* **B2 adrenergic receptors and morphological changes of the enteric nervous system in colorectal adenocarcinoma**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Raluca Niculina Ciurea |
| **Author** | Ion Rogoveanu |
| **Author** | Daniel Pirici |
| **Author** | Georgică-Costinel Târtea |
| **Author** | Costin Teodor Streba |
| **Author** | Cristina Florescu |
| **Author** | Bogdan Cătălin |
| **Author** | Ileana Puiu |
| **Author** | Elena-Anca Târtea |
| **Author** | Cristin Constantin Vere |
| **Abstract** | B2 adrenergic receptors and morphological changes of the enteric nervous system in colorectal adenocarcinoma |
| **Date** | Feb 21, 2017 |
| **Language** | en |
| **Library Catalog** | www.wjgnet.com |
| **URL** | <https://www.wjgnet.com/1007-9327/full/v23/i7/1250.htm> |
| **Accessed** | 6/15/2025, 4:10:11 PM |
| **Extra** | Publisher: Baishideng Publishing Group Inc. |
| **Volume** | 23 |
| **Pages** | 1250-1261 |
| **Publication** | World Journal of Gastroenterology |
| **DOI** | [10.3748/wjg.v23.i7.1250](http://doi.org/10.3748/wjg.v23.i7.1250) |
| **Issue** | 7 |
| **Date Added** | 6/15/2025, 4:10:11 PM |
| **Modified** | 6/15/2025, 4:10:11 PM |

* **Attachments**
  + Full Text
* **Blockade of beta-adrenergic receptors reduces cancer growth and enhances the response to anti-CTLA4 therapy by modulating the tumor microenvironment**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Klaire Yixin Fjæstad |
| **Author** | Anne Mette Askehøj Rømer |
| **Author** | Victor Goitea |
| **Author** | Astrid Zedlitz Johansen |
| **Author** | Marie-Louise Thorseth |
| **Author** | Marco Carretta |
| **Author** | Lars Henning Engelholm |
| **Author** | Lars Grøntved |
| **Author** | Niels Junker |
| **Author** | Daniel Hargbøl Madsen |
| **Abstract** | The development of immune checkpoint inhibitors (ICI) marks an important breakthrough of cancer therapies in the past years. However, only a limited fraction of patients benefit from such treatments, prompting the search for immune modulating agents that can improve the therapeutic efficacy. The nonselective beta blocker, propranolol, which for decades has been prescribed for the treatment of cardiovascular conditions, has recently been used successfully to treat metastatic angiosarcoma. These results have led to an orphan drug designation by the European Medicines Agency for the treatment of soft tissue sarcomas. The anti-tumor effects of propranolol are suggested to involve the reduction of cancer cell proliferation as well as angiogenesis. Here, we show that oral administration of propranolol delays tumor progression of MCA205 fibrosarcoma model and MC38 colon cancer model and increases the survival rate of tumor bearing mice. Propranolol works by reducing tumor angiogenesis and facilitating an anti-tumoral microenvironment with increased T cell infiltration and reduced infiltration of myeloid-derived suppressor cells (MDSCs). Using T cell deficient mice, we demonstrate that the full anti-tumor effect of propranolol requires the presence of T cells. Flow cytometry-based analysis and RNA sequencing of FACS-sorted cells show that propranolol treatment leads to an upregulation of PD-L1 on tumor associated macrophages (TAMs) and changes in their chemokine expression profile. Lastly, we observe that the co-administration of propranolol significantly enhances the efficacy of anti-CTLA4 therapy. Our results identify propranolol as an immune modulating agent, which can improve immune checkpoint inhibitor therapies in soft tissue sarcoma patients and potentially in other cancers. |
| **Date** | 2022-02 |
| **Language** | en |
| **Library Catalog** | www.nature.com |
| **URL** | <https://www.nature.com/articles/s41388-021-02170-0> |
| **Accessed** | 6/15/2025, 4:10:24 PM |
| **Rights** | 2022 The Author(s) |
| **Extra** | Publisher: Nature Publishing Group |
| **Volume** | 41 |
| **Pages** | 1364-1375 |
| **Publication** | Oncogene |
| **DOI** | [10.1038/s41388-021-02170-0](http://doi.org/10.1038/s41388-021-02170-0) |
| **Issue** | 9 |
| **ISSN** | 1476-5594 |
| **Date Added** | 6/15/2025, 4:10:24 PM |
| **Modified** | 6/15/2025, 4:10:24 PM |

* **Tags:**
  + Cancer microenvironment
  + Tumour angiogenesis
  + Tumour immunology

**Attachments**

* + Full Text PDF
* **Changes in AmotL2 Expression in Cells of the Human Enteral Nervous System in Oxaliplatin-Induced Enteric Neuropathy**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Rebeca González-Fernández |
| **Author** | Rita Martín-Ramírez |
| **Author** | María-del-Carmen Maeso |
| **Author** | Alberto Lázaro |
| **Author** | Julio Ávila |
| **Author** | Pablo Martín-Vasallo |
| **Author** | Manuel Morales |
| **Abstract** | Gastrointestinal (GI) toxicity is a common side effect in patients undergoing oxaliplatin (OxPt)-based chemotherapy for colorectal cancer (CRC). Frequently, this complication persists in the long term and could affect the efficacy of the treatment and the patient’s life quality. This long-term GI toxicity is thought to be related to OxPt-induced enteral neuropathy. AmotL2 is a member of the Angiomotin family of proteins, which play a role in cell survival, neurite outgrowth, synaptic maturation, oxidative stress protection, and inflammation. In order to assess the role of AmotL2 in OxPt-induced enteral neuropathy, we studied the expression of AmotL2 in cells of the enteric nervous system (ENS) of untreated and OxPt-treated CRC patients and its relationship with inflammation, using immunofluorescence confocal microscopy. Our results in human samples show that the total number of neurons and glial cells decreased in OxPt-treated patients, and TNF-α and AmotL2 expression was increased and colocalized in both neurons and glia. AmotL2 differential expression between OxPt-treated and untreated CRC patients shows the involvement of this scaffold protein in the inflammatory component and toxicity by OxPt in the ENS. |
| **Date** | 2024/9 |
| **Language** | en |
| **Library Catalog** | www.mdpi.com |
| **URL** | <https://www.mdpi.com/2227-9059/12/9/1952> |
| **Accessed** | 6/15/2025, 4:10:49 PM |
| **Rights** | http://creativecommons.org/licenses/by/3.0/ |
| **Extra** | Number: 9 Publisher: Multidisciplinary Digital Publishing Institute |
| **Volume** | 12 |
| **Pages** | 1952 |
| **Publication** | Biomedicines |
| **DOI** | [10.3390/biomedicines12091952](http://doi.org/10.3390/biomedicines12091952) |
| **Issue** | 9 |
| **ISSN** | 2227-9059 |
| **Date Added** | 6/15/2025, 4:10:49 PM |
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* **Tags:**
  + AmotL2
  + enteral nervous system
  + enteral nervous system toxicity
  + gastrointestinal chemotherapy toxicity
  + oxaliplatin toxicity

**Attachments**

* + Full Text PDF
* **Colorectal Cancer Invasion and Atrophy of the Enteric Nervous System: Potential Feedback and Impact on Cancer Progression**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Janusz Godlewski |
| **Author** | Zbigniew Kmiec |
| **Abstract** | Colorectal cancer (CRC) invasion within the large intestine wall results in the replacement of normal tissue architecture by tumour mass. Cancer cells digest the extracellular matrix (ECM) by the release of proteolytic enzymes. The disintegration of matrix ground substance activates several deposited growth factors which stimulate cell proliferation. Stromal (mainly fibroblasts), immune and cancer cells dominate in this area and become involved in a network of multimodal interactions which significantly induce proliferation of colon cancer cells, inhibit their apoptosis and promote their spreading within the local tumour microenvironment. Cancer invasion destroys nerve fibres and neurons of the local enteric nervous system (ENS) and induces subsequent atrophy of the submucosal and myenteric plexuses in areas adjacent to the cancer boundary. Interestingly, the reduction of plexuses’ size is accompanied by the increased number of galanin-immunoreactive neurons and increased galanin content in parts of the colon located close to the tumour. Galanin, a neuroprotective peptide, may inhibit the extrinsic pathway of apoptosis and in this way promote cancer cell survival. The possible role of acetylcholine and some ENS neuropeptides was also discussed. Invasion of cancer cells spreads along nerve fibres with the involvement of locally-released neutrophins which promote, via their specific receptors, cancer cell proliferation and pro-survival signalling pathways. Thus, during CRC development cancer cells and neurons of the ENS release many neurotransmitters/neuropeptides which affect key cellular signalling pathways promoting cancer cell proliferation and pro-survival phenotype. The multiple interactions between ENS neurons, cancer cells and other cell types present in the colon wall increase cancer cell invasiveness and have a negative impact on the course of CRC. |
| **Date** | 2020/1 |
| **Language** | en |
| **Short Title** | Colorectal Cancer Invasion and Atrophy of the Enteric Nervous System |
| **Library Catalog** | www.mdpi.com |
| **URL** | <https://www.mdpi.com/1422-0067/21/9/3391> |
| **Accessed** | 6/15/2025, 4:10:04 PM |
| **Rights** | http://creativecommons.org/licenses/by/3.0/ |
| **Extra** | Number: 9 Publisher: Multidisciplinary Digital Publishing Institute |
| **Volume** | 21 |
| **Pages** | 3391 |
| **Publication** | International Journal of Molecular Sciences |
| **DOI** | [10.3390/ijms21093391](http://doi.org/10.3390/ijms21093391) |
| **Issue** | 9 |
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* **Tags:**
  + colorectal cancer
  + tumour microenvironment
  + enteric nervous system
  + Ach
  + cancer invasion
  + galanin
  + neuropeptides
  + neurotrophins
  + perineural invasion
  + TrkB

**Attachments**

* + Full Text PDF
* **DRD4 Interacts with TGF-β Receptors to Drive Colorectal Cancer Metastasis Independently of Dopamine Signaling Pathway**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Yuan Zhou |
| **Author** | Jinlong Tang |
| **Author** | Menghan Weng |
| **Author** | Honghe Zhang |
| **Author** | Maode Lai |
| **Abstract** | The functional and pharmacological significance of dopamine receptor D4 (DRD4) in psychiatric and neurological disorders is well elucidated. However, the roles of DRD4 in colorectal cancer (CRC) remain unclear. This study observes a significant upregulation of DRD4 expression in clinical samples, which is negatively correlated with patient prognosis. In vitro, overexpression of DRD4 causes a constitutive activation of β-Arrestin2/PP2A/AKT independent of dopamine. Interestingly, this classical signaling pathway is not associated with the phenotype of DRD4-promoted migration and invasion in CRC cells. Instead, DRD4 interacts with transforming growth factor beta receptors (TGFBR1 and TGFBR2) to activate Smad2 phosphorylation and promote Smad2/Smad4 complex nucleus translocation. Then, SNAI1 and JAG1 are transcriptionally activated to induce epithelial-mesenchymal transition and enhance the metastatic potential of CRC. Notably, the COOH-terminal domain is identified as the key intracellular region for the pro-metastatic roles of DRD4. Furthermore, treatment with a TGFBR1 inhibitor combined with a BMP inhibitor effectively counteracts the pro-metastatic effects induced by DRD4 both in vitro and in vivo. In conclusion, these findings uncover an unconventional role for DRD4 beyond its classic function as a neurotransmitter receptor. The intracellular signaling of DRD4 interacting with TGFBR1 can be targeted pharmacologically for CRC therapy. |
| **Date** | 2025 |
| **Language** | en |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1002/advs.202413953> |
| **Accessed** | 6/15/2025, 4:10:35 PM |
| **Rights** | © 2024 The Author(s). Advanced Science published by Wiley-VCH GmbH |
| **Extra** | \_eprint: https://advanced.onlinelibrary.wiley.com/doi/pdf/10.1002/advs.202413953 |
| **Volume** | 12 |
| **Pages** | 2413953 |
| **Publication** | Advanced Science |
| **DOI** | [10.1002/advs.202413953](http://doi.org/10.1002/advs.202413953) |
| **Issue** | 6 |
| **ISSN** | 2198-3844 |
| **Date Added** | 6/15/2025, 4:10:35 PM |
| **Modified** | 6/15/2025, 4:10:35 PM |

* **Tags:**
  + TGFBR2
  + colorectal cancer
  + DRD4
  + TGF-β
  + TGFBR1

**Attachments**

* + Full Text PDF
* **Galanin Receptors (GALR1, GALR2, and GALR3) Immunoexpression in Enteric Plexuses of Colorectal Cancer Patients: Correlation with the Clinico-Pathological Parameters**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Jacek Kiezun |
| **Author** | Marta Kiezun |
| **Author** | Bartlomiej Emil Krazinski |
| **Author** | Lukasz Paukszto |
| **Author** | Anna Koprowicz-Wielguszewska |
| **Author** | Zbigniew Kmiec |
| **Author** | Janusz Godlewski |
| **Abstract** | Galanin (GAL) is an important neurotransmitter released by the enteric nervous system (ENS) neurons located in the muscularis externa and submucosa enteric plexuses that acts by binding to GAL receptors 1, 2 and 3 (GALR1, 2 and 3). In our previous studies, the GAL immunoexpression was compared in colorectal cancer (CRC) tissue and the adjacent parts of the large intestine wall including myenteric and submucosal plexuses. Recently we have also found that expression levels of GALR1 and GALR3 proteins are elevated in CRC tissue as compared with their expression in epithelial cells of unchanged mucosa. Moreover, higher GALR3 immunoreactivity in CRC cells correlated with better prognosis of CRC patients. To understand the distribution of GALRs in enteric plexuses distal and close to CRC invasion, in the present study we decided to evaluate GALRs expression within the myenteric and submucosal plexuses located proximally and distally to the cancer invasion and correlated the GALRs expression levels with the clinico-pathological data of CRC patients. The immunohistochemical and immunofluorescent methods showed only slightly decreased immunoexpression of GALR1 and GALR3 in myenteric plexuses close to cancer but did not reveal any correlation in the immunoexpression of all three GAL receptors in myenteric plexuses and tumour progression. No significant changes were found between the expression levels of GALRs in submucosal plexuses distal and close to the tumour. However, elevated GALR1 expression in submucosal plexuses in vicinity of CRC correlated with poor prognosis, higher tumour grading and shorter overall survival. When myenteric plexuses undergo morphological and functional alterations characteristic for atrophy, GALRs maintain or only slightly decrease their expression status. In contrast, the correlation between high expression of GALR1 in the submucosal plexuses and overall survival of CRC patients suggest that GAL and GALRs can act as a components of local neuro-paracrine pro-proliferative pathways accelerating the invasion and metastasis of cancer cell. The obtained results suggest an important role of GALR1 in submucosal plexuses function during the progression of CRC and imply that GALR1 expression in submucosal plexuses of ENS could be an important predictive factor for CRC progression. |
| **Date** | 2022/12 |
| **Language** | en |
| **Short Title** | Galanin Receptors (GALR1, GALR2, and GALR3) Immunoexpression in Enteric Plexuses of Colorectal Cancer Patients |
| **Library Catalog** | www.mdpi.com |
| **URL** | <https://www.mdpi.com/2218-273X/12/12/1769> |
| **Accessed** | 6/15/2025, 4:10:45 PM |
| **Rights** | http://creativecommons.org/licenses/by/3.0/ |
| **Extra** | Number: 12 Publisher: Multidisciplinary Digital Publishing Institute |
| **Volume** | 12 |
| **Pages** | 1769 |
| **Publication** | Biomolecules |
| **DOI** | [10.3390/biom12121769](http://doi.org/10.3390/biom12121769) |
| **Issue** | 12 |
| **ISSN** | 2218-273X |
| **Date Added** | 6/15/2025, 4:10:45 PM |
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* **Tags:**
  + colorectal cancer
  + prognosis
  + enteric plexuses
  + galanin receptors
  + immunohistochemistry

**Attachments**

* + Full Text PDF
* **High expression of substance P and its receptor neurokinin-1 receptor in colorectal cancer is associated with tumor progression and prognosis**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Xiao-Yi Chen |
| **Author** | Guo-Qing Ru |
| **Author** | Ying-Yu Ma |
| **Author** | Jun Xie |
| **Author** | Wan-Yuan Chen |
| **Author** | Hui-Ju Wang |
| **Author** | Shi-Bing Wang |
| **Author** | Li Li |
| **Author** | Ke-Tao Jin |
| **Author** | Xiang-Lei He |
| **Author** | Xiao-Zhou Mou |
| **Abstract** | High expression of substance P and its receptor neurokinin-1 receptor in colorectal cancer is associated with tumor progression and prognosis Xiao-Yi Chen,1,\* Guo-Qing Ru,2,\* Ying-Yu Ma,1 Jun Xie,3 Wan-Yuan Chen,2 Hui-Ju Wang,1 Shi-Bing Wang,1 Li Li,1 Ke-Tao Jin,4 Xiang-Lei He,2 Xiao-Zhou Mou1 1Clinical Research Institute, 2Department of Pathology, Zhejiang Provincial People&rsquo;s Hospital, Hangzhou, 3Department of Anus-Intestines, Affiliated Hospital of Shaoxing University, 4Department of Gastrointestinal Surgery, Shaoxing People&rsquo;s Hospital, Shaoxing Hospital of Zhejiang University, Shaoxing, People&rsquo;s Republic of China \*These authors contributed equally to&nbsp;this work Background: Epidemiologic evidence suggests that chronic inflammation and/or chronic infection is associated with cancer development, and the inflammatory process may play a crucial role in the carcinogenesis and prognosis of colorectal cancer (CRC). Substance P (SP) belongs to the family of tachykinins and acts as an immunomodulator, binding to the neurokinin-1 receptor (NK1R) to initiate tumor cell proliferation, angiogenesis, and migration, steps that are critical for tumor cell invasion and metastasis. It is suggested that SP/NK1R signaling may play an important role in cancer progression and metastasis. However, the exact involvement and significance of SP and NK1R in CRC pathologies remain to be adequately deciphered.Patients and methods: We performed immunohistochemistry staining on tissue microarrays containing 267 pairs of CRC and adjacent normal tissues to evaluate the clinical significance of SP or NK1R in the progression and prognosis of CRC. We also explored the potential correlation between SP and NK1R in CRC development.Results: Expression levels of SP and NK1R were upregulated in CRC compared with their expressions in adjacent normal tissues (P&lt;0.001). High expression of SP in CRC was significantly associated with lymph node metastasis (P&lt;0.001). We also found that high expression of NK1R in CRC was significantly related to TNM (tumor node metastasis) stage (P=0.010) and lymph node metastasis (P=0.019). A high correlation between SP and NK1R expression was also observed (r=0.419, P&lt;0.001). Survival analysis showed that CRC patients with high expression of SP or NK1R have a poor prognosis when compared to patients with low SP or NK1R expression (log rank test, P&lt;0.05). Multivariate analysis using Cox regression model showed that survival was independently correlated with lymph node metastasis, distant metastasis, and SP expression (P&lt;0.05).Conclusion: Upregulation of SP-NK1R may play a crucial role in CRC progression. Moreover, SP-NK1R expression may also be used as a predictor for CRC prognosis. Keywords: SP, NK1R, CRC, progression, prognosis |
| **Date** | 2016/06/16 |
| **Language** | English |
| **Library Catalog** | www.dovepress.com |
| **URL** | <https://www.dovepress.com/high-expression-of-substance-p-and-its-receptor-neurokinin-1-receptor--peer-reviewed-fulltext-article-OTT> |
| **Accessed** | 6/15/2025, 4:10:30 PM |
| **Extra** | Publisher: Dove Press |
| **Volume** | 9 |
| **Pages** | 3595-3602 |
| **Publication** | OncoTargets and Therapy |
| **DOI** | [10.2147/OTT.S102356](http://doi.org/10.2147/OTT.S102356) |
| **Journal Abbr** | OTT |
| **Date Added** | 6/15/2025, 4:10:30 PM |
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* **Attachments**
  + Full Text PDF
* **Molecular insights into oxaliplatin-induced peripheral neuropathy in colorectal cancer: Unraveling a potential signature.**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Suneeta Modekurty |
| **Author** | Michael Iglesia |
| **Author** | Katrina Sophia Pedersen |
| **Author** | Carolina Salvador |
| **Author** | Simon Haroutounian |
| **Author** | Kian-Huat Lim |
| **Author** | Nikolaos Trikalinos |
| **Author** | Rama Suresh |
| **Author** | Olivia Aranha |
| **Author** | Patrick Grierson |
| **Author** | Benjamin R. Tan |
| **Author** | Moh'd M. Khushman |
| **Abstract** | e15506Background: Oxaliplatin (OXA) is a platinum chemotherapy utilized for treating patients with colorectal cancer (CRC). OXA-induced peripheral neuropathy (OXAIPN) stands as the primary non-hematological dose-limiting toxicity. Despite its clinical significance, there exists no reliable molecular predictive biomarker of OXAIPN in current clinical practice. In this study, we delved into the molecular signature associated with OXAIPN in CRC. Methods: OXAIPN-related genes were curated through an extensive literature review. Utilizing publicly available bulk transcriptomic data from the Illumina HiSeq 2500 platform, encompassing tumor and adjacent normal tissues from 18 individuals with CRC, we identified differentially expressed genes (DEGs). Furthermore, single-cell RNA sequencing (scRNA-seq) data from 10X genomics, including normal and tumor tissues from 3 CRC patients, underwent analysis using Seurat and sctype R packages to unveil DEGs associated with cancer cells. Functional and pathway enrichment analysis was performed using the Genecodis4 web-based tool. To validate the inhibition of a curated list of neuropathy-associated genes, RNA-seq data from CRC cell lines (HCT116 and DLD1) treated with Oxaliplatin were processed, and DEGs were determined. Results: A total of 1367 OXAIPN-related genes were identified. Bulk transcriptomic data analysis revealed 715 DEGs, while scRNA-seq analysis uncovered 2,854 DEGs. Noteworthy, upregulated genes from scRNA-seq analysis, including LGALS4, SPINK4, TFF3, REG4, and REG1A, were associated with tumor proliferation through epithelial-mesenchymal transitions, oxidative stress, dysregulated immune system, and inflammation. In CRC cell lines (HCT116 and DLD1), the administration of oxaliplatin resulted in the downregulation of proteins involved in axon excitability (NGF, SOD1, ROBO1, CNTNAP2, and KCNMB1), normal sensory neuron function (SOX10, APOE, SST, S1PR1, and KCND3), voltage-gated sodium (SCNN1B, SCNN1G, SCNN1A, SCN1B, and SCN2B), calcium (CACNA2D2, CACNA1A, CACNA1C, CACNA1E, and CACNA1F), and potassium channels (KCND3, KCNMB1, KCNMA1, KCNJ2, and KCNN4). Conclusions: A molecular signature associated with OXAIPN was identified in patients with CRC and validated in CRC cell lines (HCT116 and DLD1). Further studies to reproduce and evaluate its potential in predicting OXAIPN in CRC patients in the clinic are warranted. |
| **Date** | 2024-06 |
| **Short Title** | Molecular insights into oxaliplatin-induced peripheral neuropathy in colorectal cancer |
| **Library Catalog** | ascopubs.org (Atypon) |
| **URL** | <https://ascopubs.org/doi/10.1200/JCO.2024.42.16_suppl.e15506> |
| **Accessed** | 6/15/2025, 4:10:55 PM |
| **Extra** | Publisher: Wolters Kluwer |
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| **Pages** | e15506-e15506 |
| **Publication** | Journal of Clinical Oncology |
| **DOI** | [10.1200/JCO.2024.42.16\_suppl.e15506](http://doi.org/10.1200/JCO.2024.42.16_suppl.e15506) |
| **Issue** | 16\_suppl |
| **Journal Abbr** | JCO |
| **ISSN** | 0732-183X |
| **Date Added** | 6/15/2025, 4:10:55 PM |
| **Modified** | 6/15/2025, 4:10:55 PM |

* **Perineural invasion in colorectal cancer: mechanisms of action and clinical relevance**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Hao Wang |
| **Author** | Ruixue Huo |
| **Author** | Kexin He |
| **Author** | Li Cheng |
| **Author** | Shan Zhang |
| **Author** | Minhao Yu |
| **Author** | Wei Zhao |
| **Author** | Hui Li |
| **Author** | Junli Xue |
| **Abstract** | In recent years, the significance of the nervous system in the tumor microenvironment has gained increasing attention. The bidirectional communication between nerves and cancer cells plays a critical role in tumor initiation and progression. Perineural invasion (PNI) occurs when tumor cells invade the nerve sheath and/or encircle more than 33% of the nerve circumference. PNI is a common feature in various malignancies and is associated with tumor invasion, metastasis, cancer-related pain, and unfavorable clinical outcomes. The colon and rectum are highly innervated organs, and accumulating studies support PNI as a histopathologic feature of colorectal cancer (CRC). Therefore, it is essential to investigate the role of nerves in CRC and comprehend the mechanisms of PNI to impede tumor progression and improve patient survival. |
| **Date** | 2024-02-01 |
| **Language** | en |
| **Short Title** | Perineural invasion in colorectal cancer |
| **Library Catalog** | Springer Link |
| **URL** | <https://doi.org/10.1007/s13402-023-00857-y> |
| **Accessed** | 6/15/2025, 4:10:41 PM |
| **Volume** | 47 |
| **Pages** | 1-17 |
| **Publication** | Cellular Oncology |
| **DOI** | [10.1007/s13402-023-00857-y](http://doi.org/10.1007/s13402-023-00857-y) |
| **Issue** | 1 |
| **Journal Abbr** | Cell Oncol. |
| **ISSN** | 2211-3436 |
| **Date Added** | 6/15/2025, 4:10:41 PM |
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* **Tags:**
  + Tumor microenvironment
  + Prognosis
  + Rectal cancer
  + Colorectal cancer
  + Enteric Nervous System
  + Colorectal Surgery
  + Cell Invasion
  + Colorectal innervation
  + Neurotrophins
  + Perineural invasion
  + Peripheral Nervous System

**Attachments**

* + Full Text PDF

## A comprehensive review of engineered exosomes from the preparation strategy to therapeutic applications

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Xiying Fan |
| **Author** | Yiwen Zhang |
| **Author** | Wenshuai Liu |
| **Author** | Mingzheng Shao |
| **Author** | Yibo Gong |
| **Author** | Tingya Wang |
| **Author** | Song Xue |
| **Author** | Rui Nian |
| **Abstract** | Exosomes exhibit high bioavailability, biological stability, targeted specificity, low toxicity, and low immunogenicity in shuttling various bioactive molecules such as proteins, lipids, RNA, and DNA. Natural exosomes, however, have limited production, targeting abilities, and therapeutic efficacy in clinical trials. On the other hand, engineered exosomes have demonstrated long-term circulation, high stability, targeted delivery, and efficient intracellular drug release, garnering significant attention. The engineered exosomes bring new insights into developing next-generation drug delivery systems and show enormous potential in therapeutic applications, such as tumor therapies, diabetes management, cardiovascular disease, and tissue regeneration and repair. In this review, we provide an overview of recent advancements associated with engineered exosomes by focusing on the state-of-the-art strategies for cell engineering and exosome engineering. Exosome isolation methods, including traditional and emerging approaches, are systematically compared along with advancements in characterization methods. Current challenges and future opportunities are further discussed in terms of the preparation and application of engineered exosomes. |
| **Date** | 2024-07-09 |
| **Language** | en |
| **Library Catalog** | pubs.rsc.org |
| **URL** | <https://pubs.rsc.org/en/content/articlelanding/2024/bm/d4bm00558a> |
| **Accessed** | 6/15/2025, 4:13:35 PM |
| **Extra** | Publisher: The Royal Society of Chemistry |
| **Volume** | 12 |
| **Pages** | 3500-3521 |
| **Publication** | Biomaterials Science |
| **DOI** | [10.1039/D4BM00558A](http://doi.org/10.1039/D4BM00558A) |
| **Issue** | 14 |
| **Journal Abbr** | Biomater. Sci. |
| **ISSN** | 2047-4849 |
| **Date Added** | 6/15/2025, 4:13:35 PM |
| **Modified** | 6/15/2025, 4:13:35 PM |

## Advanced glycation end products in children with type 1 diabetes and early reduced diastolic heart function

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Leif Brunvand |
| **Author** | Martin Heier |
| **Author** | Cathrine Brunborg |
| **Author** | Kristian F. Hanssen |
| **Author** | Drude Fugelseth |
| **Author** | Knut Haakon Stensaeth |
| **Author** | Knut Dahl-Jørgensen |
| **Author** | Hanna Dis Margeirsdottir |
| **Abstract** | Reduced diastolic function is an early sign of diabetes cardiomyopathy in adults and is associated with elevated levels of HbA1c and advanced glycation end products (AGEs). |
| **Date** | 2017-05-25 |
| **Library Catalog** | BioMed Central |
| **URL** | <https://doi.org/10.1186/s12872-017-0551-0> |
| **Accessed** | 6/15/2025, 4:13:47 PM |
| **Volume** | 17 |
| **Pages** | 133 |
| **Publication** | BMC Cardiovascular Disorders |
| **DOI** | [10.1186/s12872-017-0551-0](http://doi.org/10.1186/s12872-017-0551-0) |
| **Issue** | 1 |
| **Journal Abbr** | BMC Cardiovascular Disorders |
| **ISSN** | 1471-2261 |
| **Date Added** | 6/15/2025, 4:13:47 PM |
| **Modified** | 6/15/2025, 4:13:47 PM |

### Tags:

* + Color Tissue Doppler Imaging
  + Diabetic Cardiomyopathy
  + Diastolic Function
  + Distensibility Coefficient (DC)
  + Glycemic Burden

### Attachments

* + Full Text PDF

## Advanced Glycation End Products, Measured as Skin Autofluorescence, During Normal Pregnancy and Pregnancy Complicated by Diabetes Mellitus

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Wendela L. de Ranitz-Greven |
| **Author** | Lotte Kaasenbrood |
| **Author** | Wendy K. Poucki |
| **Author** | Jeanette Hamerling |
| **Author** | Dieuwke C. Bos |
| **Author** | Gerard H.A. Visser |
| **Author** | Douwe H. Biesma |
| **Author** | Joline W.J. Beulens |
| **Author** | Harold W. de Valk |
| **Abstract** | Background: Advanced glycation end products (AGEs) accumulate with age and in diabetes mellitus (DM). AGEs can be measured by the AGE Reader (DiagnOptics Technologies BV, Groningen, The Netherlands) using skin autofluorescence (SAF). SAF is related to chronic diabetes complications. In a previous study we reported that SAF is comparable in patients with gestational DM (GDM) and controls at 27 weeks of gestation. In the current study we investigated SAF at multiple time points during pregnancy in pregnancies complicated by DM (type 1 or type 2) or GDM and in controls. Furthermore, the relation between SAF levels and adverse pregnancy outcomes was investigated.Subjects and Methods: In this single-center prospective observational study SAF was measured during pregnancy from 26 gestational weeks onward in 79 GDM patients, 21 patients with preexistent DM (type 1 or type 2), and 55 women without diabetes. Adverse pregnancy outcomes were recorded.Results: SAF decreased slightly but significantly (β=−0.018) during normal pregnancy but not in pregnancies complicated with hyperglycemia. At the end of pregnancy SAF was higher in patients with preexistent DM (1.91 arbitrary [AU] units) compared with patients with GDM (1.71 AU) or normal pregnancy (1.66 AU) but did not differ between the latter two groups. SAF was not related to adverse pregnancy outcomes.Conclusions: The decrease in SAF during normal pregnancy could be the result of physiological changes. Because SAF was not related to adverse pregnancy outcomes, it is unlikely that the AGE Reader will be of use in daily clinical practice for GDM patients as a marker for identifying high-risk pregnancy outcomes. |
| **Date** | 2012-12 |
| **Library Catalog** | liebertpub.com (Atypon) |
| **URL** | <https://www.liebertpub.com/doi/10.1089/dia.2012.0120> |
| **Accessed** | 6/15/2025, 4:14:02 PM |
| **Extra** | Publisher: Mary Ann Liebert, Inc., publishers |
| **Volume** | 14 |
| **Pages** | 1134-1139 |
| **Publication** | Diabetes Technology & Therapeutics |
| **DOI** | [10.1089/dia.2012.0120](http://doi.org/10.1089/dia.2012.0120) |
| **Issue** | 12 |
| **ISSN** | 1520-9156 |
| **Date Added** | 6/15/2025, 4:14:02 PM |
| **Modified** | 6/15/2025, 4:14:02 PM |

## Beyond Syringes and Pills: Advances in Drug Delivery Systems for Diabetes

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Muggu S. Bhavani |
| **Author** | Ravindran Sarvanana |
| **Abstract** | Diabetes is a chronic disease that affects millions of people worldwide, and its prevalence is increasing. The two primary subtypes, type 1 and 2, have different causes and mechanisms, but both result in abnormal glucose metabolism. The standard of care for diabetes includes insulin therapy, oral anti-diabetic medications, diet, exercise, weight loss, and frequent selfmonitoring of blood glucose levels. However, these treatments have limitations that can lead to poor patient compliance and suboptimal outcomes. Alternative insulin delivery systems such as inhalers, patches, and oral sprays offer potential benefits such as increased convenience, reduced pain, and improved adherence. Non-insulin injectables, long-acting basal insulins, and GLP-1 agonists have also shown promise in improving glycemic control and reducing the risk of complications. Nanoparticlebased systems like SLNs are a novel approach that offers several advantages for diabetic management. They allow for targeted drug delivery, controlled release, and improved biocompatibility, enhancing drug efficacy and reducing side effects. SLNs have shown potential in animal models for reducing extracellular matrix degradation, inhibiting carbohydrate digestive enzymes, and enhancing the regeneration of insulin-producing beta cells. More studies are needed to validate their safety and efficacy in humans, but the potential benefits of SLNs make them a promising option for diabetes management. |
| **Date** | 2023-09-25 |
| **Language** | en |
| **Short Title** | Beyond Syringes and Pills |
| **Library Catalog** | DOI.org (Crossref) |
| **URL** | <https://impactfactor.org/PDF/IJDDT/13/IJDDT,Vol13,Issue3,Article48.pdf> |
| **Accessed** | 6/15/2025, 4:13:32 PM |
| **Rights** | http://creativecommons.org/licenses/by-nc-nd/4.0 |
| **Volume** | 13 |
| **Pages** | 1069-1077 |
| **Publication** | INTERNATIONAL JOURNAL OF DRUG DELIVERY TECHNOLOGY |
| **DOI** | [10.25258/ijddt.13.3.48](http://doi.org/10.25258/ijddt.13.3.48) |
| **Issue** | 03 |
| **Journal Abbr** | IJDDT |
| **ISSN** | 0975-4415 |
| **Date Added** | 6/15/2025, 4:13:32 PM |
| **Modified** | 6/15/2025, 4:13:33 PM |

### Attachments

* + PDF

## CD44 fucosylation on bone marrow-derived mesenchymal stem cells enhances homing and promotes enteric nervous system remodeling in diabetic mice

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Huiying Shi |
| **Author** | Chen Jiang |
| **Author** | Hailing Yao |
| **Author** | Yurui Zhang |
| **Author** | Qin Zhang |
| **Author** | Xiaohua Hou |
| **Author** | Rong Lin |
| **Abstract** | Diabetes can cause extensive enteric nervous system (ENS) injuries and gastrointestinal motility disorder. In developing possible treatments, researchers have engaged in tissue regeneration engineering with the very promising bone marrow-derived mesenchymal stem cells (BMSCs). However, BMSCs have poor homing ability to the targeted tissues after intravenous injection. Thus, we aimed to investigate whether enhancing the expression of E-selectin ligand on BMSCs could improve their homing ability and subsequently influence their role in ENS remodeling in diabetic mice. |
| **Date** | 2021-06-30 |
| **Library Catalog** | BioMed Central |
| **URL** | <https://doi.org/10.1186/s13578-021-00632-2> |
| **Accessed** | 6/15/2025, 4:13:18 PM |
| **Volume** | 11 |
| **Pages** | 118 |
| **Publication** | Cell & Bioscience |
| **DOI** | [10.1186/s13578-021-00632-2](http://doi.org/10.1186/s13578-021-00632-2) |
| **Issue** | 1 |
| **Journal Abbr** | Cell & Bioscience |
| **ISSN** | 2045-3701 |
| **Date Added** | 6/15/2025, 4:13:18 PM |
| **Modified** | 6/15/2025, 4:13:18 PM |

### Tags:

* + Diabetes
  + Enteric nervous system (ENS)
  + Bone marrow-derived mesenchymal stem cells (BMSCs)
  + Fucosylation modification
  + Gastrointestinal motility disorders

### Attachments

* + Full Text PDF

## Effect of Chemically-Induced Diabetes Mellitus on Phenotypic Variability of the Enteric Neurons in the Descending Colon in the Pig

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Michał Bulc |
| **Author** | Jarosław Całka |
| **Author** | Łukasz Zielonka |
| **Author** | Michał Dąbrowski |
| **Author** | Katarzyna Palus |
| **Abstract** | Gastrointestinal neuropathy in diabetes is one of numerous diseases resulting in abnormal functioning of the gastrointestinal tract (GIT), and it may... |
| **Date** | 2021/10/28 |
| **Language** | en |
| **Library Catalog** | sciendo.com |
| **URL** | <https://sciendo.com/article/10.2478/aoas-2020-0121> |
| **Accessed** | 6/15/2025, 4:12:50 PM |
| **Volume** | 21 |
| **Pages** | 1403-1422 |
| **Publication** | Annals of Animal Science |
| **DOI** | [10.2478/aoas-2020-0121](http://doi.org/10.2478/aoas-2020-0121) |
| **Issue** | 4 |
| **Date Added** | 6/15/2025, 4:12:50 PM |
| **Modified** | 6/15/2025, 4:12:50 PM |

### Attachments

* + Full Text PDF

## Electroacupuncture at ST36 Improve the Gastric Motility by Affecting Neurotransmitters in the Enteric Nervous System in Type 2 Diabetic Rats

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Xu Han |
| **Author** | Xiaoyan Chen |
| **Author** | Xuan Wang |
| **Author** | Meirong Gong |
| **Author** | Mengjiang Lu |
| **Author** | Zhi Yu |
| **Author** | Bin Xu |
| **Author** | Jinhong Yuan |
| **Abstract** | Electroacupuncture (EA) can effectively relieve hyperglycemia and gastric emptying disorders in diabetic gastroparesis (DGP). However, the effect of EA on type 2 diabetes mellitus (T2DM) gastroparesis and its mechanism in the enteric nervous system (ENS) are rarely studied. We investigated the therapeutic effect of EA at ST36 and its effect on the main inhibitory and excitatory neurotransmitters in the ENS in DGP rats. Male Sprague-Dawley (SD) rats were fed a high-fat diet for 2 weeks and injected with streptozotocin (STZ) at 35 mg/kg to induce T2DM. T2DM rats were divided into the diabetic mellitus (DM) group and the EA group. The control (CON) group comprised normal rats without any intervention. EA treatment was started 6 weeks after the induction of DM and continued for 5 weeks. The body weight and food intake of the rats were recorded every week. Blood glucose, insulin, glucose tolerance, gastric emptying, and antral motility were measured after treatment. The expression of protein gene product 9.5 (PGP9.5), neuronal nitric oxide synthase (nNOS), and choline acetyltransferase (ChAT) in gastric antrum were quantified by western blotting and quantitative real-time reverse transcription polymerase chain reaction (qRT-PCR). The T2DM gastroparesis model was successfully established. EA treatment reduced the body weight, food intake, and blood glucose; improved glucose intolerance and insulin resistance; increased the gastric emptying rate, the mean antral pressure, and the amplitude of antral motility; and decreased the frequency of antral motility compared with those in the DM group. EA treatment increased the expression level of nNOS, ChAT, and PGP9.5 proteins, and nNOS and ChAT mRNA. The results suggested that EA at ST36 could ameliorate DGP, partly restore the damage to general neurons, and increase nNOS and ChAT in the gastric antrum. EA improved DGP partly via reducing the loss of inhibitory and excitatory neurotransmitters in the ENS. |
| **Date** | 2021 |
| **Language** | en |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1155/2021/6666323> |
| **Accessed** | 6/15/2025, 4:12:41 PM |
| **Rights** | Copyright © 2021 Xu Han et al. |
| **Extra** | \_eprint: https://onlinelibrary.wiley.com/doi/pdf/10.1155/2021/6666323 |
| **Volume** | 2021 |
| **Pages** | 6666323 |
| **Publication** | Evidence-Based Complementary and Alternative Medicine |
| **DOI** | [10.1155/2021/6666323](http://doi.org/10.1155/2021/6666323) |
| **Issue** | 1 |
| **ISSN** | 1741-4288 |
| **Date Added** | 6/15/2025, 4:12:41 PM |
| **Modified** | 6/15/2025, 4:12:41 PM |

### Attachments

* + Full Text PDF

## Lactobacilli -induced Generation of Reactive Oxygen Species via Formyl Peptide Receptor-1 (FPR1) Regulates Intestinal Motility in Mice

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Bindu Chandrasekharan |
| **Author** | Bejan Saeedi |
| **Author** | M Ashfaqul Alam |
| **Author** | Shanthi Srinivasan |
| **Author** | Malu Tansey |
| **Author** | Rheinallt Jones |
| **Author** | Asma Nusrat |
| **Author** | Andrew S Neish |
| **Abstract** | Rationale Various clinical conditions like diabetes and inflammatory diseases of the gut are associated with gastrointestinal (GI) motility disorders. Despite the increased consumption of beneficial commensal microbes marketed as ‘probiotics’, their mechanism of action on the enteric nervous system (ENS) is still unclear. Aim We studied the effects of the widely used probiotic and normal commensal Lactobacillus rhamnosus GG (LGG) on ENS and GI motility. Methods Conventional (Conv), formyl peptide receptor-1 (FPR1 KO) and formyl peptide receptor-2 (FPR2 KO) knockout mice were gavaged with hanks buffered salt solution (HBSS, negative control) or LGG. Mice were sacrificed after 2 h, and the jejunum was cryofixed and immunostained for phospho-Erk (p44/42 MAPK, mitogen activated protein kinase). In a separate experiment, mice were intra peritoneally injected with a fluorescent hydro-cy3 dye prior to HBSS/LGG gavage, and production of reactive oxygen species (ROS) was assessed in the longitudinal muscle myenteric plexus (LMMP) by confocal imaging after 2h. Ileum was assayed for gene expression of neuropeptides and Hand-2 (transcription factor promoting enteric neuronal differentiation) by real time polymerase chain reaction (qRT-PCR). Fluorescence in situ hybridization (FISH) was done on ileal cryosections from conventional mice using FPR1 and peripherin (pan neuronal marker) RNA probes. Conv mice were gavaged daily with HBSS or LGG for 2 weeks, and motility was assessed from stool frequency, total gastrointestinal transit time and ex vivo studies on isolated circular muscle strips by isometric muscle recording. Results LGG stimulated myenteric ROS production, enhanced Erk 1/2 phosphorylation and upregulated choline acetyl transferase (ChAT) neurons (P < 0.001) in Conv and FPR2 KO mice. These effects were abrogated in FPR1 KO mice, suggesting that LGG-mediated signaling in the ENS is redox-dependent and requires FPR1(P < 0.001), localized on enteric neurons by FISH assay. Functionally, LGG gavage for 2 weeks significantly improved stool frequency, reduced total GI transit time and enhanced ileal circular muscle strip contractions (P < 0.05). Conclusions Our study demonstrates for the first time, the presence of FPR1 on enteric neurons, and the LGG-FPR1-dependent redox-signaling pathway that could be exploited to improve GI motility. Support or Funding Information We acknowledge support from the U.S. National Institutes of Health grant AI64462 (A.S.N.) and DK089763 (A.N. and A.S.N.) This abstract is from the Experimental Biology 2019 Meeting. There is no full text article associated with this abstract published in The FASEB Journal. |
| **Date** | 2019 |
| **Language** | en |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1096/fasebj.2019.33.1_supplement.763.1> |
| **Accessed** | 6/15/2025, 4:13:43 PM |
| **Rights** | © 2019 FASEB |
| **Extra** | \_eprint: https://faseb.onlinelibrary.wiley.com/doi/pdf/10.1096/fasebj.2019.33.1\_supplement.763.1 |
| **Volume** | 33 |
| **Pages** | 763.1-763.1 |
| **Publication** | The FASEB Journal |
| **DOI** | [10.1096/fasebj.2019.33.1\_supplement.763.1](http://doi.org/10.1096/fasebj.2019.33.1_supplement.763.1) |
| **Issue** | S1 |
| **ISSN** | 1530-6860 |
| **Date Added** | 6/15/2025, 4:13:43 PM |
| **Modified** | 6/15/2025, 4:13:43 PM |

## Long-Term Oncologic Outcome following Duodenum-Preserving Pancreatic Head Resection for Benign Tumors, Cystic Neoplasms, and Neuroendocrine Tumors: Systematic Review and Meta-analysis

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Hans G Beger |
| **Author** | Benjamin Mayer |
| **Author** | Bertram Poch |
| **Date** | 2024 |
| **URL** | <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11164799/> |
| **Volume** | 31 |
| **Pages** | 4637–4653 |
| **Publication** | Annals of Surgical Oncology |
| **DOI** | [10.1245/s10434-024-15222-y](http://doi.org/10.1245/s10434-024-15222-y) |
| **Issue** | 7 |
| **Date Added** | 4/16/2025, 11:10:32 PM |
| **Modified** | 6/16/2025, 1:12:21 PM |

### Tags:

* + Adult
  + Female
  + Humans
  + Male
  + Treatment Outcome
  + Animals
  + Disease Models, Animal
  + Mice
  + STING
  + Quality of Life
  + Retrospective Studies
  + Diabetes
  + Signal Transduction
  + Cell Differentiation
  + Cell Line
  + Neoplasm Recurrence, Local
  + Cell Movement
  + Mammals
  + Neurons
  + immune cells
  + inflammation
  + Homeostasis
  + Gastroenterology
  + intestinal organoids
  + Regeneration
  + microbiota
  + Pancreas
  + inflammatory bowel disease
  + \*Cell- and Tissue-Based Therapy/methods
  + \*Bile Duct Neoplasms
  + \*Bile Duct Neoplasms/surgery
  + \*Cell Lineage
  + \*Cholangiocarcinoma
  + \*Cholangiocarcinoma/pathology
  + \*Colitis, Ulcerative/drug therapy
  + \*Cystadenocarcinoma/diagnostic imaging/surgery
  + \*Cystadenoma/diagnostic imaging/surgery
  + \*Cysts/pathology
  + \*Diabetes Mellitus, Experimental/complications/genetics/metabolism
  + \*Enteric Nervous System
  + \*Enteric Nervous System/pathology
  + \*Hyperglycemia/genetics/metabolism
  + \*Hypothalamo-Hypophyseal System
  + \*Inflammatory Bowel Diseases/drug therapy
  + \*Liver Neoplasms/diagnostic imaging/surgery
  + \*Liver Neoplasms/surgery
  + \*Microbiota
  + \*MicroRNAs/metabolism
  + \*Neoplasms, Cystic, Mucinous, and Serous
  + \*Neuroglia/physiology
  + \*Zebrafish
  + 16S RNA sequencing
  + Acinar cell carcinoma
  + Aging
  + antibiotics
  + Bile Ducts, Intrahepatic
  + Bile Ducts, Intrahepatic/surgery
  + Biliary
  + Biliary cystadenocarcinoma
  + Biliary cystadenoma
  + Brain
  + Brain-Gut Axis
  + Brain/physiology
  + Cell Separation
  + Chemical coding
  + Chick Embryo
  + circVPS13A
  + Cistoadenocarcinoma
  + Cistoadenoma
  + Clinicopathological criteria, Surgical outcomes
  + Colon/drug effects/pathology
  + Cystadenocarcinoma
  + Cystadenoma
  + cystic liver lesions
  + Cystic liver neoplasm
  + Cytology
  + Developmental disorders
  + diabetes
  + diabetes mellitus
  + Drug Discovery/\*methods
  + Embryonic stem cells
  + ENS
  + ENS neuropathies
  + enteric glia
  + enteric glia communications
  + Enteric glia communications
  + enteric glia diversity
  + enteric nervous system
  + Enteric nervous system
  + Enteric Nervous System
  + enteric nervous system (ENS)
  + Enteric nervous system (ENS)
  + Enteric Nervous System/\*pathology
  + Enteric neural precursor cells (ENPCs)
  + enteric progenitor cell
  + Fecal microbiota transplantation
  + Frantz's tumor
  + gastrointestinal complications
  + gastrointestinal diseases
  + Gastrointestinal Diseases
  + Gastrointestinal Diseases/pathology
  + gastrointestinal tract
  + Gastrointestinal Tract/drug effects/pathology
  + glia
  + Glial Cell Line-Derived Neurotrophic Factor/genetics
  + glucagon-like peptide 1
  + Growth Disorders
  + growth retardation
  + gut brain axis
  + gut microbiota
  + gut-brain axis
  + gut–brain axis
  + hepatic cystadenocarcinoma
  + hepatic cystadenoma
  + Hepatic simple cyst
  + hepatobiliary cystadenocarcinoma
  + hepatobiliary cystadenoma
  + Hirschsprung disease
  + Hirschsprung Disease/\*drug therapy/\*pathology/therapy
  + homeostasis
  + Imaging modalities
  + In Situ Hybridization, Fluorescence
  + Inflammatory bowel diseases
  + Intraductal papillary biliary neoplasms
  + intraductal papillary neoplasms of bile duct
  + irritable bowel syndrome
  + L-Fucose
  + Liver Diseases
  + Management
  + microbial metabolites
  + microbiota-gut-brain axis
  + Microbiota-gut-brain axis
  + Mucinous biliary cystic tumors, Biliary cystadenoma
  + mucinous cystic neoplasm
  + Mucinous cystic neoplasms
  + Mucinous neoplasm
  + muscularis macrophages
  + myenteric neurons
  + Neoplasia mucinosa quística
  + Neoplasia papilar intraductal biliar
  + Neoplasia quística hepática
  + Neural Crest
  + neural crest cell
  + neurodegeneration
  + Neuroglia
  + Neurons/drug effects/\*pathology
  + offspring
  + P2X7 receptor
  + pancreatectomy
  + Pancreatectomy
  + Pancreatic neoplasms
  + Pancreatic Neoplasms
  + Pancreatic surgery
  + pancreatic tumor
  + Parkinson’s disease
  + pediatric pancreatic neoplasm
  + Pepstatins/metabolism
  + Pituitary-Adrenal System
  + pluripotent stem cells (PSCs)
  + Pluripotent Stem Cells/pathology
  + preconception
  + probiotic
  + Purinergic signaling
  + Receptor, Endothelin B/metabolism
  + Receptors, Purinergic P2X7
  + RNA, Circular/genetics
  + Rotenone-induced mouse model
  + short-chain fatty acids
  + Solid pseudopapillary tumor
  + Stem-cell differentiation
  + submucosal neurons
  + Submucous Plexus
  + surgical outcome
  + surgical resection
  + three-dimensional (3D)
  + type 2 diabetes
  + zebrafish

### Notes:

* + e14603 NMO-00132-2023
  + e14603 NMO-00132-2023

### Attachments

* + Full Text
  + Full Text
  + Full Text PDF
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  + PubMed Central Full Text PDF
  + PubMed Central Full Text PDF
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  + PubMed Central Link
  + PubMed entry

## The advanced glycation end product Nepsilon-(carboxymethyl)lysine is increased in serum from children and adolescents with type 1 diabetes.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | T J Berg |
| **Author** | J T Clausen |
| **Author** | P A Torjesen |
| **Author** | K Dahl-Jørgensen |
| **Author** | H J Bangstad |
| **Author** | K F Hanssen |
| **Abstract** | OBJECTIVE: To investigate whether children and adolescents with type 1 diabetes have increased serum levels of the glycoxidation product Nepsilon-(carboxymethyl)lysine (CML) at an early stage of the disease. RESEARCH DESIGN AND METHODS: The serum levels of CML in 38 patients with type 1 diabetes aged 14+/-3.2 (mean+/-SD) years were compared with those in 26 control subjects aged 16+/-1.7 years. The mean duration of diabetes was 5+/-4.7 years, ranging from 0.5 to 15 years. The mean levels of HbA1c were 10.3+/-2.5% in the patient group. The serum levels of CML were measured using a monoclonal anti-CML antibody in a fluoremetric immunoassay. Serum protein levels of advanced glycation end products (AGEs) were assayed using a polyclonal antibody from rabbit immunized with AGE-RNase (pAGE). RESULTS: The serum levels of CML and pAGE were significantly increased in the patient group versus the control group: 1.08 (0.45-2.97) U/ml CML (median 10-90 percentiles) vs. 0.70 (0.36-1.79) U/ml CML, P &lt; 0.03, and 6.6 (5.1-9.9) U/ml pAGE vs. 5.5 (3.7-8.2) U/ml AGEs, P &lt; 0.01. A significant relationship between CML and pAGE was found in the IDDM group, r = 0.76, P &lt; 0.001. The CML levels were not associated with the HbAlc levels (n = 23, r = -0.02, NS), cholesterol levels (n = 21, r = 0.07, NS), age, sex, or diabetes duration. CONCLUSIONS: Serum levels of CML are increased in patients with type 1 diabetes. This increase precedes the development of micro- and macrovascular complications. |
| **Date** | 1998-11-01 |
| **Library Catalog** | Silverchair |
| **URL** | <https://doi.org/10.2337/diacare.21.11.1997> |
| **Accessed** | 6/15/2025, 4:13:52 PM |
| **Volume** | 21 |
| **Pages** | 1997-2002 |
| **Publication** | Diabetes Care |
| **DOI** | [10.2337/diacare.21.11.1997](http://doi.org/10.2337/diacare.21.11.1997) |
| **Issue** | 11 |
| **Journal Abbr** | Diabetes Care |
| **ISSN** | 0149-5992 |
| **Date Added** | 6/15/2025, 4:13:52 PM |
| **Modified** | 6/15/2025, 4:13:52 PM |

### Attachments

* + Full Text PDF

## Two Fluorescent Wavelengths, 440ex/520em nm and 370ex/440em nm, Reflect Advanced Glycation and Oxidation End Products in Human Skin Without Diabetes

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Paul J. Beisswenger |
| **Author** | Scott Howell |
| **Author** | Todd Mackenzie |
| **Author** | Hugo Corstjens |
| **Author** | Neelam Muizzuddin |
| **Author** | Mary S. Matsui |
| **Abstract** | Background: Advanced glycation end products (AGEs) and oxidation products (OPs) play an important role in diabetes complications, aging, and damage from sun exposure. Measurement of skin autofluorescence (SAF) has been promoted as a noninvasive technique to measure skin AGEs, but the actual products quantified are uncertain. We have compared specific SAF measurements with analytically determined AGEs and oxidative biomarkers in skin collagen and determined if these measurements can be correlated with chronological aging and actinic exposure.Methods: SAF at four excitation (ex)/emission (em) intensities was measured on the upper inner arm (“sun protected”) and dorsal forearm (“sun exposed”) in 40 subjects without diabetes 20–60 years old. Skin collagen from the same sites was analyzed by liquid chromatography–tandem mass spectrometry for three AGEs—pentosidine, carboxymethyllysine (CML), and carboxyethyllysine (CEL)—and the OP methionine sulfoxide (MetSO).Results: There was poor correlation of AGE-associated fluorescence spectra with AGEs and OP in collagen, with only pentosidine correlating with fluorescence at 370ex/440em nm. A little-studied SAF (440ex/520em nm), possibly reflecting elastin cross-links, correlated with all AGEs and OPs. Levels of CML, pentosidine, and MetSO, but not SAF, were significantly higher in sun-exposed skin. These AGEs and OPs, as well as SAF at 370ex/440em nm and 440ex/520em nm, increased with chronological aging.Conclusions: SAF measurements at 370ex/440em nm and 335ex/385em nm, except for pentosidine, which correlated with fluorescence at 370ex/440em, correlate poorly with glycated and oxidatively modified protein in human skin and do not reflect actinic modification. A new fluorescence measurement (440ex/520em nm) appears to reflect AGEs and OPs in skin. |
| **Date** | 2012-03 |
| **Library Catalog** | liebertpub.com (Atypon) |
| **URL** | <https://www.liebertpub.com/doi/10.1089/dia.2011.0108> |
| **Accessed** | 6/15/2025, 4:13:57 PM |
| **Extra** | Publisher: Mary Ann Liebert, Inc., publishers |
| **Volume** | 14 |
| **Pages** | 285-292 |
| **Publication** | Diabetes Technology & Therapeutics |
| **DOI** | [10.1089/dia.2011.0108](http://doi.org/10.1089/dia.2011.0108) |
| **Issue** | 3 |
| **ISSN** | 1520-9156 |
| **Date Added** | 6/15/2025, 4:13:57 PM |
| **Modified** | 6/15/2025, 4:13:57 PM |

* **A Multivalent Approach to the Design and Discovery of Orally Efficacious 5-HT4 Receptor Agonists**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | R. Murray McKinnell |
| **Author** | Scott R. Armstrong |
| **Author** | David T. Beattie |
| **Author** | Seok-Ki Choi |
| **Author** | Paul R. Fatheree |
| **Author** | Roland A. L. Gendron |
| **Author** | Adam Goldblum |
| **Author** | Patrick P. Humphrey |
| **Author** | Daniel D. Long |
| **Author** | Daniel G. Marquess |
| **Author** | J. P. Shaw |
| **Author** | Jacqueline A. M. Smith |
| **Author** | S. Derek Turner |
| **Author** | Ross G. Vickery |
| **Abstract** | 5-HT4 receptor agonists such as tegaserod have demonstrated efficacy in the treatment of constipation predominant irritable bowel syndrome (IBS-C), a highly prevalent disorder characterized by chronic constipation and impairment of intestinal propulsion, abdominal bloating, and pain. The 5-HT4 receptor binding site can accommodate functionally and sterically diverse groups attached to the amine nitrogen atom of common ligands, occupying what may be termed a “secondary” binding site. Using a multivalent approach to lead discovery, we have investigated how varying the position and nature of the secondary binding group can be used as a strategy to achieve the desired 5-HT4 agonist pharmacological profile. During this study, we discovered the ability of amine-based secondary binding groups to impart exceptional gains in the binding affinity, selectivity, and functional potency of 5-HT4 agonists. Optimization of the leads generated by this approach afforded compound 26, a selective, orally efficacious 5-HT4 agonist for the potential treatment of gastrointestinal motility-related disorders. |
| **Date** | 2009-09-10 |
| **Library Catalog** | ACS Publications |
| **URL** | <https://doi.org/10.1021/jm900881j> |
| **Accessed** | 6/15/2025, 4:26:26 PM |
| **Extra** | Publisher: American Chemical Society |
| **Volume** | 52 |
| **Pages** | 5330-5343 |
| **Publication** | Journal of Medicinal Chemistry |
| **DOI** | [10.1021/jm900881j](http://doi.org/10.1021/jm900881j) |
| **Issue** | 17 |
| **Journal Abbr** | J. Med. Chem. |
| **ISSN** | 0022-2623 |
| **Date Added** | 6/15/2025, 4:26:26 PM |
| **Modified** | 6/15/2025, 4:26:26 PM |

* **A new role for serotonin: the 5-HT3 receptor in bladder afferent hypersensitivity**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Clarissa M. D. Mota |
| **Date** | 2020 |
| **Language** | en |
| **Short Title** | A new role for serotonin |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1113/JP279094> |
| **Accessed** | 6/15/2025, 4:25:46 PM |
| **Rights** | © 2019 The Authors. The Journal of Physiology © 2019 The Physiological Society |
| **Extra** | \_eprint: https://physoc.onlinelibrary.wiley.com/doi/pdf/10.1113/JP279094 |
| **Volume** | 598 |
| **Pages** | 23-24 |
| **Publication** | The Journal of Physiology |
| **DOI** | [10.1113/JP279094](http://doi.org/10.1113/JP279094) |
| **Issue** | 1 |
| **ISSN** | 1469-7793 |
| **Date Added** | 6/15/2025, 4:25:46 PM |
| **Modified** | 6/15/2025, 4:25:46 PM |

* **Tags:**
  + 5-hydroxytryptamine
  + bladder
  + sensorial
  + visceral sensitivity
* **Constipation, IBs and the 5-HT4 Receptor: What Role for Prucalopride?**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Gareth J. Sanger |
| **Author** | Eamonn M.M. Quigley |
| **Abstract** | After the problems associated with the non-selective 5-HT4 receptor agonists cisapride and tegaserod, the 5-HT4 receptor is now beginning to come in from the cold. Thus, prucalopride is now the first of a new class of drug defined by selectivity and high intrinsic activity at the 5-HT4 receptor. Prucalopride has been developed for treatment of chronic constipation rather than constipation-predominant irritable bowel syndrome (IBS). This follows the trend of first evaluating new gastrointestinal (GI) prokinetic drugs in disorders where disrupted GI motility is known to exist, rather than in a functional bowel disorder where changes in motility are uncertain. If prucalopride is not progressed towards the IBS indication, it has at least shown the way for other selective 5-HT4 receptor agonists. Most notable among these is TD-5108 (velusetrag), also characterized by good selectivity at the 5-HT4 receptor, high intrinsic activity and efficacy in patients with chronic constipation. |
| **Date** | 2010-01-01 |
| **Language** | EN |
| **Short Title** | Constipation, IBs and the 5-HT4 Receptor |
| **Library Catalog** | SAGE Journals |
| **URL** | <https://doi.org/10.4137/CGast.S4136> |
| **Accessed** | 6/15/2025, 4:25:48 PM |
| **Extra** | Publisher: SAGE Publications |
| **Volume** | 3 |
| **Pages** | CGast.S4136 |
| **Publication** | Clinical Medicine. Gastroenterology |
| **DOI** | [10.4137/CGast.S4136](http://doi.org/10.4137/CGast.S4136) |
| **ISSN** | 1178-119X |
| **Date Added** | 6/15/2025, 4:25:48 PM |
| **Modified** | 6/15/2025, 4:25:48 PM |

* **Attachments**
  + SAGE PDF Full Text
* **Do corticotropin releasing factor-1 receptors influence colonic transit and bowel function in women with irritable bowel syndrome?**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Seth Sweetser |
| **Author** | Michael Camilleri |
| **Author** | Sara J. Linker Nord |
| **Author** | Duane D. Burton |
| **Author** | Lorna Castenada |
| **Author** | Robert Croop |
| **Author** | Gary Tong |
| **Author** | Randy Dockens |
| **Author** | Alan R. Zinsmeister |
| **Abstract** | Corticotropin releasing factor (CRF), a mediator of stress response, alters gastrointestinal (GI) functions. Stress-related changes in colonic motility are blocked by selective CRF1 receptor antagonists. Our aim was to assess whether modulation of central and peripheral CRF1 receptors affects colonic transit and bowel function in female patients with diarrhea-predominant irritable bowel syndrome (D-IBS). This randomized, double-blind, placebo-controlled, 2-wk study evaluated the effects of oral pexacerfont (BMS-562086), a selective CRF1 receptor antagonist, 25 and 100 mg qd, on GI and colonic transit of solids [by validated scintigraphy with primary end point colonic geometric center (GC) at 24 h] and bowel function (by validated daily diaries) in 39 women with D-IBS. The 100-mg dose was comparable to a dose that inhibited colonic motility in stressed rats. Treatment effects were compared by analysis of covariance with baseline colonic transit as covariate. The study had 80% power (α = 0.05) to detect clinically meaningful (26%) differences in colonic transit. Thirty-nine of 55 patients fulfilled eligibility criteria (9 screen failures, 5 baseline GC24 outside prespecified range). At baseline, three treatment groups had comparable age, body mass index, and GC 24 h. Significant effects of pexacerfont relative to placebo were not detected on colonic GC24 (P = 0.53), gastric emptying, orocecal transit, ascending colon emptying half-time, and stool frequency, consistency, and ease of passage. No safety issues were identified. We conclude that in women with D-IBS, pexacerfont, 25 or 100 mg qd, does not significantly alter colonic or other regional transit or bowel function. The role of central and peripheral CRF1 receptors in bowel function in D-IBS requires further study. |
| **Date** | 2009-06 |
| **Library Catalog** | journals.physiology.org (Atypon) |
| **URL** | <https://journals.physiology.org/doi/full/10.1152/ajpgi.00011.2009> |
| **Accessed** | 6/15/2025, 4:25:31 PM |
| **Extra** | Publisher: American Physiological Society |
| **Volume** | 296 |
| **Pages** | G1299-G1306 |
| **Publication** | American Journal of Physiology-Gastrointestinal and Liver Physiology |
| **DOI** | [10.1152/ajpgi.00011.2009](http://doi.org/10.1152/ajpgi.00011.2009) |
| **Issue** | 6 |
| **ISSN** | 0193-1857 |
| **Date Added** | 6/15/2025, 4:25:31 PM |
| **Modified** | 6/15/2025, 4:25:31 PM |

* **Tags:**
  + corticotropin releasing factor
  + diarrhea-predominant irritable bowel syndrome
  + gastrointestinal transit
  + pexacerfont
  + randomized trial

**Attachments**

* + Full Text PDF
* **Efficacy and Safety of Serotonin Receptor Ligands in the Treatment of Irritable Bowel Syndrome: A Review**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Agata Binienda |
| **Author** | Martin Storr |
| **Author** | Jakub Fichna |
| **Author** | Maciej Salaga |
| **Abstract** | Background: Irritable bowel syndrome (IBS) is a chronic, recurrent bowel disorder with an unknown etiology, which is most likely multifactorial. Increased mucosal permeability, visceral hypersensitivity and activation status of intestinal mucosal immune cells cause changes in gastrointestinal (GI) motility, secretion and sensation observed in the course of IBS. Permanent, cumbersome symptoms, such as diarrhea, constipation and abdominal pain greatly lower the quality of life of IBS patients. On this basis, according to the Rome IV criteria, different forms of IBS can be distinguished. Objective: This article focuses on the role of serotonin system in the pathophysiology of IBS as a potential therapeutic target. We shortly describe several molecules, associated with serotonin receptors, mainly 5-HT3 receptor antagonists and 5-HT4 receptor agonists, that are used in the treatment of motility disorders and visceral pain in IBS patients. We summarize the findings obtained in the clinical trials and elaborate on the safety of the serotonin ligands. Although the majority of serotonin receptor ligands relieve global symptoms, there are also some adverse effects, which can be dangerous for patients. Results and Conclusion: We postulate that currently, among all serotonin-targeting compounds, ramosetron is the best treatment option for IBS-D patients, due to its exceptional efficacy in both genders as well as good tolerability. Whereas, tegaserod is highly recommended for IBS-C sufferers. Nevertheless, numerous studies on the new serotonin receptor ligands are conducted to ensure the delivery of novel compounds with improved efficacy and safety profiles. |
| **Language** | en |
| **Short Title** | Efficacy and Safety of Serotonin Receptor Ligands in the Treatment of Irritable Bowel Syndrome |
| **Library Catalog** | www.eurekaselect.com |
| **URL** | <https://www.eurekaselect.com/article/87609> |
| **Accessed** | 6/15/2025, 4:25:42 PM |
| **Publication** | http://www.eurekaselect.com |
| **Date Added** | 6/15/2025, 4:25:42 PM |
| **Modified** | 6/15/2025, 4:25:42 PM |

* **Electroacupuncture Regulates Disorders of Gut-Brain Interaction by Decreasing Corticotropin-Releasing Factor in a Rat Model of IBS**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Ying Chen |
| **Author** | Yan Zhao |
| **Author** | Dan-ni Luo |
| **Author** | Hui Zheng |
| **Author** | Ying Li |
| **Author** | Si-yuan Zhou |
| **Abstract** | Objective. Acupuncture is effective for irritable bowel syndrome (IBS); however, the mechanisms of action are not fully understood. We aim to explore the mechanism of electroacupuncture (EA) in the dual regulation of disorders of gut-brain interaction. Methods. A rat model of IBS was generated by chronic unpredictable mild stress (CUMS). Eight of 32 rats were assigned to the blank control group. The remaining 24 rats received CUMS for 14 days. Then, the rats surviving and successfully modelled were randomly divided into the CUMS group, the CUMS+EA group, and the CUMS+PB (pinaverium bromide) group. In the next 14 days of treatment, rats in the CUMS+EA group were acupunctured at ST25 (Tianshu), ST36 (Zusanli), SP6 (Sanyinjiao), and LR3 (Taichong) for 15 min every day. Rats in the CUMS+PB group were treated by the administration of gavage with 2.7 mg/mL pinaverium every day. Visceral pain threshold, the percentage of time spent in open arms (OT%) in the elevated plus maze test (EPMT), and the sucrose preference (SP%) in the sucrose preference test (SPT) were measured at baseline, day 15, and day 30. The expression of zonula occludens-1 (ZO-1), the morphology of the connective structure of intestinal epithelium, the CRF and CRF-R1 mRNA expression in the hypothalamus, and the double staining of intestinal mucosal mast cells (IMMC) and CRF-R1 were measured at the end of the experiment. Results. Compared with the blank control group, visceral pain threshold pressure, the expression of ZO-1, OT%, SP%, CRF, and CRF-R1 mRNA expression in the hypothalamus, and double staining of IMMC and CRF-R1 were decreased significantly in the CUMS group. Meanwhile, the morphology of the connective structure in the CUMS group was indistinct. Compared with the CUMS group, SP% was significantly increased in the CUMS+EA group, but there was no significant difference for it in the CUMS+PB group. The morphology of the connective structure in the two treatment groups was clear and seeable. And the expression of other parameters mentioned above was apparently increased in the two treatment groups. Compared with the CUMS+PB group, the expression of ZO-1 in the CUMS+EA group was significantly enhanced. And no obvious difference for other parameters was found between the two treatment groups. Conclusions. EA treatment can decrease the expression of hypothalamic CRF and CRF-R1, relieve anxiety and depression, meanwhile reduce the expression of CRF-R1 in the gastrointestinal mucosa, increase ZO-1 expression, and adjust tight junctions (TJs) to repair the intestinal mucosal barrier. The above roles suggest that EA may play a dual role in alleviating the gastrointestinal and psychological symptoms of IBS, suggesting a potentially dual therapeutic role for EA in regulating disorders of gut-brain interaction in IBS rats. |
| **Date** | 2019 |
| **Language** | en |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1155/2019/1759842> |
| **Accessed** | 6/15/2025, 4:26:07 PM |
| **Rights** | Copyright © 2019 Ying Chen et al. |
| **Extra** | \_eprint: https://onlinelibrary.wiley.com/doi/pdf/10.1155/2019/1759842 |
| **Volume** | 2019 |
| **Pages** | 1759842 |
| **Publication** | Gastroenterology Research and Practice |
| **DOI** | [10.1155/2019/1759842](http://doi.org/10.1155/2019/1759842) |
| **Issue** | 1 |
| **ISSN** | 1687-630X |
| **Date Added** | 6/15/2025, 4:26:07 PM |
| **Modified** | 6/15/2025, 4:26:07 PM |

* **Attachments**
  + Full Text PDF
* **Exploring the Gut-Brain Axis: A Comprehensive Review of Interactions Between the Gut Microbiota and the Central Nervous System**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Ishaan Bakshi |
| **Author** | Sandeep Dey |
| **Author** | Arya J. Raut |
| **Author** | Shreyas Katta |
| **Author** | Prashant Sharma |
| **Date** | 2024/05/11 |
| **Short Title** | Exploring the Gut-Brain Axis |
| **Library Catalog** | www.ijfmr.com |
| **URL** | <https://www.ijfmr.com/research-paper.php?id=19563> |
| **Accessed** | 6/15/2025, 4:25:20 PM |
| **Rights** | Creative Commons Attribution-ShareAlike 4.0 International License |
| **Extra** | Publisher: IJFMR |
| **Volume** | 6 |
| **Publication** | IJFMR - International Journal For Multidisciplinary Research |
| **DOI** | [10.36948/ijfmr.2024.v06i03.19563](http://doi.org/10.36948/ijfmr.2024.v06i03.19563) |
| **Issue** | 3 |
| **ISSN** | 2582-2160 |
| **Date Added** | 6/15/2025, 4:25:20 PM |
| **Modified** | 6/15/2025, 4:25:20 PM |

* **Attachments**
  + Full Text PDF
* **Impact of Enteric Nervous Cells on Irritable Bowel Syndrome: Potential Treatment Options**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Ploutarchos Pastras |
| **Author** | Ioanna Aggeletopoulou |
| **Author** | Christos Triantos |
| **Abstract** | Irritable bowel syndrome (IBS) is a condition that significantly impacts the lifestyle, health, and habits of numerous individuals worldwide. Its diagnosis and classification are based on the Rome criteria, updated periodically to reflect new research findings in this field. IBS can be classified into different types based on symptoms, each with distinct treatment approaches and some differences in their pathophysiology. The exact pathological background of IBS remains unclear, with many aspects still unknown. Recent research developments suggest that disorders in the brain-gut–microbiota axis are key contributors to the symptoms and severity of IBS. The central nervous system (CNS) interacts bidirectionally with intestinal processes within the lumen and the intestinal wall, with the autonomic nervous system, particularly the vagus nerve, playing an important role. However, the enteric nervous system (ENS) is also crucial in the pathophysiological pathway of IBS. The apeline–corticotropin-releasing factor (CRF)–toll-like receptor 4 (TLR4) signaling route via enteric glia and serotonin production in enteroendocrine cells at the enteric barrier are among the most well-understood new findings that affect IBS through the ENS. Additionally, the microbiota regulates neuronal signals, modifying enteric function by altering the number of enteric bacteria and other mechanisms. Given the limited therapeutic options currently available, it is essential to identify new treatment targets, with the brain-gut axis, particularly the enteric nervous system, being a promising focus. This study aims to delineate the molecular mechanisms that induce IBS and to suggest potential targets for future research and treatment of this potentially debilitating disease. |
| **Date** | 2024/10 |
| **Language** | en |
| **Short Title** | Impact of Enteric Nervous Cells on Irritable Bowel Syndrome |
| **Library Catalog** | www.mdpi.com |
| **URL** | <https://www.mdpi.com/2076-2607/12/10/2036> |
| **Accessed** | 6/15/2025, 4:25:12 PM |
| **Rights** | http://creativecommons.org/licenses/by/3.0/ |
| **Extra** | Number: 10 Publisher: Multidisciplinary Digital Publishing Institute |
| **Volume** | 12 |
| **Pages** | 2036 |
| **Publication** | Microorganisms |
| **DOI** | [10.3390/microorganisms12102036](http://doi.org/10.3390/microorganisms12102036) |
| **Issue** | 10 |
| **ISSN** | 2076-2607 |
| **Date Added** | 6/15/2025, 4:25:12 PM |
| **Modified** | 6/15/2025, 4:25:12 PM |

* **Tags:**
  + enteric nervous system
  + gut microbiota
  + irritable bowel syndrome
  + central nervous system
  + enteric nervous cells
  + management
  + mechanisms
  + signaling

**Attachments**

* + Full Text PDF
* **Innovations in the diagnosis, treatment, and management of disorders of gut-brain interaction (DGBI)**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Patrycja Krynicka |
| **Author** | Koulaouzidis ,George |
| **Author** | Marlicz ,Wojciech |
| **Author** | Anastasios and Koulaouzidis |
| **Abstract** | Functional dyspepsia (FD) and irritable bowel syndrome (IBS) are the most prevalent disorders of gut-brain interaction (DGBI), frequently overlapping and associated with complex pathophysiological mechanisms. Increasing evidence implicates gut microbiota alterations in driving symptoms via immune activation, altered motility, gut vascular barrier and gut-brain axis disruption. This review explores the role of gut microbiota in FD and IBS pathogenesis and symptomatology. A comprehensive literature search was conducted using PubMed, EMBASE, and Google Scholar databases, including studies published between January 2013 and March 2025. Particular focus is given to microbiota-targeted therapies such as prebiotics, probiotics, synbiotics, postbiotics, and fecal microbiota transplantation (FMT). The review also discusses multidimensional treatment strategies combining dietary and lifestyle modification, cognitive-behavioral therapy, and pharmacological neuromodulation. Recent advances in diagnostic methods, including capsule-based microbiota sampling and digital tools for remote psychogastroenterology care, are highlighted. Despite scientific progress, current DGBI management remains insufficiently personalized. Future approaches should integrate individualized microbiota profiling with targeted interventions and utilize innovative diagnostic and digital health technologies to enhance clinical outcomes in FD and IBS. |
| **Library Catalog** | Taylor and Francis+NEJM |
| **URL** | <https://doi.org/10.1080/17474124.2025.2508967> |
| **Accessed** | 6/15/2025, 4:26:20 PM |
| **Extra** | Publisher: Taylor & Francis \_eprint: https://doi.org/10.1080/17474124.2025.2508967 PMID: 40390189 |
| **Volume** | 0 |
| **Pages** | 1-14 |
| **Publication** | Expert Review of Gastroenterology & Hepatology |
| **DOI** | [10.1080/17474124.2025.2508967](http://doi.org/10.1080/17474124.2025.2508967) |
| **Issue** | 0 |
| **ISSN** | 1747-4124 |
| **Date Added** | 6/15/2025, 4:26:20 PM |
| **Modified** | 6/15/2025, 4:26:20 PM |

* **Tags:**
  + microbiota
  + irritable bowel syndrome
  + Artificial intelligence
  + functional dyspepsia
  + probiotics
  + capsule endoscopy
  + disorders of gut-brain interaction (DGBI)
  + psychogastroenterology

**Attachments**

* + Full Text PDF
* **Irritable Bowel Syndrome: Is It Really a Functional Disorder? A New Perspective on Alteration of Enteric Nervous System**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Jaehoon Jahng |
| **Author** | Yong Sung Kim |
| **Abstract** | Jaehoon Jahng, and Yong Sung Kim. J Neurogastroenterol Motil 2016;22:163-5. https://doi.org/10.5056/jnm16043 |
| **Date** | 2016/04/30 |
| **Language** | en |
| **Short Title** | Irritable Bowel Syndrome |
| **Library Catalog** | www.jnmjournal.org |
| **URL** | <https://www.jnmjournal.org/journal/view.html?doi=10.5056/jnm16043> |
| **Accessed** | 6/15/2025, 4:25:24 PM |
| **Extra** | Publisher: Korean Society of Neurogastroenterology and Motility |
| **Volume** | 22 |
| **Pages** | 163-165 |
| **Publication** | Journal of Neurogastroenterology and Motility |
| **DOI** | [10.5056/jnm16043](http://doi.org/10.5056/jnm16043) |
| **Issue** | 2 |
| **Journal Abbr** | J Neurogastroenterol Motil |
| **ISSN** | 2093-0879 |
| **Date Added** | 6/15/2025, 4:25:24 PM |
| **Modified** | 6/15/2025, 4:25:24 PM |

* **Attachments**
  + Full Text PDF
* **Long-Term Implicit Epigenetic Stress Information in the Enteric Nervous System and its Contribution to Developing and Perpetuating IBS**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Császár-Nagy Noemi |
| **Author** | Petr Bob |
| **Author** | István Bókkon |
| **Abstract** | Psychiatric and mood disorders may play an important role in the development and persistence of irritable bowel syndrome (IBS). Previously, we hypothesized that stress-induced implicit memories may persist throughout life via epigenetic processes in the enteric nervous system (ENS), independent of the central nervous system (CNS). These epigenetic memories in the ENS may contribute to developing and perpetuating IBS. Here, we further elaborate on our earlier hypothesis. That is, during pregnancy, maternal prenatal stresses perturb the HPA axis and increase circulating cortisol levels, which can affect the maternal gut microbiota. Maternal cortisol can cross the placental barrier and increase cortisol-circulating levels in the fetus. This leads to dysregulation of the HPA axis, affecting the gut microbiota, microbial metabolites, and intestinal permeability in the fetus. Microbial metabolites, such as short-chain fatty acids (which also regulate the development of fetal ENS), can modulate a range of diseases by inducing epigenetic changes. These mentioned processes suggest that stress-related, implicit, long-term epigenetic memories may be programmed into the fetal ENS during pregnancy. Subsequently, this implicit epigenetic stress information from the fetal ENS could be conveyed to the CNS through the bidirectional microbiota-gut-brain axis (MGBA), leading to perturbed functional connectivity among various brain networks and the dysregulation of affective and pain processes. |
| **Language** | en |
| **Library Catalog** | www.eurekaselect.com |
| **URL** | <https://www.eurekaselect.com/article/140226> |
| **Accessed** | 6/15/2025, 4:25:27 PM |
| **Volume** | 22 |
| **Pages** | 2100-2112 |
| **Publication** | Current Neuropharmacology |
| **DOI** | [10.2174/1570159X22666240507095700](http://doi.org/10.2174/1570159X22666240507095700) |
| **Issue** | 13 |
| **Date Added** | 6/15/2025, 4:25:27 PM |
| **Modified** | 6/15/2025, 4:25:27 PM |

* **Long-Term Oncologic Outcome following Duodenum-Preserving Pancreatic Head Resection for Benign Tumors, Cystic Neoplasms, and Neuroendocrine Tumors: Systematic Review and Meta-analysis**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Hans G Beger |
| **Author** | Benjamin Mayer |
| **Author** | Bertram Poch |
| **Date** | 2024 |
| **URL** | <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11164799/> |
| **Volume** | 31 |
| **Pages** | 4637–4653 |
| **Publication** | Annals of Surgical Oncology |
| **DOI** | [10.1245/s10434-024-15222-y](http://doi.org/10.1245/s10434-024-15222-y) |
| **Issue** | 7 |
| **Date Added** | 4/16/2025, 11:10:32 PM |
| **Modified** | 6/16/2025, 1:12:21 PM |

* **Tags:**
  + Adult
  + Female
  + Humans
  + Male
  + Treatment Outcome
  + Animals
  + Disease Models, Animal
  + Mice
  + STING
  + Quality of Life
  + Retrospective Studies
  + Diabetes
  + Signal Transduction
  + Cell Differentiation
  + Cell Line
  + Neoplasm Recurrence, Local
  + Cell Movement
  + Mammals
  + Neurons
  + immune cells
  + inflammation
  + Homeostasis
  + Gastroenterology
  + intestinal organoids
  + Regeneration
  + microbiota
  + Pancreas
  + inflammatory bowel disease
  + \*Cell- and Tissue-Based Therapy/methods
  + \*Bile Duct Neoplasms
  + \*Bile Duct Neoplasms/surgery
  + \*Cell Lineage
  + \*Cholangiocarcinoma
  + \*Cholangiocarcinoma/pathology
  + \*Colitis, Ulcerative/drug therapy
  + \*Cystadenocarcinoma/diagnostic imaging/surgery
  + \*Cystadenoma/diagnostic imaging/surgery
  + \*Cysts/pathology
  + \*Diabetes Mellitus, Experimental/complications/genetics/metabolism
  + \*Enteric Nervous System
  + \*Enteric Nervous System/pathology
  + \*Hyperglycemia/genetics/metabolism
  + \*Hypothalamo-Hypophyseal System
  + \*Inflammatory Bowel Diseases/drug therapy
  + \*Liver Neoplasms/diagnostic imaging/surgery
  + \*Liver Neoplasms/surgery
  + \*Microbiota
  + \*MicroRNAs/metabolism
  + \*Neoplasms, Cystic, Mucinous, and Serous
  + \*Neuroglia/physiology
  + \*Zebrafish
  + 16S RNA sequencing
  + Acinar cell carcinoma
  + Aging
  + antibiotics
  + Bile Ducts, Intrahepatic
  + Bile Ducts, Intrahepatic/surgery
  + Biliary
  + Biliary cystadenocarcinoma
  + Biliary cystadenoma
  + Brain
  + Brain-Gut Axis
  + Brain/physiology
  + Cell Separation
  + Chemical coding
  + Chick Embryo
  + circVPS13A
  + Cistoadenocarcinoma
  + Cistoadenoma
  + Clinicopathological criteria, Surgical outcomes
  + Colon/drug effects/pathology
  + Cystadenocarcinoma
  + Cystadenoma
  + cystic liver lesions
  + Cystic liver neoplasm
  + Cytology
  + Developmental disorders
  + diabetes
  + diabetes mellitus
  + Drug Discovery/\*methods
  + Embryonic stem cells
  + ENS
  + ENS neuropathies
  + enteric glia
  + enteric glia communications
  + Enteric glia communications
  + enteric glia diversity
  + enteric nervous system
  + Enteric nervous system
  + Enteric Nervous System
  + enteric nervous system (ENS)
  + Enteric nervous system (ENS)
  + Enteric Nervous System/\*pathology
  + Enteric neural precursor cells (ENPCs)
  + enteric progenitor cell
  + Fecal microbiota transplantation
  + Frantz's tumor
  + gastrointestinal complications
  + gastrointestinal diseases
  + Gastrointestinal Diseases
  + Gastrointestinal Diseases/pathology
  + gastrointestinal tract
  + Gastrointestinal Tract/drug effects/pathology
  + glia
  + Glial Cell Line-Derived Neurotrophic Factor/genetics
  + glucagon-like peptide 1
  + Growth Disorders
  + growth retardation
  + gut brain axis
  + gut microbiota
  + gut-brain axis
  + gut–brain axis
  + hepatic cystadenocarcinoma
  + hepatic cystadenoma
  + Hepatic simple cyst
  + hepatobiliary cystadenocarcinoma
  + hepatobiliary cystadenoma
  + Hirschsprung disease
  + Hirschsprung Disease/\*drug therapy/\*pathology/therapy
  + homeostasis
  + Imaging modalities
  + In Situ Hybridization, Fluorescence
  + Inflammatory bowel diseases
  + Intraductal papillary biliary neoplasms
  + intraductal papillary neoplasms of bile duct
  + irritable bowel syndrome
  + L-Fucose
  + Liver Diseases
  + Management
  + microbial metabolites
  + microbiota-gut-brain axis
  + Microbiota-gut-brain axis
  + Mucinous biliary cystic tumors, Biliary cystadenoma
  + mucinous cystic neoplasm
  + Mucinous cystic neoplasms
  + Mucinous neoplasm
  + muscularis macrophages
  + myenteric neurons
  + Neoplasia mucinosa quística
  + Neoplasia papilar intraductal biliar
  + Neoplasia quística hepática
  + Neural Crest
  + neural crest cell
  + neurodegeneration
  + Neuroglia
  + Neurons/drug effects/\*pathology
  + offspring
  + P2X7 receptor
  + pancreatectomy
  + Pancreatectomy
  + Pancreatic neoplasms
  + Pancreatic Neoplasms
  + Pancreatic surgery
  + pancreatic tumor
  + Parkinson’s disease
  + pediatric pancreatic neoplasm
  + Pepstatins/metabolism
  + Pituitary-Adrenal System
  + pluripotent stem cells (PSCs)
  + Pluripotent Stem Cells/pathology
  + preconception
  + probiotic
  + Purinergic signaling
  + Receptor, Endothelin B/metabolism
  + Receptors, Purinergic P2X7
  + RNA, Circular/genetics
  + Rotenone-induced mouse model
  + short-chain fatty acids
  + Solid pseudopapillary tumor
  + Stem-cell differentiation
  + submucosal neurons
  + Submucous Plexus
  + surgical outcome
  + surgical resection
  + three-dimensional (3D)
  + type 2 diabetes
  + zebrafish

**Notes:**

* + e14603 NMO-00132-2023
  + e14603 NMO-00132-2023

**Attachments**

* + Full Text
  + Full Text
  + Full Text PDF
  + Full Text PDF
  + Full Text PDF
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  + Full Text PDF
  + Full Text PDF
  + Full Text PDF
  + PubMed Central Full Text PDF
  + PubMed Central Full Text PDF
  + PubMed Central Full Text PDF
  + PubMed Central Link
  + PubMed Central Link
  + PubMed Central Link
  + PubMed Central Link
  + PubMed entry
* **Overexpression of corticotropin-releasing factor in intestinal mucosal eosinophils is associated with clinical severity in Diarrhea-Predominant Irritable Bowel Syndrome**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Eloísa Salvo-Romero |
| **Author** | Cristina Martínez |
| **Author** | Beatriz Lobo |
| **Author** | Bruno K. Rodiño-Janeiro |
| **Author** | Marc Pigrau |
| **Author** | Alejandro D. Sánchez-Chardi |
| **Author** | Ana M. González-Castro |
| **Author** | Marina Fortea |
| **Author** | Cristina Pardo-Camacho |
| **Author** | Adoración Nieto |
| **Author** | Elba Expósito |
| **Author** | Danila Guagnozzi |
| **Author** | Amanda Rodríguez-Urrutia |
| **Author** | Inés de Torres |
| **Author** | Ricard Farré |
| **Author** | Fernando Azpiroz |
| **Author** | Carmen Alonso-Cotoner |
| **Author** | Javier Santos |
| **Author** | María Vicario |
| **Abstract** | Corticotropin-releasing factor (CRF) has been identified in intestinal mucosal eosinophils and associated with psychological stress and gut dysfunction. Irritable bowel syndrome (IBS) is commonly characterized by altered intestinal motility, immune activation, and increased gut barrier permeability along with heightened susceptibility to psychosocial stress. Despite intensive research, the role of mucosal eosinophils in stress-associated gut dysfunction remains uncertain. In this study, we evaluated eosinophil activation profile and CRF content in the jejunal mucosa of diarrhea-predominant IBS (IBS-D) and healthy controls (HC) by gene/protein expression and transmission electron microscopy. We also explored the association between intestinal eosinophil CRF and chronic stress, and the potential mechanisms underlying the stress response by assessing eosinophil response to neuropeptides. We found that mucosal eosinophils displayed higher degranulation profile in IBS-D as compared to HC, with increased content of CRF in the cytoplasmic granules, which significantly correlated with IBS clinical severity, life stress background and depression. Eosinophils responded to substance P and carbachol by increasing secretory activity and CRF synthesis and release, without promoting pro-inflammatory activity, a profile similar to that found in mucosal eosinophils from IBS-D. Collectively, our results suggest that intestinal mucosal eosinophils are potential contributors to stress-mediated gut dysfunction through CRF production and release. |
| **Date** | 2020-11-26 |
| **Language** | en |
| **Library Catalog** | www.nature.com |
| **URL** | <https://www.nature.com/articles/s41598-020-77176-x> |
| **Accessed** | 6/15/2025, 4:25:38 PM |
| **Rights** | 2020 The Author(s) |
| **Extra** | Publisher: Nature Publishing Group |
| **Volume** | 10 |
| **Pages** | 20706 |
| **Publication** | Scientific Reports |
| **DOI** | [10.1038/s41598-020-77176-x](http://doi.org/10.1038/s41598-020-77176-x) |
| **Issue** | 1 |
| **Journal Abbr** | Sci Rep |
| **ISSN** | 2045-2322 |
| **Date Added** | 6/15/2025, 4:25:38 PM |
| **Modified** | 6/15/2025, 4:25:38 PM |

* **Tags:**
  + Irritable bowel syndrome
  + Mucosal immunology

**Attachments**

* + Full Text PDF
* **Pasteurized Akkermansia muciniphila improves irritable bowel syndrome-like symptoms and related behavioral disorders in mice**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Maëva Meynier |
| **Author** | Daugey ,Valentine |
| **Author** | Mallaret ,Geoffroy |
| **Author** | Gervason ,Sandie |
| **Author** | Meleine ,Mathieu |
| **Author** | Barbier ,Julie |
| **Author** | Aissouni ,Youssef |
| **Author** | Lolignier ,Stéphane |
| **Author** | Bonnet ,Mathilde |
| **Author** | Ardid ,Denis |
| **Author** | De Vos ,Willem M. |
| **Author** | Van Hul ,Matthias |
| **Author** | Suenaert ,Peter |
| **Author** | Brochot ,Amandine |
| **Author** | Cani ,Patrice D. |
| **Author** | Frédéric A. and Carvalho |
| **Abstract** | Gut – brain communications disorders in irritable bowel syndrome (IBS) are associated with intestinal microbiota composition, increased gut permeability, and psychosocial disturbances. Symptoms of IBS are difficult to medicate, and hence much research is being made into alternative approaches. This study assesses the potential of a treatment with pasteurized Akkermansia muciniphila for alleviating IBS-like symptoms in two mouse models of IBS with different etiologies. Two clinically relevant animal models were used to mimic IBS-like symptoms in C57BL6/J mice: the neonatal maternal separation (NMS) paradigm and the Citrobacter rodentium infection model. In both models, gut permeability, colonic sensitivity, fecal microbiota composition and colonic IL-22 expression were evaluated. The cognitive performance and emotional state of the animals were also assessed by several tests in the C. rodentium infection model. The neuromodulation ability of pasteurized A. muciniphila was assessed on primary neuronal cells from mice dorsal root ganglia using a ratiometric calcium imaging approach. The administration of pasteurized A. muciniphila significantly reduced colonic hypersensitivity in both IBS mouse models, accompanied by a reinforcement of the intestinal barrier function. Beneficial effects of pasteurized A. muciniphila treatment have also been observed on anxiety-like behavior and memory defects in the C. rodentium infection model. Finally, a neuroinhibitory effect exerted by pasteurized A. muciniphila was observed on neuronal cells stimulated with two algogenic substances such as capsaicin and inflammatory soup. Our findings demonstrate novel anti-hyperalgesic and neuroinhibitory properties of pasteurized A. muciniphila, which therefore may have beneficial effects in relieving pain and anxiety in subjects with IBS. |
| **Date** | 2024-12-31 |
| **Library Catalog** | Taylor and Francis+NEJM |
| **URL** | <https://doi.org/10.1080/19490976.2023.2298026> |
| **Accessed** | 6/15/2025, 4:26:14 PM |
| **Extra** | Publisher: Taylor & Francis \_eprint: https://doi.org/10.1080/19490976.2023.2298026 PMID: 38170633 |
| **Volume** | 16 |
| **Pages** | 2298026 |
| **Publication** | Gut Microbes |
| **DOI** | [10.1080/19490976.2023.2298026](http://doi.org/10.1080/19490976.2023.2298026) |
| **Issue** | 1 |
| **ISSN** | 1949-0976 |
| **Date Added** | 6/15/2025, 4:26:14 PM |
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* **Tags:**
  + IBS
  + anxiety-like disorders
  + colonic hypersensitivity
  + memory impairment
  + neuroinhibition
  + Pasteurized Akkermansia muciniphila

**Attachments**

* + Full Text PDF
* **Pathophysiological Commonality Between Irritable Bowel Syndrome and Metabolic Syndrome: Role of Corticotropin-releasing Factor–Toll-like Receptor 4–Proinflammatory Cytokine Signaling**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Tsukasa Nozu |
| **Author** | Toshikatsu Okumura |
| **Abstract** | Tsukasa Nozu and Toshikatsu Okumura. J Neurogastroenterol Motil 2022;28:173-84. https://doi.org/10.5056/jnm21002 |
| **Date** | 2022/04/30 |
| **Language** | en |
| **Short Title** | Pathophysiological Commonality Between Irritable Bowel Syndrome and Metabolic Syndrome |
| **Library Catalog** | www.jnmjournal.org |
| **URL** | <https://www.jnmjournal.org/journal/view.html?doi=10.5056/jnm21002> |
| **Accessed** | 6/15/2025, 4:25:34 PM |
| **Extra** | Publisher: The Korean Society of Neurogastroenterology and Motility |
| **Volume** | 28 |
| **Pages** | 173-184 |
| **Publication** | Journal of Neurogastroenterology and Motility |
| **DOI** | [10.5056/jnm21002](http://doi.org/10.5056/jnm21002) |
| **Issue** | 2 |
| **Journal Abbr** | J Neurogastroenterol Motil |
| **ISSN** | 2093-0879 |
| **Date Added** | 6/15/2025, 4:25:34 PM |
| **Modified** | 6/15/2025, 4:25:34 PM |

* **Attachments**
  + Full Text PDF
* **Positive allosteric modulation of endogenous delta opioid receptor signaling in the enteric nervous system is a potential treatment for gastrointestinal motility disorders**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Jesse J. DiCello |
| **Author** | Simona E. Carbone |
| **Author** | Ayame Saito |
| **Author** | Vi Pham |
| **Author** | Agata Szymaszkiewicz |
| **Author** | Arisbel B. Gondin |
| **Author** | Sadia Alvi |
| **Author** | Kiliana Marique |
| **Author** | Priyank Shenoy |
| **Author** | Nicholas A. Veldhuis |
| **Author** | Jakub Fichna |
| **Author** | Meritxell Canals |
| **Author** | Arthur Christopoulos |
| **Author** | Celine Valant |
| **Author** | Daniel P. Poole |
| **Abstract** | Download figureDownload PowerPoint |
| **Date** | 2022-01 |
| **Library Catalog** | journals.physiology.org (Atypon) |
| **URL** | <https://journals.physiology.org/doi/full/10.1152/ajpgi.00297.2021> |
| **Accessed** | 6/15/2025, 4:25:55 PM |
| **Extra** | Publisher: American Physiological Society |
| **Volume** | 322 |
| **Pages** | G66-G78 |
| **Publication** | American Journal of Physiology-Gastrointestinal and Liver Physiology |
| **DOI** | [10.1152/ajpgi.00297.2021](http://doi.org/10.1152/ajpgi.00297.2021) |
| **Issue** | 1 |
| **ISSN** | 0193-1857 |
| **Date Added** | 6/15/2025, 4:25:55 PM |
| **Modified** | 6/15/2025, 4:25:55 PM |

* **Tags:**
  + enteric nervous system
  + allosteric modulation
  + delta opioid receptor
  + G protein-coupled receptor

**Attachments**

* + Full Text PDF
* **Prokinetic actions of luminally acting 5-HT4 receptor agonists**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | John R. Konen |
| **Author** | Melody M. Haag |
| **Author** | Daria Guseva |
| **Author** | Molly Hurd |
| **Author** | Alisha A. Linton |
| **Author** | Brigitte Lavoie |
| **Author** | Colleen B. Kerrigan |
| **Author** | Emily Joyce |
| **Author** | Stephan C. Bischoff |
| **Author** | Steve Swann |
| **Author** | Luana Griffin |
| **Author** | Jun Matsukawa |
| **Author** | Matthew D. Falk |
| **Author** | Tony S. Gibson |
| **Author** | Grant W. Hennig |
| **Author** | Jill Wykosky |
| **Author** | Gary M. Mawe |
| **Abstract** | Background 5-HT4 receptor (5-HT4R) agonists exert prokinetic actions in the GI tract, but non-selective actions and potential for stimulation of non-target 5-HT4Rs have limited their use. Since 5-HT4Rs are expressed in the colonic epithelium and their stimulation accelerates colonic propulsion in vitro, we tested whether luminally acting 5-HT4R agonists promote intestinal motility. Methods Non-absorbed 5-HT4R agonists, based on prucalopride and naronapride, were assessed for potency at the 5-HT4R in vitro, and for tissue and serum distribution in vivo in mice. In vivo assessment of prokinetic potential included whole gut transit, colonic motility, fecal output, and fecal water content. Colonic motility was also studied ex vivo in mice treated in vivo. Immunofluorescence was used to evaluate receptor distribution in human intestinal mucosa. Key Results Pharmacological screening demonstrated selectivity and potency of test agonists for 5-HT4R. Bioavailability studies showed negligible serum detection. Gavage of agonists caused faster whole gut transit and colonic motility, increased fecal output, and elevated fecal water content. Prokinetic actions were blocked by a 5-HT4R antagonist and were not detected in 5-HT4R knockout mice. Agonist administration promoted motility in models of constipation. Evaluation of motility patterns ex vivo revealed enhanced contractility in the middle and distal colon. Immunoreactivity for 5-HT4R is present in the epithelial layer of the human small and large intestines. Conclusions and Inferences These findings demonstrated that stimulation of epithelial 5-HT4Rs can potentiate propulsive motility and support the concept that mucosal 5-HT4Rs could represent a safe and effective therapeutic target for the treatment of constipation. |
| **Date** | 2021 |
| **Language** | en |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1111/nmo.14026> |
| **Accessed** | 6/15/2025, 4:26:23 PM |
| **Rights** | © 2020 John Wiley & Sons Ltd |
| **Extra** | \_eprint: https://onlinelibrary.wiley.com/doi/pdf/10.1111/nmo.14026 |
| **Volume** | 33 |
| **Pages** | e14026 |
| **Publication** | Neurogastroenterology & Motility |
| **DOI** | [10.1111/nmo.14026](http://doi.org/10.1111/nmo.14026) |
| **Issue** | 4 |
| **ISSN** | 1365-2982 |
| **Date Added** | 6/15/2025, 4:26:23 PM |
| **Modified** | 6/15/2025, 4:26:23 PM |

* **Tags:**
  + constipation
  + serotonin
  + 5-HT4 receptor
  + epithelial target
  + peristalsis
  + prokinetic
* **Roles of Heart Rate Variability in Assessing Autonomic Nervous System in Functional Gastrointestinal Disorders: A Systematic Review**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | M. Khawar Ali |
| **Author** | Jiande D. Z. Chen |
| **Abstract** | Functional gastrointestinal disorders (FGID) and gastroesophageal reflux (GERD) disease affect a large global population and incur substantial health care costs. Impairment in gut-brain communication is one of the main causes of these disorders. The central nervous system (CNS) provides its inputs to the enteric nervous system (ENS) by modulating the autonomic nervous system (ANS) to control the gastrointestinal functions. Therefore, GERD and FGID’s might be associated with autonomic dysfunction, which can be identified via heart rate variability (HRV). FGIDs may be treated by restoring the autonomic dysfunction via neuromodulation. This article reviews the roles of HRV in the assessment of autonomic function and dysfunction in (i) gastroesophageal reflux (GERD), and the following FGIDs: (ii) functional dyspepsia (FD) and gastroparesis, (iii) irritable bowel syndrome (IBS) and (iv) constipation. The roles of HRV in the assessment of autonomic responses to various interventions were also reviewed. We used PUBMED, Web of Science, Elsevier/Science direct and Scopus to search the eligible studies for each disorder, which also included the keyword ‘heart rate variability’. The retrieved studies were screened and filtered to identify the most suitable studies using HRV parameters to associate the autonomic function with any of the above disorders. Studies involving both human and animal models were included. Based on analyses of HRV, GERD as well as the FGIDs were found to be associated with decreased parasympathetic activity and increased sympathetic nervous system activity with the autonomic balance shifted towards the sympathetic nervous system. In addition, the HRV methods were also reported to be able to assess the autonomic responses to various interventions (mostly neuromodulation), typically the enhancement of parasympathetic activity. In summary, GERD and FGIDs are associated with impaired autonomic dysfunction, mainly due to suppressed vagal and overactive sympathetic tone, which can be assessed noninvasively using HRV. |
| **Date** | 2023/1 |
| **Language** | en |
| **Short Title** | Roles of Heart Rate Variability in Assessing Autonomic Nervous System in Functional Gastrointestinal Disorders |
| **Library Catalog** | www.mdpi.com |
| **URL** | <https://www.mdpi.com/2075-4418/13/2/293> |
| **Accessed** | 6/15/2025, 4:26:03 PM |
| **Rights** | http://creativecommons.org/licenses/by/3.0/ |
| **Extra** | Number: 2 Publisher: Multidisciplinary Digital Publishing Institute |
| **Volume** | 13 |
| **Pages** | 293 |
| **Publication** | Diagnostics |
| **DOI** | [10.3390/diagnostics13020293](http://doi.org/10.3390/diagnostics13020293) |
| **Issue** | 2 |
| **ISSN** | 2075-4418 |
| **Date Added** | 6/15/2025, 4:26:03 PM |
| **Modified** | 6/15/2025, 4:26:03 PM |

* **Tags:**
  + irritable bowel syndrome
  + functional dyspepsia
  + constipation
  + gastroparesis
  + autonomic nervous system
  + gastroesophageal reflux disease
  + heart rate variability

**Attachments**

* + Full Text PDF
* **The neurokinin-2 receptor antagonist GR 159897 protects against neuroinflammation in the mouse enteric nervous system during colitis**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Ninotchska M Delvalle |
| **Author** | Brian Gulbransen |
| **Abstract** | Irritable bowel syndrome (IBS) is a chronic functional gastrointestinal (GI) disorder that affects 20% of Americans. The motility changes in IBS are driven by changes in the enteric nervous system (ENS). IBS has no cure, but recently, a neurokinin-2 receptor (NK2R) antagonist has been shown to improve overall symptoms in a phase II study of diarrhea-predominant IBS. However, the effects of NK2R antagonists on the ENS are not understood. We hypothesize that the beneficial effects of this antagonist on IBS are, in part, due to effects on the ENS. We tested our hypothesis by treating mice with the NK2R antagonist GR 159897 in a dinitrobenzene sulfonic acid (DNBS) model of colitis. To assess changes in the ENS, we used immunohistochemistry to quantify neuronal survival and performed a glial morphology analysis to assess reactive gliosis in the ENS. Calcium imaging recordings were performed in tissue preparations from mice expressing the genetically-encoded calcium indicator GCaMP5g expressed under the control of the SOX10 promoter (SOX10::creERT2/+; PC::G5-TdT+/−) or by loading cells with the calcium indicator dye Fluo4-AM. Our results show that treatment with GR 159897 prevents increases in glial fibrillary acid protein (GFAP) immunoreactivity (n= 3–4 mice; p= 0.0141), increases in glial process length (n= 9–12 glia; p= 0.013) and neurodegeneration (n = 3–4; p= 0.0028). Immunohistochemical and calcium imaging data show that enteric glia express NK2Rs that are activated by neurokinin-A (NKA). Glial responses to NKA were decreased in the presence of GR 159897 (n= 101–113 glia; p= 0.0001) or tetrodotoxin and were significantly reduced in samples from mice lacking glial connexin-43 hemichannels (SOX10::creERT2/+; Cx43f/f mice; n= 50–113 glia; p= 0.0001). Glial responses to NKA were completely abolished in tissue samples from SOX10::creERT2/+; Cx43f/f mice in the presence of GR 159897 (n= 34–113; p= 0.0001). In conclusion, our data demonstrate that GR 159897 provides neuroprotection during colitis through mechanisms that involve decreasing glial activity driven by NKA. We speculate that these mechanisms could explain some of the clinical benefits of current NK2R antagonists in IBS. Support or Funding InformationRO1DK103723-02S1 |
| **Date** | 2017 |
| **Language** | en |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1096/fasebj.31.1_supplement.893.2> |
| **Accessed** | 6/15/2025, 4:25:51 PM |
| **Rights** | © FASEB |
| **Extra** | \_eprint: https://faseb.onlinelibrary.wiley.com/doi/pdf/10.1096/fasebj.31.1\_supplement.893.2 |
| **Volume** | 31 |
| **Pages** | 893.2-893.2 |
| **Publication** | The FASEB Journal |
| **DOI** | [10.1096/fasebj.31.1\_supplement.893.2](http://doi.org/10.1096/fasebj.31.1_supplement.893.2) |
| **Issue** | S1 |
| **ISSN** | 1530-6860 |
| **Date Added** | 6/15/2025, 4:25:51 PM |
| **Modified** | 6/15/2025, 4:25:51 PM |

* **The Use of Fibers, Herbal Medicines and Spices in Children with Irritable Bowel Syndrome: A Narrative Review**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Daniela Pop |
| **Author** | Radu Samuel Pop |
| **Author** | Dorin Farcău |
| **Abstract** | The pathophysiology of irritable bowel syndrome in children involves multiple factors. Thus, treatment options are variable, targeting both diet and the child’s and parents’ behavior via pharmacological and psychological interventions or neuromodulation. Parents are increasingly interested in complementary and alternative therapies for children with irritable bowel syndrome, especially when other treatments have been tried without relieving the child’s symptoms. This paper examines current evidence for the benefits and side effects of herbal remedies and spices in pediatric patients with IBS. The benefits of peppermint oil, STW5, psyllium fiber, Curcuma, ginger, and other herbal medicines are discussed based on findings in the current literature. |
| **Date** | 2023/1 |
| **Language** | en |
| **Short Title** | The Use of Fibers, Herbal Medicines and Spices in Children with Irritable Bowel Syndrome |
| **Library Catalog** | www.mdpi.com |
| **URL** | <https://www.mdpi.com/2072-6643/15/20/4351> |
| **Accessed** | 6/15/2025, 4:26:30 PM |
| **Rights** | http://creativecommons.org/licenses/by/3.0/ |
| **Extra** | Number: 20 Publisher: Multidisciplinary Digital Publishing Institute |
| **Volume** | 15 |
| **Pages** | 4351 |
| **Publication** | Nutrients |
| **DOI** | [10.3390/nu15204351](http://doi.org/10.3390/nu15204351) |
| **Issue** | 20 |
| **ISSN** | 2072-6643 |
| **Date Added** | 6/15/2025, 4:26:30 PM |
| **Modified** | 6/15/2025, 4:26:30 PM |

* **Tags:**
  + irritable bowel syndrome
  + children
  + fibers
  + herbal remedies
  + peppermint oil

**Attachments**

* + Full Text PDF

## A Systematic Review of the Therapeutic Role of Gastric Pacemakers in Adults With Gastroparesis

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Medha Rajamanuri |
| **Author** | Sai Mahitha Mannava |
| **Author** | Jayksh Chhabra |
| **Author** | Guruprasad Vasant Karwarker |
| **Author** | Meher Chahal |
| **Author** | Anand Reddy Maligireddy |
| **Author** | Eiman Dai |
| **Author** | Michael Alfonso |
| **Author** | Medha Rajamanuri |
| **Author** | Sai Mahitha Mannava |
| **Author** | Jayksh Chhabra |
| **Author** | Guruprasad vasant Karwarker Jr |
| **Author** | Meher Chahal |
| **Author** | Anand Reddy Maligireddy |
| **Author** | Eiman Dai |
| **Author** | Michael Alfonso |
| **Abstract** | Gastroparesis or gastric stasis is the delayed transit of the ingested contents through the stomach in the absence of mechanical obstruction. It can have multiple etiologies, most commonly idiopathic (ID) and diabetic (DM). Gastroparesis can cause significant distress to patients as it leads to symptoms like intractable nausea and vomiting, weight loss, abdominal bloating, early satiety, etc. The pathogenesis is mainly thought to be due to the dysfunction of the gastric pacemaker cells, i.e., interstitial cells of Cajal (ICC), and their interaction with the other gastric motor function regulatory components. There are several proposed treatment options for gastroparesis. Despite that, most patients remain refractory to medical treatment and require additional interventions for symptomatic relief. One such intervention is gastric electrical stimulation or gastric pacemaker, which aids in improving gastric motility. We have searched PubMed, PubMed Central (PMC), Medline, Science Direct, and Google Scholar for articles pertaining to the use of gastric electrical stimulation in gastroparesis published in the last 10 years. The keywords used include "gastroparesis", "gastric stasis", "gastric pacemaker'', "gastric electrical stimulation", "nausea", "vomiting", "abdominal bloating", "gastric neuromodulation". We have finally included twelve studies that were the most relevant to our research question and met the quality assessment criteria. Exclusion criteria consisted of pediatric population studies, studies conducted on animals, books, and grey literature. Overall, these twelve studies helped evaluate the impact of gastric pacemakers on symptoms of gastroparesis like nausea, vomiting, weight loss, abdominal bloating, and quality of life. We found that most studies favored gastric pacemakers, improving the incidence of nausea and vomiting in patients with gastroparesis. There was a marked improvement in the BMI as well. On the other hand, most open-labeled studies showed improved quality of life and Gastroparesis Cardinal Symptom Index (GCSI) scores, while randomized controlled trials and meta-analyses did not reflect the same result. In addition, some other parameters improved with gastric pacemakers, Inflammatory markers, insulin levels (especially in diabetics), and the number of hospitalizations. In conclusion, gastric pacemaker is a potential treatment option for patients with medically refractory gastroparesis. As noted from the results of our study, nausea/vomiting, weight loss, and overall GCSI scores have shown marked improvement with gastric electrical stimulation (GES). Nevertheless, more extensive research is needed to understand better the full extent of this device’s use as a viable treatment option for patients suffering from gastroparesis. |
| **Date** | 2021/09/21 |
| **Language** | en |
| **Library Catalog** | www.cureus.com |
| **URL** | <https://www.cureus.com/articles/68426-a-systematic-review-of-the-therapeutic-role-of-gastric-pacemakers-in-adults-with-gastroparesis> |
| **Accessed** | 6/15/2025, 4:16:26 PM |
| **Extra** | Publisher: Cureus |
| **Volume** | 13 |
| **Publication** | Cureus |
| **DOI** | [10.7759/cureus.18152](http://doi.org/10.7759/cureus.18152) |
| **ISSN** | 2168-8184 |
| **Date Added** | 6/15/2025, 4:16:26 PM |
| **Modified** | 6/15/2025, 4:16:26 PM |

### Attachments

* + Full Text PDF

## Cardiac safety and clinical efficacy of high-dose domperidone for long-term treatment of gastroparesis symptoms

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Kevin Woods |
| **Author** | Mahesh Gajendran |
| **Author** | Zorisadday Gonzalez |
| **Author** | Marco Bustamante-Bernal |
| **Author** | Irene Sarosiek |
| **Author** | Karina Espino |
| **Author** | Nathan Waterhouse |
| **Author** | Tariq Siddiqui |
| **Author** | Richard McCallum |
| **Abstract** | Domperidone is an effective antiemetic used worldwide, but there have been reports of possible cardiotoxicity. Our goal was to explore the cardiac safety and clinical efficacy of long-term domperidone, titrated as high as 120 mg/day, in patients not responding or unable to tolerate other therapies for gastroparesis (GP).This retrospective cohort study was conducted at a single tertiary care academic center. We objectively assessed the safety and efficacy of domperidone through questionnaires, clinical follow-up and frequent ECGs as mandated by the Food and Drug Administration. We excluded patients with a history of dangerous arrhythmias, prolonged QTc, clinically significant electrolyte disturbances, gastrointestinal hemorrhage or obstruction, presence of a prolactinoma, pregnant or breastfeeding females, or allergy to domperidone. A total of 21 patients met the inclusion criteria for eligibility in this study (52.4% white, 42.9% Hispanic; mean age 50.1 years; 90.5% female). The mean duration of domperidone therapy was 52.3 (range 16–97) months with a mean highest dose of 80 mg/day (range 40–120 mg). Two patients (9.5%) taking 120 mg/day experienced asymptomatic meaningful QTc prolongation (>450 ms in males, >470 ms in females). One-third of patients had asymptomatic non-meaningful QTc prolongation. Palpitations or chest pain was reported in 19% of patients without ECG abnormalities or adverse cardiac events. The mean severity of vomiting and nausea was improved by 82% and 55%, respectively.Long-term treatment with high doses of domperidone (40–120 mg/day) improved GP symptoms in patients previously refractory to other medical therapies and with a satisfactory cardiovascular risk profile. |
| **Date** | 2022-06-01 |
| **Language** | EN |
| **Library Catalog** | SAGE Journals |
| **URL** | <https://doi.org/10.1136/jim-2021-001968> |
| **Accessed** | 6/15/2025, 4:16:46 PM |
| **Extra** | Publisher: SAGE Publications |
| **Volume** | 70 |
| **Pages** | 1225-1232 |
| **Publication** | Journal of Investigative Medicine |
| **DOI** | [10.1136/jim-2021-001968](http://doi.org/10.1136/jim-2021-001968) |
| **Issue** | 5 |
| **ISSN** | 1081-5589 |
| **Date Added** | 6/15/2025, 4:16:46 PM |
| **Modified** | 6/15/2025, 4:16:46 PM |

## Diabetic Gastroparesis: Epidemiology, Pathophysiology, Symptoms, and Clinical Consequences

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Olgierd Dróżdż |
| **Author** | Piotr Gacka |
| **Author** | Marcin Dołęga |
| **Author** | Dominika Musialska |
| **Author** | Maciej Rabczyński |
| **Author** | Joanna Gołda |
| **Author** | Julia Mężyk |
| **Author** | Aleksandra Snopkowska |
| **Abstract** | Diabetes mellitus affects over half a billion people worldwide and is associated with numerous complications, including diabetic gastroparesis, characterized by delayed gastric emptying without mechanical obstruction. Although diabetic gastroparesis does not affect life expectancy, it significantly impairs digestion and medication absorption, complicating glucose metabolism and health management, thus reducing quality of life. The etiology of diabetic gastroparesis is multifactorial, involving autonomic neuropathy, vagus nerve dysfunction, disturbances in interstitial cells of Cajal, nitric oxide synthesis, hyperglycemia, and oxidative stress. Symptoms include early satiety, bloating, nausea, vomiting, dysphagia, and unintentional weight loss, which complicate diabetes management by causing unpredictable glycemic control. Despite advancements in understanding diabetic gastroparesis, it remains underdiagnosed due to its often asymptomatic nature. Further research is needed to elucidate its epidemiology and pathophysiology, particularly in asymptomatic patients. This review discusses the epidemiology, pathophysiology, symptoms, and clinical consequences of diabetic gastroparesis, highlighting the need for improved diagnostic and management strategies. |
| **Date** | 2024-08-28 |
| **Language** | en |
| **Short Title** | Diabetic Gastroparesis |
| **Library Catalog** | apcz.umk.pl |
| **URL** | <https://apcz.umk.pl/QS/article/view/53928> |
| **Accessed** | 6/15/2025, 4:16:15 PM |
| **Rights** | Copyright (c) 2024 Olgierd Dróżdż, Piotr Gacka, Marcin Dołęga, Dominika Musialska, Maciej Rabczyński, Joanna Gołda, Julia Mężyk, Aleksandra Snopkowska |
| **Volume** | 21 |
| **Pages** | 53928-53928 |
| **Publication** | Quality in Sport |
| **DOI** | [10.12775/QS.2024.21.53928](http://doi.org/10.12775/QS.2024.21.53928) |
| **ISSN** | 2450-3118 |
| **Date Added** | 6/15/2025, 4:16:15 PM |
| **Modified** | 6/15/2025, 4:16:15 PM |

### Tags:

* + diabetes
  + autonomic system
  + hyperglycemia

### Attachments

* + Full Text PDF

## Diabetic Gastroparesis: Navigating Pathophysiology and Nutritional Interventions

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Alfredo Caturano |
| **Author** | Massimiliano Cavallo |
| **Author** | Davide Nilo |
| **Author** | Gaetano Vaudo |
| **Author** | Vincenzo Russo |
| **Author** | Raffaele Galiero |
| **Author** | Luca Rinaldi |
| **Author** | Raffaele Marfella |
| **Author** | Marcellino Monda |
| **Author** | Giovanni Luca |
| **Author** | Ferdinando Carlo Sasso |
| **Abstract** | Diabetic gastroparesis (DGP) delays gastric emptying in diabetes patients, notably impacting those with type 1 and long-standing type 2 diabetes. Symptoms include early satiety, fullness, appetite loss, bloating, abdominal pain, and vomiting, arising from slow stomach-to-intestine food movement. DGP’s unpredictable nature complicates diagnosis and blood glucose management, leading to severe complications like dehydration, malnutrition, and bezoar formation. Understanding DGP’s mechanisms is crucial for effective management. Vagal dysfunction, disturbances in the interstitial cells of Cajal, reduced neural nitric oxide synthase, and increased oxidative stress contribute to the complex pathophysiology. Accurate diagnosis demands a comprehensive approach, utilizing tools like gastric scintigraphy and the Gastric Emptying Breath Test. Considering the complex relationship between DGP and glycemia, managing blood glucose levels becomes paramount. Nutritional interventions, tailored to each patient, address malnutrition risks, emphasizing smaller, more frequent meals and liquid consistency. DGP’s complex nature necessitates collaborative efforts for enhanced diagnostic strategies, improved pathophysiological understanding, and compassionate management approaches. This comprehensive approach offers hope for a future where individuals with DGP can experience improved well-being and quality of life. |
| **Date** | 2024/3 |
| **Language** | en |
| **Short Title** | Diabetic Gastroparesis |
| **Library Catalog** | www.mdpi.com |
| **URL** | <https://www.mdpi.com/2624-5647/6/1/16> |
| **Accessed** | 6/15/2025, 4:16:10 PM |
| **Rights** | http://creativecommons.org/licenses/by/3.0/ |
| **Extra** | Number: 1 Publisher: Multidisciplinary Digital Publishing Institute |
| **Volume** | 6 |
| **Pages** | 214-229 |
| **Publication** | Gastrointestinal Disorders |
| **DOI** | [10.3390/gidisord6010016](http://doi.org/10.3390/gidisord6010016) |
| **Issue** | 1 |
| **ISSN** | 2624-5647 |
| **Date Added** | 6/15/2025, 4:16:10 PM |
| **Modified** | 6/15/2025, 4:16:10 PM |

### Tags:

* + diabetes
  + pathophysiology
  + diabetes complication
  + diabetic gastroparesis
  + nutritional intervention

### Attachments

* + Full Text PDF

## Editorial: finding the ideal prokinetic for gastroparesis—we are not there yet

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Sanjiv Mahadeva |
| **Abstract** | LINKED CONTENT This article is linked to Kuo et al and Camilleri & Kuo papers. To view these articles, visit https://doi.org/10.1111/apt.16451 and https://doi.org/10.1111/apt.16475 |
| **Date** | 2021 |
| **Short Title** | Editorial |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1111/apt.16470> |
| **Accessed** | 6/15/2025, 4:16:55 PM |
| **Rights** | © 2021 John Wiley & Sons Ltd |
| **Extra** | \_eprint: https://onlinelibrary.wiley.com/doi/pdf/10.1111/apt.16470 |
| **Volume** | 54 |
| **Pages** | 210-211 |
| **Publication** | Alimentary Pharmacology & Therapeutics |
| **DOI** | [10.1111/apt.16470](http://doi.org/10.1111/apt.16470) |
| **Issue** | 2 |
| **ISSN** | 1365-2036 |
| **Date Added** | 6/15/2025, 4:16:55 PM |
| **Modified** | 6/15/2025, 4:16:55 PM |

### Attachments

* + Full Text PDF

## Effects of Motilin Receptor Agonists and Ghrelin in Human motilin receptor Transgenic Mice

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Tomoe Kawamura |
| **Author** | Bunzo Matsuura |
| **Author** | Teruki Miyake |
| **Author** | Masanori Abe |
| **Author** | Yoshiou Ikeda |
| **Author** | Yoichi Hiasa |
| **Abstract** | Gastrointestinal motility is regulated by neural factors and humoral factors. Both motilin and ghrelin improve gastrointestinal motility, but many issues remain unclear. We prepared human motilin receptor transgenic (Tg) mice and performed experiments evaluating the effects of motilin, erythromycin (EM), and ghrelin. EM and ghrelin promoted gastric emptying (GE) when administered either peripherally or centrally to Tg mice. Atropine (a muscarinic receptor antagonist) counteracted GE induced by centrally administered EM, but not that induced by peripherally administered EM. The administration of EM in this model promoted the effect of mosapride (a selective serotonin 5-hydroxytryptamine 4 (5-HT4) receptor agonist), and improved loperamide (a μ-opioid receptor agonist)-induced gastroparesis. The level of acyl-ghrelin was significantly attenuated by EM administration. Thus, we have established an animal model appropriate for the evaluation of motilin receptor agonists. These data and the model are expected to facilitate the identification of novel compounds with clinical potential for relieving symptoms of dyspepsia and gastroparesis. |
| **Date** | 2019/1 |
| **Language** | en |
| **Library Catalog** | www.mdpi.com |
| **URL** | <https://www.mdpi.com/1422-0067/20/7/1521> |
| **Accessed** | 6/15/2025, 4:16:59 PM |
| **Rights** | http://creativecommons.org/licenses/by/3.0/ |
| **Extra** | Number: 7 Publisher: Multidisciplinary Digital Publishing Institute |
| **Volume** | 20 |
| **Pages** | 1521 |
| **Publication** | International Journal of Molecular Sciences |
| **DOI** | [10.3390/ijms20071521](http://doi.org/10.3390/ijms20071521) |
| **Issue** | 7 |
| **ISSN** | 1422-0067 |
| **Date Added** | 6/15/2025, 4:16:59 PM |
| **Modified** | 6/15/2025, 4:16:59 PM |

### Tags:

* + gastric emptying
  + erythromycin
  + ghrelin
  + motilin

### Attachments

* + Full Text PDF

## Efficacy and Safety of Ghrelin Agonists in Patients with Diabetic Gastroparesis: A Systematic Review and Meta-Analysis

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Seung Wook Hong |
| **Author** | Jaeyoung Chun |
| **Author** | Jihye Kim |
| **Author** | Jooyoung Lee |
| **Author** | Hyun Jung Lee |
| **Author** | Hyunsoo Chung |
| **Author** | Soo-Jeong Cho |
| **Author** | Jong Pil Im |
| **Author** | Sang Gyun Kim |
| **Author** | Joo Sung Kim |
| **Abstract** | Seung Wook Hong, Jaeyoung Chun, Jihye Kim, Jooyoung Lee, Hyun Jung Lee, Hyunsoo Chung, Soo-Jeong Cho, Jong Pil Im, Sang Gyun Kim, and Joo Sung Kim. Gut and Liver 2020;14:589-600. https://doi.org/10.5009/gnl19103 |
| **Date** | 2020/09/15 |
| **Language** | en |
| **Short Title** | Efficacy and Safety of Ghrelin Agonists in Patients with Diabetic Gastroparesis |
| **Library Catalog** | www.gutnliver.org |
| **URL** | <https://www.gutnliver.org/journal/view.html?doi=10.5009/gnl19103> |
| **Accessed** | 6/15/2025, 4:17:04 PM |
| **Extra** | Publisher: Editorial Office of Gut and Liver |
| **Volume** | 14 |
| **Pages** | 589-600 |
| **Publication** | Gut and Liver |
| **DOI** | [10.5009/gnl19103](http://doi.org/10.5009/gnl19103) |
| **Issue** | 5 |
| **Date Added** | 6/15/2025, 4:17:04 PM |
| **Modified** | 6/15/2025, 4:17:04 PM |

### Attachments

* + Full Text PDF

## Efficacy and Safety of Tradipitant in Patients With Diabetic and Idiopathic Gastroparesis in a Randomized, Placebo-Controlled Trial

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Jesse L. Carlin |
| **Author** | V. Rose Lieberman |
| **Author** | Arya Dahal |
| **Author** | Madison S. Keefe |
| **Author** | Changfu Xiao |
| **Author** | Gunther Birznieks |
| **Author** | Thomas L. Abell |
| **Author** | Anthony Lembo |
| **Author** | Henry P. Parkman |
| **Author** | Mihael H. Polymeropoulos |
| **Date** | 2021-01-01 |
| **Language** | English |
| **Library Catalog** | www.gastrojournal.org |
| **URL** | <https://www.gastrojournal.org/article/S0016-5085(20)34958-1/fulltext> |
| **Accessed** | 6/15/2025, 4:17:30 PM |
| **Extra** | Publisher: Elsevier PMID: 32693185 |
| **Volume** | 160 |
| **Pages** | 76-87.e4 |
| **Publication** | Gastroenterology |
| **DOI** | [10.1053/j.gastro.2020.07.029](http://doi.org/10.1053/j.gastro.2020.07.029) |
| **Issue** | 1 |
| **Journal Abbr** | Gastroenterology |
| **ISSN** | 0016-5085, 1528-0012 |
| **Date Added** | 6/15/2025, 4:17:30 PM |
| **Modified** | 6/15/2025, 4:17:30 PM |

### Tags:

* + Diabetes
  + ITT
  + substance P
  + American Neurogastroenterology Motility Society Gastroparesis Cardinal Symptom Index Daily Diary
  + ANMS GCSI-DD
  + CGI-S
  + Clinician Global Impression of Severity
  + Gastroparesis Cardinal Symptom Index
  + Gastroparesis Core Symptom Daily Diary
  + GCSDD
  + GCSI
  + GCSI-DD
  + intent-to-treat
  + least squares
  + LS
  + MID
  + minimally important difference
  + neurokinin-1 receptor
  + NK1R
  + PAGI-SYM
  + Patient Assessment of Gastrointestinal Disorders Symptom Severity Index
  + Patient Global Impression of Change
  + PGI-C
  + SP

### Attachments

* + Full Text PDF
  + PubMed entry

## Gastric dysmotility in Parkinson's disease is not caused by alterations of the gastric pacemaker cells

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Konstantin G. Heimrich |
| **Author** | Veit Y. P. Jacob |
| **Author** | Denise Schaller |
| **Author** | Andreas Stallmach |
| **Author** | Otto W. Witte |
| **Author** | Tino Prell |
| **Abstract** | The enteric nervous system is involved in the pathology of Parkinson´s disease and patients frequently have symptoms related to delayed gastric emptying. However, the pathophysiology of gastric dysmotility is yet not well understood. The objective of this study was to assess interdigestive gastric motility in Parkinson´s disease. Using an electromagnetic capsule system, the dominant gastric contraction frequency (primary outcome measure) and the gastric transit time were assessed in 16 patients with Parkinson´s disease and 15 young healthy controls after a fasting period of 8 h. Motor and non-motor symptoms were assessed using the Movement Disorder Society Unified Parkinson´s Disease Rating Scale III (MDS-UPDRS III), the Non-Motor Symptoms Questionnaire (NMS-Quest), and Hoehn & Yahr staging. The Gastroparesis Cardinal Symptom Index was used to record symptoms related to delayed gastric emptying. In healthy controls and patients with Parkinson's disease, the dominant contraction frequency was 3.0 cpm indicating normal function of interstitial cells of Cajal. In patients with Parkinson's disease, the gastric transit time was longer than in younger controls (56 vs. 21 min). The dominant contraction frequency and gastric transit time did not correlate with age, disease duration, Hoehn & Yahr stage, levodopa equivalent daily dose, MDS-UPDRS III, NMS-Quest, and Gastroparesis Cardinal Symptom Index. Changes of gastric motility in Parkinson´s disease are not caused by functional deficits of the gastric pacemaker cells, the interstitial cells of Cajal. Therefore, gastroparesis in Parkinson's disease can be attributed to disturbances in neurohumoral signals via the vagus nerve and myenteric plexus. |
| **Date** | 2019-07-26 |
| **Language** | en |
| **Library Catalog** | www.nature.com |
| **URL** | <https://www.nature.com/articles/s41531-019-0087-3> |
| **Accessed** | 6/15/2025, 4:16:35 PM |
| **Rights** | 2019 The Author(s) |
| **Extra** | Publisher: Nature Publishing Group |
| **Volume** | 5 |
| **Pages** | 15 |
| **Publication** | npj Parkinson's Disease |
| **DOI** | [10.1038/s41531-019-0087-3](http://doi.org/10.1038/s41531-019-0087-3) |
| **Issue** | 1 |
| **Journal Abbr** | npj Parkinsons Dis. |
| **ISSN** | 2373-8057 |
| **Date Added** | 6/15/2025, 4:16:35 PM |
| **Modified** | 6/15/2025, 4:16:35 PM |

### Tags:

* + Parkinson's disease
  + Physiology

### Attachments

* + Full Text PDF

## Gastric Electrical Stimulation for Treatment of Refractory Gastroparesis: the Current Approach to Management

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Aaron Shanker |
| **Author** | Mohammad Bashashati |
| **Author** | Ali Rezaie |
| **Abstract** | Gastroparesis is one of the more challenging entities in the landscape of gastroenterology, posing difficulties for both patients and physicians with regard to effective management and therapies. In this article, we reviewed various gastroparesis treatment options, with an emphasis on gastric electrical stimulation (GES). |
| **Date** | 2021-01-22 |
| **Language** | en |
| **Short Title** | Gastric Electrical Stimulation for Treatment of Refractory Gastroparesis |
| **Library Catalog** | Springer Link |
| **URL** | <https://doi.org/10.1007/s11894-020-00803-0> |
| **Accessed** | 6/15/2025, 4:17:44 PM |
| **Volume** | 23 |
| **Pages** | 2 |
| **Publication** | Current Gastroenterology Reports |
| **DOI** | [10.1007/s11894-020-00803-0](http://doi.org/10.1007/s11894-020-00803-0) |
| **Issue** | 2 |
| **Journal Abbr** | Curr Gastroenterol Rep |
| **ISSN** | 1534-312X |
| **Date Added** | 6/15/2025, 4:17:44 PM |
| **Modified** | 6/15/2025, 4:17:44 PM |

### Tags:

* + Abdominal pain
  + Functional gastrointestinal disorders
  + Nausea
  + Gastroparesis
  + Motility disorders
  + Brain Stimulation
  + Functional dyspepsia
  + Gastric electrical stimulation
  + Nutrition Therapy
  + Therapeutic Endoscopy
  + Vomiting

### Attachments

* + Full Text PDF

## Gastric peroral endoscopic pyloromyotomy (G-POEM) in patients with refractory gastroparesis: a review

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Grace Ann McCurdy |
| **Author** | Tonia Gooden |
| **Author** | Francesca Weis |
| **Author** | Maryam Mubashir |
| **Author** | Shazia Rashid |
| **Author** | Syed Musa Raza |
| **Author** | James Morris |
| **Author** | Qiang Cai |
| **Abstract** | Gastric peroral endoscopic pyloromyotomy (G-POEM or POP) is an endoscopic therapeutic modality for treatment of refractory gastroparesis. Since the first case reported in 2013, there are more than 200 papers published on G-POEM. In this narrative review, we summarize the short-term and long-term outcomes and review other important studies. The technical success rate is 100% and the short-term (within 1 year) success rate is about 50–80%. The procedure time is between 50 and 70 min while the average length of hospital stay was 2–3 days. The adverse event rate was around 10%. Few patients need further intervention. Three studies showed that at the 4-year follow-up, the response to G-POEM was durable, but there was a yearly recurrence rate of 13% or more. Redo G-POEM is feasible and can be of benefit for some patients. Most of the studies showed that long duration of illness is associated with poor outcomes. However, reliable predictors for successful outcomes are still unknown. Current literature indicates G-POEM is superior to gastric electric stimulator and surgical pyloroplasty. Endoflip has been used at G-POEM to predict the outcome, but the result is very preliminary. A recent sham study confirms the short-term efficacy of G-POEM. G-POEM is safe and about 50% of patients can be discharged to home on the same day. G-POEM allows for direct biopsy of the gastric muscle, which is the location of the pacemaker cells, the interstitial cells of Cajal; therefore, G-POEM may provide a new path for further research on the pathogenesis of gastroparesis. |
| **Date** | 2023-01-01 |
| **Language** | EN |
| **Short Title** | Gastric peroral endoscopic pyloromyotomy (G-POEM) in patients with refractory gastroparesis |
| **Library Catalog** | SAGE Journals |
| **URL** | <https://doi.org/10.1177/17562848231151289> |
| **Accessed** | 6/15/2025, 4:18:08 PM |
| **Extra** | Publisher: SAGE Publications Ltd STM |
| **Volume** | 16 |
| **Pages** | 17562848231151289 |
| **Publication** | Therapeutic Advances in Gastroenterology |
| **DOI** | [10.1177/17562848231151289](http://doi.org/10.1177/17562848231151289) |
| **Journal Abbr** | Therap Adv Gastroenterol |
| **ISSN** | 1756-2848 |
| **Date Added** | 6/15/2025, 4:18:08 PM |
| **Modified** | 6/15/2025, 4:18:08 PM |

### Attachments

* + SAGE PDF Full Text

## Improvement in Symptomatic Gastroparesis With Increased Vagal Nerve Stimulation

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Michael I. Dougherty |
| **Author** | Katherine Zarroli |
| **Author** | Jaideep Kapur |
| **Date** | 2021-02 |
| **Library Catalog** | neurology.org (Atypon) |
| **URL** | <https://www.neurology.org/doi/10.1212/CPJ.0000000000000775> |
| **Accessed** | 6/15/2025, 4:18:02 PM |
| **Extra** | Publisher: Wolters Kluwer |
| **Volume** | 11 |
| **Pages** | e18-e19 |
| **Publication** | Neurology Clinical Practice |
| **DOI** | [10.1212/CPJ.0000000000000775](http://doi.org/10.1212/CPJ.0000000000000775) |
| **Issue** | 1 |
| **Date Added** | 6/15/2025, 4:18:02 PM |
| **Modified** | 6/15/2025, 4:18:02 PM |

## Motion Syros: tradipitant effective in the treatment of motion sickness; a multicenter, randomized, double-blind, placebo-controlled study

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Vasilios M. Polymeropoulos |
| **Author** | Leah Kiely |
| **Author** | Margaret L. Bushman |
| **Author** | E. Blake Sutherland |
| **Author** | Abigail R. Goldberg |
| **Author** | Annalise X. Pham |
| **Author** | Cameron R. Miller |
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| **Author** | Nikolas V. Pham |
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| **Author** | Abigail K. Giles |
| **Author** | Changfu Xiao |
| **Author** | Christos M. Polymeropoulos |
| **Author** | Gunther Birznieks |
| **Author** | Mihael H. Polymeropoulos |
| **Abstract** | IntroductionMotion sickness has afflicted travelers since ancient times. Neurokinin-1 (NK1) receptor antagonists have therapeutic potential as treatments for the symptoms of motion sickness due to the widespread expression of NK1 receptors throughout important locations in the emetic pathway in the network of brainstem nuclei and the gut. This study evaluated the efficacy of tradipitant, a novel NK1 receptor antagonist, in preventing motion sickness symptoms in variable sea conditions.MethodsA total of 365 adult participants with a history of motion sickness embarked on boat trips under variable sea conditions. Study participants were distributed across 34 boat trips that took place between November 2021 and April 2023 in coastal waters of the United States. Participants were randomized 1:1:1 and received 170 mg tradipitant (n = 120), 85 mg tradipitant (n = 123) or placebo (n = 122). The symptoms of vomiting and nausea were evaluated with questionnaires every 30 min during the approximately four-hour trips. The primary efficacy endpoint for the study was the percentage of vomiting during vehicle travel. Statistical hypothesis testing was performed at the two-sided alpha level of 0.05 unless specified otherwise. Tests were declared statistically significant if the calculated p-value was ≤ 0.05.ResultsThe incidence of vomiting in both dosing arms of tradipitant was significantly lower than the placebo group across all boat trips (170 mg tradipitant = 18.3%, 85 mg tradipitant = 19.5%, placebo = 44.3%, p < 0.0001 for both dose comparisons against placebo). Tradipitant prevented severe nausea and vomiting as compared to participants taking placebo (tradipitant = 18.03%, placebo = 37.70%, p < 0.0001).DiscussionTradipitant 170 mg and 85 mg have been confirmed to be effective in the prevention of vomiting associated with motion sickness across varied sea conditions.Clinical trial registrationClinicalTrials.gov, identifier NCT04327661. |
| **Date** | 2025-03-04 |
| **Language** | English |
| **Short Title** | Motion Syros |
| **Library Catalog** | Frontiers |
| **URL** | <https://www.frontiersin.org/journals/neurology/articles/10.3389/fneur.2025.1550670/full> |
| **Accessed** | 6/15/2025, 4:17:34 PM |
| **Extra** | Publisher: Frontiers |
| **Volume** | 16 |
| **Publication** | Frontiers in Neurology |
| **DOI** | [10.3389/fneur.2025.1550670](http://doi.org/10.3389/fneur.2025.1550670) |
| **Journal Abbr** | Front. Neurol. |
| **ISSN** | 1664-2295 |
| **Date Added** | 6/15/2025, 4:17:34 PM |
| **Modified** | 6/15/2025, 4:17:34 PM |

### Tags:

* + motion sickness
  + neurokinin-1
  + seasickness
  + seasickness prevention
  + tradipitant

### Attachments

* + Full Text PDF

## Open-label pilot study: Non-invasive vagal nerve stimulation improves symptoms and gastric emptying in patients with idiopathic gastroparesis

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Andres Gottfried-Blackmore |
| **Author** | Emerald P. Adler |
| **Author** | Nielsen Fernandez-Becker |
| **Author** | John Clarke |
| **Author** | Aida Habtezion |
| **Author** | Linda Nguyen |
| **Abstract** | Background Gastroparesis, a chronic motility disorder characterized by delayed gastric emptying, abdominal pain, nausea, and vomiting, remains largely unexplained. Medical therapy is limited, reflecting the complex physiology of gastric sensorimotor function. Vagus nerve stimulation is an attractive therapeutic modality for gastroparesis, but prior methods required invasive surgery. In this open-label pilot study, we aimed to assess the benefit of non-invasive vagal nerve stimulation in patients with mild to moderate idiopathic gastroparesis. Methods Patients self-administered the gammaCore vagal nerve stimulator for 4 weeks. The gastroparesis cardinal symptom index daily diary (GCSI-dd) was assessed during a two-week run-in period, ≥4 weeks of therapy, and 4 weeks after therapy was completed. Gastric emptying and autonomic function testing were also performed. The primary endpoint was an absolute reduction in CGSI-dd of 0.75 after nVNS. Results There was a total improvement in symptom scores (2.56 ± 0.76 to 1.87 ± 1.05; P = .01), with 6/15 (40%) participants meeting our primary endpoint. Therapy was associated with a reduction in gastric emptying (T1/2 155 vs 129 minutes; P = .053, CI −0.4 to 45). Therapy did not correct autonomic function abnormalities, but was associated with modulation of reflex parasympathetic activity. Conclusions Short-term non-invasive vagal nerve stimulation led to improved cardinal symptoms and accelerated gastric emptying in a subset of patients with idiopathic gastroparesis. Responders had more severe gastric delay at baseline and clinical improvement correlated with duration of therapy, but not with improvements in gastric emptying. Larger randomized sham-controlled trials of greater duration are needed to confirm the results of this pilot study. |
| **Date** | 2020 |
| **Language** | en |
| **Short Title** | Open-label pilot study |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1111/nmo.13769> |
| **Accessed** | 6/15/2025, 4:17:58 PM |
| **Rights** | © 2019 John Wiley & Sons Ltd |
| **Extra** | \_eprint: https://onlinelibrary.wiley.com/doi/pdf/10.1111/nmo.13769 |
| **Volume** | 32 |
| **Pages** | e13769 |
| **Publication** | Neurogastroenterology & Motility |
| **DOI** | [10.1111/nmo.13769](http://doi.org/10.1111/nmo.13769) |
| **Issue** | 4 |
| **ISSN** | 1365-2982 |
| **Date Added** | 6/15/2025, 4:17:58 PM |
| **Modified** | 6/15/2025, 4:17:58 PM |

### Tags:

* + gastroparesis
  + vagal nerve stimulation
  + autonomic nervous system diseases
  + gastric emptying

## Randomized clinical trial: A phase 2b controlled study of the efficacy and safety of trazpiroben (TAK-906) for idiopathic or diabetic gastroparesis

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Jan Tack |
| **Author** | Richard McCallum |
| **Author** | Braden Kuo |
| **Author** | Susanna Y. Huh |
| **Author** | Yanwei Zhang |
| **Author** | Yaozhu J. Chen |
| **Author** | Shailly Mehrotra |
| **Author** | Henry P. Parkman |
| **Abstract** | Background Previous clinical studies of trazpiroben, a dopamine D2/D3 receptor antagonist for long-term treatment of moderate-to-severe idiopathic and diabetic gastroparesis, have shown improved symptoms of fullness. This study assessed trazpiroben efficacy, safety, and tolerability in adults with idiopathic and diabetic gastroparesis versus placebo. Methods This global, multicenter, double-blind, parallel-group, phase 2b study (NCT03544229) enrolled eligible adults aged 18–85 years with symptomatic idiopathic or diabetic gastroparesis. Randomized participants received either oral placebo or trazpiroben 5, 25, or 50 mg, administered twice daily over 12 weeks, and completed the American Neurogastroenterology and Motility Society Gastroparesis Cardinal Symptom Index-Daily Diary. Change in weekly composite score from baseline to week 12 (primary endpoint) and treatment-emergent adverse events were assessed. Data were summarized descriptively. Key Results Overall, 242 participants were enrolled (mean [standard deviation] age 55.7 [14.2] years; 75.6% female); 193 completed the study. No significant differences in change from baseline in weekly average of the daily diary composite score occurred at week 12 between placebo (least-squares mean [standard error] −1.19 [0.12]) and trazpiroben (5, 25, and 50 mg: −1.11 [0.22], −1.17 [0.12], and −1.21 [0.12], respectively). Overall, 41.4% of participants receiving trazpiroben reported treatment-emergent adverse events (placebo, 39.7%). No serious events were considered trazpiroben-related; no life-threatening or fatal events were reported. Conclusions & Inferences There was no clinically meaningful difference in efficacy between trazpiroben and placebo in treating gastroparesis, based on the primary endpoint analysis. Trazpiroben was well tolerated with no new safety concerns identified, strengthening evidence supporting its favorable safety profile. NCT number: NCT03544229. |
| **Date** | 2023 |
| **Language** | en |
| **Short Title** | Randomized clinical trial |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1111/nmo.14652> |
| **Accessed** | 6/15/2025, 4:17:39 PM |
| **Rights** | © 2023 Takeda Development Center Americas, Inc and The Authors. Neurogastroenterology & Motility published by John Wiley & Sons Ltd. |
| **Extra** | \_eprint: https://onlinelibrary.wiley.com/doi/pdf/10.1111/nmo.14652 |
| **Volume** | 35 |
| **Pages** | e14652 |
| **Publication** | Neurogastroenterology & Motility |
| **DOI** | [10.1111/nmo.14652](http://doi.org/10.1111/nmo.14652) |
| **Issue** | 10 |
| **ISSN** | 1365-2982 |
| **Date Added** | 6/15/2025, 4:17:39 PM |
| **Modified** | 6/15/2025, 4:17:39 PM |

### Tags:

* + motility
  + gastroparesis
  + gastric emptying
  + symptom score or index
  + trazpiroben

### Notes:

* + e14652 NMO-00058-2023.R1

### Attachments

* + Full Text PDF

## Safety and Efficacy of Highly Selective 5-Hydroxytryptamine Receptor 4 Agonists for Diabetic and Idiopathic Gastroparesis: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Parth Patel |
| **Author** | Eli A. Zaher |
| **Author** | Himsikhar Khataniar |
| **Author** | Mohamed A. Ebrahim |
| **Author** | Priyadarshini Loganathan |
| **Author** | Parth Patel |
| **Author** | Eli A. Zaher |
| **Author** | Himsikhar Khataniar |
| **Author** | Mohamed A. Ebrahim |
| **Author** | Priyadarshini Loganathan |
| **Abstract** | Gastroparesis significantly affects quality of life and healthcare expenditure. Effective treatment options are limited, and the utility of current prokinetic agents is inhibited by serious adverse effects. There exists an unmet need for prokinetic agents demonstrating both efficacy and an acceptable adverse effect profile. Highly selective 5-Hydroxytryptamine receptor 4 (5-HT4) agonists have exhibited clinical efficacy and safety in randomized controlled trials (RCTs). Consequently, we conducted a meta-analysis to comprehensively assess the safety and efficacy of these highly selective agents. Multiple databases, including PubMed, Scopus, and Embase, were systematically screened from inception until September 2023. Only RCTs evaluating the efficacy and safety of highly selective 5-HT4 agonists for gastroparesis were included. Key outcomes of interest included the pooled rates of Gastroparesis Cardinal Symptom Index (GCSI) scores, gastric emptying time (GET), and adverse event rates in each group. We adhered to standard meta-analysis methodology utilizing the random-effects model, with heterogeneity assessed by I2 statistics. Our analysis identified six RCTs, comprising 570 patients with diabetic (48%) or idiopathic (51%) gastroparesis, with mean ages of 46 and 45.9 years in the intervention and placebo groups, respectively. In the meta-analysis, highly selective 5-HT4 agonists demonstrated significantly superior pooled GCSI scores compared to placebo (mean difference: 4.283, (1.380, 7.186), p&lt;0.05). Pooled GET was also significantly improved with 5-HT4 agonists compared to placebo (mean difference: 2.534, (1.695, 3.373), p&lt;0.05). Although pooled rates of total adverse events were higher with 5-HT4 agonists (mean difference: 6.975, (1.042, 46.684), p&lt;0.05), rates of specific adverse events such as diarrhea, abdominal pain, and headaches were comparable. In conclusion, this meta-analysis underscores a statistically significant improvement in GET and GCSI scores among patients receiving highly selective 5-HT4 agonists (Velusetrag, Felcisetrag, Prucalopride) for both diabetic and idiopathic gastroparesis. While the overall adverse effect profile is deemed acceptable, larger studies with extended follow-up periods are needed to investigate rare and/or serious adverse events. Moreover, future high-quality RCTs comparing the efficacy and safety of these novel agents with currently available agents are essential to further validate these findings. |
| **Date** | 2024/01/08 |
| **Language** | en |
| **Short Title** | Safety and Efficacy of Highly Selective 5-Hydroxytryptamine Receptor 4 Agonists for Diabetic and Idiopathic Gastroparesis |
| **Library Catalog** | www.cureus.com |
| **URL** | <https://www.cureus.com/articles/217670-safety-and-efficacy-of-highly-selective-5-hydroxytryptamine-receptor-4-agonists-for-diabetic-and-idiopathic-gastroparesis-a-systematic-review-and-meta-analysis-of-randomized-controlled-trials> |
| **Accessed** | 6/15/2025, 4:16:50 PM |
| **Extra** | Publisher: Cureus |
| **Volume** | 16 |
| **Publication** | Cureus |
| **DOI** | [10.7759/cureus.51851](http://doi.org/10.7759/cureus.51851) |
| **ISSN** | 2168-8184 |
| **Date Added** | 6/15/2025, 4:16:50 PM |
| **Modified** | 6/15/2025, 4:16:50 PM |

### Attachments

* + Full Text PDF

## SPARC: Transcutaneous Auricular Vagal Nerve Stimulation Increases Antroduodenal Motility in Rat within a Narrow Range of Stimulus Parameters

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Matthew Peter Ward |
| **Author** | Zhenjun Tan |
| **Author** | Roberta Sclocco |
| **Author** | Braden Kuo |
| **Author** | Vitaly Napadow |
| **Author** | Thomas Nowak |
| **Author** | Terry L. Powley |
| **Abstract** | Transcutaneous auricular vagus nerve stimulation (taVNS) is a promising, non-invasive approach to modulate activity in the central nervous system, heart, lungs, stomach and other organs that receive projections from the vagus nerve. The optimal stimulus parameters for modulating stomach function are unknown, preventing further development of taVNS as a device-based treatment for motility disorders like gastroparesis. We hypothesized that taVNS parameters could be tuned to preferentially modulate antroduodenal motility with fewer off-target effects on the heart than cervical VNS. Using a custom-made stimulation and recording system (Autonomous Neural Control, or ANC), we surveyed the taVNS-mediated effects on cardiac, vagal (ventral gastric branch), antral and duodenal motility in male Sprague Dawley rats under isoflurane anesthesia (250–400 g; N = 14 rats). With custom carbon gel electrodes, we stimulated the left cymba concha at 1 or 10 Hz using 28 combinations of stimulus pulse currents and durations (0, 0.2, 0.4, 0.6, 0.8, 1.0 and 1.2 mA pulse currents in combination with 0.1, 0.2, 0.4 and 0.8 ms pulse durations), while measuring the electrocardiogram, antral electrogastrogram, and antral/duodenal motility with implanted strain gauges. The ANC software applied each stimulus parameter combination in a random order in 60 s cycles (20 s ON/40 s OFF). Stimulus pulse durations less than 0.4 ms were not associated with any significant effects on cardiac (measured from the electrocardiogram) or gastric activity (measured from the antral electrogastrogram as well as antral and duodenal strain gauge recordings), but did produce notable increases in nerve activity at the level of the ventral gastric branch (measured with an implanted bipolar cuff electrode). A pulse duration of 0.8 ms produced the most robust and consistent decrease in heart rate, increase in heart rate variability, increase in antral smooth muscle activity, and increase in antroduodenal motility, as is expected from an increase in vagal outflow. In contrast to cervical VNS, where the optimal parameters for increasing antral motility largely overlapped with those that induced severe bradycardia, the optimal taVNS parameters that increased antroduodenal motility at 1 or 10 Hz (Pulse Current: 0.2–0.6 mA | Pulse Duration: 0.4–0.8 ms) required less current, on average, than the stimulus parameters that produced the greatest reduction in heart rate and increase in heart rate variability (Pulse Current: 0.4–1.0 mA | Pulse Duration: 0.4–0.8 ms). Pulse currents greater than 0.6 mA did not have any significant effect on antroduodenal motility, supporting the value of our parameter search approach in sorting the useful from the useless stimulus parameters. These results strongly support taVNS as a viable approach to modulate gastrointestinal activity with greater specificity and control over stomach function than cervical VNS. Support or Funding Information This work was supported by NIH SPARC OT2 OD023847 |
| **Date** | 2020 |
| **Language** | en |
| **Short Title** | SPARC |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1096/fasebj.2020.34.s1.05187> |
| **Accessed** | 6/15/2025, 4:18:05 PM |
| **Rights** | © FASEB |
| **Extra** | \_eprint: https://faseb.onlinelibrary.wiley.com/doi/pdf/10.1096/fasebj.2020.34.s1.05187 |
| **Volume** | 34 |
| **Pages** | 1-1 |
| **Publication** | The FASEB Journal |
| **DOI** | [10.1096/fasebj.2020.34.s1.05187](http://doi.org/10.1096/fasebj.2020.34.s1.05187) |
| **Issue** | S1 |
| **ISSN** | 1530-6860 |
| **Date Added** | 6/15/2025, 4:18:05 PM |
| **Modified** | 6/15/2025, 4:18:05 PM |

## Transcriptome and Proteome Profiling of Primary Human Gastric Interstitial Cells of Cajal Predicts Pacemaker Networks

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Daphne Foong |
| **Author** | Meena Mikhael |
| **Author** | Jerry Zhou |
| **Author** | Ali Zarrouk |
| **Author** | Xiaodong Liu |
| **Author** | Jan Schröder |
| **Author** | Jose M. Polo |
| **Author** | Vincent Ho |
| **Author** | Michael D. O’Connor |
| **Abstract** | Daphne Foong, Meena Mikhael, Jerry Zhou, Ali Zarrouk, Xiaodong Liu, Jan Schröder, Jose M Polo, Vincent Ho, and Michael D O’Connor. J Neurogastroenterol Motil 2023;29:238-49. https://doi.org/10.5056/jnm22078 |
| **Date** | 2023/04/30 |
| **Language** | en |
| **Library Catalog** | www.jnmjournal.org |
| **URL** | <https://www.jnmjournal.org/journal/view.html?doi=10.5056/jnm22078> |
| **Accessed** | 6/15/2025, 4:16:31 PM |
| **Extra** | Publisher: The Korean Society of Neurogastroenterology and Motility |
| **Volume** | 29 |
| **Pages** | 238-249 |
| **Publication** | Journal of Neurogastroenterology and Motility |
| **DOI** | [10.5056/jnm22078](http://doi.org/10.5056/jnm22078) |
| **Issue** | 2 |
| **Journal Abbr** | J Neurogastroenterol Motil |
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| **Date Added** | 6/15/2025, 4:16:31 PM |
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### Attachments

* + Full Text PDF

## Treatment of refractory diabetic gastroparesis: Western medicine and traditional Chinese medicine therapies

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Bing Pang |
| **Author** | Qiang Zhou |
| **Author** | Jun-Ling Li |
| **Author** | Lin-Hua Zhao |
| **Author** | Xiao-Lin Tong |
| **Abstract** | Treatment of refractory diabetic gastroparesis: Western medicine and traditional Chinese medicine therapies |
| **Date** | Jun 7, 2014 |
| **Language** | en |
| **Short Title** | Treatment of refractory diabetic gastroparesis |
| **Library Catalog** | www.wjgnet.com |
| **URL** | <https://www.wjgnet.com/1007-9327/full/v20/i21/6504.htm> |
| **Accessed** | 6/15/2025, 4:18:22 PM |
| **Extra** | Publisher: Baishideng Publishing Group Inc. |
| **Volume** | 20 |
| **Pages** | 6504-6514 |
| **Publication** | World Journal of Gastroenterology |
| **DOI** | [10.3748/wjg.v20.i21.6504](http://doi.org/10.3748/wjg.v20.i21.6504) |
| **Issue** | 21 |
| **Date Added** | 6/15/2025, 4:18:22 PM |
| **Modified** | 6/15/2025, 4:18:22 PM |

### Attachments

* + Full Text

## Діабетичний гастропарез: сучасні дані щодо епідеміології, патофізіології, діагностики та лікування. Огляд літератури

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | С. М. Ткач |
| **Author** | В. І. Паньків |
| **Author** | В. Б. Доготар |
| **Author** | В. С. Юзвенко |
| **Abstract** | The analysis has been performed for the current data on the epidemiology, pathophysiology, diagnosis and treatment of diabetic gastroparesis. The search was conducted in PubMed and Medline databases. The following keywords were used: «diabetic gastroparesis», «complications of diabetes», «risk factors». Articles published in peer‑reviewed publications were taken into account. Diabetic gastroparesis is a&nbsp;serious complication of diabetes, which leads to its poor control, worsens the quality of life, increases frequency of comorbidities and mortality. This complication is characterized by abdominal distension, nausea, vomiting, weight loss and early satiety, but should be confirmed/diagnosed by scintigraphy or 13C‑octanoic breath test. Though there is no evidence that diabetic gastroparesis significantly increases mortality, this complication impairs all aspects of life. Gastroparesis carries a&nbsp;significant burden on patients, with a&nbsp;negative correlation between the severity of symptoms and their quality of life; the disease also has a&nbsp;significant negative impact on the health care system, in particular, due to increase in the number of hospitalizations and associated direct and indirect economic consequences. First‑line treatment for diabetic gastroparesis includes dietary modification, glycemic control, and fluid and electrolyte replacement. Those patients who have persistent symptoms may require pharmacological or even surgical treatment. Among pharmaceuticals, prokinetics are most often used, in particular metoclopramide, domperidone or erythromycin. Antiemetics, in particular phenothiazines and antihistamines, are also prescribed to reduce symptoms. Newer drugs under investigation include ghrelin agonists such as relamorelin, as well as serotonin receptor agonists such as prucalopride and velusetrag. In refractory cases, various options for surgical treatment or electrical stimulation of the stomach are recommended. |
| **Date** | 2022-09-30 |
| **Language** | uk |
| **Short Title** | Діабетичний гастропарез |
| **Library Catalog** | jcees.endocenter.kiev.ua |
| **URL** | <http://jcees.endocenter.kiev.ua/article/view/265352> |
| **Accessed** | 6/15/2025, 4:16:40 PM |
| **Rights** | Авторське право (c) 2022 Автори |
| **Extra** | Number: 3 |
| **Pages** | 78-86 |
| **Publication** | Clinical Endocrinology and Endocrine Surgery |
| **DOI** | [10.30978/CEES-2022-3-78](http://doi.org/10.30978/CEES-2022-3-78) |
| **Issue** | 3 |
| **ISSN** | 2519-2582 |
| **Date Added** | 6/15/2025, 4:16:40 PM |
| **Modified** | 6/15/2025, 4:16:40 PM |

### Tags:

* + лікування

## Acetylcholine from tuft cells promotes M2 macrophages polarization in Hirschsprung-associated enterocolitis

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Ziyi Zheng |
| **Author** | Lin Lin |
| **Author** | Huifang Lin |
| **Author** | Jie Zhou |
| **Author** | Zhe Wang |
| **Author** | Yang Wang |
| **Author** | Jianxin Chen |
| **Author** | Caimin Lai |
| **Author** | Renfu Li |
| **Author** | Zhiyong Shen |
| **Author** | Ming Zhong |
| **Author** | Cheng Xie |
| **Author** | Yinjian Chen |
| **Author** | Xuechao Zhang |
| **Author** | Zhongjie Guo |
| **Author** | Rui Dong |
| **Author** | Shiwei He |
| **Author** | Feng Chen |
| **Abstract** | BackgroundHirschsprung-associated enterocolitis (HAEC) is one of the most severe complications in patients with Hirschsprung’s disease (HSCR). Previous research has indicated that acetylcholine (ACH) plays an anti-inflammatory role during inflammation by acting on the α7 nicotinic acetylcholine receptor(α7nAchR) to promote the secretion of anti-inflammatory factors. However, the specific role of ACH in HAEC remains unclear. This experiment aims to explore the sources of ACH in HSCR and its anti-inflammatory mechanisms, thereby identifying new directions for the prevention and treatment of HAEC.MethodsWe analyzed single-cell transcriptome data from HSCR to identify cells that secrete ACH and observed their distribution using immunofluorescence. In Ednrb-/- mice, F4/80, iNOS, ARG-1 and CD206 were used to identify and locate M1 and M2 macrophages in different intestinal segments. Western blot, reverse transcription-quantitative polymerase chain reaction, and enzyme-linked immunosorbent assay were used to test the levels of IκBα, tumor necrosis factor-α, interleukin-10, and the macrophage activation pathway proteins JAK2 and STAT3 in different intestinal segments of Ednrb-/- mice. Organoid and cell culture techniques were used to verify the anti-inflammatory mechanism of ACH in vitro models.ResultsscRNA-seq analysis revealed that tuft cells expressed the CHAT protein. In HSCR, aganglionic segments exhibited heightened cholinergic activity compared with dilated ganglionic segments. In HAEC, inflammation was mainly concentrated in the dilated ganglionic segment and was associated with an increase in M1 macrophages, whereas the aganglionic segment showed less inflammation and was associated with an increase in M2 macrophages. Furthermore, in vitro experiments showed that intestinal organoids containing tuft cells promoted an increase in M2 macrophage markers, and ACH promoted M2 macrophage polarization.ConclusionsDifferences in inflammation among various intestinal segments in HAEC may be linked to ACH secreted by tuft cells. Drugs targeting tuft cells have the potential to become important components of HAEC treatment in the future. |
| **Date** | 2025-05-09 |
| **Language** | English |
| **Library Catalog** | Frontiers |
| **URL** | <https://www.frontiersin.org/journals/immunology/articles/10.3389/fimmu.2025.1559966/full> |
| **Accessed** | 6/15/2025, 4:20:06 PM |
| **Extra** | Publisher: Frontiers |
| **Volume** | 16 |
| **Publication** | Frontiers in Immunology |
| **DOI** | [10.3389/fimmu.2025.1559966](http://doi.org/10.3389/fimmu.2025.1559966) |
| **Journal Abbr** | Front. Immunol. |
| **ISSN** | 1664-3224 |
| **Date Added** | 6/15/2025, 4:20:06 PM |
| **Modified** | 6/15/2025, 4:20:06 PM |

### Tags:

* + macrophages
  + Hirschsprung’s disease
  + acetylcholine
  + Ednrb-/-
  + Ednrb-/- mice
  + Hirschsprung-associated enterocolitis
  + tuft cells

### Attachments

* + Full Text PDF

## Beyond the promise: evaluating and mitigating off-target effects in CRISPR gene editing for safer therapeutics

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Rui Lopes |
| **Author** | Megana K. Prasad |
| **Abstract** | Over the last decade, CRISPR has revolutionized drug development due to its potential to cure genetic diseases that currently do not have any treatment. CRISPR was adapted from bacteria for gene editing in human cells in 2012 and, remarkably, only 11 years later has seen it's very first approval as a medicine for the treatment of sickle cell disease and transfusion-dependent betathalassemia. However, the application of CRISPR systems is associated with unintended off-target and on-target alterations (including small indels, and structural variations such as translocations, inversions and large deletions), which are a source of risk for patients and a vital concern for the development of safe therapies. In recent years, a wide range of methods has been developed to detect unwanted effects of CRISPR nuclease activity. In this review, we summarize the different methods for off-target assessment, discuss their strengths and limitations, and highlight strategies to improve the safety of CRISPR systems. Finally, we discuss their relevance and application for the pre-clinical risk assessment of CRISPR therapeutics within the current regulatory context. |
| **Date** | 2024-01-18 |
| **Language** | English |
| **Short Title** | Beyond the promise |
| **Library Catalog** | Frontiers |
| **URL** | <https://www.frontiersin.org/journals/bioengineering-and-biotechnology/articles/10.3389/fbioe.2023.1339189/full> |
| **Accessed** | 6/15/2025, 4:20:35 PM |
| **Extra** | Publisher: Frontiers |
| **Volume** | 11 |
| **Publication** | Frontiers in Bioengineering and Biotechnology |
| **DOI** | [10.3389/fbioe.2023.1339189](http://doi.org/10.3389/fbioe.2023.1339189) |
| **Journal Abbr** | Front. Bioeng. Biotechnol. |
| **ISSN** | 2296-4185 |
| **Date Added** | 6/15/2025, 4:20:35 PM |
| **Modified** | 6/15/2025, 4:20:35 PM |

### Tags:

* + Safety
  + CRISPR-Cas
  + gene editing
  + Health authority. (Min
  + Off-target activity
  + Pre-clinical Development
  + Regulatory Guideline

### Attachments

* + Full Text PDF

## Cell therapy for GI motility disorders: comparison of cell sources and proposed steps for treating Hirschsprung disease

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Lincon A. Stamp |
| **Abstract** | Cell therapeutic approaches to treat a range of congenital and degenerative neuropathies are under intense investigation. There have been recent significant advancements in the development of cell therapy to treat disorders of the enteric nervous system (ENS), enteric neuropathies. These advances include the efficient generation of enteric neural progenitors from pluripotent stem cells and the rescue of a Hirschsprung disease model mouse following their transplantation into the bowel. Furthermore, a recent study provides evidence of functional innervation of the bowel muscle by neurons derived from transplanted ENS-derived neural progenitors. This mini-review discusses these recent findings, compares endogenous ENS-derived progenitors and pluripotent stem cell-derived progenitors as a cell source for therapy, and proposes the key steps for cell therapy to treat Hirschsprung disease. |
| **Date** | 2017-04 |
| **Short Title** | Cell therapy for GI motility disorders |
| **Library Catalog** | journals.physiology.org (Atypon) |
| **URL** | <https://journals.physiology.org/doi/full/10.1152/ajpgi.00018.2017> |
| **Accessed** | 6/15/2025, 4:20:18 PM |
| **Extra** | Publisher: American Physiological Society |
| **Volume** | 312 |
| **Pages** | G348-G354 |
| **Publication** | American Journal of Physiology-Gastrointestinal and Liver Physiology |
| **DOI** | [10.1152/ajpgi.00018.2017](http://doi.org/10.1152/ajpgi.00018.2017) |
| **Issue** | 4 |
| **ISSN** | 0193-1857 |
| **Date Added** | 6/15/2025, 4:20:18 PM |
| **Modified** | 6/15/2025, 4:20:18 PM |

### Attachments

* + Full Text PDF

## Development of the aganglionic colon following surgical rescue in a cell therapy model of Hirschsprung disease in rat

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | John B. Furness |
| **Author** | Enie Lei |
| **Author** | Billie Hunne |
| **Author** | Cameron D. Adams |
| **Author** | Alan J. Burns |
| **Author** | Jill Wykosky |
| **Author** | Therese E. Fazio Coles |
| **Author** | Linda J. Fothergill |
| **Author** | Juan C. Molero |
| **Author** | Ruslan V. Pustovit |
| **Author** | Lincon A. Stamp |
| **Abstract** | Patients with Hirschsprung disease lack enteric ganglia in the distal colon and propulsion of colorectal content is substantially impaired. Proposed stem cell therapies to replace neurons require surgical bypass of the aganglionic bowel during re-colonization, but there is inadequate knowledge of the consequences of bypass. We performed bypass surgery in Ednrb−/− Hirschsprung rat pups. Surgically rescued rats failed to thrive, an outcome reversed by supplying electrolyte- and glucose-enriched drinking water. Histologically, the bypassed colon had normal structure, but grew substantially less in diameter than the functional region proximal to the bypass. Extrinsic sympathetic and spinal afferent neurons projected to their normal targets, including arteries and the circular muscle, in aganglionic regions. However, although axons of intrinsic excitatory and inhibitory neurons grew into the aganglionic region, their normally dense innervation of circular muscle was not restored. Large nerve trunks that contained tyrosine hydroxylase (TH)-, calcitonin gene-related peptide (CGRP, encoded by Calca or Calcb)-, neuronal nitric oxide synthase (nNOS or NOS1)-, vasoactive intestinal peptide (VIP)- and tachykinin (encoded by Tac1)-immunoreactive axons occurred in the distal aganglionic region. We conclude that the rescued Ednrb−/− rat provides a good model for the development of cell therapies for the treatment of Hirschsprung disease. |
| **Date** | 2023-04-27 |
| **Library Catalog** | Silverchair |
| **URL** | <https://doi.org/10.1242/dmm.050055> |
| **Accessed** | 6/15/2025, 4:20:04 PM |
| **Volume** | 16 |
| **Pages** | dmm050055 |
| **Publication** | Disease Models & Mechanisms |
| **DOI** | [10.1242/dmm.050055](http://doi.org/10.1242/dmm.050055) |
| **Issue** | 6 |
| **Journal Abbr** | Disease Models & Mechanisms |
| **ISSN** | 1754-8403 |
| **Date Added** | 6/15/2025, 4:20:04 PM |
| **Modified** | 6/15/2025, 4:20:04 PM |

### Attachments

* + Full Text PDF

## Editorial: First Regulatory Approvals for CRISPR-Cas9 Therapeutic Gene Editing for Sickle Cell Disease and Transfusion-Dependent β-Thalassemia

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Dinah V. Parums |
| **Abstract** | Dear Colleagues, I wanted to share an important update on the recent regulatory approvals of CRISPR-Cas9 gene editing therapy for patients with sickl... |
| **Date** | 2024/03/01 |
| **Language** | en |
| **Short Title** | Editorial |
| **Library Catalog** | medscimonit.com |
| **URL** | <https://www.medscimonit.com/abstract/full/idArt/944204> |
| **Accessed** | 6/15/2025, 4:20:29 PM |
| **Extra** | Publisher: International Scientific Information, Inc. PMID: 38425279 |
| **Volume** | 30 |
| **Publication** | Medical Science Monitor |
| **DOI** | [10.12659/MSM.944204](http://doi.org/10.12659/MSM.944204) |
| **Journal Abbr** | Med Sci Monit |
| **ISSN** | 1234-1010, 1643-3750 |
| **Date Added** | 6/15/2025, 4:20:29 PM |
| **Modified** | 6/15/2025, 4:20:29 PM |

### Attachments

* + PubMed entry

## Hirschsprung's Disease - Review of Clinical Features, Diagnosis and Treatment

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Rafał Tkaczyk |
| **Author** | Gabriela Świątek |
| **Author** | Jakub Tomczyk |
| **Author** | Weronika Sosnowska |
| **Author** | Maria Tomkiewicz |
| **Author** | Kalina Taracha |
| **Author** | Maciej Tomkiewicz |
| **Author** | Aleksandra Brzozowska |
| **Author** | Kornelia Trusz |
| **Author** | Iwona Wanat |
| **Abstract** | Introduction and purpose: Hirschsprung's disease, also known as congenital aganglionic megacolon, is a rare congenital disorder that affects the large intestine. Due to the absence of ganglion cells, the affected segment of the colon becomes narrow and unable to relax. The disease is present from birth but may not always be immediately apparent. In this paper, we will attempt to present the current state of knowledge regarding the diagnosis and treatment of Hirschsprung's disease, based on the analysis of literature available on the PubMed platform. Description of the state of knowledge: Hirschsprung's disease (HSCR), also known as congenital aganglionosis of the colon, involves abnormal migration, proliferation, and differentiation of neural crest cells, leading to the absence of autonomic nerve ganglia within the colon. HSCR is associated with mutations in several genes, with RET, GDNF, EDNRB and SOX10 being identified as the main causes of the disease. Mutations in the RET gene are associated with the hereditary form of Hirschsprung's disease. Symptoms of HSCR appear in newborns and may include bilious vomiting, diarrhea associated with enterocolitis, failure to pass meconium within the first 24 hours of life, impaired peristalsis, jaundice, feeding difficulties, and progressive abdominal distension. Summary: Diagnosis is typically made based on clinical presentation, imaging studies, and biopsy. Treatment usually involves surgery to remove the affected segment of the colon and reconnect the healthy portions. Although postoperative complications are relatively common, long-term studies suggest that the majority of children with Hirschsprung's disease function well in society. |
| **Date** | 2023-08-25 |
| **Language** | en |
| **Library Catalog** | apcz.umk.pl |
| **URL** | <https://apcz.umk.pl/JEHS/article/view/45365> |
| **Accessed** | 6/15/2025, 4:19:46 PM |
| **Rights** | Copyright (c) 2023 Rafał Tkaczyk, Gabriela Świątek, Jakub Tomczyk, Weronika Sosnowska, Maria Tomkiewicz, Kalina Taracha, Maciej Tomkiewicz, Aleksandra Brzozowska, Kornelia Trusz, Iwona Wanat |
| **Extra** | Number: 1 |
| **Volume** | 46 |
| **Pages** | 134-145 |
| **Publication** | Journal of Education, Health and Sport |
| **DOI** | [10.12775/JEHS.2023.46.01.009](http://doi.org/10.12775/JEHS.2023.46.01.009) |
| **Issue** | 1 |
| **ISSN** | 2391-8306 |
| **Date Added** | 6/15/2025, 4:19:46 PM |
| **Modified** | 6/15/2025, 4:19:46 PM |

### Tags:

* + HAEC
  + Hirschsprung's disease
  + HSCR
  + Intestinal aganglionosis

### Attachments

* + Full Text PDF

## Human Pluripotent Stem Cell-Based Models for Hirschsprung Disease: From 2-D Cell to 3-D Organoid Model

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Kathy Nga-Chu Lui |
| **Author** | Elly Sau-Wai Ngan |
| **Abstract** | Hirschsprung disease (HSCR) is a complex congenital disorder caused by defects in the development of the enteric nervous system (ENS). It is attributed to failures of the enteric neural crest stem cells (ENCCs) to proliferate, differentiate and/or migrate, leading to the absence of enteric neurons in the distal colon, resulting in colonic motility dysfunction. Due to the oligogenic nature of the disease, some HSCR conditions could not be phenocopied in animal models. Building the patient-based disease model using human induced pluripotent stem cells (hPSC) has opened up a new opportunity to untangle the unknowns of the disease. The expanding armamentarium of hPSC-based therapies provides needed new tools for developing cell-replacement therapy for HSCR. Here we summarize the recent studies of hPSC-based models of ENS in 2-D and 3-D culture systems. These studies have highlighted how hPSC-based models complement the population-based genetic screens and bioinformatic approaches for the discovery of new HSCR susceptibility genes and provide a human model for the close-to-physiological functional studies. We will also discuss the potential applications of these hPSC-based models in translational medicines and their advantages and limitations. The use of these hPSC-based models for drug discovery or cell replacement therapy likely leads to new treatment strategies for HSCR in the future. Further improvements in incorporating hPSC-based models with the human-mouse chimera model and organ-on-a-chip system for establishing a better disease model of HSCR and for drug discovery will further propel us to success in the development of an efficacious treatment for HSCR. |
| **Date** | 2022/1 |
| **Language** | en |
| **Short Title** | Human Pluripotent Stem Cell-Based Models for Hirschsprung Disease |
| **Library Catalog** | www.mdpi.com |
| **URL** | <https://www.mdpi.com/2073-4409/11/21/3428> |
| **Accessed** | 6/15/2025, 4:20:10 PM |
| **Rights** | http://creativecommons.org/licenses/by/3.0/ |
| **Extra** | Number: 21 Publisher: Multidisciplinary Digital Publishing Institute |
| **Volume** | 11 |
| **Pages** | 3428 |
| **Publication** | Cells |
| **DOI** | [10.3390/cells11213428](http://doi.org/10.3390/cells11213428) |
| **Issue** | 21 |
| **ISSN** | 2073-4409 |
| **Date Added** | 6/15/2025, 4:20:10 PM |
| **Modified** | 6/15/2025, 4:20:10 PM |

### Tags:

* + induced pluripotent stem cells
  + enteric nervous system
  + Hirschsprung disease
  + colonic organoids
  + disease modeling

### Attachments

* + Full Text PDF

## Long-Term Oncologic Outcome following Duodenum-Preserving Pancreatic Head Resection for Benign Tumors, Cystic Neoplasms, and Neuroendocrine Tumors: Systematic Review and Meta-analysis

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Hans G Beger |
| **Author** | Benjamin Mayer |
| **Author** | Bertram Poch |
| **Date** | 2024 |
| **URL** | <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11164799/> |
| **Volume** | 31 |
| **Pages** | 4637–4653 |
| **Publication** | Annals of Surgical Oncology |
| **DOI** | [10.1245/s10434-024-15222-y](http://doi.org/10.1245/s10434-024-15222-y) |
| **Issue** | 7 |
| **Date Added** | 4/16/2025, 11:10:32 PM |
| **Modified** | 6/16/2025, 1:12:21 PM |

### Tags:

* + Adult
  + Female
  + Humans
  + Male
  + Treatment Outcome
  + Animals
  + Disease Models, Animal
  + Mice
  + STING
  + Quality of Life
  + Retrospective Studies
  + Diabetes
  + Signal Transduction
  + Cell Differentiation
  + Cell Line
  + Neoplasm Recurrence, Local
  + Cell Movement
  + Mammals
  + Neurons
  + immune cells
  + inflammation
  + Homeostasis
  + Gastroenterology
  + intestinal organoids
  + Regeneration
  + microbiota
  + Pancreas
  + inflammatory bowel disease
  + \*Cell- and Tissue-Based Therapy/methods
  + \*Bile Duct Neoplasms
  + \*Bile Duct Neoplasms/surgery
  + \*Cell Lineage
  + \*Cholangiocarcinoma
  + \*Cholangiocarcinoma/pathology
  + \*Colitis, Ulcerative/drug therapy
  + \*Cystadenocarcinoma/diagnostic imaging/surgery
  + \*Cystadenoma/diagnostic imaging/surgery
  + \*Cysts/pathology
  + \*Diabetes Mellitus, Experimental/complications/genetics/metabolism
  + \*Enteric Nervous System
  + \*Enteric Nervous System/pathology
  + \*Hyperglycemia/genetics/metabolism
  + \*Hypothalamo-Hypophyseal System
  + \*Inflammatory Bowel Diseases/drug therapy
  + \*Liver Neoplasms/diagnostic imaging/surgery
  + \*Liver Neoplasms/surgery
  + \*Microbiota
  + \*MicroRNAs/metabolism
  + \*Neoplasms, Cystic, Mucinous, and Serous
  + \*Neuroglia/physiology
  + \*Zebrafish
  + 16S RNA sequencing
  + Acinar cell carcinoma
  + Aging
  + antibiotics
  + Bile Ducts, Intrahepatic
  + Bile Ducts, Intrahepatic/surgery
  + Biliary
  + Biliary cystadenocarcinoma
  + Biliary cystadenoma
  + Brain
  + Brain-Gut Axis
  + Brain/physiology
  + Cell Separation
  + Chemical coding
  + Chick Embryo
  + circVPS13A
  + Cistoadenocarcinoma
  + Cistoadenoma
  + Clinicopathological criteria, Surgical outcomes
  + Colon/drug effects/pathology
  + Cystadenocarcinoma
  + Cystadenoma
  + cystic liver lesions
  + Cystic liver neoplasm
  + Cytology
  + Developmental disorders
  + diabetes
  + diabetes mellitus
  + Drug Discovery/\*methods
  + Embryonic stem cells
  + ENS
  + ENS neuropathies
  + enteric glia
  + enteric glia communications
  + Enteric glia communications
  + enteric glia diversity
  + enteric nervous system
  + Enteric nervous system
  + Enteric Nervous System
  + enteric nervous system (ENS)
  + Enteric nervous system (ENS)
  + Enteric Nervous System/\*pathology
  + Enteric neural precursor cells (ENPCs)
  + enteric progenitor cell
  + Fecal microbiota transplantation
  + Frantz's tumor
  + gastrointestinal complications
  + gastrointestinal diseases
  + Gastrointestinal Diseases
  + Gastrointestinal Diseases/pathology
  + gastrointestinal tract
  + Gastrointestinal Tract/drug effects/pathology
  + glia
  + Glial Cell Line-Derived Neurotrophic Factor/genetics
  + glucagon-like peptide 1
  + Growth Disorders
  + growth retardation
  + gut brain axis
  + gut microbiota
  + gut-brain axis
  + gut–brain axis
  + hepatic cystadenocarcinoma
  + hepatic cystadenoma
  + Hepatic simple cyst
  + hepatobiliary cystadenocarcinoma
  + hepatobiliary cystadenoma
  + Hirschsprung disease
  + Hirschsprung Disease/\*drug therapy/\*pathology/therapy
  + homeostasis
  + Imaging modalities
  + In Situ Hybridization, Fluorescence
  + Inflammatory bowel diseases
  + Intraductal papillary biliary neoplasms
  + intraductal papillary neoplasms of bile duct
  + irritable bowel syndrome
  + L-Fucose
  + Liver Diseases
  + Management
  + microbial metabolites
  + microbiota-gut-brain axis
  + Microbiota-gut-brain axis
  + Mucinous biliary cystic tumors, Biliary cystadenoma
  + mucinous cystic neoplasm
  + Mucinous cystic neoplasms
  + Mucinous neoplasm
  + muscularis macrophages
  + myenteric neurons
  + Neoplasia mucinosa quística
  + Neoplasia papilar intraductal biliar
  + Neoplasia quística hepática
  + Neural Crest
  + neural crest cell
  + neurodegeneration
  + Neuroglia
  + Neurons/drug effects/\*pathology
  + offspring
  + P2X7 receptor
  + pancreatectomy
  + Pancreatectomy
  + Pancreatic neoplasms
  + Pancreatic Neoplasms
  + Pancreatic surgery
  + pancreatic tumor
  + Parkinson’s disease
  + pediatric pancreatic neoplasm
  + Pepstatins/metabolism
  + Pituitary-Adrenal System
  + pluripotent stem cells (PSCs)
  + Pluripotent Stem Cells/pathology
  + preconception
  + probiotic
  + Purinergic signaling
  + Receptor, Endothelin B/metabolism
  + Receptors, Purinergic P2X7
  + RNA, Circular/genetics
  + Rotenone-induced mouse model
  + short-chain fatty acids
  + Solid pseudopapillary tumor
  + Stem-cell differentiation
  + submucosal neurons
  + Submucous Plexus
  + surgical outcome
  + surgical resection
  + three-dimensional (3D)
  + type 2 diabetes
  + zebrafish

### Notes:

* + e14603 NMO-00132-2023
  + e14603 NMO-00132-2023

### Attachments

* + Full Text
  + Full Text
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  + PubMed Central Full Text PDF
  + PubMed Central Full Text PDF
  + PubMed Central Full Text PDF
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  + PubMed Central Link
  + PubMed entry

## Roles of Enteric Neural Stem Cell Niche and Enteric Nervous System Development in Hirschsprung Disease

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Yue Ji |
| **Author** | Paul Kwong-Hang Tam |
| **Author** | Clara Sze-Man Tang |
| **Abstract** | The development of the enteric nervous system (ENS) is highly modulated by the synchronized interaction between the enteric neural crest cells (ENCCs) and the neural stem cell niche comprising the gut microenvironment. Genetic defects dysregulating the cellular behaviour(s) of the ENCCs result in incomplete innervation and hence ENS dysfunction. Hirschsprung disease (HSCR) is a rare complex neurocristopathy in which the enteric neural crest-derived cells fail to colonize the distal colon. In addition to ENS defects, increasing evidence suggests that HSCR patients may have intrinsic defects in the niche impairing the extracellular matrix (ECM)-cell interaction and/or dysregulating the cellular niche factors necessary for controlling stem cell behaviour. The niche defects in patients may compromise the regenerative capacity of the stem cell-based therapy and advocate for drug- and niche-based therapies as complementary therapeutic strategies to alleviate/enhance niche-cell interaction. Here, we provide a summary of the current understandings of the role of the enteric neural stem cell niche in modulating the development of the ENS and in the pathogenesis of HSCR. Deciphering the contribution of the niche to HSCR may provide important implications to the development of regenerative medicine for HSCR. |
| **Date** | 2021/1 |
| **Language** | en |
| **Library Catalog** | www.mdpi.com |
| **URL** | <https://www.mdpi.com/1422-0067/22/18/9659> |
| **Accessed** | 6/15/2025, 4:20:00 PM |
| **Rights** | http://creativecommons.org/licenses/by/3.0/ |
| **Extra** | Number: 18 Publisher: Multidisciplinary Digital Publishing Institute |
| **Volume** | 22 |
| **Pages** | 9659 |
| **Publication** | International Journal of Molecular Sciences |
| **DOI** | [10.3390/ijms22189659](http://doi.org/10.3390/ijms22189659) |
| **Issue** | 18 |
| **ISSN** | 1422-0067 |
| **Date Added** | 6/15/2025, 4:20:00 PM |
| **Modified** | 6/15/2025, 4:20:00 PM |

### Tags:

* + enteric nervous system
  + Hirschsprung disease
  + enteric neural crest cells
  + extra-cellular matrix
  + neural stem cell niche
  + regenerative medicine

### Attachments

* + Full Text PDF

## Schwann Cells in the Aganglionic Colon of Hirschsprung Disease Can Generate Neurons for Regenerative Therapy

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Weikang Pan |
| **Author** | Ahmed A Rahman |
| **Author** | Rhian Stavely |
| **Author** | Sukhada Bhave |
| **Author** | Richard Guyer |
| **Author** | Meredith Omer |
| **Author** | Nicole Picard |
| **Author** | Allan M Goldstein |
| **Author** | Ryo Hotta |
| **Abstract** | Cell therapy offers the potential to replace the missing enteric nervous system (ENS) in patients with Hirschsprung disease (HSCR) and to restore gut function. The Schwann cell (SC) lineage has been shown to generate enteric neurons pre- and post-natally. Here, we aimed to isolate SCs from the aganglionic segment of HSCR and to determine their potential to restore motility in the aganglionic colon. Proteolipid protein 1 (PLP1) expressing SCs were isolated from the extrinsic nerve fibers present in the aganglionic segment of postnatal mice and patients with HSCR. Following 7-10 days of in vitro expansion, HSCR-derived SCs were transplanted into the aganglionic mouse colon ex vivo and in vivo. Successful engraftment and neuronal differentiation were confirmed immunohistochemically and calcium activity of transplanted cells was demonstrated by live cell imaging. Organ bath studies revealed the restoration of motor function in the recipient aganglionic smooth muscle. These results show that SCs isolated from the aganglionic segment of HSCR mouse can generate functional neurons within the aganglionic gut environment and restore the neuromuscular activity of recipient mouse colon. We conclude that HSCR-derived SCs represent a potential autologous source of neural progenitor cells for regenerative therapy in HSCR. |
| **Date** | 2022-12-01 |
| **Library Catalog** | Silverchair |
| **URL** | <https://doi.org/10.1093/stcltm/szac076> |
| **Accessed** | 6/15/2025, 4:19:43 PM |
| **Volume** | 11 |
| **Pages** | 1232-1244 |
| **Publication** | Stem Cells Translational Medicine |
| **DOI** | [10.1093/stcltm/szac076](http://doi.org/10.1093/stcltm/szac076) |
| **Issue** | 12 |
| **Journal Abbr** | Stem Cells Translational Medicine |
| **ISSN** | 2157-6564 |
| **Date Added** | 6/15/2025, 4:19:43 PM |
| **Modified** | 6/15/2025, 4:19:43 PM |

### Attachments

* + Full Text PDF

## Stress-free cell aggregation by using the CEPT cocktail enhances embryoid body and organoid fitness

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Seungmi Ryu |
| **Author** | Claire Weber |
| **Author** | Pei-Hsuan Chu |
| **Author** | Ben Ernest |
| **Author** | Vukasin M Jovanovic |
| **Author** | Tao Deng |
| **Author** | Jaroslav Slamecka |
| **Author** | Hyenjong Hong |
| **Author** | Yogita Jethmalani |
| **Author** | Hannah M Baskir |
| **Author** | Jason Inman |
| **Author** | John Braisted |
| **Author** | Marissa B Hirst |
| **Author** | Anton Simeonov |
| **Author** | Ty C Voss |
| **Author** | Carlos A Tristan |
| **Author** | Ilyas Singeç |
| **Abstract** | Embryoid bodies (EBs) and self-organizing organoids derived from human pluripotent stem cells (hPSCs) recapitulate tissue development in a dish and hold great promise for disease modeling and drug development. However, current protocols are hampered by cellular stress and apoptosis during cell aggregation, resulting in variability and impaired cell differentiation. Here, we demonstrate that EBs and various organoid models (e.g., brain, gut, kidney) can be optimized by using the small molecule cocktail named CEPT (chroman 1, emricasan, polyamines, trans-ISRIB), a polypharmacological approach that ensures cytoprotection and cell survival. Application of CEPT for just 24 h during cell aggregation has long-lasting consequences affecting morphogenesis, gene expression, cellular differentiation, and organoid function. Various qualification methods confirmed that CEPT treatment enhanced experimental reproducibility and consistently improved EB and organoid fitness as compared to the widely used ROCK inhibitor Y-27632. Collectively, we discovered that stress-free cell aggregation and superior cell survival in the presence of CEPT are critical quality control determinants that establish a robust foundation for bioengineering complex tissue and organ models. |
| **Date** | 2023-12 |
| **Language** | en |
| **Library Catalog** | Institute of Physics |
| **URL** | <https://dx.doi.org/10.1088/1758-5090/ad0d13> |
| **Accessed** | 6/15/2025, 4:20:26 PM |
| **Extra** | Publisher: IOP Publishing |
| **Volume** | 16 |
| **Pages** | 015016 |
| **Publication** | Biofabrication |
| **DOI** | [10.1088/1758-5090/ad0d13](http://doi.org/10.1088/1758-5090/ad0d13) |
| **Issue** | 1 |
| **Journal Abbr** | Biofabrication |
| **ISSN** | 1758-5090 |
| **Date Added** | 6/15/2025, 4:20:26 PM |
| **Modified** | 6/15/2025, 4:20:26 PM |

### Attachments

* + IOP Full Text PDF

## The <i>RET</i> gene encodes RET protein, which triggers intracellular signaling pathways for enteric neurogenesis, and <i>RET</i> mutation results in Hirschsprung's disease

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Chacchu Bhattarai |
| **Author** | Phanindra Prasad Poudel |
| **Author** | Arnab Ghosh |
| **Author** | Sneha Guruprasad Kalthur |
| **Author** | Chacchu Bhattarai |
| **Author** | Phanindra Prasad Poudel |
| **Author** | Arnab Ghosh |
| **Author** | Sneha Guruprasad Kalthur |
| **Abstract** | Enteric neurons and ganglia are derived from vagal and sacral neural crest cells, which undergo migration from the neural tube to the gut wall. In the gut wall, they first undergo rostrocaudal migration followed by migration from the superficial to deep layers. After migration, they proliferate and differentiate into the enteric plexus. Expression of the Rearranged During Transfection (RET) gene and its protein RET plays a crucial role in the formation of enteric neurons. This review describes the molecular mechanism by which the RET gene and the RET protein influence the development of enteric neurons. Vagal neural crest cells give rise to enteric neurons and glia of the foregut and midgut while sacral neural crest cells give rise to neurons of the hindgut. Interaction of RET protein with its ligands (glial cell derived neurotrophic factor (GDNF), neurturin (NRTN), and artemin (ARTN)) and its co-receptors (GDNF receptor alpha proteins (GFRα1-4)) activates the Phosphoinositide-3-kinase-protein kinase B (PI3K-PKB/AKT), RAS mitogen-activated protein kinase (RAS/MAPK) and phospholipase Cγ (PLCγ) signaling pathways, which control the survival, migration, proliferation, differentiation, and maturation of the vagal and sacral neural crest cells into enteric neurons. Abnormalities of the RET gene result in Hirschsprung's disease. |
| **Date** | 2022 |
| **Language** | en |
| **Library Catalog** | www.aimspress.com |
| **URL** | <http://www.aimspress.com/article/doi/10.3934/Neuroscience.2022008> |
| **Accessed** | 6/15/2025, 4:19:53 PM |
| **Rights** | 2022 The Author(s) |
| **Extra** | Cc\_license\_type: cc\_by Number: neurosci-09-01-008 Primary\_atype: AIMS Neuroscience Subject\_term: Review Subject\_term\_id: Review |
| **Volume** | 9 |
| **Pages** | 128-149 |
| **Publication** | AIMS Neuroscience |
| **DOI** | [10.3934/Neuroscience.2022008](http://doi.org/10.3934/Neuroscience.2022008) |
| **Issue** | 1 |
| **Journal Abbr** | AIMSN |
| **ISSN** | 2373-7972 |
| **Date Added** | 6/15/2025, 4:19:53 PM |
| **Modified** | 6/15/2025, 4:19:53 PM |

* **Anti-inflammatory effects of vagal nerve stimulation with a special attention to intestinal barrier dysfunction**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Bruno Bonaz |
| **Abstract** | The vagus nerve (VN), the longest nerve of the organism innervating the gastrointestinal tract, is a mixed nerve with anti-inflammatory properties through its afferents, activating the hypothalamic–pituitary adrenal axis, and its efferents through the cholinergic anti-inflammatory pathway inhibiting the release of pro-inflammatory cytokines (e.g., TNFα) by splenic and gut macrophages. In addition, the VN is also able to modulate the permeability of the intestinal barrier although the VN does not innervate directly the intestinal epithelium. Targeting the VN through VN stimulation (VNS) has been developed in experimental model of intestinal inflammation and in inflammatory bowel disease (IBD) and might be of interest to decrease intestinal permeability in gastrointestinal disorders with intestinal barrier defect such as IBD, irritable bowel syndrome (IBS), and celiac disease. In this issue of neurogastroenterology and motility, Mogilevski et al. report that a brief non-invasive transcutaneous auricular VNS in healthy volunteers consistently reduces the permeability of the small intestine induced by intravenous administration of the stress peptide corticotropin releasing hormone, known to increase intestinal permeability and to inhibit the VN. In this review, we outline the mechanistic underpinning the effect of stress, of the VN and VNS on intestinal permeability. In particular, the VN can act on intestinal permeability through enteric nerves, and/or cells such as enteric glial cells. We also review the existing evidence of the effects VNS on intestinal permeability in models such as burn intestinal injury and traumatic brain injury, which pave the way for future clinical trials in IBD, IBS, and celiac disease. |
| **Date** | 2022 |
| **Language** | en |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1111/nmo.14456> |
| **Accessed** | 6/15/2025, 4:23:30 PM |
| **Rights** | © 2022 The Author. Neurogastroenterology & Motility published by John Wiley & Sons Ltd. |
| **Extra** | \_eprint: https://onlinelibrary.wiley.com/doi/pdf/10.1111/nmo.14456 |
| **Volume** | 34 |
| **Pages** | e14456 |
| **Publication** | Neurogastroenterology & Motility |
| **DOI** | [10.1111/nmo.14456](http://doi.org/10.1111/nmo.14456) |
| **Issue** | 10 |
| **ISSN** | 1365-2982 |
| **Date Added** | 6/15/2025, 4:23:30 PM |
| **Modified** | 6/15/2025, 4:23:30 PM |

* **Tags:**
  + inflammation
  + enteric glial cells
  + vagus nerve
  + stress
  + cholinergic anti-inflammatory pathway
  + intestinal barrier
  + vagal nerve stimulation

**Notes:**

* + e14456 NMO-00271-2022.R1

**Attachments**

* + Full Text PDF
* **Efficacy of Fecal Microbiota Transplantation for Recurrent C. Difficile Infection in Inflammatory Bowel Disease**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Raseen Tariq |
| **Author** | Molly B Disbrow |
| **Author** | John K Dibaise |
| **Author** | Robert Orenstein |
| **Author** | Srishti Saha |
| **Author** | Dipesh Solanky |
| **Author** | Edward V Loftus |
| **Author** | Darrell S Pardi |
| **Author** | Sahil Khanna |
| **Abstract** | Clostridioides difficile infection (CDI) is associated with poor outcomes in inflammatory bowel disease (IBD) patients. Data are scarce on efficacy of fecal microbiota transplant (FMT) for recurrent CDI in IBD patients.We reviewed health records of IBD patients (18 years of age or older) with recurrent CDI who underwent FMT. Outcomes of FMT for CDI were assessed on the basis of symptoms and stool test results.We included 145 patients (75 women [51.7%]; median age, 46 years). Median IBD duration was 8 (range, 0–47) years, 36.6% had Crohn disease, 61.4% had ulcerative colitis, and 2.1% had indeterminate colitis. Median number of prior CDI episodes was 3 (range, 3–20), and 61.4% had received vancomycin taper. Diarrhea resolved after FMT in 48 patients (33.1%) without further testing. Ninety-five patients (65.5%) underwent CDI testing owing to post-FMT recurrent diarrhea; 29 (20.0%) had positive results. After FMT, 2 patients received empiric treatment of recurrent CDI without symptom resolution, suggesting IBD was the cause of symptoms. The overall cure rate of CDI after FMT was 80.0%, without CDI recurrence at median follow-up of 9.3 (range, 0.1–51) months. Forty-three patients (29.7%) had planned IBD therapy escalation after CDI resolution; none de-escalated or discontinued IBD therapy. Overall, 7.6% had worsening IBD symptoms after FMT that were treated as new IBD flares. No clinical predictors of FMT failure were identified.Few patients had new IBD flare after FMT. Fecal microbiota transplantation effectively treats recurrent CDI in IBD patients but has no apparent beneficial effect on the IBD course. |
| **Date** | 2020-08-20 |
| **Library Catalog** | Silverchair |
| **URL** | <https://doi.org/10.1093/ibd/izz299> |
| **Accessed** | 6/15/2025, 4:23:19 PM |
| **Volume** | 26 |
| **Pages** | 1415-1420 |
| **Publication** | Inflammatory Bowel Diseases |
| **DOI** | [10.1093/ibd/izz299](http://doi.org/10.1093/ibd/izz299) |
| **Issue** | 9 |
| **Journal Abbr** | Inflammatory Bowel Diseases |
| **ISSN** | 1078-0998 |
| **Date Added** | 6/15/2025, 4:23:19 PM |
| **Modified** | 6/15/2025, 4:23:19 PM |

* **Guidance for Fecal Microbiota Transplantation Trials in Ulcerative Colitis: The Second ROME Consensus Conference**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Loris R Lopetuso |
| **Author** | Sara Deleu |
| **Author** | Pierluigi Puca |
| **Author** | Maria Teresa Abreu |
| **Author** | Alessandro Armuzzi |
| **Author** | Giovanni Barbara |
| **Author** | Flavio Caprioli |
| **Author** | Siew Chieng |
| **Author** | Samuel Paul Costello |
| **Author** | Andrea Damiani |
| **Author** | Silvio Danese |
| **Author** | Federica Del Chierico |
| **Author** | Geert D’Haens |
| **Author** | Iris Dotan |
| **Author** | Federica Facciotti |
| **Author** | Gwen Falony |
| **Author** | Massimo Claudio Fantini |
| **Author** | Gionata Fiorino |
| **Author** | Paolo Gionchetti |
| **Author** | Lihi Godny |
| **Author** | Ailsa Hart |
| **Author** | Juozas Kupčinskas |
| **Author** | Tariq Iqbal |
| **Author** | Lucrezia Laterza |
| **Author** | Letizia Lombardini |
| **Author** | Nitsan Maharshak |
| **Author** | Giovanni Marasco |
| **Author** | Luca Masucci |
| **Author** | Alfredo Papa |
| **Author** | Sudarshan Paramsothy |
| **Author** | Valentina Petito |
| **Author** | Daniele Piovani |
| **Author** | Daniela Pugliese |
| **Author** | Lorenza Putignani |
| **Author** | Jeroen Raes |
| **Author** | Davide Giuseppe Ribaldone |
| **Author** | Maurizio Sanguinetti |
| **Author** | Edoardo Vincenzo Savarino |
| **Author** | Harry Sokol |
| **Author** | Stefania Vetrano |
| **Author** | Gianluca Ianiro |
| **Author** | Giovanni Cammarota |
| **Author** | Fabio Cominelli |
| **Author** | Theresa T Pizarro |
| **Author** | Herbert Tilg |
| **Author** | Antonio Gasbarrini |
| **Author** | Severine Vermeire |
| **Author** | Franco Scaldaferri |
| **Abstract** | Fecal microbiota transplantation (FMT) is emerging as a potential treatment modality for individuals living with inflammatory bowel disease (IBD). Despite its promise, the effectiveness of FMT for treating IBD, particularly for ulcerative colitis (UC), still requires thorough clinical investigation. Notwithstanding differences in methodologies, current studies demonstrate its potential for inducing remission in UC patients. Therefore, standardized and robust randomized clinical trials (RCTs) are needed to further support its efficacy for managing UC. The aim of the second Rome Consensus Conference was to address gaps and uncertainties identified in previous research regarding FMT and to offer a robust framework for future studies applied to the treatment of UC.Global experts in the field of clinical IBD, mucosal immunology, and microbiology (N = 48) gathered to address the need for standardized clinical trials in FMT investigation. The group focused on key issues, such as stool donation, donor selection, characterization of fecal biomass, potential administration routes, as well as the process of induction, maintenance, and endpoint readouts.The consensus achieved during this conference established standardization of methods and protocols to enhance the current quality of research, with the aim of eventual implementation of FMT in managing UC and the ultimate goal of improving patient outcomes.The aim of this consensus was to establish a standardized framework and to discuss critical methodological issues to enhance evidence-based quality of procedure and define the role of future fecal microbiota transplantation trials in managing patients living with ulcerative colitis. |
| **Date** | 2025-02-11 |
| **Short Title** | Guidance for Fecal Microbiota Transplantation Trials in Ulcerative Colitis |
| **Library Catalog** | Silverchair |
| **URL** | <https://doi.org/10.1093/ibd/izaf013> |
| **Accessed** | 6/15/2025, 4:23:16 PM |
| **Pages** | izaf013 |
| **Publication** | Inflammatory Bowel Diseases |
| **DOI** | [10.1093/ibd/izaf013](http://doi.org/10.1093/ibd/izaf013) |
| **Journal Abbr** | Inflammatory Bowel Diseases |
| **ISSN** | 1536-4844 |
| **Date Added** | 6/15/2025, 4:23:16 PM |
| **Modified** | 6/15/2025, 4:23:16 PM |

* **Attachments**
  + Full Text PDF
* **Increased Numbers of Enteric Glial Cells in the Peyer’s Patches and Enhanced Intestinal Permeability by Glial Cell Mediators in Patients with Ileal Crohn’s Disease**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Olga Biskou |
| **Author** | Felipe Meira de-Faria |
| **Author** | Susanna M. Walter |
| **Author** | Martin E. Winberg |
| **Author** | Staffan Haapaniemi |
| **Author** | Pär Myrelid |
| **Author** | Johan D. Söderholm |
| **Author** | Åsa V. Keita |
| **Abstract** | Enteric glial cells (EGC) are known to regulate gastrointestinal functions; however, their role in Crohn’s disease (CD) is elusive. Microscopic erosions over the ileal Peyer’s patches are early signs of CD. The aim of this work was to assess the localization of EGC in the follicle and interfollicular region of the Peyer’s patches and in the lamina propria and study the effects of EGC mediators on barrier function in CD patients and non-inflammatory bowel disease (non-IBD) controls. EGC markers, glial fibrillary acidic protein (GFAP), and S100 calcium-binding protein β (S100β) were quantified by immunofluorescence and Western blotting. Both markers showed significantly more EGC in the Peyer’s patches and lamina propria of CD patients compared to the non-IBD controls. In CD patients there were significantly more EGC in Peyer’s patches compared to lamina propria, while the opposite pattern was seen in controls. Barrier function studies using Ussing chambers showed increased paracellular permeability by EGC mediators in CD patients, whereas permeability decreased by the mediators in controls. We show the accumulation of EGC in Peyer’s patches of CD patients. Moreover, EGC mediators induced barrier dysfunction in CD patients. Thus, EGC might have harmful impacts on ongoing inflammation and contribute to the pathophysiology of the disease. |
| **Date** | 2022/1 |
| **Language** | en |
| **Library Catalog** | www.mdpi.com |
| **URL** | <https://www.mdpi.com/2073-4409/11/3/335> |
| **Accessed** | 6/15/2025, 4:22:46 PM |
| **Rights** | http://creativecommons.org/licenses/by/3.0/ |
| **Extra** | Number: 3 Publisher: Multidisciplinary Digital Publishing Institute |
| **Volume** | 11 |
| **Pages** | 335 |
| **Publication** | Cells |
| **DOI** | [10.3390/cells11030335](http://doi.org/10.3390/cells11030335) |
| **Issue** | 3 |
| **ISSN** | 2073-4409 |
| **Date Added** | 6/15/2025, 4:22:46 PM |
| **Modified** | 6/15/2025, 4:22:46 PM |

* **Tags:**
  + enteric nervous system
  + follicle-associated epithelium
  + gut inflammation
  + neuro-immune interactions

**Attachments**

* + Full Text PDF
* **Inflammatory Bowel Disease Outcomes Following Fecal Microbiota Transplantation for Recurrent C. difficile Infection**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Jessica R Allegretti |
| **Author** | Colleen R Kelly |
| **Author** | Ari Grinspan |
| **Author** | Benjamin H Mullish |
| **Author** | Jonathan Hurtado |
| **Author** | Madeline Carrellas |
| **Author** | Jenna Marcus |
| **Author** | Julian R Marchesi |
| **Author** | Julie A K McDonald |
| **Author** | Ylaine Gerardin |
| **Author** | Michael Silverstein |
| **Author** | Alexandros Pechlivanis |
| **Author** | Grace F Barker |
| **Author** | Jesus Miguens Blanco |
| **Author** | James L Alexander |
| **Author** | Kate I Gallagher |
| **Author** | Will Pettee |
| **Author** | Emmalee Phelps |
| **Author** | Sara Nemes |
| **Author** | Sashidhar V Sagi |
| **Author** | Matthew Bohm |
| **Author** | Zain Kassam |
| **Author** | Monika Fischer |
| **Abstract** | Recurrent Clostridioides difficile infection (CDI) in patients with inflammatory bowel disease (IBD) is a clinical challenge. Fecal microbiota transplantation (FMT) has emerged as a recurrent CDI therapy. Anecdotal concerns exist regarding worsening of IBD activity; however, prospective data among IBD patients are limited.Secondary analysis from an open-label, prospective, multicenter cohort study among IBD patients with 2 or more CDI episodes was performed. Participants underwent a single FMT by colonoscopy (250 mL, healthy universal donor). Secondary IBD-related outcomes included rate of de novo IBD flares, worsening IBD, and IBD improvement—all based on Mayo or Harvey-Bradshaw index (HBI) scores. Stool samples were collected for microbiome and targeted metabolomic profiling.Fifty patients enrolled in the study, among which 15 had Crohn’s disease (mean HBI, 5.8 ± 3.4) and 35 had ulcerative colitis (mean partial Mayo score, 4.2 ± 2.1). Overall, 49 patients received treatment. Among the Crohn’s disease cohort, 73.3% (11 of 15) had IBD improvement, and 4 (26.6%) had no disease activity change. Among the ulcerative colitis cohort, 62% (22 of 34) had IBD improvement, 29.4% (11 of 34) had no change, and 4% (1 of 34) experienced a de novo flare. Alpha diversity significantly increased post-FMT, and ulcerative colitis patients became more similar to the donor than Crohn’s disease patients (P = 0.04).This prospective trial assessing FMT in IBD-CDI patients suggests IBD outcomes are better than reported in retrospective studies. |
| **Date** | 2021-09-01 |
| **Library Catalog** | Silverchair |
| **URL** | <https://doi.org/10.1093/ibd/izaa283> |
| **Accessed** | 6/15/2025, 4:23:23 PM |
| **Volume** | 27 |
| **Pages** | 1371-1378 |
| **Publication** | Inflammatory Bowel Diseases |
| **DOI** | [10.1093/ibd/izaa283](http://doi.org/10.1093/ibd/izaa283) |
| **Issue** | 9 |
| **Journal Abbr** | Inflammatory Bowel Diseases |
| **ISSN** | 1078-0998 |
| **Date Added** | 6/15/2025, 4:23:23 PM |
| **Modified** | 6/15/2025, 4:23:23 PM |

* **Attachments**
  + Full Text PDF
* **Intestinal macrophages and their interaction with the enteric nervous system in health and inflammatory bowel disease**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Elisa Meroni |
| **Author** | Nathalie Stakenborg |
| **Author** | Maria Francesca Viola |
| **Author** | Guy E. Boeckxstaens |
| **Abstract** | Over the past decades, there has been an increasing understanding of cellular and molecular mechanisms that mediate modulation of the immune system by the autonomic nervous system. The discovery that vagal nerve stimulation (VNS) attenuates endotoxin-induced experimental sepsis paved the way for further studies investigating neuro-immune interaction. In particular, great attention is now given to intestinal macrophages: several studies report the existence of both intrinsic and extrinsic neural mechanisms by which intestinal immune homoeostasis can be regulated in different layers of the intestine, mainly by affecting macrophage activation through neurotransmitter release. Given the important role of inflammation in numerous disease processes, such as inflammatory bowel disease (IBD), cholinergic anti-inflammatory mechanisms are under intense investigation both from a basic and clinical science perspective in immune-mediated diseases such as IBD. This review discusses recent insights on the cross-talk between enteric neurons and the immune system, especially focusing on macrophages, and provides an overview of basic and translational aspects of the cholinergic anti-inflammatory response as therapeutic alternative to reinstall immune homoeostasis in intestinal chronic inflammation. |
| **Date** | 2019 |
| **Language** | en |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1111/apha.13163> |
| **Accessed** | 6/15/2025, 4:22:44 PM |
| **Rights** | © 2018 The Authors. Acta Physiologica published by John Wiley & Sons Ltd on behalf of Scandinavian Physiological Society |
| **Extra** | \_eprint: https://onlinelibrary.wiley.com/doi/pdf/10.1111/apha.13163 |
| **Volume** | 225 |
| **Pages** | e13163 |
| **Publication** | Acta Physiologica |
| **DOI** | [10.1111/apha.13163](http://doi.org/10.1111/apha.13163) |
| **Issue** | 3 |
| **ISSN** | 1748-1716 |
| **Date Added** | 6/15/2025, 4:22:44 PM |
| **Modified** | 6/15/2025, 4:22:44 PM |

* **Tags:**
  + inflammatory bowel disease
  + enteric nervous system
  + macrophages
  + cholinergic anti-inflammatory pathway
  + vagal nerve stimulation

**Attachments**

* + Full Text PDF
* **Involvement of MAPK/NF-κB Signaling in the Activation of the Cholinergic Anti-Inflammatory Pathway in Experimental Colitis by Chronic Vagus Nerve Stimulation**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Peng Sun |
| **Author** | Kewen Zhou |
| **Author** | Sheng Wang |
| **Author** | Ping Li |
| **Author** | Sijuan Chen |
| **Author** | Guiping Lin |
| **Author** | Yan Zhao |
| **Author** | Tinghuai Wang |
| **Abstract** | BackgroundAutonomic nervous system dysfunction is implicated in the etiopathogenesis of inflammatory bowel diseases (IBD). Therapies that increase cardiovagal activity, such as Mind-Body interventions, are currently confirmed to be effective in clinical trials in IBD. However, a poor understanding of pathophysiological mechanisms limits the popularization of therapies in clinical practice. The aim of the present study was to explore the mechanisms of these therapies against 2,4,6-trinitrobenzenesulfonic acid (TNBS)-induced colitis in rats using a chronic vagus nerve stimulation model in vivo, as well as the lipopolysaccharide (LPS)-induced inflammatory response in human epithelial colorectal adenocarcinoma cells (Caco-2) by acetylcholine in vitro. Methods and ResultsColitis was induced in rats with rectal instillation of TNBS, and the effect of chronic VNS (0.25 mA, 20 Hz, 500 ms) on colonic inflammation was evaluated. Inflammatory responses were assessed by disease activity index (DAI), histological scores, myeloperoxidase (MPO) activity, inducible nitric oxide synthase (iNOS), TNF-α and IL-6 production. The expression of Mitogen-activated protein kinases (MAPK) family members, IκB-α, and nuclear NF-κB p65 were studied by immunoblotting. Heart rate variability (HRV) analysis was also applied to assess the sympathetic-vagal balance. DAI, histological scores, MPO activity, iNOS, TNF-α and IL-6 levels were significantly decreased by chronic VNS. Moreover, both VNS and acetylcholine reduced the phosphorylation of MAPKs and prevented the nuclear translocation of NF-κB p65. Methyllycaconitine (MLA) only reversed the inhibitory effect on p-ERK and intranuclear NF-κB p65 expression by ACh in vitro, no significant change was observed in the expression of p-p38 MAPK or p-JNK by MLA. ConclusionVagal activity modification contributes to the beneficial effects of the cholinergic anti-inflammatory pathway in IBD-related inflamed colonic mucosa based on the activation of MAPKs and nuclear translocation of NF-κB. Our work may provide key pathophysiological mechanistic evidence for novel therapeutic strategies that increase the cardiovagal activity in IBD patients. |
| **Date** | Aug 2, 2013 |
| **Language** | en |
| **Library Catalog** | PLoS Journals |
| **URL** | <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0069424> |
| **Accessed** | 6/15/2025, 4:23:01 PM |
| **Extra** | Publisher: Public Library of Science |
| **Volume** | 8 |
| **Pages** | e69424 |
| **Publication** | PLOS ONE |
| **DOI** | [10.1371/journal.pone.0069424](http://doi.org/10.1371/journal.pone.0069424) |
| **Issue** | 8 |
| **Journal Abbr** | PLOS ONE |
| **ISSN** | 1932-6203 |
| **Date Added** | 6/15/2025, 4:23:01 PM |
| **Modified** | 6/15/2025, 4:23:01 PM |

* **Tags:**
  + Inflammation
  + Colon
  + Inflammatory bowel disease
  + Colitis
  + Acetylcholine
  + Caco-2 cells
  + MAPK signaling cascades
  + Transcription factors

**Attachments**

* + Full Text PDF
* **Is-there a place for vagus nerve stimulation in inflammatory bowel diseases?**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Bruno Bonaz |
| **Abstract** | The vagus nerve (VN), the longest nerve of the organism that innervates the gastrointestinal tract, is a mixed nerve composed of 80% of afferent and 20% of efferent fibers. The VN has anti-inflammatory properties, in particular an anti-TNFα effect through the cholinergic anti-inflammatory pathway. The VN is a key component of the autonomic nervous system, i.e. the parasympathetic nervous system. An imbalance of the autonomic nervous system, as represented by a low vagal tone, is described in many diseases and has a pro-inflammatory role. Inflammatory bowel diseases (IBD) are chronic disorders of the gastro-intestinal tract where TNFα is a key cytokine. VN stimulation (VNS), classically used for the treatment of drug resistant epilepsy and depression, would be of interest in the treatment of IBD. We have recently reported in a 6 month follow-up pilot study that VNS improves active Crohn’s disease. Preliminary data of another pilot study confirm this interest. Similarly, VNS has recently been reported to improve rheumatoid arthritis, another TNFα mediated disease. Bioelectronic Medicine, as represented by VNS, opens new therapeutic avenues in the treatment of such chronic inflammatory disorders. In the present manuscript, we will focus on the interest of VNS in IBD. |
| **Date** | 2018-04-03 |
| **Library Catalog** | BioMed Central |
| **URL** | <https://doi.org/10.1186/s42234-018-0004-9> |
| **Accessed** | 6/15/2025, 4:23:04 PM |
| **Volume** | 4 |
| **Pages** | 4 |
| **Publication** | Bioelectronic Medicine |
| **DOI** | [10.1186/s42234-018-0004-9](http://doi.org/10.1186/s42234-018-0004-9) |
| **Issue** | 1 |
| **Journal Abbr** | Bioelectronic Medicine |
| **ISSN** | 2332-8886 |
| **Date Added** | 6/15/2025, 4:23:04 PM |
| **Modified** | 6/15/2025, 4:23:04 PM |

* **Tags:**
  + Inflammatory bowel diseases
  + Vagus nerve
  + Vagus nerve stimulation
  + Cholinergic anti-inflammatory pathway

**Attachments**

* + Full Text PDF
* **Long-Term Oncologic Outcome following Duodenum-Preserving Pancreatic Head Resection for Benign Tumors, Cystic Neoplasms, and Neuroendocrine Tumors: Systematic Review and Meta-analysis**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Hans G Beger |
| **Author** | Benjamin Mayer |
| **Author** | Bertram Poch |
| **Date** | 2024 |
| **URL** | <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11164799/> |
| **Volume** | 31 |
| **Pages** | 4637–4653 |
| **Publication** | Annals of Surgical Oncology |
| **DOI** | [10.1245/s10434-024-15222-y](http://doi.org/10.1245/s10434-024-15222-y) |
| **Issue** | 7 |
| **Date Added** | 4/16/2025, 11:10:32 PM |
| **Modified** | 6/16/2025, 1:12:21 PM |

* **Tags:**
  + Adult
  + Female
  + Humans
  + Male
  + Treatment Outcome
  + Animals
  + Disease Models, Animal
  + Mice
  + STING
  + Quality of Life
  + Retrospective Studies
  + Diabetes
  + Signal Transduction
  + Cell Differentiation
  + Cell Line
  + Neoplasm Recurrence, Local
  + Cell Movement
  + Mammals
  + Neurons
  + immune cells
  + inflammation
  + Homeostasis
  + Gastroenterology
  + intestinal organoids
  + Regeneration
  + microbiota
  + Pancreas
  + inflammatory bowel disease
  + \*Cell- and Tissue-Based Therapy/methods
  + \*Bile Duct Neoplasms
  + \*Bile Duct Neoplasms/surgery
  + \*Cell Lineage
  + \*Cholangiocarcinoma
  + \*Cholangiocarcinoma/pathology
  + \*Colitis, Ulcerative/drug therapy
  + \*Cystadenocarcinoma/diagnostic imaging/surgery
  + \*Cystadenoma/diagnostic imaging/surgery
  + \*Cysts/pathology
  + \*Diabetes Mellitus, Experimental/complications/genetics/metabolism
  + \*Enteric Nervous System
  + \*Enteric Nervous System/pathology
  + \*Hyperglycemia/genetics/metabolism
  + \*Hypothalamo-Hypophyseal System
  + \*Inflammatory Bowel Diseases/drug therapy
  + \*Liver Neoplasms/diagnostic imaging/surgery
  + \*Liver Neoplasms/surgery
  + \*Microbiota
  + \*MicroRNAs/metabolism
  + \*Neoplasms, Cystic, Mucinous, and Serous
  + \*Neuroglia/physiology
  + \*Zebrafish
  + 16S RNA sequencing
  + Acinar cell carcinoma
  + Aging
  + antibiotics
  + Bile Ducts, Intrahepatic
  + Bile Ducts, Intrahepatic/surgery
  + Biliary
  + Biliary cystadenocarcinoma
  + Biliary cystadenoma
  + Brain
  + Brain-Gut Axis
  + Brain/physiology
  + Cell Separation
  + Chemical coding
  + Chick Embryo
  + circVPS13A
  + Cistoadenocarcinoma
  + Cistoadenoma
  + Clinicopathological criteria, Surgical outcomes
  + Colon/drug effects/pathology
  + Cystadenocarcinoma
  + Cystadenoma
  + cystic liver lesions
  + Cystic liver neoplasm
  + Cytology
  + Developmental disorders
  + diabetes
  + diabetes mellitus
  + Drug Discovery/\*methods
  + Embryonic stem cells
  + ENS
  + ENS neuropathies
  + enteric glia
  + enteric glia communications
  + Enteric glia communications
  + enteric glia diversity
  + enteric nervous system
  + Enteric nervous system
  + Enteric Nervous System
  + enteric nervous system (ENS)
  + Enteric nervous system (ENS)
  + Enteric Nervous System/\*pathology
  + Enteric neural precursor cells (ENPCs)
  + enteric progenitor cell
  + Fecal microbiota transplantation
  + Frantz's tumor
  + gastrointestinal complications
  + gastrointestinal diseases
  + Gastrointestinal Diseases
  + Gastrointestinal Diseases/pathology
  + gastrointestinal tract
  + Gastrointestinal Tract/drug effects/pathology
  + glia
  + Glial Cell Line-Derived Neurotrophic Factor/genetics
  + glucagon-like peptide 1
  + Growth Disorders
  + growth retardation
  + gut brain axis
  + gut microbiota
  + gut-brain axis
  + gut–brain axis
  + hepatic cystadenocarcinoma
  + hepatic cystadenoma
  + Hepatic simple cyst
  + hepatobiliary cystadenocarcinoma
  + hepatobiliary cystadenoma
  + Hirschsprung disease
  + Hirschsprung Disease/\*drug therapy/\*pathology/therapy
  + homeostasis
  + Imaging modalities
  + In Situ Hybridization, Fluorescence
  + Inflammatory bowel diseases
  + Intraductal papillary biliary neoplasms
  + intraductal papillary neoplasms of bile duct
  + irritable bowel syndrome
  + L-Fucose
  + Liver Diseases
  + Management
  + microbial metabolites
  + microbiota-gut-brain axis
  + Microbiota-gut-brain axis
  + Mucinous biliary cystic tumors, Biliary cystadenoma
  + mucinous cystic neoplasm
  + Mucinous cystic neoplasms
  + Mucinous neoplasm
  + muscularis macrophages
  + myenteric neurons
  + Neoplasia mucinosa quística
  + Neoplasia papilar intraductal biliar
  + Neoplasia quística hepática
  + Neural Crest
  + neural crest cell
  + neurodegeneration
  + Neuroglia
  + Neurons/drug effects/\*pathology
  + offspring
  + P2X7 receptor
  + pancreatectomy
  + Pancreatectomy
  + Pancreatic neoplasms
  + Pancreatic Neoplasms
  + Pancreatic surgery
  + pancreatic tumor
  + Parkinson’s disease
  + pediatric pancreatic neoplasm
  + Pepstatins/metabolism
  + Pituitary-Adrenal System
  + pluripotent stem cells (PSCs)
  + Pluripotent Stem Cells/pathology
  + preconception
  + probiotic
  + Purinergic signaling
  + Receptor, Endothelin B/metabolism
  + Receptors, Purinergic P2X7
  + RNA, Circular/genetics
  + Rotenone-induced mouse model
  + short-chain fatty acids
  + Solid pseudopapillary tumor
  + Stem-cell differentiation
  + submucosal neurons
  + Submucous Plexus
  + surgical outcome
  + surgical resection
  + three-dimensional (3D)
  + type 2 diabetes
  + zebrafish

**Notes:**

* + e14603 NMO-00132-2023
  + e14603 NMO-00132-2023

**Attachments**

* + Full Text
  + Full Text
  + Full Text PDF
  + Full Text PDF
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  + PubMed Central Full Text PDF
  + PubMed Central Full Text PDF
  + PubMed Central Full Text PDF
  + PubMed Central Link
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  + PubMed entry
* **P0174 Enteric glial cells-derived NGF prevents necroptosis of intestinal epithelial cells and alleviates DSS-induced colitis**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Z Min |
| **Author** | Y Zhang |
| **Author** | C Hu |
| **Author** | X Song |
| **Author** | H Guo |
| **Abstract** | The maintenance and repair of the intestinal epithelial barrier (IEB) is a multifaceted process that requires the coordinated participation of different cell types within the gastrointestinal tract. Studies have shown that ablation of enteric glial cells (EGCs) can lead to intestinal epithelial cell necrosis and destruction of the IEB. However, the specific role of EGCs in it remains ambiguous. The aim of this study was to elucidate the potential role of EGCs in regulating IEB and intestinal inflammation.In this study，we employed immunofluorescence, western blot, ELISA, and gene expression profiling to assess the expression of GFAP (a marker for EGCs), NGF, and necroptosis-associated proteins in intestinal tissues from IBD patients. In addition, DSS-induced colitis mouse models, in vitro co-culture systems, and transcriptomic analysis were used to explore the effects of EGCs and NGF on IECs necroptosis and inflammation.In intestinal tissues of IBD patients, reduced expression of GFAP and S100β suggests damage to EGCs. Additionally, we found that NGF in intestinal tissues primarily originates from EGCs. Diminished NGF secretion due to EGCs damage correlates with increased necroptosis of IECs. Exogenous administration of NGF inhibits DSS-induced necroptosis of IECs and alleviates colonic inflammation. Ablation of EGCs exacerbates necroptosis of IECs, disruption of IEB, and intestinal inflammation following DSS treatment. In vitro co-culture experiments demonstrate that EGCs suppress necroptosis of IECs induced by T/S/Z mix. Further flow cytometry and TEM results confirm that NGF effectively mitigates T/S/Z mix-induced necroptosis of IECs.Transcriptomic sequencing indicated that RNF126 is a downstream target in the NGF signaling pathway, potentially mediating the protective effects of EGCs-derived NGF on IECs.Based on the findings from this study, it is evident that EGCs play a crucial role in maintaining intestinal homeostasis through their production of NGF. Reduced NGF secretion from damaged EGCs correlates with increased necroptosis of IECs, exacerbating inflammation in colonic tissues. Exogenous NGF administration effectively attenuates this process, highlighting its therapeutic potential in IBD. Furthermore, transcriptomic analysis identified RNF126 as a downstream mediator in the NGF signaling pathway, its specific role remains speculative and requires further investigation to elucidate its mechanistic involvement in mediating the protective effects of NGF. In conclusion, these findings emphasize the intricate interplay between EGCs, NGF signaling, and IEC survival, pointing towards novel therapeutic strategies targeting this pathway in IBD management. |
| **Date** | 2025-01-01 |
| **Library Catalog** | Silverchair |
| **URL** | <https://doi.org/10.1093/ecco-jcc/jjae190.0348> |
| **Accessed** | 6/15/2025, 4:22:54 PM |
| **Volume** | 19 |
| **Pages** | i575 |
| **Publication** | Journal of Crohn's and Colitis |
| **DOI** | [10.1093/ecco-jcc/jjae190.0348](http://doi.org/10.1093/ecco-jcc/jjae190.0348) |
| **Issue** | Supplement\_1 |
| **Journal Abbr** | Journal of Crohn's and Colitis |
| **ISSN** | 1876-4479 |
| **Date Added** | 6/15/2025, 4:22:54 PM |
| **Modified** | 6/15/2025, 4:22:54 PM |

* **Attachments**
  + Full Text PDF
* **P0180 Bifidobacterium longum alleviates dextran sulfate sodium-induced colitis through the differential regulation of Toll-like receptor 5 on enteric glial cells**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Q S Zeng |
| **Author** | M Zou |
| **Author** | H Gan |
| **Abstract** | Inflammatory bowel disease (IBD) is a chronic immune-associated disease arising from gastrointestinal dysbiosis and subsequent immunological dysfunction. Numerous studies have reported the beneficial effects of probiotics, such as Bifidobacterium longum (BL), on IBD, while the related mechanism behind these effects have not been fully elucidated. Enteric nervous system abnormalities have increasingly been tied to the pathogenesis of IBD, with a particular focus on the role of enteric glial cells (EGC) in this context. In this study, we aim to explore the mechanism of probiotics in the treatment of IBD from the perspective of EGC.On base of C57BL/6 mouse, TLR5 of EGC knockdown mouse model (TLR5 KD mouse) was constructed by adeno-associated virus (serum type 6) (AAV6) which carried the interference sequence of TLR5 gene (AAV6-TLR5-RNAi). Experimental colitis was induced by dextran sulfate sodium (DSS). Mice were treated with phosphate buffer solution (PBS) or BL. Disease activity index (DAI) and histological score were applied to assess the severity of colitis. The level of GDNF、IL-1β of colonic tissue were measured by ELISA. The expression of glial fibrillary acidic protein (GFAP)、toll-like receptor 5 (TLR5)、cleaved caspase-3 of colonic tissue were tested by immunofluorescence staining and quantitative PCR (qPCR).EGC cell line, EGC CRL2690, was exposed to probiotic (Bifidobacterium longum; BL) bacteria and pathogenic (Enterohemorrhagic Escherichia coli; EHEC). Cell apoptosis rate was assessed by flow cytometry. TLRs expression in EGC CRL2690 were evaluated at both baseline and after exposure to bacteria by qPCR and western blot analysis. GDNF and IL-1β release from EGC CRL2690, following exposure to bacteria, were measured in the presence or absence of specific TLR and pathway inhibitors.The results showed that BL ameliorated DSS-induced colitis accompanied by increased expression of GDNF, while pathogenic EHEC aggravated DSS-induced colitis combined with decreased expression of GDNF. Mechanistically, BL could up-regulate the secretion of GDNF via TLR5/p38 MAPK pathway in EGC, which was different from EHEC, which could up-regulate the secretion of IL-1β through TLR2/NF-κB pathway.Our results suggested a new possible mechanism whereby probiotics ameliorate DSS-induced colitis in mice by regulating EGC via TLR5, namely, BL promotes GDNF secretion in EGC through activation of p38 MAPK signaling pathway by TLR5. Meanwhile, our results suggested that probiotic, pathogenic bacteria appeared to influence the development of intestinal inflammation by differentially modulating the secretion function of EGC via different TLRs. |
| **Date** | 2025-01-01 |
| **Library Catalog** | Silverchair |
| **URL** | <https://doi.org/10.1093/ecco-jcc/jjae190.0354> |
| **Accessed** | 6/15/2025, 4:23:12 PM |
| **Volume** | 19 |
| **Pages** | i581 |
| **Publication** | Journal of Crohn's and Colitis |
| **DOI** | [10.1093/ecco-jcc/jjae190.0354](http://doi.org/10.1093/ecco-jcc/jjae190.0354) |
| **Issue** | Supplement\_1 |
| **Journal Abbr** | Journal of Crohn's and Colitis |
| **ISSN** | 1876-4479 |
| **Date Added** | 6/15/2025, 4:23:12 PM |
| **Modified** | 6/15/2025, 4:23:12 PM |

* **Attachments**
  + Full Text PDF
* **Phytocannabinoids Reduce Inflammation of Primed Macrophages and Enteric Glial Cells: An In Vitro Study**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Gal Cohen |
| **Author** | Ofer Gover |
| **Author** | Betty Schwartz |
| **Abstract** | Intestinal inflammation is mediated by a subset of cells populating the intestine, such as enteric glial cells (EGC) and macrophages. Different studies indicate that phytocannabinoids could play a possible role in the treatment of inflammatory bowel disease (IBD) by relieving the symptoms involved in the disease. Phytocannabinoids act through the endocannabinoid system, which is distributed throughout the mammalian body in the cells of the immune system and in the intestinal cells. Our in vitro study analyzed the putative anti-inflammatory effect of nine selected pure cannabinoids in J774A1 macrophage cells and EGCs triggered to undergo inflammation with lipopolysaccharide (LPS). The anti-inflammatory effect of several phytocannabinoids was measured by their ability to reduce TNFα transcription and translation in J774A1 macrophages and to diminish S100B and GFAP secretion and transcription in EGCs. Our results demonstrate that THC at the lower concentrations tested exerted the most effective anti-inflammatory effect in both J774A1 macrophages and EGCs compared to the other phytocannabinoids tested herein. We then performed RNA-seq analysis of EGCs exposed to LPS in the presence or absence of THC or THC-COOH. Transcriptomic analysis of these EGCs revealed 23 differentially expressed genes (DEG) compared to the treatment with only LPS. Pretreatment with THC resulted in 26 DEG, and pretreatment with THC-COOH resulted in 25 DEG. To evaluate which biological pathways were affected by the different phytocannabinoid treatments, we used the Ingenuity platform. We show that THC treatment affects the mTOR and RAR signaling pathway, while THC-COOH mainly affects the IL6 signaling pathway. |
| **Date** | 2023/1 |
| **Language** | en |
| **Short Title** | Phytocannabinoids Reduce Inflammation of Primed Macrophages and Enteric Glial Cells |
| **Library Catalog** | www.mdpi.com |
| **URL** | <https://www.mdpi.com/1422-0067/24/19/14628> |
| **Accessed** | 6/15/2025, 4:23:26 PM |
| **Rights** | http://creativecommons.org/licenses/by/3.0/ |
| **Extra** | Number: 19 Publisher: Multidisciplinary Digital Publishing Institute |
| **Volume** | 24 |
| **Pages** | 14628 |
| **Publication** | International Journal of Molecular Sciences |
| **DOI** | [10.3390/ijms241914628](http://doi.org/10.3390/ijms241914628) |
| **Issue** | 19 |
| **ISSN** | 1422-0067 |
| **Date Added** | 6/15/2025, 4:23:26 PM |
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* **Tags:**
  + enteric glial cells
  + J774A1 M1 macrophages
  + phytocannabinoids

**Attachments**

* + Full Text PDF
* **Vagus nerve-mediated intestinal immune regulation: therapeutic implications of inflammatory bowel diseases**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Yohei Mikami |
| **Author** | Junya Tsunoda |
| **Author** | Hiroki Kiyohara |
| **Author** | Nobuhito Taniki |
| **Author** | Toshiaki Teratani |
| **Author** | Takanori Kanai |
| **Abstract** | The pathophysiology of inflammatory bowel diseases (IBDs) involves immunological, genetic and environmental factors. Through its ability to sense environmental stimuli, the autonomic nervous system plays a key role in the development and persistence of IBDs. The vagus nerve (VN), which contains sensory and motor neurons, travels throughout the body to innervate the gut and other visceral organs in the thoracic and abdominopelvic cavities. Recent studies show that the VN has anti-inflammatory effects via the release of acetylcholine, in what is known as the cholinergic anti-inflammatory pathway (CAIP). In the gut immune system, the CAIP is proposed to be activated directly by signals from the gut and indirectly by signals from the liver, which receives gut-derived bioactive substances via the portal vein and senses the status of the gut. The gut–brain axis and liver–brain–gut reflex arc regulate a wide variety of peripheral immune cells to maintain homeostasis in the gut. Therefore, targeting the neural reflex by methods such as VN stimulation is now under investigation for suppressing intestinal inflammation associated with IBDs. In this review, we describe the role of the VN in the regulation of intestinal immunity, and we discuss novel therapeutic approaches for IBDs that target neuroimmune interactions. |
| **Date** | 2022-02-01 |
| **Short Title** | Vagus nerve-mediated intestinal immune regulation |
| **Library Catalog** | Silverchair |
| **URL** | <https://doi.org/10.1093/intimm/dxab039> |
| **Accessed** | 6/15/2025, 4:23:33 PM |
| **Volume** | 34 |
| **Pages** | 97-106 |
| **Publication** | International Immunology |
| **DOI** | [10.1093/intimm/dxab039](http://doi.org/10.1093/intimm/dxab039) |
| **Issue** | 2 |
| **Journal Abbr** | International Immunology |
| **ISSN** | 1460-2377 |
| **Date Added** | 6/15/2025, 4:23:33 PM |
| **Modified** | 6/15/2025, 4:23:33 PM |

* **Attachments**
  + Full Text PDF
* **WKB ameliorates DSS-induced colitis through inhibiting enteric glial cells activation and altering the intestinal microbiota**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Qi Sun |
| **Author** | Bai-Rong Li |
| **Author** | Dong-Hao Li |
| **Author** | Xiao-Ying Wang |
| **Author** | Qian-Yi Wang |
| **Author** | Zhi-Meng Jiang |
| **Author** | Shou-Bin Ning |
| **Author** | Tao Sun |
| **Abstract** | Inflammatory bowel disease (IBD) is a chronic condition influenced by diet, which affects gut microbiota and immune functions. The rising prevalence of IBD, linked to Western diets in developing countries, highlights the need for dietary interventions. This study aimed to assess the impact of white kidney beans (WKB) on gut inflammation and microbiota changes, focusing on their effects on enteric glial cells (EGCs) and immune activity in colitis. |
| **Date** | 2025-01-21 |
| **Library Catalog** | BioMed Central |
| **URL** | <https://doi.org/10.1186/s12967-025-06085-2> |
| **Accessed** | 6/15/2025, 4:23:38 PM |
| **Volume** | 23 |
| **Pages** | 93 |
| **Publication** | Journal of Translational Medicine |
| **DOI** | [10.1186/s12967-025-06085-2](http://doi.org/10.1186/s12967-025-06085-2) |
| **Issue** | 1 |
| **Journal Abbr** | Journal of Translational Medicine |
| **ISSN** | 1479-5876 |
| **Date Added** | 6/15/2025, 4:23:38 PM |
| **Modified** | 6/15/2025, 4:23:38 PM |

* **Tags:**
  + Microbiota
  + Enteric glial cells
  + Inflammatory bowel disease
  + Colitis
  + Th1/Th17/Treg balance
  + White kidney beans

**Attachments**

* + Full Text PDF

## Chronic Intestinal Pseudo-obstruction: Assessment and Management

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Frances L. Connor |
| **Author** | Carlo Di Lorenzo |
| **Date** | 2006-02-01 |
| **Language** | English |
| **Short Title** | Chronic Intestinal Pseudo-obstruction |
| **Library Catalog** | www.gastrojournal.org |
| **URL** | <https://www.gastrojournal.org/article/S0016-5085(05)02411-X/fulltext> |
| **Accessed** | 6/15/2025, 4:39:01 PM |
| **Extra** | Publisher: Elsevier |
| **Volume** | 130 |
| **Pages** | S29-S36 |
| **Publication** | Gastroenterology |
| **DOI** | [10.1053/j.gastro.2005.06.081](http://doi.org/10.1053/j.gastro.2005.06.081) |
| **Issue** | 2 |
| **Journal Abbr** | Gastroenterology |
| **ISSN** | 0016-5085, 1528-0012 |
| **Date Added** | 6/15/2025, 4:39:01 PM |
| **Modified** | 6/15/2025, 4:39:01 PM |

### Tags:

* + chronic intestinal pseudo-obstruction
  + CIPO

### Attachments

* + Full Text PDF

## Comprehensive analysis of adverse drug reactions associated with teduglutide: post-marketing insights and safety implications

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Praneeth Kudaravalli |
| **Author** | Andrews ,Michael B. |
| **Author** | Douglas G. and Adler |
| **Abstract** | Intestinal failure often necessitates teduglutide, a glucagon-like peptide-2 (GLP-2) analog that enhances intestinal adaptation by increasing absorptive surface area, thereby reducing reliance on intravenous supplementation (IVS). This study analyzes adverse drug reactions (ADRs) associated with teduglutide when used to treat short bowel syndrome (SBS) to inform clinical practice and enhance post-marketing surveillance. Retrospective analysis was conducted using the FDA Adverse Event Reporting System (FAERS) database. ADRs reported from teduglutide’s FDA approval in 2012 through 20 August 2024 were analyzed using descriptive statistics and presented as [N (%)] or [median (IQR)]. Of the 4,533 reports, 2,669 were females, and patients had a median age of 56 years, with 2,787 reports involving hospitalization and 443 associated with death. Gastrointestinal ADRs were the most frequently reported (N = 3,881), followed by infections (N = 2,273), cardiovascular events (N = 1,318), weight changes (N = 754), neuropsychiatric concerns (N = 651), and device-related infections (N = 618) were prominent. Mortality associated ADRs included infections (N = 222), gastrointestinal events (N = 172), and cardiovascular complications (N = 132). Teduglutide is associated with significant ADRs necessitating vigilant monitoring while managing SBS patients, particularly for gastrointestinal health and infection risks. FAERS data limitations restrict causality determination, highlighting the need for further research to optimize safety. |
| **Short Title** | Comprehensive analysis of adverse drug reactions associated with teduglutide |
| **Library Catalog** | Taylor and Francis+NEJM |
| **URL** | <https://doi.org/10.1080/14740338.2025.2493355> |
| **Accessed** | 6/15/2025, 4:39:22 PM |
| **Extra** | Publisher: Taylor & Francis \_eprint: https://doi.org/10.1080/14740338.2025.2493355 PMID: 40219687 |
| **Volume** | 0 |
| **Pages** | 1-6 |
| **Publication** | Expert Opinion on Drug Safety |
| **DOI** | [10.1080/14740338.2025.2493355](http://doi.org/10.1080/14740338.2025.2493355) |
| **Issue** | 0 |
| **ISSN** | 1474-0338 |
| **Date Added** | 6/15/2025, 4:39:22 PM |
| **Modified** | 6/15/2025, 4:39:22 PM |

### Tags:

* + short bowel syndrome
  + Adverse drug reactions
  + adverse events
  + FAERS
  + teduglutide

## Impact of cryopreservation on viability, gene expression and function of enteric nervous system derived neurospheres

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Sabine Heumüller-Klug |
| **Author** | Kristina Maurer |
| **Author** | María Á Tapia-Laliena |
| **Author** | Carsten Sticht |
| **Author** | Anne Christmann |
| **Author** | Handan Mörz |
| **Author** | Rasul Khasanov |
| **Author** | Elvira Wink |
| **Author** | Steven Schulte |
| **Author** | Wolfgang Greffrath |
| **Author** | Rolf-Detlef Treede |
| **Author** | Lucas M. Wessel |
| **Author** | Karl-Herbert Schäfer |
| **Abstract** | Impairment of both the central and peripheral nervous system is a major cause of mortality and disability. It varies from affection of the brain to various types of enteric dysganglionosis. Congenital enteric dysganglionosis is characterized by the local absence of intrinsic innervation due to deficits in either migration, proliferation or differentiation of neural stem cells. Despite surgery, children´s quality of life is reduced. Neural stem cell transplantation seems a promising therapeutic approach, requiring huge amounts of cells and multiple approaches to fully colonize diseased areas completely. A combination of expansion and storage of neural stem cells is needed until a sufficient amount of cells is generated. This must be combined with suitable cell transplantation strategies, that cover all the area affected. Cryopreservation provides the possibility to store cells for long time, unfortunately with side effects, i.e. upon vitality. In this study we investigate the impact of different freezing protocols (M1-M4) upon enteric neural stem cell survival, protein and gene expression, and cell function. Freezing enteric nervous system derived neurospheres (ENSdN) following slow-freezing protocols (M1-3) resulted in higher survival rates than flash-freezing (M4). RNA expression profiles were least affected by freezing protocols M1/2, whereas protein expression of ENSdN remained unchanged after treatment with protocol M1 only. Cells treated with the most promising freezing protocol (M1, slow freezing in fetal calf serum plus 10 % DMSO) were subsequently investigated using single-cell calcium imaging. Freezing of ENSdN did not alter the increase in intracellular calcium in response to a specific set of stimuli. Single cells could be assigned to functional subgroups according to response patterns and a significant shift towards cells responding to nicotine was observed after freezing. The results demonstrate that cryopreservation of ENSdN is possible with reduced viability, only slight changes in protein/gene expression patterns and without impact on neuronal function of different enteric nervous system cell subtypes, with the exception of a subtle upregulation of cells expressing nicotinergic acetylcholine receptors. In summary, cryopreservation presents a good method to store sufficient amounts of enteric neural stem cells without neuronal impairment, in order to enable subsequent transplantation of cells into compromised tissues. |
| **Date** | 2023-06-12 |
| **Language** | English |
| **Library Catalog** | Frontiers |
| **URL** | <https://www.frontiersin.org/journals/cell-and-developmental-biology/articles/10.3389/fcell.2023.1196472/full> |
| **Accessed** | 6/15/2025, 4:39:57 PM |
| **Extra** | Publisher: Frontiers |
| **Volume** | 11 |
| **Publication** | Frontiers in Cell and Developmental Biology |
| **DOI** | [10.3389/fcell.2023.1196472](http://doi.org/10.3389/fcell.2023.1196472) |
| **Journal Abbr** | Front. Cell Dev. Biol. |
| **ISSN** | 2296-634X |
| **Date Added** | 6/15/2025, 4:39:57 PM |
| **Modified** | 6/15/2025, 4:39:57 PM |

### Tags:

* + Enteric Nervous System
  + Aganglionosis
  + Calcium imagaing
  + Cell Transplantation
  + Cryopreservation
  + enteric neurospheres
  + Freezing

### Attachments

* + Full Text PDF

## Long-Term Oncologic Outcome following Duodenum-Preserving Pancreatic Head Resection for Benign Tumors, Cystic Neoplasms, and Neuroendocrine Tumors: Systematic Review and Meta-analysis

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Hans G Beger |
| **Author** | Benjamin Mayer |
| **Author** | Bertram Poch |
| **Date** | 2024 |
| **URL** | <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11164799/> |
| **Volume** | 31 |
| **Pages** | 4637–4653 |
| **Publication** | Annals of Surgical Oncology |
| **DOI** | [10.1245/s10434-024-15222-y](http://doi.org/10.1245/s10434-024-15222-y) |
| **Issue** | 7 |
| **Date Added** | 4/16/2025, 11:10:32 PM |
| **Modified** | 6/16/2025, 1:12:21 PM |

### Tags:

* + Adult
  + Female
  + Humans
  + Male
  + Treatment Outcome
  + Animals
  + Disease Models, Animal
  + Mice
  + STING
  + Quality of Life
  + Retrospective Studies
  + Diabetes
  + Signal Transduction
  + Cell Differentiation
  + Cell Line
  + Neoplasm Recurrence, Local
  + Cell Movement
  + Mammals
  + Neurons
  + immune cells
  + inflammation
  + Homeostasis
  + Gastroenterology
  + intestinal organoids
  + Regeneration
  + microbiota
  + Pancreas
  + inflammatory bowel disease
  + \*Cell- and Tissue-Based Therapy/methods
  + \*Bile Duct Neoplasms
  + \*Bile Duct Neoplasms/surgery
  + \*Cell Lineage
  + \*Cholangiocarcinoma
  + \*Cholangiocarcinoma/pathology
  + \*Colitis, Ulcerative/drug therapy
  + \*Cystadenocarcinoma/diagnostic imaging/surgery
  + \*Cystadenoma/diagnostic imaging/surgery
  + \*Cysts/pathology
  + \*Diabetes Mellitus, Experimental/complications/genetics/metabolism
  + \*Enteric Nervous System
  + \*Enteric Nervous System/pathology
  + \*Hyperglycemia/genetics/metabolism
  + \*Hypothalamo-Hypophyseal System
  + \*Inflammatory Bowel Diseases/drug therapy
  + \*Liver Neoplasms/diagnostic imaging/surgery
  + \*Liver Neoplasms/surgery
  + \*Microbiota
  + \*MicroRNAs/metabolism
  + \*Neoplasms, Cystic, Mucinous, and Serous
  + \*Neuroglia/physiology
  + \*Zebrafish
  + 16S RNA sequencing
  + Acinar cell carcinoma
  + Aging
  + antibiotics
  + Bile Ducts, Intrahepatic
  + Bile Ducts, Intrahepatic/surgery
  + Biliary
  + Biliary cystadenocarcinoma
  + Biliary cystadenoma
  + Brain
  + Brain-Gut Axis
  + Brain/physiology
  + Cell Separation
  + Chemical coding
  + Chick Embryo
  + circVPS13A
  + Cistoadenocarcinoma
  + Cistoadenoma
  + Clinicopathological criteria, Surgical outcomes
  + Colon/drug effects/pathology
  + Cystadenocarcinoma
  + Cystadenoma
  + cystic liver lesions
  + Cystic liver neoplasm
  + Cytology
  + Developmental disorders
  + diabetes
  + diabetes mellitus
  + Drug Discovery/\*methods
  + Embryonic stem cells
  + ENS
  + ENS neuropathies
  + enteric glia
  + enteric glia communications
  + Enteric glia communications
  + enteric glia diversity
  + enteric nervous system
  + Enteric nervous system
  + Enteric Nervous System
  + enteric nervous system (ENS)
  + Enteric nervous system (ENS)
  + Enteric Nervous System/\*pathology
  + Enteric neural precursor cells (ENPCs)
  + enteric progenitor cell
  + Fecal microbiota transplantation
  + Frantz's tumor
  + gastrointestinal complications
  + gastrointestinal diseases
  + Gastrointestinal Diseases
  + Gastrointestinal Diseases/pathology
  + gastrointestinal tract
  + Gastrointestinal Tract/drug effects/pathology
  + glia
  + Glial Cell Line-Derived Neurotrophic Factor/genetics
  + glucagon-like peptide 1
  + Growth Disorders
  + growth retardation
  + gut brain axis
  + gut microbiota
  + gut-brain axis
  + gut–brain axis
  + hepatic cystadenocarcinoma
  + hepatic cystadenoma
  + Hepatic simple cyst
  + hepatobiliary cystadenocarcinoma
  + hepatobiliary cystadenoma
  + Hirschsprung disease
  + Hirschsprung Disease/\*drug therapy/\*pathology/therapy
  + homeostasis
  + Imaging modalities
  + In Situ Hybridization, Fluorescence
  + Inflammatory bowel diseases
  + Intraductal papillary biliary neoplasms
  + intraductal papillary neoplasms of bile duct
  + irritable bowel syndrome
  + L-Fucose
  + Liver Diseases
  + Management
  + microbial metabolites
  + microbiota-gut-brain axis
  + Microbiota-gut-brain axis
  + Mucinous biliary cystic tumors, Biliary cystadenoma
  + mucinous cystic neoplasm
  + Mucinous cystic neoplasms
  + Mucinous neoplasm
  + muscularis macrophages
  + myenteric neurons
  + Neoplasia mucinosa quística
  + Neoplasia papilar intraductal biliar
  + Neoplasia quística hepática
  + Neural Crest
  + neural crest cell
  + neurodegeneration
  + Neuroglia
  + Neurons/drug effects/\*pathology
  + offspring
  + P2X7 receptor
  + pancreatectomy
  + Pancreatectomy
  + Pancreatic neoplasms
  + Pancreatic Neoplasms
  + Pancreatic surgery
  + pancreatic tumor
  + Parkinson’s disease
  + pediatric pancreatic neoplasm
  + Pepstatins/metabolism
  + Pituitary-Adrenal System
  + pluripotent stem cells (PSCs)
  + Pluripotent Stem Cells/pathology
  + preconception
  + probiotic
  + Purinergic signaling
  + Receptor, Endothelin B/metabolism
  + Receptors, Purinergic P2X7
  + RNA, Circular/genetics
  + Rotenone-induced mouse model
  + short-chain fatty acids
  + Solid pseudopapillary tumor
  + Stem-cell differentiation
  + submucosal neurons
  + Submucous Plexus
  + surgical outcome
  + surgical resection
  + three-dimensional (3D)
  + type 2 diabetes
  + zebrafish

### Notes:

* + e14603 NMO-00132-2023
  + e14603 NMO-00132-2023

### Attachments

* + Full Text
  + Full Text
  + Full Text PDF
  + Full Text PDF
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  + PubMed Central Link
  + PubMed Central Link
  + PubMed Central Link
  + PubMed Central Link
  + PubMed entry

## Muscle hypertrophy and neuroplasticity in the small bowel in short bowel syndrome

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Rasul Khasanov |
| **Author** | Daniel Svoboda |
| **Author** | María Ángeles Tapia-Laliena |
| **Author** | Martina Kohl |
| **Author** | Silke Maas-Omlor |
| **Author** | Cornelia Irene Hagl |
| **Author** | Lucas M. Wessel |
| **Author** | Karl-Herbert Schäfer |
| **Abstract** | Short bowel syndrome (SBS) is a severe, life-threatening condition and one of the leading causes of intestinal failure in children. Here we were interested in changes in muscle layers and especially in the myenteric plexus of the enteric nervous system (ENS) of the small bowel in the context of intestinal adaptation. Twelve rats underwent a massive resection of the small intestine to induce SBS. Sham laparotomy without small bowel transection was performed in 10 rats. Two weeks after surgery, the remaining jejunum and ileum were harvested and studied. Samples of human small bowel were obtained from patients who underwent resection of small bowel segments due to a medical indication. Morphological changes in the muscle layers and the expression of nestin, a marker for neuronal plasticity, were studied. Following SBS, muscle tissue increases significantly in both parts of the small bowel, i.e., jejunum and ileum. The leading pathophysiological mechanism of these changes is hypertrophy. Additionally, we observed an increased nestin expression in the myenteric plexus in the remaining bowel with SBS. Our human data also showed that in patients with SBS, the proportion of stem cells in the myenteric plexus had risen by more than twofold. Our findings suggest that the ENS is tightly connected to changes in intestinal muscle layers and is critically involved in the process of intestinal adaptation to SBS. |
| **Date** | 2023-11-01 |
| **Language** | en |
| **Library Catalog** | Springer Link |
| **URL** | <https://doi.org/10.1007/s00418-023-02214-4> |
| **Accessed** | 6/15/2025, 4:39:09 PM |
| **Volume** | 160 |
| **Pages** | 391-405 |
| **Publication** | Histochemistry and Cell Biology |
| **DOI** | [10.1007/s00418-023-02214-4](http://doi.org/10.1007/s00418-023-02214-4) |
| **Issue** | 5 |
| **Journal Abbr** | Histochem Cell Biol |
| **ISSN** | 1432-119X |
| **Date Added** | 6/15/2025, 4:39:09 PM |
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### Tags:

* + ENS
  + Enteric Nervous System
  + Enteric neuropathies
  + Irritable bowel syndrome
  + Short bowel syndrome
  + Bowel resection
  + Enteric neurons
  + Muscle Physiology
  + Nestin
  + PGP 9.5
  + Short-term potentiation
  + Skeletal Muscle

### Attachments

* + Full Text PDF

## Safety and Efficacy of the Glucagon-like Peptide 2 (GLP-2) Analog Apraglutide in Patients with Steroid-Refractory Gastrointestinal Acute Graft-Versus-Host Disease (aGvHD) in Combination with Best Available Therapy: Results from a Multicenter, Randomized, Single-Blind, Proof-of-Concept, Phase 2 Stargaze Trial

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Robert Zeiser |
| **Author** | Hannah Choe |
| **Author** | Holger Adelmann |
| **Author** | Nader N. Youssef |
| **Author** | Anastasia Eremeeva |
| **Author** | François Collin |
| **Author** | Yi-Bin Chen |
| **Abstract** | Introduction:Acute graft-versus-host disease (aGvHD) is a severe and life-threatening condition that often develops after allogeneic hematopoietic cell transplantation (alloHCT). Approximately 50% of patients (pts) who receive systemic glucocorticoids (GCs) as first-line treatment do not achieve an adequate and durable response and become steroid refractory (SR). Among pts with grade II-IV aGvHD, ~70% have gastrointestinal (GI) involvement, a key driver of morbidity and mortality. GI aGvHD is often steroid-refractory, and despite recent improvements with the availability of ruxolitinib (RUX) as second-line therapy, an unmet need remains for non-immunosuppressive treatments. Preclinical studies have suggested that glucagon-like peptide 2 (GLP-2) analogs protect and regenerate Paneth cells and intestinal stem cells and thus have the potential to improve clinical outcomes in GI aGvHD (Norona J, et al. Blood 2020). The aims of STARGAZE, the first prospective trial of a GLP-2 analog in SR GI aGvHD, are to assess the safety, tolerability, and preliminary efficacy of the GLP-2 analog apraglutide (APRA) in combination with best available therapy in pts with SR lower-GI aGvHD.Methods: In the STARGAZE phase 2 trial (NCT05415410), pts received APRA subcutaneously, once weekly, until Week 7 (up to Week 12 if no lower-GI aGvHD complete response [CR] at Week 8, plus optional treatment up to Week 25), with a follow-up period of up to 2 years after the first dose of APRA. APRA was initiated within 5 days of starting RUX as second-line therapy in pts with an inadequate response to GCs. Eligible pts (aged ≥12 years with grade II-IV SR aGvHD and stage 1-4 lower-GI aGvHD) weighing ≥50 kg were randomized 1:1 to high- or low-dose APRA arms; pts weighing 40.0-49.9 kg received a fixed dose of APRA. The primary endpoints assessed safety and tolerability of APRA. Secondary endpoints included all-organ and lower-GI overall response rates (ORRs) and CR rates on Days 28, 56, and 91. Durable overall response was assessed from Day 28 to Day 56 and from Day 56 to Day 91. Specific values in this prespecified interim analysis may be subject to change in the final analysis.Results: This fully recruited study enrolled 31 pts (high-dose APRA: n=15; low-dose APRA: n=15; fixed dose: n=1); baseline and disease characteristics were well balanced across arms. Twenty-seven (87.1%) pts had grade III-IV aGvHD and 20 (64.5%) pts had lower-GI stage 3-4 aGvHD. APRA was well tolerated, with an acceptable safety profile; most adverse events were non-serious and assessed as not related to APRA treatment, including in the 11 pts who had fatal events. On Days 28, 56, and 91, all-organ ORRs were 58.1%, 51.6%, and 45.2%, respectively, with CR rates of 25.8%, 29.0%, and 29.0%, respectively. Lower-GI ORRs were 54.8%, 51.6%, and 48.4%, respectively, with CR rates of 29.0%, 29.0%, and 32.3%, respectively. Durable overall response from Day 28 to Day 56 was 45.2% for both all-organ and lower-GI ORRs. Durable overall response from Day 56 to Day 91 was 41.9% for the all-organ ORR and 45.2% for the lower-GI ORR.Conclusions: The results of STARGAZE, the first prospective trial of a GLP-2 analog in SR lower-GI aGvHD, show that APRA was well tolerated and efficacious when added to RUX in the second-line setting. The majority of pts receiving APRA plus RUX had an overall response (all-organ and/or lower-GI response) at Days 28 and 56. Notably, durable overall responses were observed from Day 28 to Day 56 and from Day 56 to Day 91. The outcomes, based on the novel regenerative mechanism of action of APRA, are encouraging in this severely ill population. |
| **Date** | 2024-11-05 |
| **Short Title** | Safety and Efficacy of the Glucagon-like Peptide 2 (GLP-2) Analog Apraglutide in Patients with Steroid-Refractory Gastrointestinal Acute Graft-Versus-Host Disease (aGvHD) in Combination with Best Available Therapy |
| **Library Catalog** | Silverchair |
| **URL** | <https://doi.org/10.1182/blood-2024-198360> |
| **Accessed** | 6/15/2025, 4:39:18 PM |
| **Volume** | 144 |
| **Pages** | 100 |
| **Publication** | Blood |
| **DOI** | [10.1182/blood-2024-198360](http://doi.org/10.1182/blood-2024-198360) |
| **Issue** | Supplement 1 |
| **Journal Abbr** | Blood |
| **ISSN** | 0006-4971 |
| **Date Added** | 6/15/2025, 4:39:18 PM |
| **Modified** | 6/15/2025, 4:39:18 PM |

### Attachments

* + Full Text PDF

## <p>Serotonin Type 6 and 7 Receptors as a Novel Therapeutic Target for the Treatment of Schizophrenia</p>

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Etsay Weldekidan Tsegay |
| **Author** | Desalegn Getnet Demise |
| **Author** | Nigus Alemu Hailu |
| **Author** | Zenawi Hagos Gufue |
| **Abstract** | Serotonin Type 6 and 7 Receptors as a Novel Therapeutic Target for the Treatment of Schizophrenia |
| **Date** | 2020/10/28 |
| **Language** | English |
| **Library Catalog** | www.dovepress.com |
| **URL** | <https://www.dovepress.com/serotonin-type-6-and-7-receptors-as-a-novel-therapeutic-target-for-the-peer-reviewed-fulltext-article-NDT> |
| **Accessed** | 6/15/2025, 4:49:41 PM |
| **Extra** | Publisher: Dove Press |
| **Volume** | 16 |
| **Pages** | 2499-2509 |
| **Publication** | Neuropsychiatric Disease and Treatment |
| **DOI** | [10.2147/NDT.S263424](http://doi.org/10.2147/NDT.S263424) |
| **Journal Abbr** | NDT |
| **Date Added** | 6/15/2025, 4:49:41 PM |
| **Modified** | 6/15/2025, 4:49:41 PM |

### Attachments

* + Full Text PDF

## Challenges and Trends of Implantable Functional Electrical Neural Stimulators: System Architecture and Parameters

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Mostafa Katebi |
| **Author** | Abbas Erfanian |
| **Author** | Mohammad Azim Karami |
| **Author** | Mohamad Sawan |
| **Abstract** | Electrical neural stimulators (ENS) play a crucial role in medical applications and have emerged as promising therapeutic techniques for neurological disorders. The purpose of designing this device in medicine and research is to provide therapeutic benefits, aid in rehabilitation, restore sensory perception, advance scientific knowledge, and enable personalized treatment approaches. The utilization of ENS can significantly improve the quality of life for individuals with neurological disorders and contribute to advancements in neuroscience. Recently, there has been a growing inclination towards implantable biomedical microsystems, which has enticed biomedical engineers and researchers to integrate and implement electrical neural stimulators using CMOS technology. Thus, we present this review to provide a comprehensive overview of integrated circuits in the ENS field. The review aims to discuss the operational principles, design considerations, and approaches while highlighting advancements, applications, and future directions. The review begins with an introduction, emphasizing the necessity of stimulation and the fundamental principles of the ENS. It then discusses the various stimulation patterns, exploring how these patterns can modify neural circuits and restore normal function, as well as the circuit implementations involved in generating the stimulation. Design considerations specific to stimulators are also discussed. Furthermore, the review summarizes the state-of-the-art circuits and systems for the ENS, employing a top-down approach that covers specifications, circuits, and system design. Additionally, it briefly provides an overview of experimental approaches and results from various biomedical tests. Finally, this review outlines future directions, trends, and challenges for enhancing precision, safety, and patient outcomes in stimulation therapies. |
| **Date** | 2024 |
| **Short Title** | Challenges and Trends of Implantable Functional Electrical Neural Stimulators |
| **Library Catalog** | IEEE Xplore |
| **URL** | <https://ieeexplore.ieee.org/document/10606500> |
| **Accessed** | 6/15/2025, 4:51:47 PM |
| **Volume** | 12 |
| **Pages** | 103203-103236 |
| **Publication** | IEEE Access |
| **DOI** | [10.1109/ACCESS.2024.3432611](http://doi.org/10.1109/ACCESS.2024.3432611) |
| **ISSN** | 2169-3536 |
| **Date Added** | 6/15/2025, 4:51:47 PM |
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### Tags:

* + anodic/cathodic phase
  + biphasic
  + charge-balance
  + current stimulator
  + Delays
  + Electric potential
  + electrical neural stimulator (ENS)
  + Electrical stimulation
  + Electrodes
  + Functional electrical neural stimulation (FENS)
  + H-bridge
  + Impedance
  + implantable medical devices (IMD)
  + Implants
  + Market research
  + Medical treatment
  + monophasic
  + Reviews
  + Tissue damage
  + voltage compliance
  + Voltage control
  + voltage stimulator

### Attachments

* + Full Text PDF

## Gut microbiota composition and functional changes in inflammatory bowel disease and irritable bowel syndrome

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Arnau Vich Vila |
| **Author** | Floris Imhann |
| **Author** | Valerie Collij |
| **Author** | Soesma A. Jankipersadsing |
| **Author** | Thomas Gurry |
| **Author** | Zlatan Mujagic |
| **Author** | Alexander Kurilshikov |
| **Author** | Marc Jan Bonder |
| **Author** | Xiaofang Jiang |
| **Author** | Ettje F. Tigchelaar |
| **Author** | Jackie Dekens |
| **Author** | Vera Peters |
| **Author** | Michiel D. Voskuil |
| **Author** | Marijn C. Visschedijk |
| **Author** | Hendrik M. van Dullemen |
| **Author** | Daniel Keszthelyi |
| **Author** | Morris A. Swertz |
| **Author** | Lude Franke |
| **Author** | Rudi Alberts |
| **Author** | Eleonora A. M. Festen |
| **Author** | Gerard Dijkstra |
| **Author** | Ad A. M. Masclee |
| **Author** | Marten H. Hofker |
| **Author** | Ramnik J. Xavier |
| **Author** | Eric J. Alm |
| **Author** | Jingyuan Fu |
| **Author** | Cisca Wijmenga |
| **Author** | Daisy M. A. E. Jonkers |
| **Author** | Alexandra Zhernakova |
| **Author** | Rinse K. Weersma |
| **Abstract** | Changes in the gut microbiota have been associated with two of the most common gastrointestinal diseases, inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS). Here, we performed a case-control analysis using shotgun metagenomic sequencing of stool samples from 1792 individuals with IBD and IBS compared with control individuals in the general population. Despite substantial overlap between the gut microbiome of patients with IBD and IBS compared with control individuals, we were able to use gut microbiota composition differences to distinguish patients with IBD from those with IBS. By combining species-level profiles and strain-level profiles with bacterial growth rates, metabolic functions, antibiotic resistance, and virulence factor analyses, we identified key bacterial species that may be involved in two common gastrointestinal diseases. |
| **Date** | 2018-12-19 |
| **Library Catalog** | science.org (Atypon) |
| **URL** | <https://www.science.org/doi/10.1126/scitranslmed.aap8914> |
| **Accessed** | 6/15/2025, 4:51:14 PM |
| **Extra** | Publisher: American Association for the Advancement of Science |
| **Volume** | 10 |
| **Pages** | eaap8914 |
| **Publication** | Science Translational Medicine |
| **DOI** | [10.1126/scitranslmed.aap8914](http://doi.org/10.1126/scitranslmed.aap8914) |
| **Issue** | 472 |
| **Date Added** | 6/15/2025, 4:51:14 PM |
| **Modified** | 6/15/2025, 4:51:14 PM |

### Attachments

* + Full Text

## Intestinal Epithelial Serotonin as a Novel Target for Treating Disorders of Gut-Brain Interaction and Mood

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Lin Y. Hung |
| **Author** | Nuno D. Alves |
| **Author** | Andrew Del Colle |
| **Author** | Ardesheer Talati |
| **Author** | Sarah A. Najjar |
| **Author** | Virginie Bouchard |
| **Author** | Virginie Gillet |
| **Author** | Yan Tong |
| **Author** | Zixing Huang |
| **Author** | Kirsteen N. Browning |
| **Author** | Jialiang Hua |
| **Author** | Ying Liu |
| **Author** | James O. Woodruff |
| **Author** | Daniel Juarez |
| **Author** | Melissa Medina |
| **Author** | Jonathan Posner |
| **Author** | Raquel Tonello |
| **Author** | Nazli Yalcinkaya |
| **Author** | Narek Israelyan |
| **Author** | Roey Ringel |
| **Author** | Letao Yang |
| **Author** | Kam W. Leong |
| **Author** | Mu Yang |
| **Author** | Ji Ying Sze |
| **Author** | Tor Savidge |
| **Author** | Jay Gingrich |
| **Author** | Robert J. Shulman |
| **Author** | Michael D. Gershon |
| **Author** | Annie Ouellet |
| **Author** | Larissa Takser |
| **Author** | Mark S. Ansorge |
| **Author** | Kara Gross Margolis |
| **Date** | 2025-04-01 |
| **Language** | English |
| **Library Catalog** | www.gastrojournal.org |
| **URL** | <https://www.gastrojournal.org/article/S0016-5085(24)05751-2/fulltext> |
| **Accessed** | 6/15/2025, 4:49:51 PM |
| **Extra** | Publisher: Elsevier PMID: 39672518 |
| **Volume** | 168 |
| **Pages** | 754-768 |
| **Publication** | Gastroenterology |
| **DOI** | [10.1053/j.gastro.2024.11.012](http://doi.org/10.1053/j.gastro.2024.11.012) |
| **Issue** | 4 |
| **Journal Abbr** | Gastroenterology |
| **ISSN** | 0016-5085, 1528-0012 |
| **Date Added** | 6/15/2025, 4:49:51 PM |
| **Modified** | 6/15/2025, 4:49:51 PM |

### Tags:

* + ENS
  + enteric nervous system
  + disorders of gut-brain interaction
  + 5-HT
  + gastrointestinal
  + central nervous system
  + CNS
  + GI
  + 5-hydroxtryptamine
  + CCK-SAP
  + cholecystokinin conjugated to saporin
  + CMMC
  + colonic migrating motor complex
  + DGBI
  + Disorders of Gut-Brain Interaction
  + EC
  + elevated plus maze
  + enterochromaffin
  + EPM
  + HC
  + healthy control
  + In Utero SSRI
  + intraperitoneal injection of 6-hydroxydopamine
  + IP-6-OHDA
  + knockout
  + KO
  + LDB
  + light-dark box
  + Mood
  + novelty-suppressed feeding test
  + NSFT
  + OFT
  + open field test
  + paraformaldehyde
  + Patient Health Questionnaire-9
  + PBS
  + PFA
  + phosphate-buffered saline
  + PHQ-9
  + PMD
  + prenatal maternal depression
  + selective serotonin reuptake inhibitor
  + serotonin and norepinephrine reuptake inhibitor
  + serotonin reuptake transporter
  + SERT
  + SNRI
  + SSRI
  + tail suspension test
  + Tam
  + tamoxifen
  + TPH1
  + tryptophan hydroxylase 1
  + TST
  + Vagal Afferent Signaling
  + wild type
  + WT

### Attachments

* + Full Text PDF
  + PubMed entry

## Long-Term Oncologic Outcome following Duodenum-Preserving Pancreatic Head Resection for Benign Tumors, Cystic Neoplasms, and Neuroendocrine Tumors: Systematic Review and Meta-analysis

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Hans G Beger |
| **Author** | Benjamin Mayer |
| **Author** | Bertram Poch |
| **Date** | 2024 |
| **URL** | <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11164799/> |
| **Volume** | 31 |
| **Pages** | 4637–4653 |
| **Publication** | Annals of Surgical Oncology |
| **DOI** | [10.1245/s10434-024-15222-y](http://doi.org/10.1245/s10434-024-15222-y) |
| **Issue** | 7 |
| **Date Added** | 4/16/2025, 11:10:32 PM |
| **Modified** | 6/16/2025, 1:12:21 PM |

### Tags:

* + Adult
  + Female
  + Humans
  + Male
  + Treatment Outcome
  + Animals
  + Disease Models, Animal
  + Mice
  + STING
  + Quality of Life
  + Retrospective Studies
  + Diabetes
  + Signal Transduction
  + Cell Differentiation
  + Cell Line
  + Neoplasm Recurrence, Local
  + Cell Movement
  + Mammals
  + Neurons
  + immune cells
  + inflammation
  + Homeostasis
  + Gastroenterology
  + intestinal organoids
  + Regeneration
  + microbiota
  + Pancreas
  + inflammatory bowel disease
  + \*Cell- and Tissue-Based Therapy/methods
  + \*Bile Duct Neoplasms
  + \*Bile Duct Neoplasms/surgery
  + \*Cell Lineage
  + \*Cholangiocarcinoma
  + \*Cholangiocarcinoma/pathology
  + \*Colitis, Ulcerative/drug therapy
  + \*Cystadenocarcinoma/diagnostic imaging/surgery
  + \*Cystadenoma/diagnostic imaging/surgery
  + \*Cysts/pathology
  + \*Diabetes Mellitus, Experimental/complications/genetics/metabolism
  + \*Enteric Nervous System
  + \*Enteric Nervous System/pathology
  + \*Hyperglycemia/genetics/metabolism
  + \*Hypothalamo-Hypophyseal System
  + \*Inflammatory Bowel Diseases/drug therapy
  + \*Liver Neoplasms/diagnostic imaging/surgery
  + \*Liver Neoplasms/surgery
  + \*Microbiota
  + \*MicroRNAs/metabolism
  + \*Neoplasms, Cystic, Mucinous, and Serous
  + \*Neuroglia/physiology
  + \*Zebrafish
  + 16S RNA sequencing
  + Acinar cell carcinoma
  + Aging
  + antibiotics
  + Bile Ducts, Intrahepatic
  + Bile Ducts, Intrahepatic/surgery
  + Biliary
  + Biliary cystadenocarcinoma
  + Biliary cystadenoma
  + Brain
  + Brain-Gut Axis
  + Brain/physiology
  + Cell Separation
  + Chemical coding
  + Chick Embryo
  + circVPS13A
  + Cistoadenocarcinoma
  + Cistoadenoma
  + Clinicopathological criteria, Surgical outcomes
  + Colon/drug effects/pathology
  + Cystadenocarcinoma
  + Cystadenoma
  + cystic liver lesions
  + Cystic liver neoplasm
  + Cytology
  + Developmental disorders
  + diabetes
  + diabetes mellitus
  + Drug Discovery/\*methods
  + Embryonic stem cells
  + ENS
  + ENS neuropathies
  + enteric glia
  + enteric glia communications
  + Enteric glia communications
  + enteric glia diversity
  + enteric nervous system
  + Enteric nervous system
  + Enteric Nervous System
  + enteric nervous system (ENS)
  + Enteric nervous system (ENS)
  + Enteric Nervous System/\*pathology
  + Enteric neural precursor cells (ENPCs)
  + enteric progenitor cell
  + Fecal microbiota transplantation
  + Frantz's tumor
  + gastrointestinal complications
  + gastrointestinal diseases
  + Gastrointestinal Diseases
  + Gastrointestinal Diseases/pathology
  + gastrointestinal tract
  + Gastrointestinal Tract/drug effects/pathology
  + glia
  + Glial Cell Line-Derived Neurotrophic Factor/genetics
  + glucagon-like peptide 1
  + Growth Disorders
  + growth retardation
  + gut brain axis
  + gut microbiota
  + gut-brain axis
  + gut–brain axis
  + hepatic cystadenocarcinoma
  + hepatic cystadenoma
  + Hepatic simple cyst
  + hepatobiliary cystadenocarcinoma
  + hepatobiliary cystadenoma
  + Hirschsprung disease
  + Hirschsprung Disease/\*drug therapy/\*pathology/therapy
  + homeostasis
  + Imaging modalities
  + In Situ Hybridization, Fluorescence
  + Inflammatory bowel diseases
  + Intraductal papillary biliary neoplasms
  + intraductal papillary neoplasms of bile duct
  + irritable bowel syndrome
  + L-Fucose
  + Liver Diseases
  + Management
  + microbial metabolites
  + microbiota-gut-brain axis
  + Microbiota-gut-brain axis
  + Mucinous biliary cystic tumors, Biliary cystadenoma
  + mucinous cystic neoplasm
  + Mucinous cystic neoplasms
  + Mucinous neoplasm
  + muscularis macrophages
  + myenteric neurons
  + Neoplasia mucinosa quística
  + Neoplasia papilar intraductal biliar
  + Neoplasia quística hepática
  + Neural Crest
  + neural crest cell
  + neurodegeneration
  + Neuroglia
  + Neurons/drug effects/\*pathology
  + offspring
  + P2X7 receptor
  + pancreatectomy
  + Pancreatectomy
  + Pancreatic neoplasms
  + Pancreatic Neoplasms
  + Pancreatic surgery
  + pancreatic tumor
  + Parkinson’s disease
  + pediatric pancreatic neoplasm
  + Pepstatins/metabolism
  + Pituitary-Adrenal System
  + pluripotent stem cells (PSCs)
  + Pluripotent Stem Cells/pathology
  + preconception
  + probiotic
  + Purinergic signaling
  + Receptor, Endothelin B/metabolism
  + Receptors, Purinergic P2X7
  + RNA, Circular/genetics
  + Rotenone-induced mouse model
  + short-chain fatty acids
  + Solid pseudopapillary tumor
  + Stem-cell differentiation
  + submucosal neurons
  + Submucous Plexus
  + surgical outcome
  + surgical resection
  + three-dimensional (3D)
  + type 2 diabetes
  + zebrafish

### Notes:

* + e14603 NMO-00132-2023
  + e14603 NMO-00132-2023

### Attachments

* + Full Text
  + Full Text
  + Full Text PDF
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  + Full Text PDF
  + Full Text PDF
  + PubMed Central Full Text PDF
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  + PubMed Central Full Text PDF
  + PubMed Central Link
  + PubMed Central Link
  + PubMed Central Link
  + PubMed Central Link
  + PubMed entry

## MEsenchymal StEm cells for Multiple Sclerosis (MESEMS): a randomized, double blind, cross-over phase I/II clinical trial with autologous mesenchymal stem cells for the therapy of multiple sclerosis

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Antonio Uccelli |
| **Author** | Alice Laroni |
| **Author** | Lou Brundin |
| **Author** | Michel Clanet |
| **Author** | Oscar Fernandez |
| **Author** | Seyed Massood Nabavi |
| **Author** | Paolo A. Muraro |
| **Author** | Roberto S. Oliveri |
| **Author** | Ernst W. Radue |
| **Author** | Johann Sellner |
| **Author** | Per Soelberg Sorensen |
| **Author** | Maria Pia Sormani |
| **Author** | Jens Thomas Wuerfel |
| **Author** | Mario A. Battaglia |
| **Author** | Mark S. Freedman |
| **Author** | Alice Laroni |
| **Author** | Antonio Uccelli |
| **Author** | Bruno Bonetti |
| **Author** | Carolina Rush |
| **Author** | Concepción Herrera |
| **Author** | Cristina Ramo Tello |
| **Author** | David Miller |
| **Author** | David Szwajcer |
| **Author** | Dirk Strunk |
| **Author** | Donna Wall |
| **Author** | Eduardo Aguera-Morales |
| **Author** | Ernst W. Radue |
| **Author** | Eva Rohde |
| **Author** | Francesco Dazzi |
| **Author** | Giancarlo Comi |
| **Author** | Gianvito Martino |
| **Author** | Guillermo Izquierdo Ayuso |
| **Author** | H. Rabinovitch |
| **Author** | Heather MacLean |
| **Author** | James Marriott |
| **Author** | Jens Thomas Wuerfel |
| **Author** | Johann Sellner |
| **Author** | Juan Racosta |
| **Author** | Leila Arab |
| **Author** | Lou Brundin |
| **Author** | Maria Pia Sormani |
| **Author** | Mario A. Battaglia |
| **Author** | Mario Gimona |
| **Author** | Mark S. Freedman |
| **Author** | Martino Introna |
| **Author** | Michel Clanet |
| **Author** | Morten Blinkenberg |
| **Author** | Naser Aghdami |
| **Author** | Óscar Fernández |
| **Author** | Paolo A. Muraro |
| **Author** | Per Soelberg Sorensen |
| **Author** | Rehiana Ali |
| **Author** | Reza Vosoughi |
| **Author** | Richard Nicholas |
| **Author** | Roberto S. Oliveri |
| **Author** | Ruth Ann Marrie |
| **Author** | Seyed Massood Nabavi |
| **Author** | Shahedeh Karimi |
| **Author** | on behalf of the MESEMS study group |
| **Abstract** | Multiple sclerosis (MS) is an inflammatory disease of the central nervous system with a degenerative component, leading to irreversible disability. Mesenchymal stem cells (MSC) have been shown to prevent inflammation and neurodegeneration in animal models of MS, but no large phase II clinical trials have yet assessed the exploratory efficacy of MSC for MS. |
| **Date** | 2019-05-09 |
| **Short Title** | MEsenchymal StEm cells for Multiple Sclerosis (MESEMS) |
| **Library Catalog** | BioMed Central |
| **URL** | <https://doi.org/10.1186/s13063-019-3346-z> |
| **Accessed** | 6/15/2025, 4:52:20 PM |
| **Volume** | 20 |
| **Pages** | 263 |
| **Publication** | Trials |
| **DOI** | [10.1186/s13063-019-3346-z](http://doi.org/10.1186/s13063-019-3346-z) |
| **Issue** | 1 |
| **Journal Abbr** | Trials |
| **ISSN** | 1745-6215 |
| **Date Added** | 6/15/2025, 4:52:20 PM |
| **Modified** | 6/15/2025, 4:52:20 PM |

### Tags:

* + Clinical trial
  + Mesenchymal stem cells
  + Mesenchymal stromal cells
  + Multiple sclerosis

### Attachments

* + Full Text PDF

## New Developments in Prokinetic Therapy for Gastric Motility Disorders

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Michael Camilleri |
| **Author** | Jessica Atieh |
| **Abstract** | Prokinetic agents are medications that enhance coordinated gastrointestinal motility and transit of content in the gastrointestinal tract, mainly by amplifying and coordinating the gastrointestinal muscular contractions. In addition to dietary therapy, prokinetics are the first line therapy to improve gastric emptying and symptoms, balancing benefits and risks of treatment. The Food and Drug Administration (FDA) of the United States recommends use of metoclopramide for less than 12 weeks’ duration due to the risk of reversible or irreversible extrapyramidal side effects. Domperidone can be prescribed through the FDA’s Expanded Access to Investigational Drugs Program. Macrolides are used off label and are associated with tachyphylaxis and variable duration of efficacy. Aprepitant relieves some symptoms of gastroparesis. There are newer agents in the pipeline targeting diverse gastric (fundic, antral and pyloric) motor functions, including novel 5-HT4 agonists, D2/3 antagonist, NK1 antagonist, and ghrelin agonist. Novel targets with potential to improve gastric motor functions include the pylorus, macrophage/inflammatory function, oxidative stress, and neurogenesis. In the current review, we discuss the use of pharmacological approaches with potential to enhance motor functions in the management of gastroparesis. |
| **Date** | 2021-08-24 |
| **Language** | English |
| **Library Catalog** | Frontiers |
| **URL** | <https://www.frontiersin.org/journals/pharmacology/articles/10.3389/fphar.2021.711500/full> |
| **Accessed** | 6/15/2025, 4:49:55 PM |
| **Extra** | Publisher: Frontiers |
| **Volume** | 12 |
| **Publication** | Frontiers in Pharmacology |
| **DOI** | [10.3389/fphar.2021.711500](http://doi.org/10.3389/fphar.2021.711500) |
| **Journal Abbr** | Front. Pharmacol. |
| **ISSN** | 1663-9812 |
| **Date Added** | 6/15/2025, 4:49:55 PM |
| **Modified** | 6/15/2025, 4:49:55 PM |

### Tags:

* + Aprepitant
  + Domperidone
  + Erythromycin
  + functional dyspepsia
  + Gastroparesis
  + Ghrelin
  + Prucalopride
  + Relamorelin

### Attachments

* + Full Text PDF

## Patients with Multiple Functional Gastrointestinal Disorders (FGIDs) Show Increased Illness Severity: A Cross-Sectional Study in a Tertiary Care FGID Specialty Clinic

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Sabrina Berens |
| **Author** | Felicitas Engel |
| **Author** | Annika Gauss |
| **Author** | Jonas Tesarz |
| **Author** | Wolfgang Herzog |
| **Author** | Beate Niesler |
| **Author** | Esther Stroe-Kunold |
| **Author** | Rainer Schaefert |
| **Abstract** | Objectives. Overlaps between different functional gastrointestinal disorders (FGIDs) are common. However, little is known about the impact of this overlap on patients’ health status. This study is aimed at analyzing the differences between patients with multiple as compared to one single FGID. Methods. A retrospective, cross-sectional study was conducted with patients presenting to a tertiary care FGID specialty clinic between 06/2012 and 01/2015 (n = 294). They were characterized primarily according to their GI symptom severity (IBS-SSS) and secondarily to their physical as well as psychosocial symptom burden, quality of life, health care utilization, and work-related impairment. Differences between patients with >1 vs. 1 FGID were analyzed. Results. Of the 294 patients, 92.2% fulfilled the Rome III criteria for any FGID, and 48.0% had >1 FGIDs. FGID patients had a median age of 38 [23.0] years; 72.0% were female. Median GI symptom severity (IBS-SSS) scores were 339 [126] and 232 [163] in patients with >1 and 1 FGID, respectively (p < .001). Furthermore, patients with >1 FGIDs had higher general somatic symptom severity, higher illness anxiety, lower quality of life, and more work-related impairment. Almost no differences were found regarding their somatic as well as mental comorbidities. Conclusions. Multiple FGIDs are associated with an increased risk for complicated courses of illness as reflected in higher GI and somatic symptom severity, as well as stronger psychosocial and diet- and work-related impairment. Stepped and interdisciplinary models of care including psychosocial expertise and dietary advice are needed, especially for patients with multiple FGIDs. |
| **Date** | 2020 |
| **Language** | en |
| **Short Title** | Patients with Multiple Functional Gastrointestinal Disorders (FGIDs) Show Increased Illness Severity |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1155/2020/9086340> |
| **Accessed** | 6/15/2025, 4:50:04 PM |
| **Rights** | Copyright © 2020 Sabrina Berens et al. |
| **Extra** | \_eprint: https://onlinelibrary.wiley.com/doi/pdf/10.1155/2020/9086340 |
| **Volume** | 2020 |
| **Pages** | 9086340 |
| **Publication** | Gastroenterology Research and Practice |
| **DOI** | [10.1155/2020/9086340](http://doi.org/10.1155/2020/9086340) |
| **Issue** | 1 |
| **ISSN** | 1687-630X |
| **Date Added** | 6/15/2025, 4:50:04 PM |
| **Modified** | 6/15/2025, 4:50:04 PM |

### Attachments

* + Full Text PDF

## Redox regulation in regenerative medicine and tissue engineering: The paradox of oxygen

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Mireille M.J.P.E. Sthijns |
| **Author** | Clemens A. van Blitterswijk |
| **Author** | Vanessa L.S. LaPointe |
| **Abstract** | One of the biggest challenges in tissue engineering and regenerative medicine is to incorporate a functioning vasculature to overcome the consequences of a lack of oxygen and nutrients in the tissue construct. Otherwise, decreased oxygen tension leads to incomplete metabolism and the formation of the so-called reactive oxygen species (ROS). Cells have many endogenous antioxidant systems to ensure a balance between ROS and antioxidants, but if this balance is disrupted by factors such as high levels of ROS due to long-term hypoxia, there will be tissue damage and dysfunction. Current attempts to solve the oxygen problem in the field rarely take into account the importance of the redox balance and are instead centred on releasing or generating oxygen. The first problem with this approach is that although oxygen is necessary for life, it is paradoxically also a highly toxic molecule. Furthermore, although some oxygen-generating biomaterials produce oxygen, they also generate hydrogen peroxide, a ROS, as an intermediate product. In this review, we discuss why it would be a superior strategy to supplement oxygen delivery with molecules to safeguard the important redox balance. Redox sensor proteins that can stimulate the anaerobic metabolism, angiogenesis, and enhancement of endogenous antioxidant systems are discussed as promising targets. We propose that redox regulating biomaterials have the potential to tackle some of the challenges related to angiogenesis and that the knowledge in this review will help scientists in tissue engineering and regenerative medicine realize this aim. |
| **Date** | 2018 |
| **Language** | en |
| **Short Title** | Redox regulation in regenerative medicine and tissue engineering |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1002/term.2730> |
| **Accessed** | 6/15/2025, 4:51:28 PM |
| **Rights** | © 2018 The Authors. Journal of Tissue Engineering and Regenerative Medicine Published by John Wiley & Sons Ltd |
| **Extra** | \_eprint: https://onlinelibrary.wiley.com/doi/pdf/10.1002/term.2730 |
| **Volume** | 12 |
| **Pages** | 2013-2020 |
| **Publication** | Journal of Tissue Engineering and Regenerative Medicine |
| **DOI** | [10.1002/term.2730](http://doi.org/10.1002/term.2730) |
| **Issue** | 10 |
| **ISSN** | 1932-7005 |
| **Date Added** | 6/15/2025, 4:51:28 PM |
| **Modified** | 6/15/2025, 4:51:28 PM |

### Tags:

* + oxygen
  + pancreas
  + bone
  + heart
  + HIF
  + Nrf2
  + redox
  + redox regulating biomaterials

### Attachments

* + Full Text PDF

## THE AUTONOMIC NERVOUS SYSTEM: BASIC ANATOMY AND PHYSIOLOGY

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Eduardo E. Benarroch |
| **Abstract** | and respiratory tracts, micturition, and sexual function. The autonomic system consists of three subdivisions: the sympathetic, parasympathetic, and enteric nervous systems. The sympathetic and parasympathetic systems each have a central preganglionic neuron in the brain stem or spinal cord and a peripheral neuron in the autonomic ganglia. The enteric nervous system consists of neurons located in ganglia within the walls of the gut. A major component of the autonomic control systems consists of visceral afferent pathways. These pathways convey signals from the periphery that trigger visceral reflexes, transmit visceral pain, and regulate visceral function via antidromic release of neurochemical signals. The central control of autonomic function depends on a neuronal network distributed throughout the neuraxis. These neurons receive numerous afferent inputs and integrate this information according to the type of stimulus and current behavioral state. After these converging inputs have been evaluated, a specific pattern of autonomic outflow is relayed to the periphery. The central autonomic network consists of neurons in the insular and anterior cingulate cortex, amygdala, hypothalamus, periaqueductal gray, parabrachial nucleus, nucleus of the solitary tract, ventrolateral reticular formation, and medullary raphe.... |
| **Date** | December 2007 |
| **Language** | en-US |
| **Short Title** | THE AUTONOMIC NERVOUS SYSTEM |
| **Library Catalog** | journals.lww.com |
| **URL** | <https://journals.lww.com/continuum/abstract/2007/12000/the_autonomic_nervous_system__basic_anatomy_and.3.aspx> |
| **Accessed** | 6/15/2025, 4:49:12 PM |
| **Volume** | 13 |
| **Pages** | 13 |
| **Publication** | CONTINUUM: Lifelong Learning in Neurology |
| **DOI** | [10.1212/01.CON.0000299964.20642.9a](http://doi.org/10.1212/01.CON.0000299964.20642.9a) |
| **Issue** | 6 |
| **ISSN** | 1080-2371 |
| **Date Added** | 6/15/2025, 4:49:12 PM |
| **Modified** | 6/15/2025, 4:49:12 PM |

### Attachments

* + Snapshot

## The Enteric Nervous System III: A Target for Pharmacological Treatment

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Mark Berner Hansen |
| **Abstract** | Abstract: The past decade has seen major advances in the pharmacological understanding of the nervous system of the gastrointestinal tract, the enteric nervous system, and its importance for gut functions in several states of disease. Indeed, the enteric nervous system has become a promising target in the treatment of many gastrointestinal symptoms and disorders. Some of these new therapeutic concepts, such as botulinum toxin for achalasia and serotonergic drugs for functional bowel diseases, are already in clinical use. This paper is part 3 of three Minireviews in Pharmacology & Toxicology, and presents the neurogastrointestinal pharmacological therapeutic options in gastrointestinal pain, functional gastrointestinal disorders, inflammatory bowel diseases, cancer and related conditions with focus on future drug targets. The diagnosis of gastrointestinal neuropathy, the role of serotonin and related neuroendocrine transmitters, serotonergic drugs, and neurotrophic factors in neurogastrointestinal pharmacology will be addressed in this context. |
| **Date** | 2003 |
| **Language** | en |
| **Short Title** | The Enteric Nervous System III |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1034/j.1600-0773.2003.930101.x> |
| **Accessed** | 6/15/2025, 4:49:29 PM |
| **Extra** | \_eprint: https://onlinelibrary.wiley.com/doi/pdf/10.1034/j.1600-0773.2003.930101.x |
| **Volume** | 93 |
| **Pages** | 1-13 |
| **Publication** | Pharmacology & Toxicology |
| **DOI** | [10.1034/j.1600-0773.2003.930101.x](http://doi.org/10.1034/j.1600-0773.2003.930101.x) |
| **Issue** | 1 |
| **ISSN** | 1600-0773 |
| **Date Added** | 6/15/2025, 4:49:29 PM |
| **Modified** | 6/15/2025, 4:49:29 PM |

### Attachments

* + Full Text PDF

## The Generation of Hybrid Electrospun Nanofiber Layer with Extracellular Matrix Derived from Human Pluripotent Stem Cells, for Regenerative Medicine Applications

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Ronit Shtrichman |
| **Author** | Naama Zeevi-Levin |
| **Author** | Rinat Zaid |
| **Author** | Efrat Barak |
| **Author** | Bettina Fishman |
| **Author** | Anna Ziskind |
| **Author** | Rita Shulman |
| **Author** | Atara Novak |
| **Author** | Ron Avrahami |
| **Author** | Erella Livne |
| **Author** | Lior Lowenstein |
| **Author** | Eyal Zussman |
| **Author** | Joseph Itskovitz-Eldor |
| **Abstract** | Extracellular matrix (ECM) has been utilized as a biological scaffold for tissue engineering applications in a variety of body systems, due to its bioactivity and biocompatibility. In the current study we developed a modified protocol for the efficient and reproducible derivation of mesenchymal progenitor cells (MPCs) from human embryonic stem cells as well as human induced pluripotent stem cells (hiPSCs) originating from hair follicle keratinocytes (HFKTs). ECM was produced from these MPCs and characterized in comparison to adipose mesenchymal stem cell ECM, demonstrating robust ECM generation by the excised HFKT-iPSC-MPCs. Exploiting the advantages of electrospinning we generated two types of electrospun biodegradable nanofiber layers (NFLs), fabricated from polycaprolactone (PCL) and poly(lactic-co-glycolic acid) (PLGA), which provide mechanical support for cell seeding and ECM generation. Elucidating the optimized decellularization treatment we were able to generate an available “off-the-shelf” implantable product (NFL-ECM). Using rat subcutaneous transplantation model we demonstrate that this stem-cell-derived construct is biocompatible and biodegradable and holds great potential for tissue regeneration applications. |
| **Date** | 2014-10 |
| **Library Catalog** | liebertpub.com (Atypon) |
| **URL** | <https://www.liebertpub.com/doi/10.1089/ten.tea.2013.0705> |
| **Accessed** | 6/15/2025, 4:52:05 PM |
| **Extra** | Publisher: Mary Ann Liebert, Inc., publishers |
| **Volume** | 20 |
| **Pages** | 2756-2767 |
| **Publication** | Tissue Engineering Part A |
| **DOI** | [10.1089/ten.tea.2013.0705](http://doi.org/10.1089/ten.tea.2013.0705) |
| **Issue** | 19-20 |
| **ISSN** | 1937-3341 |
| **Date Added** | 6/15/2025, 4:52:05 PM |
| **Modified** | 6/15/2025, 4:52:05 PM |

## Tissue Engineering and Regenerative Medicine: A Year in Review

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Rachael H. Harrison |
| **Author** | Jean-Philippe St-Pierre |
| **Author** | Molly M. Stevens |
| **Abstract** | It is an exciting time to be involved in tissue engineering and regenerative medicine (TERM) research. Despite its relative youth, the field is expanding fast and breaking new ground in both the laboratory and clinically. In this “Year in Review,” we highlight some of the high-impact advances in the field. Building upon last year's article, we have identified the recent “hot topics” and the key publications pertaining to these themes as well as ideas that have high potential to direct the field. Based on a modified methodology grounded on last year's approach, we have identified and summarized some of the most impactful publications in five main themes: (1) pluripotent stem cells: efforts and hurdles to translation, (2) tissue engineering: complex scaffolds and advanced materials, (3) directing the cell phenotype: growth factor and biomolecule presentation, (4) characterization: imaging and beyond, and (5) translation: preclinical to clinical. We have complemented our review of the research directions highlighted within these trend-setting studies with a discussion of additional articles along the same themes that have recently been published and have yet to surface in citation analyses. We conclude with a discussion of some really interesting studies that provide a glimpse of the high potential for innovation of TERM research. |
| **Date** | 2014-02 |
| **Short Title** | Tissue Engineering and Regenerative Medicine |
| **Library Catalog** | liebertpub.com (Atypon) |
| **URL** | <https://www.liebertpub.com/doi/10.1089/ten.teb.2013.0668> |
| **Accessed** | 6/15/2025, 4:51:33 PM |
| **Extra** | Publisher: Mary Ann Liebert, Inc., publishers |
| **Volume** | 20 |
| **Pages** | 1-16 |
| **Publication** | Tissue Engineering Part B: Reviews |
| **DOI** | [10.1089/ten.teb.2013.0668](http://doi.org/10.1089/ten.teb.2013.0668) |
| **Issue** | 1 |
| **ISSN** | 1937-3368 |
| **Date Added** | 6/15/2025, 4:51:33 PM |
| **Modified** | 6/15/2025, 4:51:33 PM |

## Tissue Engineering in the Gut: Developments in Neuromusculature

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Khalil N. Bitar |
| **Author** | Shreya Raghavan |
| **Author** | Elie Zakhem |
| **Date** | 2014-06-01 |
| **Language** | English |
| **Short Title** | Tissue Engineering in the Gut |
| **Library Catalog** | www.gastrojournal.org |
| **URL** | <https://www.gastrojournal.org/article/S0016-5085(14)00428-4/fulltext> |
| **Accessed** | 6/15/2025, 4:51:22 PM |
| **Extra** | Publisher: Elsevier PMID: 24681129 |
| **Volume** | 146 |
| **Pages** | 1614-1624 |
| **Publication** | Gastroenterology |
| **DOI** | [10.1053/j.gastro.2014.03.044](http://doi.org/10.1053/j.gastro.2014.03.044) |
| **Issue** | 7 |
| **Journal Abbr** | Gastroenterology |
| **ISSN** | 0016-5085, 1528-0012 |
| **Date Added** | 6/15/2025, 4:51:22 PM |
| **Modified** | 6/15/2025, 4:51:22 PM |

### Tags:

* + VIP
  + ENS
  + enteric nervous system
  + Enteric Nervous System
  + gastrointestinal
  + central nervous system
  + CNS
  + GI
  + IAS
  + ICC
  + internal anal sphincter
  + interstitial cells of Cajal
  + Intestinal Tissue Engineering
  + LES
  + lower esophageal sphincter
  + Neoinnervation
  + Smooth Muscle
  + vasoactive intestinal peptide

### Attachments

* + Full Text PDF
  + PubMed entry

## Use of prokinetic agents in hospitalised adult patients: A scoping review

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Vera Crone |
| **Author** | Morten Hylander Møller |
| **Author** | Emilie Stokholm Bækgaard |
| **Author** | Anders Perner |
| **Author** | Peter Bytzer |
| **Author** | Waleed Alhazzani |
| **Author** | Mette Krag |
| **Abstract** | Background Gastrointestinal motility is important for adequate uptake of fluids and nutrition but is often impaired in hospitalised patients. Prokinetic agents enhance gastrointestinal motility and are prescribed for many hospitalised patients. In this scoping review, we aimed to systematically describe the body of evidence on the use of prokinetic agents in hospitalised patients. We hypothesised, that the body of evidence would be limited and derive from heterogeneous populations. Methods We conducted this scoping review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews statement. We searched Medline, Embase, Epistemonikos and the Cochrane Library for studies assessing the use of prokinetic agents on any indication and outcome in adult hospitalised patients. We used a modified version of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) to assess the certainty of evidence. Results We included 102 studies with a total of 8830 patients. Eighty-six studies were clinical trials (84%), and 52 (60%) of these were conducted in the intensive care unit, with feeding intolerance as the main indication. In the non-intensive care setting the indications were wider; most studies assessed use of prokinetic agents before gastroscopy to improve visualisation. The most studied prokinetic agent was metoclopramide (49% of studies) followed by erythromycin (31%). In total 147 outcomes were assessed with only 67% of the included studies assessing patient-centred outcomes, and with gastric emptying as the most frequently reported outcome. Overall, the data provided no firm evidence on the balance between the desirable and undesirable effects of prokinetic agents. Conclusions In this scoping review, we found that the studies addressing prokinetic agents in hospitalised adults had considerable variations in indications, drugs and outcomes assessed, and that the certainty of evidence was judged to be low to very low. |
| **Date** | 2023 |
| **Language** | en |
| **Short Title** | Use of prokinetic agents in hospitalised adult patients |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1111/aas.14222> |
| **Accessed** | 6/15/2025, 4:51:41 PM |
| **Rights** | © 2023 The Authors. Acta Anaesthesiologica Scandinavica published by John Wiley & Sons Ltd on behalf of Acta Anaesthesiologica Scandinavica Foundation. |
| **Extra** | \_eprint: https://onlinelibrary.wiley.com/doi/pdf/10.1111/aas.14222 |
| **Volume** | 67 |
| **Pages** | 588-598 |
| **Publication** | Acta Anaesthesiologica Scandinavica |
| **DOI** | [10.1111/aas.14222](http://doi.org/10.1111/aas.14222) |
| **Issue** | 5 |
| **ISSN** | 1399-6576 |
| **Date Added** | 6/15/2025, 4:51:41 PM |
| **Modified** | 6/15/2025, 4:51:41 PM |

### Tags:

* + gastrointestinal motility
  + feeding intolerance
  + hospitalised patients
  + prokinetic agents
  + scoping review

### Attachments

* + Full Text PDF

## Communication between the gut microbiota and peripheral nervous system in health and chronic disease

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Tyler M. Cook |
| **Author** | Virginie and Mansuy-Aubert |
| **Abstract** | Trillions of bacteria reside within our gastrointestinal tract, ideally forming a mutually beneficial relationship between us. However, persistent changes in diet and lifestyle in the western diet and lifestyle contribute to a damaging of the gut microbiota-host symbiosis leading to diseases such as obesity and irritable bowel syndrome. Many symptoms and comorbidities associated with these diseases stem from dysfunctional signaling in peripheral neurons. Our peripheral nervous system (PNS) is comprised of a variety of sensory, autonomic, and enteric neurons which coordinate key homeostatic functions such as gastrointestinal motility, digestion, immunity, feeding behavior, glucose and lipid homeostasis, and more. The composition and signaling of bacteria in our gut dramatically influences how our peripheral neurons regulate these functions, and we are just beginning to uncover the molecular mechanisms mediating this communication. In this review, we cover the general anatomy and function of the PNS, and then we discuss how the molecules secreted or stimulated by gut microbes signal through the PNS to alter host development and physiology. Finally, we discuss how leveraging the power of our gut microbes on peripheral nervous system signaling may offer effective therapies to counteract the rise in chronic diseases crippling the western world. |
| **Date** | 2022-12-31 |
| **Library Catalog** | Taylor and Francis+NEJM |
| **URL** | <https://doi.org/10.1080/19490976.2022.2068365> |
| **Accessed** | 6/15/2025, 4:31:18 PM |
| **Extra** | Publisher: Taylor & Francis \_eprint: https://doi.org/10.1080/19490976.2022.2068365 PMID: 35482894 |
| **Volume** | 14 |
| **Pages** | 2068365 |
| **Publication** | Gut Microbes |
| **DOI** | [10.1080/19490976.2022.2068365](http://doi.org/10.1080/19490976.2022.2068365) |
| **Issue** | 1 |
| **ISSN** | 1949-0976 |
| **Date Added** | 6/15/2025, 4:31:18 PM |
| **Modified** | 6/15/2025, 4:31:18 PM |

### Tags:

* + Gut microbiota/ microbiota metabolites/PNS/neuronal sensing/obesity

### Attachments

* + Full Text PDF

## Diet-Induced Obesity Blunts Sensitivity of Intestinal Enteric Neurons: FIRST Evidence of Modulation of Activity of Enteric Neurons by Luminal Nutrients

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Ava Grandberry |
| **Author** | Naomi Rajesh |
| **Author** | Robert Murphy |
| **Author** | Sinju Sundaresan |
| **Abstract** | The enteric nervous system (ENS) has well-established roles in gut motility, epithelial secretion, and blood flow. However, its role in luminal nutrient sensing remains elusive. Given that the nerve endings of enteric neurons terminate at the basolateral surface of epithelial cells and do not contact the luminal milieu, the involvement of enteric neurons in luminal sensing is thought to be indirect and secondary to epithelial nutrient absorption. Our study demonstrates that intestinal enteric neurons are activated by dietary glucose and oleic acid, in the absence of mucosal enterocytes and enteroendocrine cells (EECs). Using primary enteric neuronal cultures generated from the intestinal submucosa, after exclusion of the mucosa, muscle layers, glial, and smooth muscle cells, we studied neuronal activation using intracellular Ca2+ transients as a surrogate. We show that diet-induced obesity (DIO) blunts the sensitivity of enteric neurons, as evidenced by lower (42%–52%), delayed (22–34 s), and sustained peak fluorescence (1.5–3.7-fold), and prolonged decay time (1158–1432 s). These findings significantly advance the field of enteric neuronal circuitry by revealing an unexplored, critical physiological function with potential therapeutic roles in the amelioration of obesity and associated comorbidities, including type 2 diabetes. |
| **Date** | 2025 |
| **Language** | en |
| **Short Title** | Diet-Induced Obesity Blunts Sensitivity of Intestinal Enteric Neurons |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1096/fj.202500069R> |
| **Accessed** | 6/15/2025, 4:30:48 PM |
| **Rights** | © 2025 The Author(s). The FASEB Journal published by Wiley Periodicals LLC on behalf of Federation of American Societies for Experimental Biology. |
| **Extra** | \_eprint: https://faseb.onlinelibrary.wiley.com/doi/pdf/10.1096/fj.202500069R |
| **Volume** | 39 |
| **Pages** | e70584 |
| **Publication** | The FASEB Journal |
| **DOI** | [10.1096/fj.202500069R](http://doi.org/10.1096/fj.202500069R) |
| **Issue** | 9 |
| **ISSN** | 1530-6860 |
| **Date Added** | 6/15/2025, 4:30:48 PM |
| **Modified** | 6/15/2025, 4:30:48 PM |

### Notes:

* + e70584 202500069R

### Attachments

* + Full Text PDF

## Diet-microbiome-ENS connection: impact of the cafeteria diet

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Arun Balasubramaniam |
| **Author** | Shanthi Srinivasan |
| **Date** | 2025-03 |
| **Short Title** | Diet-microbiome-ENS connection |
| **Library Catalog** | journals.physiology.org (Atypon) |
| **URL** | <https://journals.physiology.org/doi/full/10.1152/ajpgi.00391.2024> |
| **Accessed** | 6/15/2025, 4:30:51 PM |
| **Extra** | Publisher: American Physiological Society |
| **Volume** | 328 |
| **Pages** | G179-G181 |
| **Publication** | American Journal of Physiology-Gastrointestinal and Liver Physiology |
| **DOI** | [10.1152/ajpgi.00391.2024](http://doi.org/10.1152/ajpgi.00391.2024) |
| **Issue** | 3 |
| **ISSN** | 0193-1857 |
| **Date Added** | 6/15/2025, 4:30:52 PM |
| **Modified** | 6/15/2025, 4:30:52 PM |

### Tags:

* + enteric nervous system
  + gut microbiota
  + gut-brain axis
  + gastrointestinal motility
  + cafeteria diet

### Attachments

* + Full Text PDF

## Dysregulation of Metabolic Peptides in the Gut–Brain Axis Promotes Hyperinsulinemia, Obesity, and Neurodegeneration

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Camille Green |
| **Author** | Vandana Zaman |
| **Author** | Kayce Blumenstock |
| **Author** | Narendra L. Banik |
| **Author** | Azizul Haque |
| **Abstract** | Metabolic peptides can influence metabolic processes and contribute to both inflammatory and/or anti-inflammatory responses. Studies have shown that there are thousands of metabolic peptides, made up of short chains of amino acids, that the human body produces. These peptides are crucial for regulating many different processes like metabolism and cell signaling, as they bind to receptors on various cells. This review will cover the role of three specific metabolic peptides and their roles in hyperinsulinemia, diabetes, inflammation, and neurodegeneration, as well as their roles in type 3 diabetes and dementia. The metabolic peptides glucagon-like peptide 1 (GLP-1), gastric inhibitor polypeptide (GIP), and pancreatic peptide (PP) will be discussed, as dysregulation within their processes can lead to the development of various inflammatory and neurodegenerative diseases. Research has been able to closely investigate the connections between these metabolic peptides and their links to the gut–brain axis, highlighting changes made in the gut that can lead to dysfunction in processes in the brain, as well as changes made in the brain that can lead to dysregulation in the gut. The role of metabolic peptides in the development and potentially reversal of diseases such as obesity, hyperinsulinemia, and type 2 diabetes will also be discussed. Furthermore, we review the potential links between these conditions and neuroinflammation and the development of neurodegenerative diseases like dementia, specifically Parkinson’s disease and Alzheimer’s disease. |
| **Date** | 2025/1 |
| **Language** | en |
| **Library Catalog** | www.mdpi.com |
| **URL** | <https://www.mdpi.com/2227-9059/13/1/132> |
| **Accessed** | 6/15/2025, 4:31:10 PM |
| **Rights** | http://creativecommons.org/licenses/by/3.0/ |
| **Extra** | Number: 1 Publisher: Multidisciplinary Digital Publishing Institute |
| **Volume** | 13 |
| **Pages** | 132 |
| **Publication** | Biomedicines |
| **DOI** | [10.3390/biomedicines13010132](http://doi.org/10.3390/biomedicines13010132) |
| **Issue** | 1 |
| **ISSN** | 2227-9059 |
| **Date Added** | 6/15/2025, 4:31:10 PM |
| **Modified** | 6/15/2025, 4:31:10 PM |

### Tags:

* + inflammation
  + diabetes
  + gut–brain axis
  + neurodegeneration
  + hormonal peptides
  + hyperinsulinemia

### Attachments

* + Full Text PDF

## Enteric glial NLRP3 inflammasome contributes to gut mucosal barrier alterations in a mouse model of diet-induced obesity

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Vanessa D'Antongiovanni |
| **Author** | Matteo Fornai |
| **Author** | Rocchina Colucci |
| **Author** | Anna Nericcio |
| **Author** | Laura Benvenuti |
| **Author** | Clelia Di Salvo |
| **Author** | Cristina Segnani |
| **Author** | Clarissa Pierucci |
| **Author** | Chiara Ippolito |
| **Author** | Zoltan H. Nemeth |
| **Author** | György Haskó |
| **Author** | Nunzia Bernardini |
| **Author** | Luca Antonioli |
| **Author** | Carolina Pellegrini |
| **Abstract** | Aim In the present study, we investigated the involvement of NLRP3 inflammasome in the intestinal epithelial barrier (IEB) changes associated with obesity, and its role in the interplay between enteric glia and intestinal epithelial cells (IECs). Methods Wild-type C57BL/6J and NLRP3-KO (−/−) mice were fed with high-fat diet (HFD) or standard diet for 8 weeks. Colonic IEB integrity and inflammasome activation were assessed. Immunolocalization of colonic mucosal GFAP- and NLRP3-positive cells along with in vitro coculture experiments with enteric glial cells (EGCs) and IECs allowed to investigate the potential link between altered IEB, enteric gliosis, and NLRP3 activation. Results HFD mice showed increased body weight, altered IEB integrity, increased GFAP-positive glial cells, and NLRP3 inflammasome hyperactivation. HFD-NLRP3−/− mice showed a lower increase in body weight, an improvement in IEB integrity and an absence of enteric gliosis. Coculture experiments showed that palmitate and lipopolysaccharide contribute to IEB damage and promote enteric gliosis with consequent hyperactivation of enteric glial NLRP3/caspase-1/IL-1β signaling. Enteric glial-derived IL-1β release exacerbates the IEB alterations. Such an effect was abrogated upon incubation with anakinra (IL-1β receptor antagonist) and with conditioned medium derived from silenced-NLRP3 glial cells. Conclusion HFD intake elicits mucosal enteric gliotic processes characterized by a hyperactivation of NLRP3/caspase-1/IL-1β signaling pathway, that contributes to further exacerbate the disruption of intestinal mucosal barrier integrity. However, we cannot rule out the contribution of NLRP3 inflammasome activation from other cells, such as immune cells, in IEB alterations associated with obesity. Overall, our results suggest that enteric glial NLRP3 inflammasome might represent an interesting molecular target for the development of novel pharmacological approaches aimed at managing the enteric inflammation and intestinal mucosal dysfunctions associated with obesity. |
| **Date** | 2025 |
| **Language** | en |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1111/apha.14232> |
| **Accessed** | 6/15/2025, 4:31:01 PM |
| **Rights** | © 2024 The Author(s). Acta Physiologica published by John Wiley & Sons Ltd on behalf of Scandinavian Physiological Society. |
| **Extra** | \_eprint: https://onlinelibrary.wiley.com/doi/pdf/10.1111/apha.14232 |
| **Volume** | 241 |
| **Pages** | e14232 |
| **Publication** | Acta Physiologica |
| **DOI** | [10.1111/apha.14232](http://doi.org/10.1111/apha.14232) |
| **Issue** | 1 |
| **ISSN** | 1748-1716 |
| **Date Added** | 6/15/2025, 4:31:01 PM |
| **Modified** | 6/15/2025, 4:31:01 PM |

### Tags:

* + obesity
  + enteric glia
  + high fat-diet
  + inflammasome
  + intestinal epithelial barrier
  + intestinal inflammation
  + mucosal inflammation

### Notes:

* + e14232 APH-2024-03-0132.R1

### Attachments

* + Full Text PDF

## Gut microbiota and sirtuins in obesity-related inflammation and bowel dysfunction

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Shaheen E. Lakhan |
| **Author** | Annette Kirchgessner |
| **Abstract** | Obesity is a chronic disease characterized by persistent low-grade inflammation with alterations in gut motility. Motor abnormalities suggest that obesity has effects on the enteric nervous system (ENS), which controls virtually all gut functions. Recent studies have revealed that the gut microbiota can affect obesity and increase inflammatory tone by modulating mucosal barrier function. Furthermore, the observation that inflammatory conditions influence the excitability of enteric neurons may add to the gut dysfunction in obesity. In this article, we discuss recent advances in understanding the role of gut microbiota and inflammation in the pathogenesis of obesity and obesity-related gastrointestinal dysfunction. The potential contribution of sirtuins in protecting or regulating the circuitry of the ENS under inflamed states is also considered. |
| **Date** | 2011-11-24 |
| **Library Catalog** | BioMed Central |
| **URL** | <https://doi.org/10.1186/1479-5876-9-202> |
| **Accessed** | 6/15/2025, 4:30:44 PM |
| **Volume** | 9 |
| **Pages** | 202 |
| **Publication** | Journal of Translational Medicine |
| **DOI** | [10.1186/1479-5876-9-202](http://doi.org/10.1186/1479-5876-9-202) |
| **Issue** | 1 |
| **Journal Abbr** | Journal of Translational Medicine |
| **ISSN** | 1479-5876 |
| **Date Added** | 6/15/2025, 4:30:44 PM |
| **Modified** | 6/15/2025, 4:30:44 PM |

### Tags:

* + Obesity
  + Enteric Nervous System
  + Irritable Bowel Syndrome
  + Resveratrol
  + SIRT1 Expression

### Attachments

* + Full Text PDF

## Gut-Brain Axis: Role of Microbiome, Metabolomics, Hormones, and Stress in Mental Health Disorders

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Ankita Verma |
| **Author** | Sabra S. Inslicht |
| **Author** | Aditi Bhargava |
| **Abstract** | The influence of gut microbiome, metabolites, omics, hormones, and stress on general and mental health is increasingly being recognized. Ancient cultures recognized the importance of diet and gut health on the overall health of an individual. Western science and modern scientific methods are beginning to unravel the foundations and mechanisms behind some of the ancient beliefs and customs. The gut microbiome, an organ itself, is now thought to influence almost all other organs, ranging from the brain to the reproductive systems. Gut microbiome, metabolites, hormones, and biological sex also influence a myriad of health conditions that range from mental health disorders, obesity, gastrointestinal disorders, and cardiovascular diseases to reproductive health. Here, we review the history and current understanding of the gut–brain axis bidirectional talk in various mental health disorders with special emphasis on anxiety and depressive disorders, whose prevalence has increased by over 50% in the past three decades with COVID-19 pandemic being the biggest risk factor in the last few years. The vagal nerve is an important contributor to this bidirectional talk, but other pathways also contribute, and most remain understudied. Probiotics containing Lactobacillus and Bifidobacterium species seem to have the most impact on improvement in mental health symptoms, but the challenge appears to be maintaining sustained levels, especially since neither Lactobacillus nor Bifidobacterium can permanently colonize the gut. Ancient endogenous retroviral DNA in the human genome is also linked to several psychiatric disorders, including depression. These discoveries reveal the complex and intricately intertwined nature of gut health with mental health disorders. |
| **Date** | 2024/1 |
| **Language** | en |
| **Short Title** | Gut-Brain Axis |
| **Library Catalog** | www.mdpi.com |
| **URL** | <https://www.mdpi.com/2073-4409/13/17/1436> |
| **Accessed** | 6/15/2025, 4:31:21 PM |
| **Rights** | http://creativecommons.org/licenses/by/3.0/ |
| **Extra** | Number: 17 Publisher: Multidisciplinary Digital Publishing Institute |
| **Volume** | 13 |
| **Pages** | 1436 |
| **Publication** | Cells |
| **DOI** | [10.3390/cells13171436](http://doi.org/10.3390/cells13171436) |
| **Issue** | 17 |
| **ISSN** | 2073-4409 |
| **Date Added** | 6/15/2025, 4:31:21 PM |
| **Modified** | 6/15/2025, 4:31:21 PM |

### Tags:

* + depression
  + metabolomics
  + placebo
  + PTSD
  + sex differences

### Attachments

* + Full Text PDF

## High-fat diets on the enteric nervous system: Possible interactions and mechanisms underlying dysmotility

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Patricia Pereira Almeida |
| **Author** | Luisa Valdetaro |
| **Author** | Beatriz Bastos de Moraes Thomasi |
| **Author** | Milena Barcza Stockler-Pinto |
| **Author** | Ana Lúcia Tavares-Gomes |
| **Abstract** | Obesity is a chronic disease that affects various physiological systems. Among them, the gastrointestinal tract appears to be a main target of this disease. High-fat diet (HFD) animal models can help recapitulate the classic signs of obesity and present a series of gastrointestinal alterations, mainly dysmotility. Because intestinal motility is governed by the enteric nervous system (ENS), enteric neurons, and glial cells have been studied in HFD models. Given the importance of the ENS in general gut physiology, this review aims to discuss the relationship between HFD-induced neuroplasticity and gut dysmotility observed in experimental models. Furthermore, we highlight components of the gut environment that might influence enteric neuroplasticity, including gut microbiota, enteric glio-epithelial unit, serotonin release, immune cells, and disturbances such as inflammation and oxidative stress. |
| **Date** | 2022 |
| **Language** | en |
| **Short Title** | High-fat diets on the enteric nervous system |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1111/obr.13404> |
| **Accessed** | 6/15/2025, 4:30:42 PM |
| **Rights** | © 2021 World Obesity Federation |
| **Extra** | \_eprint: https://onlinelibrary.wiley.com/doi/pdf/10.1111/obr.13404 |
| **Volume** | 23 |
| **Pages** | e13404 |
| **Publication** | Obesity Reviews |
| **DOI** | [10.1111/obr.13404](http://doi.org/10.1111/obr.13404) |
| **Issue** | 4 |
| **ISSN** | 1467-789X |
| **Date Added** | 6/15/2025, 4:30:42 PM |
| **Modified** | 6/15/2025, 4:30:42 PM |

### Tags:

* + enteric nervous system
  + high-fat diet
  + dysmotility
  + enteric neuroplasticity

## NLRP3 at the crossroads between immune/inflammatory responses and enteric neuroplastic remodelling in a mouse model of diet-induced obesity

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Carolina Pellegrini |
| **Author** | Matteo Fornai |
| **Author** | Laura Benvenuti |
| **Author** | Rocchina Colucci |
| **Author** | Valentina Caputi |
| **Author** | Pablo Palazon-Riquelme |
| **Author** | Maria Cecilia Giron |
| **Author** | Anna Nericcio |
| **Author** | Francesca Garelli |
| **Author** | Vanessa D'Antongiovanni |
| **Author** | Cristina Segnani |
| **Author** | Chiara Ippolito |
| **Author** | Monica Nannipieri |
| **Author** | Gloria Lopez-Castejon |
| **Author** | Pablo Pelegrin |
| **Author** | György Haskó |
| **Author** | Nunzia Bernardini |
| **Author** | Corrado Blandizzi |
| **Author** | Luca Antonioli |
| **Abstract** | Background and Purpose Enteric neurogenic/inflammation contributes to bowel dysmotility in obesity. We examined the role of NLRP3 in colonic neuromuscular dysfunctions in mice with high-fat diet (HFD)-induced obesity. Experimental Approach Wild-type C57BL/6J and NLRP3-KO (Nlrp3−/−) mice were fed with HFD or standard diet for 8 weeks. The activation of inflammasome pathways in colonic tissues from obese mice was assessed. The role of NLRP3 in in vivo colonic transit and in vitro tachykininergic contractions and substance P distribution was evaluated. The effect of substance P on NLRP3 signalling was tested in cultured cells. Key Results HFD mice displayed increased body and epididymal fat weight, cholesterol levels, plasma resistin levels and plasma and colonic IL-1β levels, colonic inflammasome adaptor protein apoptosis-associated speck-like protein containing caspase-recruitment domain (ASC) and caspase-1 mRNA expression and ASC immunopositivity in macrophages. Colonic tachykininergic contractions were enhanced in HFD mice. HFD NLRP3−/− mice developed lower increase in body and epididymal fat weight, cholesterol levels, systemic and bowel inflammation. In HFD Nlrp3−/− mice, the functional alterations of tachykinergic pathways and faecal output were normalized. In THP-1 cells, substance P promoted IL-1β release. This effect was inhibited upon incubation with caspase-1 inhibitor or NK1 antagonist and not observed in ASC−/− cells. Conclusion and Implications In obesity, NLRP3 regulates an interplay between the shaping of enteric immune/inflammatory responses and the activation of substance P/NK1 pathways underlying the onset of colonic dysmotility. Identifying NLRP3 as a therapeutic target for the treatment of bowel symptoms related to obesity. |
| **Date** | 2021 |
| **Language** | en |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1111/bph.15532> |
| **Accessed** | 6/15/2025, 4:30:55 PM |
| **Rights** | © 2021 The Authors. British Journal of Pharmacology published by John Wiley & Sons Ltd on behalf of British Pharmacological Society. |
| **Extra** | \_eprint: https://bpspubs.onlinelibrary.wiley.com/doi/pdf/10.1111/bph.15532 |
| **Volume** | 178 |
| **Pages** | 3924-3942 |
| **Publication** | British Journal of Pharmacology |
| **DOI** | [10.1111/bph.15532](http://doi.org/10.1111/bph.15532) |
| **Issue** | 19 |
| **ISSN** | 1476-5381 |
| **Date Added** | 6/15/2025, 4:30:55 PM |
| **Modified** | 6/15/2025, 4:30:55 PM |

### Tags:

* + obesity
  + inflammation
  + colonic motility
  + macrophages
  + high-fat diet
  + NLRP3 inflammasome
  + substance P
  + tachykinin neurotransmission

### Attachments

* + Full Text PDF

## Nutritional Recommendations for Adult Bariatric Surgery Patients: Clinical Practice

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Shiri Sherf Dagan |
| **Author** | Ariela Goldenshluger |
| **Author** | Inbal Globus |
| **Author** | Chaya Schweiger |
| **Author** | Yafit Kessler |
| **Author** | Galit Kowen Sandbank |
| **Author** | Tair Ben-Porat |
| **Author** | Tali Sinai |
| **Abstract** | Bariatric surgery is currently the most effective treatment for morbid obesity and its associated metabolic complications. To ensure long-term postoperative success, patients must be prepared to adopt comprehensive lifestyle changes. This review summarizes the current evidence and expert opinions with regard to nutritional care in the perioperative and long-term postoperative periods. A literature search was performed with the use of different lines of searches for narrative reviews. Nutritional recommendations are divided into 3 main sections: 1) presurgery nutritional evaluation and presurgery diet and supplementation; 2) postsurgery diet progression, eating-related behaviors, and nutritional therapy for common gastrointestinal symptoms; and 3) recommendations for lifelong supplementation and advice for nutritional follow-up. We recognize the need for uniform, evidence-based nutritional guidelines for bariatric patients and summarize recommendations with the aim of optimizing long-term success and preventing complications. |
| **Date** | 2017-03-01 |
| **Short Title** | Nutritional Recommendations for Adult Bariatric Surgery Patients |
| **Library Catalog** | ScienceDirect |
| **URL** | <https://www.sciencedirect.com/science/article/pii/S2161831322007256> |
| **Accessed** | 6/15/2025, 4:31:33 PM |
| **Volume** | 8 |
| **Pages** | 382-394 |
| **Publication** | Advances in Nutrition |
| **DOI** | [10.3945/an.116.014258](http://doi.org/10.3945/an.116.014258) |
| **Issue** | 2 |
| **Journal Abbr** | Advances in Nutrition |
| **ISSN** | 2161-8313 |
| **Date Added** | 6/15/2025, 4:31:33 PM |
| **Modified** | 6/15/2025, 4:31:33 PM |

### Tags:

* + bariatric surgery
  + obesity
  + dietary supplements
  + eating-related behaviors
  + nutrition care

### Attachments

* + Full Text

## Orally Ingested Self-Powered Stimulators for Targeted Gut–Brain Axis Electrostimulation to Treat Obesity and Metabolic Disorders

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Cam-Hoa Mac |
| **Author** | Hsien-Meng Tai |
| **Author** | Sheng-Min Huang |
| **Author** | Hsu-Hsia Peng |
| **Author** | Amit Kumar Sharma |
| **Author** | Giang Le Thi Nguyen |
| **Author** | Pei-Ju Chang |
| **Author** | Jui-To Wang |
| **Author** | Yen Chang |
| **Author** | Yu-Jung Lin |
| **Author** | Hsing-Wen Sung |
| **Abstract** | Obesity is a significant health concern that often leads to metabolic dysfunction and chronic diseases. This study introduces a novel approach to combat obesity using orally ingested self-powered electrostimulators. These electrostimulators consist of piezoelectric BaTiO3 (BTO) particles conjugated with capsaicin (Cap) and aim to activate the vagus nerve. Upon ingestion by diet-induced obese (DIO) mice, the BTO@Cap particles specifically target and bind to Cap-sensitive sensory nerve endings in the gastric mucosa. In response to stomach peristalsis, these particles generate electrical signals. The signals travel via the gut–brain axis, ultimately influencing the hypothalamus. By enhancing satiety signals in the brain, this neuromodulatory intervention reduces food intake, promotes energy metabolism, and demonstrates minimal toxicity. Over a 3-week period of daily treatments, DIO mice treated with BTO@Cap particles show a significant reduction in body weight compared to control mice, while maintaining their general locomotor activity. Furthermore, this BTO@Cap particle-based treatment mitigates various metabolic alterations associated with obesity. Importantly, this noninvasive and easy-to-administer intervention holds potential for addressing other intracerebral neurological diseases. |
| **Date** | 2024 |
| **Language** | en |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1002/adma.202310351> |
| **Accessed** | 6/15/2025, 4:31:07 PM |
| **Rights** | © 2024 Wiley-VCH GmbH |
| **Extra** | \_eprint: https://advanced.onlinelibrary.wiley.com/doi/pdf/10.1002/adma.202310351 |
| **Volume** | 36 |
| **Pages** | 2310351 |
| **Publication** | Advanced Materials |
| **DOI** | [10.1002/adma.202310351](http://doi.org/10.1002/adma.202310351) |
| **Issue** | 21 |
| **ISSN** | 1521-4095 |
| **Date Added** | 6/15/2025, 4:31:07 PM |
| **Modified** | 6/15/2025, 4:31:07 PM |

### Tags:

* + capsaicin
  + metabolic dysfunction
  + piezoelectric material
  + vagus nerve stimulation
  + weight control

## Probiotics, prebiotics, synbiotics and other microbiome-based innovative therapeutics to mitigate obesity and enhance longevity via the gut-brain axis

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Jacqueline L. Boyajian |
| **Author** | Paromita Islam |
| **Author** | Ahmed Abosalha |
| **Author** | Sabrina Schaly |
| **Author** | Rahul Thareja |
| **Author** | Amal Kassab |
| **Author** | Karan Arora |
| **Author** | Madison Santos |
| **Author** | Cedrique Shum-Tim |
| **Author** | Satya Prakash |
| **Abstract** | The global prevalence of obesity currently exceeds 1 billion people and is accompanied by an increase in the aging population. Obesity and aging share many hallmarks and are leading risk factors for cardiometabolic disease and premature death. Current anti-obesity and pro-longevity pharmacotherapies are limited by side effects, warranting the development of novel therapies. The gut microbiota plays a major role in human health and disease, with a dysbiotic composition evident in obese and aged individuals. The bidirectional communication system between the gut and the central nervous system, known as the gut-brain axis, may link obesity to unhealthy aging. Modulating the gut with microbiome-targeted therapies, such as biotics, is a novel strategy to treat and/or manage obesity and promote longevity. Biotics represent material derived from living or once-living organisms, many of which have therapeutic effects. Pre-, pro-, syn- and post-biotics may beneficially modulate gut microbial composition and function to improve obesity and the aging process. However, the investigation of biotics as next-generation therapeutics has only just begun. Further research is needed to identify therapeutic biotics and understand their mechanisms of action. Investigating the function of the gut-brain axis in obesity and aging may lead to novel therapeutic strategies for obese, aged and comorbid (e.g., sarcopenic obese) patient populations. This review discusses the interrelationship between obesity and aging, with a particular emphasis on the gut microbiome, and presents biotics as novel therapeutic agents for obesity, aging and related disease states. |
| **Date** | 2024/05/17 |
| **Language** | en |
| **Library Catalog** | www.oaepublish.com |
| **URL** | <https://www.oaepublish.com/articles/mrr.2024.05> |
| **Accessed** | 6/15/2025, 4:30:34 PM |
| **Extra** | Publisher: OAE Publishing Inc. |
| **Volume** | 3 |
| **Pages** | N/A-N/A |
| **Publication** | Microbiome Research Reports |
| **DOI** | [10.20517/mrr.2024.05](http://doi.org/10.20517/mrr.2024.05) |
| **Issue** | 3 |
| **Journal Abbr** | mrr |
| **ISSN** | ISSN 2771-5965 (Online) |
| **Date Added** | 6/15/2025, 4:30:34 PM |
| **Modified** | 6/15/2025, 4:30:34 PM |

### Attachments

* + Full Text PDF

## Regulating the Enteric Nervous System against Obesity in Mice by Electroacupuncture

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Ding Dou |
| **Author** | Qiao Qiao Chen |
| **Author** | Zhan-qiong Zhong |
| **Author** | Xiu-wen Xia |
| **Author** | Wei-Jun Ding |
| **Abstract** | Background and Objectives: The enteric nervous system (ENS) dominates the onset of obesity and has been shown to regulate nutrient absorption and energy metabolism. Methods and Study Design: This study was performed to investigate the role of electroacupuncture in regulating ENS function in obese mice. Obese mice were obtained by high-fat diet. 16S rRNA pyrosequencing, Western blotting, quantitative PCR, and neurotransmitter analysis were used for this purpose. Results: Body weight, Lee index, serum lipid, leptin, and adiponectin levels, and other basic indices were significantly ameliorated after electroacupuncture intervention. The pathological ENS scores, serum neurotransmitter levels, and intestinal transit rate were markedly changed in obese mice. Moreover, electroacupuncture promoted the diversity of gut microbiota. No significant differences were observed 21 and 28 days after electroacupuncture. Conclusions: These results suggested ENS may be a new treatment approach to obesity. |
| **Date** | 2020-06-09 |
| **Library Catalog** | Silverchair |
| **URL** | <https://doi.org/10.1159/000506483> |
| **Accessed** | 6/15/2025, 4:30:38 PM |
| **Volume** | 27 |
| **Pages** | 48-57 |
| **Publication** | Neuroimmunomodulation |
| **DOI** | [10.1159/000506483](http://doi.org/10.1159/000506483) |
| **Issue** | 1 |
| **Journal Abbr** | Neuroimmunomodulation |
| **ISSN** | 1021-7401 |
| **Date Added** | 6/15/2025, 4:30:38 PM |
| **Modified** | 6/15/2025, 4:30:38 PM |

## Reversal of High Fat Diet-Induced Obesity, Systemic Inflammation, and Astrogliosis by the NLRP3 Inflammasome Inhibitors NT-0249 and NT-0796

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Peter Thornton |
| **Author** | Valérie Reader |
| **Author** | Zsofia Digby |
| **Author** | Pamela Smolak |
| **Author** | Nicola Lindsay |
| **Author** | David Harrison |
| **Author** | Nick Clarke |
| **Author** | Alan P. Watt |
| **Date** | 2024-03-01 |
| **Language** | English |
| **Library Catalog** | jpet.aspetjournals.org |
| **URL** | <https://jpet.aspetjournals.org/article/S0022-3565(24)17213-8/fulltext> |
| **Accessed** | 6/15/2025, 4:31:13 PM |
| **Extra** | Publisher: Elsevier PMID: 38336379 |
| **Volume** | 388 |
| **Pages** | 813-826 |
| **Publication** | The Journal of Pharmacology and Experimental Therapeutics |
| **DOI** | [10.1124/jpet.123.002013](http://doi.org/10.1124/jpet.123.002013) |
| **Issue** | 3 |
| **Journal Abbr** | The Journal of Pharmacology and Experimental Therapeutics |
| **ISSN** | 0022-3565, 1521-0103 |
| **Date Added** | 6/15/2025, 4:31:13 PM |
| **Modified** | 6/15/2025, 4:31:13 PM |

### Tags:

* + GFAP
  + GLP-1
  + (2R)-2-{[(1
  + 2
  + 3
  + 5
  + 6
  + 7-hexahydro-s-indacen-4-yl)carbamoyl][(1-methyl-1H-pyrazol-4-yl)({[(2S)-oxolan-2-yl]methyl})sulfamoyl]azanide
  + 7-hexahydro-s-indacen-4-yl)carbamoyl]oxy}-3-(pyrimidin-2-yl)propanoate
  + 7-hexahydro-s-indacen-4-yl)carbamoyl]oxy}-3-(pyrimidin-2-yl)propanoic acid sodium salt
  + 7-Hexahydro-s-indacene-4-yl)amino]carbonyl]-4-(1-hydroxyl-1-methylethyl)-2-furansulfonamide sodium salt
  + 773
  + and pyrin domain-containing protein 3
  + ARC
  + arcuate nucleus
  + carboxylesterase humanized
  + CP-456
  + diet-induced obesity
  + DIO
  + DMH
  + dorsomedial hypothalamic nucleus
  + glial fibrillary acidic protein
  + GLP-1RA
  + glucagon like peptide-1
  + glucagon like peptide-1 receptor agonist
  + hCES-1
  + HDL
  + HFD
  + high-density lipoprotein
  + high-fat diet
  + IL
  + IL-1RA
  + insulin tolerance test
  + interleukin
  + interleukin-1 receptor antagonist
  + ITT
  + LDL
  + lipopolysaccharide
  + low-density lipoprotein
  + LPS
  + LRR-
  + N-[[(1
  + NDT-19795
  + NLRP3
  + NOD-
  + NT-0249
  + NT-0796
  + OD
  + OGTT
  + optical density
  + oral glucose tolerance test
  + PBMC
  + PCSK9
  + peripheral blood mononuclear cell
  + propan-2-yl(2R)-2-{[(1
  + proprotein convertase subtilisin/kexin type 9
  + sodium [(1
  + soluble urokinase plasminogen activator receptor
  + soluble vascular cell adhesion molecule 1
  + suPAR
  + sVCAM-1
  + TG
  + triglycerides
  + ventromedial hypothalamic nucleus
  + VMH

### Attachments

* + Full Text PDF
  + PubMed entry

## Role of Sirtuins in Modulating Neurodegeneration of the Enteric Nervous System and Central Nervous System

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Pavithra Chandramowlishwaran |
| **Author** | Anitha Vijay |
| **Author** | Daniel Abraham |
| **Author** | Ge Li |
| **Author** | Simon Musyoka Mwangi |
| **Author** | Shanthi Srinivasan |
| **Abstract** | Neurodegeneration of the central and enteric nervous systems is a common feature of aging and aging-related diseases, and is accelerated in individuals with metabolic dysfunction including obesity and diabetes. The molecular mechanisms of neurodegeneration in both the CNS and ENS are overlapping. Sirtuins are an important family of histone deacetylases that are important for genome stability, cellular response to stress, and nutrient and hormone sensing. They are activated by calorie restriction (CR) and by the coenzyme, nicotinamide adenine dinucleotide (NAD+). Sirtuins, specifically the nuclear SIRT1 and mitochondrial SIRT3, have been shown to have predominantly neuroprotective roles in the CNS while the cytoplasmic sirtuin, SIRT2 is largely associated with neurodegeneration. A systematic study of sirtuins in the ENS and their effect on enteric neuronal growth and survival has not been conducted. Recent studies, however, also link sirtuins with important hormones such as leptin, ghrelin, melatonin, and serotonin which influence many important processes including satiety, mood, circadian rhythm, and gut homeostasis. In this review, we address emerging roles of sirtuins in modulating the metabolic challenges from aging, obesity, and diabetes that lead to neurodegeneration in the ENS and CNS. We also highlight a novel role for sirtuins along the microbiota-gut-brain axis in modulating neurodegeneration. |
| **Date** | 2020-12-22 |
| **Language** | English |
| **Library Catalog** | Frontiers |
| **URL** | <https://www.frontiersin.org/journals/neuroscience/articles/10.3389/fnins.2020.614331/full> |
| **Accessed** | 6/15/2025, 4:31:03 PM |
| **Extra** | Publisher: Frontiers |
| **Volume** | 14 |
| **Publication** | Frontiers in Neuroscience |
| **DOI** | [10.3389/fnins.2020.614331](http://doi.org/10.3389/fnins.2020.614331) |
| **Journal Abbr** | Front. Neurosci. |
| **ISSN** | 1662-453X |
| **Date Added** | 6/15/2025, 4:31:03 PM |
| **Modified** | 6/15/2025, 4:31:03 PM |

### Tags:

* + Enteric Nervous System
  + neurodegeneration
  + Central Nervous System
  + Gut Microbiota
  + Myenteric Plexus
  + neuronal survival
  + Sirtuin (SIRT)

### Attachments

* + Full Text PDF

## Significance of the Gut-Brain Axis in the Development of Overweight and Obesity

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Martyna Kuśmierska |
| **Author** | Jakub Kuśmierski |
| **Author** | Izabela Janik |
| **Author** | Anna Martyka |
| **Author** | Przemysław Ujma |
| **Abstract** | Introduction: The global obesity crisis results from inactive lifestyles and poor diets, increasing the risk of metabolic disorders. Emerging research links obesity with gut microbiome changes influenced by factors like age, genetics, and diet. Gut-brain communication via neural, endocrine, and inflammatory pathways, influenced by microbial compounds, affects nervous system function. Materials and Methods of Research: A thorough literature review was performed using PubMed and Google Scholar, employing keywords related to the gut-brain axis and obesity. Results: Obesity shifts gut microbiota composition due to factors like childbirth method, diet, antibiotics, and environment. This imbalance impacts metabolism, appetite, and insulin sensitivity. Gut microbes influence the brain, regulating energy balance and inflammation. Dysregulated tryptophan metabolism leads to insulin resistance. Gut-brain communication via the vagal nerve affects nutrient metabolism. Hormones like insulin and leptin, along with microbial metabolites, affect lipid metabolism and appetite. Gut microbiota abundance correlates with leptin signaling, and changes in ghrelin levels relate to microbiota composition. Microbial presence affects food cravings. Inflammation in obesity is linked to gut microbiota changes, mediated by bile acids and microbial metabolites. Interventions like probiotics and fecal microbiota transplantation offer potential for managing obesity. Emerging therapies like peptide D3 hold promise but require further study. Conclusion: The microbiome-gut-brain axis is vital in obesity, affecting metabolism, inflammation, and appetite. Utilizing interventions such as dietary adjustments and probiotics targeting gut-brain signaling shows promise in managing obesity. Personalized approaches are crucial due to microbiome complexity. Further research is needed to develop effective therapies for the obesity epidemic. |
| **Date** | 2024-05-17 |
| **Language** | en |
| **Library Catalog** | apcz.umk.pl |
| **URL** | <https://apcz.umk.pl/JEHS/article/view/49434> |
| **Accessed** | 6/15/2025, 4:31:24 PM |
| **Rights** | Copyright (c) 2024 Martyna Kuśmierska, Jakub Kuśmierski, Izabela Janik, Anna Martyka, Przemysław Ujma |
| **Volume** | 70 |
| **Pages** | 49434 |
| **Publication** | Journal of Education, Health and Sport |
| **DOI** | [10.12775/JEHS.2024.70.49434](http://doi.org/10.12775/JEHS.2024.70.49434) |
| **ISSN** | 2391-8306 |
| **Date Added** | 6/15/2025, 4:31:24 PM |
| **Modified** | 6/15/2025, 4:31:24 PM |

### Tags:

* + obesity
  + brain-gut axis
  + gastrointestinal microbiome
  + overweight

### Attachments

* + Full Text PDF

## Temporal Effects of Bariatric Surgery on Adipokines, Inflammation and Oxidative Stress in Subjects with Impaired Glucose Homeostasis at 4 Years of Follow-up

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Thinzar Min |
| **Author** | Sarah L. Prior |
| **Author** | Gareth Dunseath |
| **Author** | Rachel Churm |
| **Author** | Jonathan D. Barry |
| **Author** | Jeffrey W. Stephens |
| **Abstract** | Previous studies have examined changes in plasma markers of inflammation and oxidative stress up to 24 months following bariatric surgery, but there is limited evidence on the long-term effects of bariatric surgery. |
| **Date** | 2020-05-01 |
| **Language** | en |
| **Library Catalog** | Springer Link |
| **URL** | <https://doi.org/10.1007/s11695-019-04377-3> |
| **Accessed** | 6/15/2025, 4:31:36 PM |
| **Volume** | 30 |
| **Pages** | 1712-1718 |
| **Publication** | Obesity Surgery |
| **DOI** | [10.1007/s11695-019-04377-3](http://doi.org/10.1007/s11695-019-04377-3) |
| **Issue** | 5 |
| **Journal Abbr** | OBES SURG |
| **ISSN** | 1708-0428 |
| **Date Added** | 6/15/2025, 4:31:36 PM |
| **Modified** | 6/15/2025, 4:31:36 PM |

### Tags:

* + Bariatric surgery
  + Obesity
  + Diabetes
  + Cytokines
  + Inflammation
  + Bariatric Surgery
  + Surgery
  + Oxidative stress
  + Adipokines
  + Endocrinology
  + Neuroendocrinology
  + Plastic Surgery

### Attachments

* + Full Text PDF

## The effects of bariatric surgery on clinical profile, DNA methylation, and ageing in severely obese patients

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Eliza Fraszczyk |
| **Author** | Mirjam Luijten |
| **Author** | Annemieke M. W. Spijkerman |
| **Author** | Harold Snieder |
| **Author** | Paul F. K. Wackers |
| **Author** | Vincent W. Bloks |
| **Author** | Carolina F. Nicoletti |
| **Author** | Carla B. Nonino |
| **Author** | Ana B. Crujeiras |
| **Author** | Wim A. Buurman |
| **Author** | Jan Willem Greve |
| **Author** | Sander S. Rensen |
| **Author** | Bruce H. R. Wolffenbuttel |
| **Author** | Jana V. van Vliet-Ostaptchouk |
| **Abstract** | Severe obesity is a growing, worldwide burden and conventional therapies including radical change of diet and/or increased physical activity have limited results. Bariatric surgery has been proposed as an alternative therapy showing promising results. It leads to substantial weight loss and improvement of comorbidities such as type 2 diabetes. Increased adiposity is associated with changes in epigenetic profile, including DNA methylation. We investigated the effect of bariatric surgery on clinical profile, DNA methylation, and biological age estimated using Horvath’s epigenetic clock. |
| **Date** | 2020-01-20 |
| **Library Catalog** | BioMed Central |
| **URL** | <https://doi.org/10.1186/s13148-019-0790-2> |
| **Accessed** | 6/15/2025, 4:31:38 PM |
| **Volume** | 12 |
| **Pages** | 14 |
| **Publication** | Clinical Epigenetics |
| **DOI** | [10.1186/s13148-019-0790-2](http://doi.org/10.1186/s13148-019-0790-2) |
| **Issue** | 1 |
| **Journal Abbr** | Clinical Epigenetics |
| **ISSN** | 1868-7083 |
| **Date Added** | 6/15/2025, 4:31:38 PM |
| **Modified** | 6/15/2025, 4:31:38 PM |

### Tags:

* + Bariatric surgery
  + Obesity
  + Epigenetics
  + Biological age
  + DNA methylation
  + Epigenetic clock
  + EWAS
  + Morbid obesity

### Attachments

* + Full Text PDF

## The NLRP3 inflammasome instigates obesity-induced inflammation and insulin resistance

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Bolormaa Vandanmagsar |
| **Author** | Yun-Hee Youm |
| **Author** | Anthony Ravussin |
| **Author** | Jose E. Galgani |
| **Author** | Krisztian Stadler |
| **Author** | Randall L. Mynatt |
| **Author** | Eric Ravussin |
| **Author** | Jacqueline M. Stephens |
| **Author** | Vishwa Deep Dixit |
| **Abstract** | Obesity is generally considered an inflammatory state. Vishwa Dixit and his colleagues have now shown that excess dietary lipids leads to the activation of the Nlrp3 inflammasome, a sensor of the innate immune system, and that its genetic deficiency results in decreased inflammation and improved insulin sensitivity. These results suggest a possible new therapeutic avenue to treat the effects of obesity. |
| **Date** | 2011-02 |
| **Language** | en |
| **Library Catalog** | www.nature.com |
| **URL** | <https://www.nature.com/articles/nm.2279> |
| **Accessed** | 6/15/2025, 4:30:58 PM |
| **Rights** | 2011 Springer Nature America, Inc. |
| **Extra** | Publisher: Nature Publishing Group |
| **Volume** | 17 |
| **Pages** | 179-188 |
| **Publication** | Nature Medicine |
| **DOI** | [10.1038/nm.2279](http://doi.org/10.1038/nm.2279) |
| **Issue** | 2 |
| **Journal Abbr** | Nat Med |
| **ISSN** | 1546-170X |
| **Date Added** | 6/15/2025, 4:30:58 PM |
| **Modified** | 6/15/2025, 4:30:58 PM |

### Tags:

* + Type 2 diabetes
  + Obesity
  + Inflammasome
  + Insulin signalling

## Assessment of gastrointestinal function and enteric nervous system changes over time in the A53T mouse model of Parkinson’s disease

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Myat Noe Han |
| **Author** | Madeleine R. Di Natale |
| **Author** | Enie Lei |
| **Author** | John B. Furness |
| **Author** | David I. Finkelstein |
| **Author** | Marlene M. Hao |
| **Author** | Shanti Diwakarla |
| **Author** | Rachel M. McQuade |
| **Abstract** | Gastrointestinal (GI) dysfunctions, including constipation and delayed stomach emptying, are prevalent and debilitating non-motor symptoms of Parkinson’s disease (PD). These symptoms have been associated with damage in the enteric nervous system (ENS) and the accumulation of pathogenic alpha-synuclein (α-Syn) within the GI tract. While motor deficits and dopaminergic neuron loss in the central nervous system (CNS) of the A53T mouse model are well-characterised, the temporal relationship between GI dysfunction, ENS pathology, and motor symptoms remains unclear. This study aimed to investigate functional alterations in the GI tract at the early stages of the disease, before the appearance of motor deficits, both in vivo and ex vivo. Early colonic motility deficits observed in A53T mice, measured via bead expulsion, preceded motor impairments emerged at 36 weeks. Although whole-gut transit remained unchanged, reduced faecal output was concurrent with marked colonic dysmotility at 36 weeks. Despite a lack of significant neuronal loss, a greater number of enteric neurons in A53T mice showed signs of neuronal hypertrophy and increased nuclear translocation of HuC/D proteins indicative of neuronal stress at 12 and 36 weeks. Calcium imaging revealed differential enteric neuron activity, characterised by exaggerated calcium transients at 12 weeks that normalized by 36 weeks. Furthermore, a reduction in enteric glial populations was observed as early as 12 weeks in both the ileum and colon of A53T mice. These findings provide compelling evidence that ENS pathology, including neuronal stress, disrupted calcium signalling, and glial cell loss, precedes the onset of motor symptoms and may contribute to early GI dysfunction in PD. |
| **Date** | 2025-03-12 |
| **Library Catalog** | BioMed Central |
| **URL** | <https://doi.org/10.1186/s40478-025-01956-7> |
| **Accessed** | 6/15/2025, 4:34:25 PM |
| **Volume** | 13 |
| **Pages** | 58 |
| **Publication** | Acta Neuropathologica Communications |
| **DOI** | [10.1186/s40478-025-01956-7](http://doi.org/10.1186/s40478-025-01956-7) |
| **Issue** | 1 |
| **Journal Abbr** | Acta Neuropathologica Communications |
| **ISSN** | 2051-5960 |
| **Date Added** | 6/15/2025, 4:34:25 PM |
| **Modified** | 6/15/2025, 4:34:25 PM |

### Tags:

* + Enteric nervous system
  + Parkinson’s disease
  + Constipation
  + A53T
  + Gastrointestinal dysfunction

### Attachments

* + Full Text PDF

## Beyond the Microbiota: Understanding the Role of the Enteric Nervous System in Parkinson’s Disease from Mice to Human

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Martina Montanari |
| **Author** | Paola Imbriani |
| **Author** | Paola Bonsi |
| **Author** | Giuseppina Martella |
| **Author** | Antonella Peppe |
| **Abstract** | The enteric nervous system (ENS) is a nerve network composed of neurons and glial cells that regulates the motor and secretory functions of the gastrointestinal (GI) tract. There is abundant evidence of mutual communication between the brain and the GI tract. Dysfunction of these connections appears to be involved in the pathophysiology of Parkinson’s disease (PD). Alterations in the ENS have been shown to occur very early in PD, even before central nervous system (CNS) involvement. Post-mortem studies of PD patients have shown aggregation of α-synuclein (αS) in specific subtypes of neurons in the ENS. Subsequently, αS spreads retrogradely in the CNS through preganglionic vagal fibers to this nerve’s dorsal motor nucleus (DMV) and other central nervous structures. Here, we highlight the role of the ENS in PD pathogenesis based on evidence observed in animal models and using a translational perspective. While acknowledging the putative role of the microbiome in the gut–brain axis (GBA), this review provides a comprehensive view of the ENS not only as a “second brain”, but also as a window into the “first brain”, a potentially crucial element in the search for new therapeutic approaches that can delay and even cure the disease. |
| **Date** | 2023/6 |
| **Language** | en |
| **Short Title** | Beyond the Microbiota |
| **Library Catalog** | www.mdpi.com |
| **URL** | <https://www.mdpi.com/2227-9059/11/6/1560> |
| **Accessed** | 6/15/2025, 4:33:54 PM |
| **Rights** | http://creativecommons.org/licenses/by/3.0/ |
| **Extra** | Number: 6 Publisher: Multidisciplinary Digital Publishing Institute |
| **Volume** | 11 |
| **Pages** | 1560 |
| **Publication** | Biomedicines |
| **DOI** | [10.3390/biomedicines11061560](http://doi.org/10.3390/biomedicines11061560) |
| **Issue** | 6 |
| **ISSN** | 2227-9059 |
| **Date Added** | 6/15/2025, 4:33:54 PM |
| **Modified** | 6/15/2025, 4:33:54 PM |

### Tags:

* + microbiota
  + enteric nervous system
  + gut–brain axis
  + Parkinson’s disease
  + central nervous system
  + non-motor symptoms
  + clinical evidence
  + gastrointestinal dysfunction
  + glia cells
  + neurons
  + rodent models

### Attachments

* + Full Text PDF

## Effect of probiotic supplementation on gastrointestinal motility, inflammation, motor, non-motor symptoms and mental health in Parkinson’s disease: a meta-analysis of randomized controlled trials

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Jong Mi Park |
| **Author** | Sang Chul Lee |
| **Author** | Chorom Ham |
| **Author** | Yong Wook Kim |
| **Abstract** | Parkinson’s disease (PD) is the second most common neurodegenerative disease worldwide. Gut dysbiosis is hypothesized to cause PD; therefore, whether probiotics can be used as adjuvants in the treatment of PD is being actively investigated. |
| **Date** | 2023-03-06 |
| **Short Title** | Effect of probiotic supplementation on gastrointestinal motility, inflammation, motor, non-motor symptoms and mental health in Parkinson’s disease |
| **Library Catalog** | BioMed Central |
| **URL** | <https://doi.org/10.1186/s13099-023-00536-1> |
| **Accessed** | 6/15/2025, 4:35:06 PM |
| **Volume** | 15 |
| **Pages** | 9 |
| **Publication** | Gut Pathogens |
| **DOI** | [10.1186/s13099-023-00536-1](http://doi.org/10.1186/s13099-023-00536-1) |
| **Issue** | 1 |
| **Journal Abbr** | Gut Pathogens |
| **ISSN** | 1757-4749 |
| **Date Added** | 6/15/2025, 4:35:06 PM |
| **Modified** | 6/15/2025, 4:35:06 PM |

### Tags:

* + Inflammation
  + Parkinson’s disease
  + Gastrointestinal motility
  + Meta-analysis
  + Probiotics

### Attachments

* + Full Text PDF

## Efficacy of fecal microbiota transplantation in patients with Parkinson’s disease: clinical trial results from a randomized, placebo-controlled design

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Yi Cheng |
| **Author** | Tan ,Guohua |
| **Author** | Zhu ,Qihui |
| **Author** | Wang ,Chun |
| **Author** | Ruan ,Guangcong |
| **Author** | Ying ,Senhong |
| **Author** | Qie ,Jinlong |
| **Author** | Hu ,Xiaofei |
| **Author** | Xiao ,Zhifeng |
| **Author** | Xu ,Fenghua |
| **Author** | Chen ,Lu |
| **Author** | Chen ,Minjia |
| **Author** | Pei ,Yang |
| **Author** | Zhang ,Hao |
| **Author** | Tian ,Yuting |
| **Author** | Chen ,Dongfeng |
| **Author** | Liu ,Xingyin |
| **Author** | Huang ,Heqing |
| **Author** | Yanling and Wei |
| **Abstract** | The occurrence and development of Parkinson’s disease (PD) have been demonstrated to be related to gut dysbiosis, however, the impact of fecal microbiota transplantation (FMT) on microbiota engraftment in PD patients is uncertain. We performed a randomized, placebo-controlled trial at the Department of Neurology, Army Medical University Southwest Hospital in China (ChiCTR1900021405) from February 2019 to December 2019. Fifty-six participants with mild to moderate PD (Hoehn-Yahr stage 1–3) were randomly assigned to the FMT and placebo group, 27 patients in the FMT group and 27 in the placebo group completed the whole trial. During the follow-up, no severe adverse effect was observed, and patients with FMT treatment showed significant improvement in PD-related autonomic symptoms compared with the placebo group at the end of this trial (MDS-UPDRS total score, group×time effect, B = -6.56 [−12.98, −0.13], P < 0.05). Additionally, FMT improved gastrointestinal disorders and a marked increase in the complexity of the microecological system in patients. This study demonstrated that FMT through oral administration is clinically feasible and has the potential to improve the effectiveness of current medications in the clinical symptoms of PD patients. |
| **Date** | 2023-12-18 |
| **Short Title** | Efficacy of fecal microbiota transplantation in patients with Parkinson’s disease |
| **Library Catalog** | Taylor and Francis+NEJM |
| **URL** | <https://doi.org/10.1080/19490976.2023.2284247> |
| **Accessed** | 6/15/2025, 4:35:20 PM |
| **Extra** | Publisher: Taylor & Francis \_eprint: https://doi.org/10.1080/19490976.2023.2284247 PMID: 38057970 |
| **Volume** | 15 |
| **Pages** | 2284247 |
| **Publication** | Gut Microbes |
| **DOI** | [10.1080/19490976.2023.2284247](http://doi.org/10.1080/19490976.2023.2284247) |
| **Issue** | 2 |
| **ISSN** | 1949-0976 |
| **Date Added** | 6/15/2025, 4:35:20 PM |
| **Modified** | 6/15/2025, 4:35:20 PM |

### Tags:

* + gut microbiota
  + microbiota-gut-brain axis
  + Parkinson’s disease
  + fecal microbiota transplantation
  + clinical trial

### Attachments

* + Full Text PDF

## Fecal microbiota transplantation in Parkinson's disease—A randomized repeat-dose, placebo-controlled clinical pilot study

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Herbert L. DuPont |
| **Author** | Jessika Suescun |
| **Author** | Zhi-Dong Jiang |
| **Author** | Eric L. Brown |
| **Author** | Heather T. Essigmann |
| **Author** | Ashley S. Alexander |
| **Author** | Andrew W. DuPont |
| **Author** | Tehseen Iqbal |
| **Author** | Netanya S. Utay |
| **Author** | Michael Newmark |
| **Author** | Mya C. Schiess |
| **Abstract** | Background and purpose: The intestinal microbiome plays a primary role in the pathogenesis of neurodegenerative disorders and may provide an opportunity for disease modification. We performed a pilot clinical study looking at the safety of fecal microbiota transplantation (FMT), its effect on the microbiome, and improvement of symptoms in Parkinson's disease.Methods: This was a randomized, double-blind placebo-controlled pilot study, wherein orally administered lyophilized fecal microbiota transplantation product or matching placebo was given to 12 subjects with mild to moderate Parkinson's disease with constipation twice weekly for 12 weeks. Subjects were followed for safety and clinical improvement for 9 additional months (total study duration 12 months). Results: FMT caused non-severe transient upper gastrointestinal symptoms. One subject receiving FMT was diagnosed with unrelated metastatic cancer and was removed from the trial. Beta diversity (taxa) of the microbiome, was similar comparing placebo and FMT groups at baseline, however, for subjects randomized to FMT, it increased significantly at 6 weeks (p=0.008) and 13 weeks (p=0.0008). After treatment with FMT, proportions of selective firmicute genera increased significantly, while proportion of microbiota belonging to Proteobacteria were significantly reduced. Objective motor findings showed only temporary improvement while subjective symptom improvements were reported compared to baseline in the group receiving FMT. Constipation, gut transient times (NS), and gut motility index (p=0.0374) were improved in the FMT group Conclusions: Subjects with Parkinson's disease tolerated multi-dose-FMT, and experienced increased diversity of the intestinal microbiome that was associated with reduction in constipation and improved gut transit and intestinal motility. FMT administration improved subjective motor and non-motor symptoms. |
| **Date** | 2023-03-02 |
| **Language** | English |
| **Library Catalog** | Frontiers |
| **URL** | <https://www.frontiersin.org/journals/neurology/articles/10.3389/fneur.2023.1104759/full> |
| **Accessed** | 6/15/2025, 4:35:15 PM |
| **Extra** | Publisher: Frontiers |
| **Volume** | 14 |
| **Publication** | Frontiers in Neurology |
| **DOI** | [10.3389/fneur.2023.1104759](http://doi.org/10.3389/fneur.2023.1104759) |
| **Journal Abbr** | Front. Neurol. |
| **ISSN** | 1664-2295 |
| **Date Added** | 6/15/2025, 4:35:15 PM |
| **Modified** | 6/15/2025, 4:35:15 PM |

### Tags:

* + Dysbiosis
  + microbiome
  + Constipation
  + Parkinson's disease
  + fecal microbiota transplantation

### Attachments

* + Full Text PDF

## Gut-directed therapy in Parkinson’s disease

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Laura Benvenuti |
| **Author** | Clelia Di Salvo |
| **Author** | Gabriele Bellini |
| **Author** | Luisa Seguella |
| **Author** | Francesco Rettura |
| **Author** | Giuseppe Esposito |
| **Author** | Luca Antonioli |
| **Author** | Roberto Ceravolo |
| **Author** | Nunzia Bernardini |
| **Author** | Carolina Pellegrini |
| **Author** | Matteo Fornai |
| **Abstract** | Parkinson’s disease (PD) is a common and slow-progressing neurodegenerative disorder characterized by motor and non-motor symptoms, including gastrointestinal (GI) dysfunctions. Over the last years, the microbiota-gut-brain (MGB) axis is emerging as a bacterial-neuro-immune ascending pathway that contributes to the progression of PD. Indeed, PD patients are characterized by changes in gut microbiota composition, alterations of intestinal epithelial barrier (IEB) and enteric neurogenic/inflammatory responses that, besides determining intestinal disturbances, contribute to brain pathology. In this context, despite the causal relationship between gut dysbiosis, impaired MGB axis and PD remains to be elucidated, emerging evidence shows that MGB axis modulation can represent a suitable therapeutical strategy for the treatment of PD. This review provides an overview of the available knowledge about the beneficial effects of gut-directed therapies, including dietary interventions, prebiotics, probiotics, synbiotics and fecal microbiota transplantation (FMT), in both PD patients and animal models. In this context, particular attention has been devoted to the mechanisms by which the modulation of MGB axis could halt or slow down PD pathology and, most importantly, how these approaches can be included in the clinical practice. |
| **Date** | 2024-06-21 |
| **Language** | English |
| **Library Catalog** | Frontiers |
| **URL** | <https://www.frontiersin.org/journals/pharmacology/articles/10.3389/fphar.2024.1407925/full> |
| **Accessed** | 6/15/2025, 4:36:07 PM |
| **Extra** | Publisher: Frontiers |
| **Volume** | 15 |
| **Publication** | Frontiers in Pharmacology |
| **DOI** | [10.3389/fphar.2024.1407925](http://doi.org/10.3389/fphar.2024.1407925) |
| **Journal Abbr** | Front. Pharmacol. |
| **ISSN** | 1663-9812 |
| **Date Added** | 6/15/2025, 4:36:07 PM |
| **Modified** | 6/15/2025, 4:36:07 PM |

### Tags:

* + Enteric Nervous System
  + Microbiota-gut-brain axis
  + Probiotics
  + Parkinson's disease
  + enteric inflammation
  + fecal microbiota transplantation
  + Prebiotics

### Attachments

* + Full Text PDF

## High-Throughput Screening Methodology to Identify Alpha-Synuclein Aggregation Inhibitors

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Jordi Pujols |
| **Author** | Samuel Peña-Díaz |
| **Author** | María Conde-Giménez |
| **Author** | Francisca Pinheiro |
| **Author** | Susanna Navarro |
| **Author** | Javier Sancho |
| **Author** | Salvador Ventura |
| **Abstract** | An increasing number of neurodegenerative diseases are being found to be associated with the abnormal accumulation of aggregated proteins in the brain. In Parkinson’s disease, this process involves the aggregation of alpha-synuclein (α-syn) into intraneuronal inclusions. Thus, compounds that inhibit α-syn aggregation represent a promising therapeutic strategy as disease-modifying agents for neurodegeneration. The formation of α-syn amyloid aggregates can be reproduced in vitro by incubation of the recombinant protein. However, the in vitro aggregation of α-syn is exceedingly slow and highly irreproducible, therefore precluding fast high throughput anti-aggregation drug screening. Here, we present a simple and easy-to-implement in-plate method for screening large chemical libraries in the search for α-syn aggregation modulators. It allows us to monitor aggregation kinetics with high reproducibility, while being faster and requiring lower protein amounts than conventional aggregation assays. We illustrate how the approach enables the identification of strong aggregation inhibitors in a library of more than 14,000 compounds. |
| **Date** | 2017/3 |
| **Language** | en |
| **Library Catalog** | www.mdpi.com |
| **URL** | <https://www.mdpi.com/1422-0067/18/3/478> |
| **Accessed** | 6/15/2025, 4:34:37 PM |
| **Rights** | http://creativecommons.org/licenses/by/3.0/ |
| **Extra** | Number: 3 Publisher: Multidisciplinary Digital Publishing Institute |
| **Volume** | 18 |
| **Pages** | 478 |
| **Publication** | International Journal of Molecular Sciences |
| **DOI** | [10.3390/ijms18030478](http://doi.org/10.3390/ijms18030478) |
| **Issue** | 3 |
| **ISSN** | 1422-0067 |
| **Date Added** | 6/15/2025, 4:34:37 PM |
| **Modified** | 6/15/2025, 4:34:37 PM |

### Tags:

* + α-synuclein
  + amyloid
  + high-throughput screening
  + Parkinson disease
  + protein aggregation

### Attachments

* + Full Text PDF

## Immediate modulatory effects of transcutaneous vagus nerve stimulation on patients with Parkinson’s disease: a crossover self-controlled fMRI study

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Chengwei Fu |
| **Author** | Xiaoyan Hou |
| **Author** | Chunye Zheng |
| **Author** | Yue Zhang |
| **Author** | Zhijie Gao |
| **Author** | Zhaoxian Yan |
| **Author** | Yongsong Ye |
| **Author** | Bo Liu |
| **Abstract** | Background: Previous studies have evaluated the safety and efficacy of transcutaneous auricular vagus nerve stimulation (taVNS) for the treatment of Parkinson’s disease (PD). However, the mechanism underlying the effect of taVNS on PD remains to be elucidated. This study aimed to investigate the immediate effects of taVNS in PD patients.Methods: This crossover self-controlled study included 50 PD patients. Each patient underwent three sessions of resting-state functional magnetic resonance imaging (rs-fMRI) under three conditions: real taVNS, sham taVNS, and no taVNS intervention. We analyzed whole-brain amplitude of low-frequency fluctuations (ALFF) from preprocessed fMRI data across different intervention conditions. ALFF values in altered brain regions were correlated with clinical symptoms in PD patients.Results: Forty-seven participants completed the study and were included in the final analysis. Real taVNS was associated with a widespread decrease in ALFF in the right hemisphere, including the superior parietal lobule, precentral gyrus, postcentral gyrus, middle occipital gyrus, and cuneus (voxel P < 0.001, GRF corrected). The ALFF value in the right superior parietal lobule during real taVNS was negatively correlated with the Unified Parkinson’s Disease Rating Scale Part Ⅲ (r = -0.417, P = 0.004, Bonferroni corrected).Conclusion: TaVNS could immediately modulate the functional activity of brain regions involved in superior parietal lobule, precentral gyrus, postcentral gyrus, middle occipital gyrus, and cuneus. These findings offer preliminary insights into the mechanism of taVNS in treating PD and bolster confidence in its long-term therapeutic potential. TaVNS appears to reduce ALFF values in specific brain regions, suggesting a potential modulation mechanism for treating PD. |
| **Date** | 2024-10-23 |
| **Language** | English |
| **Short Title** | Immediate modulatory effects of transcutaneous vagus nerve stimulation on patients with Parkinson’s disease |
| **Library Catalog** | Frontiers |
| **URL** | <https://www.frontiersin.org/journals/aging-neuroscience/articles/10.3389/fnagi.2024.1444703/full> |
| **Accessed** | 6/15/2025, 4:35:41 PM |
| **Extra** | Publisher: Frontiers |
| **Volume** | 16 |
| **Publication** | Frontiers in Aging Neuroscience |
| **DOI** | [10.3389/fnagi.2024.1444703](http://doi.org/10.3389/fnagi.2024.1444703) |
| **Journal Abbr** | Front. Aging Neurosci. |
| **ISSN** | 1663-4365 |
| **Date Added** | 6/15/2025, 4:35:41 PM |
| **Modified** | 6/15/2025, 4:35:41 PM |

### Tags:

* + Parkinson's disease
  + Amplitude of low-frequency fluctuations
  + functional magnetic resonance imaging
  + Neuroimaging
  + Transcutaneous auricular vagus nerve stimulation

### Attachments

* + Full Text PDF

## Impaired Phasic Discharge of Locus Coeruleus Neurons Based on Persistent High Tonic Discharge—A New Hypothesis With Potential Implications for Neurodegenerative Diseases

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Kathrin Janitzky |
| **Abstract** | The locus coeruleus (LC) is a small brainstem nucleus with widely distributed noradrenergic projections to the whole brain, and loss of LC neurons is a prominent feature of age-related neurodegenerative diseases, such as Alzheimer`s disease (AD) and Parkinson's disease (PD). This article discusses the hypothesis that in early stages of neurodegenerative diseases, the discharge mode of LC neurons could be changed to a persistent high tonic discharge, which in turn might impair phasic discharge. Since phasic discharge of LC neurons is required for the release of high amounts of norepinephrine (NE) in the brain to promote anti-inflammatory and neuroprotective effects, persistent high tonic discharge of LC neurons could be a key factor in the progression of neurodegenerative diseases. Transcutaneous vagal stimulation (t-VNS), a non-invasive technique that potentially increases phasic discharge of LC neurons could therefore provide a non-pharmacological treatment approach in specific disease stages. This article focusses on LC vulnerability in neurodegenerative diseases, discusses the hypothesis that a persistent high tonic discharge of LC neurons might affect neurodegenerative processes, and finally reflects on t-VNS as a potentially useful clinical tool in specific stages of AD and PD. |
| **Date** | 2020-05-12 |
| **Language** | English |
| **Library Catalog** | Frontiers |
| **URL** | <https://www.frontiersin.org/journals/neurology/articles/10.3389/fneur.2020.00371/full> |
| **Accessed** | 6/15/2025, 4:36:19 PM |
| **Extra** | Publisher: Frontiers |
| **Volume** | 11 |
| **Publication** | Frontiers in Neurology |
| **DOI** | [10.3389/fneur.2020.00371](http://doi.org/10.3389/fneur.2020.00371) |
| **Journal Abbr** | Front. Neurol. |
| **ISSN** | 1664-2295 |
| **Date Added** | 6/15/2025, 4:36:19 PM |
| **Modified** | 6/15/2025, 4:36:19 PM |

### Tags:

* + neurodegeneration
  + Alzheimers`s disease
  + Locus Coeruleus
  + Neuroprotection
  + Norepinephrine
  + Parkinson's disease
  + phasic and tonic discharge
  + transcutaneous vagal stimulation

### Attachments

* + Full Text PDF

## Long-Term Oncologic Outcome following Duodenum-Preserving Pancreatic Head Resection for Benign Tumors, Cystic Neoplasms, and Neuroendocrine Tumors: Systematic Review and Meta-analysis

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Hans G Beger |
| **Author** | Benjamin Mayer |
| **Author** | Bertram Poch |
| **Date** | 2024 |
| **URL** | <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11164799/> |
| **Volume** | 31 |
| **Pages** | 4637–4653 |
| **Publication** | Annals of Surgical Oncology |
| **DOI** | [10.1245/s10434-024-15222-y](http://doi.org/10.1245/s10434-024-15222-y) |
| **Issue** | 7 |
| **Date Added** | 4/16/2025, 11:10:32 PM |
| **Modified** | 6/16/2025, 1:12:21 PM |

### Tags:

* + Adult
  + Female
  + Humans
  + Male
  + Treatment Outcome
  + Animals
  + Disease Models, Animal
  + Mice
  + STING
  + Quality of Life
  + Retrospective Studies
  + Diabetes
  + Signal Transduction
  + Cell Differentiation
  + Cell Line
  + Neoplasm Recurrence, Local
  + Cell Movement
  + Mammals
  + Neurons
  + immune cells
  + inflammation
  + Homeostasis
  + Gastroenterology
  + intestinal organoids
  + Regeneration
  + microbiota
  + Pancreas
  + inflammatory bowel disease
  + \*Cell- and Tissue-Based Therapy/methods
  + \*Bile Duct Neoplasms
  + \*Bile Duct Neoplasms/surgery
  + \*Cell Lineage
  + \*Cholangiocarcinoma
  + \*Cholangiocarcinoma/pathology
  + \*Colitis, Ulcerative/drug therapy
  + \*Cystadenocarcinoma/diagnostic imaging/surgery
  + \*Cystadenoma/diagnostic imaging/surgery
  + \*Cysts/pathology
  + \*Diabetes Mellitus, Experimental/complications/genetics/metabolism
  + \*Enteric Nervous System
  + \*Enteric Nervous System/pathology
  + \*Hyperglycemia/genetics/metabolism
  + \*Hypothalamo-Hypophyseal System
  + \*Inflammatory Bowel Diseases/drug therapy
  + \*Liver Neoplasms/diagnostic imaging/surgery
  + \*Liver Neoplasms/surgery
  + \*Microbiota
  + \*MicroRNAs/metabolism
  + \*Neoplasms, Cystic, Mucinous, and Serous
  + \*Neuroglia/physiology
  + \*Zebrafish
  + 16S RNA sequencing
  + Acinar cell carcinoma
  + Aging
  + antibiotics
  + Bile Ducts, Intrahepatic
  + Bile Ducts, Intrahepatic/surgery
  + Biliary
  + Biliary cystadenocarcinoma
  + Biliary cystadenoma
  + Brain
  + Brain-Gut Axis
  + Brain/physiology
  + Cell Separation
  + Chemical coding
  + Chick Embryo
  + circVPS13A
  + Cistoadenocarcinoma
  + Cistoadenoma
  + Clinicopathological criteria, Surgical outcomes
  + Colon/drug effects/pathology
  + Cystadenocarcinoma
  + Cystadenoma
  + cystic liver lesions
  + Cystic liver neoplasm
  + Cytology
  + Developmental disorders
  + diabetes
  + diabetes mellitus
  + Drug Discovery/\*methods
  + Embryonic stem cells
  + ENS
  + ENS neuropathies
  + enteric glia
  + enteric glia communications
  + Enteric glia communications
  + enteric glia diversity
  + enteric nervous system
  + Enteric nervous system
  + Enteric Nervous System
  + enteric nervous system (ENS)
  + Enteric nervous system (ENS)
  + Enteric Nervous System/\*pathology
  + Enteric neural precursor cells (ENPCs)
  + enteric progenitor cell
  + Fecal microbiota transplantation
  + Frantz's tumor
  + gastrointestinal complications
  + gastrointestinal diseases
  + Gastrointestinal Diseases
  + Gastrointestinal Diseases/pathology
  + gastrointestinal tract
  + Gastrointestinal Tract/drug effects/pathology
  + glia
  + Glial Cell Line-Derived Neurotrophic Factor/genetics
  + glucagon-like peptide 1
  + Growth Disorders
  + growth retardation
  + gut brain axis
  + gut microbiota
  + gut-brain axis
  + gut–brain axis
  + hepatic cystadenocarcinoma
  + hepatic cystadenoma
  + Hepatic simple cyst
  + hepatobiliary cystadenocarcinoma
  + hepatobiliary cystadenoma
  + Hirschsprung disease
  + Hirschsprung Disease/\*drug therapy/\*pathology/therapy
  + homeostasis
  + Imaging modalities
  + In Situ Hybridization, Fluorescence
  + Inflammatory bowel diseases
  + Intraductal papillary biliary neoplasms
  + intraductal papillary neoplasms of bile duct
  + irritable bowel syndrome
  + L-Fucose
  + Liver Diseases
  + Management
  + microbial metabolites
  + microbiota-gut-brain axis
  + Microbiota-gut-brain axis
  + Mucinous biliary cystic tumors, Biliary cystadenoma
  + mucinous cystic neoplasm
  + Mucinous cystic neoplasms
  + Mucinous neoplasm
  + muscularis macrophages
  + myenteric neurons
  + Neoplasia mucinosa quística
  + Neoplasia papilar intraductal biliar
  + Neoplasia quística hepática
  + Neural Crest
  + neural crest cell
  + neurodegeneration
  + Neuroglia
  + Neurons/drug effects/\*pathology
  + offspring
  + P2X7 receptor
  + pancreatectomy
  + Pancreatectomy
  + Pancreatic neoplasms
  + Pancreatic Neoplasms
  + Pancreatic surgery
  + pancreatic tumor
  + Parkinson’s disease
  + pediatric pancreatic neoplasm
  + Pepstatins/metabolism
  + Pituitary-Adrenal System
  + pluripotent stem cells (PSCs)
  + Pluripotent Stem Cells/pathology
  + preconception
  + probiotic
  + Purinergic signaling
  + Receptor, Endothelin B/metabolism
  + Receptors, Purinergic P2X7
  + RNA, Circular/genetics
  + Rotenone-induced mouse model
  + short-chain fatty acids
  + Solid pseudopapillary tumor
  + Stem-cell differentiation
  + submucosal neurons
  + Submucous Plexus
  + surgical outcome
  + surgical resection
  + three-dimensional (3D)
  + type 2 diabetes
  + zebrafish

### Notes:

* + e14603 NMO-00132-2023
  + e14603 NMO-00132-2023

### Attachments

* + Full Text
  + Full Text
  + Full Text PDF
  + Full Text PDF
  + Full Text PDF
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  + Full Text PDF
  + Full Text PDF
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  + PubMed Central Full Text PDF
  + PubMed Central Full Text PDF
  + PubMed Central Full Text PDF
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  + PubMed Central Link
  + PubMed entry

## MicroRNAs regulation in Parkinson’s disease, and their potential role as diagnostic and therapeutic targets

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Nour Shaheen |
| **Author** | Ahmed Shaheen |
| **Author** | Mahmoud Osama |
| **Author** | Abdulqadir J. Nashwan |
| **Author** | Vishal Bharmauria |
| **Author** | Oliver Flouty |
| **Abstract** | MicroRNAs (miRNAs) are small non-coding RNA molecules that regulate gene expression by binding to target messenger RNA (mRNA) molecules and promoting their degradation or blocking their translation. Parkinson’s disease (PD) is a neurodegenerative disorder caused by the loss of dopaminergic neurons in the substantia nigra. There is increasing evidence to suggest that miRNAs play a role in the pathogenesis of PD. Studies have identified several miRNAs that are dysregulated in the brains of PD patients, and animal models of the disease. MiRNA expression dysregulation contributes to the onset and progression of PD by modulating neuroinflammation, oxidative stress, and protein aggregation genes. Moreover, miRNAs have emerged as potential therapeutic targets for PD. This review elucidates the changes in miRNA expression profiles associated with PD, emphasising their potential as diagnostic biomarkers and therapeutic targets, and detailing specific miRNAs implicated in PD and their downstream targets. |
| **Date** | 2024-10-05 |
| **Language** | en |
| **Library Catalog** | www.nature.com |
| **URL** | <https://www.nature.com/articles/s41531-024-00791-2> |
| **Accessed** | 6/15/2025, 4:36:14 PM |
| **Rights** | 2024 The Author(s) |
| **Extra** | Publisher: Nature Publishing Group |
| **Volume** | 10 |
| **Pages** | 186 |
| **Publication** | npj Parkinson's Disease |
| **DOI** | [10.1038/s41531-024-00791-2](http://doi.org/10.1038/s41531-024-00791-2) |
| **Issue** | 1 |
| **Journal Abbr** | npj Parkinsons Dis. |
| **ISSN** | 2373-8057 |
| **Date Added** | 6/15/2025, 4:36:14 PM |
| **Modified** | 6/15/2025, 4:36:14 PM |

### Tags:

* + Epigenetics
  + Predictive markers

### Attachments

* + Full Text PDF

## Pathophysiological Changes in the Enteric Nervous System of Rotenone-Exposed Mice as Early Radiological Markers for Parkinson's Disease

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Gabriela Schaffernicht |
| **Author** | Qi Shang |
| **Author** | Alicia Stievenard |
| **Author** | Kai Bötzel |
| **Author** | Yanina Dening |
| **Author** | Romy Kempe |
| **Author** | Magali Toussaint |
| **Author** | Daniel Gündel |
| **Author** | Mathias Kranz |
| **Author** | Heinz Reichmann |
| **Author** | Christel Vanbesien-Mailliot |
| **Author** | Peter Brust |
| **Author** | Marianne Dieterich |
| **Author** | Richard H. W. Funk |
| **Author** | Ursula Ravens |
| **Author** | Francisco Pan-Montojo |
| **Abstract** | Parkinson’s disease (PD) is known to involve the peripheral nervous system (PNS) and the enteric nervous system (ENS). Functional changes in PNS and ENS appear early in the course of the disease and are responsible for some of the non-motor symptoms observed in PD patients like constipation, that can precede the appearance of motor symptoms by years. Here we analyzed the effect of the pesticide rotenone, a mitochondrial Complex I inhibitor, on the function and neuronal composition of the ENS by measuring intestinal contractility in a tissue bath and by analyzing related protein expression. Our results show that rotenone changes the normal physiological response of the intestine to carbachol, dopamine and electric field stimulation (EFS). Changes in the reaction to EFS seem to be related to the reduction in the cholinergic input but also related to the noradrenergic input, as suggested by the noradrenergic noncholinergic (NANC) reaction to the EFS in rotenone-exposed mice. The magnitude and direction of these alterations varies between intestinal regions and exposure times and is associated with an early up-regulation of dopaminergic, cholinergic and adrenergic receptors and an irregular reduction in the amount of enteric neurons in rotenone-exposed mice. The early appearance of these alterations, that start occurring before the substantia nigra is affected in this mouse model, suggests that these alterations could be also observed in patients before the onset of motor symptoms and makes them ideal potential candidates to be used as radiological markers for the detection of Parkinson´s disease in its early stages. |
| **Date** | 2021-03-22 |
| **Language** | English |
| **Library Catalog** | Frontiers |
| **URL** | <https://www.frontiersin.org/journals/neurology/articles/10.3389/fneur.2021.642604/full> |
| **Accessed** | 6/15/2025, 4:34:00 PM |
| **Extra** | Publisher: Frontiers |
| **Volume** | 12 |
| **Publication** | Frontiers in Neurology |
| **DOI** | [10.3389/fneur.2021.642604](http://doi.org/10.3389/fneur.2021.642604) |
| **Journal Abbr** | Front. Neurol. |
| **ISSN** | 1664-2295 |
| **Date Added** | 6/15/2025, 4:34:00 PM |
| **Modified** | 6/15/2025, 4:34:00 PM |

### Tags:

* + biomarker
  + Enteric Nervous System
  + non-motor symptoms
  + parkinson´s disease
  + pathophysiology

### Attachments

* + Full Text PDF

## Probiotic Formulation VSL#3 Interacts with Mesenchymal Stromal Cells To Protect Dopaminergic Neurons via Centrally and Peripherally Suppressing NOD-Like Receptor Protein 3 Inflammasome-Mediated Inflammation in Parkinson’s Disease Mice

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Liping Zhou |
| **Author** | Deqiang Han |
| **Author** | Xingzhe Wang |
| **Author** | Zhiguo Chen |
| **Abstract** | Systemic immunomodulation is increasingly recognized among the beneficial effects of mesenchymal stromal cells (MSCs) in treatment of Parkinson’s disease (PD), while the underlying mechanism is not fully understood. With the growing popularity of using probiotics as an adjuvant approach in PD treatment, concerns about the added effects of probiotics have been raised. In addition to the molecular mechanism mediating the neuroprotective effects of MSCs, the combined effects of a probiotic formulation, VSL#3, and MSC infusion were also evaluated in PD mice. The animals were weekly treated with human MSCs (hMSCs) via the tail vein, VSL#3 via the gastrointestinal tract, or their combination six times. hMSCs, VSL#3 alone, and their combination markedly ameliorated the decreased striatal dopamine content, loss of dopaminergic neurons in the substantia nigra, increased levels of proinflammatory cytokines in serum, as well as tumor necrosis factor alpha (TNF-α) and interleukin-1β (IL-1β) mRNAs in striatum and peripheral tissues induced by MPTP. Furthermore, hMSCs, VSL#3, and their combination notably downregulated mRNA expression of NOD-like receptor protein 3 (NLRP3) and caspase-1 in brain and peripheral tissues of PD mice. These results suggest that hMSCs, VSL#3, and their combination prevent neurodegenerative changes in PD mice via anti-inflammatory activities in both the central and peripheral systems, possibly through suppressing the NLRP3 inflammasome. Moreover, two-way analysis of variance (ANOVA) indicated that VSL#3 interacts with hMSCs to attenuate neurodegeneration and inhibit NLRP3 inflammasome-mediated inflammation without altering the effects of hMSCs. Major findings of our study support the usage of probiotic formulation VSL#3 as an adjuvant therapy to hMSC infusion in PD treatment.IMPORTANCE This study provides evidence for the neuroprotective activities of human umbilical cord MSCs from the aspect of anti-inflammation actions. hMSCs inhibit the NLRP3 inflammasome and MPTP-induced inflammation in both brain and periphery to relieve the degenerative changes in dopaminergic neurons in PD mice. Furthermore, as an additional therapeutic agent, probiotic formulation VSL#3 interacts with hMSCs in suppressing the NLRP3 inflammasome as well as the central and peripheral anti-inflammatory effects to exert neuroprotective actions in PD mice without altering the actions of hMSCs, suggesting the potential of VSL#3 as an adjuvant therapy in PD treatment. The findings of the present study give a further understanding of the anti-inflammatory activity and the molecular mechanism for the beneficial effects of MSCs as well as the potential application of probiotic formulation as an adjuvant approach to MSC therapy in PD treatment. |
| **Date** | 2023-02-02 |
| **Library Catalog** | journals.asm.org (Atypon) |
| **URL** | <https://journals.asm.org/doi/10.1128/spectrum.03208-22> |
| **Accessed** | 6/15/2025, 4:36:01 PM |
| **Extra** | Publisher: American Society for Microbiology |
| **Volume** | 11 |
| **Pages** | e03208-22 |
| **Publication** | Microbiology Spectrum |
| **DOI** | [10.1128/spectrum.03208-22](http://doi.org/10.1128/spectrum.03208-22) |
| **Issue** | 2 |
| **Date Added** | 6/15/2025, 4:36:01 PM |
| **Modified** | 6/15/2025, 4:36:01 PM |

### Attachments

* + Full Text PDF

## Probiotics synergized with conventional regimen in managing Parkinson’s disease

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Hairong Sun |
| **Author** | Feiyan Zhao |
| **Author** | Yuanyuan Liu |
| **Author** | Teng Ma |
| **Author** | Hao Jin |
| **Author** | Keyu Quan |
| **Author** | Bing Leng |
| **Author** | Junwu Zhao |
| **Author** | Xiaoling Yuan |
| **Author** | Zhenguang Li |
| **Author** | Fang Li |
| **Author** | Lai-Yu Kwok |
| **Author** | Shukun Zhang |
| **Author** | Zhihong Sun |
| **Author** | Jinbiao Zhang |
| **Author** | Heping Zhang |
| **Abstract** | Parkinson’s disease (PD) is mainly managed by pharmacological therapy (e.g., Benserazide and dopamine agonists). However, prolonged use of these drugs would gradually diminish their dopaminergic effect. Gut dysbiosis was observed in some patients with PD, suggesting close association between the gut microbiome and PD. Probiotics modulate the host’s gut microbiota beneficially. A 3-month randomized, double-blind, placebo-controlled clinical trial was conducted to investigate the beneficial effect of probiotic co-administration in patients with PD. Eighty-two PD patients were recruited and randomly divided into probiotic [n = 48; Bifidobacterium animalis subsp. lactis Probio-M8 (Probio-M8), Benserazide, dopamine agonists] and placebo (n = 34; placebo, Benserazide, dopamine agonists) groups. Finally, 45 and 29 patients from Probio-M8 and placebo groups provided complete fecal and serum samples for further omics analysis, respectively. The results showed that Probio-M8 co-administration conferred added benefits by improving sleep quality, alleviating anxiety, and gastrointestinal symptoms. Metagenomic analysis showed that, after the intervention, there were significantly more species-level genome bins (SGBs) of Bifidobacterium animalis, Ruminococcaceae, and Lachnospira, while less Lactobacillus fermentum and Klebsiella oxytoca in Probio-M8 group (P < 0.05). Interestingly, Lactobacillus fermentum correlated positively with the scores of UPDRS-III, HAMA, HAMD-17, and negatively with MMSE. Klebsiella oxytoca correlated negatively with feces hardness. Moreover, co-administering Probio-M8 increased SGBs involved in tryptophan degradation, gamma-aminobutyric acid, short-chain fatty acids, and secondary bile acid biosynthesis, as well as serum acetic acid and dopamine levels (P < 0.05). Taken together, Probio-M8 synergized with the conventional regimen and strengthened the clinical efficacy in managing PD, accompanied by modifications of the host’s gut microbiome, gut microbial metabolic potential, and serum metabolites. |
| **Date** | 2022-05-24 |
| **Language** | en |
| **Library Catalog** | www.nature.com |
| **URL** | <https://www.nature.com/articles/s41531-022-00327-6> |
| **Accessed** | 6/15/2025, 4:35:11 PM |
| **Rights** | 2022 The Author(s) |
| **Extra** | Publisher: Nature Publishing Group |
| **Volume** | 8 |
| **Pages** | 62 |
| **Publication** | npj Parkinson's Disease |
| **DOI** | [10.1038/s41531-022-00327-6](http://doi.org/10.1038/s41531-022-00327-6) |
| **Issue** | 1 |
| **Journal Abbr** | npj Parkinsons Dis. |
| **ISSN** | 2373-8057 |
| **Date Added** | 6/15/2025, 4:35:11 PM |
| **Modified** | 6/15/2025, 4:35:11 PM |

### Tags:

* + Parkinson's disease

### Attachments

* + Full Text PDF

## Seeding Propensity and Characteristics of Pathogenic αSyn Assemblies in Formalin-Fixed Human Tissue from the Enteric Nervous System, Olfactory Bulb, and Brainstem in Cases Staged for Parkinson’s Disease

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Alexis Fenyi |
| **Author** | Charles Duyckaerts |
| **Author** | Luc Bousset |
| **Author** | Heiko Braak |
| **Author** | Kelly Del Tredici |
| **Author** | Ronald Melki |
| **Author** | on behalf of the Brainbank Neuro-CEB Neuropathology Network |
| **Abstract** | We investigated α-synuclein’s (αSyn) seeding activity in tissue from the brain and enteric nervous system. Specifically, we assessed the seeding propensity of pathogenic αSyn in formalin-fixed tissue from the gastric cardia and five brain regions of 29 individuals (12 Parkinson’s disease, 8 incidental Lewy body disease, 9 controls) using a protein misfolding cyclic amplification assay. The structural characteristics of the resultant αSyn assemblies were determined by limited proteolysis and transmission electron microscopy. We show that fixed tissue from Parkinson’s disease (PD) and incidental Lewy body disease (ILBD) seeds the aggregation of monomeric αSyn into fibrillar assemblies. Significant variations in the characteristics of fibrillar assemblies derived from different regions even within the same individual were observed. This finding suggests that fixation stabilizes seeds with an otherwise limited seeding propensity, that yield assemblies with different intrinsic structures (i.e., strains). The lag phase preceding fibril assembly for patients ≥80 was significantly shorter than in other age groups, suggesting the existence of increased numbers of seeds or a higher seeding potential of pathogenic αSyn with time. Seeding activity did not diminish in late-stage disease. No statistically significant difference in the seeding efficiency of specific regions was found, nor was there a relationship between seeding efficiency and the load of pathogenic αSyn in a particular region at a given neuropathological stage. |
| **Date** | 2021/1 |
| **Language** | en |
| **Library Catalog** | www.mdpi.com |
| **URL** | <https://www.mdpi.com/2073-4409/10/1/139> |
| **Accessed** | 6/15/2025, 4:34:11 PM |
| **Rights** | http://creativecommons.org/licenses/by/3.0/ |
| **Extra** | Number: 1 Publisher: Multidisciplinary Digital Publishing Institute |
| **Volume** | 10 |
| **Pages** | 139 |
| **Publication** | Cells |
| **DOI** | [10.3390/cells10010139](http://doi.org/10.3390/cells10010139) |
| **Issue** | 1 |
| **ISSN** | 2073-4409 |
| **Date Added** | 6/15/2025, 4:34:11 PM |
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### Tags:

* + enteric nervous system
  + Parkinson’s disease
  + alpha-synuclein
  + incidental Lewy body disease
  + Lewy body disease
  + prion-like
  + protein misfolding cyclic amplification (PMCA)
  + synuclein strains
  + synucleinopathy

### Attachments

* + Full Text PDF

## Squalamine Restores the Function of the Enteric Nervous System in Mouse Models of Parkinson’s Disease

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Christine L. West |
| **Author** | Yu-Kang Mao |
| **Author** | Thilini Delungahawatta |
| **Author** | Jessica Y. Amin |
| **Author** | Sohana Farhin |
| **Author** | Rachel M. McQuade |
| **Author** | Shanti Diwakarla |
| **Author** | Ruslan Pustovit |
| **Author** | Andrew M. Stanisz |
| **Author** | John Bienenstock |
| **Author** | Denise Barbut |
| **Author** | Michael Zasloff |
| **Author** | John B. Furness |
| **Author** | Wolfgang A. Kunze |
| **Abstract** | Background:Parkinson’s disease (PD) is a progressive neurodegenerative disorder thought to be caused by accumulation of α-synuclein (α-syn) within the brain, autonomic nerves, and the enteric nervous system (ENS). Involvement of the ENS in PD often precedes the onset of the classic motor signs of PD by many years at a time when severe constipation represents a major morbidity. Studies conducted in vitro and in vivo, have shown that squalamine, a zwitterionic amphipathic aminosterol, originally isolated from the liver of the dogfish shark, effectively displaces membrane-bound α-syn.Objective:Here we explore the electrophysiological effect of squalamine on the gastrointestinal (GI) tract of mouse models of PD engineered to express the highly aggregating A53T human α-syn mutant.Methods:GI motility and in vivo response to oral squalamine in PD model mice and controls were assessed using an in vitro tissue motility protocol and via fecal pellet output. Vagal afferent response to squalamine was measured using extracellular mesenteric nerve recordings from the jejunum. Whole cell patch clamp was performed to measure response to squalamine in the myenteric plexus.Results:Squalamine effectively restores disordered colonic motility in vivo and within minutes of local application to the bowel. We show that topical squalamine exposure to intrinsic primary afferent neurons (IPANs) of the ENS rapidly restores excitability.Conclusion:These observations may help to explain how squalamine may promote gut propulsive activity through local effects on IPANs in the ENS, and further support its possible utility in the treatment of constipation in patients with PD. |
| **Date** | 2020-09-30 |
| **Language** | EN |
| **Library Catalog** | SAGE Journals |
| **URL** | <https://journals.sagepub.com/action/showAbstract> |
| **Accessed** | 6/15/2025, 4:34:32 PM |
| **Extra** | Publisher: SAGE Publications |
| **Volume** | 10 |
| **Pages** | 1477-1491 |
| **Publication** | Journal of Parkinson’s Disease |
| **DOI** | [10.3233/JPD-202076](http://doi.org/10.3233/JPD-202076) |
| **Issue** | 4 |
| **ISSN** | 1877-7171 |
| **Date Added** | 6/15/2025, 4:34:32 PM |
| **Modified** | 6/15/2025, 4:34:32 PM |

### Attachments

* + SAGE PDF Full Text

## The Baseline Structure of the Enteric Nervous System and Its Role in Parkinson’s Disease

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Gianfranco Natale |
| **Author** | Larisa Ryskalin |
| **Author** | Gabriele Morucci |
| **Author** | Gloria Lazzeri |
| **Author** | Alessandro Frati |
| **Author** | Francesco Fornai |
| **Abstract** | The gastrointestinal (GI) tract is provided with a peculiar nervous network, known as the enteric nervous system (ENS), which is dedicated to the fine control of digestive functions. This forms a complex network, which includes several types of neurons, as well as glial cells. Despite extensive studies, a comprehensive classification of these neurons is still lacking. The complexity of ENS is magnified by a multiple control of the central nervous system, and bidirectional communication between various central nervous areas and the gut occurs. This lends substance to the complexity of the microbiota–gut–brain axis, which represents the network governing homeostasis through nervous, endocrine, immune, and metabolic pathways. The present manuscript is dedicated to identifying various neuronal cytotypes belonging to ENS in baseline conditions. The second part of the study provides evidence on how these very same neurons are altered during Parkinson’s disease. In fact, although being defined as a movement disorder, Parkinson’s disease features a number of degenerative alterations, which often anticipate motor symptoms. Among these, the GI tract is often involved, and for this reason, it is important to assess its normal and pathological structure. A deeper knowledge of the ENS is expected to improve the understanding of diagnosis and treatment of Parkinson’s disease. |
| **Date** | 2021/8 |
| **Language** | en |
| **Library Catalog** | www.mdpi.com |
| **URL** | <https://www.mdpi.com/2075-1729/11/8/732> |
| **Accessed** | 6/15/2025, 4:35:49 PM |
| **Rights** | http://creativecommons.org/licenses/by/3.0/ |
| **Extra** | Number: 8 Publisher: Multidisciplinary Digital Publishing Institute |
| **Volume** | 11 |
| **Pages** | 732 |
| **Publication** | Life |
| **DOI** | [10.3390/life11080732](http://doi.org/10.3390/life11080732) |
| **Issue** | 8 |
| **ISSN** | 2075-1729 |
| **Date Added** | 6/15/2025, 4:35:49 PM |
| **Modified** | 6/15/2025, 4:35:49 PM |

### Tags:

* + enteric nervous system
  + gastrointestinal tract
  + neurodegeneration
  + Parkinson’s disease
  + dopamine
  + microbiota–gut–brain axis
  + α-synuclein

### Attachments

* + Full Text PDF

## The effect of electroacupuncture at ST25 on Parkinson's disease constipation through regulation of autophagy in the enteric nervous system

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Li-Zhe-Xiong Song |
| **Author** | Na Xu |
| **Author** | Zhi Yu |
| **Author** | Hui Yang |
| **Author** | Cheng-cheng Xu |
| **Author** | Zi Qiu |
| **Author** | Jing-wen Dai |
| **Author** | Bin Xu |
| **Author** | Xuan-ming Hu |
| **Abstract** | The effectiveness and safety of electroacupuncture (EA) for constipation have been confirmed by numerous clinical studies and experiments, and there are also studies on the efficacy of EA for Parkinson's disease (PD) motor symptoms. However, there are few researches on EA for PD constipation. Autophagy is thought to be involved in the mechanistic process of EA in the central nervous system (CNS) intervention in Parkinson's pathology. However, whether it has the same effect on the enteric nervous system (ENS) has not been elucidated. Therefore, we investigated whether EA at Tianshu (ST25) acupoint promotes the clearance of α-Syn and damaged mitochondria aggregated in the ENS in a model of rotenone-induced PD constipation. This study evaluated constipation symptoms by stool characteristics, excretion volume, and water content, and the expression levels of colonic ATG5, LC3II, and Parkin were detected by Western Blot (WB) and Real-Time Quantitative PCR (RT-qPCR). The relationship between the location of α-Syn and Parkin in the colonic ENS was observed by immunofluorescence (IF). The results showed that EA intervention significantly relieved the symptoms of rotenone-induced constipation in PD rats, reversed the rotenone-induced down-regulation of colonic ATG5, LC3II, and Parkin expression, and the positional relationship between colonic α-Syn and Parkin proved to be highly correlated. It is suggested that EA might be helpful in treating PD constipation by modulating Parkin-induced mitochondrial autophagy. |
| **Date** | 2023 |
| **Language** | en |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1002/ar.25148> |
| **Accessed** | 6/15/2025, 4:34:49 PM |
| **Rights** | © 2023 The Authors. The Anatomical Record published by Wiley Periodicals LLC on behalf of American Association for Anatomy. |
| **Extra** | \_eprint: https://anatomypubs.onlinelibrary.wiley.com/doi/pdf/10.1002/ar.25148 |
| **Volume** | 306 |
| **Pages** | 3214-3228 |
| **Publication** | The Anatomical Record |
| **DOI** | [10.1002/ar.25148](http://doi.org/10.1002/ar.25148) |
| **Issue** | 12 |
| **ISSN** | 1932-8494 |
| **Date Added** | 6/15/2025, 4:34:50 PM |
| **Modified** | 6/15/2025, 4:34:50 PM |

### Tags:

* + autophagy
  + acupuncture
  + Parkin
  + Parkinson's disease constipation
  + rotenone
  + α-Syn
  + α-突触核蛋白
  + 关键词
  + 帕金森便秘
  + 自噬
  + 针灸
  + 鱼藤酮

### Attachments

* + Full Text PDF

## The genetic background of Parkinson’s disease and novel therapeutic targets

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | András Salamon |
| **Author** | Zádori ,Dénes |
| **Author** | Szpisjak ,László |
| **Author** | Klivényi ,Péter |
| **Author** | László and Vécsei |
| **Abstract** | Parkinson’s disease (PD) is the second most common neurodegenerative disease worldwide. The median age of disease onset is around 60 years. From a genetic point of view, PD is basically considered a sporadic, idiopathic disease, however, hereditary components can be detected in 5–10% of patients. Expanding data are available regarding the targeted molecular therapy of the disease. The aim of this current review article is to provide brief clinical and molecular insight into three important genetic forms (LRRK2, SNCA, GBA) of hereditary PD subtypes and to present the human clinical trials in relation to these forms of the disease. These small hereditary subgroups are crucially important in drug development, because the general trend is that clinical trials that treat PD patients as a large group, without any separation, do not meet expectations. As a result, no long term conclusions can currently be drawn regarding the effectiveness of the molecules tested in these phase 1 and 2 studies. Further precise studies are needed in the near future. |
| **Date** | 2022-10-03 |
| **Library Catalog** | Taylor and Francis+NEJM |
| **URL** | <https://doi.org/10.1080/14728222.2022.2153037> |
| **Accessed** | 6/15/2025, 4:36:33 PM |
| **Extra** | Publisher: Taylor & Francis \_eprint: https://doi.org/10.1080/14728222.2022.2153037 PMID: 36524726 |
| **Volume** | 26 |
| **Pages** | 827-836 |
| **Publication** | Expert Opinion on Therapeutic Targets |
| **DOI** | [10.1080/14728222.2022.2153037](http://doi.org/10.1080/14728222.2022.2153037) |
| **Issue** | 10 |
| **ISSN** | 1472-8222 |
| **Date Added** | 6/15/2025, 4:36:33 PM |
| **Modified** | 6/15/2025, 4:36:33 PM |

### Tags:

* + Parkinson’s disease
  + GBA
  + genetic
  + LRRK2
  + SNCA

### Attachments

* + Accepted Version

## The Impact of Probiotics on Clinical Symptoms and Peripheral Cytokines Levels in Parkinson’s Disease: Preliminary In Vivo Data

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Luca Magistrelli |
| **Author** | Elena Contaldi |
| **Author** | Annalisa Visciglia |
| **Author** | Giovanni Deusebio |
| **Author** | Marco Pane |
| **Author** | Angela Amoruso |
| **Abstract** | Introduction. Previous studies have shown that probiotics have positive effects on both motor and non-motor symptoms in Parkinson’s disease (PD). Additionally, in preclinical settings, probiotics have demonstrated the ability to counteract neuronal loss and alpha-synuclein aggregation, important pathological hallmarks of PD. Notably, preliminary in vitro studies have revealed the immunomodulatory properties of probiotics. This study aims to evaluate the impact of probiotics on symptoms and peripheral cytokines levels in PD patients compared to placebo. Methods. Patients were enrolled and blindly randomized to receive either active probiotics (comprising Bifidobacterium animalis subsp. lactis BS01 LMG P-21384, Bifidobacterium longum BL03 DSM 16603, Bifidobacterium adolescentis BA02 DSM 18351, Fructo-oligosaccharides and Maltodextrin-Group A) or placebo (Maltodextrin-Group B). Clinical evaluations and plasma levels cytokines (TNF-α, IFN-γ, IL-6, and TGF-β) were also assessed at enrollment and after 12 weeks. Anti-parkinsonian therapy remained stable throughout the study. Results. Forty PD patients were recruited. After 12 weeks, Group A showed significant improvement in motor symptoms (UPDRS III: 13.89 ± 4.08 vs. 12.74 ± 4.57, p = 0.028) and non-motor symptoms (NMSS: 34.32 ± 21.41 vs. 30.11 ± 19.89, p = 0.041), with notable improvement in the gastrointestinal sub-item (3.79 ± 4.14 vs. 1.89 ± 2.54, p = 0.021). A reduction of IFN-γ levels was observed in both groups, but group A also showed a significant decrease in IL-6 and a slight increase in the anti-inflammatory cytokine TGF-β. Conclusions. Our data suggest that probiotics may modulate peripheral cytokines levels and improve clinical symptoms in PD patients. Probiotics may, therefore, represent a valuable adjunctive therapy to conventional anti-parkinsonian drugs. |
| **Date** | 2024/11 |
| **Language** | en |
| **Short Title** | The Impact of Probiotics on Clinical Symptoms and Peripheral Cytokines Levels in Parkinson’s Disease |
| **Library Catalog** | www.mdpi.com |
| **URL** | <https://www.mdpi.com/2076-3425/14/11/1147> |
| **Accessed** | 6/15/2025, 4:34:55 PM |
| **Rights** | http://creativecommons.org/licenses/by/3.0/ |
| **Extra** | Number: 11 Publisher: Multidisciplinary Digital Publishing Institute |
| **Volume** | 14 |
| **Pages** | 1147 |
| **Publication** | Brain Sciences |
| **DOI** | [10.3390/brainsci14111147](http://doi.org/10.3390/brainsci14111147) |
| **Issue** | 11 |
| **ISSN** | 2076-3425 |
| **Date Added** | 6/15/2025, 4:34:55 PM |
| **Modified** | 6/15/2025, 4:34:55 PM |

### Tags:

* + Parkinson’s disease
  + neuroinflammation
  + probiotics

### Attachments

* + Full Text PDF

## The PROB-PD trial: a pilot, randomised, placebo-controlled study protocol to evaluate the feasibility and potential efficacy of probiotics in modulating peripheral immunity in subjects with Parkinson’s disease

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Stefano Martini |
| **Author** | Franca Marino |
| **Author** | Luca Magistrelli |
| **Author** | Elena Contaldi |
| **Author** | Marco Cosentino |
| **Author** | Cristoforo Comi |
| **Abstract** | Parkinson’s disease (PD) is a common neurodegenerative disease. No disease-modifying treatment is available, and therapy is symptomatic. The histopathologic hallmark is the loss of dopaminergic neurons and accumulation of α-synuclein (α-syn) in surviving neurons, but the underlying pathophysiology is unclear. Inflammatory mechanisms seem to play a prominent role, with an imbalance of immune functions and neurotoxicity caused by reactive oxygen species (ROS). Involvement of peripheral adaptive immunity, with an imbalance in T cell subpopulations and in the expression of transcriptional factors in CD4+ T cells, has also been reported. Although clinical presentation is defined by motor symptoms, patients also report non-motor symptoms, often before the onset of a clinically established disease. Etiopathogenesis of PD is unknown, but an initial aggregation of α-syn in the gut, with subsequent propagation along the vagus nerve to the brain has been hypothesised. Interestingly, in an α-syn overexpressing murine model, the absence of gut microbiota prevented both microglia activation and motor impairment, thus pointing to a fundamental role of microbiota in the development of PD. Magistrelli et al. showed that in peripheral blood mononuclear cells of PD patients, probiotics modulate the in vitro production of cytokines toward an anti-inflammatory profile and reduce the production of ROS. |
| **Date** | 2023-05-08 |
| **Short Title** | The PROB-PD trial |
| **Library Catalog** | BioMed Central |
| **URL** | <https://doi.org/10.1186/s40814-023-01306-1> |
| **Accessed** | 6/15/2025, 4:36:28 PM |
| **Volume** | 9 |
| **Pages** | 77 |
| **Publication** | Pilot and Feasibility Studies |
| **DOI** | [10.1186/s40814-023-01306-1](http://doi.org/10.1186/s40814-023-01306-1) |
| **Issue** | 1 |
| **Journal Abbr** | Pilot and Feasibility Studies |
| **ISSN** | 2055-5784 |
| **Date Added** | 6/15/2025, 4:36:28 PM |
| **Modified** | 6/15/2025, 4:36:28 PM |

### Tags:

* + Innate immunity
  + Inflammation
  + Parkinson’s disease
  + Peripheral immunity
  + Probiotics

### Attachments

* + Full Text PDF

## Transcutaneous vagal nerve stimulation improves gastroenteric complaints in Parkinson’s disease patients

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Oliver Kaut |
| **Author** | Laura Janocha |
| **Author** | Tobias J. Weismüller |
| **Author** | Ullrich Wüllner |
| **Abstract** | BACKGROUND:Gastrointestinal dysfunctions are common in Parkinson’s disease. Their management is still challenging and new treatment options are needed.OBJECTIVE:To test whether transcutaneous vagal nerve stimulation can improve gastrointestinal dysfunction in patients with Parkinson’s disease.METHODS:We performed a randomized double-blind pilot study enrolling patients suffering from Parkinson’s disease with gastroenteric complaints. Patients were randomized to use either a sham-device or to stimulate the vagal nerve with an electric device over the course of four weeks with four stimulations per day. Ten patients (aged 69.6±4.6 years) were randomized for the intervention group, and nine patients (aged 67.2±6.3 years) used a sham-device. Clinical outcome was evaluated using the Gastrointestinal Symptom Rating Scale whereas gastrointestinal motility was measured with the 13C-octanoic acid breath test.RESULTS:In the treatment group, vagal nerve stimulation improved the Gastrointestinal Symptom Rating Scale comparing before and after stimulation (before, 8.7±6.09; after 5.67±3.08; p-value 0.48). This improvement was not observed in the sham group (before, 7.44±4.85; after, 5.67±3.08; p-value 0.16). In the 13C-octanoic acid breath test no significant changes were detectable.CONCLUSIONS:Vagal nerve stimulation is well tolerated with no side effects and may be a promising non-invasive therapy option to improve gastroenteric symptoms in Parkinson’s disease. |
| **Date** | 2019-12-18 |
| **Language** | EN |
| **Library Catalog** | SAGE Journals |
| **URL** | <https://journals.sagepub.com/action/showAbstract> |
| **Accessed** | 6/15/2025, 4:35:35 PM |
| **Extra** | Publisher: SAGE Publications |
| **Volume** | 45 |
| **Pages** | 449-451 |
| **Publication** | NeuroRehabilitation |
| **DOI** | [10.3233/NRE-192909](http://doi.org/10.3233/NRE-192909) |
| **Issue** | 4 |
| **ISSN** | 1053-8135 |
| **Date Added** | 6/15/2025, 4:35:35 PM |
| **Modified** | 6/15/2025, 4:35:35 PM |

* **Anatomical and physiological considerations in short bowel syndrome: Emphasis on intestinal adaptation and the role of enterohormones**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Kelly A. Tappenden |
| **Abstract** | Short bowel syndrome (SBS)–associated intestinal failure (IF) is a complex, life-threatening condition that requires complex care of multiple factors impacting the patient's long-term prognosis. Various etiologies result in SBS-IF, with three primary anatomical subtypes occurring following intestinal resection. Depending on the extent and segment(s) of the intestine resected, malabsorption can be nutrient specific or sweeping; however, such issues and the associated prognosis for the patient can be predicted with analysis of the residual intestine, along with baseline nutrient and fluid deficits and extent of malabsorption. The provision of parenteral nutrition/intravenous (PN-IV) fluids and antisymptomatic agents is fundamental; however, optimal management should focus on intestinal rehabilitation, wherein intestinal adaptation is prioritized and PN-IV fluids are weaned over time. Key strategies to maximize intestinal adaptation include hyperphagic consumption of an individualized SBS diet and the appropriate use of trophic agents, such as a glucagon-like peptide 2 analog. |
| **Date** | 2023 |
| **Language** | en |
| **Short Title** | Anatomical and physiological considerations in short bowel syndrome |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1002/ncp.10991> |
| **Accessed** | 6/15/2025, 4:42:37 PM |
| **Rights** | © 2023 The Authors. Nutrition in Clinical Practice published by Wiley Periodicals LLC on behalf of American Society for Parenteral and Enteral Nutrition. |
| **Extra** | \_eprint: https://aspenjournals.onlinelibrary.wiley.com/doi/pdf/10.1002/ncp.10991 |
| **Volume** | 38 |
| **Pages** | S27-S34 |
| **Publication** | Nutrition in Clinical Practice |
| **DOI** | [10.1002/ncp.10991](http://doi.org/10.1002/ncp.10991) |
| **Issue** | S1 |
| **ISSN** | 1941-2452 |
| **Date Added** | 6/15/2025, 4:42:37 PM |
| **Modified** | 6/15/2025, 4:42:37 PM |

* **Tags:**
  + intestinal failure
  + glucagon-like peptide 2
  + intestinal rehabilitation
  + malabsorption
  + parenteral nutrition
  + short bowel syndrome

**Attachments**

* + Full Text PDF
* **Glucagon-Like Peptide-2 and the Enteric Nervous System Are Components of Cell-Cell Communication Pathway Regulating Intestinal Na+/Glucose Co-transport**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Andrew W. Moran |
| **Author** | Miran A. Al-Rammahi |
| **Author** | Daniel J. Batchelor |
| **Author** | David M. Bravo |
| **Author** | Soraya P. Shirazi-Beechey |
| **Abstract** | The Na+/glucose cotransporter 1, SGLT1 is the major route for transport of dietary glucose from the lumen of the intestine into absorptive enterocytes. Sensing of dietary sugars and artificial sweeteners by the sweet taste receptor, T1R2-T1R3, expressed in the enteroendocrine L-cell regulates SGLT1 expression in neighboring absorptive enterocytes. However, the mechanism by which sugar sensing by the enteroendocrine cell is communicated to the absorptive enterocytes is not known. Here, we show that glucagon-like peptide-2 (GLP-2) secreted from the enteroendocrine cell in response to luminal sugars regulates SGLT1 mRNA and protein expression in absorptive enterocytes, via the enteric neurons. Glucose and artificial sweeteners induced secretion of GLP-2 from mouse small intestine, which was inhibited by the sweet-taste receptor inhibitor, gurmarin. In wild type mice there was an increase in sugar-induced SGLT1 mRNA and protein abundance that was not observed in GLP-2 receptor knockout mice. GLP-2 receptor is expressed in enteric neurons, and not in absorptive enterocytes ruling out a paracrine effect of GLP-2. Electric field stimulation of the intestine resulted in upregulation of SGLT1 expression that was abolished by the nerve blocking agent tetrodotoxin. We conclude that GLP-2 and the enteric nervous system are components of the enteroendocrine-absorptive enterocyte communication pathway regulating intestinal glucose transport. |
| **Date** | 2018-10-26 |
| **Language** | English |
| **Library Catalog** | Frontiers |
| **URL** | <https://www.frontiersin.org/journals/nutrition/articles/10.3389/fnut.2018.00101/full> |
| **Accessed** | 6/15/2025, 4:42:51 PM |
| **Extra** | Publisher: Frontiers |
| **Volume** | 5 |
| **Publication** | Frontiers in Nutrition |
| **DOI** | [10.3389/fnut.2018.00101](http://doi.org/10.3389/fnut.2018.00101) |
| **Journal Abbr** | Front. Nutr. |
| **ISSN** | 2296-861X |
| **Date Added** | 6/15/2025, 4:42:51 PM |
| **Modified** | 6/15/2025, 4:42:51 PM |

* **Tags:**
  + Glucose
  + intestine
  + GLP-2
  + regulation
  + SGLT1

**Attachments**

* + Full Text PDF
* **Intestinal microbiome in short bowel syndrome: diagnostic and therapeutic opportunities**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Fariha Chowdhury |
| **Author** | Lee Hill |
| **Author** | Nyah Shah |
| **Author** | Jelena Popov |
| **Author** | Paige Cheveldayoff |
| **Author** | Nikhil Pai |
| **Abstract** | Purpose of review  The intestinal microbiome plays a strong, complementary role in the development and integrity of the intestinal epithelium. This biology is crucial for intestinal adaptation, particularly after the mucosal insults that lead to short bowel syndrome (SBS). The purpose of this review is to discuss relationships between the intestinal microbiota and the physiology of intestinal adaptation. Recent findings  We will address interactions between the intestinal microbiome and nutritional metabolism, factors leading to dysbiosis in SBS, and common compositional differences of the gut microbiome in SBS patients as compared to healthy controls. We will also discuss novel opportunities to expand diagnostic and therapeutic interventions in this population, by using our knowledge of the microbiome to manipulate luminal bacteria and study their resultant metabolites. As microbial therapeutics advance across so many fields of medicine, this review is timely in its advocacy for ongoing research that focuses on the SBS population. Our review will discuss 4 key areas: 1) physiology of the intestinal microbiome in SBS, 2) clinical and therapeutic insults that lead to a state of dysbiosis, 3) currently available evidence on microbiome-based approaches to SBS management, and 4) opportunities and innovations to inspire future research. Summary  The clinical implications of this review are both current, and potential. Understanding how the microbiome impacts intestinal adaptation and host physiology may enhance our understanding of why we experience such clinical variability in SBS patients’ outcomes. This review may also expand clinicians’ understanding of what ‘personalized medicine’ can mean for this patient population, and how we may someday consider our nutritional, therapeutic, and prognostic recommendations based on our patients’ host, and microbial physiology. |
| **Date** | November 2023 |
| **Language** | en-US |
| **Short Title** | Intestinal microbiome in short bowel syndrome |
| **Library Catalog** | journals.lww.com |
| **URL** | <https://journals.lww.com/co-gastroenterology/abstract/2023/11000/intestinal_microbiome_in_short_bowel_syndrome_.3.aspx> |
| **Accessed** | 6/15/2025, 4:42:40 PM |
| **Volume** | 39 |
| **Pages** | 463 |
| **Publication** | Current Opinion in Gastroenterology |
| **DOI** | [10.1097/MOG.0000000000000970](http://doi.org/10.1097/MOG.0000000000000970) |
| **Issue** | 6 |
| **ISSN** | 0267-1379 |
| **Date Added** | 6/15/2025, 4:42:40 PM |
| **Modified** | 6/15/2025, 4:42:40 PM |

* **Lactobacillus rhamnosus GG maintains gut microbiota stability and promotes intestinal adaptation via activated intestinal farnesoid X receptor signaling in short bowel syndrome**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Linling Gui |
| **Author** | Xufei Duan |
| **Author** | Hanfei Wang |
| **Author** | Hua Xie |
| **Author** | Ruyi Zhang |
| **Author** | Weiwei Jiang |
| **Author** | Weibing Tang |
| **Abstract** | Intestinal farnesoid X receptor (FXR) signaling plays a critical role in maintaining intestinal microbiota stability. In this study, we investigated the probiotic Lactobacillus rhamnosus GG (LGG) and its ability to promote intestinal adaptation and stabilize the gut microbiota by activating intestinal FXR signaling in short bowel syndrome (SBS). In patients with type I SBS, fecal microbial α-diversity was decreased, Proteobacteria abundance was increased, and Firmicutes, Actinobacteria, and Bacteroidetes abundance levels were decreased. In vitro, LGG supernatant (LGGs) upregulated FXR expression in Caco-2 cells and ileum organoids. In vivo, LGG supplementation significantly improved intestinal morphology in wild-type (WT) SBS mice, including increased villus height, crypt depth and goblet cell numbers. Serum fibroblast growth factor 15 (FGF15) levels increased and fecal Proteobacteria abundance decreased, while secondary bile acids rose and primary bile acids declined in WT SBS mice after LGG supplementation. In addition, LGG supplementation also increased occludin and FXR expression in WT SBS mice, but not in intestinal FXR knockout (FXRInt-KO) SBS animals. SBS disrupts FXR signaling and gut microbiota equilibrium. LGG counteracts these effects by activating intestinal FXR, which stabilizes microbiota composition, protects the mucosal barrier, and promotes intestinal adaptation both in vitro and in vivo. |
| **Date** | 2025-05-27 |
| **Language** | en |
| **Library Catalog** | www.nature.com |
| **URL** | <https://www.nature.com/articles/s42003-025-08254-x> |
| **Accessed** | 6/15/2025, 4:43:27 PM |
| **Rights** | 2025 The Author(s) |
| **Extra** | Publisher: Nature Publishing Group |
| **Volume** | 8 |
| **Pages** | 816 |
| **Publication** | Communications Biology |
| **DOI** | [10.1038/s42003-025-08254-x](http://doi.org/10.1038/s42003-025-08254-x) |
| **Issue** | 1 |
| **Journal Abbr** | Commun Biol |
| **ISSN** | 2399-3642 |
| **Date Added** | 6/15/2025, 4:43:27 PM |
| **Modified** | 6/15/2025, 4:43:27 PM |

* **Tags:**
  + Dysbiosis
  + Applied microbiology

**Attachments**

* + Full Text PDF
* **Long-Term Oncologic Outcome following Duodenum-Preserving Pancreatic Head Resection for Benign Tumors, Cystic Neoplasms, and Neuroendocrine Tumors: Systematic Review and Meta-analysis**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Hans G Beger |
| **Author** | Benjamin Mayer |
| **Author** | Bertram Poch |
| **Date** | 2024 |
| **URL** | <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11164799/> |
| **Volume** | 31 |
| **Pages** | 4637–4653 |
| **Publication** | Annals of Surgical Oncology |
| **DOI** | [10.1245/s10434-024-15222-y](http://doi.org/10.1245/s10434-024-15222-y) |
| **Issue** | 7 |
| **Date Added** | 4/16/2025, 11:10:32 PM |
| **Modified** | 6/16/2025, 1:12:21 PM |

* **Tags:**
  + Adult
  + Female
  + Humans
  + Male
  + Treatment Outcome
  + Animals
  + Disease Models, Animal
  + Mice
  + STING
  + Quality of Life
  + Retrospective Studies
  + Diabetes
  + Signal Transduction
  + Cell Differentiation
  + Cell Line
  + Neoplasm Recurrence, Local
  + Cell Movement
  + Mammals
  + Neurons
  + immune cells
  + inflammation
  + Homeostasis
  + Gastroenterology
  + intestinal organoids
  + Regeneration
  + microbiota
  + Pancreas
  + inflammatory bowel disease
  + \*Cell- and Tissue-Based Therapy/methods
  + \*Bile Duct Neoplasms
  + \*Bile Duct Neoplasms/surgery
  + \*Cell Lineage
  + \*Cholangiocarcinoma
  + \*Cholangiocarcinoma/pathology
  + \*Colitis, Ulcerative/drug therapy
  + \*Cystadenocarcinoma/diagnostic imaging/surgery
  + \*Cystadenoma/diagnostic imaging/surgery
  + \*Cysts/pathology
  + \*Diabetes Mellitus, Experimental/complications/genetics/metabolism
  + \*Enteric Nervous System
  + \*Enteric Nervous System/pathology
  + \*Hyperglycemia/genetics/metabolism
  + \*Hypothalamo-Hypophyseal System
  + \*Inflammatory Bowel Diseases/drug therapy
  + \*Liver Neoplasms/diagnostic imaging/surgery
  + \*Liver Neoplasms/surgery
  + \*Microbiota
  + \*MicroRNAs/metabolism
  + \*Neoplasms, Cystic, Mucinous, and Serous
  + \*Neuroglia/physiology
  + \*Zebrafish
  + 16S RNA sequencing
  + Acinar cell carcinoma
  + Aging
  + antibiotics
  + Bile Ducts, Intrahepatic
  + Bile Ducts, Intrahepatic/surgery
  + Biliary
  + Biliary cystadenocarcinoma
  + Biliary cystadenoma
  + Brain
  + Brain-Gut Axis
  + Brain/physiology
  + Cell Separation
  + Chemical coding
  + Chick Embryo
  + circVPS13A
  + Cistoadenocarcinoma
  + Cistoadenoma
  + Clinicopathological criteria, Surgical outcomes
  + Colon/drug effects/pathology
  + Cystadenocarcinoma
  + Cystadenoma
  + cystic liver lesions
  + Cystic liver neoplasm
  + Cytology
  + Developmental disorders
  + diabetes
  + diabetes mellitus
  + Drug Discovery/\*methods
  + Embryonic stem cells
  + ENS
  + ENS neuropathies
  + enteric glia
  + enteric glia communications
  + Enteric glia communications
  + enteric glia diversity
  + enteric nervous system
  + Enteric nervous system
  + Enteric Nervous System
  + enteric nervous system (ENS)
  + Enteric nervous system (ENS)
  + Enteric Nervous System/\*pathology
  + Enteric neural precursor cells (ENPCs)
  + enteric progenitor cell
  + Fecal microbiota transplantation
  + Frantz's tumor
  + gastrointestinal complications
  + gastrointestinal diseases
  + Gastrointestinal Diseases
  + Gastrointestinal Diseases/pathology
  + gastrointestinal tract
  + Gastrointestinal Tract/drug effects/pathology
  + glia
  + Glial Cell Line-Derived Neurotrophic Factor/genetics
  + glucagon-like peptide 1
  + Growth Disorders
  + growth retardation
  + gut brain axis
  + gut microbiota
  + gut-brain axis
  + gut–brain axis
  + hepatic cystadenocarcinoma
  + hepatic cystadenoma
  + Hepatic simple cyst
  + hepatobiliary cystadenocarcinoma
  + hepatobiliary cystadenoma
  + Hirschsprung disease
  + Hirschsprung Disease/\*drug therapy/\*pathology/therapy
  + homeostasis
  + Imaging modalities
  + In Situ Hybridization, Fluorescence
  + Inflammatory bowel diseases
  + Intraductal papillary biliary neoplasms
  + intraductal papillary neoplasms of bile duct
  + irritable bowel syndrome
  + L-Fucose
  + Liver Diseases
  + Management
  + microbial metabolites
  + microbiota-gut-brain axis
  + Microbiota-gut-brain axis
  + Mucinous biliary cystic tumors, Biliary cystadenoma
  + mucinous cystic neoplasm
  + Mucinous cystic neoplasms
  + Mucinous neoplasm
  + muscularis macrophages
  + myenteric neurons
  + Neoplasia mucinosa quística
  + Neoplasia papilar intraductal biliar
  + Neoplasia quística hepática
  + Neural Crest
  + neural crest cell
  + neurodegeneration
  + Neuroglia
  + Neurons/drug effects/\*pathology
  + offspring
  + P2X7 receptor
  + pancreatectomy
  + Pancreatectomy
  + Pancreatic neoplasms
  + Pancreatic Neoplasms
  + Pancreatic surgery
  + pancreatic tumor
  + Parkinson’s disease
  + pediatric pancreatic neoplasm
  + Pepstatins/metabolism
  + Pituitary-Adrenal System
  + pluripotent stem cells (PSCs)
  + Pluripotent Stem Cells/pathology
  + preconception
  + probiotic
  + Purinergic signaling
  + Receptor, Endothelin B/metabolism
  + Receptors, Purinergic P2X7
  + RNA, Circular/genetics
  + Rotenone-induced mouse model
  + short-chain fatty acids
  + Solid pseudopapillary tumor
  + Stem-cell differentiation
  + submucosal neurons
  + Submucous Plexus
  + surgical outcome
  + surgical resection
  + three-dimensional (3D)
  + type 2 diabetes
  + zebrafish

**Notes:**

* + e14603 NMO-00132-2023
  + e14603 NMO-00132-2023

**Attachments**

* + Full Text
  + Full Text
  + Full Text PDF
  + Full Text PDF
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  + PubMed Central Full Text PDF
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  + PubMed Central Link
  + PubMed Central Link
  + PubMed Central Link
  + PubMed Central Link
  + PubMed entry
* **Physical organogenesis of the gut**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Nicolas R. Chevalier |
| **Abstract** | The gut has been a central subject of organogenesis since Caspar Friedrich Wolff’s seminal 1769 work ‘De Formatione Intestinorum’. Today, we are moving from a purely genetic understanding of cell specification to a model in which genetics codes for layers of physical–mechanical and electrical properties that drive organogenesis such that organ function and morphogenesis are deeply intertwined. This Review provides an up-to-date survey of the extrinsic and intrinsic mechanical forces acting on the embryonic vertebrate gut during development and of their role in all aspects of intestinal morphogenesis: enteric nervous system formation, epithelium structuring, muscle orientation and differentiation, anisotropic growth and the development of myogenic and neurogenic motility. I outline numerous implications of this biomechanical perspective in the etiology and treatment of pathologies, such as short bowel syndrome, dysmotility, interstitial cells of Cajal-related disorders and Hirschsprung disease. |
| **Date** | 2022-08-18 |
| **Library Catalog** | Silverchair |
| **URL** | <https://doi.org/10.1242/dev.200765> |
| **Accessed** | 6/15/2025, 4:42:32 PM |
| **Volume** | 149 |
| **Pages** | dev200765 |
| **Publication** | Development |
| **DOI** | [10.1242/dev.200765](http://doi.org/10.1242/dev.200765) |
| **Issue** | 16 |
| **Journal Abbr** | Development |
| **ISSN** | 0950-1991 |
| **Date Added** | 6/15/2025, 4:42:32 PM |
| **Modified** | 6/15/2025, 4:42:32 PM |

* **Attachments**
  + Full Text PDF
* **Role of glial cell-line derived neurotropic factor family receptor α2 in the actions of the glucagon-like peptides on the murine intestine**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Sean C. McDonagh |
| **Author** | Jenny Lee |
| **Author** | Angelo Izzo |
| **Author** | Patricia L. Brubaker |
| **Abstract** | The intestinal glucagon-like peptides GLP-1 and GLP-2 inhibit intestinal motility, whereas GLP-2 also stimulates growth of the intestinal mucosa. However, the mechanisms of action of these peptides in the intestine remain poorly characterized. To determine the role of the enteric nervous system in the actions of GLP-1 and GLP-2 on the intestine, the glial cell line-derived neurotropic factor family receptor α2 (GFRα2) knockout (KO) mouse was employed. The mice exhibited decreased cholinergic staining, as well as reduced mRNA transcripts for substance P-ergic excitatory motoneurons in the enteric nervous system (ENS) (P < 0.05). Examination of parameters of intestinal growth (including small and large intestinal weight and small intestinal villus height, crypt depth, and crypt cell proliferation) demonstrated no differences between wild-type and KO mice in either basal or GLP-2-stimulated mucosal growth. Nonetheless, KO mice exhibited reduced numbers of synaptophysin-positive enteroendocrine cells (P < 0.05), as well as a markedly impaired basal gastrointestinal (GI) transit rate (P < 0.05). Furthermore, acute administration of GLP-1 and GLP-2 significantly inhibited transit rates in wild-type mice (P < 0.05–0.01) but had no effect in GFRα2 KO mice. Despite these changes, expression of mRNA transcripts for the GLP receptors was not reduced in the ENS of KO animals, suggesting that GLP-1 and -2 modulate intestinal transit through enhancement of inhibitory input to cholinergic/substance P-ergic excitatory motoneurons. Together, these findings demonstrate a role for GFRα2-expressing enteric neurons in the downstream signaling of the glucagon-like peptides to inhibit GI motility, but not in intestinal growth. |
| **Date** | 2007-08 |
| **Library Catalog** | journals.physiology.org (Atypon) |
| **URL** | <https://journals.physiology.org/doi/full/10.1152/ajpgi.00424.2006> |
| **Accessed** | 6/15/2025, 4:43:07 PM |
| **Extra** | Publisher: American Physiological Society |
| **Volume** | 293 |
| **Pages** | G461-G468 |
| **Publication** | American Journal of Physiology-Gastrointestinal and Liver Physiology |
| **DOI** | [10.1152/ajpgi.00424.2006](http://doi.org/10.1152/ajpgi.00424.2006) |
| **Issue** | 2 |
| **ISSN** | 0193-1857 |
| **Date Added** | 6/15/2025, 4:43:07 PM |
| **Modified** | 6/15/2025, 4:43:07 PM |

* **Tags:**
  + enteric nervous system
  + GFRα2
  + GLP-1
  + GLP-2
  + growth
  + motility

**Attachments**

* + Full Text PDF
* **Short-chain fatty acids mediate enteric and central nervous ... : Neural Regeneration Research**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Shimin Pang |
| **Author** | Zhili Ren |
| **Author** | Hui Ding |
| **Author** | Piu Chan |
| **Abstract** | Short-chain fatty acids, metabolites produced by the fermentation of dietary fiber by gut microbiota, have garnered significant attention due to their correlation with neurodegenerative diseases, particularly Parkinson’s disease. In this review, we summarize the changes in short-chain fatty acid levels and the abundance of short-chain fatty acid-producing bacteria in various samples from patients with Parkinson’s disease, highlighting the critical role of gut homeostasis imbalance in the pathogenesis and progression of the disease. Focusing on the nervous system, we discuss the molecular mechanisms by which short-chain fatty acids influence the homeostasis of both the enteric nervous system and the central nervous system. We identify key processes, including the activation of G protein-coupled receptors and the inhibition of histone deacetylases by short-chain fatty acids. Importantly, structural or functional disruptions in the enteric nervous system mediated by these fatty acids may lead to abnormal α-synuclein expression and gastrointestinal dysmotility, which could serve as an initiating event in Parkinson’s disease. Furthermore, we propose that short-chain fatty acids help establish communication between the enteric nervous system and the central nervous system via the vagal nerve, immune circulation, and endocrine signaling. This communication may shed light on their potential role in the transmission of α-synuclein from the gut to the brain. Finally, we elucidate novel treatment strategies for Parkinson’s disease that target short-chain fatty acids and examine the challenges associated with translating short-chain fatty acid-based therapies into clinical practice. In conclusion, this review emphasizes the pivotal role of short-chain fatty acids in regulating gut–brain axis integrity and their significance in the pathogenesis of Parkinson’s disease from the perspective of the nervous system. Moreover, it highlights the potential value of short-chain fatty acids in early intervention for Parkinson’s disease. Future research into the molecular mechanisms of short-chain fatty acids and their synergistic interactions with other gut metabolites is likely to advance the clinical translation of innovative short-chain fatty acid-based therapies for Parkinson’s disease. |
| **Language** | en-US |
| **Short Title** | Short-chain fatty acids mediate enteric and central nervous ... |
| **Library Catalog** | journals.lww.com |
| **URL** | <https://journals.lww.com/nrronline/abstract/9900/short_chain_fatty_acids_mediate_enteric_and.798.aspx> |
| **Accessed** | 6/15/2025, 4:43:31 PM |
| **Date Added** | 6/15/2025, 4:43:31 PM |
| **Modified** | 6/15/2025, 4:43:31 PM |

* **Synergy of glucagon-like peptide-2 and epidermal growth factor coadministration on intestinal adaptation in neonatal piglets with short bowel syndrome**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | David W. Lim |
| **Author** | Crystal L. Levesque |
| **Author** | Donna F. Vine |
| **Author** | Mitsuru Muto |
| **Author** | Jacob R. Koepke |
| **Author** | Patrick N. Nation |
| **Author** | Pamela R. Wizzard |
| **Author** | Julang Li |
| **Author** | David L. Bigam |
| **Author** | Patricia L. Brubaker |
| **Author** | Justine M. Turner |
| **Author** | Paul W. Wales |
| **Abstract** | Glucagon-like peptide-2 (GLP-2) and epidermal growth factor (EGF) treatment enhance intestinal adaptation. To determine whether these growth factors exert synergistic effects on intestinal growth and function, GLP-2 and EGF-containing media (EGF-cm) were administered, alone and in combination, in neonatal piglet models of short bowel syndrome (SBS). Neonatal Landrace-Large White piglets were block randomized to 75% midintestinal [jejunoileal (JI) group] or distal intestinal [jejunocolic (JC) group] resection or sham control, with 7-day infusion of saline (control), intravenous human GLP-2 (11 nmol·kg−1·day−1) alone, enteral EGF-cm (80 μg·kg−1·day−1) alone, or GLP-2 and EGF-cm in combination. Adaptation was assessed by intestinal length, histopathology, Üssing chamber analysis, and real-time quantitative PCR of intestinal growth factors. Combined EGF-cm and GLP-2 treatment increased intestinal length in all three surgical models (P < 0.01). EGF-cm alone selectively increased bowel weight per length and jejunal villus height in the JI group only. The JC group demonstrated increased intestinal weight and villus height (P < 0.01) when given either GLP-2 alone or in combination with EGF-cm, with no effect of EGF-cm alone. Jejunal permeability of mannitol and polyethylene glycol decreased with combination therapy in both SBS groups (P < 0.05). No difference was observed in fat absorption or body weight gain. IGF-1 mRNA was differentially expressed in JI vs. JC piglets with treatment. Combined treatment with GLP-2 and EGF-cm induced intestinal lengthening and decreased permeability, in addition to the trophic effects of GLP-2 alone. Our findings demonstrate the benefits of novel combination GLP-2 and EGF treatment for neonatal SBS, especially in the JC model representing most human infants with SBS. NEW & NOTEWORTHY Glucagon-like peptide-2 (GLP-2) and epidermal growth factor (EGF) are intestinotrophic, with demonstrated benefit in both animal models and human studies of short bowel syndrome (SBS). The current research shows that over and above known trophic effects, the combination of GLP-2 and EGF synergistically lengthens the bowel in neonatal piglet models of SBS. Most notable benefit occurred with resection of the terminal ileum, the common clinical anatomy seen in neonatal SBS and associated with least de novo lengthening postsurgery. |
| **Date** | 2017-04 |
| **Library Catalog** | journals.physiology.org (Atypon) |
| **URL** | <https://journals.physiology.org/doi/full/10.1152/ajpgi.00281.2016> |
| **Accessed** | 6/15/2025, 4:43:13 PM |
| **Extra** | Publisher: American Physiological Society |
| **Volume** | 312 |
| **Pages** | G390-G404 |
| **Publication** | American Journal of Physiology-Gastrointestinal and Liver Physiology |
| **DOI** | [10.1152/ajpgi.00281.2016](http://doi.org/10.1152/ajpgi.00281.2016) |
| **Issue** | 4 |
| **ISSN** | 0193-1857 |
| **Date Added** | 6/15/2025, 4:43:13 PM |
| **Modified** | 6/15/2025, 4:43:13 PM |

* **Tags:**
  + growth factors
  + intestinal failure
  + intestinal growth
  + preclinical
  + trophic peptides

**Attachments**

* + Full Text PDF
* **The effect of hepatocyte growth factor on intestinal adaption in an experimental model of short bowel syndrome**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | George Bagias |
| **Author** | Evangelos P. Misiakos |
| **Author** | Anestis Charalampopoulos |
| **Author** | Nick Zavras |
| **Author** | Stratigoula Sakellariou |
| **Author** | Dimitrios Schizas |
| **Author** | Igor Sukhotnik |
| **Author** | Evangelos Giamarelos |
| **Author** | Emmanouil Pikoulis |
| **Abstract** | Nowadays, the standard therapy for patients with short bowel syndrome is parenteral nutrition (PN). Various growth factors have been tested to achieve weaning from prolonged PN administration. We evaluated the effect of hepatocyte growth factor (HGF) on structural intestinal adaptation and cell proliferation in a rat model of SBS. |
| **Date** | 2023-01-11 |
| **Language** | en |
| **Library Catalog** | Springer Link |
| **URL** | <https://doi.org/10.1007/s00383-022-05341-6> |
| **Accessed** | 6/15/2025, 4:43:18 PM |
| **Volume** | 39 |
| **Pages** | 80 |
| **Publication** | Pediatric Surgery International |
| **DOI** | [10.1007/s00383-022-05341-6](http://doi.org/10.1007/s00383-022-05341-6) |
| **Issue** | 1 |
| **Journal Abbr** | Pediatr Surg Int |
| **ISSN** | 1437-9813 |
| **Date Added** | 6/15/2025, 4:43:18 PM |
| **Modified** | 6/15/2025, 4:43:18 PM |

* **Tags:**
  + Cell proliferation
  + Gene up-regulation
  + Growth Factor Signalling
  + Haematopoietic cell growth factor
  + Hepatic Physiology
  + Hepatocyte growth factor
  + Intestinal adaptation
  + Intestinal stem cells
  + Intrauterine growth
  + Short bowel syndrome

**Attachments**

* + Submitted Version
* **Xenotransplanted human organoids identify transepithelial zinc transport as a key mediator of intestinal adaptation**

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Maame Efua S. Sampah |
| **Author** | Hannah Moore |
| **Author** | Raheel Ahmad |
| **Author** | Johannes Duess |
| **Author** | Peng Lu |
| **Author** | Carla Lopez |
| **Author** | Steve Steinway |
| **Author** | Daniel Scheese |
| **Author** | Zachariah Raouf |
| **Author** | Koichi Tsuboi |
| **Author** | Jeffrey Ding |
| **Author** | Connor Caputo |
| **Author** | Madison McFarland |
| **Author** | William B. Fulton |
| **Author** | Sanxia Wang |
| **Author** | Meghan Wang |
| **Author** | Thomas Prindle |
| **Author** | Vered Gazit |
| **Author** | Deborah C. Rubin |
| **Author** | Samuel Alaish |
| **Author** | Chhinder P. Sodhi |
| **Author** | David J. Hackam |
| **Abstract** | Short bowel syndrome (SBS) leads to severe morbidity and mortality. Intestinal adaptation is crucial in improving outcomes. To understand the human gene pathways associated with adaptation, we perform single-cell transcriptomic analysis of human small intestinal organoids explanted from mice with experimental SBS. We show that transmembrane ion pathways, specifically the transepithelial zinc transport pathway genes SLC39A4 and SLC39A5, are upregulated in SBS. This discovery is corroborated by an external dataset, bulk RT-qPCR, and Western blots. Oral zinc supplementation is shown to improve survival and weight gain of SBS mice and increase the proliferation of intestinal crypt cells in vitro. Finally, we identify the upregulation of SLC39A5 and associated transcription factor KLF5 in biopsied intestinal tissue specimens from patients with SBS. Thus, we identify zinc supplementation as a potential therapy for SBS and describe a xenotransplantation model that provides a platform for discovery in other intestinal diseases. |
| **Date** | 2024-10-07 |
| **Language** | en |
| **Library Catalog** | www.nature.com |
| **URL** | <https://www.nature.com/articles/s41467-024-52216-6> |
| **Accessed** | 6/15/2025, 4:43:56 PM |
| **Rights** | 2024 The Author(s) |
| **Extra** | Publisher: Nature Publishing Group |
| **Volume** | 15 |
| **Pages** | 8613 |
| **Publication** | Nature Communications |
| **DOI** | [10.1038/s41467-024-52216-6](http://doi.org/10.1038/s41467-024-52216-6) |
| **Issue** | 1 |
| **Journal Abbr** | Nat Commun |
| **ISSN** | 2041-1723 |
| **Date Added** | 6/15/2025, 4:43:56 PM |
| **Modified** | 6/15/2025, 4:43:56 PM |

* **Tags:**
  + Animal disease models
  + Experimental models of disease
  + Intestinal diseases

**Attachments**

* + Full Text PDF

## Agrin Inhibition in Enteric Neural Stem Cells Enhances Their Migration Following Colonic Transplantation

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Jessica L Mueller |
| **Author** | Rhian Stavely |
| **Author** | Richard A Guyer |
| **Author** | Ádám Soos |
| **Author** | Sukhada Bhave |
| **Author** | Chris Han |
| **Author** | Ryo Hotta |
| **Author** | Nandor Nagy |
| **Author** | Allan M Goldstein |
| **Abstract** | Regenerative cell therapy to replenish the missing neurons and glia in the aganglionic segment of Hirschsprung disease represents a promising treatment option. However, the success of cell therapies for this condition are hindered by poor migration of the transplanted cells. This limitation is in part due to a markedly less permissive extracellular environment in the postnatal gut than that of the embryo. Coordinated interactions between enteric neural crest-derived cells (ENCDCs) and their local environment drive migration along the embryonic gut during development of the enteric nervous system. Modifying transplanted cells, or the postnatal extracellular environment, to better recapitulate embryonic ENCDC migration could be leveraged to improve the engraftment and coverage of stem cell transplants. We compared the transcriptomes of ENCDCs from the embryonic intestine to that of postnatal-derived neurospheres and identified 89 extracellular matrix (ECM)-associated genes that are differentially expressed. Agrin, a heparin sulfate proteoglycan with a known inhibitory effect on ENCDC migration, was highly over-expressed by postnatal-derived neurospheres. Using a function-blocking antibody and a shRNA-expressing lentivirus, we show that inhibiting agrin promotes ENCDC migration in vitro and following cell transplantation ex vivo and in vivo. This enhanced migration is associated with an increased proportion of GFAP + cells, whose migration is especially enhanced. |
| **Date** | 2024-05-01 |
| **Library Catalog** | Silverchair |
| **URL** | <https://doi.org/10.1093/stcltm/szae013> |
| **Accessed** | 6/15/2025, 4:46:45 PM |
| **Volume** | 13 |
| **Pages** | 490-504 |
| **Publication** | Stem Cells Translational Medicine |
| **DOI** | [10.1093/stcltm/szae013](http://doi.org/10.1093/stcltm/szae013) |
| **Issue** | 5 |
| **Journal Abbr** | Stem Cells Translational Medicine |
| **ISSN** | 2157-6564 |
| **Date Added** | 6/15/2025, 4:46:45 PM |
| **Modified** | 6/15/2025, 4:46:45 PM |

### Attachments

* + Full Text PDF

## Characterization and transplantation of enteric neural crest cells from human induced pluripotent stem cells

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | W. Li |
| **Author** | L. Huang |
| **Author** | J. Zeng |
| **Author** | W. Lin |
| **Author** | K. Li |
| **Author** | J. Sun |
| **Author** | W. Huang |
| **Author** | J. Chen |
| **Author** | G. Wang |
| **Author** | Q. Ke |
| **Author** | J. Duan |
| **Author** | X. Lai |
| **Author** | R. Chen |
| **Author** | M. Liu |
| **Author** | Y. Liu |
| **Author** | T. Wang |
| **Author** | X. Yang |
| **Author** | Y. Chen |
| **Author** | H. Xia |
| **Author** | A. P. Xiang |
| **Abstract** | The enteric nervous system (ENS) is recognized as a second brain because of its complexity and its largely autonomic control of bowel function. Recent progress in studying the interactions between the ENS and the central nervous system (CNS) has implicated alterations of the gut/brain axis as a possible mechanism in the pathophysiology of autism spectrum disorders (ASDs), Parkinson’s disease (PD) and other human CNS disorders, whereas the underlying mechanisms are largely unknown because of the lack of good model systems. Human induced pluripotent stem cells (hiPSCs) have the ability to proliferate indefinitely and differentiate into cells of all three germ layers, thus making iPSCs an ideal source of cells for disease modelling and cell therapy. Here, hiPSCs were induced to differentiate into neural crest stem cells (NCSCs) efficiently. When co-cultured with smooth muscle layers of ganglionic gut tissue, the NCSCs differentiated into different subtypes of mature enteric-like neurons expressing nitric oxide synthase (nNOS), vasoactive intestinal polypeptide (VIP), choline acetyltransferase (ChAT) or calretinin with typical electrophysiological characteristics of functional neurons. Furthermore, when they were transplanted into aneural or aganglionic chick, mouse or human gut tissues in ovo, in vitro or in vivo, hiPSC-derived NCSCs showed extensive migration and neural differentiation capacity, generating neurons and glial cells that expressed phenotypic markers characteristic of the enteric nervous system. Our results indicate that enteric NCSCs derived from hiPSCs supply a powerful tool for studying the pathogenesis of gastrointestinal disorders and brain/gut dysfunction and represent a potentially ideal cell source for enteric neural transplantation treatments. |
| **Date** | 2018-03 |
| **Language** | en |
| **Library Catalog** | www.nature.com |
| **URL** | <https://www.nature.com/articles/mp2016191> |
| **Accessed** | 6/15/2025, 4:45:49 PM |
| **Rights** | 2018 The Author(s) |
| **Extra** | Publisher: Nature Publishing Group |
| **Volume** | 23 |
| **Pages** | 499-508 |
| **Publication** | Molecular Psychiatry |
| **DOI** | [10.1038/mp.2016.191](http://doi.org/10.1038/mp.2016.191) |
| **Issue** | 3 |
| **Journal Abbr** | Mol Psychiatry |
| **ISSN** | 1476-5578 |
| **Date Added** | 6/15/2025, 4:45:49 PM |
| **Modified** | 6/15/2025, 4:45:49 PM |

### Tags:

* + Cell biology
  + Neuroscience
  + Stem cells

### Attachments

* + Full Text PDF

## Enteric mesenchymal cells support the growth of postnatal enteric neural stem cells

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Rhian Stavely |
| **Author** | Sukhada Bhave |
| **Author** | Wing Lam N. Ho |
| **Author** | Minhal Ahmed |
| **Author** | Weikang Pan |
| **Author** | Ahmed A. Rahman |
| **Author** | Jessica Ulloa |
| **Author** | Nicole Bousquet |
| **Author** | Meredith Omer |
| **Author** | Richard Guyer |
| **Author** | Nandor Nagy |
| **Author** | Allan M. Goldstein |
| **Author** | Ryo Hotta |
| **Abstract** | Interplay between embryonic enteric neural stem cells (ENSCs) and enteric mesenchymal cells (EMCs) in the embryonic gut is essential for normal development of the enteric nervous system. Disruption of these interactions underlies the pathogenesis of intestinal aganglionosis in Hirschsprung disease (HSCR). ENSC therapy has been proposed as a possible treatment for HSCR, but whether the survival and development of postnatal-derived ENSCs similarly rely on signals from the mesenchymal environment is unknown and has important implications for developing protocols to expand ENSCs for cell transplantation therapy. Enteric neural crest-derived cells (ENCDCs) and EMCs were cultured from the small intestine of Wnt1-Rosa26-tdTomato mice. EMCs promoted the expansion of ENCDCs 9.5-fold by inducing ENSC properties, including expression of Nes, Sox10, Sox2, and Ngfr. EMCs enhanced the neurosphere-forming ability of ENCDCs, and this persisted after withdrawal of the EMCs. These effects were mediated by paracrine factors and several ligands known to support neural stem cells were identified in EMCs. Using the optimized expansion procedures, neurospheres were generated from small intestine of the Ednrb −/− mouse model of HSCR. These ENSCs had similar proliferative and migratory capacity to Ednrb +/+ ENSCs, albeit neurospheres contained fewer neurons. ENSCs derived from Ednrb −/− mice generated functional neurons with similar calcium responses to Ednrb +/+ ENSCs and survived after transplantation into the aganglionic colon of Ednrb −/− recipients. EMCs act as supporting cells to ENSCs postnatally via an array of synergistically acting paracrine signaling factors. These properties can be leveraged to expand autologous ENSCs from patients with HSCR mutations for therapeutic application. |
| **Date** | 2021-09-01 |
| **Library Catalog** | Silverchair |
| **URL** | <https://doi.org/10.1002/stem.3388> |
| **Accessed** | 6/15/2025, 4:45:38 PM |
| **Volume** | 39 |
| **Pages** | 1236-1252 |
| **Publication** | Stem Cells |
| **DOI** | [10.1002/stem.3388](http://doi.org/10.1002/stem.3388) |
| **Issue** | 9 |
| **Journal Abbr** | Stem Cells |
| **ISSN** | 1066-5099 |
| **Date Added** | 6/15/2025, 4:45:38 PM |
| **Modified** | 6/15/2025, 4:45:38 PM |

### Attachments

* + Full Text PDF

## Enteric neural stem cell transplant restores gut motility in mice with Hirschsprung disease

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Ahmed A. Rahman |
| **Author** | Takahiro Ohkura |
| **Author** | Sukhada Bhave |
| **Author** | Weikang Pan |
| **Author** | Kensuke Ohishi |
| **Author** | Leah Ott |
| **Author** | Christopher Han |
| **Author** | Abigail Leavitt |
| **Author** | Rhian Stavely |
| **Author** | Alan J. Burns |
| **Author** | Allan M. Goldstein |
| **Author** | Ryo Hotta |
| **Date** | 2024/09/10 |
| **Language** | en |
| **Library Catalog** | insight.jci.org |
| **URL** | <https://insight.jci.org/articles/view/179755> |
| **Accessed** | 6/15/2025, 4:45:29 PM |
| **Extra** | Publisher: American Society for Clinical Investigation PMID: 0 |
| **Volume** | 9 |
| **Publication** | JCI Insight |
| **DOI** | [10.1172/jci.insight.179755](http://doi.org/10.1172/jci.insight.179755) |
| **Issue** | 17 |
| **Journal Abbr** | JCI Insight |
| **ISSN** | 0021-9738 |
| **Date Added** | 6/15/2025, 4:45:29 PM |
| **Modified** | 6/15/2025, 4:45:29 PM |

### Attachments

* + Full Text PDF
  + PubMed entry

## Epithelial Stem Cells and Tissue Engineered Intestine

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Richard M. Day |
| **Abstract** | The intestinal mucosa has an amazing regenerative capacity, enabling rapid restoration of its physiological functions following injury. The ability to do this resides with the epithelial stem cells located within glandular invaginations in the mucosal surface. Recent advances toward the isolation and characterization of epithelial stem cells has paved the way for exploring novel therapeutic approaches for gastrointestinal disease. Possible stem cell-based therapy of gastrointestinal disorders range from the repair of damaged mucosa through to tissue engineering of artificial intestinal constructs for patients with short bowel syndrome. Before these benefits are realized further information is required on the biological characteristics of intestinal stem cells, their interactions with surrounding cells, and the environment in which they reside. This includes discovering markers to assist in the identification and purification of stem cell populations and techniques to manipulate the cells both in vivo and in vitro. Because intestinal transplantation for patients still represents a significant challenge, it is hoped that one day a tissue-engineered intestine will provide a feasible option for patients with short bowel syndrome. This review aims to introduce the reader to the main characteristics of epithelial stem cells and provide an overview of the current status of intestinal tissue engineering and the problems still being faced. |
| **Language** | en |
| **Library Catalog** | www.eurekaselect.com |
| **URL** | <https://www.eurekaselect.com/article/1661> |
| **Accessed** | 6/15/2025, 4:47:00 PM |
| **Publication** | http://www.eurekaselect.com |
| **Date Added** | 6/15/2025, 4:47:00 PM |
| **Modified** | 6/15/2025, 4:47:00 PM |

## Generation of tissue-engineered small intestine using embryonic stem cell-derived human intestinal organoids

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Stacy R. Finkbeiner |
| **Author** | Jennifer J. Freeman |
| **Author** | Minna M. Wieck |
| **Author** | Wael El-Nachef |
| **Author** | Christopher H. Altheim |
| **Author** | Yu-Hwai Tsai |
| **Author** | Sha Huang |
| **Author** | Rachel Dyal |
| **Author** | Eric S. White |
| **Author** | Tracy C. Grikscheit |
| **Author** | Daniel H. Teitelbaum |
| **Author** | Jason R. Spence |
| **Abstract** | Short bowel syndrome (SBS) is characterized by poor nutrient absorption due to a deficit of healthy intestine. Current treatment practices rely on providing supportive medical therapy with parenteral nutrition; while life saving, such interventions are not curative and are still associated with significant co-morbidities. As approaches to lengthen remaining intestinal tissue have been met with only limited success and intestinal transplants have poor survival outcomes, new approaches to treating SBS are necessary. Human intestine derived from embryonic stem cells (hESCs) or induced pluripotent stem cells (iPSCs), called human intestinal organoids (HIOs), have the potential to offer a personalized and scalable source of intestine for regenerative therapies. However, given that HIOs are small three-dimensional structures grown in vitro, methods to generate usable HIO-derived constructs are needed. We investigated the ability of hESCs or HIOs to populate acellular porcine intestinal matrices and artificial polyglycolic/poly L lactic acid (PGA/PLLA) scaffolds, and examined the ability of matrix/scaffolds to thrive when transplanted in vivo. Our results demonstrate that the acellular matrix alone is not sufficient to instruct hESC differentiation towards an endodermal or intestinal fate. We observed that while HIOs reseed acellular porcine matrices in vitro, the HIO-reseeded matrices do not thrive when transplanted in vivo. In contrast, HIO-seeded PGA/PLLA scaffolds thrive in vivo and develop into tissue that looks nearly identical to adult human intestinal tissue. Our results suggest that HIO-seeded PGA/PLLA scaffolds are a promising avenue for developing the mucosal component of tissue engineered human small intestine, which need to be explored further to develop them into fully functional tissue. |
| **Date** | 2015-10-12 |
| **Library Catalog** | Silverchair |
| **URL** | <https://doi.org/10.1242/bio.013235> |
| **Accessed** | 6/15/2025, 4:46:51 PM |
| **Volume** | 4 |
| **Pages** | 1462-1472 |
| **Publication** | Biology Open |
| **DOI** | [10.1242/bio.013235](http://doi.org/10.1242/bio.013235) |
| **Issue** | 11 |
| **Journal Abbr** | Biology Open |
| **ISSN** | 2046-6390 |
| **Date Added** | 6/15/2025, 4:46:51 PM |
| **Modified** | 6/15/2025, 4:46:51 PM |

### Attachments

* + Full Text PDF

## In Vivo Transplantation of Enteric Neural Crest Cells into Mouse Gut; Engraftment, Functional Integration and Long-Term Safety

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Julie E. Cooper |
| **Author** | Conor J. McCann |
| **Author** | Dipa Natarajan |
| **Author** | Shanas Choudhury |
| **Author** | Werend Boesmans |
| **Author** | Jean-Marie Delalande |
| **Author** | Pieter Vanden Berghe |
| **Author** | Alan J. Burns |
| **Author** | Nikhil Thapar |
| **Abstract** | Objectives Enteric neuropathies are severe gastrointestinal disorders with unsatisfactory outcomes. We aimed to investigate the potential of enteric neural stem cell therapy approaches for such disorders by transplanting mouse enteric neural crest cells (ENCCs) into ganglionic and aganglionic mouse gut in vivo and analysing functional integration and long-term safety. Design Neurospheres generated from yellow fluorescent protein (YFP) expressing ENCCs selected from postnatal Wnt1-cre;R26R-YFP/YFP murine gut were transplanted into ganglionic hindgut of wild-type littermates or aganglionic hindgut of Ednrbtm1Ywa mice (lacking functional endothelin receptor type-B). Intestines were then assessed for ENCC integration and differentiation using immunohistochemistry, cell function using calcium imaging, and long-term safety using PCR to detect off-target YFP expression. Results YFP+ ENCCs engrafted, proliferated and differentiated into enteric neurons and glia within recipient ganglionic gut. Transplanted cells and their projections spread along the endogenous myenteric plexus to form branching networks. Electrical point stimulation of endogenous nerve fibres resulted in calcium transients (F/F0 = 1.16±0.01;43 cells, n = 6) in YFP+ transplanted ENCCs (abolished with TTX). Long-term follow-up (24 months) showed transplanted ENCCs did not give rise to tumours or spread to other organs (PCR negative in extraintestinal sites). In aganglionic gut ENCCs similarly spread and differentiated to form neuronal and glial networks with projections closely associated with endogenous neural networks of the transition zone. Conclusions Transplanted ENCCs successfully engrafted into recipient ganglionic and aganglionic gut showing appropriate spread, localisation and, importantly, functional integration without any long-term safety issues. This study provides key support for the development and use of enteric neural stem cell therapies. |
| **Date** | Jan 29, 2016 |
| **Language** | en |
| **Library Catalog** | PLoS Journals |
| **URL** | <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0147989> |
| **Accessed** | 6/15/2025, 4:45:43 PM |
| **Extra** | Publisher: Public Library of Science |
| **Volume** | 11 |
| **Pages** | e0147989 |
| **Publication** | PLOS ONE |
| **DOI** | [10.1371/journal.pone.0147989](http://doi.org/10.1371/journal.pone.0147989) |
| **Issue** | 1 |
| **Journal Abbr** | PLOS ONE |
| **ISSN** | 1932-6203 |
| **Date Added** | 6/15/2025, 4:45:43 PM |
| **Modified** | 6/15/2025, 4:45:43 PM |

### Tags:

* + Neurons
  + Liver transplantation
  + Cardiac transplantation
  + Gastrointestinal tract
  + Neural networks
  + Neuropathy
  + Neurospheres
  + Yellow fluorescent protein

### Attachments

* + Full Text PDF

## Inhibition of ROCK signaling pathway accelerates enteric neural crest cell-based therapy after transplantation in a rat hypoganglionic model

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Yuying Zhao |
| **Author** | Xin Ge |
| **Author** | Hui Yu |
| **Author** | Laura E. Kuil |
| **Author** | Maria M. Alves |
| **Author** | Donghao Tian |
| **Author** | Qiang Huang |
| **Author** | Xinlin Chen |
| **Author** | Robert M. W. Hofstra |
| **Author** | Ya Gao |
| **Abstract** | Background Hirschsprung's disease (HSCR) is a congenital gastrointestinal disorder, characterized by enteric ganglia absence in part or entire of the colon, due to abnormal colonization and migration of enteric neural crest cells (ENCCs) during development. Currently, besides surgery which is the main therapy for HSCR, the potential of stem cell-based transplantation was investigated as an alternative option. Although promising, it has limitations, including poor survival, differentiation, and migration of the grafted cells. We hypothesized that modulation of extracellular factors during transplantation could promote ENCCs proliferation and migration, leading to increased transplantation efficiency. Considering that the RhoA/ROCK pathway is highly involved in cytoskeletal dynamics and neurite growth, our study explored the effect of inhibition of this pathway to improve the success of ENCCs transplantation. Methods Enteric neural crest cells were isolated from rat embryos and labeled with a GFP-tag. Cell viability, apoptosis, differentiation, and migration assays were performed with and without RhoA/ROCK inhibition. Labeled ENCCs were transplanted into the muscle layer of an induced hypoganglionic rat model followed by intraperitoneal injections of ROCK inhibitor. The transplanted segments were collected 3 weeks after for histological analysis. Key Results Our results showed that inhibition of ROCK increased viable cell number, differentiation, and migration of ENCCs in vitro. Moreover, transplantation of labeled ENCCs into the hypoganglionic model showed enhanced distribution of grafted ENCCs, upon treatment with ROCK inhibitor. Conclusions and Inferences ROCK inhibitors influence ENCCs growth and migration in vitro and in vivo, and should be considered to improve the efficiency of ENCCs transplantation. |
| **Date** | 2020 |
| **Language** | en |
| **Library Catalog** | Wiley Online Library |
| **URL** | <https://onlinelibrary.wiley.com/doi/abs/10.1111/nmo.13895> |
| **Accessed** | 6/15/2025, 4:46:01 PM |
| **Rights** | © 2020 John Wiley & Sons Ltd |
| **Extra** | \_eprint: https://onlinelibrary.wiley.com/doi/pdf/10.1111/nmo.13895 |
| **Volume** | 32 |
| **Pages** | e13895 |
| **Publication** | Neurogastroenterology & Motility |
| **DOI** | [10.1111/nmo.13895](http://doi.org/10.1111/nmo.13895) |
| **Issue** | 9 |
| **ISSN** | 1365-2982 |
| **Date Added** | 6/15/2025, 4:46:02 PM |
| **Modified** | 6/15/2025, 4:46:02 PM |

### Tags:

* + enteric nervous system
  + transplantation
  + ENCCs
  + hirschsprung's disease
  + RhoA/ROCK pathway

### Attachments

* + Full Text

## Long-Term Oncologic Outcome following Duodenum-Preserving Pancreatic Head Resection for Benign Tumors, Cystic Neoplasms, and Neuroendocrine Tumors: Systematic Review and Meta-analysis

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Hans G Beger |
| **Author** | Benjamin Mayer |
| **Author** | Bertram Poch |
| **Date** | 2024 |
| **URL** | <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11164799/> |
| **Volume** | 31 |
| **Pages** | 4637–4653 |
| **Publication** | Annals of Surgical Oncology |
| **DOI** | [10.1245/s10434-024-15222-y](http://doi.org/10.1245/s10434-024-15222-y) |
| **Issue** | 7 |
| **Date Added** | 4/16/2025, 11:10:32 PM |
| **Modified** | 6/16/2025, 1:12:21 PM |

### Tags:

* + Adult
  + Female
  + Humans
  + Male
  + Treatment Outcome
  + Animals
  + Disease Models, Animal
  + Mice
  + STING
  + Quality of Life
  + Retrospective Studies
  + Diabetes
  + Signal Transduction
  + Cell Differentiation
  + Cell Line
  + Neoplasm Recurrence, Local
  + Cell Movement
  + Mammals
  + Neurons
  + immune cells
  + inflammation
  + Homeostasis
  + Gastroenterology
  + intestinal organoids
  + Regeneration
  + microbiota
  + Pancreas
  + inflammatory bowel disease
  + \*Cell- and Tissue-Based Therapy/methods
  + \*Bile Duct Neoplasms
  + \*Bile Duct Neoplasms/surgery
  + \*Cell Lineage
  + \*Cholangiocarcinoma
  + \*Cholangiocarcinoma/pathology
  + \*Colitis, Ulcerative/drug therapy
  + \*Cystadenocarcinoma/diagnostic imaging/surgery
  + \*Cystadenoma/diagnostic imaging/surgery
  + \*Cysts/pathology
  + \*Diabetes Mellitus, Experimental/complications/genetics/metabolism
  + \*Enteric Nervous System
  + \*Enteric Nervous System/pathology
  + \*Hyperglycemia/genetics/metabolism
  + \*Hypothalamo-Hypophyseal System
  + \*Inflammatory Bowel Diseases/drug therapy
  + \*Liver Neoplasms/diagnostic imaging/surgery
  + \*Liver Neoplasms/surgery
  + \*Microbiota
  + \*MicroRNAs/metabolism
  + \*Neoplasms, Cystic, Mucinous, and Serous
  + \*Neuroglia/physiology
  + \*Zebrafish
  + 16S RNA sequencing
  + Acinar cell carcinoma
  + Aging
  + antibiotics
  + Bile Ducts, Intrahepatic
  + Bile Ducts, Intrahepatic/surgery
  + Biliary
  + Biliary cystadenocarcinoma
  + Biliary cystadenoma
  + Brain
  + Brain-Gut Axis
  + Brain/physiology
  + Cell Separation
  + Chemical coding
  + Chick Embryo
  + circVPS13A
  + Cistoadenocarcinoma
  + Cistoadenoma
  + Clinicopathological criteria, Surgical outcomes
  + Colon/drug effects/pathology
  + Cystadenocarcinoma
  + Cystadenoma
  + cystic liver lesions
  + Cystic liver neoplasm
  + Cytology
  + Developmental disorders
  + diabetes
  + diabetes mellitus
  + Drug Discovery/\*methods
  + Embryonic stem cells
  + ENS
  + ENS neuropathies
  + enteric glia
  + enteric glia communications
  + Enteric glia communications
  + enteric glia diversity
  + enteric nervous system
  + Enteric nervous system
  + Enteric Nervous System
  + enteric nervous system (ENS)
  + Enteric nervous system (ENS)
  + Enteric Nervous System/\*pathology
  + Enteric neural precursor cells (ENPCs)
  + enteric progenitor cell
  + Fecal microbiota transplantation
  + Frantz's tumor
  + gastrointestinal complications
  + gastrointestinal diseases
  + Gastrointestinal Diseases
  + Gastrointestinal Diseases/pathology
  + gastrointestinal tract
  + Gastrointestinal Tract/drug effects/pathology
  + glia
  + Glial Cell Line-Derived Neurotrophic Factor/genetics
  + glucagon-like peptide 1
  + Growth Disorders
  + growth retardation
  + gut brain axis
  + gut microbiota
  + gut-brain axis
  + gut–brain axis
  + hepatic cystadenocarcinoma
  + hepatic cystadenoma
  + Hepatic simple cyst
  + hepatobiliary cystadenocarcinoma
  + hepatobiliary cystadenoma
  + Hirschsprung disease
  + Hirschsprung Disease/\*drug therapy/\*pathology/therapy
  + homeostasis
  + Imaging modalities
  + In Situ Hybridization, Fluorescence
  + Inflammatory bowel diseases
  + Intraductal papillary biliary neoplasms
  + intraductal papillary neoplasms of bile duct
  + irritable bowel syndrome
  + L-Fucose
  + Liver Diseases
  + Management
  + microbial metabolites
  + microbiota-gut-brain axis
  + Microbiota-gut-brain axis
  + Mucinous biliary cystic tumors, Biliary cystadenoma
  + mucinous cystic neoplasm
  + Mucinous cystic neoplasms
  + Mucinous neoplasm
  + muscularis macrophages
  + myenteric neurons
  + Neoplasia mucinosa quística
  + Neoplasia papilar intraductal biliar
  + Neoplasia quística hepática
  + Neural Crest
  + neural crest cell
  + neurodegeneration
  + Neuroglia
  + Neurons/drug effects/\*pathology
  + offspring
  + P2X7 receptor
  + pancreatectomy
  + Pancreatectomy
  + Pancreatic neoplasms
  + Pancreatic Neoplasms
  + Pancreatic surgery
  + pancreatic tumor
  + Parkinson’s disease
  + pediatric pancreatic neoplasm
  + Pepstatins/metabolism
  + Pituitary-Adrenal System
  + pluripotent stem cells (PSCs)
  + Pluripotent Stem Cells/pathology
  + preconception
  + probiotic
  + Purinergic signaling
  + Receptor, Endothelin B/metabolism
  + Receptors, Purinergic P2X7
  + RNA, Circular/genetics
  + Rotenone-induced mouse model
  + short-chain fatty acids
  + Solid pseudopapillary tumor
  + Stem-cell differentiation
  + submucosal neurons
  + Submucous Plexus
  + surgical outcome
  + surgical resection
  + three-dimensional (3D)
  + type 2 diabetes
  + zebrafish

### Notes:

* + e14603 NMO-00132-2023
  + e14603 NMO-00132-2023

### Attachments

* + Full Text
  + Full Text
  + Full Text PDF
  + Full Text PDF
  + Full Text PDF
  + Full Text PDF
  + Full Text PDF
  + Full Text PDF
  + Full Text PDF
  + Full Text PDF
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  + PubMed Central Full Text PDF
  + PubMed Central Full Text PDF
  + PubMed Central Full Text PDF
  + PubMed Central Link
  + PubMed Central Link
  + PubMed Central Link
  + PubMed Central Link
  + PubMed entry

## Magnesium ions regulate the Warburg effect to promote the differentiation of enteric neural crest cells into neurons

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Qiongqian Xu |
| **Author** | Xixi He |
| **Author** | Yaru Mou |
| **Author** | Dong Sun |
| **Author** | Xintao Zhang |
| **Author** | Jichang Han |
| **Author** | Xiaoyang Liu |
| **Author** | Xingjian Liu |
| **Author** | Xue Ren |
| **Author** | Dongming Wang |
| **Author** | Jian Wang |
| **Author** | Chuncan Ma |
| **Author** | Qiangye Zhang |
| **Author** | Aiwu Li |
| **Abstract** | Understanding how enteric neural crest cells (ENCCs) differentiate into neurons is crucial for neurogenesis therapy and gastrointestinal disease research. This study explores how magnesium ions regulate the glycolytic pathway to enhance ENCCs differentiation into neurons. |
| **Date** | 2025-01-23 |
| **Library Catalog** | BioMed Central |
| **URL** | <https://doi.org/10.1186/s13287-024-04121-4> |
| **Accessed** | 6/15/2025, 4:45:56 PM |
| **Volume** | 16 |
| **Pages** | 19 |
| **Publication** | Stem Cell Research & Therapy |
| **DOI** | [10.1186/s13287-024-04121-4](http://doi.org/10.1186/s13287-024-04121-4) |
| **Issue** | 1 |
| **Journal Abbr** | Stem Cell Research & Therapy |
| **ISSN** | 1757-6512 |
| **Date Added** | 6/15/2025, 4:45:56 PM |
| **Modified** | 6/15/2025, 4:45:56 PM |

### Tags:

* + Neurons
  + Differentiation
  + Enteric neural crest cells
  + Magnesium Ions
  + Warburg effect

### Attachments

* + Full Text PDF

## Mesenchymal stem cell therapy in patients with small bowel transplantation: Single center experience

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Sel&ccedil Sait Murat Doğan |
| **Author** | Uk Kılın&ccedil |
| **Author** | Ey&uuml |
| **Author** | P Kebap&ccedil |
| **Author** | Cem Tuğmen I |
| **Author** | Maşallah Baran Rkan |
| **Author** | Cezmi Karaca Lmez |
| **Abstract** | Mesenchymal stem cell therapy in patients with small bowel transplantation: Single center experience |
| **Date** | Jul 7, 2014 |
| **Language** | en |
| **Short Title** | Mesenchymal stem cell therapy in patients with small bowel transplantation |
| **Library Catalog** | www.wjgnet.com |
| **URL** | <https://www.wjgnet.com/1007-9327/full/v20/i25/8215.htm> |
| **Accessed** | 6/15/2025, 4:46:10 PM |
| **Extra** | Publisher: Baishideng Publishing Group Inc. |
| **Volume** | 20 |
| **Pages** | 8215-8220 |
| **Publication** | World Journal of Gastroenterology |
| **DOI** | [10.3748/wjg.v20.i25.8215](http://doi.org/10.3748/wjg.v20.i25.8215) |
| **Issue** | 25 |
| **Date Added** | 6/15/2025, 4:46:10 PM |
| **Modified** | 6/15/2025, 4:46:10 PM |

### Attachments

* + Full Text

## Spray Delivery of Intestinal Organoids to Reconstitute Epithelium on Decellularized Native Extracellular Matrix

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Dana M. Schwartz |
| **Author** | Meryem O. Pehlivaner Kara |
| **Author** | Allan M. Goldstein |
| **Author** | Harald C. Ott |
| **Author** | Adam K. Ekenseair |
| **Abstract** | The native extracellular matrix (ECM) serves as a unique platform for tissue engineering because it provides an organ-specific scaffold in terms of both matrix composition and tissue architecture. However, efficacious cell-seeding techniques for recellularizing the ECM constructs with appropriate cell types to restore biological function remain under development. In this study, the impact of spraying as a seeding technique for repopulation of decellularized small intestine was investigated. In a series of experiments, CaCo-2 cells were first used to investigate the effect of spray device type and pressure on cell viability and to optimize parameters for seeding intestinal epithelial cells. High cell viability and a homogeneous cell distribution were obtained when cell suspensions were sprayed through an airbrush at low pressure. Next, the effect of seeding method and spray pressure on the size and dispersal of intestinal organoids, a more complex and clinically relevant intestinal stem cell population, was evaluated. The feasibility of seeding intestinal epithelial cells onto decellularized scaffolds was next studied using sprayed CaCo-2 cells, which survived the spray-seeding process and formed a monolayer on the scaffold. Finally, airbrush seeding was used to spray intestinal organoids onto the scaffolds, with cell survival and tissue architecture evaluated after 1 week of culture. Organoids seeded through pipetting onto the decellularized scaffold survived, but demonstrated aggregation, with cells organized around multiple small lumens. In contrast, organoids airbrush spray seeded at 0.35 bar onto the decellularized scaffold not only engrafted but also demonstrated formation of an epithelial monolayer that resembled the absorptive surface found on intestinal villi. The results suggest that seeding cells through airbrush spraying holds great potential for use in tissue engineering, especially for large-scale tubular organ recellularization. |
| **Date** | 2017-09 |
| **Library Catalog** | liebertpub.com (Atypon) |
| **URL** | <https://www.liebertpub.com/doi/10.1089/ten.tec.2017.0269> |
| **Accessed** | 6/15/2025, 4:46:39 PM |
| **Extra** | Publisher: Mary Ann Liebert, Inc., publishers |
| **Volume** | 23 |
| **Pages** | 565-573 |
| **Publication** | Tissue Engineering Part C: Methods |
| **DOI** | [10.1089/ten.tec.2017.0269](http://doi.org/10.1089/ten.tec.2017.0269) |
| **Issue** | 9 |
| **ISSN** | 1937-3384 |
| **Date Added** | 6/15/2025, 4:46:39 PM |
| **Modified** | 6/15/2025, 4:46:39 PM |

### Attachments

* + Full Text

## Activation of KCNQ (K(V)7) K(+) channels in enteric neurons inhibits epithelial Cl(-) secretion in mouse distal colon.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Andrew J. Nickerson |
| **Author** | Trey S. Rottgen |
| **Author** | Vazhaikkurichi M. Rajendran |
| **Abstract** | Voltage-gated Kv7 (KCNQ family) K(+) channels are expressed in many neuronal populations and play an important role in regulating membrane potential by generating a hyperpolarizing K(+) current and decreasing cell excitability. However, the role of K(V)7 channels in the neural regulation of intestinal epithelial Cl(-) secretion is not known. Cl(-) secretion in mouse distal colon was measured as a function of short-circuit current (I(SC)), and pharmacological approaches were used to test the hypothesis that activation of K(V)7 channels in enteric neurons would inhibit epithelial Cl(-) secretion. Flupirtine, a nonselective K(V)7 activator, inhibited basal Cl(-) secretion in mouse distal colon and abolished or attenuated the effects of drugs that target various components of enteric neurotransmission, including tetrodotoxin (Na(V) channel blocker), veratridine (Na(V) channel activator), nicotine (nicotinic acetylcholine receptor agonist), and hexamethonium (nicotinic antagonist). In contrast, flupritine did not block the response to epithelium-targeted agents VIP (endogenous VPAC receptor ligand) or carbachol (nonselective cholinergic agonist). Flupirtine inhibited Cl(-) secretion in both full-thickness and seromuscular-stripped distal colon (containing the submucosal, but not myenteric plexus) but generated no response in epithelial T84 cell monolayers. K(V)7.2 and K(V)7.3 channel proteins were detected by immunofluorescence in whole mount preparations of the submucosa from mouse distal colon. ICA 110381 (K(V)7.2/7.3 specific activator) inhibited Cl(-) secretion comparably to flupirtine. We conclude that K(V)7 channel activators inhibit neurally driven Cl(-) secretion in the colonic epithelium and may therefore have therapeutic benefit in treating pathologies associated with hyperexcitable enteric nervous system, such as irritable bowel syndrome with diarrhea (IBS-D). |
| **Date** | 2021 Jun 1 |
| **Language** | eng |
| **Extra** | Place: United States PMID: 33852365 PMCID: PMC8285638 |
| **Volume** | 320 |
| **Pages** | C1074-C1087 |
| **Publication** | American journal of physiology. Cell physiology |
| **DOI** | [10.1152/ajpcell.00536.2020](http://doi.org/10.1152/ajpcell.00536.2020) |
| **Issue** | 6 |
| **Journal Abbr** | Am J Physiol Cell Physiol |
| **ISSN** | 1522-1563 0363-6143 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Female
  + Humans
  + Male
  + Animals
  + Mice
  + Cell Line, Tumor
  + Mice, Inbred BALB C
  + enteric nervous system
  + Aminopyridines/pharmacology
  + Carbachol/pharmacology
  + Chlorides/\*metabolism
  + Cholinergic Agonists/pharmacology
  + Colon/drug effects/\*metabolism
  + colonic epithelium
  + Enteric Nervous System/\*drug effects/metabolism
  + Epithelial Cells/drug effects/\*metabolism
  + flupirtine
  + Intestinal Mucosa/drug effects/metabolism
  + irritable bowel syndrome with diarrhea
  + KCNQ Potassium Channels/\*metabolism
  + Membrane Potentials/drug effects/physiology
  + Neurons/drug effects/\*metabolism
  + Synaptic Transmission/drug effects
  + Ussing chamber

## Agmatine as a potential therapeutic intervention in bipolar depression: the preclinical landscape.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Devon Watts |
| **Author** | Bianca Pfaffenseller |
| **Author** | Bianca Wollenhaupt-Aguiar |
| **Author** | Luiza Paul Géa |
| **Author** | Taiane De Azevedo Cardoso |
| **Author** | Flavio Kapczinski |
| **Abstract** | Present antidepressant treatments are only helpful in a quarter of patients with bipolar depression, and new strategies are warranted. Increasing evidence suggests that accelerated polyamine metabolism is associated with the pathophysiology of depression. Polyamines regulate stress responses, inflammation, and neuronal signaling in the central and enteric nervous system. Agmatine is a promising target of altered polyamine metabolism considering its unique ability to regulate intracellular polyamine content and neuroprotective effects. Areas covered: This review discusses the polyamine system and its relationship to the central and enteric nervous system, focusing on results from preclinical studies supporting the relationship between agmatine and the pathophysiology of depression. We also discussed the main mechanisms underlying the antidepressant and neuroprotective effects of agmatine. Expert opinion: Our review points out the possible relationship between polyamines and the pathophysiology of depression. It discusses the efficacy of agmatine in several models of depressive-like behaviour, and suggests that it may prove to be an efficacious adjunctive treatment in bipolar depression. Furthermore, it discusses a proposed pathway linking systemic inflammation, observed in a subset of bipolar disorder patients, to abnormal polyamine metabolism and associated changes in the epithelial gut barrier and blood-brain barrier. |
| **Date** | 2019 Apr |
| **Language** | eng |
| **Extra** | Place: England PMID: 30764678 |
| **Volume** | 23 |
| **Pages** | 327-339 |
| **Publication** | Expert opinion on therapeutic targets |
| **DOI** | [10.1080/14728222.2019.1581764](http://doi.org/10.1080/14728222.2019.1581764) |
| **Issue** | 4 |
| **Journal Abbr** | Expert Opin Ther Targets |
| **ISSN** | 1744-7631 1472-8222 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/11/2025, 2:32:24 PM |

### Tags:

* + Humans
  + Animals
  + gut-brain axis
  + Neuroprotective Agents/pharmacology
  + Agmatine
  + Agmatine/\*pharmacology
  + Antidepressive Agents/\*pharmacology
  + bipolar depression
  + Bipolar Disorder/\*drug therapy/physiopathology
  + blood-brain barrier
  + Blood-Brain Barrier/embryology
  + leaky-gut
  + polyamines
  + Polyamines/metabolism

## Agonist-dependent development of delta opioid receptor tolerance in the colon.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Jesse J. DiCello |
| **Author** | Ayame Saito |
| **Author** | Pradeep Rajasekhar |
| **Author** | Benjamin W. Sebastian |
| **Author** | Rachel M. McQuade |
| **Author** | Arisbel B. Gondin |
| **Author** | Nicholas A. Veldhuis |
| **Author** | Meritxell Canals |
| **Author** | Simona E. Carbone |
| **Author** | Daniel P. Poole |
| **Abstract** | The use of opioid analgesics is severely limited due to the development of intractable constipation, mediated through activation of mu opioid receptors (MOR) expressed by enteric neurons. The related delta opioid receptor (DOR) is an emerging therapeutic target for chronic pain, depression and anxiety. Whether DOR agonists also promote sustained inhibition of colonic transit is unknown. This study examined acute and chronic tolerance to SNC80 and ARM390, which were full and partial DOR agonists in neural pathways controlling colonic motility, respectively. Excitatory pathways developed acute and chronic tolerance to SNC80, whereas only chronic tolerance developed in inhibitory pathways. Both pathways remained functional after acute or chronic ARM390 exposure. Propagating colonic motor patterns were significantly reduced after acute or chronic SNC80 treatment, but not by ARM390 pre-treatment. These findings demonstrate that SNC80 has a prolonged inhibitory effect on propagating colonic motility. ARM390 had no effect on motor patterns and thus may have fewer gastrointestinal side-effects. |
| **Date** | 2019 Aug |
| **Language** | eng |
| **Extra** | Place: Switzerland PMID: 30904952 PMCID: PMC11105391 |
| **Volume** | 76 |
| **Pages** | 3033-3050 |
| **Publication** | Cellular and molecular life sciences : CMLS |
| **DOI** | [10.1007/s00018-019-03077-6](http://doi.org/10.1007/s00018-019-03077-6) |
| **Issue** | 15 |
| **Journal Abbr** | Cell Mol Life Sci |
| **ISSN** | 1420-9071 1420-682X |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Animals
  + Mice
  + Mice, Inbred C57BL
  + Neurons/metabolism
  + Enteric nervous system
  + Electric Stimulation
  + \*Drug Tolerance
  + Analgesics, Opioid/\*pharmacology
  + Benzamides/pharmacology
  + Colon motility
  + Colon/\*drug effects/physiology
  + Endocytosis
  + GPCR regulation
  + Microscopy, Confocal
  + Muscle Contraction/drug effects
  + Opioid receptor
  + Piperazines/pharmacology
  + Receptors, Opioid, delta/agonists/\*metabolism
  + Receptors, Opioid, mu/agonists/metabolism

## Alterations of Prostanoid Expression and Intestinal Epithelial Barrier Functions in Ileus.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Anne Bessard |
| **Author** | Claire Cardaillac |
| **Author** | Thibauld Oullier |
| **Author** | Nicolas Cenac |
| **Author** | Malvyne Rolli-Derkinderen |
| **Author** | Michel Neunlist |
| **Author** | Aurélien Venara |
| **Abstract** | INTRODUCTION: Intestinal manipulation (IM)-induced inflammation could contribute to postoperative ileus (POI) pathophysiology via the modulation of prostanoid pathways. To identify the prostanoids involved, we aimed to characterize the profile of prostanoids and their synthesis enzyme expression in a murine model of POI and to determine whether the altered prostanoids could contribute to POI. METHODS: Four or 14 h after IM in mice, gastrointestinal (GI) motility and intestinal epithelial barrier (IEB) permeability were assessed in vivo and ex vivo in Ussing chambers. Using high sensitivity liquid chromatography-tandem mass spectrometry, we characterized the tissue profile of polyunsaturated fatty acid metabolites in our experimental model. Finally, we evaluated in vivo the effects of the prostanoids studied upon IM-induced gut dysfunctions. RESULTS: We first showed that 14 h after IM was significantly faster than jejunal transit at 4 h post-IM, although it remained significantly increased compared to the control. In contrast, we showed that IM-induced inflammation increase in jejunum permeability was similar after four and 14 h. We next showed that expression of prostacyclin synthase and hemopoietic prostaglandin-D synthase mRNA and their products were significantly reduced 14 h after IM as compared to controls. Furthermore, 15-deoxy-delta 12,14-Prostaglandin J2 reduced the IM-induced inflammation increase in IEB permeability but had no effect on GI motility. In contrast, PGI(2) increased IM-induced IEB permeability and motility dysfunctions. CONCLUSIONS: Arachidonic acid derivative contributes differentially to GI dysfunction in POI. The decrease of 15-deoxy-delta 12,14-Prostaglandin J2 levels induced by IM could contribute to impaired GI dysfunctions in POI and could be considered as putative therapeutic targets to restore barrier dysfunctions associated with POI. |
| **Date** | 2024 Apr |
| **Language** | eng |
| **Rights** | Copyright © 2024 Elsevier Inc. All rights reserved. |
| **Extra** | Place: United States PMID: 38277953 |
| **Volume** | 296 |
| **Pages** | 165-173 |
| **Publication** | The Journal of surgical research |
| **DOI** | [10.1016/j.jss.2023.12.018](http://doi.org/10.1016/j.jss.2023.12.018) |
| **Journal Abbr** | J Surg Res |
| **ISSN** | 1095-8673 0022-4804 |
| **Date Added** | 6/11/2025, 2:32:27 PM |
| **Modified** | 6/11/2025, 2:32:27 PM |

### Tags:

* + Animals
  + Mice
  + Postoperative Complications
  + Gastrointestinal Motility
  + Inflammation/metabolism
  + Pathophysiology
  + Postoperative ileus
  + \*Ileus/etiology
  + \*Prostaglandins/pharmacology
  + Jejunum
  + Murine
  + Prostanoid

## Altered enteric expression of the homeobox transcription factor Phox2b in patients with diverticular disease.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | François Cossais |
| **Author** | Christina Lange |
| **Author** | Martina Barrenschee |
| **Author** | Marie Möding |
| **Author** | Michael Ebsen |
| **Author** | Ilka Vogel |
| **Author** | Martina Böttner |
| **Author** | Thilo Wedel |
| **Abstract** | BACKGROUND: Diverticular disease, a major gastrointestinal disorder, is associated with modifications of the enteric nervous system, encompassing alterations of neurochemical coding and of the tyrosine receptor kinase Ret/GDNF pathway. However, molecular factors underlying these changes remain to be determined. OBJECTIVES: We aimed to characterise the expression of Phox2b, an essential regulator of Ret and of neuronal subtype development, in the adult human enteric nervous system, and to evaluate its potential involvement in acute diverticulitis. METHODS: Site-specific gene expression of Phox2b in the adult colon was analysed by quantitative polymerase chain reaction. Colonic specimens of adult controls and patients with diverticulitis were subjected to quantitative polymerase chain reaction for Phox2b and dual-label immunochemistry for Phox2b and the neuronal markers RET and tyrosine hydroxylase or the glial marker S100β. RESULTS: The results indicate that Phox2b is physiologically expressed in myenteric neuronal and glial subpopulations in the adult enteric nervous system. Messenger RNA expression of Phox2b was increased in patients with diverticulitis and both neuronal, and glial protein expression of Phox2b were altered in these patients. CONCLUSIONS: Alterations of Phox2b expression may contribute to the enteric neuropathy observed in diverticular disease. Future studies are required to characterise the functions of Phox2b in the adult enteric nervous system and to determine its potential as a therapeutic target in gastrointestinal disorders. |
| **Date** | 2019 Apr |
| **Language** | eng |
| **Extra** | Place: England PMID: 31019703 PMCID: PMC6466753 |
| **Volume** | 7 |
| **Pages** | 349-357 |
| **Publication** | United European gastroenterology journal |
| **DOI** | [10.1177/2050640618824913](http://doi.org/10.1177/2050640618824913) |
| **Issue** | 3 |
| **Journal Abbr** | United European Gastroenterol J |
| **ISSN** | 2050-6406 2050-6414 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Aged
  + Female
  + Humans
  + Male
  + Retrospective Studies
  + Gene Expression
  + Colon/metabolism/pathology
  + Diverticular disease
  + Diverticular Diseases/\*metabolism
  + Dopaminergic Neurons/metabolism
  + enteric glial cells
  + Enteric Nervous System/\*metabolism/pathology
  + enteric neurons
  + enteric neuropathy
  + Homeodomain Proteins/\*genetics/\*metabolism
  + Intestinal Pseudo-Obstruction/metabolism
  + Neuroglia/metabolism
  + phox2b
  + Proto-Oncogene Proteins c-ret/metabolism
  + Ret
  + RNA, Messenger/genetics
  + S100 Calcium Binding Protein beta Subunit/metabolism
  + S100β
  + TH
  + Transcription Factors/\*genetics/\*metabolism
  + Tyrosine 3-Monooxygenase/metabolism

## Altered epithelial barrier functions in the colon of patients with spina bifida.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Charlène Brochard |
| **Author** | Guillaume Bouguen |
| **Author** | Raphael Olivier |
| **Author** | Tony Durand |
| **Author** | Sébastien Henno |
| **Author** | Benoît Peyronnet |
| **Author** | Mael Pagenault |
| **Author** | Chloé Lefèvre |
| **Author** | Gaëlle Boudry |
| **Author** | Mikael Croyal |
| **Author** | Alain Fautrel |
| **Author** | Maxime Esvan |
| **Author** | Alain Ropert |
| **Author** | Anne Dariel |
| **Author** | Laurent Siproudhis |
| **Author** | Michel Neunlist |
| **Abstract** | Our objectives were to better characterize the colorectal function of patients with Spina Bifida (SB). Patients with SB and healthy volunteers (HVs) completed prospectively a standardized questionnaire, clinical evaluation, rectal barostat, colonoscopy with biopsies and faecal collection. The data from 36 adults with SB (age: 38.8 [34.1-47.2]) were compared with those of 16 HVs (age: 39.0 [31.0-46.5]). Compared to HVs, rectal compliance was lower in patients with SB (p = 0.01), whereas rectal tone was higher (p = 0.0015). Ex vivo paracellular permeability was increased in patients with SB (p = 0.0008) and inversely correlated with rectal compliance (r = - 0.563, p = 0.002). The expression of key tight junction proteins and inflammatory markers was comparable between SB and HVs, except for an increase in Claudin-1 immunoreactivity (p = 0.04) in SB compared to HVs. TGFβ1 and GDNF mRNAs were expressed at higher levels in patients with SB (p = 0.02 and p = 0.008). The levels of acetate, propionate and butyrate in faecal samples were reduced (p = 0.04, p = 0.01, and p = 0.02, respectively). Our findings provide evidence that anorectal and epithelial functions are altered in patients with SB. The alterations in these key functions might represent new therapeutic targets, in particular using microbiota-derived approaches.Clinical Trials: NCT02440984 and NCT03054415. |
| **Date** | 2022 May 3 |
| **Language** | eng |
| **Rights** | © 2022. The Author(s). |
| **Extra** | Place: England PMID: 35505001 PMCID: PMC9065040 |
| **Volume** | 12 |
| **Pages** | 7196 |
| **Publication** | Scientific reports |
| **DOI** | [10.1038/s41598-022-11289-3](http://doi.org/10.1038/s41598-022-11289-3) |
| **Issue** | 1 |
| **Journal Abbr** | Sci Rep |
| **ISSN** | 2045-2322 |
| **Date Added** | 6/11/2025, 2:32:27 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Adult
  + Humans
  + Colon
  + Surveys and Questionnaires
  + \*Spinal Dysraphism
  + Colonoscopy
  + Rectum

## Are We Close to Targeting Enteric Glia in Gastrointestinal Diseases and Motility Disorders?

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Brian D. Gulbransen |
| **Author** | Fievos L. Christofi |
| **Date** | 2018 Aug |
| **Language** | eng |
| **Extra** | Place: United States PMID: 29964042 PMCID: PMC6452442 |
| **Volume** | 155 |
| **Pages** | 245-251 |
| **Publication** | Gastroenterology |
| **DOI** | [10.1053/j.gastro.2018.06.050](http://doi.org/10.1053/j.gastro.2018.06.050) |
| **Issue** | 2 |
| **Journal Abbr** | Gastroenterology |
| **ISSN** | 1528-0012 0016-5085 |
| **Date Added** | 6/11/2025, 2:32:27 PM |
| **Modified** | 6/11/2025, 2:32:27 PM |

### Tags:

* + Humans
  + Calcium/physiology
  + Connexins/antagonists & inhibitors/physiology
  + Enteric Nervous System/drug effects/\*physiology
  + Gastrointestinal Agents/therapeutic use
  + Gastrointestinal Diseases/drug therapy/\*physiopathology
  + Gastrointestinal Motility/drug effects/\*physiology
  + Gastrointestinal Tract/\*innervation/physiology
  + Neuroglia/drug effects/\*physiology
  + Purinergic P2X Receptor Antagonists/therapeutic use

## Blockage of the P2X7 Receptor Attenuates Harmful Changes Produced by Ischemia and Reperfusion in the Myenteric Plexus.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Kelly Palombit |
| **Author** | Cristina Eusébio Mendes |
| **Author** | Wothan Tavares-de-Lima |
| **Author** | Maria Luiza Barreto-Chaves |
| **Author** | Patricia Castelucci |
| **Abstract** | INTRODUCTION: Our work analyzed the effects of a P2X7 receptor antagonist, Brilliant Blue G (BBG), on rat ileum myenteric plexus following ischemia and reperfusion (ISR) induced by 45 min of ileal artery occlusion with an atraumatic vascular clamp with 24 h (ISR 24-h group) or 14 d of reperfusion (ISR 14-d group). MATERIAL AND METHODS: Either BBG (50 mg/kg or 100 mg/kg, BBG50 or BBG100 groups) or saline (vehicle) was administered subcutaneously 1 h after ischemia in the ISR 24-h group or once daily for the 5 d after ischemia in the ISR 14-d group (n = 5 per group). We evaluated the neuronal density and profile area by examining the number of neutrophils in the intestinal layers, protein expression levels of the P2X7 receptor, intestinal motility and immunoreactivity for the P2X7 receptor, nitric oxide synthase, neurofilament-200, and choline acetyl transferase in myenteric neurons. RESULTS: The neuronal density and profile area were restored by BBG following ISR. The ischemic groups showed alterations in P2X7 receptor protein expression and the number of neutrophils in the intestine and decreased intestinal motility, all of which were recovered by BBG treatment. CONCLUSION: We concluded that ISR morphologically and functionally affected the intestine and that its effects were reversed by BBG treatment, suggesting the P2X7 receptor as a therapeutic target. |
| **Date** | 2019 Jul |
| **Language** | eng |
| **Extra** | Place: United States PMID: 30734238 |
| **Volume** | 64 |
| **Pages** | 1815-1829 |
| **Publication** | Digestive diseases and sciences |
| **DOI** | [10.1007/s10620-019-05496-8](http://doi.org/10.1007/s10620-019-05496-8) |
| **Issue** | 7 |
| **Journal Abbr** | Dig Dis Sci |
| **ISSN** | 1573-2568 0163-2116 |
| **Date Added** | 6/11/2025, 2:32:27 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Male
  + Animals
  + Disease Models, Animal
  + Rats, Wistar
  + Signal Transduction/drug effects
  + P2X7 receptor
  + Brilliant Blue G
  + Cytoprotection
  + Gastrointestinal Motility/drug effects
  + Ileum
  + Ileum/\*innervation
  + Ischemia and reperfusion
  + Mesenteric Ischemia/\*drug therapy/metabolism/pathology/physiopathology
  + Myenteric plexus
  + Myenteric Plexus/\*drug effects/metabolism/pathology
  + Neurons/\*drug effects/metabolism/pathology
  + Neutrophil Infiltration/drug effects
  + Purinergic P2X Receptor Antagonists/\*pharmacology
  + Receptors, Purinergic P2X7/\*drug effects/metabolism
  + Reperfusion Injury/metabolism/pathology/physiopathology/\*prevention & control
  + Rosaniline Dyes/\*pharmacology

## Calcium-sensing receptor: A new target for therapy of diarrhea.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Sam Xianjun Cheng |
| **Abstract** | Management of acute diarrhea remains a global challenge, particularly in resource-limiting countries. Oral rehydration solution (ORS), a passive rehydrating therapy developed approximately 40 years ago, remains the mainstay treatment. Although ORS is effective for hydration, since it does not inhibit enterotoxin-mediated excessive secretion, reduced absorption and compromised barrier function - the primary mechanisms of diarrhea, ORS does not offer a rapid relief of diarrhea symptom. There are a few alternative therapies available, yet the use of these drugs is limited by their expense, lack of availability and/or safety concerns. Novel anti-diarrheal therapeutic approaches, particularly those simple affordable therapies, are needed. This article explores intestinal calcium-sensing receptor (CaSR), a newly uncovered target for therapy of diarrhea. Unlike others, targeting this host antidiarrheal receptor system appears "all-inclusive": it is anti-secretory, pro-absorptive, anti-motility, and anti-inflammatory. Thus, activating CaSR reverses changes of both secretory and inflammatory diarrheas. Considering its unique property of using simple nutrients such as calcium, polyamines, and certain amino acids/oligopeptides as activators, it is possible that through targeting of CaSR with a combination of specific nutrients, novel oral rehydrating solutions that are inexpensive and practical to use in all countries may be developed. |
| **Date** | 2016 Mar 7 |
| **Language** | eng |
| **Extra** | Place: United States PMID: 26973410 PMCID: PMC4777994 |
| **Volume** | 22 |
| **Pages** | 2711-2724 |
| **Publication** | World journal of gastroenterology |
| **DOI** | [10.3748/wjg.v22.i9.2711](http://doi.org/10.3748/wjg.v22.i9.2711) |
| **Issue** | 9 |
| **Journal Abbr** | World J Gastroenterol |
| **ISSN** | 2219-2840 1007-9327 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/11/2025, 2:32:24 PM |

### Tags:

* + Humans
  + Animals
  + Disease Models, Animal
  + Signal Transduction/drug effects
  + Mice, Knockout
  + Molecular Targeted Therapy
  + Intestinal Mucosa/metabolism
  + Enteric nervous system
  + Gastrointestinal Motility/drug effects
  + Cost-Benefit Analysis
  + Genotype
  + Intestinal permeability
  + Anti-secretory
  + Antidiarrheals/economics/\*therapeutic use
  + Cholera toxin
  + Diarrhea/\*drug therapy/economics/metabolism/physiopathology
  + Drug Costs
  + Drug Design
  + Escherichia coli heat stable toxin
  + Inflammatory diarrhea
  + Intestinal barrier function
  + Intestines/\*drug effects/physiopathology
  + Oral rehydration solution
  + Permeability
  + Pro-absorptive
  + Receptors, Calcium-Sensing/\*agonists/metabolism
  + Receptors, G-Protein-Coupled/deficiency/genetics
  + Secretory diarrhea

## Centrally Targeted Pharmacotherapy for Chronic Abdominal Pain: Understanding and Management.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Hans Törnblom |
| **Author** | Douglas A. Drossman |
| **Abstract** | Chronic abdominal pain has a widespread impact on the individual and the society. Identifying and explaining mechanisms of importance for the pain experience within a biopsychosocial context are central in order to select treatment that has a chance for symptom reduction. With current knowledge of brain-gut interactions, chronic abdominal pain, which mostly appears in functional gastrointestinal disorders, to a large extent involves pain mechanisms residing within the brain. As such, the use of centrally targeted pharmacotherapy as an effective treatment option is obvious in a selected number of patients. The antidepressants are most common, but also other classes of medications can be used, either alone or in combination. The latter option refers to when there is insufficient effect of one drug alone or side effects limiting dosage, and when combined in lower doses, certain drugs give rise to augmentation effects. This chapter outlines basic mechanisms of importance for the understanding of chronic abdominal pain and the pharmacologic treatment options. |
| **Date** | 2017 |
| **Language** | eng |
| **Extra** | Place: Germany PMID: 28204956 |
| **Volume** | 239 |
| **Pages** | 417-440 |
| **Publication** | Handbook of experimental pharmacology |
| **DOI** | [10.1007/164\_2016\_106](http://doi.org/10.1007/164_2016_106) |
| **Journal Abbr** | Handb Exp Pharmacol |
| **ISSN** | 0171-2004 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Animals
  + Signal Transduction/drug effects
  + Abdominal pain
  + Abdominal Pain/\*drug therapy/metabolism/physiopathology
  + Analgesics/\*therapeutic use
  + Antidepressants
  + Brain–gut axis
  + Brain/\*drug effects/metabolism/physiopathology
  + Chronic Pain/\*drug therapy/metabolism/physiopathology
  + Enteric Nervous System/\*drug effects/metabolism/physiopathology
  + Functional gastrointestinal disorders
  + Gastrointestinal Tract/\*innervation
  + Pain Perception/drug effects
  + Pain Threshold/drug effects
  + Treatment

## Colonic 5-HT(4) receptors are targets for novel prokinetic drugs.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | James J. Galligan |
| **Abstract** | 5-HT(4) receptors are G protein-coupled receptors that link to the stimulatory protein Gs which activates adenylate cyclase to increase intracellular cyclic AMP which then activates protein kinase A (PKA). 5-HT(4) receptors are expressed by neurons in the central and peripheral nervous systems especially the enteric nervous system (ENS). In general, 5-HT(4) receptors are stimulatory and their activation in the ENS enhances neurotransmitter release and propulsive motility patterns. 5-HT(4) receptors are expressed by enterochromaffin (EC) cells, Goblet cells, and most enteric neurons. The study by Konen and colleagues in this issue of Neurogastroenterology and Motility features two novel 5-HT(4) receptor agonists (5-HT(4) -LA1 and 5-HT(4) -LA-2) that are not absorbed from the gastrointestinal tract of mice and act locally in the colonic mucosa to stimulate propulsive motility. The authors show that 5-HT(4) -LA1 and 5-HT(4) -LA2 were not absorbed from the colon and that both drugs stimulated colonic transit when administered by gavage. Both agonists stimulated colonic glass bead expulsion, and 5-HT(4) LA1 activation stimulated fecal output and increased fecal water content. These effects were detected in young and aged mice. 5-HT(4) receptors were also localized to the epithelium of the human duodenum, ileum, and colon. These studies highlight novel 5-HT(4) receptor agonists that have prokinetic actions on the GI tract. These drugs are not absorbed and act locally in the gut mucosa to stimulate propulsive motility while minimizing access to systemic 5-HT(4) receptors and avoiding potential unwanted side effects. |
| **Date** | 2021 Apr |
| **Language** | eng |
| **Rights** | © 2021 John Wiley & Sons Ltd. |
| **Extra** | Place: England PMID: 33749067 |
| **Volume** | 33 |
| **Pages** | e14125 |
| **Publication** | Neurogastroenterology and motility |
| **DOI** | [10.1111/nmo.14125](http://doi.org/10.1111/nmo.14125) |
| **Issue** | 4 |
| **Journal Abbr** | Neurogastroenterol Motil |
| **ISSN** | 1365-2982 1350-1925 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/11/2025, 2:32:24 PM |

### Tags:

* + Humans
  + Animals
  + 5-HT4 receptors
  + colon motility
  + Colon/\*drug effects/metabolism
  + Drug Delivery Systems/\*methods
  + Gastrointestinal Diseases/\*drug therapy/metabolism
  + Gastrointestinal Motility/\*drug effects/physiology
  + prokinetic drugs
  + Receptors, Serotonin, 5-HT4/metabolism
  + Serotonin 5-HT4 Receptor Agonists/\*administration & dosage/metabolism

## Concise Review: Cellular and Molecular Mechanisms of Postnatal Injury-Induced Enteric Neurogenesis.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Raleigh Jonscher |
| **Author** | Jaime Belkind-Gerson |
| **Abstract** | Although still controversial, there is increasing agreement that postnatal neurogenesis occurs in the enteric nervous system (ENS) in response to injury. Following acute colitis, there is significant cell death of enteric neurons and evidence suggests that subsequent neural regeneration follows. An enteric neural stem/progenitor cell population with neurogenic potential has been identified in culture; in vivo, compensatory neurogenesis is driven by enteric glia and may also include de-differentiated Schwann cells. Recent evidence suggests that changes in the enteric microenvironment due to injury-associated increases in glial cell-derived neurotrophic factor (GDNF), serotonin (5-hydroxytryptamine [HT]), products from the gut microbiome, and possibly endocannabinoids may lead to the transdifferentiation of mature enteric glia and may reprogram recruited Schwann cells. Targeting neurogenic pathways presents a promising avenue toward the development of new and innovative treatments for acquired damage to the ENS. In this review, we discuss potential sources of newly generated adult enteric neurons, the involvement of GDNF, 5-HT, endocannabinoids, and lipopolysaccharide, as well as therapeutic applications of this evolving work. Stem Cells 2019;37:1136-1143. |
| **Date** | 2019 Sep |
| **Language** | eng |
| **Rights** | ©AlphaMed Press 2019. |
| **Extra** | Place: England PMID: 31145813 |
| **Volume** | 37 |
| **Pages** | 1136-1143 |
| **Publication** | Stem cells (Dayton, Ohio) |
| **DOI** | [10.1002/stem.3045](http://doi.org/10.1002/stem.3045) |
| **Issue** | 9 |
| **Journal Abbr** | Stem Cells |
| **ISSN** | 1549-4918 1066-5099 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/11/2025, 2:32:24 PM |

### Tags:

* + Humans
  + Animals
  + Cell Proliferation/physiology
  + Colitis/pathology/physiopathology
  + Enteric Nervous System/cytology/\*physiology
  + Intestines/pathology/physiopathology
  + Nerve Regeneration/physiology
  + Neural Stem Cells/cytology/\*physiology
  + Neurogenesis/\*physiology
  + Neurons/cytology/\*physiology

## Connecting the Dots: The Interplay Between Stroke and the Gut-Brain Axis.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Pooja M. Murthy |
| **Author** | Jayashankar Ca |
| **Author** | Venkataramana Kandi |
| **Author** | Mithun K. Reddy |
| **Author** | Ganaraja V. Harikrishna |
| **Author** | Kavitha Reddy |
| **Author** | Ramya Jp |
| **Author** | Ankush N. Reddy |
| **Author** | Jigya Narang |
| **Abstract** | This article discusses the interplay between the gut-brain axis and stroke, a multifaceted neurological disorder that affects millions of people worldwide. The gut-brain axis is a bidirectional communication network linking the central nervous system (CNS) to the gastrointestinal tract (GIT), including the enteric nervous system (ENS), vagus nerve, and gut microbiota. Dysbiosis in the gut microbiota, alterations in the ENS and vagus nerve, and gut motility changes have been linked to increased inflammation and oxidative stress, which are contributing factors in the development and progression of stroke. Research on animals has shown that modifying the gut microbiota can impact the results of a stroke. Germ-free mice displayed improved neurological function and decreased infarct volumes, indicating a positive effect. Furthermore, studies in stroke patients have shown alterations in the gut microbiota composition, indicating that targeting dysbiosis could be a potential therapeutic strategy for stroke. The review suggests that targeting the gut-brain axis may represent a potential therapeutic approach to reduce the morbidity and mortality associated with stroke. |
| **Date** | 2023 Apr |
| **Language** | eng |
| **Rights** | Copyright © 2023, Murthy et al. |
| **Extra** | Place: United States PMID: 37182027 PMCID: PMC10168015 |
| **Volume** | 15 |
| **Pages** | e37324 |
| **Publication** | Cureus |
| **DOI** | [10.7759/cureus.37324](http://doi.org/10.7759/cureus.37324) |
| **Issue** | 4 |
| **Journal Abbr** | Cureus |
| **ISSN** | 2168-8184 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + gastrointestinal tract
  + gut-brain axis
  + dysbiosis
  + stroke
  + therapeutic approach

## Constipation Caused by Anti-calcitonin Gene-Related Peptide Migraine Therapeutics Explained by Antagonism of Calcitonin Gene-Related Peptide's Motor-Stimulating and Prosecretory Function in the Intestine.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Peter Holzer |
| **Author** | Ulrike Holzer-Petsche |
| **Abstract** | The development of small-molecule calcitonin gene-related peptide (CGRP) receptor antagonists (gepants) and of monoclonal antibodies targeting the CGRP system has been a major advance in the management of migraine. In the randomized controlled trials before regulatory approval, the safety of these anti-CGRP migraine therapeutics was considered favorable and to stay within the expected profile. Post-approval real-world surveys reveal, however, constipation to be a major adverse event which may affect more than 50% of patients treated with erenumab (an antibody targeting the CGRP receptor), fremanezumab or galcanezumab (antibodies targeting CGRP). In this review article we address the question whether constipation caused by inhibition of CGRP signaling can be mechanistically deduced from the known pharmacological actions and pathophysiological implications of CGRP in the digestive tract. CGRP in the gut is expressed by two distinct neuronal populations: extrinsic primary afferent nerve fibers and distinct neurons of the intrinsic enteric nervous system. In particular, CGRP is a major messenger of enteric sensory neurons which in response to mucosal stimulation activate both ascending excitatory and descending inhibitory neuronal pathways that enable propulsive (peristaltic) motor activity to take place. In addition, CGRP is able to stimulate ion and water secretion into the intestinal lumen. The motor-stimulating and prosecretory actions of CGRP combine in accelerating intestinal transit, an activity profile that has been confirmed by the ability of CGRP to induce diarrhea in mice, dogs and humans. We therefore conclude that the constipation elicited by antibodies targeting CGRP or its receptor results from interference with the physiological function of CGRP in the small and large intestine in which it contributes to the maintenance of peristaltic motor activity, ion and water secretion and intestinal transit. |
| **Date** | 2021 |
| **Language** | eng |
| **Rights** | Copyright © 2022 Holzer and Holzer-Petsche. |
| **Extra** | Place: Switzerland PMID: 35087426 PMCID: PMC8787053 |
| **Volume** | 12 |
| **Pages** | 820006 |
| **Publication** | Frontiers in physiology |
| **DOI** | [10.3389/fphys.2021.820006](http://doi.org/10.3389/fphys.2021.820006) |
| **Journal Abbr** | Front Physiol |
| **ISSN** | 1664-042X |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/11/2025, 2:32:26 PM |

### Tags:

* + diarrhea
  + calcitonin gene-related peptide (CGRP)
  + CGRP antibodies
  + CGRP receptor antagonists (gepants)
  + CGRP receptor antibodies
  + constipation
  + migraine
  + peristaltic motor activity

## Decoding the neuroimmune axis in colorectal cancer: From neural circuitry to therapeutic innovation.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Ying Li |
| **Author** | Sheng-Ya Yang |
| **Author** | Ying-Ru Zhang |
| **Author** | Yan Wang |
| **Abstract** | The nervous and immune systems are two major components that maintain body homeostasis, with their functional roles often overlapping significantly. Both systems are capable of identifying, integrating, and organizing responsive reactions to various external stimuli. The gut, referred to as the "second brain" and the largest immune organ in the body, serves as the most frequent focal site for neuroimmune interactions. Colorectal cancer (CRC), as the predominant solid tumor arising in this neuroimmune-rich microenvironment, remains understudied through the lens of neuroimmune regulatory mechanisms. This review systematically synthesizes current evidence to elucidate the neuroimmune axis in CRC pathogenesis, with particular emphasis on neuroimmune crosstalk-mediated remodeling of tumor immunity. We comprehensively catalog the immunomodulatory effects exerted by principal neuroregulatory mediators, categorized as: (1) neurotransmitters (glutamate, glutamine, γ-aminobutyric acid, epinephrine, norepinephrine, dopamine, serotonin, acetylcholine, and gaseous signaling molecules); (2) neuropeptides (substance P, calcitonin gene-related peptide, vasoactive intestinal peptide); and (3) neurotrophic factors. Furthermore, we critically evaluate the translational prospects and therapeutic challenges of targeting neuroimmune pathways and propose strategic priorities and research focuses for advancing the development of neuroimmune interaction-related therapeutic approaches in CRC. |
| **Date** | 2025 Jun |
| **Language** | eng |
| **Rights** | Copyright © 2025 Elsevier Ltd. All rights reserved. |
| **Extra** | Place: England PMID: 40274426 |
| **Volume** | 83 |
| **Pages** | 3-17 |
| **Publication** | Cytokine & growth factor reviews |
| **DOI** | [10.1016/j.cytogfr.2025.04.001](http://doi.org/10.1016/j.cytogfr.2025.04.001) |
| **Journal Abbr** | Cytokine Growth Factor Rev |
| **ISSN** | 1879-0305 1359-6101 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/11/2025, 2:32:26 PM |

### Tags:

* + Humans
  + Animals
  + Tumor Microenvironment/immunology
  + Colorectal cancer
  + Enteric nervous system
  + Gut-brain axis
  + \*Colorectal Neoplasms/immunology/therapy/pathology
  + \*Neuroimmunomodulation/immunology
  + Neuroimmune Interactions
  + Neuropeptides/immunology
  + Neurotransmitter
  + Neurotransmitter Agents/immunology

## Designing poly(gamma-aminobutyric acid)-based nanoparticles for the treatment of major depressive disorders.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Bui Duc Tri |
| **Author** | Babita Shashni |
| **Author** | Hirofumi Matsui |
| **Author** | Yukio Nagasaki |
| **Abstract** | Major depressive disorder (MDD) is a worldwide concern owing to its negative impact on the quality of life. Gamma-aminobutyric acid (GABA), an essential neurotransmitter in the brain, is important for regulating the enteric nervous system and gut-brain dual communication (gut-brain axis), thus providing gastrointestinal GABA and GABA-related pathways with possible targets for MDD treatment. However, the use of GABA for this disease remains limited due to its poor pharmacokinetic properties, including the low permeability through the blood-brain barrier, and the rapid clearance from the gastrointestinal tract. Since poly(amino acid)s are advantageous for improving the beneficial bioactivities of conventional amino acids, poly(gamma-aminobutyric acid) (poly(GABA)) is a potential candidate for MDD therapy. Nevertheless, the non-water-soluble and non-dispersible characteristics of poly(GABA) render difficulty in administering its conventional forms in vitro/in vivo, thereby hindering its therapeutic applications. Therefore, this study proposes a new design for poly(GABA) in nanoparticle form, which is composed of the amphiphilic diblock copolymers of poly(GABA) and poly(ethylene glycol), providing a suitable formulation for medication applications. Herein, we report on a new orally deliverable poly(GABA)-based nanoparticles (Nano(GABA)) in aqueous media and their efficacy on mouse depression models. Nano(GABA) treatment efficiently attenuated depression-like symptoms as evidenced by behavioral tests (forced swimming tests and tail suspension tests) and stress biomarkers (corticosterone). These findings suggest that the newly designed poly(GABA)-based nanoparticles are a promising candidate for the treatment of depression. STATEMENT OF SIGNIFICANCE: This research is the first to report the preparation of poly(GABA)-based nanoparticles in aqueous conditions with beneficial physical properties to open the gate for medical and pharmaceutical applications of poly (GABA). It is also a pioneer in using poly(GABA)-based materials for major depressive disorder therapeutics in vivo. Oral administration of Nano(GABA) attenuates depressive-like symptoms by targeting the enteric nervous system possibly through modulation of the gut-brain axis pathways with negligible toxicity, suggesting that Nano(GABA) is a promising therapeutic agent for major depressive disorders. |
| **Date** | 2023 Aug |
| **Language** | eng |
| **Rights** | Copyright © 2023. Published by Elsevier B.V. |
| **Extra** | Place: Netherlands PMID: 37336293 |
| **Volume** | 360 |
| **Pages** | 110-121 |
| **Publication** | Journal of controlled release : official journal of the Controlled Release Society |
| **DOI** | [10.1016/j.jconrel.2023.06.021](http://doi.org/10.1016/j.jconrel.2023.06.021) |
| **Journal Abbr** | J Control Release |
| **ISSN** | 1873-4995 0168-3659 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/11/2025, 2:32:25 PM |

### Tags:

* + Animals
  + Mice
  + Quality of Life
  + Gut-brain axis
  + Brain/metabolism
  + \*Depressive Disorder, Major/drug therapy/diagnosis/metabolism
  + Blood-Brain Barrier/metabolism
  + GABA
  + gamma-Aminobutyric Acid
  + Major depressive disorder
  + Nanoparticle
  + Poly(GABA)

## Differential contribution of estrogen receptors to the intestinal therapeutic effects of 17β-estradiol in a murine model of Parkinson's disease.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Andrée-Anne Poirier |
| **Author** | Mélissa Côté |
| **Author** | Mélanie Bourque |
| **Author** | Hend Jarras |
| **Author** | Jérôme Lamontagne-Proulx |
| **Author** | Marc Morissette |
| **Author** | Thérèse Di Paolo |
| **Author** | Denis Soulet |
| **Abstract** | Beneficial effects of estrogens have been reported in Parkinson's disease (PD) for many years. We previously reported their neuroprotective and anti-inflammatory potentials in the enteric nervous system of the intestine, a region possibly affected during the early stages of the disease according to Braak's hypothesis. Three different estrogen receptors have been characterized to date: the estrogen receptor alpha (ERα), the estrogen receptor beta (ERβ) and the G protein coupled estrogen receptor 1 (GPER1). The aim of the present study was to decipher the individual contribution of each estrogen receptor to the therapeutic properties of 17β-estradiol (E2) in the myenteric plexus of the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) mouse model of PD. Different agonists, 4,4',4''-(4-propyl-[1H]-pyrazole-1,3,5-triyl)trisphenol (PPT; ERα), 2,3-bis(4-hydroxyphenyl)-propionitrile (DPN; ERβ), G1 (GPER1), and antagonists, ICI 182,780 (ERα and ERβ), G15 (GPER1), were used to analyze the involvement of each receptor. We confirmed that G1 protects dopamine (DA) neurons to a similar extent as E2. An anti-inflammatory effect on proinflammatory macrophages and cultured human monocytes was also demonstrated with E2 and G1. The effects of PPT and DPN were less potent than G1 with only a partial neuroprotection of DA neurons by PPT and a partial reduction of interleukin (IL)- 1β production in monocytes by PPT and DPN. Overall, the present results indicate that the positive outcomes of estrogens are mainly through activation of GPER1. Therefore, this suggests that targeting GPER1 could be a promising approach for future estrogen-based hormone therapies during early PD. |
| **Date** | 2022 Sep |
| **Language** | eng |
| **Rights** | Copyright © 2022. Published by Elsevier Inc. |
| **Extra** | Place: United States PMID: 35781029 |
| **Volume** | 187 |
| **Pages** | 85-97 |
| **Publication** | Brain research bulletin |
| **DOI** | [10.1016/j.brainresbull.2022.06.019](http://doi.org/10.1016/j.brainresbull.2022.06.019) |
| **Journal Abbr** | Brain Res Bull |
| **ISSN** | 1873-2747 0361-9230 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/11/2025, 2:32:26 PM |

### Tags:

* + Humans
  + Animals
  + Disease Models, Animal
  + Mice
  + Intestines
  + Inflammation
  + Enteric nervous system
  + \*Parkinson Disease/drug therapy
  + \*Receptors, Estrogen/metabolism
  + Anti-Inflammatory Agents
  + Estradiol/pharmacology/therapeutic use
  + Estrogen receptor
  + Estrogen Receptor alpha/metabolism
  + Estrogen Receptor beta/agonists
  + Estrogens/pharmacology
  + GPER1
  + Gut
  + MPTP

## Distinct gut microbiome characteristics and dynamics in patients with Parkinson's disease based on the presence of premotor rapid-eye movement sleep behavior disorders.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Jae-Yun Lee |
| **Author** | Sungyang Jo |
| **Author** | Jihyun Lee |
| **Author** | Moongwan Choi |
| **Author** | Kijeong Kim |
| **Author** | Sangjin Lee |
| **Author** | Hyun Sik Kim |
| **Author** | Jin-Woo Bae |
| **Author** | Sun Ju Chung |
| **Abstract** | BACKGROUND: Alpha-synuclein aggregation, a hallmark of Parkinson's disease (PD), is hypothesized to often begin in the enteric or peripheral nervous system in "body-first" PD and progresses through the vagus nerve to the brain, therefore REM sleep behavior disorder (RBD) precedes the PD diagnosis. In contrast, "brain-first" PD begins in the central nervous system. Evidence that gut microbiome imbalances observed in PD and idiopathic RBD exhibit similar trends supports body-first and brain-first hypothesis and highlights the role of microbiota in PD pathogenesis. However, further investigation is needed to understand distinct microbiome changes in body-first versus brain-first PD over the disease progression. RESULTS: Our investigation involved 104 patients with PD and 85 of their spouses as healthy controls (HC), with 57 patients (54.8%) categorized as PD-RBD(+) and 47 patients (45.2%) as PD-RBD(-) based on RBD presence before the PD diagnosis. We evaluated the microbiome differences between these groups over the disease progression through taxonomic and functional differential abundance analyses and carbohydrate-active enzyme (CAZyme) profiles based on metagenome-assembled genomes. The PD-RBD(+) gut microbiome showed a relatively stable microbiome composition irrespective of disease stage. In contrast, PD-RBD(-) microbiome exhibited a relatively dynamic microbiome change as the disease progressed. In early-stage PD-RBD(+), Escherichia and Akkermansia, associated with pathogenic biofilm formation and host mucin degradation, respectively, were enriched, which was supported by functional analysis. We discovered that genes of the UDP-GlcNAc synthesis/recycling pathway negatively correlated with biofilm formation; this finding was further validated in a separate cohort. Furthermore, fiber intake-associated taxa were decreased in early-stage PD-RBD(+) and the biased mucin-degrading capacity of CAZyme compared to fiber degradation. CONCLUSION: We determined that the gut microbiome dynamics in patients with PD according to the disease progression depend on the presence of premotor RBD. Notably, early-stage PD-RBD(+) demonstrated distinct gut microbial characteristics, potentially contributing to exacerbation of PD pathophysiology. This outcome may contribute to the development of new therapeutic strategies targeting the gut microbiome in PD. Video Abstract. |
| **Date** | 2025 Apr 30 |
| **Language** | eng |
| **Rights** | © 2025. The Author(s). |
| **Extra** | Place: England PMID: 40307949 PMCID: PMC12042535 |
| **Volume** | 13 |
| **Pages** | 108 |
| **Publication** | Microbiome |
| **DOI** | [10.1186/s40168-025-02095-w](http://doi.org/10.1186/s40168-025-02095-w) |
| **Issue** | 1 |
| **Journal Abbr** | Microbiome |
| **ISSN** | 2049-2618 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/11/2025, 2:32:25 PM |

### Tags:

* + Aged
  + Female
  + Humans
  + Male
  + Middle Aged
  + Disease Progression
  + Parkinson’s disease
  + Feces/microbiology
  + RNA, Ribosomal, 16S/genetics
  + Microbiome
  + \*Bacteria/classification/genetics/isolation & purification
  + \*Gastrointestinal Microbiome/genetics
  + \*Parkinson Disease/microbiology/complications
  + \*REM Sleep Behavior Disorder/microbiology
  + Biofilm
  + Carbohydrate-active enzymes
  + Rapid eye movement sleep behavior disorders

## Distribution of muscarinic acetylcholine receptor subtypes in the murine small intestine.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Eleanor D. Muise |
| **Author** | Neeru Gandotra |
| **Author** | John J. Tackett |
| **Author** | Michaela C. Bamdad |
| **Author** | Robert A. Cowles |
| **Abstract** | AIMS: Serotonin stimulates enterocyte turnover in the small intestine and studies suggest this is mediated by neuronal signaling via a cholinergic pathway. Distribution of the five known muscarinic receptor subtypes (mAChRs) in the small intestine has not been fully studied, and their role in intestinal growth is unknown. We hypothesized that mAChRs have distinct anatomic distributions within the bowel, and that mAChRs present within intestinal crypts mediate the effects of acetylcholine on the small intestinal mucosa. MAIN METHODS: Small intestine from male C57BL/6 mice ages 2, 4, 6, and 8weeks were harvested. RNA was isolated and cDNA synthesized for PCR-amplification of subtype specific mAChRs. Ileum was fixed with Nakane, embedded in epon, and immunofluorescence microscopy performed using polyclonal antibodies specific to each mAChR1-5. KEY FINDINGS: All five mAChR subtypes were present in the mouse duodenum, jejunum, and ileum at all ages by RT-PCR. Immunofluorescence microscopy suggested the presence of mAChR1-5 in association with mature enterocytes along the villus and within the myenteric plexus. Only mAChR2 clearly localized to the crypt stem cell compartment, specifically co-localizing with Paneth cells at crypt bases. SIGNIFICANCE: Muscarinic receptors are widely distributed along the entire alimentary tract. mAChR2 appears to localize to the crypt stem cell compartment, suggesting it is a plausible regulator of stem cell activity. The location of mAChR2 to the crypt makes it a potential therapeutic target for treatment of intestinal disease such as short bowel syndrome. The exact cellular location and action of each mAChR requires further study. |
| **Date** | 2017 Jan 15 |
| **Language** | eng |
| **Rights** | Copyright © 2016 Elsevier Inc. All rights reserved. |
| **Extra** | Place: Netherlands PMID: 27866962 |
| **Volume** | 169 |
| **Pages** | 6-10 |
| **Publication** | Life sciences |
| **DOI** | [10.1016/j.lfs.2016.10.030](http://doi.org/10.1016/j.lfs.2016.10.030) |
| **Journal Abbr** | Life Sci |
| **ISSN** | 1879-0631 0024-3205 |
| **Date Added** | 6/11/2025, 2:32:27 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Male
  + Animals
  + Mice, Inbred C57BL
  + Enteric nervous system
  + Microscopy, Fluorescence
  + Fluorescent Antibody Technique
  + Intestinal crypt
  + Intestinal Mucosa/\*chemistry/cytology/growth & development/\*ultrastructure
  + Intestine, Small/\*chemistry/cytology/growth & development/\*ultrastructure
  + Muscarinic acetylcholine receptor
  + Paneth cell
  + Receptors, Muscarinic/\*analysis
  + Stem cell compartment
  + Stem Cells/chemistry/cytology

## Early-Life Stress Induced by Neonatal Maternal Separation Leads to Intestinal 5-HT Accumulation and Causes Intestinal Dysfunction.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Ding Yang |
| **Author** | Rulan Bai |
| **Author** | Chengzhong Li |
| **Author** | Yan Sun |
| **Author** | Hongyu Jing |
| **Author** | Zixu Wang |
| **Author** | Yaoxing Chen |
| **Author** | Yulan Dong |
| **Abstract** | BACKGROUND: The early childhood period is a critical development stage, and experiencing stress during this time may increase the risk of gastrointestinal disorders, including irritable bowel syndrome (IBS). Neonatal maternal separation (NMS) in rodent models has been shown to cause bowel dysfunctions similar to IBS, and 5-HT is considered to be a key regulator regulating intestinal function, but the precise underlying mechanisms remain unclear. RESULTS: We established a maternal separation stress mouse model to simulate early-life stress, exploring the expression patterns of 5-HT under chronic stress and its mechanisms affecting gut function. We observed a significant increase in 5-HT expression due to NMS, leading to disruptions in intestinal structure and function. However, inhibiting 5-HT reversed these effects, suggesting its potential as a therapeutic target. Furthermore, our research revealed that excess 5-HT in mice with early life stress increased intestinal neural network density and promoted excitatory motor neuron expression. Mechanistically, 5-HT activated the Wnt signaling pathway through the 5-HT(4) receptor, promoting neurogenesis within the intestinal nervous system. CONCLUSION: These findings shed light on the intricate changes induced by early life stress in the intestines, confirming the regulatory role of 5-HT in the enteric nervous system and providing potential insights for the development of novel therapies for gastrointestinal disorders. |
| **Date** | 2024 |
| **Language** | eng |
| **Rights** | © 2024 Yang et al. |
| **Extra** | Place: New Zealand PMID: 39588137 PMCID: PMC11586501 |
| **Volume** | 17 |
| **Pages** | 8945-8964 |
| **Publication** | Journal of inflammation research |
| **DOI** | [10.2147/JIR.S488290](http://doi.org/10.2147/JIR.S488290) |
| **Journal Abbr** | J Inflamm Res |
| **ISSN** | 1178-7031 |
| **Date Added** | 6/11/2025, 2:32:27 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + 5-HT
  + early-life stress
  + IBS
  + neurogenesis

## Effects of aged garlic extract on aging?related changes in gastrointestinal function and enteric nervous system cells.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Kensuke Ohishi |
| **Author** | Ahmed A. Rahman |
| **Author** | Takahiro Ohkura |
| **Author** | Alan J. Burns |
| **Author** | Allan M. Goldstein |
| **Author** | Ryo Hotta |
| **Abstract** | Dysmotility of the gastrointestinal (GI) tract is commonly seen in elderly individuals, where it causes significant morbidity and can lead to more severe conditions, including sarcopenia and frailty. Although the precise mechanisms underlying aging-related GI dysmotility are not fully understood, neuronal loss or degeneration in the enteric nervous system (ENS) may be involved. Aged garlic extract (AGE) has been shown to have several beneficial effects in the GI tract; however, it is not known whether AGE can improve GI motility in older animals. The aim of the present study was to examine the effects of AGE on the ENS and gut motility in older mice and elucidate potential mechanisms of action. An AGE-formulated diet was given to 18-month-old female mice for 2 weeks. Organ bath studies and cell culture demonstrated that AGE: i) Altered gut contractile activity; ii) enhanced viability of ENS cells; and iii) exhibited neuroprotective effects on the ENS via reduction in oxidative stress. These findings suggest that AGE could be used to develop novel dietary therapeutics for aging-related GI dysmotility by targeting the associated loss and damage of the ENS. |
| **Date** | 2025 May |
| **Language** | eng |
| **Rights** | Copyright: © 2025 Ohishi et al. |
| **Extra** | Place: Greece PMID: 40171138 PMCID: PMC11959352 |
| **Volume** | 29 |
| **Pages** | 103 |
| **Publication** | Experimental and therapeutic medicine |
| **DOI** | [10.3892/etm.2025.12853](http://doi.org/10.3892/etm.2025.12853) |
| **Issue** | 5 |
| **Journal Abbr** | Exp Ther Med |
| **ISSN** | 1792-1015 1792-0981 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + enteric nervous system
  + oxidative stress
  + aged garlic extract
  + aging
  + intestinal motility
  + neuronal nitric oxide synthase
  + neuroprotection

## Emerging epigenetic dynamics in gut-microglia brain axis: experimental and clinical implications for accelerated brain aging in schizophrenia.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Benneth Ben-Azu |
| **Author** | Elisabetta C. Del Re |
| **Author** | Jared VanderZwaag |
| **Author** | Micaël Carrier |
| **Author** | Matcheri Keshavan |
| **Author** | Mohammadparsa Khakpour |
| **Author** | Marie-Ève Tremblay |
| **Abstract** | Brain aging, which involves a progressive loss of neuronal functions, has been reported to be premature in probands affected by schizophrenia (SCZ). Evidence shows that SCZ and accelerated aging are linked to changes in epigenetic clocks. Recent cross-sectional magnetic resonance imaging analyses have uncovered reduced brain reserves and connectivity in patients with SCZ compared to typically aging individuals. These data may indicate early abnormalities of neuronal function following cyto-architectural alterations in SCZ. The current mechanistic knowledge on brain aging, epigenetic changes, and their neuropsychiatric disease association remains incomplete. With this review, we explore and summarize evidence that the dynamics of gut-resident bacteria can modulate molecular brain function and contribute to age-related neurodegenerative disorders. It is known that environmental factors such as mode of birth, dietary habits, stress, pollution, and infections can modulate the microbiota system to regulate intrinsic neuronal activity and brain reserves through the vagus nerve and enteric nervous system. Microbiota-derived molecules can trigger continuous activation of the microglial sensome, groups of receptors and proteins that permit microglia to remodel the brain neurochemistry based on complex environmental activities. This remodeling causes aberrant brain plasticity as early as fetal developmental stages, and after the onset of first-episode psychosis. In the central nervous system, microglia, the resident immune surveillance cells, are involved in neurogenesis, phagocytosis of synapses and neurological dysfunction. Here, we review recent emerging experimental and clinical evidence regarding the gut-brain microglia axis involvement in SCZ pathology and etiology, the hypothesis of brain reserve and accelerated aging induced by dietary habits, stress, pollution, infections, and other factors. We also include in our review the possibilities and consequences of gut dysbiosis activities on microglial function and dysfunction, together with the effects of antipsychotics on the gut microbiome: therapeutic and adverse effects, role of fecal microbiota transplant and psychobiotics on microglial sensomes, brain reserves and SCZ-derived accelerated aging. We end the review with suggestions that may be applicable to the clinical setting. For example, we propose that psychobiotics might contribute to antipsychotic-induced therapeutic benefits or adverse effects, as well as reduce the aging process through the gut-brain microglia axis. Overall, we hope that this review will help increase the understanding of SCZ pathogenesis as related to chronobiology and the gut microbiome, as well as reveal new concepts that will serve as novel treatment targets for SCZ. |
| **Date** | 2023 |
| **Language** | eng |
| **Rights** | Copyright © 2023 Ben-Azu, del Re, VanderZwaag, Carrier, Keshavan, Khakpour and Tremblay. |
| **Extra** | Place: Switzerland PMID: 37256150 PMCID: PMC10225712 |
| **Volume** | 17 |
| **Pages** | 1139357 |
| **Publication** | Frontiers in cellular neuroscience |
| **DOI** | [10.3389/fncel.2023.1139357](http://doi.org/10.3389/fncel.2023.1139357) |
| **Journal Abbr** | Front Cell Neurosci |
| **ISSN** | 1662-5102 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/11/2025, 2:32:25 PM |

### Tags:

* + microbiome
  + aging
  + dysbiosis
  + epigenetics
  + microglia
  + psychobiotics
  + schizophrenia
  + vagus nerve

## Emerging role of fecal microbiota therapy in the treatment of gastrointestinal and extra-gastrointestinal diseases.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | P. C. Konturek |
| **Author** | D. Haziri |
| **Author** | T. Brzozowski |
| **Author** | T. Hess |
| **Author** | S. Heyman |
| **Author** | S. Kwiecien |
| **Author** | S. J. Konturek |
| **Author** | J. Koziel |
| **Abstract** | In the recent decade our understanding of the role of the human gut microbiome has been revolutionized by advances in development of molecular methods. Approximately, up to 100 trillion (10(14)) microorganisms per human body colonize the intestinal tract making an additional acquired organ that provides many vital functions to the host. A healthy gut microbiome can be defined by the presence of the various classes of microbes that enhance metabolism, resistance to infection and inflammation, prevention against cancer and autoimmunity and that positively influence so called braingut axis. Diet represents one of the most important driving forces that besides environmental and genetic factors, can define and influence the microbial composition of the gut. Aging process due to different changes in gut physiology (i.e. gastric hypochlorhydria, motility disorders, use of drugs, degenerative changes in enteric nervous system) has a profound effect on the composition, diversity and functional features of gut microbiota. A perturbed aged gut microbiome has been associated with the increasing number of gastrointestinal (e.g. Clostridium difficile infection - CDI) and non-gastrointestinal diseases (metabolic syndrome, diabetes mellitus, fatty liver disease, atherosclerosis etc.). Fecal microbiota transplantation (FMT) is a highly effective method in the treatment of refractory CDI. FMT is the term used when stool is taken from a healthy individual and instilled during endoscopy (colonoscopy or enteroscopy) into a gut of the sick person to cure certain disease. FMT represents an effective therapy in patient with recurrent CDI and the effectiveness of FMT in the prevention of CDI recurrence had reached approx. 90%. There is also an increasing evidence that the manipulation of gut microbiota by FMT represents a promising therapeutic method in patients with inflammatory bowel disease and irritable bowel syndrome. There is also an increased interest in the role of FMT for the treatment of metabolic syndrome and obesity which collectively present the greatest health challenge in the developed world nowadays. Targeting of gut microbiota by FMT represents an exciting new frontier in the prevention and management of gastrointestinal and non-gastrointestinal diseases that awaits further studies in preclinical and clinical settings. |
| **Date** | 2015 Aug |
| **Language** | eng |
| **Extra** | Place: Poland PMID: 26348073 |
| **Volume** | 66 |
| **Pages** | 483-491 |
| **Publication** | Journal of physiology and pharmacology : an official journal of the Polish Physiological Society |
| **Issue** | 4 |
| **Journal Abbr** | J Physiol Pharmacol |
| **ISSN** | 1899-1505 0867-5910 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Animals
  + \*Gastrointestinal Microbiome
  + Feces/\*microbiology
  + Gastrointestinal Diseases/\*therapy

## Engineered liposomes targeting the gut-CNS Axis for comprehensive therapy of spinal cord injury.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Xue Wang |
| **Author** | Jin Wu |
| **Author** | Xinlong Liu |
| **Author** | Kaicheng Tang |
| **Author** | Liting Cheng |
| **Author** | Jie Li |
| **Author** | Yixuan Tang |
| **Author** | Xiangrong Song |
| **Author** | Xiaoyou Wang |
| **Author** | Chong Li |
| **Abstract** | Effective curative therapies for spinal cord injury (SCI), which is often accompanied by intestinal complications, are lacking. Potential therapeutic targets include astrocytes and their enteric nervous system counterpart, enteric glial cells (EGCs). Based on shared biomarkers and similar functions of both cell types, we designed an orally administered targeted delivery system in which the neuropeptide apamin, stabilized by sulfur replacement with selenium, was adopted as a targeting moiety, and the liposome surface was protected with a non-covalent cross-linked chitosan oligosaccharide lactate layer. The system effectively permeated through oral absorption barriers, targeted local EGCs and astrocytes after systemic circulation, allowing for comprehensive SCI therapy. Given the involvement of the gut-organ axis in a growing number of diseases, our research may shed light on new aspects of the oral administration route as a bypass for multiple interventions and targeted therapy. |
| **Date** | 2021 Mar 10 |
| **Language** | eng |
| **Rights** | Copyright © 2021 Elsevier B.V. All rights reserved. |
| **Extra** | Place: Netherlands PMID: 33485884 |
| **Volume** | 331 |
| **Pages** | 390-403 |
| **Publication** | Journal of controlled release : official journal of the Controlled Release Society |
| **DOI** | [10.1016/j.jconrel.2021.01.032](http://doi.org/10.1016/j.jconrel.2021.01.032) |
| **Journal Abbr** | J Control Release |
| **ISSN** | 1873-4995 0168-3659 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Neuroglia
  + \*Liposomes
  + \*Spinal Cord Injuries/drug therapy
  + Astrocytes
  + Enteric glial cells
  + Gut-CNS axis
  + Oral delivery
  + Spinal Cord
  + Spinal cord injury

## Enteric Glia and Brain Astroglia: Complex Communication in Health and Disease along the Gut-Brain Axis.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Vanessa D'Antongiovanni |
| **Author** | Carolina Pellegrini |
| **Author** | Luca Antonioli |
| **Author** | Chiara Ippolito |
| **Author** | Cristina Segnani |
| **Author** | Laura Benvenuti |
| **Author** | Antonio D'Amati |
| **Author** | Mariella Errede |
| **Author** | Daniela Virgintino |
| **Author** | Matteo Fornai |
| **Author** | Nunzia Bernardini |
| **Abstract** | Several studies have provided interesting evidence about the role of the bidirectional communication between the gut and brain in the onset and development of several pathologic conditions, including inflammatory bowel diseases (IBDs), neurodegenerative diseases, and related comorbidities. Indeed, patients with IBD can experience neurologic disorders, including depression and cognitive impairment, besides typical intestinal symptoms. In parallel, patients with neurodegenerative disease, such as Parkinson disease and Alzheimer disease, are often characterized by the occurrence of functional gastrointestinal disorders. In this context, enteric glial cells and brain astrocytes are emerging as pivotal players in the initiation/maintenance of neuroinflammatory responses, which appear to contribute to the alterations of intestinal and neurologic functions observed in patients with IBD and neurodegenerative disorders. The present review was conceived to provide a comprehensive and critical overview of the available knowledge on the morphologic, molecular, and functional changes occurring in the enteric glia and brain astroglia in IBDs and neurologic disorders. In addition, our intent is to identify whether such alterations could represent a common denominator involved in the onset of comorbidities associated with the aforementioned disorders. This might help to identify putative targets useful to develop novel pharmacologic approaches for the therapeutic management of such disturbances. |
| **Date** | 2024 Aug |
| **Language** | eng |
| **Extra** | Place: United States PMID: 37052336 |
| **Volume** | 30 |
| **Pages** | 493-510 |
| **Publication** | The Neuroscientist : a review journal bringing neurobiology, neurology and psychiatry |
| **DOI** | [10.1177/10738584231163460](http://doi.org/10.1177/10738584231163460) |
| **Issue** | 4 |
| **Journal Abbr** | Neuroscientist |
| **ISSN** | 1089-4098 1073-8584 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
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### Tags:

* + Humans
  + Animals
  + \*Brain-Gut Axis/physiology
  + gut-brain axis
  + IBD
  + enteric glial cells
  + Parkinson disease
  + \*Astrocytes/metabolism/physiology
  + \*Brain/physiopathology
  + \*Enteric Nervous System/physiopathology/physiology
  + \*Neuroglia/physiology/metabolism
  + Alzheimer disease
  + astrocytes
  + Inflammatory Bowel Diseases/physiopathology/pathology/metabolism
  + Neurodegenerative Diseases/physiopathology/pathology/metabolism

## Enteric Glia: A New Player in Abdominal Pain.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Wilmarie Morales-Soto |
| **Author** | Brian D. Gulbransen |
| **Abstract** | Chronic abdominal pain is the most common gastrointestinal issue and contributes to the pathophysiology of functional bowel disorders and inflammatory bowel disease. Current theories suggest that neuronal plasticity and broad alterations along the brain-gut axis contribute to the development of chronic abdominal pain, but the specific mechanisms involved in chronic abdominal pain remain incompletely understood. Accumulating evidence implicates glial cells in the development and maintenance of chronic pain. Astrocytes and microglia in the central nervous system and satellite glia in dorsal root ganglia contribute to chronic pain states through reactive gliosis, the modification of glial networks, and the synthesis and release of neuromodulators. In addition, new data suggest that enteric glia, a unique type of peripheral glia found within the enteric nervous system, have the potential to modify visceral perception through interactions with neurons and immune cells. Understanding these emerging roles of enteric glia is important to fully understand the mechanisms that drive chronic pain and to identify novel therapeutic targets. In this review, we discuss enteric glial cell signaling mechanisms that have the potential to influence chronic abdominal pain. |
| **Date** | 2019 |
| **Language** | eng |
| **Rights** | Copyright © 2019 The Authors. Published by Elsevier Inc. All rights reserved. |
| **Extra** | Place: United States PMID: 30739868 PMCID: PMC6369218 |
| **Volume** | 7 |
| **Pages** | 433-445 |
| **Publication** | Cellular and molecular gastroenterology and hepatology |
| **DOI** | [10.1016/j.jcmgh.2018.11.005](http://doi.org/10.1016/j.jcmgh.2018.11.005) |
| **Issue** | 2 |
| **Journal Abbr** | Cell Mol Gastroenterol Hepatol |
| **ISSN** | 2352-345X |
| **Date Added** | 6/11/2025, 2:32:23 PM |
| **Modified** | 6/11/2025, 2:32:23 PM |

### Tags:

* + Humans
  + Animals
  + Inflammation
  + Brain-Gut Axis
  + ENS
  + Enteric Nervous System/\*pathology
  + Abdominal Pain
  + Enteric Glia
  + Abdominal Pain/\*pathology
  + Chronic Pain
  + Chronic Pain/pathology
  + Glial Cells
  + Hyperalgesia/pathology
  + Neuroglia/\*pathology
  + Nociceptors/metabolism

## Enteric Glial Cells: A New Frontier in Neurogastroenterology and Clinical Target for Inflammatory Bowel Diseases.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Fernando Ochoa-Cortes |
| **Author** | Fabio Turco |
| **Author** | Andromeda Linan-Rico |
| **Author** | Suren Soghomonyan |
| **Author** | Emmett Whitaker |
| **Author** | Sven Wehner |
| **Author** | Rosario Cuomo |
| **Author** | Fievos L. Christofi |
| **Abstract** | The word "glia" is derived from the Greek word "γλoια," glue of the enteric nervous system, and for many years, enteric glial cells (EGCs) were believed to provide mainly structural support. However, EGCs as astrocytes in the central nervous system may serve a much more vital and active role in the enteric nervous system, and in homeostatic regulation of gastrointestinal functions. The emphasis of this review will be on emerging concepts supported by basic, translational, and/or clinical studies, implicating EGCs in neuron-to-glial (neuroglial) communication, motility, interactions with other cells in the gut microenvironment, infection, and inflammatory bowel diseases. The concept of the "reactive glial phenotype" is explored as it relates to inflammatory bowel diseases, bacterial and viral infections, postoperative ileus, functional gastrointestinal disorders, and motility disorders. The main theme of this review is that EGCs are emerging as a new frontier in neurogastroenterology and a potential therapeutic target. New technological innovations in neuroimaging techniques are facilitating progress in the field, and an update is provided on exciting new translational studies. Gaps in our knowledge are discussed for further research. Restoring normal EGC function may prove to be an efficient strategy to dampen inflammation. Probiotics, palmitoylethanolamide (peroxisome proliferator-activated receptor-α), interleukin-1 antagonists (anakinra), and interventions acting on nitric oxide, receptor for advanced glycation end products, S100B, or purinergic signaling pathways are relevant clinical targets on EGCs with therapeutic potential. |
| **Date** | 2016 Feb |
| **Language** | eng |
| **Extra** | Place: England PMID: 26689598 PMCID: PMC4718179 |
| **Volume** | 22 |
| **Pages** | 433-449 |
| **Publication** | Inflammatory bowel diseases |
| **DOI** | [10.1097/MIB.0000000000000667](http://doi.org/10.1097/MIB.0000000000000667) |
| **Issue** | 2 |
| **Journal Abbr** | Inflamm Bowel Dis |
| **ISSN** | 1536-4844 1078-0998 |
| **Date Added** | 6/11/2025, 2:32:23 PM |
| **Modified** | 6/11/2025, 2:32:23 PM |

### Tags:

* + Humans
  + Cell Communication
  + Prognosis
  + Signal Transduction
  + \*Cytoprotection
  + \*Gastroenterology
  + Enteric Nervous System/\*cytology
  + Inflammatory Bowel Diseases/\*prevention & control
  + Neuroglia/\*cytology

## Enteric Nervous System and Its Relationship with Neurological Diseases.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | María José Luesma |
| **Author** | Liberto López-Marco |
| **Author** | Marta Monzón |
| **Author** | Sonia Santander |
| **Abstract** | The enteric nervous system (ENS) is a fundamental component of the gastrointestinal system, composed of a vast network of neurons and glial cells. It operates autonomously but is interconnected with the central nervous system (CNS) through the vagus nerve. This communication, known as the gut-brain axis, influences the bidirectional communication between the brain and the gut. Background/Objectives: This study aimed to review neurological pathologies related to the ENS. Methods: To this end, a comprehensive literature search was conducted in the "PubMed" database. Articles available in "free format" were selected, applying the filters "Humans" and limiting the search to publications from the last ten years. Results: The ENS has been linked to various neurological diseases, from autism spectrum disorder to Parkinson's disease including neurological infection with the varicella zoster virus (VZV), even sharing pathologies with the CNS. This finding suggests that the ENS could serve as an early diagnostic marker or therapeutic target for neurological diseases. Gastrointestinal symptoms often precede CNS symptoms, and the ENS's accessibility aids in diagnosis and treatment. Parkinson's patients may show intestinal lesions up to twenty years before CNS symptoms, underscoring the potential for early diagnosis. However, challenges include developing standardized diagnostic protocols and the uneven distribution of dopaminergic neurons in the ENS. Continued research is needed to explore the ENS's potential in improving disease prognosis. Conclusions: The ENS is a promising area for early diagnosis and therapeutic development. Nevertheless, it is essential to continue research in this area, especially to gain a deeper understanding of its organization, function, and regenerative capacity. |
| **Date** | 2024 Sep 20 |
| **Language** | eng |
| **Extra** | Place: Switzerland PMID: 39337066 PMCID: PMC11433641 |
| **Volume** | 13 |
| **Publication** | Journal of clinical medicine |
| **DOI** | [10.3390/jcm13185579](http://doi.org/10.3390/jcm13185579) |
| **Issue** | 18 |
| **Journal Abbr** | J Clin Med |
| **ISSN** | 2077-0383 |
| **Date Added** | 6/11/2025, 2:32:23 PM |
| **Modified** | 6/11/2025, 2:32:23 PM |

### Tags:

* + enteric nervous system (ENS)
  + central nervous system (CNS)
  + gastrointestinal system
  + glial cells
  + neurological diseases
  + varicella zoster virus (VZV)

## Enteric nervous system dysfunction as a driver of central nervous system disorders: The Forgotten brain in neurological disease.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Orabi Hajjeh |
| **Author** | Islam Rajab |
| **Author** | Mohammad Bdair |
| **Author** | Sarah Saife |
| **Author** | Anwar Zahran |
| **Author** | Iyad Nazzal |
| **Author** | Mohammad Ibrahem AbuZahra |
| **Author** | Hammam Jallad |
| **Author** | Maram M. Abukhalil |
| **Author** | Mira Hallak |
| **Author** | Osama S. Al-Said |
| **Author** | Rama Al-Braik |
| **Author** | Zaid Sawaftah |
| **Author** | Fathi Milhem |
| **Author** | Omar Almur |
| **Author** | Sakeena Saife |
| **Author** | Mohammed Aburemaileh |
| **Author** | Anfal Abuhilal |
| **Abstract** | The Enteric Nervous System (ENS), often called the "second brain," is a complex network of neurons and glial cells within the gastrointestinal (GI) tract. It functions autonomously while maintaining close communication with the central nervous system (CNS) via the gut-brain axis (GBA). ENS dysfunction plays a crucial role in neurodegenerative and neurodevelopmental disorders, including Parkinson's disease, Alzheimer's disease, and autism spectrum disorder. Disruptions such as altered neurotransmission, gut microbiota imbalance, and neuroinflammation contribute to disease pathogenesis. The GBA enables bidirectional communication through the vagus nerve, gut hormones, immune signaling, and microbial metabolites, linking gut health to neurological function. ENS dysregulation is implicated in conditions like irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD), influencing systemic and CNS pathology through neuroinflammation and impaired barrier integrity. This review highlights emerging therapeutic strategies targeting ENS dysfunction, including prebiotics, probiotics, fecal microbiota transplantation (FMT), and vagus nerve stimulation, which offer novel ways to modulate gut-brain interactions. Unlike previous perspectives that view the ENS as a passive disease marker, this review repositions it as an active driver of neurological disorders. By integrating advances in ENS biomarkers, therapeutic targets, and GBA modulation, this article presents a paradigm shift-emphasizing ENS dysfunction as a fundamental mechanism in neurodegeneration and neurodevelopmental disorders. This perspective paves the way for innovative diagnostics, personalized gut-targeted therapies, and a deeper understanding of the ENS's role in brain health and disease. |
| **Date** | 2025 Apr 19 |
| **Language** | eng |
| **Rights** | Copyright © 2025 International Brain Research Organization (IBRO). Published by Elsevier Inc. All rights reserved. |
| **Extra** | Place: United States PMID: 40088964 |
| **Volume** | 572 |
| **Pages** | 232-247 |
| **Publication** | Neuroscience |
| **DOI** | [10.1016/j.neuroscience.2025.03.015](http://doi.org/10.1016/j.neuroscience.2025.03.015) |
| **Journal Abbr** | Neuroscience |
| **ISSN** | 1873-7544 0306-4522 |
| **Date Added** | 6/11/2025, 2:32:23 PM |
| **Modified** | 6/11/2025, 2:32:23 PM |

### Tags:

* + Humans
  + Animals
  + Enteric Nervous System
  + Microbiota
  + Gastrointestinal Microbiome/physiology
  + \*Brain/physiopathology
  + Neuroinflammation
  + \*Central Nervous System Diseases/physiopathology/therapy
  + \*Enteric Nervous System/physiopathology
  + Brain-Gut Axis/physiology
  + Gut-Brain Axis
  + Neurodegenerative diseases
  + Therapeutic targets
  + Vagus nerve stimulation

## Enteric nervous system manifestations of neurodegenerative disease.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Alcmène Chalazonitis |
| **Author** | Meenakshi Rao |
| **Abstract** | Neurological disorders cause gastrointestinal (GI) symptoms that are debilitating and markedly diminish quality of life in patients. The enteric nervous system (ENS), the intrinsic nervous system of the GI tract that is often referred to as "the second brain", shares many features with the central nervous system. The ENS plays an essential role in regulating many GI functions including motility and fluid secretion. Enteric neuronal degeneration could therefore be responsible for the GI symptoms commonly observed in neurological conditions. Here we describe the organization and functions of the ENS and then review the evidence for ENS involvement in two common neurodegenerative disorders, Parkinson's disease (PD) and Alzheimer's disease (AD). Data from patients as well as animal models suggest that PD affects distinct subsets of neurons and glia in the ENS, and that the ENS may participate in the pathogenesis of this disorder. While there has been great enthusiasm for the possibility of sampling the ENS for diagnosis or therapeutic monitoring of PD, further work is needed to determine which enteric neurons are most affected and how ENS function could be modulated to ameliorate GI symptoms in patients. Although AD is far more common than PD and AD patients also experience GI symptoms, understanding of ENS dysfunction in AD is in its infancy. Much work remains to be done in both of these fields to determine how the ENS contributes to and/or is altered by these disorders, and how to target the ENS for more effective treatment of GI comorbidities. |
| **Date** | 2018 Aug 15 |
| **Language** | eng |
| **Rights** | Copyright © 2018 Elsevier B.V. All rights reserved. |
| **Extra** | Place: Netherlands PMID: 29360466 PMCID: PMC6003851 |
| **Volume** | 1693 |
| **Pages** | 207-213 |
| **Publication** | Brain research |
| **DOI** | [10.1016/j.brainres.2018.01.011](http://doi.org/10.1016/j.brainres.2018.01.011) |
| **Issue** | Pt B |
| **Journal Abbr** | Brain Res |
| **ISSN** | 1872-6240 0006-8993 |
| **Date Added** | 6/11/2025, 2:32:23 PM |
| **Modified** | 6/11/2025, 2:32:23 PM |

### Tags:

* + Humans
  + Animals
  + Enteric nervous system
  + Parkinson’s disease
  + Enteric Nervous System/\*physiopathology
  + Alzheimer’s disease
  + Neurodegeneration
  + Gastrointestinal Tract/\*pathology
  + Neurodegenerative Diseases/\*pathology

## Enteric neuropathy and the vagus nerve: Therapeutic implications.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Bruno Bonaz |
| **Abstract** | Enteric neuropathies are characterized by abnormalities of gut innervation, which includes the enteric nervous system, inducing severe gut dysmotility among other dysfunctions. Most of the gastrointestinal tract is innervated by the vagus nerve, the efferent branches of which have close interconnections with the enteric nervous system and whose afferents are distributed throughout the different layers of the digestive wall. The vagus nerve is a key element of the autonomic nervous system, involved in the stress response, at the interface of the microbiota-gut-brain axis, has anti-inflammatory and prokinetic properties, modulates intestinal permeability, and has a significant capacity of plasticity and regeneration. Targeting these properties of the vagus nerve, with vagus nerve stimulation (or non-stimulation/ pharmacological methods), could be of interest in the therapeutic management of enteric neuropathies. |
| **Date** | 2024 Jun 14 |
| **Language** | eng |
| **Rights** | © 2024 The Author(s). Neurogastroenterology & Motility published by John Wiley & Sons Ltd. |
| **Extra** | Place: England PMID: 38873822 |
| **Pages** | e14842 |
| **Publication** | Neurogastroenterology and motility |
| **DOI** | [10.1111/nmo.14842](http://doi.org/10.1111/nmo.14842) |
| **Journal Abbr** | Neurogastroenterol Motil |
| **ISSN** | 1365-2982 1350-1925 |
| **Date Added** | 6/11/2025, 2:32:23 PM |
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### Tags:

* + microbiota
  + enteric nervous system
  + motility
  + vagus nerve stimulation
  + enteric neuropathies
  + vagus nerve
  + autonomic nervous system
  + intestinal permeability
  + neuroplasticity
  + stress

## Enteric neuroplasticity and dysmotility in inflammatory disease: key players and possible therapeutic targets.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Estelle T. Spear |
| **Author** | Gary M. Mawe |
| **Abstract** | Intestinal functions, including motility and secretion, are locally controlled by enteric neural networks housed within the wall of the gut. The fidelity of these functions depends on the precision of intercellular signaling among cellular elements, including enteric neurons, epithelial cells, immune cells, and glia, all of which are vulnerable to disruptive influences during inflammatory events. This review article describes current knowledge regarding inflammation-induced neuroplasticity along key elements of enteric neural circuits, what is known about the causes of these changes, and possible therapeutic targets for protecting and/or repairing the integrity of intrinsic enteric neurotransmission. Changes that have been detected in response to inflammation include increased epithelial serotonin availability, hyperexcitability of intrinsic primary afferent neurons, facilitation of synaptic activity among enteric neurons, and attenuated purinergic neuromuscular transmission. Dysfunctional propulsive motility has been detected in models of colitis, where causes include the changes described above, and in models of multiple sclerosis and other autoimmune conditions, where autoantibodies are thought to mediate dysmotility. Other cells implicated in inflammation-induced neuroplasticity include muscularis macrophages and enteric glia. Targeted treatments that are discussed include 5-hydroxytryptamine receptor 4 agonists, cyclooxygenase inhibitors, antioxidants, B cell depletion therapy, and activation of anti-inflammatory pathways. |
| **Date** | 2019 Dec 1 |
| **Language** | eng |
| **Extra** | Place: United States PMID: 31604034 PMCID: PMC6962496 |
| **Volume** | 317 |
| **Pages** | G853-G861 |
| **Publication** | American journal of physiology. Gastrointestinal and liver physiology |
| **DOI** | [10.1152/ajpgi.00206.2019](http://doi.org/10.1152/ajpgi.00206.2019) |
| **Issue** | 6 |
| **Journal Abbr** | Am J Physiol Gastrointest Liver Physiol |
| **ISSN** | 1522-1547 0193-1857 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Animals
  + enteric nervous system
  + glia
  + \*Enteric Nervous System/immunology/physiopathology
  + \*Inflammation/immunology/physiopathology/therapy
  + autoantibody
  + Cell Communication/\*physiology
  + gastrointestinal motility
  + Gastrointestinal Motility/\*immunology
  + macrophage
  + Nervous System Autoimmune Disease, Experimental
  + Neuronal Plasticity/\*immunology

## EphrinB2/ephB2 activation facilitates colonic synaptic potentiation and plasticity contributing to long-term visceral hypersensitivity in irritable bowel syndrome.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Lei Zhang |
| **Author** | Ruiyun Wang |
| **Author** | Yuhua Chen |
| **Author** | Pengcheng Yang |
| **Author** | Tao Bai |
| **Author** | Jun Song |
| **Author** | Xiaohua Hou |
| **Abstract** | AIMS: Sustained visceral hypersensitivity is a hallmark of irritable bowel syndrome (IBS) could be partially explained by enteric neural remodeling. Particularly, synaptic plasticity in the enteric nervous system, a form of enteric "memory", has been speculated as a participant in the pain maintenance in IBS. This study aimed to elucidate the role of ephrinB2/ephB2 in enteric synaptic plasticity and visceral pain in IBS. MATERIALS AND METHODS: EphrinB2/ephB2 expression and synaptic plasticity were assessed in colonic tissues from IBS patients, and rats induced by Trichinella spiralis infection and those treated with ephB2-Fc (an ephB2 receptor blocker) or ifenprodil (a selective NR2B antagonist). Furthermore, abdominal withdrawal reflex scores to colorectal distention and mesenteric afferent firing were assessed. EphrinB2-Fc(an ephB2 receptor activator) induced enteric synaptic plasticity was further evaluated in longitudinal muscle-myenteric plexus(LMMP) cultures and primary cultured myenteric neurons. KEY FINDINGS: EphrinB2/ephB2 was specifically expressed in colonic nerves and upregulated in IBS patients and rats, which was correlated with pain severity. The functional synaptic plasticity, visceral sensitivity to colorectal distention and colonic mesenteric afferent activity to mechanical and chemical stimulus were enhanced in IBS rats, and were blocked by ephB2-Fc or ifenprodil treatment. EphrinB2-Fc promoted the phosphorylation of NR2B in IBS rats and LMMP cultures, and could mediate sustained neural activation via increased [Ca(2+)](i) and raised expression of synaptic plasticity-related early immediate genes, including c-fos and arc. SIGNIFICANCE: EphrinB2/ephB2 facilitated NR2B-mediated synaptic potentiation in the enteric nervous system that may be a novel explanation and potential therapeutic target for sustained pain hypersensitivity in IBS. |
| **Date** | 2022 Apr 15 |
| **Language** | eng |
| **Rights** | Copyright © 2022. Published by Elsevier Inc. |
| **Extra** | Place: Netherlands PMID: 35183555 |
| **Volume** | 295 |
| **Pages** | 120419 |
| **Publication** | Life sciences |
| **DOI** | [10.1016/j.lfs.2022.120419](http://doi.org/10.1016/j.lfs.2022.120419) |
| **Journal Abbr** | Life Sci |
| **ISSN** | 1879-0631 0024-3205 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/11/2025, 2:32:25 PM |

### Tags:

* + Adult
  + Female
  + Humans
  + Male
  + Middle Aged
  + Animals
  + Rats
  + Rats, Sprague-Dawley
  + China
  + Enteric nervous system
  + Pain Measurement
  + Irritable bowel syndrome
  + Colon/metabolism
  + Enteric Nervous System/physiology
  + Ephrin-B2/\*metabolism/physiology
  + Ephrinb2/ephB2
  + Hyperalgesia/metabolism
  + Irritable Bowel Syndrome/metabolism/\*physiopathology
  + Neuronal Plasticity/physiology
  + Receptor, EphB2/\*metabolism/physiology
  + Synaptic plasticity
  + Synaptic Potentials/physiology
  + Visceral hypersensitivity
  + Visceral Pain/metabolism

## Fecal Calprotectin as a Marker of the Gut Immune System Activation Is Elevated in Parkinson's Disease.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Agata Mulak |
| **Author** | Magdalena Koszewicz |
| **Author** | Magdalena Panek-Jeziorna |
| **Author** | Ewa Koziorowska-Gawron |
| **Author** | Sławomir Budrewicz |
| **Abstract** | INTRODUCTION: Alpha-synucleinopathy constituting a characteristic feature of Parkinson's disease (PD) occurs at all levels of the brain-gut axis including the enteric nervous system (ENS). Lesions in the ENS may be connected with gut inflammation, increased intestinal permeability and dysmotility contributing to the pathogenesis of PD and its gastrointestinal manifestations. AIMS: To evaluate fecal calprotectin and zonulin as biomarkers of gut inflammation and intestinal barrier dysfunction in PD patients. METHODS: Quantitative evaluation of fecal biomarkers was performed by ELISA tests in 35 PD patients and 20 healthy controls. Additionally, patients filled out a short questionnaire concerning gastrointestinal symptoms. RESULTS: Median fecal calprotectin level (μg/g) was significantly higher in PD patients compared to the controls: 54.5 (29.0-137.9) vs. 9.7 (5.2-23.3), p < 0.0001. Applying age-related reference ranges, the increased fecal calprotectin level was found in 43% of PD patients and in none of the control subjects (p < 0.001). No correlation between fecal calprotectin level and PD duration was observed. No statistically significant difference between the groups regarding zonulin level was found. The most frequent bowel symptoms reported by PD patients included constipation (69% of subjects), feeling of incomplete evacuation (51%), bloating (51%), abdominal pain (20%), and alternating bowel movement pattern (17%). CONCLUSION: The evaluation of fecal calprotectin level may be a useful tool to detect the signs of gut immune system activation present in a remarkable number of PD patients, also in the early stage of the disease. Calprotectin may constitute a critical link between amyloid formation and neuroinflammatory cascades serving as a prospective diagnostic and therapeutic target. |
| **Date** | 2019 |
| **Language** | eng |
| **Rights** | Copyright © 2019 Mulak, Koszewicz, Panek-Jeziorna, Koziorowska-Gawron and Budrewicz. |
| **Extra** | Place: Switzerland PMID: 31611762 PMCID: PMC6776883 |
| **Volume** | 13 |
| **Pages** | 992 |
| **Publication** | Frontiers in neuroscience |
| **DOI** | [10.3389/fnins.2019.00992](http://doi.org/10.3389/fnins.2019.00992) |
| **Journal Abbr** | Front Neurosci |
| **ISSN** | 1662-4548 1662-453X |
| **Date Added** | 6/11/2025, 2:32:27 PM |
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### Tags:

* + Parkinson’s disease
  + brain-gut axis
  + intestinal inflammation
  + fecal calprotectin
  + inflammatory marker

## Functional roles of the microbiota-gut-brain axis in Alzheimer's disease: Implications of gut microbiota-targeted therapy.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Si-Ran Zhong |
| **Author** | Qi Kuang |
| **Author** | Fan Zhang |
| **Author** | Ben Chen |
| **Author** | Zhen-Guo Zhong |
| **Abstract** | Increasing scientific evidence demonstrates that the gut microbiota influences normal physiological homeostasis and contributes to pathogenesis, ranging from obesity to neurodegenerative diseases, such as Alzheimer's disease (AD). Gut microbiota can interact with the central nervous system (CNS) through the microbiota-gut-brain axis. The interaction is mediated by microbial secretions, metabolic interventions, and neural stimulation. Here, we review and summarize the regulatory pathways (immune, neural, neuroendocrine, or metabolic systems) in the microbiota-gut-brain axis in AD pathogenesis. Besides, we highlight the significant roles of the intestinal epithelial barrier and blood-brain barrier (BBB) in the microbiota-gut-brain axis. During the progression of AD, there is a gradual shift in the gut microbiota and host co-metabolic relationship, leading to gut dysbiosis, and the imbalance of microbial secretions and metabolites, such as lipopolysaccharides (LPS) and short-chain fatty acids (SCFAs). These products may affect the CNS metabolic state and immune balance through the microbiota-gut-brain axis. Further, we summarize the potential microbiota-gut-brain axis-targeted therapy including carbohydrates, probiotics, dietary measures, and propose new strategies toward the development of anti-AD drugs. Taken together, the data in this review suggest that remodeling the gut microbiota may present a tractable strategy in the management and development of new therapeutics against AD and other neurodegenerative diseases. |
| **Date** | 2021 Jan 1 |
| **Language** | eng |
| **Rights** | © 2021 Si-Ran Zhong et al., published by De Gruyter. |
| **Extra** | Place: Germany PMID: 35070442 PMCID: PMC8724360 |
| **Volume** | 12 |
| **Pages** | 581-600 |
| **Publication** | Translational neuroscience |
| **DOI** | [10.1515/tnsci-2020-0206](http://doi.org/10.1515/tnsci-2020-0206) |
| **Issue** | 1 |
| **Journal Abbr** | Transl Neurosci |
| **ISSN** | 2081-3856 2081-6936 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/11/2025, 2:32:25 PM |

### Tags:

* + enteric nervous system
  + gut microbiota
  + microbiota-gut-brain axis
  + short-chain fatty acids
  + lipopolysaccharides
  + Alzheimer’s disease
  + Bacteroides
  + blood–brain barrier
  + microbial amyloid
  + oligosaccharides

## G protein-coupled receptor trafficking and signaling: new insights into the enteric nervous system.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Simona E. Carbone |
| **Author** | Nicholas A. Veldhuis |
| **Author** | Arisbel B. Gondin |
| **Author** | Daniel P. Poole |
| **Abstract** | G protein-coupled receptors (GPCRs) are essential for the neurogenic control of gastrointestinal (GI) function and are important and emerging therapeutic targets in the gut. Detailed knowledge of both the distribution and functional expression of GPCRs in the enteric nervous system (ENS) is critical toward advancing our understanding of how these receptors contribute to GI function during physiological and pathophysiological states. Equally important, but less well defined, is the complex relationship between receptor expression, ligand binding, signaling, and trafficking within enteric neurons. Neuronal GPCRs are internalized following exposure to agonists and under pathological conditions, such as intestinal inflammation. However, the relationship between the intracellular distribution of GPCRs and their signaling outputs in this setting remains a "black box". This review will briefly summarize current knowledge of agonist-evoked GPCR trafficking and location-specific signaling in the ENS and identifies key areas where future research could be focused. Greater understanding of the cellular and molecular mechanisms involved in regulating GPCR signaling in the ENS will provide new insights into GI function and may open novel avenues for therapeutic targeting of GPCRs for the treatment of digestive disorders. |
| **Date** | 2019 Apr 1 |
| **Language** | eng |
| **Extra** | Place: United States PMID: 30702900 |
| **Volume** | 316 |
| **Pages** | G446-G452 |
| **Publication** | American journal of physiology. Gastrointestinal and liver physiology |
| **DOI** | [10.1152/ajpgi.00406.2018](http://doi.org/10.1152/ajpgi.00406.2018) |
| **Issue** | 4 |
| **Journal Abbr** | Am J Physiol Gastrointest Liver Physiol |
| **ISSN** | 1522-1547 0193-1857 |
| **Date Added** | 6/11/2025, 2:32:23 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Animals
  + Drug Discovery
  + Signal Transduction
  + enteric nervous system
  + endocytosis
  + Receptors, G-Protein-Coupled/\*metabolism
  + \*Protein Transport/drug effects/physiology
  + Enteric Nervous System/\*physiology
  + Enterocytes/\*physiology
  + GPCR, location-specific signaling
  + receptor trafficking

## G Protein-Coupled Receptor Trafficking and Signalling in the Enteric Nervous System: The Past, Present and Future.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Daniel P. Poole |
| **Author** | Nigel W. Bunnett |
| **Abstract** | G protein-coupled receptors (GPCRs) enable cells to detect and respond to changes in their extracellular environment. With over 800 members, the GPCR family includes receptors for a diverse range of agonists including olfactants, neurotransmitters and hormones. Importantly, GPCRs represent a major therapeutic target, with approximately 50 % of all current drugs acting at some aspect of GPCR signalling (Audet and Bouvier 2008). GPCRs are widely expressed by all cell types in the gastrointestinal (GI) tract and are major regulators of every aspect of gut function. Many GPCRs are internalised upon activation, and this represents one of the mechanisms through which G protein-signalling is terminated. The latency between the endocytosis of GPCRs and their recycling and resensitization is a major determinant of the cell's ability to respond to subsequent exposure to agonists. |
| **Date** | 2016 |
| **Language** | eng |
| **Extra** | Place: United States PMID: 27379642 PMCID: PMC11450630 |
| **Volume** | 891 |
| **Pages** | 145-152 |
| **Publication** | Advances in experimental medicine and biology |
| **DOI** | [10.1007/978-3-319-27592-5\_14](http://doi.org/10.1007/978-3-319-27592-5_14) |
| **Journal Abbr** | Adv Exp Med Biol |
| **ISSN** | 0065-2598 2214-8019 |
| **Date Added** | 6/11/2025, 2:32:23 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Animals
  + Protein Transport
  + Enteric Nervous System/\*metabolism
  + GTP-Binding Proteins/\*metabolism
  + Receptors, G-Protein-Coupled/\*metabolism
  + Signal Transduction/\*physiology

## Gastrointestinal Dysfunction in Parkinson's Disease: Current and Potential Therapeutics.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Myat Noe Han |
| **Author** | David I. Finkelstein |
| **Author** | Rachel M. McQuade |
| **Author** | Shanti Diwakarla |
| **Abstract** | Abnormalities in the gastrointestinal (GI) tract of Parkinson's disease (PD) sufferers were first reported over 200 years ago; however, the extent and role of GI dysfunction in PD disease progression is still unknown. GI dysfunctions, including dysphagia, gastroparesis, and constipation, are amongst the most prevalent non-motor symptoms in PD. These symptoms not only impact patient quality of life, but also complicate disease management. Conventional treatment pathways for GI dysfunctions (i.e., constipation), such as increasing fibre and fluid intake, and the use of over-the-counter laxatives, are generally ineffective in PD patients, and approved compounds such as guanylate cyclase C agonists and selective 5-hyroxytryptamine 4 receptor agonists have demonstrated limited efficacy. Thus, identification of potential targets for novel therapies to alleviate PD-induced GI dysfunctions are essential to improve clinical outcomes and quality of life in people with PD. Unlike the central nervous system (CNS), where PD pathology and the mechanisms involved in CNS damage are relatively well characterised, the effect of PD at the cellular and tissue level in the enteric nervous system (ENS) remains unclear, making it difficult to alleviate or reverse GI symptoms. However, the resurgence of interest in understanding how the GI tract is involved in various disease states, such as PD, has resulted in the identification of novel therapeutic avenues. This review focuses on common PD-related GI symptoms, and summarizes the current treatments available and their limitations. We propose that by targeting the intestinal barrier, ENS, and/or the gut microbiome, may prove successful in alleviating PD-related GI symptoms, and discuss emerging therapies and potential drugs that could be repurposed to target these areas. |
| **Date** | 2022 Jan 21 |
| **Language** | eng |
| **Extra** | Place: Switzerland PMID: 35207632 PMCID: PMC8875119 |
| **Volume** | 12 |
| **Publication** | Journal of personalized medicine |
| **DOI** | [10.3390/jpm12020144](http://doi.org/10.3390/jpm12020144) |
| **Issue** | 2 |
| **Journal Abbr** | J Pers Med |
| **ISSN** | 2075-4426 |
| **Date Added** | 6/11/2025, 2:32:23 PM |
| **Modified** | 6/11/2025, 2:32:23 PM |

### Tags:

* + enteric nervous system
  + Parkinson’s disease
  + enteric neuropathy
  + gastrointestinal dysfunction
  + constipation
  + dysphagia
  + gastroparesis
  + unmet therapeutic need

## Gastrointestinal neuromuscular apparatus: An underestimated target of gut microbiota.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Michele Pier Luca Guarino |
| **Author** | Michele Cicala |
| **Author** | Lorenza Putignani |
| **Author** | Carola Severi |
| **Abstract** | Over the last few years, the importance of the resident intestinal microbiota in the pathogenesis of several gastro-intestinal diseases has been largely investigated. Growing evidence suggest that microbiota can influence gastro-intestinal motility. The current working hypothesis is that dysbiosis-driven mucosal alterations induce the production of several inflammatory/immune mediators which affect gut neuro-muscular functions. Besides these indirect mucosal-mediated effects, the present review highlights that recent evidence suggests that microbiota can directly affect enteric nerves and smooth muscle cells functions through its metabolic products or bacterial molecular components translocated from the intestinal lumen. Toll-like receptors, the bacterial recognition receptors, are expressed both on enteric nerves and smooth muscle and are emerging as potential mediators between microbiota and the enteric neuromuscular apparatus. Furthermore, the ongoing studies on probiotics support the hypothesis that the neuromuscular apparatus may represent a target of intervention, thus opening new physiopathological and therapeutic scenarios. |
| **Date** | 2016 Dec 7 |
| **Language** | eng |
| **Extra** | Place: United States PMID: 28018095 PMCID: PMC5143755 |
| **Volume** | 22 |
| **Pages** | 9871-9879 |
| **Publication** | World journal of gastroenterology |
| **DOI** | [10.3748/wjg.v22.i45.9871](http://doi.org/10.3748/wjg.v22.i45.9871) |
| **Issue** | 45 |
| **Journal Abbr** | World J Gastroenterol |
| **ISSN** | 2219-2840 1007-9327 |
| **Date Added** | 6/11/2025, 2:32:23 PM |
| **Modified** | 6/11/2025, 2:32:23 PM |

### Tags:

* + Humans
  + Enteric nervous system
  + Gastrointestinal Microbiome/\*physiology
  + Gastrointestinal Motility/\*physiology
  + Gastrointestinal motility
  + Microbiota
  + Irritable bowel syndrome
  + Smooth muscle
  + Probiotics
  + Dysbiosis/metabolism/\*physiopathology
  + Enteric Nervous System/\*physiology/physiopathology
  + Gastrointestinal Tract/metabolism/physiology/physiopathology
  + Muscle, Smooth/metabolism/\*physiology/physiopathology
  + Toll-Like Receptors/metabolism

## Gastrointestinal Physiology and Function.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Beverley Greenwood-Van Meerveld |
| **Author** | Anthony C. Johnson |
| **Author** | David Grundy |
| **Abstract** | The gastrointestinal (GI) system is responsible for the digestion and absorption of ingested food and liquids. Due to the complexity of the GI tract and the substantial volume of material that could be covered under the scope of GI physiology, this chapter briefly reviews the overall function of the GI tract, and discusses the major factors affecting GI physiology and function, including the intestinal microbiota, chronic stress, inflammation, and aging with a focus on the neural regulation of the GI tract and an emphasis on basic brain-gut interactions that serve to modulate the GI tract. GI diseases refer to diseases of the esophagus, stomach, small intestine, colon, and rectum. The major symptoms of common GI disorders include recurrent abdominal pain and bloating, heartburn, indigestion/dyspepsia, nausea and vomiting, diarrhea, and constipation. GI disorders rank among the most prevalent disorders, with the most common including esophageal and swallowing disorders, gastric and peptic ulcer disease, gastroparesis or delayed gastric emptying, irritable bowel syndrome (IBS), and inflammatory bowel disease (IBD). Many GI disorders are difficult to diagnose and their symptoms are not effectively managed. Thus, basic research is required to drive the development of novel therapeutics which are urgently needed. One approach is to enhance our understanding of gut physiology and pathophysiology especially as it relates to gut-brain communications since they have clinical relevance to a number of GI complaints and represent a therapeutic target for the treatment of conditions including inflammatory diseases of the GI tract such as IBD and functional gut disorders such as IBS. |
| **Date** | 2017 |
| **Language** | eng |
| **Extra** | Place: Germany PMID: 28176047 |
| **Volume** | 239 |
| **Pages** | 1-16 |
| **Publication** | Handbook of experimental pharmacology |
| **DOI** | [10.1007/164\_2016\_118](http://doi.org/10.1007/164_2016_118) |
| **Journal Abbr** | Handb Exp Pharmacol |
| **ISSN** | 0171-2004 |
| **Date Added** | 6/11/2025, 2:32:22 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Animals
  + Inflammation
  + Colon
  + Enteric nervous system (ENS)
  + Gastrointestinal Motility
  + Stress
  + Absorption
  + Barrier function
  + Central nervous system (CNS)
  + Constipation
  + Diarrhea
  + Digestion
  + Enteric Nervous System/\*physiopathology
  + Epithelial barrier
  + Gastric Juice/metabolism
  + Gastrointestinal Absorption
  + Gastrointestinal Diseases/immunology/\*physiopathology
  + Gastrointestinal Tract/immunology/innervation/metabolism/physiopathology
  + Gut microbiome
  + Inflammatory bowel disease (IBD)
  + Intestinal permeability
  + Intestinal Secretions/metabolism
  + Irritable bowel syndrome (IBS)
  + Mucosa
  + Secretion
  + Small intestine
  + Smooth muscle
  + Visceral pain

## Gastrointestinal problems, mechanisms and possible therapeutic directions in Gulf war illness: a mini review.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Diana A. Kimono |
| **Abstract** | By its nature, Gulf war illness (GWI) is multisymptomatic and affects several organ systems in the body. Along with other symptoms, veterans who suffer from GWI commonly report chronic gastrointestinal issues such as constipation, pain, indigestion, etc. However, until recently, most attention has been focused on neurological disturbances such as cognitive impairments, chronic fatigue, and chronic pain among affected veterans. With such high prevalence of gastrointestinal problems among Gulf war (GW) veterans, it is surprising that there is little research to investigate the mechanisms behind these issues. This review summarizes all the available works on the mechanisms behind gastrointestinal problems in GWI that have been published to date in various databases. Generally, these studies, which were done in rodent models, in vitro and human cohorts propose that an altered microbiome, a reactive enteric nervous system or a leaky gut among other possible mechanisms are the major drivers of gastrointestinal problems reported in GWI. This review aims to draw attention to the gastrointestinal tract as an important player in GWI disease pathology and a potential therapeutic target. |
| **Date** | 2021 Sep 9 |
| **Language** | eng |
| **Rights** | © 2021. The Author(s). |
| **Extra** | Place: England PMID: 34503577 PMCID: PMC8431926 |
| **Volume** | 8 |
| **Pages** | 50 |
| **Publication** | Military Medical Research |
| **DOI** | [10.1186/s40779-021-00341-4](http://doi.org/10.1186/s40779-021-00341-4) |
| **Issue** | 1 |
| **Journal Abbr** | Mil Med Res |
| **ISSN** | 2054-9369 2095-7467 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/11/2025, 2:32:24 PM |

### Tags:

* + Humans
  + Enteric nervous system
  + Microbiome
  + GI
  + Enteric Nervous System/drug effects/physiopathology
  + Gastrointestinal
  + Gastrointestinal Diseases/\*etiology/physiopathology
  + Gastrointestinal Microbiome/immunology/physiology
  + Gulf war illness
  + GWI
  + Leaky gut
  + Persian Gulf Syndrome/\*complications/physiopathology
  + Veterans/statistics & numerical data

## Genome-Wide Association Studies of Diarrhea Frequency and Duration in the First Year of Life in Bangladeshi Infants.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Rebecca M. Munday |
| **Author** | Rashidul Haque |
| **Author** | Genevieve L. Wojcik |
| **Author** | Poonum Korpe |
| **Author** | Uma Nayak |
| **Author** | Beth D. Kirkpatrick |
| **Author** | William A. Jr Petri |
| **Author** | Priya Duggal |
| **Abstract** | BACKGROUND: Diarrhea is the second leading cause of death in children under 5 years old worldwide. Known diarrhea risk factors include sanitation, water sources, and pathogens but do not fully explain the heterogeneity in frequency and duration of diarrhea in young children. We evaluated the role of host genetics in diarrhea. METHODS: Using 3 well-characterized birth cohorts from an impoverished area of Dhaka, Bangladesh, we compared infants with no diarrhea in the first year of life to those with an abundance, measured by either frequency or duration. We performed a genome-wide association analysis for each cohort under an additive model and then meta-analyzed across the studies. RESULTS: For diarrhea frequency, we identified 2 genome-wide significant loci associated with not having any diarrhea, on chromosome 21 within the noncoding RNA AP000959 (C allele odds ratio [OR] = 0.31, P = 4.01 × 10-8), and on chromosome 8 within SAMD12 (T allele OR = 0.35, P = 4.74 × 10-7). For duration of diarrhea, we identified 2 loci associated with no diarrhea, including the same locus on chromosome 21 (C allele OR = 0.31, P = 1.59 × 10-8) and another locus on chromosome 17 near WSCD1 (C allele OR = 0.35, P = 1.09 × 10-7). CONCLUSIONS: These loci are in or near genes involved in enteric nervous system development and intestinal inflammation and may be potential targets for diarrhea therapeutics. |
| **Date** | 2023 Oct 18 |
| **Language** | eng |
| **Rights** | © The Author(s) 2023. Published by Oxford University Press on behalf of Infectious Diseases Society of America. All rights reserved. For permissions, please e-mail: journals.permissions@oup.com. |
| **Extra** | Place: United States PMID: 36967705 PMCID: PMC11007397 |
| **Volume** | 228 |
| **Pages** | 979-989 |
| **Publication** | The Journal of infectious diseases |
| **DOI** | [10.1093/infdis/jiad068](http://doi.org/10.1093/infdis/jiad068) |
| **Issue** | 8 |
| **Journal Abbr** | J Infect Dis |
| **ISSN** | 1537-6613 0022-1899 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Infant
  + Child
  + Alleles
  + \*Diarrhea/epidemiology/genetics
  + \*Genome-Wide Association Study
  + association
  + Bangladesh/epidemiology
  + Child, Preschool
  + diarrhea
  + enterics
  + GWAS
  + host genetics
  + malnutrition
  + Risk Factors

## Ghrelin and Motilin Control Systems in GI Physiology and Therapeutics.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Gareth J. Sanger |
| **Author** | John Broad |
| **Author** | Brid Callaghan |
| **Author** | John B. Furness |
| **Abstract** | Ghrelin and motilin are released from gastrointestinal endocrine cells during hunger, to act through G protein-coupled receptors that have closely related amino acid sequences. The actions of ghrelin are more complex than motilin because ghrelin also exists outside the GI tract, it is processed to des-acyl ghrelin which has activity, ghrelin can exist in truncated forms and retain activity, the ghrelin receptor can have constitutive activity and is subject to biased agonism and finally additional ghrelin-like and des-acyl ghrelin receptors are proposed. Both ghrelin and motilin can stimulate gastric emptying, acting via different pathways, perhaps influenced by biased agonism at the receptors, but research is revealing additional pathways of activity. For example, it is becoming apparent that reduction of nausea may be a key therapeutic target for ghrelin receptor agonists and perhaps for compounds that modulate the constitutive activity of the ghrelin receptor. Reduction of nausea may be the mechanism through which gastroparesis symptoms are reduced. Intriguingly, a potential ability of motilin to influence nausea is also becoming apparent. Ghrelin interacts with digestive function through its effects on appetite, and ghrelin antagonists may have a place in treating Prader-Willi syndrome. Unlike motilin, ghrelin receptor agonists also have the potential to treat constipation by acting at the lumbosacral defecation centres. In conclusion, agonists of both ghrelin and motilin receptors hold potential as treatments for specific subsets of digestive system disorders. |
| **Date** | 2017 |
| **Language** | eng |
| **Extra** | Place: Germany PMID: 28035532 |
| **Volume** | 239 |
| **Pages** | 379-416 |
| **Publication** | Handbook of experimental pharmacology |
| **DOI** | [10.1007/164\_2016\_104](http://doi.org/10.1007/164_2016_104) |
| **Journal Abbr** | Handb Exp Pharmacol |
| **ISSN** | 0171-2004 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/11/2025, 2:32:25 PM |

### Tags:

* + Humans
  + Animals
  + Colon
  + Nausea
  + Stomach
  + Constipation
  + Gastroparesis
  + Ghrelin
  + Gastrointestinal tract
  + Gastrointestinal Agents/therapeutic use
  + \*Gastrointestinal Motility/drug effects
  + \*Signal Transduction/drug effects
  + Gastrointestinal Tract/drug effects/innervation/\*metabolism/physiopathology
  + Appetite
  + Appetite Regulation
  + Des-acyl ghrelin
  + Enteric Nervous System/metabolism/physiopathology
  + Gastrointestinal Diseases/drug therapy/\*metabolism/physiopathology
  + Ghrelin/\*metabolism
  + Human
  + Motilin
  + Motilin/\*metabolism
  + Neural Pathways/metabolism
  + Obestatin
  + Prader-Willi syndrome
  + Receptor
  + Receptors, Gastrointestinal Hormone/agonists/metabolism
  + Receptors, Ghrelin/agonists/metabolism
  + Receptors, Neuropeptide/agonists/metabolism

## Glial A(2B) Adenosine Receptors Modulate Abnormal Tachykininergic Responses and Prevent Enteric Inflammation Associated with High Fat Diet-Induced Obesity.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Vanessa D'Antongiovanni |
| **Author** | Laura Benvenuti |
| **Author** | Matteo Fornai |
| **Author** | Carolina Pellegrini |
| **Author** | Renè van den Wijngaard |
| **Author** | Silvia Cerantola |
| **Author** | Maria Cecilia Giron |
| **Author** | Valentina Caputi |
| **Author** | Rocchina Colucci |
| **Author** | Gyorgy Haskó |
| **Author** | Zoltán H. Németh |
| **Author** | Corrado Blandizzi |
| **Author** | Luca Antonioli |
| **Abstract** | The role played by adenosine A(2B) receptors (A(2B)Rs) in the regulation of enteric glial cell (EGC) functions remains unclear. This study was aimed at investigating the involvement of A(2B)Rs in the control of EGC functions in a model of obesity. C57BL/6 mice were fed with standard diet (SD) or high fat diet (HFD) for eight weeks. Colonic tachykininergic contractions were recorded in the presence of BAY60-6583 (A(2B)Rs agonist), MRS1754 (A(2B)Rs antagonist), and the gliotoxin fluorocitrate. Immunofluorescence distribution of HuC/D, S100β, and A(2B)Rs was assessed in whole mount preparations of colonic myenteric plexus. To mimic HFD, EGCs were incubated in vitro with palmitate (PA) and lipopolysaccharide (LPS), in the absence or in the presence of A(2B)R ligands. Toll-like receptor 4 (TLR4) expression was assessed by Western blot analysis. Interleukin-1β (IL-1β), substance P (SP), and glial cell derived neurotrophic factor (GDNF) release were determined by enzyme-linked immunosorbent assay (ELISA) assays. MRS1754 enhanced electrically evoked tachykininergic contractions of colonic preparations from HFD mice. BAY60-6583 decreased the evoked tachykininergic contractions, with higher efficacy in HFD mice. Such effects were blunted upon incubation with fluorocitrate. In in vitro experiments on EGCs, PA and LPS increased TLR4 expression as well as IL-1β, GDNF, and SP release. Incubation with BAY60-6583 reduced TLR4 expression as well as IL-1β, GDNF, and SP release. Such effects were blunted by MRS1754. The present results suggest that A(2B)Rs, expressed on EGCs, participate in the modulation of enteric inflammation and altered tachykininergic responses associated with obesity, thus representing a potential therapeutic target. |
| **Date** | 2020 May 18 |
| **Language** | eng |
| **Extra** | Place: Switzerland PMID: 32443525 PMCID: PMC7290602 |
| **Volume** | 9 |
| **Publication** | Cells |
| **DOI** | [10.3390/cells9051245](http://doi.org/10.3390/cells9051245) |
| **Issue** | 5 |
| **Journal Abbr** | Cells |
| **ISSN** | 2073-4409 |
| **Date Added** | 6/11/2025, 2:32:27 PM |
| **Modified** | 6/11/2025, 2:32:27 PM |

### Tags:

* + Male
  + Animals
  + Models, Biological
  + Cells, Cultured
  + obesity
  + Mice, Inbred C57BL
  + enteric glia
  + Enteric Nervous System/\*pathology
  + Aminopyridines/pharmacology
  + enteric inflammation
  + substance P
  + Acetamides/pharmacology
  + adenosine A2B receptors
  + Body Weight/drug effects
  + Citrates/pharmacology
  + colonic motor dysfunction
  + Diet, High-Fat
  + Feeding Behavior/drug effects
  + glial cell derived neurotrophic factor
  + Inflammation/\*pathology
  + Interleukin-1beta/metabolism
  + interleukin-1β
  + Lipopolysaccharides/pharmacology
  + Mice, Obese
  + Nerve Growth Factors/metabolism
  + Neuroglia/drug effects/\*metabolism
  + Obesity/\*pathology
  + Palmitic Acid/pharmacology
  + Purines/pharmacology
  + Receptor, Adenosine A2B/\*metabolism
  + S100 Proteins/metabolism
  + Substance P/metabolism
  + tachykininergic contraction
  + Tachykinins/\*metabolism
  + toll-like receptor 4
  + Toll-Like Receptor 4/metabolism

## Glial Cells as Possible Targets of Neuroprotection through Neurotrophic and Antioxidative Molecules in the Central and Enteric Nervous Systems in Parkinson's Disease.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Nami Isooka |
| **Author** | Ikuko Miyazaki |
| **Author** | Masato Asanuma |
| **Abstract** | Parkinson's disease (PD) is the second most common neurodegenerative disease worldwide. The loss of nigrostriatal dopaminergic neurons produces its characteristic motor symptoms, but PD patients also have non-motor symptoms such as constipation and orthostatic hypotension. The pathological hallmark of PD is the presence of α-synuclein-containing Lewy bodies and neurites in the brain. However, the PD pathology is observed in not only the central nervous system (CNS) but also in parts of the peripheral nervous system such as the enteric nervous system (ENS). Since constipation is a typical prodromal non-motor symptom in PD, often preceding motor symptoms by 10-20 years, it has been hypothesized that PD pathology propagates from the ENS to the CNS via the vagal nerve. Discovery of pharmacological and other methods to halt this progression of neurodegeneration in PD has the potential to improve millions of lives. Astrocytes protect neurons in the CNS by secretion of neurotrophic and antioxidative factors. Similarly, astrocyte-like enteric glial cells (EGCs) are known to secrete neuroprotective factors in the ENS. In this article, we summarize the neuroprotective function of astrocytes and EGCs and discuss therapeutic strategies for the prevention of neurodegeneration in PD targeting neurotrophic and antioxidative molecules in glial cells. |
| **Date** | 2021 |
| **Language** | eng |
| **Extra** | Place: Japan PMID: 34703037 |
| **Volume** | 75 |
| **Pages** | 549-556 |
| **Publication** | Acta medica Okayama |
| **DOI** | [10.18926/AMO/62767](http://doi.org/10.18926/AMO/62767) |
| **Issue** | 5 |
| **Journal Abbr** | Acta Med Okayama |
| **ISSN** | 0386-300X |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/11/2025, 2:32:24 PM |

### Tags:

* + Humans
  + Parkinson’s disease
  + Antioxidants/\*metabolism
  + antioxidative molecule
  + astrocyte
  + Central Nervous System/cytology/\*drug effects
  + enteric glial cell
  + Enteric Nervous System/cytology/\*drug effects
  + Neuroglia/\*drug effects
  + Neuroprotective Agents/\*pharmacology
  + neurotrophic factor
  + Parkinson Disease/\*drug therapy

## Glutamate regulates gliosis of BMSCs to promote ENS regeneration through α-KG and H3K9/H3K27 demethylation.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Mengke Fan |
| **Author** | Huiying Shi |
| **Author** | Hailing Yao |
| **Author** | Weijun Wang |
| **Author** | Yurui Zhang |
| **Author** | Chen Jiang |
| **Author** | Rong Lin |
| **Abstract** | BACKGROUND: There is a lack of effective therapies for enteric nervous system (ENS) injury. Our previous study showed that transplanted bone marrow-derived mesenchymal stem cells (BMSCs) play a "glia-like cells" role in initiating ENS regeneration in denervated mice. Cellular energy metabolism is an important factor in maintaining the biological characteristics of stem cells. However, how cellular energy metabolism regulates the fate of BMSCs in the ENS-injured microenvironment is unclear. METHODS: The biological characteristics, energy metabolism, and histone methylation levels of BMSCs following ENS injury were determined. Then, glutamate dehydrogenase 1 (Glud1) which catalyzes the oxidative deamination of glutamate to α-KG was overexpressed (OE) in BMSCs. Further, OE-Glud1 BMSCs were targeted-transplanted into the ENS injury site of denervated mice to determine their effects on ENS regeneration. RESULTS: In vitro, in the ENS-injured high-glutamate microenvironment, the ratio of α-ketoglutarate (α-KG) to succinate (P < 0.05), the histone demethylation level (P < 0.05), the protein expression of glial cell markers (P < 0.05), and the gene expression of Glud1 (P < 0.05) were significantly increased. And the binding of H3K9me3 to the GFAP, S100B, and GDNF promoter was enhanced (P < 0.05). Moreover, α-KG treatment increased the monomethylation and decreased the trimethylation on H3K9 (P < 0.01) and H3K27 (P < 0.05) in BMSCs and significantly upregulated the protein expression of glial cell markers (P < 0.01), which was reversed by the α-KG competitive inhibitor D-2-hydroxyglutarate (P < 0.05). Besides, overexpression of Glud1 in BMSCs exhibited increases in monomethylation and decreases in trimethylation on H3K9 (P < 0.05) and H3K27 (P < 0.05), and upregulated protein expression of glial cell markers (P < 0.01). In vivo, BMSCs overexpressing Glud1 had a strong promotion effect on ENS regeneration in denervated mice through H3K9/H3K27 demethylation (P < 0.05), and upregulating the expression of glial cell protein (P < 0.05). CONCLUSIONS: BMSCs overexpressing Glud1 promote the expression of glial cell markers and ENS remodeling in denervated mice through regulating intracellular α-KG and H3K9/H3K27 demethylation. |
| **Date** | 2022 Jun 17 |
| **Language** | eng |
| **Rights** | © 2022. The Author(s). |
| **Extra** | Place: England PMID: 35715822 PMCID: PMC9205030 |
| **Volume** | 13 |
| **Pages** | 255 |
| **Publication** | Stem cell research & therapy |
| **DOI** | [10.1186/s13287-022-02936-7](http://doi.org/10.1186/s13287-022-02936-7) |
| **Issue** | 1 |
| **Journal Abbr** | Stem Cell Res Ther |
| **ISSN** | 1757-6512 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Animals
  + Mice
  + \*Enteric Nervous System/metabolism
  + \*Gliosis/metabolism
  + \*Histones/drug effects/genetics/metabolism
  + \*Ketoglutaric Acids/metabolism
  + Bone Marrow Cells/metabolism
  + Bone marrow-derived mesenchymal stem cells (BMSCs)
  + Demethylation
  + Glud1 (glutamate dehydrogenase 1)
  + Glutamic Acid/metabolism
  + Histone methylation
  + Mesenchymal Stem Cell Transplantation
  + α-ketoglutarate (α-KG)

## Gut-Brain Axis, Neurodegeneration and Mental Health: A Personalized Medicine Perspective.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Alisha Chunduri |
| **Author** | S. Deepak Mohan Reddy |
| **Author** | M. Jahanavi |
| **Author** | C. Nagendranatha Reddy |
| **Abstract** | Neurological conditions such as neurodegenerative diseases and mental health disorders are a result of multifactorial underpinnings, leading to individual-based complex phenotypes. Demystification of these multifactorial connections will promote disease diagnosis and treatment. Personalized treatment rather than a one-size-fits-all approach would enable us to cater to the unmet healthcare needs based on protein-protein and gene-environment interactions. Gut-brain axis, as the name suggests, is a two-way biochemical communication pathway between the central nervous system (CNS) and enteric nervous system (ENS), enabling a mutual influence between brain and peripheral intestinal functions. The gut microbiota is a major component of this bidirectional communication, the composition of which is varied depending on the age, and disease conditions, among other factors. Gut microbiota profile is typically unique and personalized therapeutic intervention can aid in treating or delaying neurodegeneration and mental health conditions. Besides, research on the gut microbial influence on these conditions is gaining attention, and a better understanding of this concept can lead to identification of novel targeted therapies. |
| **Date** | 2022 Dec |
| **Language** | eng |
| **Rights** | © Association of Microbiologists of India 2022, Springer Nature or its licensor holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law. |
| **Extra** | Place: India PMID: 36458229 PMCID: PMC9705676 |
| **Volume** | 62 |
| **Pages** | 505-515 |
| **Publication** | Indian journal of microbiology |
| **DOI** | [10.1007/s12088-022-01033-w](http://doi.org/10.1007/s12088-022-01033-w) |
| **Issue** | 4 |
| **Journal Abbr** | Indian J Microbiol |
| **ISSN** | 0046-8991 0973-7715 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/11/2025, 2:32:24 PM |

### Tags:

* + Personalized medicine
  + Gut microbiota
  + Gut–brain axis
  + Mental health
  + Neurodegeneration

## Gut-brain communication in COVID-19: molecular mechanisms, mediators, biomarkers, and therapeutics.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Tameena Wais |
| **Author** | Mehde Hasan |
| **Author** | Vikrant Rai |
| **Author** | Devendra K. Agrawal |
| **Abstract** | INTRODUCTION: Infection with COVID-19 results in acute respiratory symptoms followed by long COVID multi-organ effects presenting with neurological, cardiovascular, musculoskeletal, and gastrointestinal (GI) manifestations. Temporal relationship between gastrointestinal and neurological symptoms is unclear but warranted for exploring better clinical care for COVID-19 patients. AREAS COVERED: We critically reviewed the temporal relationship between gut-brain axis after SARS-CoV-2 infection and the molecular mechanisms involved in neuroinvasion following GI infection. Mediators are identified that could serve as biomarkers and therapeutic targets in SARS-CoV-2. We discussed the potential therapeutic approaches to mitigate the effects of GI infection with SARS-CoV-2. EXPERT OPINION: Altered gut microbiota cause increased expression of various mediators, including zonulin causing disruption of tight junction. This stimulates enteric nervous system and signals to CNS precipitating neurological sequalae. Published reports suggest potential role of cytokines, immune cells, B(0)AT1 (SLC6A19), ACE2, TMRSS2, TMPRSS4, IFN-γ, IL-17A, zonulin, and altered gut microbiome in gut-brain axis and associated neurological sequalae. Targeting these mediators and gut microbiome to improve immunity will be of therapeutic significance. In-depth research and well-designed large-scale population-based clinical trials with multidisciplinary and collaborative approaches are warranted. Investigating the temporal relationship between organs involved in long-term sequalae is critical due to evolving variants of SARS-CoV-2. |
| **Date** | 2022 Sep |
| **Language** | eng |
| **Extra** | Place: England PMID: 35868344 PMCID: PMC9388545 |
| **Volume** | 18 |
| **Pages** | 947-960 |
| **Publication** | Expert review of clinical immunology |
| **DOI** | [10.1080/1744666X.2022.2105697](http://doi.org/10.1080/1744666X.2022.2105697) |
| **Issue** | 9 |
| **Journal Abbr** | Expert Rev Clin Immunol |
| **ISSN** | 1744-8409 1744-666X |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + SARS-CoV-2
  + COVID-19
  + Biomarkers
  + Brain
  + enteric nervous system
  + gastrointestinal tract
  + \*Brain-Gut Axis
  + \*COVID-19/complications
  + \*Gastrointestinal Diseases
  + ACE-2 receptor
  + Gut-brain axis
  + Post-Acute COVID-19 Syndrome

## HDCA alleviates Parkinson's disease symptoms by promoting autophagic degradation of α-synuclein in enteric neurons.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Ren-Yu Kong |
| **Author** | Jin-Bao Zhang |
| **Author** | Xu Miao |
| **Author** | Xiao-Yu Yao |
| **Author** | Mei-Hua Pan |
| **Author** | Xin Yin |
| **Author** | Rui-Qin Yao |
| **Author** | Chao Ren |
| **Abstract** | INTRODUCTION: Bile acids (BAs) are emerging as key modulators of Parkinson's disease (PD) through gut-brain interactions, yet their therapeutic potential remains underutilized. While BA imbalances contribute to PD pathogenesis, the specific subspecies regulating α-synuclein (α-syn) homeostasis and their mechanisms in enteric neurons-critical sites for PD initiation-require systematic investigation. OBJECTIVE: To investigate whether hyodeoxycholic acid (HDCA), a secondary BA with documented neuroprotective properties but unproven efficacy in synucleinopathy, modulates α-syn clearance through enteric neuronal autophagy to mitigate PD progression. METHODS: A53T transgenic mice underwent behavioral assessments for PD phenotyping. State-of-the-art UPLC/MS-based metabolomics quantified BA profiles. Pharmacological interventions using target-specific inhibitors (Gly-MCA, T0070907, VER-155,008) dissected the FXR-PPARγ-HSPA8 pathway. Multiscale analyses spanning immunofluorescence, western blotting, and LC3B autophagy flux reporter assays elucidated α-syn aggregation and autophagic dynamics in primary enteric neurons. RESULTS: HDCA decline correlated with PD severity, positioning it as a novel biomarker for gut-brain axis dysfunction in PD. HDCA supplementation not only alleviated motor/non-motor deficits but also conferred dual neuroprotection-reducing colonic α-syn oligomers and preserving nigral dopaminergic neurons. Mechanistic decoding revealed HDCA's unparalleled capacity to activate enteric neuronal autophagy via FXR-PPARγ-HSPA8 signaling, a pathway previously unrecognized in PD therapeutics. CONCLUSION: Our study reveals a novel gut-brain axis where HDCA depletion drives PD pathogenesis via FXR-PPARγ-HSPA8-mediated autophagic dysfunction in enteric neurons. PD-associated HDCA deficiency directly impairs α-syn clearance, identifying HDCA as both a gut-derived synucleinopathy biomarker and a therapeutic target. |
| **Date** | 2025 Jul |
| **Language** | eng |
| **Rights** | Copyright © 2025 Elsevier GmbH. All rights reserved. |
| **Extra** | Place: Germany PMID: 40252434 |
| **Volume** | 142 |
| **Pages** | 156749 |
| **Publication** | Phytomedicine : international journal of phytotherapy and phytopharmacology |
| **DOI** | [10.1016/j.phymed.2025.156749](http://doi.org/10.1016/j.phymed.2025.156749) |
| **Journal Abbr** | Phytomedicine |
| **ISSN** | 1618-095X 0944-7113 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/11/2025, 2:32:26 PM |

### Tags:

* + Male
  + Animals
  + Mice
  + Mice, Inbred C57BL
  + Mice, Transgenic
  + Autophagy
  + Parkinson's disease
  + \*alpha-Synuclein/metabolism
  + \*Autophagy/drug effects
  + \*Neurons/drug effects/metabolism
  + \*Parkinson Disease/drug therapy/metabolism
  + Alpha-synuclein
  + Enteric Nervous System/drug effects
  + Heat shock protein 8
  + Hyodeoxycholic acid
  + Neuroprotective Agents/pharmacology
  + PPAR gamma/metabolism
  + PPARγ

## Herpes Simplex Virus Type 1 Infects Enteric Neurons and Triggers Gut Dysfunction via Macrophage Recruitment.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Paola Brun |
| **Author** | Marsela Qesari |
| **Author** | Peggy C. Marconi |
| **Author** | Andromachi Kotsafti |
| **Author** | Andrea Porzionato |
| **Author** | Veronica Macchi |
| **Author** | Reto A. Schwendener |
| **Author** | Marco Scarpa |
| **Author** | Maria C. Giron |
| **Author** | Giorgio Palù |
| **Author** | Arianna Calistri |
| **Author** | Ignazio Castagliuolo |
| **Abstract** | Herpes Simplex Virus type 1 (HSV-1), a neurotropic pathogen widespread in human population, infects the enteric nervous system (ENS) in humans and rodents and causes intestinal neuromuscular dysfunction in rats. Although infiltration of inflammatory cells in the myenteric plexus and neurodegeneration of enteric nerves are common features of patients suffering from functional intestinal disorders, the proof of a pathogenic link with HSV-1 is still unsettled mainly because the underlying mechanisms are largely unknown. In this study we demonstrated that following intragastrical administration HSV-1 infects neurons within the myenteric plexus resulting in functional and structural alterations of the ENS. By infecting mice with HSV-1 replication-defective strain we revealed that gastrointestinal neuromuscular anomalies were however independent of viral replication. Indeed, enteric neurons exposed to UV-inactivated HSV-1 produced monocyte chemoattractant protein-1 (MCP-1/CCL2) to recruit activated macrophages in the longitudinal muscle myenteric plexus. Infiltrating macrophages produced reactive oxygen and nitrogen species and directly harmed enteric neurons resulting in gastrointestinal dysmotility. In HSV-1 infected mice intestinal neuromuscular dysfunctions were ameliorated by in vivo administration of (i) liposomes containing dichloromethylene bisphosphonic acid (clodronate) to deplete tissue macrophages, (ii) CCR2 chemokine receptor antagonist RS504393 to block the CCL2/CCR2 pathway, (iii) Nω-Nitro-L-arginine methyl ester hydrochloride (L-NAME) and AR-C 102222 to quench production of nitrogen reactive species produced via iNOS. Overall these data demonstrate that HSV-1 infection makes enteric neurons recruit macrophages via production of a specific chemoattractant factor. The resulting inflammatory reaction is mandatory for intestinal dysmotility. These findings provide insights into the neuro-immune communication that occurs in the ENS following HSV-1 infection and allow recognition of an original pathophysiologic mechanism underlying gastrointestinal diseases as well as identification of novel therapeutic targets. |
| **Date** | 2018 |
| **Language** | eng |
| **Extra** | Place: Switzerland PMID: 29600197 PMCID: PMC5862801 |
| **Volume** | 8 |
| **Pages** | 74 |
| **Publication** | Frontiers in cellular and infection microbiology |
| **DOI** | [10.3389/fcimb.2018.00074](http://doi.org/10.3389/fcimb.2018.00074) |
| **Journal Abbr** | Front Cell Infect Microbiol |
| **ISSN** | 2235-2988 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/11/2025, 2:32:26 PM |

### Tags:

* + Male
  + Animals
  + Disease Models, Animal
  + Mice
  + Rats
  + Mice, Inbred C57BL
  + Virus Replication
  + inflammation
  + Adaptive Immunity
  + Arginine/analogs & derivatives/metabolism
  + Chemokine CCL2/metabolism
  + Clodronic Acid
  + Enteric Nervous System/\*drug effects/metabolism/pathology/\*virology
  + enteric neuropathies
  + Gastrointestinal Motility/\*drug effects
  + Herpes Simplex/immunology/\*metabolism/pathology/virology
  + Herpesvirus 1, Human/\*pathogenicity
  + Ileum/immunology/pathology/virology
  + Inflammation/metabolism
  + Liposomes/metabolism
  + macrophage recruitment
  + Macrophages/\*metabolism
  + Myenteric Plexus/drug effects/metabolism/pathology/virology
  + neuromuscular dysfunction
  + Neurons/\*drug effects/virology
  + neurotropic virus
  + NG-Nitroarginine Methyl Ester/metabolism
  + Reactive Nitrogen Species/metabolism/toxicity
  + Reactive Oxygen Species/metabolism/toxicity
  + Receptors, Chemokine
  + Virus Internalization

## Hidden Role of Gut Microbiome Dysbiosis in Schizophrenia: Antipsychotics or Psychobiotics as Therapeutics?

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Nayla Munawar |
| **Author** | Khansa Ahsan |
| **Author** | Khalid Muhammad |
| **Author** | Aftab Ahmad |
| **Author** | Munir A. Anwar |
| **Author** | Iltaf Shah |
| **Author** | Ahlam Khalifa Al Ameri |
| **Author** | Fadwa Al Mughairbi |
| **Abstract** | Schizophrenia is a chronic, heterogeneous neurodevelopmental disorder that has complex symptoms and uncertain etiology. Mounting evidence indicates the involvement of genetics and epigenetic disturbances, alteration in gut microbiome, immune system abnormalities, and environmental influence in the disease, but a single root cause and mechanism involved has yet to be conclusively determined. Consequently, the identification of diagnostic markers and the development of psychotic drugs for the treatment of schizophrenia faces a high failure rate. This article surveys the etiology of schizophrenia with a particular focus on gut microbiota regulation and the microbial signaling system that correlates with the brain through the vagus nerve, enteric nervous system, immune system, and production of postbiotics. Gut microbially produced molecules may lay the groundwork for further investigations into the role of gut microbiota dysbiosis and the pathophysiology of schizophrenia. Current treatment of schizophrenia is limited to psychotherapy and antipsychotic drugs that have significant side effects. Therefore, alternative therapeutic options merit exploration. The use of psychobiotics alone or in combination with antipsychotics may promote the development of novel therapeutic strategies. In view of the individual gut microbiome structure and personalized response to antipsychotic drugs, a tailored and targeted manipulation of gut microbial diversity naturally by novel prebiotics (non-digestible fiber) may be a successful alternative therapeutic for the treatment of schizophrenia patients. |
| **Date** | 2021 Jul 18 |
| **Language** | eng |
| **Extra** | Place: Switzerland PMID: 34299291 PMCID: PMC8307070 |
| **Volume** | 22 |
| **Publication** | International journal of molecular sciences |
| **DOI** | [10.3390/ijms22147671](http://doi.org/10.3390/ijms22147671) |
| **Issue** | 14 |
| **Journal Abbr** | Int J Mol Sci |
| **ISSN** | 1422-0067 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/11/2025, 2:32:25 PM |

### Tags:

* + Humans
  + dysbiosis
  + probiotics
  + schizophrenia
  + Antipsychotic Agents/\*therapeutic use
  + antipsychotics
  + Brain/microbiology
  + Dysbiosis/immunology/metabolism/microbiology
  + Gastrointestinal Microbiome/\*drug effects/physiology
  + gut microbiome
  + Immune System
  + postbiotics
  + prebiotics
  + Prebiotics/microbiology
  + Probiotics/\*therapeutic use
  + Schizophrenia/\*microbiology/\*therapy

## Host Gut Motility Promotes Competitive Exclusion within a Model Intestinal Microbiota.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Travis J. Wiles |
| **Author** | Matthew Jemielita |
| **Author** | Ryan P. Baker |
| **Author** | Brandon H. Schlomann |
| **Author** | Savannah L. Logan |
| **Author** | Julia Ganz |
| **Author** | Ellie Melancon |
| **Author** | Judith S. Eisen |
| **Author** | Karen Guillemin |
| **Author** | Raghuveer Parthasarathy |
| **Abstract** | The gut microbiota is a complex consortium of microorganisms with the ability to influence important aspects of host health and development. Harnessing this "microbial organ" for biomedical applications requires clarifying the degree to which host and bacterial factors act alone or in combination to govern the stability of specific lineages. To address this issue, we combined bacteriological manipulation and light sheet fluorescence microscopy to monitor the dynamics of a defined two-species microbiota within a vertebrate gut. We observed that the interplay between each population and the gut environment produces distinct spatiotemporal patterns. As a consequence, one species dominates while the other experiences sudden drops in abundance that are well fit by a stochastic mathematical model. Modeling revealed that direct bacterial competition could only partially explain the observed phenomena, suggesting that a host factor is also important in shaping the community. We hypothesized the host determinant to be gut motility, and tested this mechanism by measuring colonization in hosts with enteric nervous system dysfunction due to a mutation in the ret locus, which in humans is associated with the intestinal motility disorder known as Hirschsprung disease. In mutant hosts we found reduced gut motility and, confirming our hypothesis, robust coexistence of both bacterial species. This study provides evidence that host-mediated spatial structuring and stochastic perturbation of communities can drive bacterial population dynamics within the gut, and it reveals a new facet of the intestinal host-microbe interface by demonstrating the capacity of the enteric nervous system to influence the microbiota. Ultimately, these findings suggest that therapeutic strategies targeting the intestinal ecosystem should consider the dynamic physical nature of the gut environment. |
| **Date** | 2016 Jul |
| **Language** | eng |
| **Extra** | Place: United States PMID: 27458727 PMCID: PMC4961409 |
| **Volume** | 14 |
| **Pages** | e1002517 |
| **Publication** | PLoS biology |
| **DOI** | [10.1371/journal.pbio.1002517](http://doi.org/10.1371/journal.pbio.1002517) |
| **Issue** | 7 |
| **Journal Abbr** | PLoS Biol |
| **ISSN** | 1545-7885 1544-9173 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
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### Tags:

* + Animals
  + Mutation
  + Species Specificity
  + Aeromonas veronii/physiology
  + Antibiosis/physiology
  + Gastrointestinal Microbiome/\*physiology
  + Gastrointestinal Motility/\*physiology
  + Gastrointestinal Tract/\*microbiology
  + Larva/genetics/microbiology/physiology
  + Microbiota/\*physiology
  + Microscopy, Fluorescence
  + Population Dynamics
  + Vibrio cholerae/physiology
  + Zebrafish

## Human Enteric Glia Diversity in Health and Disease: New Avenues for the Treatment of Hirschsprung Disease.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Jonathan D. Windster |
| **Author** | Naomi J. M. Kakiailatu |
| **Author** | Laura E. Kuil |
| **Author** | Agne Antanaviciute |
| **Author** | Andrea Sacchetti |
| **Author** | Katherine C. MacKenzie |
| **Author** | Joke Peulen-Zink |
| **Author** | Tsung W. Kan |
| **Author** | Eric Bindels |
| **Author** | Emma de Pater |
| **Author** | Michail Doukas |
| **Author** | Thierry P. P. van den Bosch |
| **Author** | Soheil Yousefi |
| **Author** | Tahsin-Stefan Barakat |
| **Author** | Conny J. H. M. Meeussen |
| **Author** | Pim C. E. J. Sloots |
| **Author** | Rene M. H. Wijnen |
| **Author** | Kaushal Parikh |
| **Author** | Werend Boesmans |
| **Author** | Veerle Melotte |
| **Author** | Robert M. W. Hofstra |
| **Author** | Alison Simmons |
| **Author** | Maria M. Alves |
| **Abstract** | BACKGROUND & AIMS: The enteric nervous system (ENS), which is composed of neurons and glia, regulates intestinal motility. Hirschsprung disease (HSCR) results from defects in ENS formation; however, although neuronal aspects have been studied extensively, enteric glia remain disregarded. This study aimed to explore enteric glia diversity in health and disease. METHODS: Full-thickness intestinal resection material from pediatric controls and patients with HSCR was collected, dissociated, and enriched for the ENS population through fluorescence-activated cell sorting. Single-cell RNA sequencing was performed to uncover the transcriptomic diversity of the ENS in controls and HSCR patients, as well as in wild-type and ret mutant zebrafish. Immunofluorescence and fluorescence in situ hybridization confirmed the presence of distinct subtypes. RESULTS: Two major enteric glial classes emerged in the pediatric intestine: Schwann-like enteric glia, which are reminiscent of Schwann cells, and enteric glia expressing classical glial markers. Comparative analysis with previously published datasets confirmed our classification and revealed that although classical enteric glia are predominant prenatally, Schwann-like enteric glia become more abundant postnatally. In HSCR, ganglionic segments mirrored controls and aganglionic segments featured only Schwann-like enteric glia. Leveraging the regenerative potential of Schwann cells, we explored therapeutic options using a ret mutant zebrafish. Prucalopride, a serotonin-receptor (5-HT) agonist, induced neurogenesis partially rescuing the HSCR phenotype in ret(+/-) mutants. CONCLUSIONS: Two major enteric glial classes were identified in the pediatric intestine, highlighting the significant postnatal contribution of Schwann-like enteric glia to glial heterogeneity. Crucially, these glial subtypes persist in aganglionic segments of patients with HSCR, offering a new target for their treatment using 5-HT agonists. |
| **Date** | 2025 May |
| **Language** | eng |
| **Rights** | Copyright © 2025 The Authors. Published by Elsevier Inc. All rights reserved. |
| **Extra** | Place: United States PMID: 39725172 |
| **Volume** | 168 |
| **Pages** | 965-979.e12 |
| **Publication** | Gastroenterology |
| **DOI** | [10.1053/j.gastro.2024.12.011](http://doi.org/10.1053/j.gastro.2024.12.011) |
| **Issue** | 5 |
| **Journal Abbr** | Gastroenterology |
| **ISSN** | 1528-0012 0016-5085 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/11/2025, 2:32:24 PM |

### Tags:

* + Female
  + Humans
  + Male
  + Animals
  + Disease Models, Animal
  + Transcriptome
  + Single-Cell Analysis
  + Infant
  + Child
  + ENS
  + Zebrafish
  + Child, Preschool
  + Case-Control Studies
  + Prucalopride
  + \*Enteric Nervous System/pathology/metabolism/drug effects/cytology
  + \*Hirschsprung Disease/pathology/genetics/metabolism/drug therapy
  + \*Neuroglia/metabolism/pathology/drug effects
  + Enteric Glia
  + Hirschsprung Disease
  + Proto-Oncogene Proteins c-ret/genetics
  + Schwann Cells
  + Schwann Cells/pathology/metabolism
  + Single-Cell RNA Sequencing

## Hyaluronan Regulates Neuronal and Immune Function in the Rat Small Intestine and Colonic Microbiota after Ischemic/Reperfusion Injury.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Annalisa Bosi |
| **Author** | Davide Banfi |
| **Author** | Michela Bistoletti |
| **Author** | Lucia Martina Catizzone |
| **Author** | Anna Maria Chiaravalli |
| **Author** | Paola Moretto |
| **Author** | Elisabetta Moro |
| **Author** | Evgenia Karousou |
| **Author** | Manuela Viola |
| **Author** | Maria Cecilia Giron |
| **Author** | Francesca Crema |
| **Author** | Carlo Rossetti |
| **Author** | Giorgio Binelli |
| **Author** | Alberto Passi |
| **Author** | Davide Vigetti |
| **Author** | Cristina Giaroni |
| **Author** | Andreina Baj |
| **Abstract** | BACKGROUND: Intestinal ischemia and reperfusion (IRI) injury induces acute and long-lasting damage to the neuromuscular compartment and dysmotility. This study aims to evaluate the pathogenetic role of hyaluronan (HA), a glycosaminoglycan component of the extracellular matrix, as a modulator of the enteric neuronal and immune function and of the colonic microbiota during in vivo IRI in the rat small intestine. METHODS: mesenteric ischemia was induced in anesthetized adult male rats for 60 min, followed by 24 h reperfusion. Injured, sham-operated and non-injured animals were treated with the HA synthesis inhibitor, 4-methylumbelliferone (4-MU 25 mg/kg). Fecal microbiota composition was evaluated by Next Generation Sequencing. Neutrophil infiltration, HA homeostasis and toll like receptor (TLR2 and TLR4) expression in the small intestine were evaluated by immunohistochemical and biomolecular approaches (qRT-PCR and Western blotting). Neuromuscular responses were studied in vitro, in the absence and presence of the selective TLR2/4 inhibitor, Sparstolonin B (SsnB 10, 30 µM). RESULTS: 4-MU significantly reduced IRI-induced enhancement of potentially harmful Escherichia and Enterococcus bacteria. After IRI, HA levels, neutrophil infiltration, and TLR2 and TLR4 expression were significantly enhanced in the muscularis propria, and were significantly reduced to baseline levels by 4-MU. In the injured, but not in the non-injured and sham-operated groups, SsnB reduced both electrical field-stimulated (EFS, 0.1-40 Hz) contractions and EFS-induced (10 Hz) non-cholinergic non-adrenergic relaxations. CONCLUSIONS: enhanced HA levels after intestinal IRI favors harmful bacteria overgrowth, increases neutrophil infiltration and promotes the upregulation of bacterial target receptors, TLR2 and TLR4, in the muscularis propria, inducing a pro-inflammatory state. TLR2 and TLR4 activation may, however, underlay a provisional benefit on excitatory and inhibitory neuronal pathways underlying peristalsis. |
| **Date** | 2022 Oct 25 |
| **Language** | eng |
| **Extra** | Place: Switzerland PMID: 36359764 PMCID: PMC9657036 |
| **Volume** | 11 |
| **Publication** | Cells |
| **DOI** | [10.3390/cells11213370](http://doi.org/10.3390/cells11213370) |
| **Issue** | 21 |
| **Journal Abbr** | Cells |
| **ISSN** | 2073-4409 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/11/2025, 2:32:26 PM |

### Tags:

* + Male
  + Animals
  + Rats
  + microbiota
  + \*Microbiota
  + enteric nervous system
  + Toll-Like Receptor 4/metabolism
  + \*Reperfusion Injury/metabolism
  + Hyaluronic Acid/metabolism
  + Immunity
  + intestinal ischemia/reperfusion injury
  + intestinal neuromuscular function
  + Intestine, Small/metabolism
  + TLRs
  + Toll-Like Receptor 2/metabolism

## Hyperglycemic stress induces oxidative damage of enteric glial cells by triggering redoxosomes/p66SHC activation.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Yanmin Jiang |
| **Author** | Lan Xu |
| **Author** | Xue Zhu |
| **Author** | Xiaowei Zhu |
| **Author** | Xiang Xu |
| **Author** | Jianbo Li |
| **Abstract** | OBJECTIVES: Diabetic gastrointestinal dysfunction (DGD) is a serious complication of diabetic mellitus (DM), affecting the enteric nervous system (ENS), particular enteric glial cells (EGCs). This study aimed to elucidate the effects and underlying molecular mechanisms of hyperglycemic stress on EGCs in in vitro and in vivo models of DM. METHODS: In in vitro studies, enteric glial cell line CRL-2690 was exposed to hyperglycemia stress, and cell viability, cell apoptosis and oxidative damage were assessed. In in vivo studies, STZ-induced diabetic mice were constructed, and cell apoptosis and oxidative damage of EGCs in the duodenum of DM mice were assessed. RESULTS: The results showed that hyperglycemic stress markedly induced oxidative damage of EGCs in in vitro and in vivo models of DM. This damage was found to be dependent on the activation of redoxosomes, which involved the phosphorylation of SRC and Vav2, the up-regulation of active RAC1-GTP, and the activation of NADPH oxidase (NOX). Moreover, inhibitors of redoxosomes, such as the RAC1 inhibitor NSC23766 and the NOX inhibitor VAS2870, effectively mitigated the hyperglycemic stress-induced oxidative damage of EGCs. Additionally, inhibition of p66SHC, a downstream target of redoxosomes, attenuated oxidative damage of EGCs under hyperglycemic stress. DISCUSSION: Our findings suggest that the redoxosomes/p66SHC signaling is involved in the oxidative damage of EGCs during the pathological process of DGD. This signaling cascade may represent a potential therapeutic target for the treatment of DGD. |
| **Date** | 2024 Dec |
| **Language** | eng |
| **Extra** | Place: England PMID: 38444386 PMCID: PMC10919305 |
| **Volume** | 29 |
| **Pages** | 2324234 |
| **Publication** | Redox report : communications in free radical research |
| **DOI** | [10.1080/13510002.2024.2324234](http://doi.org/10.1080/13510002.2024.2324234) |
| **Issue** | 1 |
| **Journal Abbr** | Redox Rep |
| **ISSN** | 1743-2928 1351-0002 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/11/2025, 2:32:24 PM |

### Tags:

* + Animals
  + Mice
  + Neuroglia
  + Oxidative Stress
  + enteric glial cells
  + \*Diabetes Mellitus, Experimental
  + Diabetic gastrointestinal dysfunction
  + hyperglycemic stress
  + NADPH Oxidases
  + redoxosomes/p66SHC signaling
  + Src Homology 2 Domain-Containing, Transforming Protein 1

## Hypnosis and Cognitive Behavioral Therapies for the Management of Gastrointestinal Disorders.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Olafur S. Palsson |
| **Author** | Sarah Ballou |
| **Abstract** | PURPOSE OF REVIEW: To review the nature, current evidence of efficacy, recent developments, and future prospects for cognitive behavioral therapy (CBT) and gut-directed hypnotherapy, the two best established psychological interventions for managing gastrointestinal (GI) disorders. RECENT FINDINGS: New large randomized controlled trials are showing that cost-effective therapy delivery formats (telephone-based, Internet-based, fewer therapist sessions, or group therapy) are effective for treating GI disorders. CBT and hypnotherapy can produce substantial improvement in the digestive tract symptoms, psychological well-being, and quality of life of GI patients. However, they have long been hampered by limited scalability and significant cost, and only been sufficiently tested for a few GI health problems. Through adoption of more cost-effective therapy formats and teletherapy, and by expanding the scope of efficacy testing to additional GI treatment targets, these interventions have the potential to become widely available options for improving clinical outcomes for patients with hard-to-treat GI disorders. |
| **Date** | 2020 Jun 3 |
| **Language** | eng |
| **Extra** | Place: United States PMID: 32495233 |
| **Volume** | 22 |
| **Pages** | 31 |
| **Publication** | Current gastroenterology reports |
| **DOI** | [10.1007/s11894-020-00769-z](http://doi.org/10.1007/s11894-020-00769-z) |
| **Issue** | 7 |
| **Journal Abbr** | Curr Gastroenterol Rep |
| **ISSN** | 1534-312X 1522-8037 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Quality of Life
  + Functional gastrointestinal disorders
  + \*Cognitive Behavioral Therapy
  + \*Hypnosis
  + Brain-gut axis
  + Central Nervous System/physiology/physiopathology
  + Cognitive behavioral therapy
  + Dyspepsia/psychology/therapy
  + Enteric Nervous System/physiology/physiopathology
  + Gastrointestinal Diseases/physiopathology/psychology/\*therapy
  + Hypnotherapy
  + Inflammatory Bowel Diseases/psychology/therapy
  + Irritable Bowel Syndrome/psychology/therapy
  + Stress, Psychological/physiopathology
  + Telemedicine

## Identification of Arginine-Vasopressin Receptor 1a (Avpr1a/Avpr1a) as a Novel Candidate Gene for Chronic Visceral Pain Sheds Light on the Potential Role of Enteric Neurons in the Development of Visceral Hypersensitivity.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Leena Kader |
| **Author** | Adam B. Willits |
| **Author** | Sebastian Meriano |
| **Author** | Julie A. Christianson |
| **Author** | Jun-Ho La |
| **Author** | Bin Feng |
| **Author** | Brittany Knight |
| **Author** | Gulum Kosova |
| **Author** | Jennifer J. Deberry |
| **Author** | Matthew D. Coates |
| **Author** | Jeffrey S. Hyams |
| **Author** | Kyle M. Baumbauer |
| **Author** | Erin E. Young |
| **Abstract** | Chronic abdominal pain in the absence of ongoing disease is the hallmark of disorders of gut-brain interaction (DGBIs), including irritable bowel syndrome (IBS). While the etiology of DGBIs remains poorly understood, there is evidence that both genetic and environmental factors play a role. In this study, we report the identification and validation of arginine-vasopressin receptor 1A (Avpr1a) as a novel candidate gene for visceral hypersensitivity (VH), a primary peripheral mechanism underlying abdominal pain in DGBI/IBS. Comparing 2 C57BL/6 (BL/6) substrains (C57BL/6NTac and C57BL/6J) revealed differential susceptibility to the development of chronic VH following intrarectal zymosan instillation, a validated preclinical model for postinflammatory IBS. Using whole-genome sequencing, we identified a single-nucleotide polymorphism differentiating the 2 strains in the 5' intergenic region upstream of Avpr1a, encoding the protein Avpr1a. We used behavioral, histological, and molecular approaches to identify distal colon-specific gene expression and neuronal hyperresponsiveness covarying with Avpr1a genotype and VH susceptibility. While the 2 BL/6 substrains did not differ across other gastrointestinal phenotypes (eg, fecal water retention), VH-susceptible BL/6NTac mice had higher colonic Avpr1a mRNA and protein expression. These results parallel findings that patients' colonic Avpr1a mRNA expression corresponded to higher pain ratings. Moreover, neurons of the enteric nervous system were hyperresponsive to the Avpr1a agonist arginine-vasopressin, suggesting a role for enteric neurons in the pathology underlying VH. Taken together, these findings implicate differential regulation of Avpr1a as a novel mechanism of VH susceptibility as well as a potential therapeutic target specific to VH. PERSPECTIVE: This article presents evidence of Avpr1a as a novel candidate gene for VH in a mouse model of IBS. Avpr1a genotype and/or tissue-specific expression represents a potential biomarker for chronic abdominal pain susceptibility. |
| **Date** | 2024 Sep |
| **Language** | eng |
| **Rights** | Copyright © 2024 The Authors. Published by Elsevier Inc. All rights reserved. |
| **Extra** | Place: United States PMID: 38768798 PMCID: PMC11571697 |
| **Volume** | 25 |
| **Pages** | 104572 |
| **Publication** | The journal of pain |
| **DOI** | [10.1016/j.jpain.2024.104572](http://doi.org/10.1016/j.jpain.2024.104572) |
| **Issue** | 9 |
| **Journal Abbr** | J Pain |
| **ISSN** | 1528-8447 1526-5900 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/11/2025, 2:32:26 PM |

### Tags:

* + Male
  + Animals
  + Disease Models, Animal
  + Mice
  + Neurons/metabolism
  + \*Mice, Inbred C57BL
  + Colon
  + enteric nervous system
  + disorders of gut-brain interaction
  + genetics
  + visceral hypersensitivity
  + Irritable bowel syndrome
  + \*Chronic Pain/genetics
  + \*Receptors, Vasopressin/genetics
  + \*Visceral Pain/genetics
  + Enteric Nervous System/metabolism
  + Hyperalgesia/genetics
  + Irritable Bowel Syndrome/genetics
  + Polymorphism, Single Nucleotide

## Identification of arginine-vasopressin receptor 1a (Avpr1a/AVPR1A) as a novel candidate gene for chronic visceral pain.

|  |  |
| --- | --- |
| **Item Type** | Preprint |
| **Author** | Leena Kader |
| **Author** | Adam Willits |
| **Author** | Sebastian Meriano |
| **Author** | Julie A. Christianson |
| **Author** | Jun-Ho La |
| **Author** | Bin Feng |
| **Author** | Brittany Knight |
| **Author** | Gulum Kosova |
| **Author** | Jennifer Deberry |
| **Author** | Matthew Coates |
| **Author** | Jeffrey Hyams |
| **Author** | Kyle Baumbauer |
| **Author** | Erin E. Young |
| **Abstract** | Chronic abdominal pain in the absence of ongoing disease is the hallmark of disorders of gut-brain interaction (DGBIs), including irritable bowel syndrome (IBS). While the etiology of DGBIs remains poorly understood, there is evidence that both genetic and environmental factors play a role. In this study, we report the identification and validation of Avpr1a as a novel candidate gene for visceral hypersensitivity (VH), a primary peripheral mechanism underlying abdominal pain in DGBI/IBS. Comparing two C57BL/6 (BL/6) substrains (C57BL/6NTac and C57BL/6J) revealed differential susceptibility to the development of chronic VH following intrarectal zymosan (ZYM) instillation, a validated preclinical model for post-inflammatory IBS. Using whole genome sequencing, we identified a SNP differentiating the two strains in the 5' intergenic region upstream of Avpr1a, encoding the protein arginine-vasopressin receptor 1A (AVPR1A). We used behavioral, histological, and molecular approaches to identify distal colon-specific gene expression differences and neuronal hyperresponsiveness covarying with Avpr1a genotype and VH susceptibility. While the two BL/6 substrains did not differ across other gastrointestinal (GI) phenotypes (e.g., GI motility), VH-susceptible BL/6NTac mice had higher colonic Avpr1a mRNA and protein expression. Moreover, neurons of the enteric nervous system were hyperresponsive to the AVPR1A agonist AVP, suggesting a role for enteric neurons in the pathology underlying VH. These results parallel our findings that patients' colonic Avpr1a mRNA expression was higher in patients with higher pain ratings. Taken together, these findings implicate differential regulation of Avpr1a as a novel mechanism of VH-susceptibility as well as a potential therapeutic target specific to VH. |
| **Date** | 2023 Dec 19 |
| **Language** | eng |
| **Extra** | ISSN: 2692-8205 Journal Abbreviation: bioRxiv Pages: 2023.12.19.572390 Publication Title: bioRxiv : the preprint server for biology PMID: 38187732 PMCID: PMC10769202 |
| **Place** | United States |
| **DOI** | [10.1101/2023.12.19.572390](http://doi.org/10.1101/2023.12.19.572390) |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + enteric nervous system
  + irritable bowel syndrome
  + disorders of gut-brain interaction
  + genetics
  + visceral hypersensitivity

## IL-7 receptor influences anti-TNF responsiveness and T cell gut homing in inflammatory bowel disease.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Lyssia Belarif |
| **Author** | Richard Danger |
| **Author** | Laetitia Kermarrec |
| **Author** | Véronique Nerrière-Daguin |
| **Author** | Sabrina Pengam |
| **Author** | Tony Durand |
| **Author** | Caroline Mary |
| **Author** | Elise Kerdreux |
| **Author** | Vanessa Gauttier |
| **Author** | Aneta Kucik |
| **Author** | Virginie Thepenier |
| **Author** | Jerome C. Martin |
| **Author** | Christie Chang |
| **Author** | Adeeb Rahman |
| **Author** | Nina Salabert-Le Guen |
| **Author** | Cécile Braudeau |
| **Author** | Ahmed Abidi |
| **Author** | Grégoire David |
| **Author** | Florent Malard |
| **Author** | Celine Takoudju |
| **Author** | Bernard Martinet |
| **Author** | Nathalie Gérard |
| **Author** | Isabelle Neveu |
| **Author** | Michel Neunlist |
| **Author** | Emmanuel Coron |
| **Author** | Thomas T. MacDonald |
| **Author** | Pierre Desreumaux |
| **Author** | Hoa-Le Mai |
| **Author** | Stephanie Le Bas-Bernardet |
| **Author** | Jean-François Mosnier |
| **Author** | Miriam Merad |
| **Author** | Régis Josien |
| **Author** | Sophie Brouard |
| **Author** | Jean-Paul Soulillou |
| **Author** | Gilles Blancho |
| **Author** | Arnaud Bourreille |
| **Author** | Philippe Naveilhan |
| **Author** | Bernard Vanhove |
| **Author** | Nicolas Poirier |
| **Abstract** | It remains unknown what causes inflammatory bowel disease (IBD), including signaling networks perpetuating chronic gastrointestinal inflammation in Crohn's disease (CD) and ulcerative colitis (UC), in humans. According to an analysis of up to 500 patients with IBD and 100 controls, we report that key transcripts of the IL-7 receptor (IL-7R) pathway are accumulated in inflamed colon tissues of severe CD and UC patients not responding to either immunosuppressive/corticosteroid, anti-TNF, or anti-α4β7 therapies. High expression of both IL7R and IL-7R signaling signature in the colon before treatment is strongly associated with nonresponsiveness to anti-TNF therapy. While in mice IL-7 is known to play a role in systemic inflammation, we found that in humans IL-7 also controlled α4β7 integrin expression and imprinted gut-homing specificity on T cells. IL-7R blockade reduced human T cell homing to the gut and colonic inflammation in vivo in humanized mouse models, and altered effector T cells in colon explants from UC patients grown ex vivo. Our findings show that failure of current treatments for CD and UC is strongly associated with an overexpressed IL-7R signaling pathway and point to IL-7R as a relevant therapeutic target and potential biomarker to fill an unmet need in clinical IBD detection and treatment. |
| **Date** | 2019 Apr 2 |
| **Language** | eng |
| **Extra** | Place: United States PMID: 30939120 PMCID: PMC6486337 |
| **Volume** | 129 |
| **Pages** | 1910-1925 |
| **Publication** | The Journal of clinical investigation |
| **DOI** | [10.1172/JCI121668](http://doi.org/10.1172/JCI121668) |
| **Issue** | 5 |
| **Journal Abbr** | J Clin Invest |
| **ISSN** | 1558-8238 0021-9738 |
| **Date Added** | 6/11/2025, 2:32:27 PM |
| **Modified** | 6/11/2025, 2:32:27 PM |

### Tags:

* + Adult
  + Aged
  + Female
  + Humans
  + Male
  + Middle Aged
  + Animals
  + Mice
  + T cells
  + Young Adult
  + Signal Transduction
  + Gene Expression Profiling
  + Cytokines
  + Mice, SCID
  + Mice, Inbred NOD
  + Intestinal Mucosa/metabolism
  + Gene Expression Regulation
  + Cytokines/metabolism
  + Inflammation
  + Gastroenterology
  + Adolescent
  + Endoscopy
  + Colitis, Ulcerative/\*metabolism
  + Colon/\*metabolism/pathology
  + Crohn Disease/\*metabolism
  + Graft vs Host Disease/metabolism
  + Immunology
  + Inflammatory bowel disease
  + Integrins/metabolism
  + Leukocytes, Mononuclear/cytology
  + Receptors, Interleukin-7/\*metabolism
  + T-Lymphocytes/\*cytology
  + Tumor Necrosis Factor-alpha/\*antagonists & inhibitors

## Immune landscape of the enteric nervous system differentiates Parkinson's disease patients from controls: The PADUA-CESNE cohort.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Marta Campagnolo |
| **Author** | Luca Weis |
| **Author** | Michele Sandre |
| **Author** | Aleksandar Tushevski |
| **Author** | Francesco Paolo Russo |
| **Author** | Edoardo Savarino |
| **Author** | Miryam Carecchio |
| **Author** | Elena Stocco |
| **Author** | Veronica Macchi |
| **Author** | Raffaele De Caro |
| **Author** | Piero Parchi |
| **Author** | Luigi Bubacco |
| **Author** | Andrea Porzionato |
| **Author** | Angelo Antonini |
| **Author** | Aron Emmi |
| **Abstract** | BACKGROUND: Gastrointestinal dysfunction has emerged as a prominent early feature of Parkinson's Disease, shedding new light on the pivotal role of the enteric nervous system in its pathophysiology. However, the role of immune-cell clusters and inflammatory and glial markers in the gut pathogenetic process needs further elucidation. OBJECTIVES: We aimed to study duodenum tissue samples to characterize PD's enteric nervous system pathology further. Twenty patients with advanced PD, six with early PD, and 18 matched controls were included in the PADUA-CESNE cohort. METHODS: Duodenal biopsies from 26 patients with early to advanced stage PD and 18 age-matched HCs were evaluated for the presence of surface markers (CD3+, CD4+, CD8+, CD20+, CD68+, HLA-DR), presence of misfolded alpha-synuclein and enteric glial alteration (GFAP). Correlation of immulogic pattern and clinical characteristic were analyzed. RESULTS: The findings validate that in patients with Parkinson's Disease, the activation and reactive gliosis are linked to the neurodegeneration triggered by the presence of misfolded alpha-synuclein in the enteric nervous system. This process intensifies from the initial to the advanced stages of the disease. The clusters of T- and B-lymphocytes in the enteric system, along with the overall expression of HLA-DR in antigen-presenting cells, exceeded those in the control group. Conversely, no differences in terms of macrophage populations were found. CONCLUSIONS: These findings broaden our understanding of the mechanisms underlying the enteric nervous system's involvement in PD and point to the gastrointestinal system as a potential therapeutic target, especially in the early stages of the disease. Moreover, our results propose a role of T- and B-lymphocytes in maintaining inflammation and ultimately influencing alpha-synuclein misfolding and aggregation. |
| **Date** | 2024 Oct 1 |
| **Language** | eng |
| **Rights** | Copyright © 2024 The Authors. Published by Elsevier Inc. All rights reserved. |
| **Extra** | Place: United States PMID: 39048026 |
| **Volume** | 200 |
| **Pages** | 106609 |
| **Publication** | Neurobiology of disease |
| **DOI** | [10.1016/j.nbd.2024.106609](http://doi.org/10.1016/j.nbd.2024.106609) |
| **Journal Abbr** | Neurobiol Dis |
| **ISSN** | 1095-953X 0969-9961 |
| **Date Added** | 6/11/2025, 2:32:23 PM |
| **Modified** | 6/11/2025, 2:32:23 PM |

### Tags:

* + Aged
  + Female
  + Humans
  + Male
  + Middle Aged
  + Cohort Studies
  + Biomarkers
  + Inflammation
  + Gut
  + Alpha-synuclein
  + Immune system
  + \*Enteric Nervous System/immunology/pathology/metabolism
  + \*Parkinson Disease/immunology/metabolism/pathology
  + alpha-Synuclein/metabolism/immunology
  + Duodenum/immunology/pathology/metabolism
  + Parkinson's disease's

## Impact of chemotherapy on gastrointestinal functions and the enteric nervous system.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Jonathan Escalante |
| **Author** | Rachel M. McQuade |
| **Author** | Vanesa Stojanovska |
| **Author** | Kulmira Nurgali |
| **Abstract** | Chemotherapy is the main treatment for many cancers, including colorectal cancer, a type of cancer with some of the highest prevalence and mortality rates worldwide. Although chemotherapeutic drugs have greatly improved the survival rates of cancer patients, there are many side-effects associated with their use. The gastrointestinal side-effects of chemotherapy often lead to dose reduction or even discontinuation of treatment, which in turn affects the clinical outcome. Gastrointestinal side-effects, such as chemotherapy-induced diarrhea and constipation, may persist many years after treatment, greatly reducing quality of life. Current treatments for these side-effects have many adverse effects themselves; therefore, new approaches are needed to address this problem. Changes in the enteric nervous system located within the gastrointestinal tract and controlling its functions have been implicated in many disorders. Recent studies providing insight into the association between chemotherapy-induced damage to enteric neurons and gastrointestinal dysfunction have highlighted the enteric nervous system as a potential therapeutic target to alleviate chemotherapy-induced toxicity which may improve both clinical outcomes and the quality of patients' lives. |
| **Date** | 2017 Nov |
| **Language** | eng |
| **Rights** | Copyright © 2017 Elsevier B.V. All rights reserved. |
| **Extra** | Place: Ireland PMID: 28545907 |
| **Volume** | 105 |
| **Pages** | 23-29 |
| **Publication** | Maturitas |
| **DOI** | [10.1016/j.maturitas.2017.04.021](http://doi.org/10.1016/j.maturitas.2017.04.021) |
| **Journal Abbr** | Maturitas |
| **ISSN** | 1873-4111 0378-5122 |
| **Date Added** | 6/11/2025, 2:32:23 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Animals
  + Quality of Life
  + Chemotherapy
  + Antineoplastic Agents/\*adverse effects
  + Chemotherapy-induced constipation
  + Chemotherapy-induced diarrhea
  + Colorectal Neoplasms/\*drug therapy/physiopathology
  + Constipation/\*chemically induced
  + Diarrhea/\*chemically induced
  + Enteric Nervous System/\*drug effects/physiology
  + Enteric neuropathy

## Impact of Intestinal Peptides on the Enteric Nervous System: Novel Approaches to Control Glucose Metabolism and Food Intake.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Anne Abot |
| **Author** | Patrice D. Cani |
| **Author** | Claude Knauf |
| **Abstract** | The gut is one of the most important sources of bioactive peptides in the body. In addition to their direct actions in the brain and/or peripheral tissues, the intestinal peptides can also have an impact on enteric nervous neurons. By modifying the endogenousproduction of these peptides, one may expect modify the "local" physiology such as glucose absorption, but also could have a "global" action via the gut-brain axis. Due to the various origins of gut peptides (i.e., nutrients, intestinal wall, gut microbiota) and the heterogeneity of enteric neurons population, the potential physiological parameters control by the interaction between the two partners are multiple. In this review, we will exclusively focus on the role of enteric nervous system as a potential target of gut peptides to control glucose metabolism and food intake. Potential therapeutic strategies based on per os administration of gut peptides to treat type 2 diabetes will be described. |
| **Date** | 2018 |
| **Language** | eng |
| **Extra** | Place: Switzerland PMID: 29988396 PMCID: PMC6023997 |
| **Volume** | 9 |
| **Pages** | 328 |
| **Publication** | Frontiers in endocrinology |
| **DOI** | [10.3389/fendo.2018.00328](http://doi.org/10.3389/fendo.2018.00328) |
| **Journal Abbr** | Front Endocrinol (Lausanne) |
| **ISSN** | 1664-2392 |
| **Date Added** | 6/11/2025, 2:32:23 PM |
| **Modified** | 6/11/2025, 2:32:23 PM |

### Tags:

* + diabetes
  + enteric nervous system
  + bioactive peptides
  + food intake
  + glucose metabolism

## Impact of Siponimod on Enteric and Central Nervous System Pathology in Late-Stage Experimental Autoimmune Encephalomyelitis.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Alicia Weier |
| **Author** | Michael Enders |
| **Author** | Philipp Kirchner |
| **Author** | Arif Ekici |
| **Author** | Marc Bigaud |
| **Author** | Christopher Kapitza |
| **Author** | Jürgen Wörl |
| **Author** | Stefanie Kuerten |
| **Abstract** | Multiple sclerosis (MS) is an autoimmune disease of the central nervous system (CNS). Although immune modulation and suppression are effective during relapsing-remitting MS, secondary progressive MS (SPMS) requires neuroregenerative therapeutic options that act on the CNS. The sphingosine-1-phosphate receptor modulator siponimod is the only approved drug for SPMS. In the pivotal trial, siponimod reduced disease progression and brain atrophy compared with placebo. The enteric nervous system (ENS) was recently identified as an additional autoimmune target in MS. We investigated the effects of siponimod on the ENS and CNS in the experimental autoimmune encephalomyelitis model of MS. Mice with late-stage disease were treated with siponimod, fingolimod, or sham. The clinical disease was monitored daily, and treatment success was verified using mass spectrometry and flow cytometry, which revealed peripheral lymphopenia in siponimod- and fingolimod-treated mice. We evaluated the mRNA expression, ultrastructure, and histopathology of the ENS and CNS. Single-cell RNA sequencing revealed an upregulation of proinflammatory genes in spinal cord astrocytes and ependymal cells in siponimod-treated mice. However, differences in CNS and ENS histopathology and ultrastructural pathology between the treatment groups were absent. Thus, our data suggest that siponimod and fingolimod act on the peripheral immune system and do not have pronounced direct neuroprotective effects. |
| **Date** | 2022 Nov 17 |
| **Language** | eng |
| **Extra** | Place: Switzerland PMID: 36430692 PMCID: PMC9695324 |
| **Volume** | 23 |
| **Publication** | International journal of molecular sciences |
| **DOI** | [10.3390/ijms232214209](http://doi.org/10.3390/ijms232214209) |
| **Issue** | 22 |
| **Journal Abbr** | Int J Mol Sci |
| **ISSN** | 1422-0067 |
| **Date Added** | 6/11/2025, 2:32:23 PM |
| **Modified** | 6/11/2025, 2:32:23 PM |

### Tags:

* + Animals
  + Mice
  + enteric nervous system
  + central nervous system
  + \*Encephalomyelitis, Autoimmune, Experimental/drug therapy
  + \*Multiple Sclerosis/drug therapy/pathology
  + Benzyl Compounds/pharmacology
  + Central Nervous System/pathology
  + experimental autoimmune encephalomyelitis
  + fingolimod
  + Fingolimod Hydrochloride/pharmacology/therapeutic use
  + multiple sclerosis
  + siponimod

## Inflammation-associated changes in DOR expression and function in the mouse colon.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Jesse J. DiCello |
| **Author** | Ayame Saito |
| **Author** | Pradeep Rajasekhar |
| **Author** | Emily M. Eriksson |
| **Author** | Rachel M. McQuade |
| **Author** | Cameron J. Nowell |
| **Author** | Benjamin W. Sebastian |
| **Author** | Jakub Fichna |
| **Author** | Nicholas A. Veldhuis |
| **Author** | Meritxell Canals |
| **Author** | Nigel W. Bunnett |
| **Author** | Simona E. Carbone |
| **Author** | Daniel P. Poole |
| **Abstract** | Endogenous opioids activate opioid receptors (ORs) in the enteric nervous system to control intestinal motility and secretion. The μ-OR mediates the deleterious side effects of opioid analgesics, including constipation, respiratory depression, and addiction. Although the δ-OR (DOR) is a promising target for analgesia, the function and regulation of DOR in the colon are poorly understood. This study provides evidence that endogenous opioids activate DOR in myenteric neurons that may regulate colonic motility. The DOR agonists DADLE, deltorphin II, and SNC80 inhibited electrically evoked contractions and induced neurogenic contractions in the mouse colon. Electrical, chemical, and mechanical stimulation of the colon evoked the release of endogenous opioids, which stimulated endocytosis of DOR in the soma and proximal neurites of myenteric neurons of transgenic mice expressing DOR fused to enhanced green fluorescent protein. In contrast, DOR was not internalized in nerve fibers within the circular muscle. Administration of dextran sulfate sodium induced acute colitis, which was accompanied by DOR endocytosis and an increased density of DOR-positive nerve fibers within the circular muscle. The potency with which SNC80 inhibited neurogenic contractions was significantly enhanced in the inflamed colon. This study demonstrates that DOR-expressing neurons in the mouse colon can be activated by exogenous and endogenous opioids. Activated DOR traffics to endosomes and inhibits neurogenic motility of the colon. DOR signaling is enhanced during intestinal inflammation. This study demonstrates functional expression of DOR by myenteric neurons and supports the therapeutic targeting of DOR in the enteric nervous system. NEW & NOTEWORTHY DOR is activated during physiologically relevant reflex stimulation. Agonist-evoked DOR endocytosis is spatially and temporally regulated. A significant proportion of DOR is internalized in myenteric neurons during inflammation. The relative proportion of all myenteric neurons that expressed DOR and the overlap with the nNOS-positive population are increased in inflammation. DOR-specific innervation of the circular muscle is increased in inflammation, and this is consistent with enhanced responsiveness to the DOR agonist SNC80. |
| **Date** | 2018 Oct 1 |
| **Language** | eng |
| **Extra** | Place: United States PMID: 29927325 PMCID: PMC6230691 |
| **Volume** | 315 |
| **Pages** | G544-G559 |
| **Publication** | American journal of physiology. Gastrointestinal and liver physiology |
| **DOI** | [10.1152/ajpgi.00025.2018](http://doi.org/10.1152/ajpgi.00025.2018) |
| **Issue** | 4 |
| **Journal Abbr** | Am J Physiol Gastrointest Liver Physiol |
| **ISSN** | 1522-1547 0193-1857 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Female
  + Male
  + Animals
  + Mice
  + Mice, Inbred C57BL
  + enteric nervous system
  + Benzamides/pharmacology
  + Endocytosis
  + Piperazines/pharmacology
  + \*Gastrointestinal Motility
  + Colitis, Ulcerative/\*metabolism
  + Colon/\*metabolism/physiology/physiopathology
  + endocytosis
  + Enkephalin, Leucine-2-Alanine/metabolism
  + Enteric Nervous System/\*metabolism/physiology/physiopathology
  + G protein-coupled receptor, intestinal motility
  + Muscle Contraction
  + Oligopeptides/metabolism
  + opioid receptor
  + Receptors, Opioid, delta/agonists/genetics/\*metabolism

## Inflammatory bowel disease therapeutic strategies by modulation of the microbiota: how and when to introduce pre-, pro-, syn-, or postbiotics?

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Amélie Lê |
| **Author** | Marine Mantel |
| **Author** | Justine Marchix |
| **Author** | Marie Bodinier |
| **Author** | Gwénaël Jan |
| **Author** | Malvyne Rolli-Derkinderen |
| **Abstract** | Inflammatory bowel diseases (IBD), a heterogeneous group of inflammatory conditions that encompass both ulcerative colitis and Crohn's disease, represent a major public health concern. The etiology of IBD is not yet fully understood and no cure is available, with current treatments only showing long-term effectiveness in a minority of patients. A need to increase our knowledge on IBD pathophysiology is growing, to define preventive measures, to improve disease outcome, and to develop new effective and lasting treatments. IBD pathogenesis is sustained by aberrant immune responses, associated with alterations of the intestinal epithelial barrier (IEB), modifications of the enteric nervous system, and changes in microbiota composition. Currently, most of the treatments target the inflammation and the immune system, but holistic approaches targeting lifestyle and diet improvements are emerging. As dysbiosis is involved in IBD pathogenesis, pre-, pro-, syn-, and postbiotics are used/tested to reduce the inflammation or strengthen the IEB. The present review will resume these works, pointing out the stage of life, the duration, and the environmental conditions that should go along with microbiota or microbiota-derived treatments. |
| **Date** | 2022 Dec 1 |
| **Language** | eng |
| **Extra** | Place: United States PMID: 36165557 |
| **Volume** | 323 |
| **Pages** | G523-G553 |
| **Publication** | American journal of physiology. Gastrointestinal and liver physiology |
| **DOI** | [10.1152/ajpgi.00002.2022](http://doi.org/10.1152/ajpgi.00002.2022) |
| **Issue** | 6 |
| **Journal Abbr** | Am J Physiol Gastrointest Liver Physiol |
| **ISSN** | 1522-1547 0193-1857 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/11/2025, 2:32:25 PM |

### Tags:

* + Humans
  + Inflammation
  + microbiota
  + \*Microbiota
  + probiotic
  + \*Inflammatory Bowel Diseases
  + IBD
  + \*Colitis, Ulcerative/pathology
  + Dysbiosis/therapy
  + n − 6
  + prebiotic

## Ingestible transiently anchoring electronics for microstimulation and conductive signaling.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Alex Abramson |
| **Author** | David Dellal |
| **Author** | Yong Lin Kong |
| **Author** | Jianlin Zhou |
| **Author** | Yuan Gao |
| **Author** | Joy Collins |
| **Author** | Siddartha Tamang |
| **Author** | Jacob Wainer |
| **Author** | Rebecca McManus |
| **Author** | Alison Hayward |
| **Author** | Morten Revsgaard Frederiksen |
| **Author** | Jorrit J. Water |
| **Author** | Brian Jensen |
| **Author** | Niclas Roxhed |
| **Author** | Robert Langer |
| **Author** | Giovanni Traverso |
| **Abstract** | Ingestible electronic devices enable noninvasive evaluation and diagnosis of pathologies in the gastrointestinal (GI) tract but generally cannot therapeutically interact with the tissue wall. Here, we report the development of an orally administered electrical stimulation device characterized in ex vivo human tissue and in in vivo swine models, which transiently anchored itself to the stomach by autonomously inserting electrically conductive, hooked probes. The probes provided stimulation to the tissue via timed electrical pulses that could be used as a treatment for gastric motility disorders. To demonstrate interaction with stomach muscle tissue, we used the electrical stimulation to induce acute muscular contractions. Pulses conductively signaled the probes' successful anchoring and detachment events to a parenterally placed device. The ability to anchor into and electrically interact with targeted GI tissues controlled by the enteric nervous system introduces opportunities to treat a multitude of associated pathologies. |
| **Date** | 2020 Aug |
| **Language** | eng |
| **Rights** | Copyright © 2020 The Authors, some rights reserved; exclusive licensee American Association for the Advancement of Science. No claim to original U.S. Government Works. Distributed under a Creative Commons Attribution License 4.0 (CC BY). |
| **Extra** | Place: United States PMID: 32923616 PMCID: PMC7455191 |
| **Volume** | 6 |
| **Pages** | eaaz0127 |
| **Publication** | Science advances |
| **DOI** | [10.1126/sciadv.aaz0127](http://doi.org/10.1126/sciadv.aaz0127) |
| **Issue** | 35 |
| **Journal Abbr** | Sci Adv |
| **ISSN** | 2375-2548 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/11/2025, 2:32:26 PM |

## Inhibition of APE1/Ref-1 Redox Signaling Alleviates Intestinal Dysfunction and Damage to Myenteric Neurons in a Mouse Model of Spontaneous Chronic Colitis.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Lauren Sahakian |
| **Author** | Rhiannon T. Filippone |
| **Author** | Rhian Stavely |
| **Author** | Ainsley M. Robinson |
| **Author** | Xu Sean Yan |
| **Author** | Raquel Abalo |
| **Author** | Rajaraman Eri |
| **Author** | Joel C. Bornstein |
| **Author** | Mark R. Kelley |
| **Author** | Kulmira Nurgali |
| **Abstract** | BACKGROUND: Inflammatory bowel disease (IBD) associates with damage to the enteric nervous system (ENS), leading to gastrointestinal (GI) dysfunction. Oxidative stress is important for the pathophysiology of inflammation-induced enteric neuropathy and GI dysfunction. Apurinic/apyrimidinic endonuclease 1/redox factor-1 (APE1/Ref-1) is a dual functioning protein that is an essential regulator of the cellular response to oxidative stress. In this study, we aimed to determine whether an APE1/Ref-1 redox domain inhibitor, APX3330, alleviates inflammation-induced oxidative stress that leads to enteric neuropathy in the Winnie murine model of spontaneous chronic colitis. METHODS: Winnie mice received APX3330 or vehicle via intraperitoneal injections over 2 weeks and were compared with C57BL/6 controls. In vivo disease activity and GI transit were evaluated. Ex vivo experiments were performed to assess functional parameters of colonic motility, immune cell infiltration, and changes to the ENS. RESULTS: Targeting APE1/Ref-1 redox activity with APX3330 improved disease severity, reduced immune cell infiltration, restored GI function ,and provided neuroprotective effects to the enteric nervous system. Inhibition of APE1/Ref-1 redox signaling leading to reduced mitochondrial superoxide production, oxidative DNA damage, and translocation of high mobility group box 1 protein (HMGB1) was involved in neuroprotective effects of APX3330 in enteric neurons. CONCLUSIONS: This study is the first to investigate inhibition of APE1/Ref-1's redox activity via APX3330 in an animal model of chronic intestinal inflammation. Inhibition of the redox function of APE1/Ref-1 is a novel strategy that might lead to a possible application of APX3330 for the treatment of IBD. |
| **Date** | 2021 Feb 16 |
| **Language** | eng |
| **Rights** | © 2020 Crohn’s & Colitis Foundation. Published by Oxford University Press. All rights reserved. For permissions, please e-mail: journals.permissions@oup.com. |
| **Extra** | Place: England PMID: 32618996 PMCID: PMC8287929 |
| **Volume** | 27 |
| **Pages** | 388-406 |
| **Publication** | Inflammatory bowel diseases |
| **DOI** | [10.1093/ibd/izaa161](http://doi.org/10.1093/ibd/izaa161) |
| **Issue** | 3 |
| **Journal Abbr** | Inflamm Bowel Dis |
| **ISSN** | 1536-4844 1078-0998 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Animals
  + Disease Models, Animal
  + Mice
  + Mice, Inbred C57BL
  + DNA damage
  + Neurons
  + Inflammation/drug therapy
  + enteric nervous system
  + \*Colitis/chemically induced/drug therapy
  + \*Intestinal Pseudo-Obstruction
  + APE1/Ref-1
  + APX3330
  + chronic intestinal inflammation
  + DNA-(Apurinic or Apyrimidinic Site) Lyase/\*metabolism
  + IBD
  + Neuroprotective Agents/\*therapeutic use
  + Oxidation-Reduction
  + oxidative stress
  + Oxidative Stress

## Insights into the Role of Opioid Receptors in the GI Tract: Experimental Evidence and Therapeutic Relevance.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | James J. Galligan |
| **Author** | Catia Sternini |
| **Abstract** | Opioid drugs are prescribed extensively for pain treatment but when used chronically they induce constipation that can progress to opioid-induced bowel dysfunction. Opioid drugs interact with three classes of opioid receptors: mu opioid receptors (MORs), delta opioid receptors (DOR), and kappa opioid receptors (KORs), but opioid drugs mostly target the MORs. Upon stimulation, opioid receptors couple to inhibitory Gi/Go proteins that activate or inhibit downstream effector proteins. MOR and DOR couple to inhibition of adenylate cyclase and voltage-gated Ca(2+) channels and to activation of K(+) channels resulting in reduced neuronal activity and neurotransmitter release. KORs couple to inhibition of Ca(2+) channels and neurotransmitter release. In the gastrointestinal tract, opioid receptors are localized to enteric neurons, interstitial cells of Cajal, and immune cells. In humans, MOR, DOR, and KOR link to inhibition of acetylcholine release from enteric interneurons and motor neurons and purine/nitric oxide release from inhibitory motor neurons causing inhibition of propulsive motility patterns. MOR and DOR activation also results in inhibition of submucosal secretomotor neurons reducing active Cl(-) secretion and passive water movement into the colonic lumen. Together, these effects on motility and secretion account for the constipation caused by opioid receptor agonists. Tolerance develops to the analgesic effects of opioid receptor agonists but not to the constipating actions. This may be due to differences in trafficking and downstream signaling in enteric nerves in the colon compared to the small intestine and in neuronal pain pathways. Further studies of differential opioid receptor desensitization and tolerance in subsets of enteric neurons may identify new drug or other treatment strategies of opioid-induced bowel dysfunction. |
| **Date** | 2017 |
| **Language** | eng |
| **Extra** | Place: Germany PMID: 28204957 PMCID: PMC6310692 |
| **Volume** | 239 |
| **Pages** | 363-378 |
| **Publication** | Handbook of experimental pharmacology |
| **DOI** | [10.1007/164\_2016\_116](http://doi.org/10.1007/164_2016_116) |
| **Journal Abbr** | Handb Exp Pharmacol |
| **ISSN** | 0171-2004 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/11/2025, 2:32:26 PM |

### Tags:

* + Humans
  + Animals
  + Protein Transport
  + Enteric nervous system
  + Constipation
  + \*Gastrointestinal Motility/drug effects
  + \*Signal Transduction/drug effects
  + Analgesics, Opioid/adverse effects
  + Constipation/chemically induced/physiopathology
  + Drug tolerance
  + Drug Tolerance
  + Enteric Nervous System/drug effects/\*metabolism/physiopathology
  + Gastrointestinal Tract/drug effects/innervation/\*metabolism/physiopathology
  + Opiates
  + Receptors, Opioid/drug effects/\*metabolism

## Interaction between the Renin-Angiotensin System and Enteric Neurotransmission Contributes to Colonic Dysmotility in the TNBS-Induced Model of Colitis.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Mariana Ferreira-Duarte |
| **Author** | Tiago Rodrigues-Pinto |
| **Author** | Teresa Sousa |
| **Author** | Miguel A. Faria |
| **Author** | Maria Sofia Rocha |
| **Author** | Daniela Menezes-Pinto |
| **Author** | Marisa Esteves-Monteiro |
| **Author** | Fernando Magro |
| **Author** | Patrícia Dias-Pereira |
| **Author** | Margarida Duarte-Araújo |
| **Author** | Manuela Morato |
| **Abstract** | Angiotensin II (Ang II) regulates colon contraction, acting not only directly on smooth muscle but also indirectly, interfering with myenteric neuromodulation mediated by the activation of AT(1) /AT(2) receptors. In this article, we aimed to explore which mediators and cells were involved in Ang II-mediated colonic contraction in the TNBS-induced rat model of colitis. The contractile responses to Ang II were evaluated in distinct regions of the colon of control animals or animals with colitis in the absence and presence of different antagonists/inhibitors. Endogenous levels of Ang II in the colon were assessed by ELISA and the number of AT(1)/AT(2) receptors by qPCR. Ang II caused AT(1) receptor-mediated colonic contraction that was markedly decreased along the colons of TNBS-induced rats, consistent with reduced AT(1) mRNA expression. However, the effect mediated by Ang II is much more intricate, involving (in addition to smooth muscle cells and nerve terminals) ICC and EGC, which communicate by releasing ACh and NO in a complex mechanism that changes colitis, unveiling new therapeutic targets. |
| **Date** | 2021 May 3 |
| **Language** | eng |
| **Extra** | Place: Switzerland PMID: 34063607 PMCID: PMC8125095 |
| **Volume** | 22 |
| **Publication** | International journal of molecular sciences |
| **DOI** | [10.3390/ijms22094836](http://doi.org/10.3390/ijms22094836) |
| **Issue** | 9 |
| **Journal Abbr** | Int J Mol Sci |
| **ISSN** | 1422-0067 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/11/2025, 2:32:26 PM |

### Tags:

* + Humans
  + Male
  + Animals
  + Rats
  + inflammatory bowel disease
  + IBD
  + nitric oxide
  + Colon/metabolism/pathology
  + enteric glial cells
  + ICC
  + interstitial cells of Cajal
  + angiotensin II
  + Angiotensin II/\*genetics
  + Angiotensin Receptor Antagonists/pharmacology
  + AT1 and AT2 receptors
  + Colitis/\*genetics/physiopathology
  + colonic dysmotility
  + EGC
  + Enteric Nervous System/metabolism/pathology
  + Inflammatory Bowel Diseases/\*genetics/pathology
  + Interstitial Cells of Cajal/metabolism/pathology
  + Muscle Contraction/genetics/physiology
  + Muscle, Smooth, Vascular/drug effects
  + Neuroglia/metabolism/pathology
  + Nitric Oxide/metabolism
  + Receptor, Angiotensin, Type 1/genetics
  + Receptor, Angiotensin, Type 2/genetics
  + Renin-Angiotensin System/\*genetics
  + Synaptic Transmission/genetics
  + TNBS-induced colitis

## Intestinal Enteroendocrine Cells: Present and Future Druggable Targets.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Roger Atanga |
| **Author** | Varsha Singh |
| **Author** | Julie G. In |
| **Abstract** | Enteroendocrine cells are specialized secretory lineage cells in the small and large intestines that secrete hormones and peptides in response to luminal contents. The various hormones and peptides can act upon neighboring cells and as part of the endocrine system, circulate systemically via immune cells and the enteric nervous system. Locally, enteroendocrine cells have a major role in gastrointestinal motility, nutrient sensing, and glucose metabolism. Targeting the intestinal enteroendocrine cells or mimicking hormone secretion has been an important field of study in obesity and other metabolic diseases. Studies on the importance of these cells in inflammatory and auto-immune diseases have only recently been reported. The rapid global increase in metabolic and inflammatory diseases suggests that increased understanding and novel therapies are needed. This review will focus on the association between enteroendocrine changes and metabolic and inflammatory disease progression and conclude with the future of enteroendocrine cells as potential druggable targets. |
| **Date** | 2023 May 16 |
| **Language** | eng |
| **Extra** | Place: Switzerland PMID: 37240181 PMCID: PMC10218851 |
| **Volume** | 24 |
| **Publication** | International journal of molecular sciences |
| **DOI** | [10.3390/ijms24108836](http://doi.org/10.3390/ijms24108836) |
| **Issue** | 10 |
| **Journal Abbr** | Int J Mol Sci |
| **ISSN** | 1422-0067 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + therapeutics
  + Biological Transport
  + inflammatory bowel disease
  + Hormones/metabolism
  + \*Enteroendocrine Cells/metabolism
  + \*Intestines
  + enteroendocrine cells
  + intestinal hormones
  + metabolic disease
  + Peptides/metabolism

## Iron Dysregulation and Inflammagens Related to Oral and Gut Health Are Central to the Development of Parkinson's Disease.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Marthinus Janse van Vuuren |
| **Author** | Theodore Albertus Nell |
| **Author** | Jonathan Ambrose Carr |
| **Author** | Douglas B. Kell |
| **Author** | Etheresia Pretorius |
| **Abstract** | Neuronal lesions in Parkinson's disease (PD) are commonly associated with α-synuclein (α-Syn)-induced cell damage that are present both in the central and peripheral nervous systems of patients, with the enteric nervous system also being especially vulnerable. Here, we bring together evidence that the development and presence of PD depends on specific sets of interlinking factors that include neuroinflammation, systemic inflammation, α-Syn-induced cell damage, vascular dysfunction, iron dysregulation, and gut and periodontal dysbiosis. We argue that there is significant evidence that bacterial inflammagens fuel this systemic inflammation, and might be central to the development of PD. We also discuss the processes whereby bacterial inflammagens may be involved in causing nucleation of proteins, including of α-Syn. Lastly, we review evidence that iron chelation, pre-and probiotics, as well as antibiotics and faecal transplant treatment might be valuable treatments in PD. A most important consideration, however, is that these therapeutic options need to be validated and tested in randomized controlled clinical trials. However, targeting underlying mechanisms of PD, including gut dysbiosis and iron toxicity, have potentially opened up possibilities of a wide variety of novel treatments, which may relieve the characteristic motor and nonmotor deficits of PD, and may even slow the progression and/or accompanying gut-related conditions of the disease. |
| **Date** | 2020 Dec 29 |
| **Language** | eng |
| **Extra** | Place: Switzerland PMID: 33383805 PMCID: PMC7823713 |
| **Volume** | 11 |
| **Publication** | Biomolecules |
| **DOI** | [10.3390/biom11010030](http://doi.org/10.3390/biom11010030) |
| **Issue** | 1 |
| **Journal Abbr** | Biomolecules |
| **ISSN** | 2218-273X |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/11/2025, 2:32:25 PM |

### Tags:

* + Humans
  + Animals
  + iron
  + Parkinson’s disease
  + Oxidative Stress
  + alpha-Synuclein/metabolism
  + amyloid and α-synuclein
  + bacteria
  + Dysbiosis/complications/\*metabolism/physiopathology
  + Gastrointestinal Microbiome
  + gingipains
  + Inflammation/complications/\*metabolism/physiopathology
  + Iron/\*metabolism
  + lipopolysaccharides
  + Mouth/microbiology
  + Parkinson Disease/etiology/\*metabolism/physiopathology

## Irritable Bowel Syndrome and Stress-Related Psychiatric Co-morbidities: Focus on Early Life Stress.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Siobhain M. O'Mahony |
| **Author** | Gerard Clarke |
| **Author** | Timothy G. Dinan |
| **Author** | John F. Cryan |
| **Abstract** | Irritable bowel syndrome is a functional gastrointestinal disorder, with stress playing a major role in onset and exacerbation of symptoms such as abdominal pain and altered bowel movements. Stress-related disorders including anxiety and depression often precede the development of irritable bowel syndrome and vice versa. Stressor exposure during early life has the potential to increase an individual's susceptibility to both irritable bowel syndrome and psychiatric disease indicating that there may be a common origin for these disorders. Moreover, adverse early life events significantly impact upon many of the communication pathways within the brain-gut-microbiota axis, which allows bidirectional interaction between the central nervous system and the gastrointestinal tract. This axis is proposed to be perturbed in irritable bowel syndrome and studies now indicate that dysfunction of this axis is also seen in psychiatric disease. Here we review the co-morbidity of irritable bowel syndrome and psychiatric disease with their common origin in mind in relation to the impact of early life stress on the developing brain-gut-microbiota axis. We also discuss the therapeutic potential of targeting this axis in these diseases. |
| **Date** | 2017 |
| **Language** | eng |
| **Extra** | Place: Germany PMID: 28233180 |
| **Volume** | 239 |
| **Pages** | 219-246 |
| **Publication** | Handbook of experimental pharmacology |
| **DOI** | [10.1007/164\_2016\_128](http://doi.org/10.1007/164_2016_128) |
| **Journal Abbr** | Handb Exp Pharmacol |
| **ISSN** | 0171-2004 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/11/2025, 2:32:25 PM |

### Tags:

* + Humans
  + Animals
  + Comorbidity
  + Prognosis
  + Host-Pathogen Interactions
  + Risk Factors
  + Age Factors
  + Irritable bowel syndrome
  + Enteric Nervous System/\*physiopathology
  + Gastrointestinal Microbiome
  + Brain-gut-microbiota axis
  + Brain/physiopathology
  + Depression
  + Early life stress
  + Health Status
  + Intestines/\*innervation/microbiology
  + Irritable Bowel Syndrome/epidemiology/physiopathology/\*psychology/therapy
  + Psychiatric disease
  + Stress, Psychological/epidemiology/physiopathology/\*psychology/therapy

## Long-Term Oncologic Outcome following Duodenum-Preserving Pancreatic Head Resection for Benign Tumors, Cystic Neoplasms, and Neuroendocrine Tumors: Systematic Review and Meta-analysis

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Hans G Beger |
| **Author** | Benjamin Mayer |
| **Author** | Bertram Poch |
| **Date** | 2024 |
| **URL** | <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11164799/> |
| **Volume** | 31 |
| **Pages** | 4637–4653 |
| **Publication** | Annals of Surgical Oncology |
| **DOI** | [10.1245/s10434-024-15222-y](http://doi.org/10.1245/s10434-024-15222-y) |
| **Issue** | 7 |
| **Date Added** | 4/16/2025, 11:10:32 PM |
| **Modified** | 6/16/2025, 1:12:21 PM |

### Tags:

* + Adult
  + Female
  + Humans
  + Male
  + Treatment Outcome
  + Animals
  + Disease Models, Animal
  + Mice
  + STING
  + Quality of Life
  + Retrospective Studies
  + Diabetes
  + Signal Transduction
  + Cell Differentiation
  + Cell Line
  + Neoplasm Recurrence, Local
  + Cell Movement
  + Mammals
  + Neurons
  + immune cells
  + inflammation
  + Homeostasis
  + Gastroenterology
  + intestinal organoids
  + Regeneration
  + microbiota
  + Pancreas
  + inflammatory bowel disease
  + \*Cell- and Tissue-Based Therapy/methods
  + \*Bile Duct Neoplasms
  + \*Bile Duct Neoplasms/surgery
  + \*Cell Lineage
  + \*Cholangiocarcinoma
  + \*Cholangiocarcinoma/pathology
  + \*Colitis, Ulcerative/drug therapy
  + \*Cystadenocarcinoma/diagnostic imaging/surgery
  + \*Cystadenoma/diagnostic imaging/surgery
  + \*Cysts/pathology
  + \*Diabetes Mellitus, Experimental/complications/genetics/metabolism
  + \*Enteric Nervous System
  + \*Enteric Nervous System/pathology
  + \*Hyperglycemia/genetics/metabolism
  + \*Hypothalamo-Hypophyseal System
  + \*Inflammatory Bowel Diseases/drug therapy
  + \*Liver Neoplasms/diagnostic imaging/surgery
  + \*Liver Neoplasms/surgery
  + \*Microbiota
  + \*MicroRNAs/metabolism
  + \*Neoplasms, Cystic, Mucinous, and Serous
  + \*Neuroglia/physiology
  + \*Zebrafish
  + 16S RNA sequencing
  + Acinar cell carcinoma
  + Aging
  + antibiotics
  + Bile Ducts, Intrahepatic
  + Bile Ducts, Intrahepatic/surgery
  + Biliary
  + Biliary cystadenocarcinoma
  + Biliary cystadenoma
  + Brain
  + Brain-Gut Axis
  + Brain/physiology
  + Cell Separation
  + Chemical coding
  + Chick Embryo
  + circVPS13A
  + Cistoadenocarcinoma
  + Cistoadenoma
  + Clinicopathological criteria, Surgical outcomes
  + Colon/drug effects/pathology
  + Cystadenocarcinoma
  + Cystadenoma
  + cystic liver lesions
  + Cystic liver neoplasm
  + Cytology
  + Developmental disorders
  + diabetes
  + diabetes mellitus
  + Drug Discovery/\*methods
  + Embryonic stem cells
  + ENS
  + ENS neuropathies
  + enteric glia
  + enteric glia communications
  + Enteric glia communications
  + enteric glia diversity
  + enteric nervous system
  + Enteric nervous system
  + Enteric Nervous System
  + enteric nervous system (ENS)
  + Enteric nervous system (ENS)
  + Enteric Nervous System/\*pathology
  + Enteric neural precursor cells (ENPCs)
  + enteric progenitor cell
  + Fecal microbiota transplantation
  + Frantz's tumor
  + gastrointestinal complications
  + gastrointestinal diseases
  + Gastrointestinal Diseases
  + Gastrointestinal Diseases/pathology
  + gastrointestinal tract
  + Gastrointestinal Tract/drug effects/pathology
  + glia
  + Glial Cell Line-Derived Neurotrophic Factor/genetics
  + glucagon-like peptide 1
  + Growth Disorders
  + growth retardation
  + gut brain axis
  + gut microbiota
  + gut-brain axis
  + gut–brain axis
  + hepatic cystadenocarcinoma
  + hepatic cystadenoma
  + Hepatic simple cyst
  + hepatobiliary cystadenocarcinoma
  + hepatobiliary cystadenoma
  + Hirschsprung disease
  + Hirschsprung Disease/\*drug therapy/\*pathology/therapy
  + homeostasis
  + Imaging modalities
  + In Situ Hybridization, Fluorescence
  + Inflammatory bowel diseases
  + Intraductal papillary biliary neoplasms
  + intraductal papillary neoplasms of bile duct
  + irritable bowel syndrome
  + L-Fucose
  + Liver Diseases
  + Management
  + microbial metabolites
  + microbiota-gut-brain axis
  + Microbiota-gut-brain axis
  + Mucinous biliary cystic tumors, Biliary cystadenoma
  + mucinous cystic neoplasm
  + Mucinous cystic neoplasms
  + Mucinous neoplasm
  + muscularis macrophages
  + myenteric neurons
  + Neoplasia mucinosa quística
  + Neoplasia papilar intraductal biliar
  + Neoplasia quística hepática
  + Neural Crest
  + neural crest cell
  + neurodegeneration
  + Neuroglia
  + Neurons/drug effects/\*pathology
  + offspring
  + P2X7 receptor
  + pancreatectomy
  + Pancreatectomy
  + Pancreatic neoplasms
  + Pancreatic Neoplasms
  + Pancreatic surgery
  + pancreatic tumor
  + Parkinson’s disease
  + pediatric pancreatic neoplasm
  + Pepstatins/metabolism
  + Pituitary-Adrenal System
  + pluripotent stem cells (PSCs)
  + Pluripotent Stem Cells/pathology
  + preconception
  + probiotic
  + Purinergic signaling
  + Receptor, Endothelin B/metabolism
  + Receptors, Purinergic P2X7
  + RNA, Circular/genetics
  + Rotenone-induced mouse model
  + short-chain fatty acids
  + Solid pseudopapillary tumor
  + Stem-cell differentiation
  + submucosal neurons
  + Submucous Plexus
  + surgical outcome
  + surgical resection
  + three-dimensional (3D)
  + type 2 diabetes
  + zebrafish

### Notes:

* + e14603 NMO-00132-2023
  + e14603 NMO-00132-2023

### Attachments

* + Full Text
  + Full Text
  + Full Text PDF
  + Full Text PDF
  + Full Text PDF
  + Full Text PDF
  + Full Text PDF
  + Full Text PDF
  + Full Text PDF
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## Macrophage regulation of the "second brain": CD163 intestinal macrophages interact with inhibitory interneurons to regulate colonic motility - evidence from the Cx3cr1-Dtr rat model.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Jackson L. K. Yip |
| **Author** | Soniya Xavier |
| **Author** | Gayathri K. Balasuriya |
| **Author** | Elisa L. Hill-Yardin |
| **Author** | Sarah J. Spencer |
| **Abstract** | Intestinal macrophages are well-studied for their conventional roles in the immune response against pathogens and protecting the gut from chronic inflammation. However, these macrophages may also have additional functional roles in gastrointestinal motility under typical conditions. This is likely to occur via both direct and indirect influences on gastrointestinal motility through interaction with myenteric neurons that contribute to the gut-brain axis, but this mechanism is yet to be properly characterised. The CX3CR1 chemokine receptor is expressed in the majority of intestinal macrophages, so we used a conditional knockout Cx3cr1-Dtr (diphtheria toxin receptor) rat model to transiently ablate these cells. We then utilized ex vivo video imaging to evaluate colonic motility. Our previous studies in brain suggested that Cx3cr1-expressing cells repopulate by 7 days after depletion in this model, so we performed our experiments at both the 48 hr (macrophage depletion) and 7-day (macrophage repopulation) time points. We also investigated whether inhibitory neuronal input driven by nitric oxide from the enteric nervous system is required for the regulation of colonic motility by intestinal macrophages. Our results demonstrated that CD163-positive resident intestinal macrophages are important in regulating colonic motility in the absence of this major inhibitory neuronal input. In addition, we show that intestinal macrophages are indispensable in maintaining a healthy intestinal structure. Our study provides a novel understanding of the interplay between the enteric nervous system and intestinal macrophages in colonic motility. We highlight intestinal macrophages as a potential therapeutic target for gastrointestinal motility disorders when inhibitory neuronal input is suppressed. |
| **Date** | 2023 |
| **Language** | eng |
| **Rights** | Copyright © 2023 Yip, Xavier, Balasuriya, Hill-Yardin and Spencer. |
| **Extra** | Place: Switzerland PMID: 37868978 PMCID: PMC10585175 |
| **Volume** | 14 |
| **Pages** | 1269890 |
| **Publication** | Frontiers in immunology |
| **DOI** | [10.3389/fimmu.2023.1269890](http://doi.org/10.3389/fimmu.2023.1269890) |
| **Journal Abbr** | Front Immunol |
| **ISSN** | 1664-3224 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Animals
  + Rats
  + Brain
  + \*Interneurons
  + \*Macrophages
  + CD163 Antigen
  + colonic motility
  + gastrointestinal
  + Heparin-binding EGF-like Growth Factor
  + macrophages
  + myenteric plexus
  + nitric oxide

## Marine Toxins and Nociception: Potential Therapeutic Use in the Treatment of Visceral Pain Associated with Gastrointestinal Disorders.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Andreina Baj |
| **Author** | Michela Bistoletti |
| **Author** | Annalisa Bosi |
| **Author** | Elisabetta Moro |
| **Author** | Cristina Giaroni |
| **Author** | Francesca Crema |
| **Abstract** | Visceral pain, of which the pathogenic basis is currently largely unknown, is a hallmark symptom of both functional disorders, such as irritable bowel syndrome, and inflammatory bowel disease. Intrinsic sensory neurons in the enteric nervous system and afferent sensory neurons of the dorsal root ganglia, connecting with the central nervous system, represent the primary neuronal pathways transducing gut visceral pain. Current pharmacological therapies have several limitations, owing to their partial efficacy and the generation of severe adverse effects. Numerous cellular targets of visceral nociception have been recognized, including, among others, channels (i.e., voltage-gated sodium channels, VGSCs, voltage-gated calcium channels, VGCCs, Transient Receptor Potential, TRP, and Acid-sensing ion channels, ASICs) and neurotransmitter pathways (i.e., GABAergic pathways), which represent attractive targets for the discovery of novel drugs. Natural biologically active compounds, such as marine toxins, able to bind with high affinity and selectivity to different visceral pain molecular mediators, may represent a useful tool (1) to improve our knowledge of the physiological and pathological relevance of each nociceptive target, and (2) to discover therapeutically valuable molecules. In this review we report the most recent literature describing the effects of marine toxin on gastrointestinal visceral pain pathways and the possible clinical implications in the treatment of chronic pain associated with gut diseases. |
| **Date** | 2019 Jul 31 |
| **Language** | eng |
| **Extra** | Place: Switzerland PMID: 31370176 PMCID: PMC6723473 |
| **Volume** | 11 |
| **Publication** | Toxins |
| **DOI** | [10.3390/toxins11080449](http://doi.org/10.3390/toxins11080449) |
| **Issue** | 8 |
| **Journal Abbr** | Toxins (Basel) |
| **ISSN** | 2072-6651 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/11/2025, 2:32:25 PM |

### Tags:

* + Humans
  + Animals
  + inflammatory bowel disease
  + irritable bowel syndrome
  + ASICs
  + GABAB
  + Gastrointestinal Diseases/\*drug therapy/physiopathology
  + marine toxins
  + Marine Toxins/\*therapeutic use
  + Nociception
  + TRPs
  + VGCCs
  + VGSCs
  + visceral pain
  + Visceral Pain/\*drug therapy/physiopathology

## Mas-related G protein-coupled receptors in gastrointestinal dysfunction and inflammatory bowel disease: A review.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Patrick Hawker |
| **Author** | Li Zhang |
| **Author** | Lu Liu |
| **Abstract** | Inflammatory bowel disease (IBD) is a chronic debilitating condition, hallmarked by persistent inflammation of the gastrointestinal tract. Despite recent advances in clinical treatments, the aetiology of IBD is unknown, and a large proportion of patients are refractory to pharmacotherapy. Understanding IBD immunopathogenesis is crucial to discern the cause of IBD and optimise treatments. Mas-related G protein-coupled receptors (Mrgprs) are a family of approximately 50 G protein-coupled receptors that were first identified over 20 years ago. Originally known for their expression in skin nociceptors and their role in transmitting the sensation of itch in the periphery, new reports have described the presence of Mrgprs in the gastrointestinal tract. In this review, we consider the impact of these findings and assess the evidence that suggests that Mrgprs may be involved in the disrupted homeostatic processes that contribute to gastrointestinal disorders and IBD. LINKED ARTICLES: This article is part of a themed issue Therapeutic Targeting of G Protein-Coupled Receptors: hot topics from the Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists 2021 Virtual Annual Scientific Meeting. To view the other articles in this section visit http://onlinelibrary.wiley.com/doi/10.1111/bph.v181.14/issuetoc. |
| **Date** | 2024 Jul |
| **Language** | eng |
| **Rights** | © 2023 The Authors. British Journal of Pharmacology published by John Wiley & Sons Ltd on behalf of British Pharmacological Society. |
| **Extra** | Place: England PMID: 36787888 |
| **Volume** | 181 |
| **Pages** | 2197-2211 |
| **Publication** | British journal of pharmacology |
| **DOI** | [10.1111/bph.16059](http://doi.org/10.1111/bph.16059) |
| **Issue** | 14 |
| **Journal Abbr** | Br J Pharmacol |
| **ISSN** | 1476-5381 0007-1188 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
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### Tags:

* + Humans
  + Animals
  + inflammation
  + inflammatory bowel disease
  + enteric nervous system
  + gastrointestinal
  + motility
  + \*Gastrointestinal Diseases/metabolism/drug therapy/physiopathology
  + \*Inflammatory Bowel Diseases/metabolism/drug therapy/physiopathology
  + \*Receptors, G-Protein-Coupled/metabolism
  + Mas‐related G protein‐coupled receptor
  + mast cell
  + Mrgpr

## Mesenchymal cells regulate enteric neural crest cell migration via RET-GFRA1b trans-signaling.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Mari Morikawa |
| **Author** | Hisayoshi Yoshizaki |
| **Author** | Yoshitomo Yasui |
| **Author** | Shoichi Nishida |
| **Author** | Yutaka Saikawa |
| **Author** | Miyuki Kohno |
| **Author** | Hideaki Okajima |
| **Abstract** | During early development, the enteric nervous system forms from the migration of enteric neural crest cells (ENCCs) from the foregut to the hindgut, where they undergo proliferation and differentiation facilitated by interactions with enteric mesenchymal cells (EMCs). This study investigates the impact on ENCC migration of EMC-ENCC communication mediated by GFRA1b expressed in EMCs. GFRA1-expressing cells in day 11-12 (E11-12) mouse embryos differentiated into smooth muscle cells from E12 onwards. Observations at E12-13.5 revealed high levels of GFRA1 expression on the anti-mesenteric side of the hindgut, correlating with enhanced ENCC migration. This indicates that GFRA1 in EMCs plays a role in ENCC migration during development. Examining GFRA1 isoforms, we found high levels of GFRA1b, which lacks amino acids 140-144, in EMCs. To assess the impact of GFRA1 isoforms on EMC-ENCC communication, we conducted neurosphere drop assays. This revealed that GFRA1b-expressing cells promoted GDNF-dependent extension and increased neurite density in ENCC neurospheres. Co-culture of ENCC mimetic cells expressing RET and GFRA1a with EMC mimetic cells expressing GFRA1a, GFRA1b, or vector alone showed that only GFRA1b-expressing co-cultured cells sustained RET phosphorylation in ENCC-mimetic cells for over 120 min upon GDNF stimulation. Our study provides evidence that GFRA1b-mediated cell-to-cell communication plays a critical role in ENCC motility in enteric nervous system development. These findings contribute to understanding the cellular interactions and signaling mechanisms that underlie enteric nervous system formation and highlight potential therapeutic targets for gastrointestinal motility disorders. |
| **Date** | 2024 May 28 |
| **Language** | eng |
| **Rights** | Copyright © 2024 Elsevier Inc. All rights reserved. |
| **Extra** | Place: United States PMID: 38581949 |
| **Volume** | 710 |
| **Pages** | 149861 |
| **Publication** | Biochemical and biophysical research communications |
| **DOI** | [10.1016/j.bbrc.2024.149861](http://doi.org/10.1016/j.bbrc.2024.149861) |
| **Journal Abbr** | Biochem Biophys Res Commun |
| **ISSN** | 1090-2104 0006-291X |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/11/2025, 2:32:25 PM |

### Tags:

* + Animals
  + Mice
  + \*Enteric Nervous System/physiology
  + \*Neural Crest/metabolism
  + Cell Differentiation/physiology
  + Cell Movement/physiology
  + Enteric mesenchymal cell
  + Enteric neural crest cell
  + Glial Cell Line-Derived Neurotrophic Factor/metabolism
  + Intercellular communication
  + Protein Isoforms/metabolism
  + Trans-RET signaling

## Microbiome-based therapies for Parkinson's disease.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Mudassir Alam |
| **Author** | Kashif Abbas |
| **Author** | Mohd Mustafa |
| **Author** | Nazura Usmani |
| **Author** | Safia Habib |
| **Abstract** | The human gut microbiome dysbiosis plays an important role in the pathogenesis of Parkinson's disease (PD). The bidirectional relationship between the enteric nervous system (ENS) and central nervous system (CNS) under the mediation of the gut-brain axis control the gastrointestinal functioning. This review article discusses key mechanisms by which modifications in the composition and function of the gut microbiota (GM) influence PD progression and motor control loss. Increased intestinal permeability, chronic inflammation, oxidative stress, α-synuclein aggregation, and neurotransmitter imbalances are some key factors that govern gastrointestinal pathology and PD progression. The bacterial taxa of the gut associated with PD development are discussed with emphasis on the enteric nervous system (ENS), as well as the impact of gut bacteria on dopamine production and levodopa metabolism. The pathophysiology and course of the disease are associated with several inflammatory markers, including TNF-α, IL-1β, and IL-6. Emerging therapeutic strategies targeting the gut microbiome include probiotics, prebiotics, synbiotics, postbiotics, and fecal microbiota transplantation (FMT). The article explored how dietary changes may affect the gut microbiota (GM) and the ways that can affect Parkinson's disease (PD), with a focus on nutrition-based, Mediterranean, and ketogenic diets. This comprehensive review synthesizes current evidence on the role of the gut microbiome in PD pathogenesis and explores its potential as a therapeutic target. Understanding these complex interactions may assist in the development of novel diagnostic tools and treatment options for this neurodegenerative disorder. |
| **Date** | 2024 |
| **Language** | eng |
| **Rights** | Copyright © 2024 Alam, Abbas, Mustafa, Usmani and Habib. |
| **Extra** | Place: Switzerland PMID: 39568727 PMCID: PMC11576319 |
| **Volume** | 11 |
| **Pages** | 1496616 |
| **Publication** | Frontiers in nutrition |
| **DOI** | [10.3389/fnut.2024.1496616](http://doi.org/10.3389/fnut.2024.1496616) |
| **Journal Abbr** | Front Nutr |
| **ISSN** | 2296-861X |
| **Date Added** | 6/11/2025, 2:32:23 PM |
| **Modified** | 6/11/2025, 2:32:23 PM |

### Tags:

* + enteric nervous system
  + gut microbiota
  + Parkinson’s disease
  + FMT
  + gut dysbiosis

## Microbiota-Gut-Brain Axis in Psychiatry: Focus on Depressive Disorders.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | I.-Ching Wang |
| **Author** | Shelly A. Buffington |
| **Author** | Ramiro Salas |
| **Abstract** | PURPOSE OF REVIEW: Gut microbiota contribute to several physiological processes in the host. The composition of the gut microbiome is associated with different neurological and neurodevelopmental diseases. In psychiatric disease, stress may be a major factor leading to gut microbiota alterations. Depressive disorders are the most prevalent mental health issues worldwide and patients often report gastrointestinal symptoms. Accordingly, evidence of gut microbial alterations in depressive disorders has been growing. Here we review current literature revealing links between the gut microbiome and brain function in the context of depression. RECENT FINDINGS: The gut-brain axis could impact the behavioral manifestation of depression and the underlying neuropathology via multiple routes: the HPA axis, immune function, the enteric nervous system, and the vagus nerve. Furthermore, we explore possible therapeutic interventions including fecal microbiota transplant or probiotic supplementation in alleviating depressive symptoms. SUMMARY: Understanding the mechanisms by which bidirectional communication along the gut-brain axis can be dysregulated in patients with depression could lead to the development of personalized, microbiome-targeted therapies for the treatment of this disorder. |
| **Date** | 2024 Dec |
| **Language** | eng |
| **Extra** | Place: Switzerland PMID: 40130013 PMCID: PMC11932714 |
| **Volume** | 11 |
| **Pages** | 222-232 |
| **Publication** | Current epidemiology reports |
| **DOI** | [10.1007/s40471-024-00349-z](http://doi.org/10.1007/s40471-024-00349-z) |
| **Issue** | 4 |
| **Journal Abbr** | Curr Epidemiol Rep |
| **ISSN** | 2196-2995 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/11/2025, 2:32:24 PM |

### Tags:

* + Gut microbiome
  + Depression
  + Fecal microbiota transfer
  + HPA-axis
  + Immune system
  + Vagus nerve

## Microbiota-Gut-Brain Axis: New Therapeutic Opportunities.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Caitríona Long-Smith |
| **Author** | Kenneth J. O'Riordan |
| **Author** | Gerard Clarke |
| **Author** | Catherine Stanton |
| **Author** | Timothy G. Dinan |
| **Author** | John F. Cryan |
| **Abstract** | The traditional fields of pharmacology and toxicology are beginning to consider the substantial impact our gut microbiota has on host physiology. The microbiota-gut-brain axis is emerging as a particular area of interest and a potential new therapeutic target for effective treatment of central nervous system disorders, in addition to being a potential cause of drug side effects. Microbiota-gut-brain axis signaling can occur via several pathways, including via the immune system, recruitment of host neurochemical signaling, direct enteric nervous system routes and the vagus nerve, and the production of bacterial metabolites. Altered gut microbial profiles have been described in several psychiatric and neurological disorders. Psychobiotics, live biotherapeutics or substances whose beneficial effects on the brain are bacterially mediated, are currently being investigated as direct and/or adjunctive therapies for psychiatric and neurodevelopmental disorders and possibly for neurodegenerative disease, and they may emerge as new therapeutic options in the clinical management of brain disorders. |
| **Date** | 2020 Jan 6 |
| **Language** | eng |
| **Extra** | Place: United States PMID: 31506009 |
| **Volume** | 60 |
| **Pages** | 477-502 |
| **Publication** | Annual review of pharmacology and toxicology |
| **DOI** | [10.1146/annurev-pharmtox-010919-023628](http://doi.org/10.1146/annurev-pharmtox-010919-023628) |
| **Journal Abbr** | Annu Rev Pharmacol Toxicol |
| **ISSN** | 1545-4304 0362-1642 |
| **Date Added** | 6/11/2025, 2:32:23 PM |
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### Tags:

* + Humans
  + Animals
  + \*Gastrointestinal Microbiome
  + microbiota-gut-brain axis
  + probiotic
  + prebiotic
  + Brain/microbiology/\*physiopathology
  + Central Nervous System Diseases/microbiology/\*physiopathology/therapy
  + Drug-Related Side Effects and Adverse Reactions/epidemiology/microbiology
  + Mental Disorders/microbiology/physiopathology/therapy
  + Neurodegenerative Diseases/microbiology/physiopathology/therapy
  + psychobiotic

## MicroRNA regulation of enteric nervous system development and disease.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Amy Marie Holland |
| **Author** | Reindert Jehoul |
| **Author** | Jorunn Vranken |
| **Author** | Stefanie Gabriele Wohl |
| **Author** | Werend Boesmans |
| **Abstract** | The enteric nervous system (ENS), an elaborate network of neurons and glia woven through the gastrointestinal tract, is integral for digestive physiology and broader human health. Commensurate with its importance, ENS dysfunction is linked to a range of debilitating gastrointestinal disorders. MicroRNAs (miRNAs), with their pleiotropic roles in post-transcriptional gene regulation, serve as key developmental effectors within the ENS. Herein, we review the regulatory dynamics of miRNAs in ENS ontogeny, showcasing specific miRNAs implicated in both congenital and acquired enteric neuropathies, such as Hirschsprung's disease (HSCR), achalasia, intestinal neuronal dysplasia (IND), chronic intestinal pseudo-obstruction (CIPO), and slow transit constipation (STC). By delineating miRNA-mediated mechanisms in these diseases, we underscore their importance for ENS homeostasis and highlight their potential as therapeutic targets. |
| **Date** | 2025 Apr |
| **Language** | eng |
| **Rights** | Copyright © 2025 Elsevier Ltd. All rights reserved. |
| **Extra** | Place: England PMID: 40089421 PMCID: PMC11981837 |
| **Volume** | 48 |
| **Pages** | 268-282 |
| **Publication** | Trends in neurosciences |
| **DOI** | [10.1016/j.tins.2025.02.004](http://doi.org/10.1016/j.tins.2025.02.004) |
| **Issue** | 4 |
| **Journal Abbr** | Trends Neurosci |
| **ISSN** | 1878-108X 0166-2236 |
| **Date Added** | 6/11/2025, 2:32:23 PM |
| **Modified** | 6/11/2025, 2:32:23 PM |

### Tags:

* + Humans
  + Animals
  + gastrointestinal
  + Hirschsprung’s disease
  + epigenetics
  + \*Enteric Nervous System/metabolism/growth & development
  + \*Gastrointestinal Diseases/genetics/metabolism
  + \*MicroRNAs/metabolism/genetics
  + gut
  + Hirschsprung Disease/genetics
  + neural crest cells
  + noncoding RNA

## Mini-review: "Enteric glia functions in nervous tissue repair: Therapeutic target or tool?".

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Mukhamad Sunardi |
| **Author** | Carla Cirillo |
| **Abstract** | In the body, nerve tissue is not only present in the central nervous system, but also in the periphery. The enteric nervous system (ENS) is a highly organized intrinsic network of neurons and glial cells grouped to form interconnected ganglia. Glial cells in the ENS are a fascinating cell population: their neurotrophic role is well established, as well as their plasticity in specific circumstances. Gene expression profiling studies indicate that ENS glia retain neurogenic potential. The identification of neurogenic glial subtype(s) and the molecular basis of glia-derived neurogenesis may have profound biological and clinical implications. In this review, we discuss the potential of using gene-editing for ENS glia and cell transplantation as therapies for enteric neuropathies. Glia in the ENS: target or tool for nerve tissue repair? |
| **Date** | 2023 Aug 24 |
| **Language** | eng |
| **Rights** | Copyright © 2023 Elsevier B.V. All rights reserved. |
| **Extra** | Place: Ireland PMID: 37393007 |
| **Volume** | 812 |
| **Pages** | 137360 |
| **Publication** | Neuroscience letters |
| **DOI** | [10.1016/j.neulet.2023.137360](http://doi.org/10.1016/j.neulet.2023.137360) |
| **Journal Abbr** | Neurosci Lett |
| **ISSN** | 1872-7972 0304-3940 |
| **Date Added** | 6/11/2025, 2:32:23 PM |
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### Tags:

* + Neurons/metabolism
  + \*Enteric Nervous System/metabolism
  + \*Nerve Tissue
  + Neurogenesis/physiology
  + Neuroglia/physiology

## Mini-review: Enteric glial cell reactions to inflammation and potential therapeutic implications for GI diseases, motility disorders, and abdominal pain.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Andromeda Linan-Rico |
| **Author** | Fernando Ochoa-Cortes |
| **Author** | Reiner Schneider |
| **Author** | Fievos L. Christofi |
| **Abstract** | Enteric glial cells are emerging as critical players in the regulation of intestinal motility, secretion, epithelial barrier function, and gut homeostasis in health and disease. Enteric glia react to intestinal inflammation by converting to a 'reactive glial phenotype' and enteric gliosis, contributing to neuroinflammation, enteric neuropathy, bowel motor dysfunction and dysmotility, diarrhea or constipation, 'leaky gut', and visceral pain. The focus of the minireview is on the impact of inflammation on enteric glia reactivity in response to diverse insults such as intestinal surgery, ischemia, infections (C. difficile infection, HIV-Tat-induced diarrhea, endotoxemia and paralytic ileus), GI diseases (inflammatory bowel diseases, diverticular disease, necrotizing enterocolitis, colorectal cancer) and functional GI disorders (postoperative ileus, chronic intestinal pseudo-obstruction, constipation, irritable bowel syndrome). Significant progress has been made in recent years on molecular pathogenic mechanisms of glial reactivity and enteric gliosis, resulting in enteric neuropathy, disruption of motility, diarrhea, visceral hypersensitivity and abdominal pain. There is a growing number of glial molecular targets with therapeutic implications that includes receptors for interleukin-1 (IL-1R), purines (P2X2R, A2BR), PPARα, lysophosphatidic acid (LPAR1), Toll-like receptor 4 (TLR4R), estrogen-β receptor (ERβ) adrenergic α-(2) (α-(2)R) and endothelin B (ETBR), connexin-43 / Colony-stimulating factor 1 signaling (Cx43/CSF1) and the S100β/RAGE signaling pathway. These exciting new developments are the subject of the minireview. Some of the findings in pre-clinical models may be translatable to humans, raising the possibility of designing future clinical trials to test therapeutic application(s). Overall, research on enteric glia has resulted in significant advances in our understanding of GI pathophysiology. |
| **Date** | 2023 Aug 24 |
| **Language** | eng |
| **Rights** | Copyright © 2023 The Authors. Published by Elsevier B.V. All rights reserved. |
| **Extra** | Place: Ireland PMID: 37451357 PMCID: PMC10952371 |
| **Volume** | 812 |
| **Pages** | 137395 |
| **Publication** | Neuroscience letters |
| **DOI** | [10.1016/j.neulet.2023.137395](http://doi.org/10.1016/j.neulet.2023.137395) |
| **Journal Abbr** | Neurosci Lett |
| **ISSN** | 1872-7972 0304-3940 |
| **Date Added** | 6/11/2025, 2:32:23 PM |
| **Modified** | 6/11/2025, 2:32:23 PM |

### Tags:

* + Humans
  + Infant, Newborn
  + \*Enteric Nervous System/pathology
  + Abdominal pain
  + Gastrointestinal Motility
  + Neuroglia/metabolism
  + Inflammation/metabolism
  + \*Clostridioides difficile
  + \*Gastrointestinal Diseases/therapy/metabolism/pathology
  + \*Intestinal Pseudo-Obstruction/therapy/metabolism/pathology
  + Abdominal Pain/metabolism/pathology
  + Constipation/metabolism
  + Diarrhea/metabolism/pathology
  + Enteric glia
  + GI diseases
  + GI disorders
  + Gliosis/metabolism
  + Motility disorders
  + Neuroinflammation

## Modulation of Ceramide-Induced Apoptosis in Enteric Neurons by Aryl Hydrocarbon Receptor Signaling: Unveiling a New Pathway beyond ER Stress.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Mallappa Anitha |
| **Author** | Supriya M. Kumar |
| **Author** | Imhoi Koo |
| **Author** | Gary H. Perdew |
| **Author** | Shanthi Srinivasan |
| **Author** | Andrew D. Patterson |
| **Abstract** | 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), a persistent organic pollutant and a potent aryl hydrocarbon receptor (AHR) ligand, causes delayed intestinal motility and affects the survival of enteric neurons. In this study, we investigated the specific signaling pathways and molecular targets involved in TCDD-induced enteric neurotoxicity. Immortalized fetal enteric neuronal (IM-FEN) cells treated with 10 nM TCDD exhibited cytotoxicity and caspase 3/7 activation, indicating apoptosis. Increased cleaved caspase-3 expression with TCDD treatment, as assessed by immunostaining in enteric neuronal cells isolated from WT mice but not in neural crest cell-specific Ahr deletion mutant mice (Wnt1Cre(+/-)/Ahr(b(fl/fl)())), emphasized the pivotal role of AHR in this process. Importantly, the apoptosis in IM-FEN cells treated with TCDD was mediated through a ceramide-dependent pathway, independent of endoplasmic reticulum stress, as evidenced by increased ceramide synthesis and the reversal of cytotoxic effects with myriocin, a potent inhibitor of ceramide biosynthesis. We identified Sptlc2 and Smpd2 as potential gene targets of AHR in ceramide regulation by a chromatin immunoprecipitation (ChIP) assay in IM-FEN cells. Additionally, TCDD downregulated phosphorylated Akt and phosphorylated Ser9-GSK-3β levels, implicating the PI3 kinase/AKT pathway in TCDD-induced neurotoxicity. Overall, this study provides important insights into the mechanisms underlying TCDD-induced enteric neurotoxicity and identifies potential targets for the development of therapeutic interventions. |
| **Date** | 2024 Aug 6 |
| **Language** | eng |
| **Extra** | Place: Switzerland PMID: 39201268 PMCID: PMC11354200 |
| **Volume** | 25 |
| **Publication** | International journal of molecular sciences |
| **DOI** | [10.3390/ijms25168581](http://doi.org/10.3390/ijms25168581) |
| **Issue** | 16 |
| **Journal Abbr** | Int J Mol Sci |
| **ISSN** | 1422-0067 |
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### Tags:

* + Male
  + Animals
  + Mice
  + Cells, Cultured
  + Tissue Culture Techniques
  + Mice, Inbred C57BL
  + Glycogen Synthase Kinase 3 beta/metabolism
  + Proto-Oncogene Proteins c-akt/metabolism
  + Mice, Transgenic
  + \*Apoptosis/drug effects
  + apoptosis
  + ENS
  + \*Ceramides/metabolism
  + \*Endoplasmic Reticulum Stress/drug effects
  + \*Enteric Nervous System/cytology/drug effects
  + \*Neurons/cytology/drug effects/metabolism
  + \*Receptors, Aryl Hydrocarbon/genetics/metabolism
  + AHR
  + ceramides
  + cytotoxicity
  + Polychlorinated Dibenzodioxins/pharmacology
  + Sphingolipids/metabolism
  + TCDD

## Molecular signalling during cross talk between gut brain axis regulation and progression of irritable bowel syndrome: A comprehensive review.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Shiv Vardan Singh |
| **Author** | Risha Ganguly |
| **Author** | Kritika Jaiswal |
| **Author** | Aditya Kumar Yadav |
| **Author** | Ramesh Kumar |
| **Author** | Abhay K. Pandey |
| **Abstract** | Irritable bowel syndrome (IBS) is a chronic functional disorder which alters gastrointestinal (GI) functions, thus leading to compromised health status. Pathophysiology of IBS is not fully understood, whereas abnormal gut brain axis (GBA) has been identified as a major etiological factor. Recent studies are suggestive for visceral hyper-sensitivity, altered gut motility and dysfunctional autonomous nervous system as the main clinical abnormalities in IBS patients. Bidirectional signalling interactions among these abnormalities are derived through various exogenous and endogenous factors, such as microbiota population and diversity, microbial metabolites, dietary uptake, and psychological abnormalities. Strategic efforts focused to study these interactions including probiotics, antibiotics and fecal transplantations in normal and germ-free animals are clearly suggestive for the pivotal role of gut microbiota in IBS etiology. Additionally, neurotransmitters act as communication tools between enteric microbiota and brain functions, where serotonin (5-hydroxytryptamine) plays a key role in pathophysiology of IBS. It regulates GI motility, pain sense and inflammatory responses particular to mucosal and brain activity. In the absence of a better understanding of various interconnected crosstalks in GBA, more scientific efforts are required in the search of novel and targeted therapies for the management of IBS. In this review, we have summarized the gut microbial composition, interconnected signalling pathways and their regulators, available therapeutics, and the gaps needed to fill for a better management of IBS. |
| **Date** | 2023 Jul 6 |
| **Language** | eng |
| **Rights** | ©The Author(s) 2023. Published by Baishideng Publishing Group Inc. All rights reserved. |
| **Extra** | Place: United States PMID: 37469740 PMCID: PMC10353503 |
| **Volume** | 11 |
| **Pages** | 4458-4476 |
| **Publication** | World journal of clinical cases |
| **DOI** | [10.12998/wjcc.v11.i19.4458](http://doi.org/10.12998/wjcc.v11.i19.4458) |
| **Issue** | 19 |
| **Journal Abbr** | World J Clin Cases |
| **ISSN** | 2307-8960 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Serotonin
  + Microbiota
  + Gut brain axis
  + Irritable bowel syndrome
  + Stress

## Molecular Targets to Alleviate Enteric Neuropathy and Gastrointestinal Dysfunction.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Lauren Sahakian |
| **Author** | Rachel McQuade |
| **Author** | Rhian Stavely |
| **Author** | Ainsley Robinson |
| **Author** | Rhiannon T. Filippone |
| **Author** | Majid Hassanzadeganroudsari |
| **Author** | Raj Eri |
| **Author** | Raquel Abalo |
| **Author** | Joel C. Bornstein |
| **Author** | Mark R. Kelley |
| **Author** | Kulmira Nurgali |
| **Abstract** | Enteric neuropathy underlies long-term gastrointestinal (GI) dysfunction associated with several pathological conditions. Our previous studies have demonstrated that structural and functional changes in the enteric nervous system (ENS) result in persistent alterations of intestinal functions long after the acute insult. These changes lead to aberrant immune response and chronic dysregulation of the epithelial barrier. Damage to the ENS is prognostic of disease progression and plays an important role in the recurrence of clinical manifestations. This suggests that the ENS is a viable therapeutic target to alleviate chronic intestinal dysfunction. Our recent studies in preclinical animal models have progressed into the development of novel therapeutic strategies for the treatment of enteric neuropathy in various chronic GI disorders. We have tested the anti-inflammatory and neuroprotective efficacy of novel compounds targeting specific molecular pathways. Ex vivo studies in human tissues freshly collected after resection surgeries provide an understanding of the molecular mechanisms involved in enteric neuropathy. In vivo treatments in animal models provide data on the efficacy and the mechanisms of actions of the novel compounds and their combinations with clinically used therapies. These novel findings provide avenues for the development of safe, cost-effective, and highly efficacious treatments of GI disorders. |
| **Date** | 2022 |
| **Language** | eng |
| **Rights** | © 2022. The Author(s), under exclusive license to Springer Nature Switzerland AG. |
| **Extra** | Place: United States PMID: 36587161 |
| **Volume** | 1383 |
| **Pages** | 221-228 |
| **Publication** | Advances in experimental medicine and biology |
| **DOI** | [10.1007/978-3-031-05843-1\_21](http://doi.org/10.1007/978-3-031-05843-1_21) |
| **Journal Abbr** | Adv Exp Med Biol |
| **ISSN** | 0065-2598 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/11/2025, 2:32:24 PM |

### Tags:

* + Humans
  + Treatment Outcome
  + Animals
  + Models, Animal
  + Chemotherapy
  + \*Enteric Nervous System/pathology
  + Enteric neuropathy
  + Inflammatory bowel disease
  + \*Gastrointestinal Diseases/drug therapy
  + \*Intestinal Pseudo-Obstruction/pathology
  + Apurinic/apyrimidinic endonuclease/redox factor-1 (APE1/Ref-1)
  + High mobility group box protein 1 (HMGB1)

## Na(+) /Ca(2+) exchanger 1 is a key mechanosensitive molecule of the esophageal myenteric neurons.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Hui Dong |
| **Author** | Bo Tang |
| **Author** | Yanfen Jiang |
| **Author** | Ravinder K. Mittal |
| **Abstract** | AIM: Our earlier studies showed that mechanical stretch activates inhibitory motor neurons of the oesophagus; however, the underlying molecular mechanisms are unclear. Here, we sought to examine if Na(+) /Ca(2+) exchanger 1 (NCX1) is responsible for the mechanosensitivity in the esophageal myenteric neurons (EMN) of rats and humans. METHODS: The function of NCX1 in primary culture of neurons was determined using calcium imaging, and mechanosensitivity was tested using osmotic stretch and direct mechanical stretch. Axial stretch-induced relaxation of the lower esophageal sphincter (LES) was also studied in vivo in rats. RESULTS: The expression and co-localization of NCX1 with nNOS were identified in the EMN from both rats and humans. The extracellular Ca(2+) entry caused by ATP through purinergic signalling in the rat EMN was significantly inhibited by selective NCX blockers. Removal of extracellular Na(+) to activate the Ca(2+) entry mode of NCX1 induced an increase in the cytoplasmic calcium ([Ca(2+) ](cyt) ), which was attenuated by NCX blockers. Osmotic stretch and mechanical stretch-induced [Ca(2+) ](cyt) signalling in the rat and human EMN were attenuated by NCX blockers as well as specific NCX1 knockdown. Osmotic stretch and mechanical stretch also induced [Ca(2+) ](cyt) signalling in the Chinese hamster ovary (CHO) cells with NCX1 over-expression, which was attenuated by NCX blockers. Finally, NCX blockade inhibited axial stretch-activated LES relaxation in vivo experiments in the rats. CONCLUSIONS: We demonstrate a novel NCX1/Ca(2+) pathway in the mechanosensitive neurons of rat and human oesophagus, which may provide a potential therapeutic target for the treatment of oesophageal motility disorders. |
| **Date** | 2019 Apr |
| **Language** | eng |
| **Rights** | © 2018 Scandinavian Physiological Society. Published by John Wiley & Sons Ltd. |
| **Extra** | Place: England PMID: 30466198 |
| **Volume** | 225 |
| **Pages** | e13223 |
| **Publication** | Acta physiologica (Oxford, England) |
| **DOI** | [10.1111/apha.13223](http://doi.org/10.1111/apha.13223) |
| **Issue** | 4 |
| **Journal Abbr** | Acta Physiol (Oxf) |
| **ISSN** | 1748-1716 1748-1708 |
| **Date Added** | 6/11/2025, 2:32:27 PM |
| **Modified** | 6/11/2025, 2:32:27 PM |

### Tags:

* + Humans
  + Animals
  + Rats
  + Rats, Sprague-Dawley
  + Neurons/metabolism
  + Calcium/metabolism
  + Primary Cell Culture
  + \*Mechanotransduction, Cellular
  + CHO Cells
  + Cricetulus
  + esophageal myenteric neurons
  + lower esophageal sphincter relaxation
  + mechanosensitive neurons
  + Myenteric Plexus/\*physiology
  + Na+/Ca2+ exchanger 1
  + Nitric Oxide Synthase Type I/metabolism
  + Receptors, Purinergic/metabolism
  + Sodium-Calcium Exchanger/\*metabolism

## Network Pharmacology-Based Strategy for Predicting Active Ingredients and Potential Targets of Gegen Qinlian Decoction for Rotavirus Enteritis.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Peicheng Zhong |
| **Author** | Lijun Song |
| **Author** | Mengyue Gao |
| **Author** | Xiaotong Wang |
| **Author** | Wenpan Tan |
| **Author** | Huanqian Lu |
| **Author** | Qian Lan |
| **Author** | Zuyi Zhao |
| **Author** | Wenchang Zhao |
| **Abstract** | MATERIALS AND METHODS: In this study, a network pharmacology-based strategy was used to elucidate the mechanism of GGQLD for the treatment of RVE. Oral bioavailability and drug-likeness were taken as the judgment criteria to search the active ingredients of GGQLD in traditional Chinese medicine systems pharmacology database and analysis platform (TCMSP). The affinity between protein and ingredients was further determined using the similarity ensemble approach to find the corresponding targets. According to the genes related to enteritis in GeneCards database, the key targets were screened by intersections between drug and disease targets. And the therapeutic mechanism was predicted using the protein-protein interactions (PPIs), the Gene Ontology (GO), and the Kyoto Encyclopedia of Genes and Genomes (KEGG) database, which was verified by detecting calcium ion concentration with the fluorescent probe. RESULT: 130 active ingredients were screened from GGQLD, including (R)-canadine, moupinamide, formononetin, and other flavonoids. They act on a total of 366 targets, which is mainly distributed in the biological process of hormone binding or signaling pathways of neuroactive ligand receptor interaction, serotonergic synapse, and calcium signaling pathway. Furthermore, serotonin receptors, adrenergic receptors, cholinergic receptors, and dopamine receptors in the enteric nervous system may be the key targets of RVE treatment by GGQLD. CONCLUSION: This study demonstrated that the potential mechanism that GGQLD can effectively improve the symptoms of RVE may depend on the regulation of calcium ions, serotonin, and gastrointestinal hormone ion that could mutually affect the intestinal nervous system. |
| **Date** | 2020 |
| **Language** | eng |
| **Rights** | Copyright © 2020 Peicheng Zhong et al. |
| **Extra** | Place: United States PMID: 32802121 PMCID: PMC7414372 |
| **Volume** | 2020 |
| **Pages** | 2957567 |
| **Publication** | Evidence-based complementary and alternative medicine : eCAM |
| **DOI** | [10.1155/2020/2957567](http://doi.org/10.1155/2020/2957567) |
| **Journal Abbr** | Evid Based Complement Alternat Med |
| **ISSN** | 1741-427X 1741-4288 |
| **Date Added** | 6/11/2025, 2:32:27 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

## Neuroimmunophysiology of the gut: advances and emerging concepts focusing on the epithelium.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Keith A. Sharkey |
| **Author** | Paul L. Beck |
| **Author** | Derek M. McKay |
| **Abstract** | The epithelial lining of the gastrointestinal tract serves as the interface for digestion and absorption of nutrients and water and as a defensive barrier. The defensive functions of the intestinal epithelium are remarkable considering that the gut lumen is home to trillions of resident bacteria, fungi and protozoa (collectively, the intestinal microbiota) that must be prevented from translocation across the epithelial barrier. Imbalances in the relationship between the intestinal microbiota and the host lead to the manifestation of diseases that range from disorders of motility and sensation (IBS) and intestinal inflammation (IBD) to behavioural and metabolic disorders, including autism and obesity. The latest discoveries shed light on the sophisticated intracellular, intercellular and interkingdom signalling mechanisms of host defence that involve epithelial and enteroendocrine cells, the enteric nervous system and the immune system. Together, they maintain homeostasis by integrating luminal signals, including those derived from the microbiota, to regulate the physiology of the gastrointestinal tract in health and disease. Therapeutic strategies are being developed that target these signalling systems to improve the resilience of the gut and treat the symptoms of gastrointestinal disease. |
| **Date** | 2018 Dec |
| **Language** | eng |
| **Extra** | Place: England PMID: 30069036 |
| **Volume** | 15 |
| **Pages** | 765-784 |
| **Publication** | Nature reviews. Gastroenterology & hepatology |
| **DOI** | [10.1038/s41575-018-0051-4](http://doi.org/10.1038/s41575-018-0051-4) |
| **Issue** | 12 |
| **Journal Abbr** | Nat Rev Gastroenterol Hepatol |
| **ISSN** | 1759-5053 1759-5045 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Animals
  + Gastrointestinal Microbiome/physiology
  + Intestinal Diseases/physiopathology
  + Intestinal Mucosa/cytology/\*physiology/physiopathology
  + Neuroimmunomodulation/\*physiology

## Neuroinflammation and the Gut Microbiota: Possible Alternative Therapeutic Targets to Counteract Alzheimer's Disease?

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Milica Cerovic |
| **Author** | Gianluigi Forloni |
| **Author** | Claudia Balducci |
| **Abstract** | Alzheimer's disease (AD) is a complex, multi-factorial disease affecting various brain systems. This complexity implies that successful therapies must be directed against several core neuropathological targets rather than single ones. The scientific community has made great efforts to identify the right AD targets beside the historic amyloid-β (Aβ). Neuroinflammation is re-emerging as determinant in the neuropathological process of AD. A new theory, still in its infancy, highlights the role of gut microbiota (GM) in the control of brain development, but also in the onset and progression of neurodegenerative diseases. Bidirectional communication between the central and the enteric nervous systems, called gut-brain axes, is largely influenced by GM and the immune system is a potential key mediator of this interaction. Growing evidence points to the role of GM in the maturation and activation of host microglia and peripheral immune cells. Several recent studies have found abnormalities in GM (dysbiosis) in AD populations. These observations raise the intriguing question whether and how GM dysbiosis could contribute to AD development through action on the immune system and whether, in a therapeutic prospective, the development of strategies preserving a healthy GM might become a valuable approach to prevent AD. Here, we review the evidence from animal models and humans of the role of GM in neuroinflammation and AD. |
| **Date** | 2019 |
| **Language** | eng |
| **Rights** | Copyright © 2019 Cerovic, Forloni and Balducci. |
| **Extra** | Place: Switzerland PMID: 31680937 PMCID: PMC6813195 |
| **Volume** | 11 |
| **Pages** | 284 |
| **Publication** | Frontiers in aging neuroscience |
| **DOI** | [10.3389/fnagi.2019.00284](http://doi.org/10.3389/fnagi.2019.00284) |
| **Journal Abbr** | Front Aging Neurosci |
| **ISSN** | 1663-4365 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/11/2025, 2:32:25 PM |

### Tags:

* + immune cells
  + therapy
  + gut microbiota
  + neuroinflammation
  + Alzhimer’s disease

## Neuropharmacology of purinergic receptors in human submucous plexus: Involvement of P2X₁, P2X₂, P2X₃ channels, P2Y and A₃ metabotropic receptors in neurotransmission.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | A. Liñán-Rico |
| **Author** | J. E. Wunderlich |
| **Author** | J. T. Enneking |
| **Author** | D. R. Tso |
| **Author** | I. Grants |
| **Author** | K. C. Williams |
| **Author** | A. Otey |
| **Author** | K. Michel |
| **Author** | M. Schemann |
| **Author** | B. Needleman |
| **Author** | A. Harzman |
| **Author** | F. L. Christofi |
| **Abstract** | RATIONALE: The role of purinergic signaling in human ENS is not well understood. We sought to further characterize the neuropharmacology of purinergic receptors in human ENS and test the hypothesis that endogenous purines are critical regulators of neurotransmission. EXPERIMENTAL APPROACH: LSCM-Fluo-4/(Ca(2+))-imaging of postsynaptic Ca(2+) transients (PSCaTs) was used as a reporter of synaptic transmission evoked by fiber tract electrical stimulation in human SMP surgical preparations. Pharmacological analysis of purinergic signaling was done in 1,556 neurons (identified by HuC/D-immunoreactivity) in 235 ganglia from 107 patients; P2XR-immunoreactivity was evaluated in 19 patients. Real-time MSORT (Di-8-ANEPPS) imaging tested effects of adenosine on fast excitatory synaptic potentials (fEPSPs). RESULTS: Synaptic transmission is sensitive to pharmacological manipulations that alter accumulation of extracellular purines: Apyrase blocks PSCaTs in a majority of neurons. An ecto-NTPDase-inhibitor 6-N,N-diethyl-D-β,γ-dibromomethyleneATP or adenosine deaminase augments PSCaTs. Blockade of reuptake/deamination of eADO inhibits PSCaTs. Adenosine inhibits fEPSPs and PSCaTs (IC50 = 25 µM), sensitive to MRS1220-antagonism (A3AR). A P2Y agonist ADPβS inhibits PSCaTs (IC50 = 111 nM) in neurons without stimulatory ADPbS responses (EC50 = 960 nM). ATP or a P2X1,2,2/3 (α,β-MeATP) agonist evokes fast, slow, biphasic Ca(2+) transients or Ca(2+) oscillations (ATP,EC50 = 400 mM). PSCaTs are sensitive to P2X1 antagonist NF279. Low (20 nM) or high (5 µM) concentrations of P2X antagonist TNP-ATP block PSCaTs in different neurons; proportions of neurons with P2XR-immunoreactivity follow the order P2X2 > P2X1 >> P2X3; P2X1 + P2X2 and P2X3 + P2X2 are co-localized. RT-PCR identified mRNA-transcripts for P2X1-7, P2Y1,2,12-14R. CONCLUSIONS: Purines are critical regulators of neurotransmission in human ENS. Purinergic signaling involves P2X1, P2X2, P2X3 channels, P2X1 + P2X2 co-localization and inhibitory P2Y or A3 receptors. These are potential novel therapeutic targets for neurogastroenterology. |
| **Date** | 2015 Aug |
| **Language** | eng |
| **Rights** | Published by Elsevier Ltd. |
| **Extra** | Place: England PMID: 25724083 PMCID: PMC4466061 |
| **Volume** | 95 |
| **Pages** | 83-99 |
| **Publication** | Neuropharmacology |
| **DOI** | [10.1016/j.neuropharm.2015.02.014](http://doi.org/10.1016/j.neuropharm.2015.02.014) |
| **Journal Abbr** | Neuropharmacology |
| **ISSN** | 1873-7064 0028-3908 |
| **Date Added** | 6/11/2025, 2:32:27 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Calcium/metabolism
  + A(3) inhibitory receptors
  + Adenosine Triphosphate/metabolism
  + ATP
  + Colectomy
  + Electric Stimulation
  + Endogenous adenosine
  + Excitatory Postsynaptic Potentials/physiology
  + Human enteric nervous system
  + Immunohistochemistry
  + Inhibitory P2Y receptors
  + Neurons/\*drug effects/\*physiology
  + P2X channels
  + Purinergic Agents/pharmacology
  + Purinergic synaptic transmission
  + Receptors, Purinergic/\*metabolism
  + Submucous plexus
  + Submucous Plexus/\*drug effects/\*physiology
  + Synaptic Transmission/drug effects/physiology
  + Voltage-Sensitive Dye Imaging

## New insights into the pathophysiology of achalasia and implications for future treatment.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Janette Furuzawa-Carballeda |
| **Author** | Samuel Torres-Landa |
| **Author** | Miguel Ángel Valdovinos |
| **Author** | Enrique Coss-Adame |
| **Author** | Luis A. Martín Del Campo |
| **Author** | Gonzalo Torres-Villalobos |
| **Abstract** | Idiopathic achalasia is an archetype esophageal motor disorder, causing significant impairment of eating ability and reducing quality of life. The pathophysiological underpinnings of this condition are loss of esophageal peristalsis and insufficient relaxation of the lower esophageal sphincter (LES). The clinical manifestations include dysphagia for both solids and liquids, regurgitation of esophageal contents, retrosternal chest pain, cough, aspiration, weight loss and heartburn. Even though idiopathic achalasia was first described more than 300 years ago, researchers are only now beginning to unravel its complex etiology and molecular pathology. The most recent findings indicate an autoimmune component, as suggested by the presence of circulating anti-myenteric plexus autoantibodies, and a genetic predisposition, as suggested by observed correlations with other well-defined genetic syndromes such as Allgrove syndrome and multiple endocrine neoplasia type 2 B syndrome. Viral agents (herpes, varicella zoster) have also been proposed as causative and promoting factors. Unfortunately, the therapeutic approaches available today do not resolve the causes of the disease, and only target the consequential changes to the involved tissues, such as destruction of the LES, rather than restoring or modifying the underlying pathology. New therapies should aim to stop the disease at early stages, thereby preventing the consequential changes from developing and inhibiting permanent damage. This review focuses on the known characteristics of idiopathic achalasia that will help promote understanding its pathogenesis and improve therapeutic management to positively impact the patient's quality of life. |
| **Date** | 2016 Sep 21 |
| **Language** | eng |
| **Extra** | Place: United States PMID: 27672286 PMCID: PMC5028805 |
| **Volume** | 22 |
| **Pages** | 7892-7907 |
| **Publication** | World journal of gastroenterology |
| **DOI** | [10.3748/wjg.v22.i35.7892](http://doi.org/10.3748/wjg.v22.i35.7892) |
| **Issue** | 35 |
| **Journal Abbr** | World J Gastroenterol |
| **ISSN** | 2219-2840 1007-9327 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/11/2025, 2:32:26 PM |

### Tags:

* + Humans
  + Quality of Life
  + Inflammation
  + Treatment
  + Achalasia
  + Adrenal Insufficiency
  + Autoantibodies/blood
  + Autoimmune disease
  + Autoimmune Diseases/metabolism
  + Deglutition Disorders/physiopathology
  + Esophageal Achalasia/diagnosis/physiopathology/\*therapy
  + Esophageal Motility Disorders/\*physiopathology
  + Esophageal Sphincter, Lower/\*physiopathology
  + Heartburn/physiopathology
  + Manometry
  + Myenteric Plexus/physiopathology
  + Pathophysiology
  + Peristalsis/physiology

## New treatment options for irritable bowel syndrome with predominant diarrhea.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | H. Christian Weber |
| **Abstract** | PURPOSE OF REVIEW: Irritable bowel syndrome (IBS) is a highly prevalent gastrointestinal disorder with negative impact on quality of life and it represents a substantial economic burden on healthcare cost. The medical management of IBS remains largely symptomatic. This review provides an update related to the most recently published diagnostic Rome IV criteria for IBS and clinical trial data for novel treatment modalities in IBS targeting the peripheral opioid receptors of the enteric nervous system and the gut microbiota. RECENT FINDINGS: The new Rome IV criteria define functional gastrointestinal disorders as disorders of the gut-brain interaction. In addition to previously introduced pharmacological treatment modalities for IBS with constipation (IBS-C) with synthetic peptides and small molecules targeting gastrointestinal receptors and ion channels, the newly Food and Drug Administration-approved mixed peripheral opioid receptor agonist/antagonist eluxadoline and the nonabsorbable antibiotic rifaximin demonstrate efficacy and safety in the treatment of IBS with predominant diarrhea (IBS-D). SUMMARY: Diagnostic criteria for functional gastrointestinal disorders, including IBS, have been revised in Rome IV and are defined as gut-brain disorders. The mixed peripheral opioid receptor agonist/antagonist eluxadoline and the antibiotic rifaximin have been recently Food and Drug Administration approved for the treatment of diarrhea-predominant IBS (IBS-D) with proven efficacy and acceptable side-effect profiles. |
| **Date** | 2017 Feb |
| **Language** | eng |
| **Extra** | Place: England PMID: 27875419 |
| **Volume** | 24 |
| **Pages** | 25-30 |
| **Publication** | Current opinion in endocrinology, diabetes, and obesity |
| **DOI** | [10.1097/MED.0000000000000302](http://doi.org/10.1097/MED.0000000000000302) |
| **Issue** | 1 |
| **Journal Abbr** | Curr Opin Endocrinol Diabetes Obes |
| **ISSN** | 1752-2978 1752-296X |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/11/2025, 2:32:25 PM |

### Tags:

* + Humans
  + Quality of Life
  + Gastrointestinal Agents/therapeutic use
  + \*Diarrhea/drug therapy/physiopathology
  + Anti-Bacterial Agents/therapeutic use
  + Constipation/drug therapy
  + Drug Therapy, Combination
  + Imidazoles/therapeutic use
  + Irritable Bowel Syndrome/diagnosis/\*drug therapy/physiopathology
  + Narcotic Antagonists/therapeutic use
  + Phenylalanine/analogs & derivatives/therapeutic use
  + Receptors, Opioid/agonists
  + Rifamycins/therapeutic use
  + Rifaximin

## Nonpharmacological Modulation of Chronic Inflammation in Parkinson's Disease: Role of Diet Interventions.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Stefania Kalampokini |
| **Author** | Anouck Becker |
| **Author** | Klaus Fassbender |
| **Author** | Epameinondas Lyros |
| **Author** | Marcus M. Unger |
| **Abstract** | Neuroinflammation is increasingly recognized as an important pathophysiological feature of neurodegenerative diseases such as Parkinson's disease (PD). Recent evidence suggests that neuroinflammation in PD might originate in the intestine and the bidirectional communication between the central and enteric nervous system, the so-called "gut-brain axis," has received growing attention due to its contribution to the pathogenesis of neurological disorders. Diet targets mediators of inflammation with various mechanisms and combined with dopaminergic treatment can exert various beneficial effects in PD. Food-based therapies may favorably modulate gut microbiota composition and enhance the intestinal epithelial integrity or decrease the proinflammatory response by direct effects on immune cells. Diets rich in pre- and probiotics, polyunsaturated fatty acids, phenols including flavonoids, and vitamins, such as the Mediterranean diet or a plant-based diet, may attenuate chronic inflammation and positively influence PD symptoms and even progression of the disease. Dietary strategies should be encouraged in the context of a healthy lifestyle with physical activity, which also has neuroimmune-modifying properties. Thus, diet adaptation appears to be an effective additive, nonpharmacological therapeutic strategy that can attenuate the chronic inflammation implicated in PD, potentially slow down degeneration, and thereby modify the course of the disease. PD patients should be highly encouraged to adopt corresponding lifestyle modifications, in order to improve not only PD symptoms, but also general quality of life. Future research should focus on planning larger clinical trials with dietary interventions in PD in order to obtain hard evidence for the hypothesized beneficial effects. |
| **Date** | 2019 |
| **Language** | eng |
| **Extra** | Place: United States PMID: 31534664 PMCID: PMC6732577 |
| **Volume** | 2019 |
| **Pages** | 7535472 |
| **Publication** | Parkinson's disease |
| **DOI** | [10.1155/2019/7535472](http://doi.org/10.1155/2019/7535472) |
| **Journal Abbr** | Parkinsons Dis |
| **ISSN** | 2090-8083 2042-0080 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/11/2025, 2:32:25 PM |

## Novel aspects of enteric serotonergic signaling in health and brain-gut disease.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Andrew Del Colle |
| **Author** | Narek Israelyan |
| **Author** | Kara Gross Margolis |
| **Abstract** | Gastrointestinal (GI) comorbidities are common in individuals with mood and behavioral dysfunction. Similarly, patients with GI problems more commonly suffer from co-morbid psychiatric diagnoses. Although the central and enteric nervous systems (CNS and ENS, respectively) have largely been studied separately, there is emerging interest in factors that may contribute to disease states involving both systems. There is strong evidence to suggest that serotonin may be an important contributor to these brain-gut conditions. Serotonin has long been recognized for its critical functions in CNS development and function. The majority of the body's serotonin, however, is produced in the GI tract, where it plays key roles in ENS development and function. Further understanding of the specific impact that enteric serotonin has on brain-gut disease may lay the foundation for the creation of novel therapeutic targets. This review summarizes the current data focusing on the important roles that serotonin plays in ENS development and motility, with a focus on novel aspects of serotonergic signaling in medical conditions in which CNS and ENS co-morbidities are common, including autism spectrum disorders and depression. |
| **Date** | 2020 Jan 1 |
| **Language** | eng |
| **Extra** | Place: United States PMID: 31682158 PMCID: PMC6985840 |
| **Volume** | 318 |
| **Pages** | G130-G143 |
| **Publication** | American journal of physiology. Gastrointestinal and liver physiology |
| **DOI** | [10.1152/ajpgi.00173.2019](http://doi.org/10.1152/ajpgi.00173.2019) |
| **Issue** | 1 |
| **Journal Abbr** | Am J Physiol Gastrointest Liver Physiol |
| **ISSN** | 1522-1547 0193-1857 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/11/2025, 2:32:24 PM |

### Tags:

* + Humans
  + Animals
  + Adolescent
  + Child
  + ENS
  + Risk Factors
  + microbiome
  + Age Factors
  + \*Gastrointestinal Motility
  + motility
  + Gastrointestinal Microbiome
  + Adolescent Behavior
  + Affect
  + brain-gut
  + Brain/\*metabolism/physiopathology
  + Child Behavior
  + Enteric Nervous System/\*metabolism/physiopathology
  + Gastrointestinal Diseases/epidemiology/\*metabolism/physiopathology/psychology
  + Gastrointestinal Tract/\*innervation/microbiology
  + Mental Disorders/embryology/\*metabolism/physiopathology/psychology
  + Neurogenesis
  + Receptors, Serotonin/metabolism
  + Serotonergic Neurons/\*metabolism
  + serotonin
  + Serotonin/\*metabolism

## Patchouli alcohol restores gut homeostasis in irritable bowel syndrome with diarrhea through myosin Va-mediated neurotransmitter regulation.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Wanyu Chen |
| **Author** | Ting Li |
| **Author** | Yukang Lin |
| **Author** | Zijun Chen |
| **Author** | Milei OuYang |
| **Author** | Ying Pei |
| **Author** | Shulin Yi |
| **Author** | Shuyan Huang |
| **Author** | Zitong Huang |
| **Author** | Lu Liao |
| **Author** | Na Zhou |
| **Author** | Jintong Lu |
| **Author** | ZhuoYing Chen |
| **Author** | Hongying Cao |
| **Author** | Bo Tan |
| **Abstract** | BACKGROUND: Patchouli alcohol (PA), the active ingredient of Pogostemonis Herba, is important in medicine and food, effectively alleviating irritable bowel syndrome with diarrhea (IBS-D) symptoms; however, its mechanism remains unclear. Myosin Va, particularly in the intestinal longitudinal muscle myenteric plexus (LMMP), modulates neurotransmitter release, restoring gastrointestinal motility. PURPOSE: To investigate the primary targets and potential mechanisms of PA in the treatment of IBS-D. STUDY DESIGN: PA treats IBS-D may involve the regulation of neurotransmitter release through the modulation of Myosin Va, and remodels neurons of colon LMMP, ultimately restores enteric nervous system (ENS) homeostasis. METHODS: The GEO database, UK Biobank (UKB) public database and Mendelian randomization (MR) were utilized to identify differentially expressed genes and risk genes in IBS-D population. Network pharmacology and molecular docking were applied to screen for targets of PA in the treatment of IBS-D and predicted the binding affinity of drug targets. We established a chronic restraint stress-induced IBS-D rat model, after that PA (5 mg/kg and 20 mg/kg) was given to treat disease, and multi-omics methods such as bacterial 16S rRNA sequencing, whole transcriptome sequencing and snRNA-seq were used to observe the therapeutic effect of PA. Then measured the expression levels of LMMP neurotransmitter and Myosin Va via in vivo and in vitro experiments. Additionally, observe the effect of PA on Myosin Va-deficient DBA(Dilute, Brown and Non-Agouti) mice, and the regulation of Myosin Va expression by PA was verified by knockdown and overexpression gene function. RESULTS: Bioinformatics analysis, Mendelian randomization and Network pharmacology suggested that neurotransmitter are PA targets in IBS-D treatment. Molecular docking predicted a strong binding affinity between PA and these targets. Multiomics indicated aberrant gastrointestinal motility, imbalanced excitatory and inhibitory neurons, and significantly reduced myosin Va expression under chronic restraint stress-induced IBS-D rat. PA treatment significantly improved these symptoms and restored intestinal microbiota homeostasis. Ex vivo experiments, DBA mice verification and gene function experiments suggested that PA treatment of IBS-D involves regulation of neurotransmitter release by modulating myosin Va and remodeling colon LMMP neurons, restoring enteric nervous system homeostasis. CONCLUSION: Our results provide a theoretical basis for PA application in IBS-D treatment. |
| **Date** | 2025 Jun |
| **Language** | eng |
| **Rights** | Copyright © 2025 Elsevier GmbH. All rights reserved. |
| **Extra** | Place: Germany PMID: 40222168 |
| **Volume** | 141 |
| **Pages** | 156681 |
| **Publication** | Phytomedicine : international journal of phytotherapy and phytopharmacology |
| **DOI** | [10.1016/j.phymed.2025.156681](http://doi.org/10.1016/j.phymed.2025.156681) |
| **Journal Abbr** | Phytomedicine |
| **ISSN** | 1618-095X 0944-7113 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/11/2025, 2:32:24 PM |

### Tags:

* + Humans
  + Male
  + Animals
  + Disease Models, Animal
  + Mice
  + Rats
  + Rats, Sprague-Dawley
  + Multiomics
  + Molecular Docking Simulation
  + Enteric nervous system
  + Gastrointestinal Motility/drug effects
  + Enteric Nervous System/drug effects
  + \*Diarrhea/drug therapy
  + \*Irritable Bowel Syndrome/drug therapy
  + \*Myosin Heavy Chains/metabolism
  + \*Myosin Type V/metabolism
  + \*Neurotransmitter Agents/metabolism
  + Diarrhea-predominant irritable bowel syndrome
  + Gastrointestinal Microbiome/drug effects
  + Homeostasis/drug effects
  + Myosin Va
  + Patchouli alcohol
  + Sesquiterpenes

## Pathogenesis of Parkinson disease--the gut-brain axis and environmental factors.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Lisa Klingelhoefer |
| **Author** | Heinz Reichmann |
| **Abstract** | Parkinson disease (PD) follows a defined clinical pattern, and a range of nonmotor symptoms precede the motor phase. The predominant early nonmotor manifestations are olfactory impairment and constipation. The pathology that accompanies these symptoms is consistent with the Braak staging system: α-synuclein in the dorsal motor nucleus of the vagus nerve, the olfactory bulb, the enteric nervous system (ENS) and the submandibular gland, each of which is a gateway to the environment. The neuropathological process that leads to PD seems to start in the ENS or the olfactory bulb and spreads via rostrocranial transmission to the substantia nigra and further into the CNS, raising the intriguing possibility that environmental substances can trigger pathogenesis. Evidence from epidemiological studies and animal models supports this hypothesis. For example, in mice, intragastric administration of the pesticide rotenone can almost completely reproduce the typical pathological and clinical features of PD. In this Review, we present clinical and pathological evidence to support the hypothesis that PD starts in the gut and spreads via trans-synaptic cell-to-cell transfer of pathology through the sympathetic and parasympathetic nervous systems to the substantia nigra and the CNS. We also consider how environmental factors might trigger pathogenesis, and the potential for therapeutically targeting the mechanisms of these initial stages. |
| **Date** | 2015 Nov |
| **Language** | eng |
| **Extra** | Place: England PMID: 26503923 |
| **Volume** | 11 |
| **Pages** | 625-636 |
| **Publication** | Nature reviews. Neurology |
| **DOI** | [10.1038/nrneurol.2015.197](http://doi.org/10.1038/nrneurol.2015.197) |
| **Issue** | 11 |
| **Journal Abbr** | Nat Rev Neurol |
| **ISSN** | 1759-4766 1759-4758 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/11/2025, 2:32:25 PM |

### Tags:

* + Humans
  + Animals
  + Brain/pathology/\*physiopathology
  + Enteric Nervous System/pathology/physiopathology
  + Gastrointestinal Tract/pathology/\*physiopathology
  + Parkinson Disease/epidemiology/pathology/\*physiopathology

## Pathophysiology and Management of Postoperative Ileus in Adults and Neonates: A Review.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Sindhu Mannava |
| **Author** | Attie Vogler |
| **Author** | Troy Markel |
| **Abstract** | Postoperative ileus (POI) is caused by enteric neural dysfunction and inflammatory response to the stress of surgery as well as the effect of anesthetics and opioid pain medications. POI results in prolonged hospital stays, increased medical costs, and diminished enteral nutrition, rendering it a problem worth tackling. Many cellular pathways are implicated in this disease process, creating numerous opportunities for targeted management strategies. There is a gap in the literature in studies exploring neonatal POI pathophysiology and treatment options. It is well known that neonatal immune and enteric nervous systems are immature, and this results in gut physiology which is distinct from adults. Neonates undergoing abdominal surgery face similar surgical stressors and exposure to medications that cause POI in adults. In this review, we aim to summarize the existing adult and neonatal literature on POI pathophysiology and management and explore applications in the neonatal population. |
| **Date** | 2024 May |
| **Language** | eng |
| **Rights** | Copyright © 2024 Elsevier Inc. All rights reserved. |
| **Extra** | Place: United States PMID: 38428262 |
| **Volume** | 297 |
| **Pages** | 9-17 |
| **Publication** | The Journal of surgical research |
| **DOI** | [10.1016/j.jss.2024.02.001](http://doi.org/10.1016/j.jss.2024.02.001) |
| **Journal Abbr** | J Surg Res |
| **ISSN** | 1095-8673 0022-4804 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/11/2025, 2:32:25 PM |

### Tags:

* + Adult
  + Humans
  + Infant, Newborn
  + \*Enteric Nervous System
  + Analgesics, Opioid
  + \*Ileus/epidemiology
  + Activity
  + Analgesia
  + Enteral Nutrition/adverse effects
  + Ileus
  + Neonate
  + Nutrition
  + Postoperative
  + Postoperative Complications/etiology

## Pediatric Neurogastroenterology and Motility: Moving Rapidly Into the Future.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Atchariya Chanpong |
| **Author** | Nikhil Thapar |
| **Abstract** | The field of pediatric neurogastroenterology and motility encompasses some of the most common and severe gastrointestinal (GI) disorders that affect children. GI motility disorders remain, in general, poorly understood, variably diagnosed, and inadequately treated. Although the field progressed relatively slowly over the last decades, the coming years will, no doubt, see it move into a prolific and dynamic era. With this review, we look forward to this brighter future for the field and highlight emerging areas that show promise and deserve focus in the coming years. This includes the role of early life programming and insult of the enteric neuromusculature as a key determinant of motility diseases and factors that are likely to be relevant in disease etiopathogenesis. We discuss several recent and futuristic developments and advancements in investigative and diagnostic tools as well as novel approaches that have been introduced in the management of GI motility disorders. These include targeted and personalized medicine in both pharmacological and multidisciplinary approaches as well as the emerging therapeutic options such as bioelectrical neuromodulation and regenerative medicine. |
| **Date** | 2023 May 1 |
| **Language** | eng |
| **Rights** | Copyright © 2023 by European Society for European Society for Pediatric Gastroenterology, Hepatology, and Nutrition and North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition. |
| **Extra** | Place: United States PMID: 36705671 |
| **Volume** | 76 |
| **Pages** | 547-552 |
| **Publication** | Journal of pediatric gastroenterology and nutrition |
| **DOI** | [10.1097/MPG.0000000000003721](http://doi.org/10.1097/MPG.0000000000003721) |
| **Issue** | 5 |
| **Journal Abbr** | J Pediatr Gastroenterol Nutr |
| **ISSN** | 1536-4801 0277-2116 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Precision Medicine
  + Child
  + \*Enteric Nervous System/pathology
  + \*Gastrointestinal Diseases/diagnosis/therapy/pathology
  + Cognition
  + Gastrointestinal Motility

## Pharmacologic Profile of Naloxegol, a Peripherally Acting µ-Opioid Receptor Antagonist, for the Treatment of Opioid-Induced Constipation.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Eike Floettmann |
| **Author** | Khanh Bui |
| **Author** | Mark Sostek |
| **Author** | Kemal Payza |
| **Author** | Michael Eldon |
| **Abstract** | Opioid-induced constipation (OIC) is a common side effect of opioid pharmacotherapy for the management of pain because opioid agonists bind to µ-opioid receptors in the enteric nervous system (ENS). Naloxegol, a polyethylene glycol derivative of naloxol, which is a derivative of naloxone and a peripherally acting µ-opioid receptor antagonist, targets the physiologic mechanisms that cause OIC. Pharmacologic measures of opioid activity and pharmacokinetic measures of central nervous system (CNS) penetration were employed to characterize the mechanism of action of naloxegol. At the human µ-opioid receptor in vitro, naloxegol was a potent inhibitor of binding (K(i) = 7.42 nM) and a neutral competitive antagonist (pA(2) - 7.95); agonist effects were <10% up to 30 μM and identical to those of naloxone. The oral doses achieving 50% of the maximal effect in the rat for antagonism of morphine-induced inhibition of gastrointestinal transit and morphine-induced antinociception in the hot plate assay were 23.1 and 55.4 mg/kg for naloxegol and 0.69 and 1.14 mg/kg by for naloxone, respectively. In the human colon adenocarcinoma cell transport assay, naloxegol was a substrate for the P-glycoprotein transporter, with low apparent permeability in the apical to basolateral direction, and penetrated the CNS 15-fold slower than naloxone in a rat brain perfusion model. Naloxegol-derived radioactivity was poorly distributed throughout the rat CNS and was eliminated from most tissues within 24 hours. These findings corroborate phase 3 clinical studies demonstrating that naloxegol relieves OIC-associated symptoms in patients with chronic noncancer pain by antagonizing the µ-opioid receptor in the ENS while preserving CNS-mediated analgesia. |
| **Date** | 2017 May |
| **Language** | eng |
| **Rights** | Copyright © 2017 The Author(s). |
| **Extra** | Place: Netherlands PMID: 28336575 PMCID: PMC5399635 |
| **Volume** | 361 |
| **Pages** | 280-291 |
| **Publication** | The Journal of pharmacology and experimental therapeutics |
| **DOI** | [10.1124/jpet.116.239061](http://doi.org/10.1124/jpet.116.239061) |
| **Issue** | 2 |
| **Journal Abbr** | J Pharmacol Exp Ther |
| **ISSN** | 1521-0103 0022-3565 |
| **Date Added** | 6/11/2025, 2:32:27 PM |
| **Modified** | 6/11/2025, 2:32:27 PM |

### Tags:

* + Female
  + Humans
  + Male
  + Animals
  + Rats
  + Rats, Sprague-Dawley
  + HEK293 Cells
  + Analgesics, Opioid/pharmacology/toxicity
  + Brain/metabolism
  + Caco-2 Cells
  + Cell Membrane Permeability
  + Constipation/chemically induced/\*drug therapy
  + Gastrointestinal Transit/drug effects
  + Morphinans/pharmacokinetics/\*pharmacology
  + Morphine/pharmacology/toxicity
  + Opiate Alkaloids/pharmacology/\*toxicity
  + Polyethylene Glycols/pharmacokinetics/\*pharmacology
  + Radioligand Assay
  + Receptors, Opioid, mu/agonists/\*antagonists & inhibitors
  + Tissue Distribution

## Pharmacology and physiology of gastrointestinal enteroendocrine cells.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | O. J. Mace |
| **Author** | B. Tehan |
| **Author** | F. Marshall |
| **Abstract** | Gastrointestinal (GI) polypeptides are secreted from enteroendocrine cells (EECs). Recent technical advances and the identification of endogenous and synthetic ligands have enabled exploration of the pharmacology and physiology of EECs. Enteroendocrine signaling pathways stimulating hormone secretion involve multiple nutrient transporters and G protein-coupled receptors (GPCRs), which are activated simultaneously under prevailing nutrient conditions in the intestine following a meal. The majority of studies investigate hormone secretion from EECs in response to single ligands and although the mechanisms behind how individual signaling pathways generate a hormonal output have been well characterized, our understanding of how these signaling pathways converge to generate a single hormone secretory response is still in its infancy. However, a picture is beginning to emerge of how nutrients and full, partial, or allosteric GPCR ligands differentially regulate the enteroendocrine system and its interaction with the enteric and central nervous system. So far, activation of multiple pathways underlies drug discovery efforts to harness the therapeutic potential of the enteroendocrine system to mimic the phenotypic changes observed in patients who have undergone Roux-en-Y gastric surgery. Typically obese patients exhibit ∼30% weight loss and greater than 80% of obese diabetics show remission of diabetes. Targeting combinations of enteroendocrine signaling pathways that work synergistically may manifest with significant, differentiated EEC secretory efficacy. Furthermore, allosteric modulators with their increased selectivity, self-limiting activity, and structural novelty may translate into more promising enteroendocrine drugs. Together with the potential to bias enteroendocrine GPCR signaling and/or to activate multiple divergent signaling pathways highlights the considerable range of therapeutic possibilities available. Here, we review the pharmacology and physiology of the EEC system. |
| **Date** | 2015 Aug |
| **Language** | eng |
| **Extra** | Place: United States PMID: 26213627 PMCID: PMC4506687 |
| **Volume** | 3 |
| **Pages** | e00155 |
| **Publication** | Pharmacology research & perspectives |
| **DOI** | [10.1002/prp2.155](http://doi.org/10.1002/prp2.155) |
| **Issue** | 4 |
| **Journal Abbr** | Pharmacol Res Perspect |
| **ISSN** | 2052-1707 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/11/2025, 2:32:24 PM |

### Tags:

* + intestine
  + diabetes
  + GLP-1
  + Chemosensing
  + enteroendocrine
  + GPCR

## Pleiotropic effect of common PHOX2B variants in Hirschsprung disease and neuroblastoma.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Jinglu Zhao |
| **Author** | Yun Zhu |
| **Author** | Xiaoli Xie |
| **Author** | Yuxiao Yao |
| **Author** | Jiao Zhang |
| **Author** | Ruizhong Zhang |
| **Author** | Lihua Huang |
| **Author** | Jiwen Cheng |
| **Author** | Huimin Xia |
| **Author** | Jing He |
| **Author** | Yan Zhang |
| **Abstract** | Hirschsprung disease (HSCR) is a heterogeneous congenital disorder that affects the enteric nervous system, while neuroblastoma is an embryonal tumor of the sympathetic nervous system. Familial cases of both HSCR and neuroblastoma appear to be functionally linked to PHOX2B, which plays a key role in the development of neural crest derivatives. However, the association between common PHOX2B variants and disease risk is contested. Additionally, large-scale examination for pleiotropy or shared genetic susceptibility in sporadic HSCR and neuroblastoma cases lacks theoretical support. Here, we report the first examination of PHOX2B in 1470 HSCR and 469 neuroblastoma patients with matched healthy controls. The PHOX2B rs28647582 polymorphism was found to be associated with HSCR (P = 2.21E-03, OR = 1.26), and each subtype of the ailment (3.22E-03 ≤ P ≤ 0.43, 1.11 ≤ OR ≤ 2.32). The association between rs28647582 and NB risk was consistent with HSCR in a recessive model, though the P value was marginal (P = 0.06). These new genetic findings indicate the potential pleiotropic effects of PHOX2B in both HSCR and neuroblastoma, which could guide the development of therapeutic targets for the treatment of related neurodevelopmental disorders. |
| **Date** | 2019 Feb 22 |
| **Language** | eng |
| **Extra** | Place: United States PMID: 30799307 PMCID: PMC6402522 |
| **Volume** | 11 |
| **Pages** | 1252-1261 |
| **Publication** | Aging |
| **DOI** | [10.18632/aging.101834](http://doi.org/10.18632/aging.101834) |
| **Issue** | 4 |
| **Journal Abbr** | Aging (Albany NY) |
| **ISSN** | 1945-4589 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/11/2025, 2:32:26 PM |

### Tags:

* + Female
  + Humans
  + Male
  + Infant
  + Infant, Newborn
  + Case-Control Studies
  + \*Genetic Predisposition to Disease
  + \*Polymorphism, Genetic
  + Hirschsprung Disease/\*genetics/metabolism
  + Hirschsprung’s disease
  + Homeodomain Proteins/\*genetics/metabolism
  + neuroblastoma
  + Neuroblastoma/\*genetics/metabolism
  + PHOX2B
  + pleiotropic effect
  + Transcription Factors/\*genetics/metabolism

## Postoperative Ileus: Pathophysiology, Current Therapeutic Approaches.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | N. Stakenborg |
| **Author** | P. J. Gomez-Pinilla |
| **Author** | G. E. Boeckxstaens |
| **Abstract** | Postoperative ileus, which develops after each abdominal surgical procedure, is an iatrogenic disorder characterized by a transient inhibition of gastrointestinal motility. Its pathophysiology is complex involving pharmacological (opioids, anesthetics), neural, and immune-mediated mechanisms. The early neural phase, triggered by activation of afferent nerves during the surgical procedure, is short lasting compared to the later inflammatory phase. The latter starts after 3-6 h and lasts several days, making it a more interesting target for treatment. Insight into the triggers and immune cells involved is of great importance for the development of new therapeutic strategies. In this chapter, the pathogenesis and the current therapeutic approaches to treat postoperative ileus are discussed. |
| **Date** | 2017 |
| **Language** | eng |
| **Extra** | Place: Germany PMID: 27999957 |
| **Volume** | 239 |
| **Pages** | 39-57 |
| **Publication** | Handbook of experimental pharmacology |
| **DOI** | [10.1007/164\_2016\_108](http://doi.org/10.1007/164_2016_108) |
| **Journal Abbr** | Handb Exp Pharmacol |
| **ISSN** | 0171-2004 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/11/2025, 2:32:24 PM |

### Tags:

* + Humans
  + Treatment Outcome
  + Animals
  + \*Laparoscopy
  + Macrophages
  + Gastrointestinal motility
  + Recovery of Function
  + Gastrointestinal Motility/\*drug effects
  + Pathophysiology
  + \*Enteric Nervous System/drug effects/physiopathology/surgery
  + \*Iatrogenic Disease
  + \*Ileum/drug effects/innervation/surgery
  + Field effect
  + Gastrointestinal Agents/\*therapeutic use
  + Ileus/etiology/physiopathology/\*therapy
  + Inflammatory phase
  + Mast cells
  + Neural phase
  + Postoperative Complications/physiopathology/\*therapy
  + Postoperative ileus

## Psychological comorbidity in gastrointestinal diseases: Update on the brain-gut-microbiome axis.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Hannibal Person |
| **Author** | Laurie Keefer |
| **Abstract** | The high comorbidity of psychological disorders in both functional and organic gastrointestinal diseases suggests the intimate and complex link between the brain and the gut. Termed the brain-gut axis, this bidirectional communication between the central nervous system and enteric nervous system relies on immune, endocrine, neural, and metabolic pathways. There is increasing evidence that the gut microbiome is a key part of this system, and dysregulation of the brain-gut-microbiome axis (BGMA) has been implicated in disorders of brain-gut interaction, including irritable bowel syndrome, and in neuropsychiatric disorders, including depression, Alzheimer's disease, and autism spectrum disorder. Further, alterations in the gut microbiome have been implicated in the pathogenesis of organic gastrointestinal diseases, including inflammatory bowel disease. The BGMA is an attractive therapeutic target, as using prebiotics, probiotics, or postbiotics to modify the gut microbiome or mimic gut microbial signals could provide novel treatment options to address these debilitating diseases. However, despite significant advancements in our understanding of the BGMA, clinical data is lacking. In this article, we will review current understanding of the comorbidity of gastrointestinal diseases and psychological disorders. We will also review the current evidence supporting the key role of the BGMA in this pathology. Finally, we will discuss the clinical implications of the BGMA in the evaluation and management of psychological and gastrointestinal disorders. |
| **Date** | 2021 Apr 20 |
| **Language** | eng |
| **Rights** | Copyright © 2020 Elsevier Inc. All rights reserved. |
| **Extra** | Place: England PMID: 33326819 PMCID: PMC8382262 |
| **Volume** | 107 |
| **Pages** | 110209 |
| **Publication** | Progress in neuro-psychopharmacology & biological psychiatry |
| **DOI** | [10.1016/j.pnpbp.2020.110209](http://doi.org/10.1016/j.pnpbp.2020.110209) |
| **Journal Abbr** | Prog Neuropsychopharmacol Biol Psychiatry |
| **ISSN** | 1878-4216 0278-5846 |
| **Date Added** | 6/11/2025, 2:32:22 PM |
| **Modified** | 6/11/2025, 2:32:22 PM |

### Tags:

* + Humans
  + Comorbidity
  + Brain/physiology
  + Gastrointestinal Microbiome/\*physiology
  + Functional gastrointestinal disorders
  + Irritable bowel syndrome
  + Inflammatory bowel disease
  + Enteric Nervous System/physiology
  + Brain-Gut Axis/\*physiology
  + Brain-gut-microbiome axis
  + Disorder of the brain-gut axis
  + Gastrointestinal Diseases/diet therapy/\*epidemiology/\*psychology
  + Irritable Bowel Syndrome/diet therapy/epidemiology/psychology
  + Mental Disorders/diet therapy/\*epidemiology/\*psychology
  + Prebiotics/administration & dosage
  + Probiotics/administration & dosage
  + Psychological treatments

## Recent drug delivery systems targeting the gut-brain-microbiome axis for the management of chronic diseases.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Debjani Ray |
| **Author** | Piyas Bose |
| **Author** | Saptarshi Mukherjee |
| **Author** | Subhadeep Roy |
| **Author** | Santanu Kaity |
| **Abstract** | In recent years, the study of microorganisms and the brain has become increasingly connected. The gut-brain-microbiome axis (GBMA), a bi-directional communication system, is the key part of how the body's bacteria and the brain interact. This system can influence the brain and behaviour. Changes in this relationship have been linked to various mental and physical health conditions. The immune system, tryptophan metabolism, the vagus nerve, and the enteric nervous system all facilitate connections between the gut and brain. Microbes produce Peptidoglycans, branched-chain amino acids, and short-chain fatty acids, which are involved in this communication. Studies suggest the gut microbiome may be involved in conditions like autism, anxiety, obesity, schizophrenia, Parkinson's disease, and Alzheimer's disease. Researchers are exploring the gut-brain connection to cure a variety of disorders, such as neurological disorders, cancers, metabolic problems, and liver diseases. Developing novel drug delivery systems is a key focus in GBMA for therapeutic targeting at various disease pathways. Notable platforms attracting significant interest include silica nanoparticle-based delivery systems for probiotic spores, composite hydrogels formulated from protein isolates and citrus pectin, and biomimetic nanosystems designed for targeted therapeutic delivery. This review summarizes different methods of delivering drugs and using dietary interventions to target the GBMA and treat these conditions in a less invasive way. By understanding how the gut and brain communicate, scientists aim to develop new and more effective therapies for these complex chronic diseases. |
| **Date** | 2025 May 25 |
| **Language** | eng |
| **Rights** | Copyright © 2025 Elsevier B.V. All rights reserved. |
| **Extra** | Place: Netherlands PMID: 40425058 |
| **Volume** | 680 |
| **Pages** | 125776 |
| **Publication** | International journal of pharmaceutics |
| **DOI** | [10.1016/j.ijpharm.2025.125776](http://doi.org/10.1016/j.ijpharm.2025.125776) |
| **Journal Abbr** | Int J Pharm |
| **ISSN** | 1873-3476 0378-5173 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Drug Delivery Systems
  + Dysbiosis
  + Gut-Brain-Microbiome-Axis
  + Microbiota
  + Signalling

## Retinoic acid in Parkinson's disease: Molecular insights, therapeutic advances, and future prospects.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Ashutosh Pareek |
| **Author** | Runjhun Singhal |
| **Author** | Aaushi Pareek |
| **Author** | Terisha Ghazi |
| **Author** | Devesh U. Kapoor |
| **Author** | Yashumati Ratan |
| **Author** | Arun Kumar Singh |
| **Author** | Vivek Jain |
| **Author** | Anil A. Chuturgoon |
| **Abstract** | Parkinson's disease (PD) is a common and progressively worsening neurodegenerative disorder characterized by abnormal protein homeostasis and the degeneration of dopaminergic neurons, particularly in the substantia nigra pars compacta. The prevalence of PD has doubled in the past 25 years, now affecting over 8.5 million individuals worldwide, underscoring the need for effective management strategies. While current pharmacological therapies provide symptom relief, they face challenges in treating advanced PD stages. Recent research highlights the therapeutic benefits of retinoic acid (RA) in PD, demonstrating its potential to mitigate neuroinflammation and oxidative stress, regulate brain aging, promote neuronal plasticity, and influence circadian rhythm gene expression and retinoid X receptor heterodimerization. Additionally, RA helps maintain intestinal homeostasis and modulates the enteric nervous system, presenting significant therapeutic potential for managing PD. This review explores RA as a promising alternative to conventional therapies by summarizing the molecular mechanisms underlying its role in PD pathophysiology and presenting up-to-date insights into both preclinical and clinical studies of RA in PD treatment. It also delves into cutting-edge formulations incorporating RA, highlighting ongoing efforts to refine therapeutic strategies by integrating RA into novel treatments. This comprehensive overview aims to advance progress in the field, contribute to the development of effective, targeted treatments for PD, and enhance patient well-being. Further research is essential to fully explore RA's therapeutic potential and validate its efficacy in PD treatment. |
| **Date** | 2024 Oct 15 |
| **Language** | eng |
| **Rights** | Copyright © 2024 The Authors. Published by Elsevier Inc. All rights reserved. |
| **Extra** | Place: Netherlands PMID: 39181315 |
| **Volume** | 355 |
| **Pages** | 123010 |
| **Publication** | Life sciences |
| **DOI** | [10.1016/j.lfs.2024.123010](http://doi.org/10.1016/j.lfs.2024.123010) |
| **Journal Abbr** | Life Sci |
| **ISSN** | 1879-0631 0024-3205 |
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### Tags:

* + Humans
  + Animals
  + Nanoparticles
  + Aging
  + Parkinson's disease
  + \*Parkinson Disease/drug therapy/metabolism
  + \*Tretinoin/therapeutic use
  + DAergic neurons
  + Oxidative Stress/drug effects
  + Retinoic acid
  + Vitamins

## Role of glutamatergic neurotransmission in the enteric nervous system and brain-gut axis in health and disease.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Viviana Filpa |
| **Author** | Elisabetta Moro |
| **Author** | Marina Protasoni |
| **Author** | Francesca Crema |
| **Author** | Gianmario Frigo |
| **Author** | Cristina Giaroni |
| **Abstract** | Several studies have been carried out in the last 30 years in the attempt to clarify the possible role of glutamate as a neurotransmitter/neuromodulator in the gastrointestinal tract. Such effort has provided immunohistochemical, biomolecular and functional data suggesting that the entire glutamatergic neurotransmitter machinery is present in the complex circuitries of the enteric nervous system (ENS), which participates to the local coordination of gastrointestinal functions. Glutamate is also involved in the regulation of the brain-gut axis, a bi-directional connection pathway between the central nervous system (CNS) and the gut. The neurotransmitter contributes to convey information, via afferent fibers, from the gut to the brain, and to send appropriate signals, via efferent fibers, from the brain to control gut secretion and motility. In analogy with the CNS, an increasing number of studies suggest that dysregulation of the enteric glutamatergic neurotransmitter machinery may lead to gastrointestinal dysfunctions. On the whole, this research field has opened the possibility to find new potential targets for development of drugs for the treatment of gastrointestinal diseases. The present review analyzes the more recent literature on enteric glutamatergic neurotransmission both in physiological and pathological conditions, such as gastroesophageal reflux, gastric acid hypersecretory diseases, inflammatory bowel disease, irritable bowel syndrome and intestinal ischemia/reperfusion injury. |
| **Date** | 2016 Dec |
| **Language** | eng |
| **Rights** | Copyright © 2016 Elsevier Ltd. All rights reserved. |
| **Extra** | Place: England PMID: 27561972 |
| **Volume** | 111 |
| **Pages** | 14-33 |
| **Publication** | Neuropharmacology |
| **DOI** | [10.1016/j.neuropharm.2016.08.024](http://doi.org/10.1016/j.neuropharm.2016.08.024) |
| **Journal Abbr** | Neuropharmacology |
| **ISSN** | 1873-7064 0028-3908 |
| **Date Added** | 6/11/2025, 2:32:23 PM |
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### Tags:

* + Humans
  + Animals
  + Enteric nervous system
  + Brain-gut axis
  + Gastrointestinal tract
  + \*Synaptic Transmission
  + Excitotoxicity
  + Gastroesophageal Reflux/physiopathology
  + Gastrointestinal Tract/innervation/\*physiology/\*physiopathology
  + Glutamate
  + Glutamic Acid/\*physiology
  + Inflammatory Bowel Diseases/physiopathology
  + Irritable Bowel Syndrome/physiopathology
  + Neurons, Afferent/physiology

## Role of stem cell growth factor/c-Kit in the pathogenesis of irritable bowel syndrome.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Yuna Chai |
| **Author** | Yusheng Huang |
| **Author** | Hongmei Tang |
| **Author** | Xing Tu |
| **Author** | Jianbo He |
| **Author** | Ting Wang |
| **Author** | Qingye Zhang |
| **Author** | Fen Xiong |
| **Author** | Detang Li |
| **Author** | Zhenwen Qiu |
| **Abstract** | Irritable bowel syndrome (IBS) is a functional bowel disease with a complicated etiopathogenesis, often characterized by gastrointestinal motility disorder and high visceral sensitivity. IBS is a comprehensive multi-systemic disorder, with the interaction of multiple factors, such as mental stress, intestinal function and flora, heredity, resulting in the disease. The existence of a common mechanism underlying the aforementioned factors is currently unknown. The lack of therapies that comprehensively address the disease symptoms, including abdominal pain and diarrhea, is a limitation of current IBS management. The current review has explored the role of the SCF/c-Kit receptor/ligand system in IBS. The SCF/c-Kit system constitutes a classical ligand/receptor tyrosine kinase signaling system that mediates inflammation and smooth muscle contraction. Additionally, it provides trophic support to neural crest-derived cell types, including the enteric nervous system and mast cells. The regulation of SCF/c-Kit on the interstitial cells of Cajal (ICC) suggest that it may play a key role in the aberrant intestinal dynamics and high visceral sensitivity observed in IBS. The role of the SCF/c-Kit system in intestinal motility, inflammation and nerve growth has been reported. From the available biomedical evidence on the pathogenesis of IBS, it has been concluded that the SCF-c-Kit system is a potential therapeutic target for rational drug design in the treatment of IBS. |
| **Date** | 2017 Apr |
| **Language** | eng |
| **Extra** | Place: Greece PMID: 28413456 PMCID: PMC5377426 |
| **Volume** | 13 |
| **Pages** | 1187-1193 |
| **Publication** | Experimental and therapeutic medicine |
| **DOI** | [10.3892/etm.2017.4133](http://doi.org/10.3892/etm.2017.4133) |
| **Issue** | 4 |
| **Journal Abbr** | Exp Ther Med |
| **ISSN** | 1792-0981 1792-1015 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
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### Tags:

* + inflammation
  + irritable bowel syndrome
  + gastrointestinal motility
  + ligand/receptor tyrosine kinase signaling system
  + neuromodulation
  + stem cell factor (SCF)/c-Kit

## Secretion of Acid Sphingomyelinase and Ceramide by Endothelial Cells Contributes to Radiation-Induced Intestinal Toxicity.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Daniela Leonetti |
| **Author** | Hala Estéphan |
| **Author** | Natacha Ripoche |
| **Author** | Nolwenn Dubois |
| **Author** | Audrey Aguesse |
| **Author** | Sébastien Gouard |
| **Author** | Lisa Brossard |
| **Author** | Sophie Chiavassa |
| **Author** | Isabelle Corre |
| **Author** | Claire Pecqueur |
| **Author** | Michel Neunlist |
| **Author** | Elie Hadchity |
| **Author** | Marie-Hélène Gaugler |
| **Author** | Maxime M. Mahé |
| **Author** | François Paris |
| **Abstract** | Ceramide-induced endothelial cell apoptosis boosts intestinal stem cell radiosensitivity. However, the molecular connection between these two cellular compartments has not been clearly elucidated. Here we report that ceramide and its related enzyme acid sphingomyelinase (ASM) are secreted by irradiated endothelial cells and act as bystander factors to enhance the radiotoxicity of intestinal epithelium. Ceramide and the two isoforms of ASM were acutely secreted in the blood serum of wild-type mice after 15 Gy radiation dose, inducing a gastrointestinal syndrome. Interestingly, serum ceramide was not enhanced in irradiated ASMKO mice, which are unable to develop intestinal failure injury. Because ASM/ceramide were secreted by primary endothelial cells, their contribution was studied in intestinal epithelium dysfunction using coculture of primary endothelial cells and intestinal T84 cells. Adding exogenous ASM or ceramide enhanced epithelial cell growth arrest and death. Conversely, blocking their secretion by endothelial cells using genetic, pharmacologic, or immunologic approaches abolished intestinal T84 cell radiosensitivity. Use of enteroid models revealed ASM and ceramide-mediated deleterious mode-of-action: when ceramide reduced the number of intestinal crypt-forming enteroids without affecting their structure, ASM induced a significant decrease of enteroid growth without affecting their number. Identification of specific and different roles for ceramide and ASM secreted by irradiated endothelial cells opens new perspectives in the understanding of intestinal epithelial dysfunction after radiation and defines a new class of potential therapeutic radiomitigators. SIGNIFICANCE: This study identifies secreted ASM and ceramide as paracrine factors enhancing intestinal epithelial dysfunction, revealing a previously unknown class of mediators of radiosensitivity. |
| **Date** | 2020 Jun 15 |
| **Language** | eng |
| **Rights** | ©2020 American Association for Cancer Research. |
| **Extra** | Place: United States PMID: 32291318 |
| **Volume** | 80 |
| **Pages** | 2651-2662 |
| **Publication** | Cancer research |
| **DOI** | [10.1158/0008-5472.CAN-19-1527](http://doi.org/10.1158/0008-5472.CAN-19-1527) |
| **Issue** | 12 |
| **Journal Abbr** | Cancer Res |
| **ISSN** | 1538-7445 0008-5472 |
| **Date Added** | 6/11/2025, 2:32:27 PM |
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### Tags:

* + Humans
  + Male
  + Animals
  + Disease Models, Animal
  + Mice
  + Coculture Techniques
  + Cells, Cultured
  + Mice, Knockout
  + Primary Cell Culture
  + Bystander Effect/radiation effects
  + Ceramides/blood/\*metabolism
  + Desipramine/pharmacology
  + Endothelial Cells/drug effects/\*metabolism/radiation effects
  + Epithelial Cells/drug effects/pathology/radiation effects
  + Intestinal Mucosa/cytology/drug effects/\*pathology/radiation effects
  + Paracrine Communication/genetics/radiation effects
  + Radiation Injuries/blood/etiology/\*pathology/prevention & control
  + Radiation Tolerance/drug effects/genetics
  + RNA, Small Interfering/metabolism
  + Sphingomyelin Phosphodiesterase/antagonists & inhibitors/blood/genetics/\*metabolism

## Serotonin attenuates tumor necrosis factor-induced intestinal inflammation by interacting with human mucosal tissue.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Veronika Bosáková |
| **Author** | Ioanna Papatheodorou |
| **Author** | Filip Kafka |
| **Author** | Zuzana Tomášiková |
| **Author** | Petros Kolovos |
| **Author** | Marcela Hortová Kohoutková |
| **Author** | Jan Frič |
| **Abstract** | The intestine hosts the largest immune system and peripheral nervous system in the human body. The gut‒brain axis orchestrates communication between the central and enteric nervous systems, playing a pivotal role in regulating overall body function and intestinal homeostasis. Here, using a human three-dimensional in vitro culture model, we investigated the effects of serotonin, a neuromodulator produced in the gut, on immune cell and intestinal tissue interactions. Serotonin attenuated the tumor necrosis factor-induced proinflammatory response, mostly by affecting the expression of chemokines. Serotonin affected the phenotype and distribution of tissue-migrating monocytes, without direct contact with the cells, by remodeling the intestinal tissue. Collectively, our results show that serotonin plays a crucial role in communication among gut-brain axis components and regulates monocyte migration and plasticity, thereby contributing to gut homeostasis and the progression of inflammation. In vivo studies focused on the role of neuromodulators in gut inflammation have shown controversial results, highlighting the importance of human experimental models. Moreover, our results emphasize the importance of human health research in human cell-based models and suggest that the serotonin signaling pathway is a new therapeutic target for inflammatory bowel disease. |
| **Date** | 2025 Feb |
| **Language** | eng |
| **Rights** | © 2025. The Author(s). |
| **Extra** | Place: United States PMID: 39894823 PMCID: PMC11873120 |
| **Volume** | 57 |
| **Pages** | 364-378 |
| **Publication** | Experimental & molecular medicine |
| **DOI** | [10.1038/s12276-025-01397-1](http://doi.org/10.1038/s12276-025-01397-1) |
| **Issue** | 2 |
| **Journal Abbr** | Exp Mol Med |
| **ISSN** | 2092-6413 1226-3613 |
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### Tags:

* + Humans
  + Signal Transduction/drug effects
  + \*Inflammation/metabolism/pathology
  + \*Intestinal Mucosa/metabolism/drug effects/pathology/immunology
  + \*Serotonin/pharmacology/metabolism
  + \*Tumor Necrosis Factor-alpha
  + Cell Movement/drug effects
  + Inflammatory Bowel Diseases/metabolism/pathology
  + Monocytes/metabolism/drug effects

## Study of the roles of caspase-3 and nuclear factor kappa B in myenteric neurons in a P2X7 receptor knockout mouse model of ulcerative colitis.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Henrique Inhauser Riceti Magalhães |
| **Author** | Felipe Alexandre Machado |
| **Author** | Roberta Figueiroa Souza |
| **Author** | Marcos Antônio Ferreira Caetano |
| **Author** | Vanessa Ribeiro Figliuolo |
| **Author** | Robson Coutinho-Silva |
| **Author** | Patricia Castelucci |
| **Abstract** | BACKGROUND: The literature indicates that the enteric nervous system is affected in inflammatory bowel diseases (IBDs) and that the P2X7 receptor triggers neuronal death. However, the mechanism by which enteric neurons are lost in IBDs is unknown. AIM: To study the role of the caspase-3 and nuclear factor kappa B (NF-κB) pathways in myenteric neurons in a P2X7 receptor knockout (KO) mouse model of IBDs. METHODS: Forty male wild-type (WT) C57BL/6 and P2X7 receptor KO mice were euthanized 24 h or 4 d after colitis induction by 2,4,6-trinitrobenzene sulfonic acid (colitis group). Mice in the sham groups were injected with vehicle. The mice were divided into eight groups (n = 5): The WT sham 24 h and 4 d groups, the WT colitis 24 h and 4 d groups, the KO sham 24 h and 4 d groups, and the KO colitis 24 h and 4 d groups. The disease activity index (DAI) was analyzed, the distal colon was collected for immunohistochemistry analyses, and immunofluorescence was performed to identify neurons immunoreactive (ir) for calretinin, P2X7 receptor, cleaved caspase-3, total caspase-3, phospho-NF-κB, and total NF-κB. We analyzed the number of calretinin-ir and P2X7 receptor-ir neurons per ganglion, the neuronal profile area (µm²), and corrected total cell fluorescence (CTCF). RESULTS: Cells double labeled for calretinin and P2X7 receptor, cleaved caspase-3, total caspase-3, phospho-NF-κB, or total NF-κB were observed in the WT colitis 24 h and 4 d groups. The number of calretinin-ir neurons per ganglion was decreased in the WT colitis 24 h and 4 d groups compared to the WT sham 24 h and 4 d groups, respectively (2.10 ± 0.13 vs 3.33 ± 0.17, P < 0.001; 2.92 ± 0.12 vs 3.70 ± 0.11, P < 0.05), but was not significantly different between the KO groups. The calretinin-ir neuronal profile area was increased in the WT colitis 24 h group compared to the WT sham 24 h group (312.60 ± 7.85 vs 278.41 ± 6.65, P < 0.05), and the nuclear profile area was decreased in the WT colitis 4 d group compared to the WT sham 4 d group (104.63 ± 2.49 vs 117.41 ± 1.14, P < 0.01). The number of P2X7 receptor-ir neurons per ganglion was decreased in the WT colitis 24 h and 4 d groups compared to the WT sham 24 h and 4 d groups, respectively (19.49 ± 0.35 vs 22.21 ± 0.18, P < 0.001; 20.35 ± 0.14 vs 22.75 ± 0.51, P < 0.001), and no P2X7 receptor-ir neurons were observed in the KO groups. Myenteric neurons showed ultrastructural changes in the WT colitis 24 h and 4 d groups and in the KO colitis 24 h group. The cleaved caspase-3 CTCF was increased in the WT colitis 24 h and 4 d groups compared to the WT sham 24 h and 4 d groups, respectively (485949 ± 14140 vs 371371 ± 16426, P < 0.001; 480381 ± 11336 vs 378365 ± 4053, P < 0.001), but was not significantly different between the KO groups. The total caspase-3 CTCF, phospho-NF-κB CTCF, and total NF-κB CTCF were not significantly different among the groups. The DAI was recovered in the KO groups. Furthermore, we demonstrated that the absence of the P2X7 receptor attenuated inflammatory infiltration, tissue damage, collagen deposition, and the decrease in the number of goblet cells in the distal colon. CONCLUSION: Ulcerative colitis affects myenteric neurons in WT mice but has a weaker effect in P2X7 receptor KO mice, and neuronal death may be associated with P2X7 receptor-mediated caspase-3 activation. The P2X7 receptor can be a therapeutic target for IBDs. |
| **Date** | 2023 Jun 14 |
| **Language** | eng |
| **Rights** | ©The Author(s) 2023. Published by Baishideng Publishing Group Inc. All rights reserved. |
| **Extra** | Place: United States PMID: 37389242 PMCID: PMC10303518 |
| **Volume** | 29 |
| **Pages** | 3440-3468 |
| **Publication** | World journal of gastroenterology |
| **DOI** | [10.3748/wjg.v29.i22.3440](http://doi.org/10.3748/wjg.v29.i22.3440) |
| **Issue** | 22 |
| **Journal Abbr** | World J Gastroenterol |
| **ISSN** | 2219-2840 1007-9327 |
| **Date Added** | 6/11/2025, 2:32:27 PM |
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### Tags:

* + Male
  + Animals
  + Mice
  + Mice, Inbred C57BL
  + Gastroenterology
  + Enteric nervous system
  + Inflammatory bowel diseases
  + P2X7 receptor
  + Purinergic signaling
  + \*Colitis
  + \*Colitis, Ulcerative/chemically induced/genetics
  + \*Inflammatory Bowel Diseases
  + Calbindin 2
  + Caspase 3
  + Cell death
  + NF-kappa B

## Suppression of PGE2/EP2 signaling alleviates Hirschsprung disease by upregulating p38 mitogen-activated protein kinase activity.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Jiao Wang |
| **Author** | Zhengke Zhi |
| **Author** | Jie Ding |
| **Author** | Na Jia |
| **Author** | Yuqing Hu |
| **Author** | Jiali Cai |
| **Author** | Hongxing Li |
| **Author** | Jie Tang |
| **Author** | Weibing Tang |
| **Author** | Xiaohua Mao |
| **Abstract** | Hirschsprung disease (HSCR) is a congenital disorder caused by the failure of enteric neural crest cells (ENCCs) to colonize the distal bowel, resulting in absence of enteric nervous system. While a range of molecules and signaling pathways have been found to contribute to HSCR development, the risk factors and pathogenesis of this disease in many patients remain unknown. We previously demonstrated that increased activity of the prostaglandin E2 (PGE2)/PGE2 receptor subtype EP2 pathway can be a risk factor for HSCR. In this study, an Ednrb-deficient mouse model of HSCR was generated and used to investigate if PGE2/EP2 pathway could be a potential therapeutic target for HSCR. We found that downregulation of PGE2/EP2 signaling by siRNA-mediated ablation of a PGE2 synthase or pharmacologic blockage of EP2 enhanced ENCC colonization in the distal bowel of Ednrb(-/-) mice and alleviated their HSCR-like symptoms. Furthermore, blockage of EP2 was shown to promote ENCC migration through upregulating p38 mitogen-activated protein kinase activity, which was downregulated in the colon of Ednrb(-/-) mice and in the distal aganglionic bowel of HSCR patients. These data provide evidence that maternal exposure during embryonic development to an environment with dysregulated activation of the PGE2/EP2 pathway may predispose genetically susceptible offspring to HSCR, and avoidance or early disruption of maternal events (e.g. inflammation) that possibly enhance PGE2/EP2 signaling during pregnancy would reduce the occurrence and severity of this disease. KEY MESSAGES : Knockdown of PTGES alleviates HSCR severity in Ednrb(-/-) mice. Blockage of EP2-mediated PGE2 signaling alleviates HSCR severity in Ednrb(-/-) mice. Blockage of EP2-mediated PGE2 signaling promotes ENCC migration via enhancing p38 activity. |
| **Date** | 2023 Sep |
| **Language** | eng |
| **Rights** | © 2023. The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature. |
| **Extra** | Place: Germany PMID: 37522903 |
| **Volume** | 101 |
| **Pages** | 1125-1139 |
| **Publication** | Journal of molecular medicine (Berlin, Germany) |
| **DOI** | [10.1007/s00109-023-02353-0](http://doi.org/10.1007/s00109-023-02353-0) |
| **Issue** | 9 |
| **Journal Abbr** | J Mol Med (Berl) |
| **ISSN** | 1432-1440 0946-2716 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
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### Tags:

* + Female
  + Animals
  + Mice
  + Dinoprostone/metabolism
  + \*Enteric Nervous System/metabolism
  + \*Hirschsprung Disease/metabolism/pathology
  + EDNRB
  + EP2
  + Hirschsprung disease (HSCR)
  + Neural crest cell
  + p38 Mitogen-Activated Protein Kinases/metabolism
  + PGE2

## Targeting enteric glial CRF-R1/Cx43 attenuates stress-induced accelerated colonic motility.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Haiqing Chang |
| **Author** | Haifeng Zhang |
| **Author** | Shiqiu Jiang |
| **Author** | Juan Hu |
| **Author** | Hongli Ma |
| **Author** | Bo Cheng |
| **Author** | Qiang Wang |
| **Author** | Yansong Li |
| **Abstract** | Stress triggers disorders in accelerated peristalsis, with corticotropin releasing factor receptor 1 (CRF-R1) playing a pivotal role. Enteric glia cells (EGCs) and glial Cx43 are known to influence gastrointestinal motility, yet their involvement in colonic motor responses to stress remains unclear. Using immunofluorescence and single-cell RNA sequencing data, we identified CRF-R1 expression in EGCs. Male C57BL/6 mice subjected to wrap restraint stress (WRS) revealed stress-induced colonic motility changes. By employing Fluoroacetate, NBI 27914, and Gap26, we elucidated the impact of glial CRF-R1/Cx43 on stress-induced colonic motor responses. Our study demonstrated CRF-R1 expression in EGCs of the small intestine and colon, along with elevated CRF levels and upregulated CRF-R1 in the distal colon under stress. Antagonizing CRF-R1 and disrupting EGC function made mice resistant to colonic stress responses. Mechanistically, increased glial Cx43 expression and activity influenced colonic motor responses in a CRF-R1-dependent manner. Our findings highlight the role of EGC-derived CRF-R1 in stress-induced colonic motor responses via Cx43 activation. Targeting CRF-R1/Cx43 signaling in EGCs may offer a promising approach to mitigate stress-induced colonic transit changes. |
| **Date** | 2025 Mar |
| **Language** | eng |
| **Rights** | Copyright © 2025 The Authors. Published by Elsevier B.V. All rights reserved. |
| **Extra** | Place: Japan PMID: 39929591 |
| **Volume** | 157 |
| **Pages** | 167-178 |
| **Publication** | Journal of pharmacological sciences |
| **DOI** | [10.1016/j.jphs.2025.01.009](http://doi.org/10.1016/j.jphs.2025.01.009) |
| **Issue** | 3 |
| **Journal Abbr** | J Pharmacol Sci |
| **ISSN** | 1347-8648 1347-8613 |
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### Tags:

* + Male
  + Animals
  + Mice
  + Mice, Inbred C57BL
  + Signal Transduction
  + Enteric Nervous System
  + Stress
  + \*Colon/physiology
  + \*Connexin 43/metabolism/physiology/genetics
  + \*Gastrointestinal Motility/physiology/genetics
  + \*Neuroglia/metabolism/physiology
  + \*Receptors, Corticotropin-Releasing Hormone/metabolism/physiology/genetics/antagonists & inhibitors
  + \*Stress, Psychological/physiopathology/complications
  + Colonic motility
  + Colonic stress responses
  + Corticotropin-Releasing Hormone/metabolism
  + CRF Receptor, Type 1
  + CRF-R1/Cx43
  + Enteric glia cells
  + Gene Expression/genetics
  + Restraint, Physical

## Targeting Enteric Neurons and Plexitis for the Management of Inflammatory Bowel Disease.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Rhian Stavely |
| **Author** | Raquel Abalo |
| **Author** | Kulmira Nurgali |
| **Abstract** | Ulcerative colitis (UC) and Crohn's disease (CD) are pathological conditions with an unknown aetiology that are characterised by severe inflammation of the intestinal tract and collectively referred to as inflammatory bowel disease (IBD). Current treatments are mostly ineffective due to their limited efficacy or toxicity, necessitating surgical resection of the affected bowel. The management of IBD is hindered by a lack of prognostic markers for clinical inflammatory relapse. Intestinal inflammation associates with the infiltration of immune cells (leukocytes) into, or surrounding the neuronal ganglia of the enteric nervous system (ENS) termed plexitis or ganglionitis. Histological observation of plexitis in unaffected intestinal regions is emerging as a vital predictive marker for IBD relapses. Plexitis associates with alterations to the structure, cellular composition, molecular expression and electrophysiological function of enteric neurons. Moreover, plexitis often occurs before the onset of gross clinical inflammation, which may indicate that plexitis can contribute to the progression of intestinal inflammation. In this review, the bilateral relationships between the ENS and inflammation are discussed. These include the effects and mechanisms of inflammation-induced enteric neuronal loss and plasticity. Additionally, the role of enteric neurons in preventing antigenic/pathogenic insult and immunomodulation is explored. While all current treatments target the inflammatory pathology of IBD, interventions that protect the ENS may offer an alternative avenue for therapeutic intervention. |
| **Date** | 2020 |
| **Language** | eng |
| **Rights** | Copyright© Bentham Science Publishers; For any queries, please email at epub@benthamscience.net. |
| **Extra** | Place: United Arab Emirates PMID: 32416686 |
| **Volume** | 21 |
| **Pages** | 1428-1439 |
| **Publication** | Current drug targets |
| **DOI** | [10.2174/1389450121666200516173242](http://doi.org/10.2174/1389450121666200516173242) |
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| **Journal Abbr** | Curr Drug Targets |
| **ISSN** | 1873-5592 1389-4501 |
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### Tags:

* + Humans
  + Animals
  + inflammation
  + inflammatory bowel disease
  + Enteric nervous system
  + Crohn’s disease
  + ulcerative colitis
  + neuroprotection
  + Enteric Nervous System/\*immunology/metabolism
  + Inflammation/immunology/metabolism
  + Inflammatory Bowel Diseases/\*immunology/\*therapy
  + neuro-immune
  + Neurons/immunology/metabolism
  + Peripheral Nervous System Diseases/\*immunology/\*therapy
  + Physical Therapy Modalities
  + plexitis

## Targeting the Enteric Nervous System to Treat Metabolic Disorders? "Enterosynes" as Therapeutic Gut Factors.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Claude Knauf |
| **Author** | Anne Abot |
| **Author** | Eve Wemelle |
| **Author** | Patrice D. Cani |
| **Abstract** | The gut-brain axis is of crucial importance for controlling glucose homeostasis. Alteration of this axis promotes the type 2 diabetes (T2D) phenotype (hyperglycaemia, insulin resistance). Recently, a new concept has emerged to demonstrate the crucial role of the enteric nervous system in the control of glycaemia via the hypothalamus. In diabetic patients and mice, modification of enteric neurons activity in the proximal part of the intestine generates a duodenal hyper-contractility that generates an aberrant message from the gut to the brain. In turn, the hypothalamus sends an aberrant efferent message that provokes a state of insulin resistance, which is characteristic of a T2D state. Targeting the enteric nervous system of the duodenum is now recognized as an innovative strategy for treatment of diabetes. By acting in the intestine, bioactive gut molecules that we called "enterosynes" can modulate the function of a specific type of neurons of the enteric nervous system to decrease the contraction of intestinal smooth muscle cells. Here, we focus on the origins of enterosynes (hormones, neurotransmitters, nutrients, microbiota, and immune factors), which could be considered therapeutic factors, and we describe their modes of action on enteric neurons. This unsuspected action of enterosynes is proposed for the treatment of T2D, but it could be applied for other therapeutic solutions that implicate communication between the gut and brain. |
| **Date** | 2020 |
| **Language** | eng |
| **Rights** | © 2019 S. Karger AG, Basel. |
| **Extra** | Place: Switzerland PMID: 31280267 |
| **Volume** | 110 |
| **Pages** | 139-146 |
| **Publication** | Neuroendocrinology |
| **DOI** | [10.1159/000500602](http://doi.org/10.1159/000500602) |
| **Issue** | 1-2 |
| **Journal Abbr** | Neuroendocrinology |
| **ISSN** | 1423-0194 0028-3835 |
| **Date Added** | 6/11/2025, 2:32:22 PM |
| **Modified** | 6/11/2025, 2:32:22 PM |

### Tags:

* + Humans
  + Animals
  + Obesity
  + Diabetes
  + Enteric nervous system
  + Diabetes Mellitus, Type 2/\*drug therapy
  + Enteric Nervous System/\*drug effects/\*physiology
  + Obesity/\*drug therapy

## Targeting the gastrointestinal tract with viral vectors: state of the art and possible applications in research and therapy.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Roeland Buckinx |
| **Author** | Jean-Pierre Timmermans |
| **Abstract** | While there is a large body of preclinical data on the use of viral vectors in gene transfer, relatively little is known about viral gene transfer in the gastrointestinal tract. Viral vector technology is especially underused in the field of neurogastroenterology when compared to brain research. This review provides an overview of the studies employing viral vectors-in particular retroviruses, adenoviruses and adeno-associated viruses-to transduce different cell types in the intestine. Early work mainly focused on mucosal transduction, but had limited success due to the harsh luminal conditions in the gastrointestinal tract and the high turnover rate of enterocytes. More recently, several studies have successfully employed viral gene transfer to target the enteric nervous system and its progenitors. Although several hurdles still need to be overcome, in particular on how to augment transduction efficiency and specific cell targeting, viral vector technology holds strong potential not only as a valid research tool in fundamental gastroenterological research but also as a therapeutic agent in translational (bio)medical research. |
| **Date** | 2016 Dec |
| **Language** | eng |
| **Extra** | Place: Germany PMID: 27665281 |
| **Volume** | 146 |
| **Pages** | 709-720 |
| **Publication** | Histochemistry and cell biology |
| **DOI** | [10.1007/s00418-016-1496-6](http://doi.org/10.1007/s00418-016-1496-6) |
| **Issue** | 6 |
| **Journal Abbr** | Histochem Cell Biol |
| **ISSN** | 1432-119X 0948-6143 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/11/2025, 2:32:25 PM |

### Tags:

* + Humans
  + Animals
  + Gastroenterology
  + \*Genetic Therapy
  + AAV
  + Adenoviridae/\*genetics
  + Adenovirus
  + Dependovirus/\*genetics
  + Gastrointestinal Tract/cytology/\*metabolism/\*virology
  + Gene therapy
  + Genetic Vectors/\*genetics
  + Retroviridae/\*genetics
  + Retrovirus

## Targeting the gut to treat multiple sclerosis.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Laura Ghezzi |
| **Author** | Claudia Cantoni |
| **Author** | Gabriela V. Pinget |
| **Author** | Yanjiao Zhou |
| **Author** | Laura Piccio |
| **Abstract** | The gut-brain axis (GBA) refers to the complex interactions between the gut microbiota and the nervous, immune, and endocrine systems, together linking brain and gut functions. Perturbations of the GBA have been reported in people with multiple sclerosis (pwMS), suggesting a possible role in disease pathogenesis and making it a potential therapeutic target. While research in the area is still in its infancy, a number of studies revealed that pwMS are more likely to exhibit altered microbiota, altered levels of short chain fatty acids and secondary bile products, and increased intestinal permeability. However, specific microbes and metabolites identified across studies and cohorts vary greatly. Small clinical and preclinical trials in pwMS and mouse models, in which microbial composition was manipulated through the use of antibiotics, fecal microbiota transplantation, and probiotic supplements, have provided promising outcomes in preventing CNS inflammation. However, results are not always consistent, and large-scale randomized controlled trials are lacking. Herein, we give an overview of how the GBA could contribute to MS pathogenesis, examine the different approaches tested to modulate the GBA, and discuss how they may impact neuroinflammation and demyelination in the CNS. |
| **Date** | 2021 Jul 1 |
| **Language** | eng |
| **Extra** | Place: United States PMID: 34196310 PMCID: PMC8245171 |
| **Volume** | 131 |
| **Publication** | The Journal of clinical investigation |
| **DOI** | [10.1172/JCI143774](http://doi.org/10.1172/JCI143774) |
| **Issue** | 13 |
| **Journal Abbr** | J Clin Invest |
| **ISSN** | 1558-8238 0021-9738 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/11/2025, 2:32:24 PM |

### Tags:

* + Humans
  + Animals
  + Disease Models, Animal
  + \*Gastrointestinal Microbiome/drug effects/immunology/physiology
  + Autoimmunity
  + Dysbiosis/immunology/physiopathology
  + Endocrine System/immunology/physiopathology
  + Enteric Nervous System/immunology/microbiology/physiopathology
  + Fecal Microbiota Transplantation
  + Intestinal Mucosa/immunology/microbiology/physiopathology
  + Models, Neurological
  + Multiple Sclerosis/etiology/microbiology/\*therapy
  + Neuroimmunomodulation
  + Probiotics/therapeutic use

## The Brain-Gut-Microbiotal Axis: A framework for understanding functional GI illness and their therapeutic interventions.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Christopher Tait |
| **Author** | Gregory S. Sayuk |
| **Abstract** | Functional gastrointestinal disorders (FGIDs), characterized by chronic abdominal complaints without a structural or biochemical cause, are common diseases that are frequently encountered by specialists in internal medicine. Collectively, irritable bowel syndrome (IBS) and functional dyspepsia are estimated to affect up to 22% of the population, and are often associated with additional somatic and pain complaints, all without an obvious structural source [1,2]. An appreciation of the current understanding of the mechanistic basis for these disorders is key to developing treatment goals and optimization of patient management strategies. In recent years, the brain-gut axis increasingly has been recognized as a central factor in the experience of functional abdominal pain disorders, including the most recent Rome IV guidelines which identify FGIDs as disorders of gut-brain interaction [3]. The brain-gut axis (BGA), simply defined, is a complex network of bidirectional communication between the central and enteric nervous systems. This axis broadly includes all the systems involved with communication between the GI tract and central nervous system (CNS), with principle inputs into this network occurring between the CNS, enteric nervous system (ENS), and autonomic nervous systems (ANS), but also includes interfaces with numerous other factors, including endocrine hormones and immune effector cells as well as interactions with the gut microbiota. Perturbances to this system have been found to play a critical role in the development of visceral hypersensitivity, bowel dysregulation, and mood. This review will summarize the principle processes involved in the neurologic and biologic function of the brain-gut axis, our current understanding of its role in functional GI disorders, and potential targets for therapeutic intervention. |
| **Date** | 2021 Feb |
| **Language** | eng |
| **Rights** | Published by Elsevier B.V. |
| **Extra** | Place: Netherlands PMID: 33423906 |
| **Volume** | 84 |
| **Pages** | 1-9 |
| **Publication** | European journal of internal medicine |
| **DOI** | [10.1016/j.ejim.2020.12.023](http://doi.org/10.1016/j.ejim.2020.12.023) |
| **Journal Abbr** | Eur J Intern Med |
| **ISSN** | 1879-0828 0953-6205 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/11/2025, 2:32:24 PM |

### Tags:

* + Humans
  + microbiota
  + \*Enteric Nervous System
  + Brain
  + enteric nervous system
  + functional gastrointestinal disorders
  + \*Gastrointestinal Diseases/therapy
  + \*Irritable Bowel Syndrome/therapy
  + Abdominal Pain
  + Brain gut axis

## The enteric nervous system is a potential autoimmune target in multiple sclerosis.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Marie Wunsch |
| **Author** | Samir Jabari |
| **Author** | Barbara Voussen |
| **Author** | Michael Enders |
| **Author** | Shanthi Srinivasan |
| **Author** | François Cossais |
| **Author** | Thilo Wedel |
| **Author** | Martina Boettner |
| **Author** | Anna Schwarz |
| **Author** | Linda Weyer |
| **Author** | Oktay Göcer |
| **Author** | Michael Schroeter |
| **Author** | Mathias Maeurer |
| **Author** | Matthias Woenckhaus |
| **Author** | Karolin Pollok |
| **Author** | Helena Radbruch |
| **Author** | Luisa Klotz |
| **Author** | Claus-Jürgen Scholz |
| **Author** | Joachim Nickel |
| **Author** | Andreas Friebe |
| **Author** | Klaus Addicks |
| **Author** | Süleyman Ergün |
| **Author** | Paul V. Lehmann |
| **Author** | Stefanie Kuerten |
| **Abstract** | Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system (CNS) in young adults that has serious negative socioeconomic effects. In addition to symptoms caused by CNS pathology, the majority of MS patients frequently exhibit gastrointestinal dysfunction, which was previously either explained by the presence of spinal cord lesions or not directly linked to the autoimmune etiology of the disease. Here, we studied the enteric nervous system (ENS) in a B cell- and antibody-dependent mouse model of MS by immunohistochemistry and electron microscopy at different stages of the disease. ENS degeneration was evident prior to the development of CNS lesions and the onset of neurological deficits in mice. The pathology was antibody mediated and caused a significant decrease in gastrointestinal motility, which was associated with ENS gliosis and neuronal loss. We identified autoantibodies against four potential target antigens derived from enteric glia and/or neurons by immunoprecipitation and mass spectrometry. Antibodies against three of the target antigens were also present in the plasma of MS patients as confirmed by ELISA. The analysis of human colon resectates provided evidence of gliosis and ENS degeneration in MS patients compared to non-MS controls. For the first time, this study establishes a pathomechanistic link between the well-established autoimmune attack on the CNS and ENS pathology in MS, which might provide a paradigm shift in our current understanding of the immunopathogenesis of the disease with broad diagnostic and therapeutic implications. |
| **Date** | 2017 Aug |
| **Language** | eng |
| **Extra** | Place: Germany PMID: 28620692 |
| **Volume** | 134 |
| **Pages** | 281-295 |
| **Publication** | Acta neuropathologica |
| **DOI** | [10.1007/s00401-017-1742-6](http://doi.org/10.1007/s00401-017-1742-6) |
| **Issue** | 2 |
| **Journal Abbr** | Acta Neuropathol |
| **ISSN** | 1432-0533 0001-6322 |
| **Date Added** | 6/11/2025, 2:32:23 PM |
| **Modified** | 6/11/2025, 2:32:23 PM |

### Tags:

* + Female
  + Humans
  + Male
  + Animals
  + Disease Models, Animal
  + Mice
  + Mice, Inbred C57BL
  + Cytokines/metabolism
  + ENS
  + Multiple sclerosis
  + CNS
  + Tubulin/metabolism
  + \*Multiple Sclerosis/complications/immunology/pathology
  + Autoantibodies
  + Autoantibodies/\*blood
  + Central Nervous System/metabolism/pathology
  + EAE
  + Enteric Nervous System/metabolism/pathology/ultrastructure
  + Freund's Adjuvant/toxicity
  + Gastrointestinal Diseases/\*etiology
  + Muscle, Smooth/pathology/ultrastructure
  + Myelin Basic Protein/immunology/metabolism/toxicity
  + Myelin-Oligodendrocyte Glycoprotein/immunology/toxicity
  + Myenteric Plexus/pathology/ultrastructure
  + Recombinant Fusion Proteins/immunology/toxicity

## The gut-brain axis: Identifying new therapeutic approaches for type 2 diabetes, obesity, and related disorders.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Paul Richards |
| **Author** | Nancy A. Thornberry |
| **Author** | Shirly Pinto |
| **Abstract** | BACKGROUND: The gut-brain axis, which mediates bidirectional communication between the gastrointestinal system and central nervous system (CNS), plays a fundamental role in multiple areas of physiology including regulating appetite, metabolism, and gastrointestinal function. The biology of the gut-brain axis is central to the efficacy of glucagon-like peptide-1 (GLP-1)-based therapies, which are now leading treatments for type 2 diabetes (T2DM) and obesity. This success and research to suggest a much broader role of gut-brain circuits in physiology and disease has led to increasing interest in targeting such circuits to discover new therapeutics. However, our current knowledge of this biology is limited, largely because the scientific tools have not been available to enable a detailed mechanistic understanding of gut-brain communication. SCOPE OF REVIEW: In this review, we provide an overview of the current understanding of how sensory information from the gastrointestinal system is communicated to the central nervous system, with an emphasis on circuits involved in regulating feeding and metabolism. We then describe how recent technologies are enabling a better understanding of this system at a molecular level and how this information is leading to novel insights into gut-brain communication. We also discuss current therapeutic approaches that leverage the gut-brain axis to treat diabetes, obesity, and related disorders and describe potential novel approaches that have been enabled by recent advances in the field. MAJOR CONCLUSIONS: The gut-brain axis is intimately involved in regulating glucose homeostasis and appetite, and this system plays a key role in mediating the efficacy of therapeutics that have had a major impact on treating T2DM and obesity. Research into the gut-brain axis has historically largely focused on studying individual components in this system, but new technologies are now enabling a better understanding of how signals from these components are orchestrated to regulate metabolism. While this work reveals a complexity of signaling even greater than previously appreciated, new insights are already being leveraged to explore fundamentally new approaches to treating metabolic diseases. |
| **Date** | 2021 Apr |
| **Language** | eng |
| **Rights** | Copyright © 2021 The Author(s). Published by Elsevier GmbH.. All rights reserved. |
| **Extra** | Place: Germany PMID: 33548501 PMCID: PMC8085592 |
| **Volume** | 46 |
| **Pages** | 101175 |
| **Publication** | Molecular metabolism |
| **DOI** | [10.1016/j.molmet.2021.101175](http://doi.org/10.1016/j.molmet.2021.101175) |
| **Journal Abbr** | Mol Metab |
| **ISSN** | 2212-8778 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/11/2025, 2:32:25 PM |

### Tags:

* + Humans
  + Animals
  + Obesity
  + Diabetes
  + Homeostasis
  + Enteric Nervous System
  + Gut-brain axis
  + Central Nervous System
  + Gastrointestinal Microbiome
  + Appetite
  + Brain/\*metabolism
  + Diabetes Mellitus, Type 2/\*metabolism
  + Gastrointestinal Tract/\*metabolism
  + Glucagon-Like Peptide 1/metabolism
  + Gut peptides
  + Metabolic Diseases/metabolism
  + Obesity/\*metabolism
  + Vagus
  + Vagus Nerve

## The microbiota-gut-brain axis in Huntington's disease: pathogenic mechanisms and therapeutic targets.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Millicent N. Ekwudo |
| **Author** | Carolina Gubert |
| **Author** | Anthony J. Hannan |
| **Abstract** | Huntington's disease (HD) is a currently incurable neurogenerative disorder and is typically characterized by progressive movement disorder (including chorea), cognitive deficits (culminating in dementia), psychiatric abnormalities (the most common of which is depression), and peripheral symptoms (including gastrointestinal dysfunction). There are currently no approved disease-modifying therapies available for HD, with death usually occurring approximately 10-25 years after onset, but some therapies hold promising potential. HD subjects are often burdened by chronic diarrhea, constipation, esophageal and gastric inflammation, and a susceptibility to diabetes. Our understanding of the microbiota-gut-brain axis in HD is in its infancy and growing evidence from preclinical and clinical studies suggests a role of gut microbial population imbalance (gut dysbiosis) in HD pathophysiology. The gut and the brain can communicate through the enteric nervous system, immune system, vagus nerve, and microbiota-derived-metabolites including short-chain fatty acids, bile acids, and branched-chain amino acids. This review summarizes supporting evidence demonstrating the alterations in bacterial and fungal composition that may be associated with HD. We focus on mechanisms through which gut dysbiosis may compromise brain and gut health, thus triggering neuroinflammatory responses, and further highlight outcomes of attempts to modulate the gut microbiota as promising therapeutic strategies for HD. Ultimately, we discuss the dearth of data and the need for more longitudinal and translational studies in this nascent field. We suggest future directions to improve our understanding of the association between gut microbes and the pathogenesis of HD, and other 'brain and body disorders'. |
| **Date** | 2025 Mar |
| **Language** | eng |
| **Rights** | © 2024 The Authors. The FEBS Journal published by John Wiley & Sons Ltd on behalf of Federation of European Biochemical Societies. |
| **Extra** | Place: England PMID: 38426291 PMCID: PMC11927060 |
| **Volume** | 292 |
| **Pages** | 1282-1315 |
| **Publication** | The FEBS journal |
| **DOI** | [10.1111/febs.17102](http://doi.org/10.1111/febs.17102) |
| **Issue** | 6 |
| **Journal Abbr** | FEBS J |
| **ISSN** | 1742-4658 1742-464X |
| **Date Added** | 6/11/2025, 2:32:25 PM |
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### Tags:

* + Humans
  + Animals
  + \*Gastrointestinal Microbiome
  + microbiota
  + neurodegeneration
  + microbiome
  + \*Brain-Gut Axis
  + \*Brain/microbiology/pathology/metabolism
  + \*Dysbiosis/microbiology/pathology
  + \*Huntington Disease/microbiology/pathology/therapy
  + diet
  + gut dysbiosis
  + gut‐brain axis
  + Huntington's disease
  + mycobiome

## The neuroprotective effects of human bone marrow mesenchymal stem cells are dose-dependent in TNBS colitis.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Ainsley M. Robinson |
| **Author** | Ahmed A. Rahman |
| **Author** | Sarah Miller |
| **Author** | Rhian Stavely |
| **Author** | Samy Sakkal |
| **Author** | Kulmira Nurgali |
| **Abstract** | BACKGROUND: The incidence of inflammatory bowel diseases (IBD) is increasing worldwide with patients experiencing severe impacts on their quality of life. It is well accepted that intestinal inflammation associates with extensive damage to the enteric nervous system (ENS), which intrinsically innervates the gastrointestinal tract and regulates all gut functions. Hence, treatments targeting the enteric neurons are plausible for alleviating IBD and associated complications. Mesenchymal stem cells (MSCs) are gaining wide recognition as a potential therapy for many diseases due to their immunomodulatory and neuroprotective qualities. However, there is a large discrepancy regarding appropriate cell doses used in both clinical trials and experimental models of disease. We have previously demonstrated that human bone marrow MSCs exhibit neuroprotective and anti-inflammatory effects in a guinea-pig model of 2,4,6-trinitrobenzene-sulfonate (TNBS)-induced colitis; but an investigation into whether this response is dose-dependent has not been conducted. METHODS: Hartley guinea-pigs were administered TNBS or sham treatment intra-rectally. Animals in the MSC treatment groups received either 1 × 10(5), 1 × 10(6) or 3 × 10(6) MSCs by enema 3 hours after induction of colitis. Colon tissues were collected 72 hours after TNBS administration to assess the effects of MSC treatments on the level of inflammation and damage to the ENS by immunohistochemical and histological analyses. RESULTS: MSCs administered at a low dose, 1 × 10(5) cells, had little or no effect on the level of immune cell infiltrate and damage to the colonic innervation was similar to the TNBS group. Treatment with 1 × 10(6) MSCs decreased the quantity of immune infiltrate and damage to nerve processes in the colonic wall, prevented myenteric neuronal loss and changes in neuronal subpopulations. Treatment with 3 × 10(6) MSCs had similar effects to 1 × 10(6) MSC treatments. CONCLUSIONS: The neuroprotective effect of MSCs in TNBS colitis is dose-dependent. Increasing doses higher than 1 × 10(6) MSCs demonstrates no further therapeutic benefit than 1 × 10(6) MSCs in preventing enteric neuropathy associated with intestinal inflammation. Furthermore, we have established an optimal dose of MSCs for future studies investigating intestinal inflammation, the enteric neurons and stem cell therapy in this model. |
| **Date** | 2017 Apr 18 |
| **Language** | eng |
| **Extra** | Place: England PMID: 28420434 PMCID: PMC5395912 |
| **Volume** | 8 |
| **Pages** | 87 |
| **Publication** | Stem cell research & therapy |
| **DOI** | [10.1186/s13287-017-0540-3](http://doi.org/10.1186/s13287-017-0540-3) |
| **Issue** | 1 |
| **Journal Abbr** | Stem Cell Res Ther |
| **ISSN** | 1757-6512 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
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### Tags:

* + Female
  + Humans
  + Male
  + Animals
  + Cell Line
  + Mesenchymal stem cells
  + Enteric neurons
  + Inflammatory bowel disease
  + Colitis, Ulcerative/etiology/\*therapy
  + Colon/cytology
  + Dose-dependence
  + Guinea Pigs
  + Intestinal inflammation
  + Mesenchymal Stem Cell Transplantation/adverse effects/\*methods
  + Mesenchymal Stem Cells/\*cytology
  + Neurons/\*cytology
  + Trinitrobenzenesulfonic Acid/toxicity

## The role of galanin in the progression and prognosis of colorectal cancer: the unfinished story.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Zbigniew Kmiec |
| **Author** | Jacek Kieżun |
| **Author** | Bartlomiej E. Krazinski |
| **Author** | Przemyslaw Kwiatkowski |
| **Author** | Janusz Godlewski |
| **Abstract** | The paper presents a summary of immunohistochemical (IHC) and biochemical investigations on the presence of galanin (Gal), one of the neuropeptides abundant in the enteric nervous systems, and three types of its receptors (GalR1-3) in colorectal cancer (CRC) tissue and non-involved colon wall and their associations with clinical-pathological data of the CRC patients. We were the first to morphologically demonstrate the presence of endogenous Gal in CRC sections and measure its content in homogenates of tumor tissue and dissected compartments of unchanged colon wall. The prominent atrophy of myenteric plexuses displaying Gal immunoreactivity (Gal-Ir) located close to the tumor invasion was found to be accompanied by higher Gal content in the tumor-adjacent muscularis externa than in tumor-distant tissue. In further studies for the first time, we demonstrated by the IHC technique the presence of the GalR1-3 receptors in the CRC tumors and the colon mucosa and found that higher GalR3-Ir in the tumor tissue correlated with longer overall survival of CRC patients. Furthermore, we discovered that lower GalR1 expression in submucosal plexuses located near the tumor correlated with a better prognosis in patients with CRC. These findings suggest that GalR1 could be considered as a novel therapeutic target in CRC. In conclusion, our morphological investigations provided novel data documenting the involvement of Gal and its receptors in the progression of CRC and showed the usefulness of the IHC technique for the prognosis of CRC patients. |
| **Date** | 2024 Mar 6 |
| **Language** | eng |
| **Extra** | Place: Italy PMID: 38568200 PMCID: PMC11017717 |
| **Volume** | 68 |
| **Publication** | European journal of histochemistry : EJH |
| **DOI** | [10.4081/ejh.2024.3990](http://doi.org/10.4081/ejh.2024.3990) |
| **Issue** | 1 |
| **Journal Abbr** | Eur J Histochem |
| **ISSN** | 2038-8306 1121-760X |
| **Date Added** | 6/11/2025, 2:32:27 PM |
| **Modified** | 6/11/2025, 2:32:27 PM |

### Tags:

* + Humans
  + Prognosis
  + \*Enteric Nervous System
  + \*Colorectal Neoplasms/diagnosis
  + Galanin

## The role of the gut-brain axis in depression: endocrine, neural, and immune pathways.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Anastasios P. Makris |
| **Author** | Minois Karianaki |
| **Author** | Konstantinos I. Tsamis |
| **Author** | Stavroula A. Paschou |
| **Abstract** | The aim of this article is to summarize the pathways connecting the gut and the brain and to highlight their role in the development of depression as well as their potential use as therapeutic targets. A literature search was conducted in PubMed using relevant keywords and their combinations up to the end of March 2020. Previously seen as a disease pertaining solely to the central nervous system, depression is now perceived as a multifactorial condition that extends beyond neurotransmitter depletion. Central to our understanding of the disease is our current knowledge of the communication between the gut and the brain, which is bidirectional and involves neural, endocrine, and immune pathways. This communication is facilitated via stress-mediated activation of the HPA axis, which stimulates the immune system and causes a decrease in microbial diversity, also known as dysbiosis. This change in the intestinal flora leads, in turn, to bacterial production of various substances which stimulate both the enteric nervous system and the vagal afferents and contribute to additional activation of the HPA axis. Concomitantly, these substances are associated with an increase in intestinal permeability, namely, the leaky gut phenomenon. The bidirectional link between the gut and the brain is of great importance for a more inclusive approach to the management of depression. It can thus be deployed for the development of novel therapeutic strategies against depression, offering promising alternatives to limited efficacy antidepressants, while combination therapy also remains a potential treatment option. |
| **Date** | 2021 Mar |
| **Language** | eng |
| **Extra** | Place: Switzerland PMID: 32827123 |
| **Volume** | 20 |
| **Pages** | 1-12 |
| **Publication** | Hormones (Athens, Greece) |
| **DOI** | [10.1007/s42000-020-00236-4](http://doi.org/10.1007/s42000-020-00236-4) |
| **Issue** | 1 |
| **Journal Abbr** | Hormones (Athens) |
| **ISSN** | 2520-8721 1109-3099 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/11/2025, 2:32:24 PM |

### Tags:

* + Humans
  + \*Gastrointestinal Microbiome
  + Gut microbiota
  + Gut-brain axis
  + Probiotics
  + Depression
  + Bacteria/classification
  + Brain/immunology/\*physiology
  + Depression/etiology/\*metabolism
  + Gastrointestinal Tract/immunology/microbiology/\*physiology
  + Hormones/\*metabolism
  + Psychological stress

## Therapeutic potential of allosteric modulators for the treatment of gastrointestinal motility disorders.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Ayame Saito |
| **Author** | Sadia Alvi |
| **Author** | Celine Valant |
| **Author** | Arthur Christopoulos |
| **Author** | Simona E. Carbone |
| **Author** | Daniel P. Poole |
| **Abstract** | Gastrointestinal motility is tightly regulated by the enteric nervous system (ENS). Disruption of coordinated enteric nervous system activity can result in dysmotility. Pharmacological treatment options for dysmotility include targeting of G protein-coupled receptors (GPCRs) expressed by neurons of the enteric nervous system. Current GPCR-targeting drugs for motility disorders bind to the highly conserved endogenous ligand-binding site and promote indiscriminate activation or inhibition of the target receptor throughout the body. This can be associated with significant side-effect liability and a loss of physiological tone. Allosteric modulators of GPCRs bind to a distinct site from the endogenous ligand, which is typically less conserved across multiple receptor subtypes and can modulate endogenous ligand signalling. Allosteric modulation of GPCRs that are important for enteric nervous system function may provide effective relief from motility disorders while limiting side-effects. This review will focus on how allosteric modulators of GPCRs may influence gastrointestinal motility, using 5-hydroxytryptamine (5-HT), acetylcholine (ACh) and opioid receptors as examples. LINKED ARTICLES: This article is part of a themed issue Therapeutic Targeting of G Protein-Coupled Receptors: hot topics from the Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists 2021 Virtual Annual Scientific Meeting. To view the other articles in this section visit http://onlinelibrary.wiley.com/doi/10.1111/bph.v181.14/issuetoc. |
| **Date** | 2024 Jul |
| **Language** | eng |
| **Rights** | © 2022 British Pharmacological Society. |
| **Extra** | Place: England PMID: 36565295 |
| **Volume** | 181 |
| **Pages** | 2232-2246 |
| **Publication** | British journal of pharmacology |
| **DOI** | [10.1111/bph.16023](http://doi.org/10.1111/bph.16023) |
| **Issue** | 14 |
| **Journal Abbr** | Br J Pharmacol |
| **ISSN** | 1476-5381 0007-1188 |
| **Date Added** | 6/11/2025, 2:32:23 PM |
| **Modified** | 6/11/2025, 2:32:23 PM |

### Tags:

* + Humans
  + Animals
  + enteric nervous system
  + gastrointestinal motility
  + \*Gastrointestinal Motility/drug effects
  + \*Gastrointestinal Diseases/drug therapy/metabolism
  + allosteric modulator
  + Allosteric Regulation/drug effects
  + G protein‐coupled receptors
  + Gastrointestinal Agents/pharmacology/therapeutic use
  + Receptors, G-Protein-Coupled/metabolism

## Therapeutic potential of serotonin 4 receptor for chronic depression and its associated comorbidity in the gut.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Lokesh Agrawal |
| **Author** | Mustafa Korkutata |
| **Author** | Sunil Kumar Vimal |
| **Author** | Manoj Kumar Yadav |
| **Author** | Sanjib Bhattacharyya |
| **Author** | Takashi Shiga |
| **Abstract** | The latest estimates from world health organization suggest that more than 450 million people are suffering from depression and other psychiatric conditions. Of these, 50-60% have been reported to have progression of gut diseases. In the last two decades, researchers introduced incipient physiological roles for serotonin (5-HT) receptors (5-HTRs), suggesting their importance as a potential pharmacological target in various psychiatric and gut diseases. A growing body of evidence suggests that 5-HT systems affect the brain-gut axis in depressive patients, which leads to gut comorbidity. Recently, preclinical trials of 5-HT4R agonists and antagonists were promising as antipsychotic and prokinetic agents. In the current review, we address the possible pharmacological role and contribution of 5-HT4R in the pathophysiology of chronic depression and associated gut abnormalities. Physiologically, during depression episodes, centers of the sympathetic and parasympathetic nervous system couple together with neuroendocrine systems to alter the function of hypothalamic-pituitary-adrenal (HPA) axis and enteric nervous system (ENS), which in turn leads to onset of gastrointestinal tract (GIT) disorders. Consecutively, the ENS governs a broad spectrum of physiological activities of gut, such as visceral pain and motility. During the stages of emotional stress, hyperactivity of the HPA axis alters the ENS response to physiological and noxious stimuli. Consecutively, stress-induced flare, swelling, hyperalgesia and altered reflexes in gut eventually lead to GIT disorders. In summary, the current review provides prospective information about the role and mechanism of 5-HT4R-based therapeutics for the treatment of depressive disorder and possible consequences for the gut via brain-gut axis interactions. This article is part of the special issue entitled 'Serotonin Research: Crossing Scales and Boundaries'. |
| **Date** | 2020 Apr |
| **Language** | eng |
| **Rights** | Copyright © 2020 Elsevier Ltd. All rights reserved. |
| **Extra** | Place: England PMID: 31982703 |
| **Volume** | 166 |
| **Pages** | 107969 |
| **Publication** | Neuropharmacology |
| **DOI** | [10.1016/j.neuropharm.2020.107969](http://doi.org/10.1016/j.neuropharm.2020.107969) |
| **Journal Abbr** | Neuropharmacology |
| **ISSN** | 1873-7064 0028-3908 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/11/2025, 2:32:25 PM |

### Tags:

* + Humans
  + Animals
  + Comorbidity
  + Gastrointestinal tract
  + 5-HT4R
  + Brain/drug effects/metabolism
  + Depression/drug therapy/\*epidemiology/\*metabolism
  + Depressive disorder
  + Gastrointestinal Diseases/drug therapy/\*epidemiology/\*metabolism
  + Gastrointestinal Microbiome/drug effects/\*physiology
  + HPA axis
  + Receptors, Serotonin, 5-HT4/\*metabolism
  + Serotonin 5-HT4 Receptor Agonists/pharmacology/therapeutic use
  + Serotonin 5-HT4 Receptor Antagonists/pharmacology/therapeutic use

## [Therapeutic strategy for Parkinson's disease: targeting zinc-binding protein in astrocytes].

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Ikuko Miyazaki |
| **Author** | Masato Asanuma |
| **Abstract** | Parkinson's disease (PD) is a progressive neurodegenerative disease with motor symptoms, such as tremor, akinesia/bradykinesia, rigidity and postural instability due to a loss of nigrostriatal dopaminergic neurons; PD patients also exhibit non-motor symptoms, such as hyposmia, orthostatic hypotension and constipation, which precede motor symptoms. Pathologically, Lewy bodies and neurites, which contains α-synuclein, are observed in the central and peripheral nervous system. To date, it is hypothesized that PD pathology appears first in the olfactory bulb and the enteric nervous system, and propagates progressively through the substantia nigra to finally reach the cerebral cortex. Major medications at present are nosotropic treatments to improve motor dysfunction in PD. Therefore, development of disease-modifying drug is required to slow or prevent PD progression. Astrocytes are known to play an important role in the maintenance of the neuronal environment and exert neuroprotective effects by production of antioxidants and neurotrophic factors and clearing toxic molecules. In the previous study, we demonstrated that astrocytes produced antioxidative molecules metallothionein (MT)-1/2 in response to oxidative stress and protected dopaminergic neurons against oxidative stress. MTs are cysteine-rich proteins possessing antioxidative properties. MTs bind to metals such as zinc (Zn) and copper (Cu) and function in metal homeostasis and detoxification; MTs regulate Zn-mediated transcriptional activation of various genes. Recently, it is reported that MTs prevent Cu-induced aggregation of α-synuclein. In this article, we review a new therapeutic strategy of neuroprotection in PD by targeting MTs in astrocytes. |
| **Date** | 2021 |
| **Language** | jpn |
| **Extra** | Place: Japan PMID: 33642534 |
| **Volume** | 156 |
| **Pages** | 76-80 |
| **Publication** | Nihon yakurigaku zasshi. Folia pharmacologica Japonica |
| **DOI** | [10.1254/fpj.20082](http://doi.org/10.1254/fpj.20082) |
| **Issue** | 2 |
| **Journal Abbr** | Nihon Yakurigaku Zasshi |
| **ISSN** | 0015-5691 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/11/2025, 2:32:25 PM |

### Tags:

* + Humans
  + Astrocytes
  + \*Parkinson Disease/drug therapy
  + \*Neurodegenerative Diseases
  + alpha-Synuclein
  + Carrier Proteins

## TNF-α disrupts the malate-aspartate shuttle, driving metabolic rewiring in iPSC-derived enteric neural lineages from Parkinson's Disease patients.

|  |  |
| --- | --- |
| **Item Type** | Preprint |
| **Author** | Bruno Ghirotto |
| **Author** | Luís Eduardo Gonçalves |
| **Author** | Vivien Ruder |
| **Author** | Christina James |
| **Author** | Elizaveta Gerasimova |
| **Author** | Tania Rizo |
| **Author** | Holger Wend |
| **Author** | Michaela Farrell |
| **Author** | Juan Atilio Gerez |
| **Author** | Natalia Cecilia Prymaczok |
| **Author** | Merel Kuijs |
| **Author** | Maiia Shulman |
| **Author** | Anne Hartebrodt |
| **Author** | Iryna Prots |
| **Author** | Arne Gessner |
| **Author** | Friederike Zunke |
| **Author** | Jürgen Winkler |
| **Author** | David B. Blumenthal |
| **Author** | Fabian J. Theis |
| **Author** | Roland Riek |
| **Author** | Claudia Günther |
| **Author** | Markus Neurath |
| **Author** | Pooja Gupta |
| **Author** | Beate Winner |
| **Abstract** | Gastrointestinal (GI) dysfunction emerges years before motor symptoms in Parkinson's disease (PD), implicating the enteric nervous system (ENS) in early disease progression. However, the mechanisms linking the PD hallmark protein, α-synuclein (α-syn), to ENS dysfunction - and whether these mechanisms are influenced by inflammation - remains elusive. Using iPSC-derived enteric neural lineages from patients with α-syn triplications, we reveal that TNF-α increases mitochondrial-α-syn interactions, disrupts the malate-aspartate shuttle, and forces a metabolic shift toward glutamine oxidation. These alterations drive mitochondrial dysfunction, characterizing metabolic impairment under cytokine stress. Interestingly, targeting glutamate metabolism with Chicago Sky Blue 6B restores mitochondrial function, reversing TNF-α-driven metabolic disruption. Our findings position the ENS as a central player in PD pathogenesis, establishing a direct link between cytokines, α-syn accumulation, metabolic stress and mitochondrial dysfunction. By uncovering a previously unrecognized metabolic vulnerability in the ENS, we highlight its potential as a therapeutic target for early PD intervention. |
| **Date** | 2025 Mar 26 |
| **Language** | eng |
| **Extra** | ISSN: 2692-8205 Journal Abbreviation: bioRxiv Pages: 2025.03.25.644826 Publication Title: bioRxiv : the preprint server for biology PMID: 40196623 PMCID: PMC11974853 |
| **Place** | United States |
| **DOI** | [10.1101/2025.03.25.644826](http://doi.org/10.1101/2025.03.25.644826) |
| **Date Added** | 6/11/2025, 2:32:27 PM |
| **Modified** | 6/11/2025, 2:32:27 PM |

### Tags:

* + enteric nervous system
  + Parkinson’s disease
  + alpha-synuclein
  + Chicago Sky Blue 6B
  + cytokines
  + malate-aspartate shuttle
  + mitochondrial dysfunction

## Toll like receptor-2 regulates production of glial-derived neurotrophic factors in murine intestinal smooth muscle cells.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Paola Brun |
| **Author** | Serena Gobbo |
| **Author** | Valentina Caputi |
| **Author** | Lisa Spagnol |
| **Author** | Giulia Schirato |
| **Author** | Matteo Pasqualin |
| **Author** | Elia Levorato |
| **Author** | Giorgio Palù |
| **Author** | Maria Cecilia Giron |
| **Author** | Ignazio Castagliuolo |
| **Abstract** | Gut microbiota-innate immunity axis is emerging as a key player to guarantee the structural and functional integrity of the enteric nervous system (ENS). Alterations in the composition of the gut microbiota, derangement in signaling of innate immune receptors such as Toll-like receptors (TLRs), and modifications in the neurochemical coding of the ENS have been associated with a variety of gastrointestinal disorders. Indeed, TLR2 activation by microbial products controls the ENS structure and regulates intestinal neuromuscular function. However, the cellular populations and the molecular mechanisms shaping the plasticity of enteric neurons in response to gut microbes are largely unexplored. In this study, smooth muscle cells (SMCs), enteric glial cells (EGCs) and macrophages/dendritic cells (MΦ/DCs) were isolated and cultured from the ileal longitudinal muscle layer of wild-type (WT) and Toll-like receptor-2 deficient (TLR2(-/-)) mice. Quantification of mRNA levels of neurotrophins at baseline and following stimulation with TLR ligands was performed by RT-PCR. To determine the role of neurotrophins in supporting the neuronal phenotype, we performed co-culture experiments of enteric neurons with the conditioned media of cells isolated from the longitudinal muscle layer of WT or TLR2(-/-) mice. The neuronal phenotype was investigated evaluating the expression of βIII-tubulin, HuC/D, and nNOS by immunocytochemistry. As detected by semi-quantitative RT-PCR, SMCs expressed mRNA coding TLR1-9. Among the tested cell populations, un-stimulated SMCs were the most prominent sources of neurotrophins. Stimulation with TLR2, TLR4, TLR5 and TLR9 ligands further increased Gdnf, Ngf, Bdnf and Lif mRNA levels in SMCs. Enteric neurons isolated from TLR2(-/-) mice exhibited smaller ganglia, fewer HuC/D(+ve) and nNOS(+ve) neurons and shorter βIII-tubulin axonal networks as compared to neurons cultured from WT mice. The co-culture with the conditioned media from WT-SMCs but not with those from WT-EGCs or WT-MΦ/DCs corrected the altered neuronal phenotype of TLR2(-/-) mice. Supplementation of TLR2(-/-) neuronal cultures with GDNF recapitulated the WT-SMC co-culture effect whereas the knockdown of GDNF expression in WT-SMCs using shRNA interference abolished the effect on TLR2(-/-) neurons. These data revealed that by exploiting the repertoire of TLRs to decode gut-microbial signals, intestinal SMCs elaborate a cocktail of neurotrophic factors that in turn supports neuronal phenotype. In this view, the SMCs represent an attractive target for novel therapeutic strategies. |
| **Date** | 2015 Sep |
| **Language** | eng |
| **Rights** | Copyright © 2015 Elsevier Inc. All rights reserved. |
| **Extra** | Place: United States PMID: 25823690 |
| **Volume** | 68 |
| **Pages** | 24-35 |
| **Publication** | Molecular and cellular neurosciences |
| **DOI** | [10.1016/j.mcn.2015.03.018](http://doi.org/10.1016/j.mcn.2015.03.018) |
| **Journal Abbr** | Mol Cell Neurosci |
| **ISSN** | 1095-9327 1044-7431 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/11/2025, 2:32:26 PM |

### Tags:

* + Male
  + Animals
  + Mice
  + Coculture Techniques
  + Cells, Cultured
  + Mice, Inbred C57BL
  + Mice, Transgenic
  + Actins/metabolism
  + Enteric nervous system
  + Neuroglia/physiology
  + Lipopolysaccharides/pharmacology
  + ELAV-Like Protein 3/metabolism
  + ELAV-Like Protein 4/metabolism
  + Gene Expression Regulation/\*genetics
  + Glial Cell Line-Derived Neurotrophic Factor/\*metabolism
  + Glial derived neurotrophic factor
  + Intestine, Small/\*cytology
  + Myocytes, Smooth Muscle/drug effects/\*metabolism
  + Neuronal integrity
  + Neurons/physiology
  + Neurotrophin
  + Quinolines/metabolism
  + Smooth muscle cell
  + Thiazoles/metabolism
  + Toll-like receptor
  + Toll-Like Receptor 2/genetics/\*metabolism
  + Tubulin/metabolism

## Transplanted ENSCs form functional connections with intestinal smooth muscle and restore colonic motility in nNOS-deficient mice.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Ryo Hotta |
| **Author** | Ahmed Rahman |
| **Author** | Sukhada Bhave |
| **Author** | Rhian Stavely |
| **Author** | Weikang Pan |
| **Author** | Shriya Srinivasan |
| **Author** | Geoffrey de Couto |
| **Author** | Luis Rodriguez-Borlado |
| **Author** | Richard Myers |
| **Author** | Alan J. Burns |
| **Author** | Allan M. Goldstein |
| **Abstract** | BACKGROUND: Enteric neuropathies, which result from abnormalities of the enteric nervous system, are associated with significant morbidity and high health-care costs, but current treatments are unsatisfactory. Cell-based therapy offers an innovative approach to replace the absent or abnormal enteric neurons and thereby restore gut function. METHODS: Enteric neuronal stem cells (ENSCs) were isolated from the gastrointestinal tract of Wnt1-Cre;R26tdTomato mice and generated neurospheres (NS). NS transplants were performed via injection into the mid-colon mesenchyme of nNOS(-/-) mouse, a model of colonic dysmotility, using either 1 (n = 12) or 3 (n = 12) injections (30 NS per injection) targeted longitudinally 1-2 mm apart. Functional outcomes were assessed up to 6 weeks later using electromyography (EMG), electrical field stimulation (EFS), optogenetics, and by measuring colorectal motility. RESULTS: Transplanted ENSCs formed nitrergic neurons in the nNOS(-/-) recipient colon. Multiple injections of ENSCs resulted in a significantly larger area of coverage compared to single injection alone and were associated with a marked improvement in colonic function, demonstrated by (1) increased colonic muscle activity by EMG recording, (2) faster rectal bead expulsion, and (3) increased fecal pellet output in vivo. Organ bath studies revealed direct neuromuscular communication by optogenetic stimulation of channelrhodopsin-expressing ENSCs and restoration of smooth muscle relaxation in response to EFS. CONCLUSIONS: These results demonstrate that transplanted ENSCs can form effective neuromuscular connections and improve colonic motor function in a model of colonic dysmotility, and additionally reveal that multiple sites of cell delivery led to an improved response, paving the way for optimized clinical trial design. |
| **Date** | 2023 Sep 4 |
| **Language** | eng |
| **Rights** | © 2023. BioMed Central Ltd., part of Springer Nature. |
| **Extra** | Place: England PMID: 37667277 PMCID: PMC10478362 |
| **Volume** | 14 |
| **Pages** | 232 |
| **Publication** | Stem cell research & therapy |
| **DOI** | [10.1186/s13287-023-03469-3](http://doi.org/10.1186/s13287-023-03469-3) |
| **Issue** | 1 |
| **Journal Abbr** | Stem Cell Res Ther |
| **ISSN** | 1757-6512 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Animals
  + Mice
  + Colon
  + Electric Stimulation
  + \*Muscle, Smooth
  + \*Neurons
  + Cell therapy
  + Cell- and Tissue-Based Therapy
  + Enteric neuropathies
  + Gastrointestinal motility
  + Nitric oxide synthase
  + Optogenetics

## Underneath the Gut-Brain Axis in IBD-Evidence of the Non-Obvious.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Lidiya V. Boldyreva |
| **Author** | Anna A. Evtushenko |
| **Author** | Maria N. Lvova |
| **Author** | Ksenia N. Morozova |
| **Author** | Elena V. Kiseleva |
| **Abstract** | The gut-brain axis (GBA) plays a pivotal role in human health and wellness by orchestrating complex bidirectional regulation and influencing numerous critical processes within the body. Over the past decade, research has increasingly focused on the GBA in the context of inflammatory bowel disease (IBD). Beyond its well-documented effects on the GBA-enteric nervous system and vagus nerve dysregulation, and gut microbiota misbalance-IBD also leads to impairments in the metabolic and cellular functions: metabolic dysregulation, mitochondrial dysfunction, cationic transport, and cytoskeleton dysregulation. These systemic effects are currently underexplored in relation to the GBA; however, they are crucial for the nervous system cells' functioning. This review summarizes the studies on the particular mechanisms of metabolic dysregulation, mitochondrial dysfunction, cationic transport, and cytoskeleton impairments in IBD. Understanding the involvement of these processes in the GBA may help find new therapeutic targets and develop systemic approaches to improve the quality of life in IBD patients. |
| **Date** | 2024 Nov 12 |
| **Language** | eng |
| **Extra** | Place: Switzerland PMID: 39596193 PMCID: PMC11594934 |
| **Volume** | 25 |
| **Publication** | International journal of molecular sciences |
| **DOI** | [10.3390/ijms252212125](http://doi.org/10.3390/ijms252212125) |
| **Issue** | 22 |
| **Journal Abbr** | Int J Mol Sci |
| **ISSN** | 1422-0067 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/11/2025, 2:32:24 PM |

### Tags:

* + Humans
  + Animals
  + \*Gastrointestinal Microbiome
  + inflammation
  + gut–brain axis
  + IBD
  + \*Brain-Gut Axis
  + Brain/metabolism
  + \*Inflammatory Bowel Diseases/metabolism
  + cationic transport
  + cytoskeleton
  + Cytoskeleton/metabolism
  + lipidome
  + metabolome
  + Mitochondria/metabolism
  + mitochondrial function

## Up-Regulation of microRNA-424 Causes an Imbalance in AKT Phosphorylation and Impairs Enteric Neural Crest Cell Migration in Hirschsprung Disease.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Ze Xu |
| **Author** | Yingnan Yan |
| **Author** | Beilin Gu |
| **Author** | Wei Cai |
| **Author** | Yang Wang |
| **Abstract** | Insights into the role of microRNAs (miRNAs) in disease pathogenesis have made them attractive therapeutic targets, and numerous miRNAs have been functionally linked to Hirschsprung disease (HSCR), a life-threatening genetic disorder due to defective migration, proliferation, and colonization of enteric neural crest cells (ENCCs) in the gut. Recent studies have demonstrated that miR-424 strongly inhibits migration in a variety of cell types and its potential target RICTOR is essential for neural crest cell development. We therefore sought to interrogate how miR-424 and RICTOR contribute to the pathogenesis of HSCR. We utilized HSCR cases and human neural cells to evaluate the miR-424-mediated regulation of RICTOR and the downstream AKT phosphorylation. We further developed an ex vivo model to assess the effects of miR-424 on ENCC migration and proliferation. Then, single-cell atlases of gene expression in both human and mouse fetal intestines were used to determine the characteristics of RICTOR and AKT expression in the developing gut. Our findings demonstrate that miR-424 levels are markedly increased in the colonic tissues of patients with HSCR and that it regulates human neural cell migration by directly targeting RICTOR. Up-regulation of miR-424 leads to decreased AKT phosphorylation levels in a RICTOR-dependent manner, and this, in turn, impairs ENCC proliferation and migration in the developing gut. Interestingly, we further identified prominent RICTOR and AKT expressions in the enteric neurons and other types of enteric neural cells in human and mouse fetal intestines. Our present study reveals the role of the miR-424/RICTOR axis in HSCR pathogenesis and indicates that miR-424 is a promising candidate for the development of targeted therapies against HSCR. |
| **Date** | 2023 Apr 4 |
| **Language** | eng |
| **Extra** | Place: Switzerland PMID: 37047673 PMCID: PMC10094892 |
| **Volume** | 24 |
| **Publication** | International journal of molecular sciences |
| **DOI** | [10.3390/ijms24076700](http://doi.org/10.3390/ijms24076700) |
| **Issue** | 7 |
| **Journal Abbr** | Int J Mol Sci |
| **ISSN** | 1422-0067 |
| **Date Added** | 6/11/2025, 2:32:27 PM |
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### Tags:

* + Humans
  + Animals
  + Mice
  + Phosphorylation
  + Transcription Factors/metabolism
  + Proto-Oncogene Proteins c-akt/metabolism
  + Cell Movement/genetics
  + \*MicroRNAs/genetics/metabolism
  + Hirschsprung disease
  + \*Enteric Nervous System/metabolism
  + \*Hirschsprung Disease/metabolism
  + AKT phosphorylation
  + enteric neural crest cells
  + miR-424
  + Neural Crest/metabolism
  + RICTOR
  + Up-Regulation

## What goes around comes around: novel pharmacological targets in the gut-brain axis.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Camila González-Arancibia |
| **Author** | Jorge Escobar-Luna |
| **Author** | Camila Barrera-Bugueño |
| **Author** | Camilo Díaz-Zepeda |
| **Author** | María P. González-Toro |
| **Author** | Loreto Olavarría-Ramírez |
| **Author** | Francesca Zanelli-Massai |
| **Author** | Martin Gotteland |
| **Author** | Javier A. Bravo |
| **Author** | Marcela Julio-Pieper |
| **Abstract** | The gut and the brain communicate bidirectionally through anatomic and humoral pathways, establishing what is known as the gut-brain axis. Therefore, interventions affecting one system will impact on the other, giving the opportunity to investigate and develop future therapeutic strategies that target both systems. Alterations in the gut-brain axis may arise as a consequence of changes in microbiota composition (dysbiosis), modifications in intestinal barrier function, impairment of enteric nervous system, unbalanced local immune response and exaggerated responses to stress, to mention a few. In this review we analyze and discuss several novel pharmacological targets within the gut-brain axis, with potential applications to improve intestinal and mental health. |
| **Date** | 2016 May |
| **Language** | eng |
| **Extra** | Place: England PMID: 27134664 PMCID: PMC4830101 |
| **Volume** | 9 |
| **Pages** | 339-353 |
| **Publication** | Therapeutic advances in gastroenterology |
| **DOI** | [10.1177/1756283X16630718](http://doi.org/10.1177/1756283X16630718) |
| **Issue** | 3 |
| **Journal Abbr** | Therap Adv Gastroenterol |
| **ISSN** | 1756-283X 1756-2848 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/11/2025, 2:32:24 PM |

### Tags:

* + enteric nervous system
  + gut–brain axis
  + vagus nerve
  + serotonin
  + interleukin 22
  + intestinal microbiota

## What substance P might tell us about the prognosis and mechanism of Parkinson's disease?

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Paola Tirassa |
| **Author** | Tommaso Schirinzi |
| **Author** | Marcello Raspa |
| **Author** | Massimo Ralli |
| **Author** | Antonio Greco |
| **Author** | Antonella Polimeni |
| **Author** | Roberta Possenti |
| **Author** | Nicola Biagio Mercuri |
| **Author** | Cinzia Severini |
| **Abstract** | The neuropeptide substance P (SP) plays an important role in neurodegenerative disorders, among which Parkinson's disease (PD). In the present work we have reviewed the involvement of SP and its preferred receptor (NK1-R) in motor and non-motor PD symptoms, in both PD animal models and patients. Despite PD is primarily a motor disorder, non-motor abnormalities, including olfactory deficits and gastrointestinal dysfunctions, can represent diagnostic PD predictors, according to the hypothesis that the olfactory and the enteric nervous system represent starting points of neurodegeneration, ascending to the brain via the sympathetic fibers and the vagus nerve. In PD patients, the α-synuclein aggregates in the olfactory bulb and the gastrointestinal tract, as well as in the dorsal motor nucleus of the vagus nerve often co-localize with SP, indicating SP-positive neurons as highly vulnerable sites of degeneration. Considering the involvement of the SP/NK1-R in both the periphery and specific brain areas, this system might represent a neuronal substrate for the symptom and disease progression, as well as a therapeutic target for PD. |
| **Date** | 2021 Dec |
| **Language** | eng |
| **Rights** | Published by Elsevier Ltd. |
| **Extra** | Place: United States PMID: 34653503 |
| **Volume** | 131 |
| **Pages** | 899-911 |
| **Publication** | Neuroscience and biobehavioral reviews |
| **DOI** | [10.1016/j.neubiorev.2021.10.008](http://doi.org/10.1016/j.neubiorev.2021.10.008) |
| **Journal Abbr** | Neurosci Biobehav Rev |
| **ISSN** | 1873-7528 0149-7634 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
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### Tags:

* + Humans
  + Animals
  + Prognosis
  + Brain
  + Parkinson’s disease
  + Gut-brain axis
  + alpha-Synuclein/metabolism
  + vagus nerve
  + \*Parkinson Disease
  + \*Substance P
  + Animal models
  + Gastrointestinal Tract/metabolism
  + Non-motor symptoms
  + Olfactory deficits
  + Substance P

## Yoga, Meditation, Mindfulness, or Hypnotherapy for GI Disorders: Similar Mechanisms of Action?

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Anjan Hamal |
| **Author** | Andrea Shin |
| **Author** | Miranda A. L. van Tilburg |
| **Abstract** | Mind-body approaches aim to improve gut symptoms and quality of life by targeting the interaction between the central nervous system and the enteric nervous system. These include treatments such as hypnotherapy, mindfulness, meditation, and yoga. Although evidence is building on efficacy of mind-body approaches, we generally lack a thorough understanding of how they work. Despite being presented as separate treatment modalities, mind-body approaches often use overlapping treatment aspects with the same mechanism of action. There is evidence that yoga, meditation, and hypnotherapy may partly draw their benefit from creating an absorbed state of attention combined with suggestions for change. This has implications for clinical application of these treatments in patients with GI disease. We propose studies on mechanisms of mind-body approaches to develop more efficacious and more precise treatments for GI diseases. |
| **Date** | 2025 May |
| **Language** | eng |
| **Rights** | © 2025 John Wiley & Sons Ltd. |
| **Extra** | Place: England PMID: 39901652 |
| **Volume** | 37 |
| **Pages** | e15014 |
| **Publication** | Neurogastroenterology and motility |
| **DOI** | [10.1111/nmo.15014](http://doi.org/10.1111/nmo.15014) |
| **Issue** | 5 |
| **Journal Abbr** | Neurogastroenterol Motil |
| **ISSN** | 1365-2982 1350-1925 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/11/2025, 2:32:25 PM |

### Tags:

* + Humans
  + irritable bowel syndrome
  + \*Gastrointestinal Diseases/therapy/psychology
  + \*Hypnosis/methods
  + \*Meditation/methods
  + \*Mindfulness/methods
  + \*Yoga
  + functional gastrointestinal disorders
  + hypnosis
  + mindfulness
  + yoga

## μ-Opioid Receptor-Mediated Enteric Glial Activation Is Involved in Morphine-Induced Constipation.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Hui Gao |
| **Author** | Yuxin Zhang |
| **Author** | Yansong Li |
| **Author** | Haiqing Chang |
| **Author** | Bo Cheng |
| **Author** | Na Li |
| **Author** | Wei Yuan |
| **Author** | Shuang Li |
| **Author** | Qiang Wang |
| **Abstract** | Among all the side effects, opioid-induced constipation (OIC) has the highest incidence rate in people who take chronic opioid therapy. Increasing evidence shows that enteric glial cells (EGCs) play a pivotal role in the modulation of gastrointestinal motility. We aim to investigate whether EGCs are involved in OIC and possible mechanisms. Eight-week male C57BL/6 mice were randomized into four groups: the control group, the morphine group, the gliotoxin fluorocitrate (FC) group, and the FC plus morphine group. OIC was induced by injection of morphine subcutaneously. Colonic motility was evaluated by in vivo motility assays and colonic migrating motor complex (CMMC) in vitro. Both the Ca(2+) responses and the release of inflammatory cytokine by EGCs were detected in vitro. Proteins were detected by immunofluorescence staining and Western blot. The morphine group showed prolonged gastrointestinal motility compared with the control group. Once EGCs were disrupted by FC, such inhibitory effect was abolished. There was a remarkable enhancement of the GFAP expression on colonic EGCs. Immunofluorescence exhibited that μ-opioid receptor (MOR) collocated with GFAP, indicating the existence of MOR in EGCs. Moreover, morphine activated the EGCs significantly through enhancing GFAP expression and Ca(2+) amplitude. Both effects can be reversed by MOR-siRNA. Morphine treatment elevated the enteric glial release of proinflammatory cytokines notably and this effect was abolished when EGCs were silenced by MOR-siRNA. The activation of EGCs via MOR and the increased proinflammatory cytokine from EGCs may be involved in morphine-induced constipation. These results provided a potential therapeutic target for OIC. |
| **Date** | 2021 Jul |
| **Language** | eng |
| **Extra** | Place: United States PMID: 33624141 |
| **Volume** | 58 |
| **Pages** | 3061-3070 |
| **Publication** | Molecular neurobiology |
| **DOI** | [10.1007/s12035-021-02286-0](http://doi.org/10.1007/s12035-021-02286-0) |
| **Issue** | 7 |
| **Journal Abbr** | Mol Neurobiol |
| **ISSN** | 1559-1182 0893-7648 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/11/2025, 2:32:26 PM |

### Tags:

* + Female
  + Male
  + Animals
  + Mice
  + Rats
  + Mice, Inbred C57BL
  + Cell Line
  + Pregnancy
  + Cytokines/metabolism
  + Gastrointestinal motility
  + Enteric glial cells
  + Neuroglia/drug effects/\*metabolism
  + Analgesics, Opioid/toxicity
  + Ca2+ responses
  + Colon/drug effects/metabolism
  + Constipation/\*chemically induced/\*metabolism
  + Enteric Nervous System/drug effects/\*metabolism
  + Inflammation Mediators/metabolism
  + Morphine/\*toxicity
  + OIC
  + Proinflammatory cytokine
  + Receptors, Opioid, mu/agonists/\*metabolism
  + μ-Opioid receptor

## Activation of KCNQ (K(V)7) K(+) channels in enteric neurons inhibits epithelial Cl(-) secretion in mouse distal colon.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Andrew J. Nickerson |
| **Author** | Trey S. Rottgen |
| **Author** | Vazhaikkurichi M. Rajendran |
| **Abstract** | Voltage-gated Kv7 (KCNQ family) K(+) channels are expressed in many neuronal populations and play an important role in regulating membrane potential by generating a hyperpolarizing K(+) current and decreasing cell excitability. However, the role of K(V)7 channels in the neural regulation of intestinal epithelial Cl(-) secretion is not known. Cl(-) secretion in mouse distal colon was measured as a function of short-circuit current (I(SC)), and pharmacological approaches were used to test the hypothesis that activation of K(V)7 channels in enteric neurons would inhibit epithelial Cl(-) secretion. Flupirtine, a nonselective K(V)7 activator, inhibited basal Cl(-) secretion in mouse distal colon and abolished or attenuated the effects of drugs that target various components of enteric neurotransmission, including tetrodotoxin (Na(V) channel blocker), veratridine (Na(V) channel activator), nicotine (nicotinic acetylcholine receptor agonist), and hexamethonium (nicotinic antagonist). In contrast, flupritine did not block the response to epithelium-targeted agents VIP (endogenous VPAC receptor ligand) or carbachol (nonselective cholinergic agonist). Flupirtine inhibited Cl(-) secretion in both full-thickness and seromuscular-stripped distal colon (containing the submucosal, but not myenteric plexus) but generated no response in epithelial T84 cell monolayers. K(V)7.2 and K(V)7.3 channel proteins were detected by immunofluorescence in whole mount preparations of the submucosa from mouse distal colon. ICA 110381 (K(V)7.2/7.3 specific activator) inhibited Cl(-) secretion comparably to flupirtine. We conclude that K(V)7 channel activators inhibit neurally driven Cl(-) secretion in the colonic epithelium and may therefore have therapeutic benefit in treating pathologies associated with hyperexcitable enteric nervous system, such as irritable bowel syndrome with diarrhea (IBS-D). |
| **Date** | 2021 Jun 1 |
| **Language** | eng |
| **Extra** | Place: United States PMID: 33852365 PMCID: PMC8285638 |
| **Volume** | 320 |
| **Pages** | C1074-C1087 |
| **Publication** | American journal of physiology. Cell physiology |
| **DOI** | [10.1152/ajpcell.00536.2020](http://doi.org/10.1152/ajpcell.00536.2020) |
| **Issue** | 6 |
| **Journal Abbr** | Am J Physiol Cell Physiol |
| **ISSN** | 1522-1563 0363-6143 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Female
  + Humans
  + Male
  + Animals
  + Mice
  + Cell Line, Tumor
  + Mice, Inbred BALB C
  + enteric nervous system
  + Aminopyridines/pharmacology
  + Carbachol/pharmacology
  + Chlorides/\*metabolism
  + Cholinergic Agonists/pharmacology
  + Colon/drug effects/\*metabolism
  + colonic epithelium
  + Enteric Nervous System/\*drug effects/metabolism
  + Epithelial Cells/drug effects/\*metabolism
  + flupirtine
  + Intestinal Mucosa/drug effects/metabolism
  + irritable bowel syndrome with diarrhea
  + KCNQ Potassium Channels/\*metabolism
  + Membrane Potentials/drug effects/physiology
  + Neurons/drug effects/\*metabolism
  + Synaptic Transmission/drug effects
  + Ussing chamber

## Agonist-dependent development of delta opioid receptor tolerance in the colon.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Jesse J. DiCello |
| **Author** | Ayame Saito |
| **Author** | Pradeep Rajasekhar |
| **Author** | Benjamin W. Sebastian |
| **Author** | Rachel M. McQuade |
| **Author** | Arisbel B. Gondin |
| **Author** | Nicholas A. Veldhuis |
| **Author** | Meritxell Canals |
| **Author** | Simona E. Carbone |
| **Author** | Daniel P. Poole |
| **Abstract** | The use of opioid analgesics is severely limited due to the development of intractable constipation, mediated through activation of mu opioid receptors (MOR) expressed by enteric neurons. The related delta opioid receptor (DOR) is an emerging therapeutic target for chronic pain, depression and anxiety. Whether DOR agonists also promote sustained inhibition of colonic transit is unknown. This study examined acute and chronic tolerance to SNC80 and ARM390, which were full and partial DOR agonists in neural pathways controlling colonic motility, respectively. Excitatory pathways developed acute and chronic tolerance to SNC80, whereas only chronic tolerance developed in inhibitory pathways. Both pathways remained functional after acute or chronic ARM390 exposure. Propagating colonic motor patterns were significantly reduced after acute or chronic SNC80 treatment, but not by ARM390 pre-treatment. These findings demonstrate that SNC80 has a prolonged inhibitory effect on propagating colonic motility. ARM390 had no effect on motor patterns and thus may have fewer gastrointestinal side-effects. |
| **Date** | 2019 Aug |
| **Language** | eng |
| **Extra** | Place: Switzerland PMID: 30904952 PMCID: PMC11105391 |
| **Volume** | 76 |
| **Pages** | 3033-3050 |
| **Publication** | Cellular and molecular life sciences : CMLS |
| **DOI** | [10.1007/s00018-019-03077-6](http://doi.org/10.1007/s00018-019-03077-6) |
| **Issue** | 15 |
| **Journal Abbr** | Cell Mol Life Sci |
| **ISSN** | 1420-9071 1420-682X |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Animals
  + Mice
  + Mice, Inbred C57BL
  + Neurons/metabolism
  + Enteric nervous system
  + Electric Stimulation
  + \*Drug Tolerance
  + Analgesics, Opioid/\*pharmacology
  + Benzamides/pharmacology
  + Colon motility
  + Colon/\*drug effects/physiology
  + Endocytosis
  + GPCR regulation
  + Microscopy, Confocal
  + Muscle Contraction/drug effects
  + Opioid receptor
  + Piperazines/pharmacology
  + Receptors, Opioid, delta/agonists/\*metabolism
  + Receptors, Opioid, mu/agonists/metabolism

## Altered enteric expression of the homeobox transcription factor Phox2b in patients with diverticular disease.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | François Cossais |
| **Author** | Christina Lange |
| **Author** | Martina Barrenschee |
| **Author** | Marie Möding |
| **Author** | Michael Ebsen |
| **Author** | Ilka Vogel |
| **Author** | Martina Böttner |
| **Author** | Thilo Wedel |
| **Abstract** | BACKGROUND: Diverticular disease, a major gastrointestinal disorder, is associated with modifications of the enteric nervous system, encompassing alterations of neurochemical coding and of the tyrosine receptor kinase Ret/GDNF pathway. However, molecular factors underlying these changes remain to be determined. OBJECTIVES: We aimed to characterise the expression of Phox2b, an essential regulator of Ret and of neuronal subtype development, in the adult human enteric nervous system, and to evaluate its potential involvement in acute diverticulitis. METHODS: Site-specific gene expression of Phox2b in the adult colon was analysed by quantitative polymerase chain reaction. Colonic specimens of adult controls and patients with diverticulitis were subjected to quantitative polymerase chain reaction for Phox2b and dual-label immunochemistry for Phox2b and the neuronal markers RET and tyrosine hydroxylase or the glial marker S100β. RESULTS: The results indicate that Phox2b is physiologically expressed in myenteric neuronal and glial subpopulations in the adult enteric nervous system. Messenger RNA expression of Phox2b was increased in patients with diverticulitis and both neuronal, and glial protein expression of Phox2b were altered in these patients. CONCLUSIONS: Alterations of Phox2b expression may contribute to the enteric neuropathy observed in diverticular disease. Future studies are required to characterise the functions of Phox2b in the adult enteric nervous system and to determine its potential as a therapeutic target in gastrointestinal disorders. |
| **Date** | 2019 Apr |
| **Language** | eng |
| **Extra** | Place: England PMID: 31019703 PMCID: PMC6466753 |
| **Volume** | 7 |
| **Pages** | 349-357 |
| **Publication** | United European gastroenterology journal |
| **DOI** | [10.1177/2050640618824913](http://doi.org/10.1177/2050640618824913) |
| **Issue** | 3 |
| **Journal Abbr** | United European Gastroenterol J |
| **ISSN** | 2050-6406 2050-6414 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Aged
  + Female
  + Humans
  + Male
  + Retrospective Studies
  + Gene Expression
  + Colon/metabolism/pathology
  + Diverticular disease
  + Diverticular Diseases/\*metabolism
  + Dopaminergic Neurons/metabolism
  + enteric glial cells
  + Enteric Nervous System/\*metabolism/pathology
  + enteric neurons
  + enteric neuropathy
  + Homeodomain Proteins/\*genetics/\*metabolism
  + Intestinal Pseudo-Obstruction/metabolism
  + Neuroglia/metabolism
  + phox2b
  + Proto-Oncogene Proteins c-ret/metabolism
  + Ret
  + RNA, Messenger/genetics
  + S100 Calcium Binding Protein beta Subunit/metabolism
  + S100β
  + TH
  + Transcription Factors/\*genetics/\*metabolism
  + Tyrosine 3-Monooxygenase/metabolism

## Altered epithelial barrier functions in the colon of patients with spina bifida.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Charlène Brochard |
| **Author** | Guillaume Bouguen |
| **Author** | Raphael Olivier |
| **Author** | Tony Durand |
| **Author** | Sébastien Henno |
| **Author** | Benoît Peyronnet |
| **Author** | Mael Pagenault |
| **Author** | Chloé Lefèvre |
| **Author** | Gaëlle Boudry |
| **Author** | Mikael Croyal |
| **Author** | Alain Fautrel |
| **Author** | Maxime Esvan |
| **Author** | Alain Ropert |
| **Author** | Anne Dariel |
| **Author** | Laurent Siproudhis |
| **Author** | Michel Neunlist |
| **Abstract** | Our objectives were to better characterize the colorectal function of patients with Spina Bifida (SB). Patients with SB and healthy volunteers (HVs) completed prospectively a standardized questionnaire, clinical evaluation, rectal barostat, colonoscopy with biopsies and faecal collection. The data from 36 adults with SB (age: 38.8 [34.1-47.2]) were compared with those of 16 HVs (age: 39.0 [31.0-46.5]). Compared to HVs, rectal compliance was lower in patients with SB (p = 0.01), whereas rectal tone was higher (p = 0.0015). Ex vivo paracellular permeability was increased in patients with SB (p = 0.0008) and inversely correlated with rectal compliance (r = - 0.563, p = 0.002). The expression of key tight junction proteins and inflammatory markers was comparable between SB and HVs, except for an increase in Claudin-1 immunoreactivity (p = 0.04) in SB compared to HVs. TGFβ1 and GDNF mRNAs were expressed at higher levels in patients with SB (p = 0.02 and p = 0.008). The levels of acetate, propionate and butyrate in faecal samples were reduced (p = 0.04, p = 0.01, and p = 0.02, respectively). Our findings provide evidence that anorectal and epithelial functions are altered in patients with SB. The alterations in these key functions might represent new therapeutic targets, in particular using microbiota-derived approaches.Clinical Trials: NCT02440984 and NCT03054415. |
| **Date** | 2022 May 3 |
| **Language** | eng |
| **Rights** | © 2022. The Author(s). |
| **Extra** | Place: England PMID: 35505001 PMCID: PMC9065040 |
| **Volume** | 12 |
| **Pages** | 7196 |
| **Publication** | Scientific reports |
| **DOI** | [10.1038/s41598-022-11289-3](http://doi.org/10.1038/s41598-022-11289-3) |
| **Issue** | 1 |
| **Journal Abbr** | Sci Rep |
| **ISSN** | 2045-2322 |
| **Date Added** | 6/11/2025, 2:32:27 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Adult
  + Humans
  + Colon
  + Surveys and Questionnaires
  + \*Spinal Dysraphism
  + Colonoscopy
  + Rectum

## Blockage of the P2X7 Receptor Attenuates Harmful Changes Produced by Ischemia and Reperfusion in the Myenteric Plexus.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Kelly Palombit |
| **Author** | Cristina Eusébio Mendes |
| **Author** | Wothan Tavares-de-Lima |
| **Author** | Maria Luiza Barreto-Chaves |
| **Author** | Patricia Castelucci |
| **Abstract** | INTRODUCTION: Our work analyzed the effects of a P2X7 receptor antagonist, Brilliant Blue G (BBG), on rat ileum myenteric plexus following ischemia and reperfusion (ISR) induced by 45 min of ileal artery occlusion with an atraumatic vascular clamp with 24 h (ISR 24-h group) or 14 d of reperfusion (ISR 14-d group). MATERIAL AND METHODS: Either BBG (50 mg/kg or 100 mg/kg, BBG50 or BBG100 groups) or saline (vehicle) was administered subcutaneously 1 h after ischemia in the ISR 24-h group or once daily for the 5 d after ischemia in the ISR 14-d group (n = 5 per group). We evaluated the neuronal density and profile area by examining the number of neutrophils in the intestinal layers, protein expression levels of the P2X7 receptor, intestinal motility and immunoreactivity for the P2X7 receptor, nitric oxide synthase, neurofilament-200, and choline acetyl transferase in myenteric neurons. RESULTS: The neuronal density and profile area were restored by BBG following ISR. The ischemic groups showed alterations in P2X7 receptor protein expression and the number of neutrophils in the intestine and decreased intestinal motility, all of which were recovered by BBG treatment. CONCLUSION: We concluded that ISR morphologically and functionally affected the intestine and that its effects were reversed by BBG treatment, suggesting the P2X7 receptor as a therapeutic target. |
| **Date** | 2019 Jul |
| **Language** | eng |
| **Extra** | Place: United States PMID: 30734238 |
| **Volume** | 64 |
| **Pages** | 1815-1829 |
| **Publication** | Digestive diseases and sciences |
| **DOI** | [10.1007/s10620-019-05496-8](http://doi.org/10.1007/s10620-019-05496-8) |
| **Issue** | 7 |
| **Journal Abbr** | Dig Dis Sci |
| **ISSN** | 1573-2568 0163-2116 |
| **Date Added** | 6/11/2025, 2:32:27 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Male
  + Animals
  + Disease Models, Animal
  + Rats, Wistar
  + Signal Transduction/drug effects
  + P2X7 receptor
  + Brilliant Blue G
  + Cytoprotection
  + Gastrointestinal Motility/drug effects
  + Ileum
  + Ileum/\*innervation
  + Ischemia and reperfusion
  + Mesenteric Ischemia/\*drug therapy/metabolism/pathology/physiopathology
  + Myenteric plexus
  + Myenteric Plexus/\*drug effects/metabolism/pathology
  + Neurons/\*drug effects/metabolism/pathology
  + Neutrophil Infiltration/drug effects
  + Purinergic P2X Receptor Antagonists/\*pharmacology
  + Receptors, Purinergic P2X7/\*drug effects/metabolism
  + Reperfusion Injury/metabolism/pathology/physiopathology/\*prevention & control
  + Rosaniline Dyes/\*pharmacology

## Centrally Targeted Pharmacotherapy for Chronic Abdominal Pain: Understanding and Management.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Hans Törnblom |
| **Author** | Douglas A. Drossman |
| **Abstract** | Chronic abdominal pain has a widespread impact on the individual and the society. Identifying and explaining mechanisms of importance for the pain experience within a biopsychosocial context are central in order to select treatment that has a chance for symptom reduction. With current knowledge of brain-gut interactions, chronic abdominal pain, which mostly appears in functional gastrointestinal disorders, to a large extent involves pain mechanisms residing within the brain. As such, the use of centrally targeted pharmacotherapy as an effective treatment option is obvious in a selected number of patients. The antidepressants are most common, but also other classes of medications can be used, either alone or in combination. The latter option refers to when there is insufficient effect of one drug alone or side effects limiting dosage, and when combined in lower doses, certain drugs give rise to augmentation effects. This chapter outlines basic mechanisms of importance for the understanding of chronic abdominal pain and the pharmacologic treatment options. |
| **Date** | 2017 |
| **Language** | eng |
| **Extra** | Place: Germany PMID: 28204956 |
| **Volume** | 239 |
| **Pages** | 417-440 |
| **Publication** | Handbook of experimental pharmacology |
| **DOI** | [10.1007/164\_2016\_106](http://doi.org/10.1007/164_2016_106) |
| **Journal Abbr** | Handb Exp Pharmacol |
| **ISSN** | 0171-2004 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Animals
  + Signal Transduction/drug effects
  + Abdominal pain
  + Abdominal Pain/\*drug therapy/metabolism/physiopathology
  + Analgesics/\*therapeutic use
  + Antidepressants
  + Brain–gut axis
  + Brain/\*drug effects/metabolism/physiopathology
  + Chronic Pain/\*drug therapy/metabolism/physiopathology
  + Enteric Nervous System/\*drug effects/metabolism/physiopathology
  + Functional gastrointestinal disorders
  + Gastrointestinal Tract/\*innervation
  + Pain Perception/drug effects
  + Pain Threshold/drug effects
  + Treatment

## Connecting the Dots: The Interplay Between Stroke and the Gut-Brain Axis.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Pooja M. Murthy |
| **Author** | Jayashankar Ca |
| **Author** | Venkataramana Kandi |
| **Author** | Mithun K. Reddy |
| **Author** | Ganaraja V. Harikrishna |
| **Author** | Kavitha Reddy |
| **Author** | Ramya Jp |
| **Author** | Ankush N. Reddy |
| **Author** | Jigya Narang |
| **Abstract** | This article discusses the interplay between the gut-brain axis and stroke, a multifaceted neurological disorder that affects millions of people worldwide. The gut-brain axis is a bidirectional communication network linking the central nervous system (CNS) to the gastrointestinal tract (GIT), including the enteric nervous system (ENS), vagus nerve, and gut microbiota. Dysbiosis in the gut microbiota, alterations in the ENS and vagus nerve, and gut motility changes have been linked to increased inflammation and oxidative stress, which are contributing factors in the development and progression of stroke. Research on animals has shown that modifying the gut microbiota can impact the results of a stroke. Germ-free mice displayed improved neurological function and decreased infarct volumes, indicating a positive effect. Furthermore, studies in stroke patients have shown alterations in the gut microbiota composition, indicating that targeting dysbiosis could be a potential therapeutic strategy for stroke. The review suggests that targeting the gut-brain axis may represent a potential therapeutic approach to reduce the morbidity and mortality associated with stroke. |
| **Date** | 2023 Apr |
| **Language** | eng |
| **Rights** | Copyright © 2023, Murthy et al. |
| **Extra** | Place: United States PMID: 37182027 PMCID: PMC10168015 |
| **Volume** | 15 |
| **Pages** | e37324 |
| **Publication** | Cureus |
| **DOI** | [10.7759/cureus.37324](http://doi.org/10.7759/cureus.37324) |
| **Issue** | 4 |
| **Journal Abbr** | Cureus |
| **ISSN** | 2168-8184 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + gastrointestinal tract
  + gut-brain axis
  + dysbiosis
  + stroke
  + therapeutic approach

## Distribution of muscarinic acetylcholine receptor subtypes in the murine small intestine.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Eleanor D. Muise |
| **Author** | Neeru Gandotra |
| **Author** | John J. Tackett |
| **Author** | Michaela C. Bamdad |
| **Author** | Robert A. Cowles |
| **Abstract** | AIMS: Serotonin stimulates enterocyte turnover in the small intestine and studies suggest this is mediated by neuronal signaling via a cholinergic pathway. Distribution of the five known muscarinic receptor subtypes (mAChRs) in the small intestine has not been fully studied, and their role in intestinal growth is unknown. We hypothesized that mAChRs have distinct anatomic distributions within the bowel, and that mAChRs present within intestinal crypts mediate the effects of acetylcholine on the small intestinal mucosa. MAIN METHODS: Small intestine from male C57BL/6 mice ages 2, 4, 6, and 8weeks were harvested. RNA was isolated and cDNA synthesized for PCR-amplification of subtype specific mAChRs. Ileum was fixed with Nakane, embedded in epon, and immunofluorescence microscopy performed using polyclonal antibodies specific to each mAChR1-5. KEY FINDINGS: All five mAChR subtypes were present in the mouse duodenum, jejunum, and ileum at all ages by RT-PCR. Immunofluorescence microscopy suggested the presence of mAChR1-5 in association with mature enterocytes along the villus and within the myenteric plexus. Only mAChR2 clearly localized to the crypt stem cell compartment, specifically co-localizing with Paneth cells at crypt bases. SIGNIFICANCE: Muscarinic receptors are widely distributed along the entire alimentary tract. mAChR2 appears to localize to the crypt stem cell compartment, suggesting it is a plausible regulator of stem cell activity. The location of mAChR2 to the crypt makes it a potential therapeutic target for treatment of intestinal disease such as short bowel syndrome. The exact cellular location and action of each mAChR requires further study. |
| **Date** | 2017 Jan 15 |
| **Language** | eng |
| **Rights** | Copyright © 2016 Elsevier Inc. All rights reserved. |
| **Extra** | Place: Netherlands PMID: 27866962 |
| **Volume** | 169 |
| **Pages** | 6-10 |
| **Publication** | Life sciences |
| **DOI** | [10.1016/j.lfs.2016.10.030](http://doi.org/10.1016/j.lfs.2016.10.030) |
| **Journal Abbr** | Life Sci |
| **ISSN** | 1879-0631 0024-3205 |
| **Date Added** | 6/11/2025, 2:32:27 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Male
  + Animals
  + Mice, Inbred C57BL
  + Enteric nervous system
  + Microscopy, Fluorescence
  + Fluorescent Antibody Technique
  + Intestinal crypt
  + Intestinal Mucosa/\*chemistry/cytology/growth & development/\*ultrastructure
  + Intestine, Small/\*chemistry/cytology/growth & development/\*ultrastructure
  + Muscarinic acetylcholine receptor
  + Paneth cell
  + Receptors, Muscarinic/\*analysis
  + Stem cell compartment
  + Stem Cells/chemistry/cytology

## Early-Life Stress Induced by Neonatal Maternal Separation Leads to Intestinal 5-HT Accumulation and Causes Intestinal Dysfunction.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Ding Yang |
| **Author** | Rulan Bai |
| **Author** | Chengzhong Li |
| **Author** | Yan Sun |
| **Author** | Hongyu Jing |
| **Author** | Zixu Wang |
| **Author** | Yaoxing Chen |
| **Author** | Yulan Dong |
| **Abstract** | BACKGROUND: The early childhood period is a critical development stage, and experiencing stress during this time may increase the risk of gastrointestinal disorders, including irritable bowel syndrome (IBS). Neonatal maternal separation (NMS) in rodent models has been shown to cause bowel dysfunctions similar to IBS, and 5-HT is considered to be a key regulator regulating intestinal function, but the precise underlying mechanisms remain unclear. RESULTS: We established a maternal separation stress mouse model to simulate early-life stress, exploring the expression patterns of 5-HT under chronic stress and its mechanisms affecting gut function. We observed a significant increase in 5-HT expression due to NMS, leading to disruptions in intestinal structure and function. However, inhibiting 5-HT reversed these effects, suggesting its potential as a therapeutic target. Furthermore, our research revealed that excess 5-HT in mice with early life stress increased intestinal neural network density and promoted excitatory motor neuron expression. Mechanistically, 5-HT activated the Wnt signaling pathway through the 5-HT(4) receptor, promoting neurogenesis within the intestinal nervous system. CONCLUSION: These findings shed light on the intricate changes induced by early life stress in the intestines, confirming the regulatory role of 5-HT in the enteric nervous system and providing potential insights for the development of novel therapies for gastrointestinal disorders. |
| **Date** | 2024 |
| **Language** | eng |
| **Rights** | © 2024 Yang et al. |
| **Extra** | Place: New Zealand PMID: 39588137 PMCID: PMC11586501 |
| **Volume** | 17 |
| **Pages** | 8945-8964 |
| **Publication** | Journal of inflammation research |
| **DOI** | [10.2147/JIR.S488290](http://doi.org/10.2147/JIR.S488290) |
| **Journal Abbr** | J Inflamm Res |
| **ISSN** | 1178-7031 |
| **Date Added** | 6/11/2025, 2:32:27 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + 5-HT
  + early-life stress
  + IBS
  + neurogenesis

## Effects of aged garlic extract on aging?related changes in gastrointestinal function and enteric nervous system cells.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Kensuke Ohishi |
| **Author** | Ahmed A. Rahman |
| **Author** | Takahiro Ohkura |
| **Author** | Alan J. Burns |
| **Author** | Allan M. Goldstein |
| **Author** | Ryo Hotta |
| **Abstract** | Dysmotility of the gastrointestinal (GI) tract is commonly seen in elderly individuals, where it causes significant morbidity and can lead to more severe conditions, including sarcopenia and frailty. Although the precise mechanisms underlying aging-related GI dysmotility are not fully understood, neuronal loss or degeneration in the enteric nervous system (ENS) may be involved. Aged garlic extract (AGE) has been shown to have several beneficial effects in the GI tract; however, it is not known whether AGE can improve GI motility in older animals. The aim of the present study was to examine the effects of AGE on the ENS and gut motility in older mice and elucidate potential mechanisms of action. An AGE-formulated diet was given to 18-month-old female mice for 2 weeks. Organ bath studies and cell culture demonstrated that AGE: i) Altered gut contractile activity; ii) enhanced viability of ENS cells; and iii) exhibited neuroprotective effects on the ENS via reduction in oxidative stress. These findings suggest that AGE could be used to develop novel dietary therapeutics for aging-related GI dysmotility by targeting the associated loss and damage of the ENS. |
| **Date** | 2025 May |
| **Language** | eng |
| **Rights** | Copyright: © 2025 Ohishi et al. |
| **Extra** | Place: Greece PMID: 40171138 PMCID: PMC11959352 |
| **Volume** | 29 |
| **Pages** | 103 |
| **Publication** | Experimental and therapeutic medicine |
| **DOI** | [10.3892/etm.2025.12853](http://doi.org/10.3892/etm.2025.12853) |
| **Issue** | 5 |
| **Journal Abbr** | Exp Ther Med |
| **ISSN** | 1792-1015 1792-0981 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + enteric nervous system
  + oxidative stress
  + aged garlic extract
  + aging
  + intestinal motility
  + neuronal nitric oxide synthase
  + neuroprotection

## Emerging role of fecal microbiota therapy in the treatment of gastrointestinal and extra-gastrointestinal diseases.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | P. C. Konturek |
| **Author** | D. Haziri |
| **Author** | T. Brzozowski |
| **Author** | T. Hess |
| **Author** | S. Heyman |
| **Author** | S. Kwiecien |
| **Author** | S. J. Konturek |
| **Author** | J. Koziel |
| **Abstract** | In the recent decade our understanding of the role of the human gut microbiome has been revolutionized by advances in development of molecular methods. Approximately, up to 100 trillion (10(14)) microorganisms per human body colonize the intestinal tract making an additional acquired organ that provides many vital functions to the host. A healthy gut microbiome can be defined by the presence of the various classes of microbes that enhance metabolism, resistance to infection and inflammation, prevention against cancer and autoimmunity and that positively influence so called braingut axis. Diet represents one of the most important driving forces that besides environmental and genetic factors, can define and influence the microbial composition of the gut. Aging process due to different changes in gut physiology (i.e. gastric hypochlorhydria, motility disorders, use of drugs, degenerative changes in enteric nervous system) has a profound effect on the composition, diversity and functional features of gut microbiota. A perturbed aged gut microbiome has been associated with the increasing number of gastrointestinal (e.g. Clostridium difficile infection - CDI) and non-gastrointestinal diseases (metabolic syndrome, diabetes mellitus, fatty liver disease, atherosclerosis etc.). Fecal microbiota transplantation (FMT) is a highly effective method in the treatment of refractory CDI. FMT is the term used when stool is taken from a healthy individual and instilled during endoscopy (colonoscopy or enteroscopy) into a gut of the sick person to cure certain disease. FMT represents an effective therapy in patient with recurrent CDI and the effectiveness of FMT in the prevention of CDI recurrence had reached approx. 90%. There is also an increasing evidence that the manipulation of gut microbiota by FMT represents a promising therapeutic method in patients with inflammatory bowel disease and irritable bowel syndrome. There is also an increased interest in the role of FMT for the treatment of metabolic syndrome and obesity which collectively present the greatest health challenge in the developed world nowadays. Targeting of gut microbiota by FMT represents an exciting new frontier in the prevention and management of gastrointestinal and non-gastrointestinal diseases that awaits further studies in preclinical and clinical settings. |
| **Date** | 2015 Aug |
| **Language** | eng |
| **Extra** | Place: Poland PMID: 26348073 |
| **Volume** | 66 |
| **Pages** | 483-491 |
| **Publication** | Journal of physiology and pharmacology : an official journal of the Polish Physiological Society |
| **Issue** | 4 |
| **Journal Abbr** | J Physiol Pharmacol |
| **ISSN** | 1899-1505 0867-5910 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Animals
  + \*Gastrointestinal Microbiome
  + Feces/\*microbiology
  + Gastrointestinal Diseases/\*therapy

## Engineered liposomes targeting the gut-CNS Axis for comprehensive therapy of spinal cord injury.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Xue Wang |
| **Author** | Jin Wu |
| **Author** | Xinlong Liu |
| **Author** | Kaicheng Tang |
| **Author** | Liting Cheng |
| **Author** | Jie Li |
| **Author** | Yixuan Tang |
| **Author** | Xiangrong Song |
| **Author** | Xiaoyou Wang |
| **Author** | Chong Li |
| **Abstract** | Effective curative therapies for spinal cord injury (SCI), which is often accompanied by intestinal complications, are lacking. Potential therapeutic targets include astrocytes and their enteric nervous system counterpart, enteric glial cells (EGCs). Based on shared biomarkers and similar functions of both cell types, we designed an orally administered targeted delivery system in which the neuropeptide apamin, stabilized by sulfur replacement with selenium, was adopted as a targeting moiety, and the liposome surface was protected with a non-covalent cross-linked chitosan oligosaccharide lactate layer. The system effectively permeated through oral absorption barriers, targeted local EGCs and astrocytes after systemic circulation, allowing for comprehensive SCI therapy. Given the involvement of the gut-organ axis in a growing number of diseases, our research may shed light on new aspects of the oral administration route as a bypass for multiple interventions and targeted therapy. |
| **Date** | 2021 Mar 10 |
| **Language** | eng |
| **Rights** | Copyright © 2021 Elsevier B.V. All rights reserved. |
| **Extra** | Place: Netherlands PMID: 33485884 |
| **Volume** | 331 |
| **Pages** | 390-403 |
| **Publication** | Journal of controlled release : official journal of the Controlled Release Society |
| **DOI** | [10.1016/j.jconrel.2021.01.032](http://doi.org/10.1016/j.jconrel.2021.01.032) |
| **Journal Abbr** | J Control Release |
| **ISSN** | 1873-4995 0168-3659 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Neuroglia
  + \*Liposomes
  + \*Spinal Cord Injuries/drug therapy
  + Astrocytes
  + Enteric glial cells
  + Gut-CNS axis
  + Oral delivery
  + Spinal Cord
  + Spinal cord injury

## Enteric neuroplasticity and dysmotility in inflammatory disease: key players and possible therapeutic targets.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Estelle T. Spear |
| **Author** | Gary M. Mawe |
| **Abstract** | Intestinal functions, including motility and secretion, are locally controlled by enteric neural networks housed within the wall of the gut. The fidelity of these functions depends on the precision of intercellular signaling among cellular elements, including enteric neurons, epithelial cells, immune cells, and glia, all of which are vulnerable to disruptive influences during inflammatory events. This review article describes current knowledge regarding inflammation-induced neuroplasticity along key elements of enteric neural circuits, what is known about the causes of these changes, and possible therapeutic targets for protecting and/or repairing the integrity of intrinsic enteric neurotransmission. Changes that have been detected in response to inflammation include increased epithelial serotonin availability, hyperexcitability of intrinsic primary afferent neurons, facilitation of synaptic activity among enteric neurons, and attenuated purinergic neuromuscular transmission. Dysfunctional propulsive motility has been detected in models of colitis, where causes include the changes described above, and in models of multiple sclerosis and other autoimmune conditions, where autoantibodies are thought to mediate dysmotility. Other cells implicated in inflammation-induced neuroplasticity include muscularis macrophages and enteric glia. Targeted treatments that are discussed include 5-hydroxytryptamine receptor 4 agonists, cyclooxygenase inhibitors, antioxidants, B cell depletion therapy, and activation of anti-inflammatory pathways. |
| **Date** | 2019 Dec 1 |
| **Language** | eng |
| **Extra** | Place: United States PMID: 31604034 PMCID: PMC6962496 |
| **Volume** | 317 |
| **Pages** | G853-G861 |
| **Publication** | American journal of physiology. Gastrointestinal and liver physiology |
| **DOI** | [10.1152/ajpgi.00206.2019](http://doi.org/10.1152/ajpgi.00206.2019) |
| **Issue** | 6 |
| **Journal Abbr** | Am J Physiol Gastrointest Liver Physiol |
| **ISSN** | 1522-1547 0193-1857 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Animals
  + enteric nervous system
  + glia
  + \*Enteric Nervous System/immunology/physiopathology
  + \*Inflammation/immunology/physiopathology/therapy
  + autoantibody
  + Cell Communication/\*physiology
  + gastrointestinal motility
  + Gastrointestinal Motility/\*immunology
  + macrophage
  + Nervous System Autoimmune Disease, Experimental
  + Neuronal Plasticity/\*immunology

## G protein-coupled receptor trafficking and signaling: new insights into the enteric nervous system.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Simona E. Carbone |
| **Author** | Nicholas A. Veldhuis |
| **Author** | Arisbel B. Gondin |
| **Author** | Daniel P. Poole |
| **Abstract** | G protein-coupled receptors (GPCRs) are essential for the neurogenic control of gastrointestinal (GI) function and are important and emerging therapeutic targets in the gut. Detailed knowledge of both the distribution and functional expression of GPCRs in the enteric nervous system (ENS) is critical toward advancing our understanding of how these receptors contribute to GI function during physiological and pathophysiological states. Equally important, but less well defined, is the complex relationship between receptor expression, ligand binding, signaling, and trafficking within enteric neurons. Neuronal GPCRs are internalized following exposure to agonists and under pathological conditions, such as intestinal inflammation. However, the relationship between the intracellular distribution of GPCRs and their signaling outputs in this setting remains a "black box". This review will briefly summarize current knowledge of agonist-evoked GPCR trafficking and location-specific signaling in the ENS and identifies key areas where future research could be focused. Greater understanding of the cellular and molecular mechanisms involved in regulating GPCR signaling in the ENS will provide new insights into GI function and may open novel avenues for therapeutic targeting of GPCRs for the treatment of digestive disorders. |
| **Date** | 2019 Apr 1 |
| **Language** | eng |
| **Extra** | Place: United States PMID: 30702900 |
| **Volume** | 316 |
| **Pages** | G446-G452 |
| **Publication** | American journal of physiology. Gastrointestinal and liver physiology |
| **DOI** | [10.1152/ajpgi.00406.2018](http://doi.org/10.1152/ajpgi.00406.2018) |
| **Issue** | 4 |
| **Journal Abbr** | Am J Physiol Gastrointest Liver Physiol |
| **ISSN** | 1522-1547 0193-1857 |
| **Date Added** | 6/11/2025, 2:32:23 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Animals
  + Drug Discovery
  + Signal Transduction
  + enteric nervous system
  + endocytosis
  + Receptors, G-Protein-Coupled/\*metabolism
  + \*Protein Transport/drug effects/physiology
  + Enteric Nervous System/\*physiology
  + Enterocytes/\*physiology
  + GPCR, location-specific signaling
  + receptor trafficking

## G Protein-Coupled Receptor Trafficking and Signalling in the Enteric Nervous System: The Past, Present and Future.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Daniel P. Poole |
| **Author** | Nigel W. Bunnett |
| **Abstract** | G protein-coupled receptors (GPCRs) enable cells to detect and respond to changes in their extracellular environment. With over 800 members, the GPCR family includes receptors for a diverse range of agonists including olfactants, neurotransmitters and hormones. Importantly, GPCRs represent a major therapeutic target, with approximately 50 % of all current drugs acting at some aspect of GPCR signalling (Audet and Bouvier 2008). GPCRs are widely expressed by all cell types in the gastrointestinal (GI) tract and are major regulators of every aspect of gut function. Many GPCRs are internalised upon activation, and this represents one of the mechanisms through which G protein-signalling is terminated. The latency between the endocytosis of GPCRs and their recycling and resensitization is a major determinant of the cell's ability to respond to subsequent exposure to agonists. |
| **Date** | 2016 |
| **Language** | eng |
| **Extra** | Place: United States PMID: 27379642 PMCID: PMC11450630 |
| **Volume** | 891 |
| **Pages** | 145-152 |
| **Publication** | Advances in experimental medicine and biology |
| **DOI** | [10.1007/978-3-319-27592-5\_14](http://doi.org/10.1007/978-3-319-27592-5_14) |
| **Journal Abbr** | Adv Exp Med Biol |
| **ISSN** | 0065-2598 2214-8019 |
| **Date Added** | 6/11/2025, 2:32:23 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Animals
  + Protein Transport
  + Enteric Nervous System/\*metabolism
  + GTP-Binding Proteins/\*metabolism
  + Receptors, G-Protein-Coupled/\*metabolism
  + Signal Transduction/\*physiology

## Gastrointestinal Physiology and Function.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Beverley Greenwood-Van Meerveld |
| **Author** | Anthony C. Johnson |
| **Author** | David Grundy |
| **Abstract** | The gastrointestinal (GI) system is responsible for the digestion and absorption of ingested food and liquids. Due to the complexity of the GI tract and the substantial volume of material that could be covered under the scope of GI physiology, this chapter briefly reviews the overall function of the GI tract, and discusses the major factors affecting GI physiology and function, including the intestinal microbiota, chronic stress, inflammation, and aging with a focus on the neural regulation of the GI tract and an emphasis on basic brain-gut interactions that serve to modulate the GI tract. GI diseases refer to diseases of the esophagus, stomach, small intestine, colon, and rectum. The major symptoms of common GI disorders include recurrent abdominal pain and bloating, heartburn, indigestion/dyspepsia, nausea and vomiting, diarrhea, and constipation. GI disorders rank among the most prevalent disorders, with the most common including esophageal and swallowing disorders, gastric and peptic ulcer disease, gastroparesis or delayed gastric emptying, irritable bowel syndrome (IBS), and inflammatory bowel disease (IBD). Many GI disorders are difficult to diagnose and their symptoms are not effectively managed. Thus, basic research is required to drive the development of novel therapeutics which are urgently needed. One approach is to enhance our understanding of gut physiology and pathophysiology especially as it relates to gut-brain communications since they have clinical relevance to a number of GI complaints and represent a therapeutic target for the treatment of conditions including inflammatory diseases of the GI tract such as IBD and functional gut disorders such as IBS. |
| **Date** | 2017 |
| **Language** | eng |
| **Extra** | Place: Germany PMID: 28176047 |
| **Volume** | 239 |
| **Pages** | 1-16 |
| **Publication** | Handbook of experimental pharmacology |
| **DOI** | [10.1007/164\_2016\_118](http://doi.org/10.1007/164_2016_118) |
| **Journal Abbr** | Handb Exp Pharmacol |
| **ISSN** | 0171-2004 |
| **Date Added** | 6/11/2025, 2:32:22 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Animals
  + Inflammation
  + Colon
  + Enteric nervous system (ENS)
  + Gastrointestinal Motility
  + Stress
  + Absorption
  + Barrier function
  + Central nervous system (CNS)
  + Constipation
  + Diarrhea
  + Digestion
  + Enteric Nervous System/\*physiopathology
  + Epithelial barrier
  + Gastric Juice/metabolism
  + Gastrointestinal Absorption
  + Gastrointestinal Diseases/immunology/\*physiopathology
  + Gastrointestinal Tract/immunology/innervation/metabolism/physiopathology
  + Gut microbiome
  + Inflammatory bowel disease (IBD)
  + Intestinal permeability
  + Intestinal Secretions/metabolism
  + Irritable bowel syndrome (IBS)
  + Mucosa
  + Secretion
  + Small intestine
  + Smooth muscle
  + Visceral pain

## Genome-Wide Association Studies of Diarrhea Frequency and Duration in the First Year of Life in Bangladeshi Infants.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Rebecca M. Munday |
| **Author** | Rashidul Haque |
| **Author** | Genevieve L. Wojcik |
| **Author** | Poonum Korpe |
| **Author** | Uma Nayak |
| **Author** | Beth D. Kirkpatrick |
| **Author** | William A. Jr Petri |
| **Author** | Priya Duggal |
| **Abstract** | BACKGROUND: Diarrhea is the second leading cause of death in children under 5 years old worldwide. Known diarrhea risk factors include sanitation, water sources, and pathogens but do not fully explain the heterogeneity in frequency and duration of diarrhea in young children. We evaluated the role of host genetics in diarrhea. METHODS: Using 3 well-characterized birth cohorts from an impoverished area of Dhaka, Bangladesh, we compared infants with no diarrhea in the first year of life to those with an abundance, measured by either frequency or duration. We performed a genome-wide association analysis for each cohort under an additive model and then meta-analyzed across the studies. RESULTS: For diarrhea frequency, we identified 2 genome-wide significant loci associated with not having any diarrhea, on chromosome 21 within the noncoding RNA AP000959 (C allele odds ratio [OR] = 0.31, P = 4.01 × 10-8), and on chromosome 8 within SAMD12 (T allele OR = 0.35, P = 4.74 × 10-7). For duration of diarrhea, we identified 2 loci associated with no diarrhea, including the same locus on chromosome 21 (C allele OR = 0.31, P = 1.59 × 10-8) and another locus on chromosome 17 near WSCD1 (C allele OR = 0.35, P = 1.09 × 10-7). CONCLUSIONS: These loci are in or near genes involved in enteric nervous system development and intestinal inflammation and may be potential targets for diarrhea therapeutics. |
| **Date** | 2023 Oct 18 |
| **Language** | eng |
| **Rights** | © The Author(s) 2023. Published by Oxford University Press on behalf of Infectious Diseases Society of America. All rights reserved. For permissions, please e-mail: journals.permissions@oup.com. |
| **Extra** | Place: United States PMID: 36967705 PMCID: PMC11007397 |
| **Volume** | 228 |
| **Pages** | 979-989 |
| **Publication** | The Journal of infectious diseases |
| **DOI** | [10.1093/infdis/jiad068](http://doi.org/10.1093/infdis/jiad068) |
| **Issue** | 8 |
| **Journal Abbr** | J Infect Dis |
| **ISSN** | 1537-6613 0022-1899 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Infant
  + Child
  + Alleles
  + \*Diarrhea/epidemiology/genetics
  + \*Genome-Wide Association Study
  + association
  + Bangladesh/epidemiology
  + Child, Preschool
  + diarrhea
  + enterics
  + GWAS
  + host genetics
  + malnutrition
  + Risk Factors

## Glutamate regulates gliosis of BMSCs to promote ENS regeneration through α-KG and H3K9/H3K27 demethylation.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Mengke Fan |
| **Author** | Huiying Shi |
| **Author** | Hailing Yao |
| **Author** | Weijun Wang |
| **Author** | Yurui Zhang |
| **Author** | Chen Jiang |
| **Author** | Rong Lin |
| **Abstract** | BACKGROUND: There is a lack of effective therapies for enteric nervous system (ENS) injury. Our previous study showed that transplanted bone marrow-derived mesenchymal stem cells (BMSCs) play a "glia-like cells" role in initiating ENS regeneration in denervated mice. Cellular energy metabolism is an important factor in maintaining the biological characteristics of stem cells. However, how cellular energy metabolism regulates the fate of BMSCs in the ENS-injured microenvironment is unclear. METHODS: The biological characteristics, energy metabolism, and histone methylation levels of BMSCs following ENS injury were determined. Then, glutamate dehydrogenase 1 (Glud1) which catalyzes the oxidative deamination of glutamate to α-KG was overexpressed (OE) in BMSCs. Further, OE-Glud1 BMSCs were targeted-transplanted into the ENS injury site of denervated mice to determine their effects on ENS regeneration. RESULTS: In vitro, in the ENS-injured high-glutamate microenvironment, the ratio of α-ketoglutarate (α-KG) to succinate (P < 0.05), the histone demethylation level (P < 0.05), the protein expression of glial cell markers (P < 0.05), and the gene expression of Glud1 (P < 0.05) were significantly increased. And the binding of H3K9me3 to the GFAP, S100B, and GDNF promoter was enhanced (P < 0.05). Moreover, α-KG treatment increased the monomethylation and decreased the trimethylation on H3K9 (P < 0.01) and H3K27 (P < 0.05) in BMSCs and significantly upregulated the protein expression of glial cell markers (P < 0.01), which was reversed by the α-KG competitive inhibitor D-2-hydroxyglutarate (P < 0.05). Besides, overexpression of Glud1 in BMSCs exhibited increases in monomethylation and decreases in trimethylation on H3K9 (P < 0.05) and H3K27 (P < 0.05), and upregulated protein expression of glial cell markers (P < 0.01). In vivo, BMSCs overexpressing Glud1 had a strong promotion effect on ENS regeneration in denervated mice through H3K9/H3K27 demethylation (P < 0.05), and upregulating the expression of glial cell protein (P < 0.05). CONCLUSIONS: BMSCs overexpressing Glud1 promote the expression of glial cell markers and ENS remodeling in denervated mice through regulating intracellular α-KG and H3K9/H3K27 demethylation. |
| **Date** | 2022 Jun 17 |
| **Language** | eng |
| **Rights** | © 2022. The Author(s). |
| **Extra** | Place: England PMID: 35715822 PMCID: PMC9205030 |
| **Volume** | 13 |
| **Pages** | 255 |
| **Publication** | Stem cell research & therapy |
| **DOI** | [10.1186/s13287-022-02936-7](http://doi.org/10.1186/s13287-022-02936-7) |
| **Issue** | 1 |
| **Journal Abbr** | Stem Cell Res Ther |
| **ISSN** | 1757-6512 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Animals
  + Mice
  + \*Enteric Nervous System/metabolism
  + \*Gliosis/metabolism
  + \*Histones/drug effects/genetics/metabolism
  + \*Ketoglutaric Acids/metabolism
  + Bone Marrow Cells/metabolism
  + Bone marrow-derived mesenchymal stem cells (BMSCs)
  + Demethylation
  + Glud1 (glutamate dehydrogenase 1)
  + Glutamic Acid/metabolism
  + Histone methylation
  + Mesenchymal Stem Cell Transplantation
  + α-ketoglutarate (α-KG)

## Gut-brain communication in COVID-19: molecular mechanisms, mediators, biomarkers, and therapeutics.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Tameena Wais |
| **Author** | Mehde Hasan |
| **Author** | Vikrant Rai |
| **Author** | Devendra K. Agrawal |
| **Abstract** | INTRODUCTION: Infection with COVID-19 results in acute respiratory symptoms followed by long COVID multi-organ effects presenting with neurological, cardiovascular, musculoskeletal, and gastrointestinal (GI) manifestations. Temporal relationship between gastrointestinal and neurological symptoms is unclear but warranted for exploring better clinical care for COVID-19 patients. AREAS COVERED: We critically reviewed the temporal relationship between gut-brain axis after SARS-CoV-2 infection and the molecular mechanisms involved in neuroinvasion following GI infection. Mediators are identified that could serve as biomarkers and therapeutic targets in SARS-CoV-2. We discussed the potential therapeutic approaches to mitigate the effects of GI infection with SARS-CoV-2. EXPERT OPINION: Altered gut microbiota cause increased expression of various mediators, including zonulin causing disruption of tight junction. This stimulates enteric nervous system and signals to CNS precipitating neurological sequalae. Published reports suggest potential role of cytokines, immune cells, B(0)AT1 (SLC6A19), ACE2, TMRSS2, TMPRSS4, IFN-γ, IL-17A, zonulin, and altered gut microbiome in gut-brain axis and associated neurological sequalae. Targeting these mediators and gut microbiome to improve immunity will be of therapeutic significance. In-depth research and well-designed large-scale population-based clinical trials with multidisciplinary and collaborative approaches are warranted. Investigating the temporal relationship between organs involved in long-term sequalae is critical due to evolving variants of SARS-CoV-2. |
| **Date** | 2022 Sep |
| **Language** | eng |
| **Extra** | Place: England PMID: 35868344 PMCID: PMC9388545 |
| **Volume** | 18 |
| **Pages** | 947-960 |
| **Publication** | Expert review of clinical immunology |
| **DOI** | [10.1080/1744666X.2022.2105697](http://doi.org/10.1080/1744666X.2022.2105697) |
| **Issue** | 9 |
| **Journal Abbr** | Expert Rev Clin Immunol |
| **ISSN** | 1744-8409 1744-666X |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + SARS-CoV-2
  + COVID-19
  + Biomarkers
  + Brain
  + enteric nervous system
  + gastrointestinal tract
  + \*Brain-Gut Axis
  + \*COVID-19/complications
  + \*Gastrointestinal Diseases
  + ACE-2 receptor
  + Gut-brain axis
  + Post-Acute COVID-19 Syndrome

## Host Gut Motility Promotes Competitive Exclusion within a Model Intestinal Microbiota.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Travis J. Wiles |
| **Author** | Matthew Jemielita |
| **Author** | Ryan P. Baker |
| **Author** | Brandon H. Schlomann |
| **Author** | Savannah L. Logan |
| **Author** | Julia Ganz |
| **Author** | Ellie Melancon |
| **Author** | Judith S. Eisen |
| **Author** | Karen Guillemin |
| **Author** | Raghuveer Parthasarathy |
| **Abstract** | The gut microbiota is a complex consortium of microorganisms with the ability to influence important aspects of host health and development. Harnessing this "microbial organ" for biomedical applications requires clarifying the degree to which host and bacterial factors act alone or in combination to govern the stability of specific lineages. To address this issue, we combined bacteriological manipulation and light sheet fluorescence microscopy to monitor the dynamics of a defined two-species microbiota within a vertebrate gut. We observed that the interplay between each population and the gut environment produces distinct spatiotemporal patterns. As a consequence, one species dominates while the other experiences sudden drops in abundance that are well fit by a stochastic mathematical model. Modeling revealed that direct bacterial competition could only partially explain the observed phenomena, suggesting that a host factor is also important in shaping the community. We hypothesized the host determinant to be gut motility, and tested this mechanism by measuring colonization in hosts with enteric nervous system dysfunction due to a mutation in the ret locus, which in humans is associated with the intestinal motility disorder known as Hirschsprung disease. In mutant hosts we found reduced gut motility and, confirming our hypothesis, robust coexistence of both bacterial species. This study provides evidence that host-mediated spatial structuring and stochastic perturbation of communities can drive bacterial population dynamics within the gut, and it reveals a new facet of the intestinal host-microbe interface by demonstrating the capacity of the enteric nervous system to influence the microbiota. Ultimately, these findings suggest that therapeutic strategies targeting the intestinal ecosystem should consider the dynamic physical nature of the gut environment. |
| **Date** | 2016 Jul |
| **Language** | eng |
| **Extra** | Place: United States PMID: 27458727 PMCID: PMC4961409 |
| **Volume** | 14 |
| **Pages** | e1002517 |
| **Publication** | PLoS biology |
| **DOI** | [10.1371/journal.pbio.1002517](http://doi.org/10.1371/journal.pbio.1002517) |
| **Issue** | 7 |
| **Journal Abbr** | PLoS Biol |
| **ISSN** | 1545-7885 1544-9173 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Animals
  + Mutation
  + Species Specificity
  + Aeromonas veronii/physiology
  + Antibiosis/physiology
  + Gastrointestinal Microbiome/\*physiology
  + Gastrointestinal Motility/\*physiology
  + Gastrointestinal Tract/\*microbiology
  + Larva/genetics/microbiology/physiology
  + Microbiota/\*physiology
  + Microscopy, Fluorescence
  + Population Dynamics
  + Vibrio cholerae/physiology
  + Zebrafish

## Hypnosis and Cognitive Behavioral Therapies for the Management of Gastrointestinal Disorders.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Olafur S. Palsson |
| **Author** | Sarah Ballou |
| **Abstract** | PURPOSE OF REVIEW: To review the nature, current evidence of efficacy, recent developments, and future prospects for cognitive behavioral therapy (CBT) and gut-directed hypnotherapy, the two best established psychological interventions for managing gastrointestinal (GI) disorders. RECENT FINDINGS: New large randomized controlled trials are showing that cost-effective therapy delivery formats (telephone-based, Internet-based, fewer therapist sessions, or group therapy) are effective for treating GI disorders. CBT and hypnotherapy can produce substantial improvement in the digestive tract symptoms, psychological well-being, and quality of life of GI patients. However, they have long been hampered by limited scalability and significant cost, and only been sufficiently tested for a few GI health problems. Through adoption of more cost-effective therapy formats and teletherapy, and by expanding the scope of efficacy testing to additional GI treatment targets, these interventions have the potential to become widely available options for improving clinical outcomes for patients with hard-to-treat GI disorders. |
| **Date** | 2020 Jun 3 |
| **Language** | eng |
| **Extra** | Place: United States PMID: 32495233 |
| **Volume** | 22 |
| **Pages** | 31 |
| **Publication** | Current gastroenterology reports |
| **DOI** | [10.1007/s11894-020-00769-z](http://doi.org/10.1007/s11894-020-00769-z) |
| **Issue** | 7 |
| **Journal Abbr** | Curr Gastroenterol Rep |
| **ISSN** | 1534-312X 1522-8037 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Quality of Life
  + Functional gastrointestinal disorders
  + \*Cognitive Behavioral Therapy
  + \*Hypnosis
  + Brain-gut axis
  + Central Nervous System/physiology/physiopathology
  + Cognitive behavioral therapy
  + Dyspepsia/psychology/therapy
  + Enteric Nervous System/physiology/physiopathology
  + Gastrointestinal Diseases/physiopathology/psychology/\*therapy
  + Hypnotherapy
  + Inflammatory Bowel Diseases/psychology/therapy
  + Irritable Bowel Syndrome/psychology/therapy
  + Stress, Psychological/physiopathology
  + Telemedicine

## Impact of chemotherapy on gastrointestinal functions and the enteric nervous system.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Jonathan Escalante |
| **Author** | Rachel M. McQuade |
| **Author** | Vanesa Stojanovska |
| **Author** | Kulmira Nurgali |
| **Abstract** | Chemotherapy is the main treatment for many cancers, including colorectal cancer, a type of cancer with some of the highest prevalence and mortality rates worldwide. Although chemotherapeutic drugs have greatly improved the survival rates of cancer patients, there are many side-effects associated with their use. The gastrointestinal side-effects of chemotherapy often lead to dose reduction or even discontinuation of treatment, which in turn affects the clinical outcome. Gastrointestinal side-effects, such as chemotherapy-induced diarrhea and constipation, may persist many years after treatment, greatly reducing quality of life. Current treatments for these side-effects have many adverse effects themselves; therefore, new approaches are needed to address this problem. Changes in the enteric nervous system located within the gastrointestinal tract and controlling its functions have been implicated in many disorders. Recent studies providing insight into the association between chemotherapy-induced damage to enteric neurons and gastrointestinal dysfunction have highlighted the enteric nervous system as a potential therapeutic target to alleviate chemotherapy-induced toxicity which may improve both clinical outcomes and the quality of patients' lives. |
| **Date** | 2017 Nov |
| **Language** | eng |
| **Rights** | Copyright © 2017 Elsevier B.V. All rights reserved. |
| **Extra** | Place: Ireland PMID: 28545907 |
| **Volume** | 105 |
| **Pages** | 23-29 |
| **Publication** | Maturitas |
| **DOI** | [10.1016/j.maturitas.2017.04.021](http://doi.org/10.1016/j.maturitas.2017.04.021) |
| **Journal Abbr** | Maturitas |
| **ISSN** | 1873-4111 0378-5122 |
| **Date Added** | 6/11/2025, 2:32:23 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Animals
  + Quality of Life
  + Chemotherapy
  + Antineoplastic Agents/\*adverse effects
  + Chemotherapy-induced constipation
  + Chemotherapy-induced diarrhea
  + Colorectal Neoplasms/\*drug therapy/physiopathology
  + Constipation/\*chemically induced
  + Diarrhea/\*chemically induced
  + Enteric Nervous System/\*drug effects/physiology
  + Enteric neuropathy

## Inflammation-associated changes in DOR expression and function in the mouse colon.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Jesse J. DiCello |
| **Author** | Ayame Saito |
| **Author** | Pradeep Rajasekhar |
| **Author** | Emily M. Eriksson |
| **Author** | Rachel M. McQuade |
| **Author** | Cameron J. Nowell |
| **Author** | Benjamin W. Sebastian |
| **Author** | Jakub Fichna |
| **Author** | Nicholas A. Veldhuis |
| **Author** | Meritxell Canals |
| **Author** | Nigel W. Bunnett |
| **Author** | Simona E. Carbone |
| **Author** | Daniel P. Poole |
| **Abstract** | Endogenous opioids activate opioid receptors (ORs) in the enteric nervous system to control intestinal motility and secretion. The μ-OR mediates the deleterious side effects of opioid analgesics, including constipation, respiratory depression, and addiction. Although the δ-OR (DOR) is a promising target for analgesia, the function and regulation of DOR in the colon are poorly understood. This study provides evidence that endogenous opioids activate DOR in myenteric neurons that may regulate colonic motility. The DOR agonists DADLE, deltorphin II, and SNC80 inhibited electrically evoked contractions and induced neurogenic contractions in the mouse colon. Electrical, chemical, and mechanical stimulation of the colon evoked the release of endogenous opioids, which stimulated endocytosis of DOR in the soma and proximal neurites of myenteric neurons of transgenic mice expressing DOR fused to enhanced green fluorescent protein. In contrast, DOR was not internalized in nerve fibers within the circular muscle. Administration of dextran sulfate sodium induced acute colitis, which was accompanied by DOR endocytosis and an increased density of DOR-positive nerve fibers within the circular muscle. The potency with which SNC80 inhibited neurogenic contractions was significantly enhanced in the inflamed colon. This study demonstrates that DOR-expressing neurons in the mouse colon can be activated by exogenous and endogenous opioids. Activated DOR traffics to endosomes and inhibits neurogenic motility of the colon. DOR signaling is enhanced during intestinal inflammation. This study demonstrates functional expression of DOR by myenteric neurons and supports the therapeutic targeting of DOR in the enteric nervous system. NEW & NOTEWORTHY DOR is activated during physiologically relevant reflex stimulation. Agonist-evoked DOR endocytosis is spatially and temporally regulated. A significant proportion of DOR is internalized in myenteric neurons during inflammation. The relative proportion of all myenteric neurons that expressed DOR and the overlap with the nNOS-positive population are increased in inflammation. DOR-specific innervation of the circular muscle is increased in inflammation, and this is consistent with enhanced responsiveness to the DOR agonist SNC80. |
| **Date** | 2018 Oct 1 |
| **Language** | eng |
| **Extra** | Place: United States PMID: 29927325 PMCID: PMC6230691 |
| **Volume** | 315 |
| **Pages** | G544-G559 |
| **Publication** | American journal of physiology. Gastrointestinal and liver physiology |
| **DOI** | [10.1152/ajpgi.00025.2018](http://doi.org/10.1152/ajpgi.00025.2018) |
| **Issue** | 4 |
| **Journal Abbr** | Am J Physiol Gastrointest Liver Physiol |
| **ISSN** | 1522-1547 0193-1857 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Female
  + Male
  + Animals
  + Mice
  + Mice, Inbred C57BL
  + enteric nervous system
  + Benzamides/pharmacology
  + Endocytosis
  + Piperazines/pharmacology
  + \*Gastrointestinal Motility
  + Colitis, Ulcerative/\*metabolism
  + Colon/\*metabolism/physiology/physiopathology
  + endocytosis
  + Enkephalin, Leucine-2-Alanine/metabolism
  + Enteric Nervous System/\*metabolism/physiology/physiopathology
  + G protein-coupled receptor, intestinal motility
  + Muscle Contraction
  + Oligopeptides/metabolism
  + opioid receptor
  + Receptors, Opioid, delta/agonists/genetics/\*metabolism

## Inhibition of APE1/Ref-1 Redox Signaling Alleviates Intestinal Dysfunction and Damage to Myenteric Neurons in a Mouse Model of Spontaneous Chronic Colitis.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Lauren Sahakian |
| **Author** | Rhiannon T. Filippone |
| **Author** | Rhian Stavely |
| **Author** | Ainsley M. Robinson |
| **Author** | Xu Sean Yan |
| **Author** | Raquel Abalo |
| **Author** | Rajaraman Eri |
| **Author** | Joel C. Bornstein |
| **Author** | Mark R. Kelley |
| **Author** | Kulmira Nurgali |
| **Abstract** | BACKGROUND: Inflammatory bowel disease (IBD) associates with damage to the enteric nervous system (ENS), leading to gastrointestinal (GI) dysfunction. Oxidative stress is important for the pathophysiology of inflammation-induced enteric neuropathy and GI dysfunction. Apurinic/apyrimidinic endonuclease 1/redox factor-1 (APE1/Ref-1) is a dual functioning protein that is an essential regulator of the cellular response to oxidative stress. In this study, we aimed to determine whether an APE1/Ref-1 redox domain inhibitor, APX3330, alleviates inflammation-induced oxidative stress that leads to enteric neuropathy in the Winnie murine model of spontaneous chronic colitis. METHODS: Winnie mice received APX3330 or vehicle via intraperitoneal injections over 2 weeks and were compared with C57BL/6 controls. In vivo disease activity and GI transit were evaluated. Ex vivo experiments were performed to assess functional parameters of colonic motility, immune cell infiltration, and changes to the ENS. RESULTS: Targeting APE1/Ref-1 redox activity with APX3330 improved disease severity, reduced immune cell infiltration, restored GI function ,and provided neuroprotective effects to the enteric nervous system. Inhibition of APE1/Ref-1 redox signaling leading to reduced mitochondrial superoxide production, oxidative DNA damage, and translocation of high mobility group box 1 protein (HMGB1) was involved in neuroprotective effects of APX3330 in enteric neurons. CONCLUSIONS: This study is the first to investigate inhibition of APE1/Ref-1's redox activity via APX3330 in an animal model of chronic intestinal inflammation. Inhibition of the redox function of APE1/Ref-1 is a novel strategy that might lead to a possible application of APX3330 for the treatment of IBD. |
| **Date** | 2021 Feb 16 |
| **Language** | eng |
| **Rights** | © 2020 Crohn’s & Colitis Foundation. Published by Oxford University Press. All rights reserved. For permissions, please e-mail: journals.permissions@oup.com. |
| **Extra** | Place: England PMID: 32618996 PMCID: PMC8287929 |
| **Volume** | 27 |
| **Pages** | 388-406 |
| **Publication** | Inflammatory bowel diseases |
| **DOI** | [10.1093/ibd/izaa161](http://doi.org/10.1093/ibd/izaa161) |
| **Issue** | 3 |
| **Journal Abbr** | Inflamm Bowel Dis |
| **ISSN** | 1536-4844 1078-0998 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Animals
  + Disease Models, Animal
  + Mice
  + Mice, Inbred C57BL
  + DNA damage
  + Neurons
  + Inflammation/drug therapy
  + enteric nervous system
  + \*Colitis/chemically induced/drug therapy
  + \*Intestinal Pseudo-Obstruction
  + APE1/Ref-1
  + APX3330
  + chronic intestinal inflammation
  + DNA-(Apurinic or Apyrimidinic Site) Lyase/\*metabolism
  + IBD
  + Neuroprotective Agents/\*therapeutic use
  + Oxidation-Reduction
  + oxidative stress
  + Oxidative Stress

## Intestinal Enteroendocrine Cells: Present and Future Druggable Targets.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Roger Atanga |
| **Author** | Varsha Singh |
| **Author** | Julie G. In |
| **Abstract** | Enteroendocrine cells are specialized secretory lineage cells in the small and large intestines that secrete hormones and peptides in response to luminal contents. The various hormones and peptides can act upon neighboring cells and as part of the endocrine system, circulate systemically via immune cells and the enteric nervous system. Locally, enteroendocrine cells have a major role in gastrointestinal motility, nutrient sensing, and glucose metabolism. Targeting the intestinal enteroendocrine cells or mimicking hormone secretion has been an important field of study in obesity and other metabolic diseases. Studies on the importance of these cells in inflammatory and auto-immune diseases have only recently been reported. The rapid global increase in metabolic and inflammatory diseases suggests that increased understanding and novel therapies are needed. This review will focus on the association between enteroendocrine changes and metabolic and inflammatory disease progression and conclude with the future of enteroendocrine cells as potential druggable targets. |
| **Date** | 2023 May 16 |
| **Language** | eng |
| **Extra** | Place: Switzerland PMID: 37240181 PMCID: PMC10218851 |
| **Volume** | 24 |
| **Publication** | International journal of molecular sciences |
| **DOI** | [10.3390/ijms24108836](http://doi.org/10.3390/ijms24108836) |
| **Issue** | 10 |
| **Journal Abbr** | Int J Mol Sci |
| **ISSN** | 1422-0067 |
| **Date Added** | 6/11/2025, 2:32:24 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + therapeutics
  + Biological Transport
  + inflammatory bowel disease
  + Hormones/metabolism
  + \*Enteroendocrine Cells/metabolism
  + \*Intestines
  + enteroendocrine cells
  + intestinal hormones
  + metabolic disease
  + Peptides/metabolism

## Long-Term Oncologic Outcome following Duodenum-Preserving Pancreatic Head Resection for Benign Tumors, Cystic Neoplasms, and Neuroendocrine Tumors: Systematic Review and Meta-analysis

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Hans G Beger |
| **Author** | Benjamin Mayer |
| **Author** | Bertram Poch |
| **Date** | 2024 |
| **URL** | <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11164799/> |
| **Volume** | 31 |
| **Pages** | 4637–4653 |
| **Publication** | Annals of Surgical Oncology |
| **DOI** | [10.1245/s10434-024-15222-y](http://doi.org/10.1245/s10434-024-15222-y) |
| **Issue** | 7 |
| **Date Added** | 4/16/2025, 11:10:32 PM |
| **Modified** | 6/16/2025, 1:12:21 PM |

### Tags:

* + Adult
  + Female
  + Humans
  + Male
  + Treatment Outcome
  + Animals
  + Disease Models, Animal
  + Mice
  + STING
  + Quality of Life
  + Retrospective Studies
  + Diabetes
  + Signal Transduction
  + Cell Differentiation
  + Cell Line
  + Neoplasm Recurrence, Local
  + Cell Movement
  + Mammals
  + Neurons
  + immune cells
  + inflammation
  + Homeostasis
  + Gastroenterology
  + intestinal organoids
  + Regeneration
  + microbiota
  + Pancreas
  + inflammatory bowel disease
  + \*Cell- and Tissue-Based Therapy/methods
  + \*Bile Duct Neoplasms
  + \*Bile Duct Neoplasms/surgery
  + \*Cell Lineage
  + \*Cholangiocarcinoma
  + \*Cholangiocarcinoma/pathology
  + \*Colitis, Ulcerative/drug therapy
  + \*Cystadenocarcinoma/diagnostic imaging/surgery
  + \*Cystadenoma/diagnostic imaging/surgery
  + \*Cysts/pathology
  + \*Diabetes Mellitus, Experimental/complications/genetics/metabolism
  + \*Enteric Nervous System
  + \*Enteric Nervous System/pathology
  + \*Hyperglycemia/genetics/metabolism
  + \*Hypothalamo-Hypophyseal System
  + \*Inflammatory Bowel Diseases/drug therapy
  + \*Liver Neoplasms/diagnostic imaging/surgery
  + \*Liver Neoplasms/surgery
  + \*Microbiota
  + \*MicroRNAs/metabolism
  + \*Neoplasms, Cystic, Mucinous, and Serous
  + \*Neuroglia/physiology
  + \*Zebrafish
  + 16S RNA sequencing
  + Acinar cell carcinoma
  + Aging
  + antibiotics
  + Bile Ducts, Intrahepatic
  + Bile Ducts, Intrahepatic/surgery
  + Biliary
  + Biliary cystadenocarcinoma
  + Biliary cystadenoma
  + Brain
  + Brain-Gut Axis
  + Brain/physiology
  + Cell Separation
  + Chemical coding
  + Chick Embryo
  + circVPS13A
  + Cistoadenocarcinoma
  + Cistoadenoma
  + Clinicopathological criteria, Surgical outcomes
  + Colon/drug effects/pathology
  + Cystadenocarcinoma
  + Cystadenoma
  + cystic liver lesions
  + Cystic liver neoplasm
  + Cytology
  + Developmental disorders
  + diabetes
  + diabetes mellitus
  + Drug Discovery/\*methods
  + Embryonic stem cells
  + ENS
  + ENS neuropathies
  + enteric glia
  + enteric glia communications
  + Enteric glia communications
  + enteric glia diversity
  + enteric nervous system
  + Enteric nervous system
  + Enteric Nervous System
  + enteric nervous system (ENS)
  + Enteric nervous system (ENS)
  + Enteric Nervous System/\*pathology
  + Enteric neural precursor cells (ENPCs)
  + enteric progenitor cell
  + Fecal microbiota transplantation
  + Frantz's tumor
  + gastrointestinal complications
  + gastrointestinal diseases
  + Gastrointestinal Diseases
  + Gastrointestinal Diseases/pathology
  + gastrointestinal tract
  + Gastrointestinal Tract/drug effects/pathology
  + glia
  + Glial Cell Line-Derived Neurotrophic Factor/genetics
  + glucagon-like peptide 1
  + Growth Disorders
  + growth retardation
  + gut brain axis
  + gut microbiota
  + gut-brain axis
  + gut–brain axis
  + hepatic cystadenocarcinoma
  + hepatic cystadenoma
  + Hepatic simple cyst
  + hepatobiliary cystadenocarcinoma
  + hepatobiliary cystadenoma
  + Hirschsprung disease
  + Hirschsprung Disease/\*drug therapy/\*pathology/therapy
  + homeostasis
  + Imaging modalities
  + In Situ Hybridization, Fluorescence
  + Inflammatory bowel diseases
  + Intraductal papillary biliary neoplasms
  + intraductal papillary neoplasms of bile duct
  + irritable bowel syndrome
  + L-Fucose
  + Liver Diseases
  + Management
  + microbial metabolites
  + microbiota-gut-brain axis
  + Microbiota-gut-brain axis
  + Mucinous biliary cystic tumors, Biliary cystadenoma
  + mucinous cystic neoplasm
  + Mucinous cystic neoplasms
  + Mucinous neoplasm
  + muscularis macrophages
  + myenteric neurons
  + Neoplasia mucinosa quística
  + Neoplasia papilar intraductal biliar
  + Neoplasia quística hepática
  + Neural Crest
  + neural crest cell
  + neurodegeneration
  + Neuroglia
  + Neurons/drug effects/\*pathology
  + offspring
  + P2X7 receptor
  + pancreatectomy
  + Pancreatectomy
  + Pancreatic neoplasms
  + Pancreatic Neoplasms
  + Pancreatic surgery
  + pancreatic tumor
  + Parkinson’s disease
  + pediatric pancreatic neoplasm
  + Pepstatins/metabolism
  + Pituitary-Adrenal System
  + pluripotent stem cells (PSCs)
  + Pluripotent Stem Cells/pathology
  + preconception
  + probiotic
  + Purinergic signaling
  + Receptor, Endothelin B/metabolism
  + Receptors, Purinergic P2X7
  + RNA, Circular/genetics
  + Rotenone-induced mouse model
  + short-chain fatty acids
  + Solid pseudopapillary tumor
  + Stem-cell differentiation
  + submucosal neurons
  + Submucous Plexus
  + surgical outcome
  + surgical resection
  + three-dimensional (3D)
  + type 2 diabetes
  + zebrafish

### Notes:

* + e14603 NMO-00132-2023
  + e14603 NMO-00132-2023

### Attachments

* + Full Text
  + Full Text
  + Full Text PDF
  + Full Text PDF
  + Full Text PDF
  + Full Text PDF
  + Full Text PDF
  + Full Text PDF
  + Full Text PDF
  + Full Text PDF
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  + PubMed Central Full Text PDF
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  + PubMed Central Link
  + PubMed Central Link
  + PubMed Central Link
  + PubMed Central Link
  + PubMed entry

## Macrophage regulation of the "second brain": CD163 intestinal macrophages interact with inhibitory interneurons to regulate colonic motility - evidence from the Cx3cr1-Dtr rat model.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Jackson L. K. Yip |
| **Author** | Soniya Xavier |
| **Author** | Gayathri K. Balasuriya |
| **Author** | Elisa L. Hill-Yardin |
| **Author** | Sarah J. Spencer |
| **Abstract** | Intestinal macrophages are well-studied for their conventional roles in the immune response against pathogens and protecting the gut from chronic inflammation. However, these macrophages may also have additional functional roles in gastrointestinal motility under typical conditions. This is likely to occur via both direct and indirect influences on gastrointestinal motility through interaction with myenteric neurons that contribute to the gut-brain axis, but this mechanism is yet to be properly characterised. The CX3CR1 chemokine receptor is expressed in the majority of intestinal macrophages, so we used a conditional knockout Cx3cr1-Dtr (diphtheria toxin receptor) rat model to transiently ablate these cells. We then utilized ex vivo video imaging to evaluate colonic motility. Our previous studies in brain suggested that Cx3cr1-expressing cells repopulate by 7 days after depletion in this model, so we performed our experiments at both the 48 hr (macrophage depletion) and 7-day (macrophage repopulation) time points. We also investigated whether inhibitory neuronal input driven by nitric oxide from the enteric nervous system is required for the regulation of colonic motility by intestinal macrophages. Our results demonstrated that CD163-positive resident intestinal macrophages are important in regulating colonic motility in the absence of this major inhibitory neuronal input. In addition, we show that intestinal macrophages are indispensable in maintaining a healthy intestinal structure. Our study provides a novel understanding of the interplay between the enteric nervous system and intestinal macrophages in colonic motility. We highlight intestinal macrophages as a potential therapeutic target for gastrointestinal motility disorders when inhibitory neuronal input is suppressed. |
| **Date** | 2023 |
| **Language** | eng |
| **Rights** | Copyright © 2023 Yip, Xavier, Balasuriya, Hill-Yardin and Spencer. |
| **Extra** | Place: Switzerland PMID: 37868978 PMCID: PMC10585175 |
| **Volume** | 14 |
| **Pages** | 1269890 |
| **Publication** | Frontiers in immunology |
| **DOI** | [10.3389/fimmu.2023.1269890](http://doi.org/10.3389/fimmu.2023.1269890) |
| **Journal Abbr** | Front Immunol |
| **ISSN** | 1664-3224 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Animals
  + Rats
  + Brain
  + \*Interneurons
  + \*Macrophages
  + CD163 Antigen
  + colonic motility
  + gastrointestinal
  + Heparin-binding EGF-like Growth Factor
  + macrophages
  + myenteric plexus
  + nitric oxide

## Mini-review: "Enteric glia functions in nervous tissue repair: Therapeutic target or tool?".

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Mukhamad Sunardi |
| **Author** | Carla Cirillo |
| **Abstract** | In the body, nerve tissue is not only present in the central nervous system, but also in the periphery. The enteric nervous system (ENS) is a highly organized intrinsic network of neurons and glial cells grouped to form interconnected ganglia. Glial cells in the ENS are a fascinating cell population: their neurotrophic role is well established, as well as their plasticity in specific circumstances. Gene expression profiling studies indicate that ENS glia retain neurogenic potential. The identification of neurogenic glial subtype(s) and the molecular basis of glia-derived neurogenesis may have profound biological and clinical implications. In this review, we discuss the potential of using gene-editing for ENS glia and cell transplantation as therapies for enteric neuropathies. Glia in the ENS: target or tool for nerve tissue repair? |
| **Date** | 2023 Aug 24 |
| **Language** | eng |
| **Rights** | Copyright © 2023 Elsevier B.V. All rights reserved. |
| **Extra** | Place: Ireland PMID: 37393007 |
| **Volume** | 812 |
| **Pages** | 137360 |
| **Publication** | Neuroscience letters |
| **DOI** | [10.1016/j.neulet.2023.137360](http://doi.org/10.1016/j.neulet.2023.137360) |
| **Journal Abbr** | Neurosci Lett |
| **ISSN** | 1872-7972 0304-3940 |
| **Date Added** | 6/11/2025, 2:32:23 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Neurons/metabolism
  + \*Enteric Nervous System/metabolism
  + \*Nerve Tissue
  + Neurogenesis/physiology
  + Neuroglia/physiology

## Modulation of Ceramide-Induced Apoptosis in Enteric Neurons by Aryl Hydrocarbon Receptor Signaling: Unveiling a New Pathway beyond ER Stress.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Mallappa Anitha |
| **Author** | Supriya M. Kumar |
| **Author** | Imhoi Koo |
| **Author** | Gary H. Perdew |
| **Author** | Shanthi Srinivasan |
| **Author** | Andrew D. Patterson |
| **Abstract** | 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), a persistent organic pollutant and a potent aryl hydrocarbon receptor (AHR) ligand, causes delayed intestinal motility and affects the survival of enteric neurons. In this study, we investigated the specific signaling pathways and molecular targets involved in TCDD-induced enteric neurotoxicity. Immortalized fetal enteric neuronal (IM-FEN) cells treated with 10 nM TCDD exhibited cytotoxicity and caspase 3/7 activation, indicating apoptosis. Increased cleaved caspase-3 expression with TCDD treatment, as assessed by immunostaining in enteric neuronal cells isolated from WT mice but not in neural crest cell-specific Ahr deletion mutant mice (Wnt1Cre(+/-)/Ahr(b(fl/fl)())), emphasized the pivotal role of AHR in this process. Importantly, the apoptosis in IM-FEN cells treated with TCDD was mediated through a ceramide-dependent pathway, independent of endoplasmic reticulum stress, as evidenced by increased ceramide synthesis and the reversal of cytotoxic effects with myriocin, a potent inhibitor of ceramide biosynthesis. We identified Sptlc2 and Smpd2 as potential gene targets of AHR in ceramide regulation by a chromatin immunoprecipitation (ChIP) assay in IM-FEN cells. Additionally, TCDD downregulated phosphorylated Akt and phosphorylated Ser9-GSK-3β levels, implicating the PI3 kinase/AKT pathway in TCDD-induced neurotoxicity. Overall, this study provides important insights into the mechanisms underlying TCDD-induced enteric neurotoxicity and identifies potential targets for the development of therapeutic interventions. |
| **Date** | 2024 Aug 6 |
| **Language** | eng |
| **Extra** | Place: Switzerland PMID: 39201268 PMCID: PMC11354200 |
| **Volume** | 25 |
| **Publication** | International journal of molecular sciences |
| **DOI** | [10.3390/ijms25168581](http://doi.org/10.3390/ijms25168581) |
| **Issue** | 16 |
| **Journal Abbr** | Int J Mol Sci |
| **ISSN** | 1422-0067 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Male
  + Animals
  + Mice
  + Cells, Cultured
  + Tissue Culture Techniques
  + Mice, Inbred C57BL
  + Glycogen Synthase Kinase 3 beta/metabolism
  + Proto-Oncogene Proteins c-akt/metabolism
  + Mice, Transgenic
  + \*Apoptosis/drug effects
  + apoptosis
  + ENS
  + \*Ceramides/metabolism
  + \*Endoplasmic Reticulum Stress/drug effects
  + \*Enteric Nervous System/cytology/drug effects
  + \*Neurons/cytology/drug effects/metabolism
  + \*Receptors, Aryl Hydrocarbon/genetics/metabolism
  + AHR
  + ceramides
  + cytotoxicity
  + Polychlorinated Dibenzodioxins/pharmacology
  + Sphingolipids/metabolism
  + TCDD

## Molecular signalling during cross talk between gut brain axis regulation and progression of irritable bowel syndrome: A comprehensive review.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Shiv Vardan Singh |
| **Author** | Risha Ganguly |
| **Author** | Kritika Jaiswal |
| **Author** | Aditya Kumar Yadav |
| **Author** | Ramesh Kumar |
| **Author** | Abhay K. Pandey |
| **Abstract** | Irritable bowel syndrome (IBS) is a chronic functional disorder which alters gastrointestinal (GI) functions, thus leading to compromised health status. Pathophysiology of IBS is not fully understood, whereas abnormal gut brain axis (GBA) has been identified as a major etiological factor. Recent studies are suggestive for visceral hyper-sensitivity, altered gut motility and dysfunctional autonomous nervous system as the main clinical abnormalities in IBS patients. Bidirectional signalling interactions among these abnormalities are derived through various exogenous and endogenous factors, such as microbiota population and diversity, microbial metabolites, dietary uptake, and psychological abnormalities. Strategic efforts focused to study these interactions including probiotics, antibiotics and fecal transplantations in normal and germ-free animals are clearly suggestive for the pivotal role of gut microbiota in IBS etiology. Additionally, neurotransmitters act as communication tools between enteric microbiota and brain functions, where serotonin (5-hydroxytryptamine) plays a key role in pathophysiology of IBS. It regulates GI motility, pain sense and inflammatory responses particular to mucosal and brain activity. In the absence of a better understanding of various interconnected crosstalks in GBA, more scientific efforts are required in the search of novel and targeted therapies for the management of IBS. In this review, we have summarized the gut microbial composition, interconnected signalling pathways and their regulators, available therapeutics, and the gaps needed to fill for a better management of IBS. |
| **Date** | 2023 Jul 6 |
| **Language** | eng |
| **Rights** | ©The Author(s) 2023. Published by Baishideng Publishing Group Inc. All rights reserved. |
| **Extra** | Place: United States PMID: 37469740 PMCID: PMC10353503 |
| **Volume** | 11 |
| **Pages** | 4458-4476 |
| **Publication** | World journal of clinical cases |
| **DOI** | [10.12998/wjcc.v11.i19.4458](http://doi.org/10.12998/wjcc.v11.i19.4458) |
| **Issue** | 19 |
| **Journal Abbr** | World J Clin Cases |
| **ISSN** | 2307-8960 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Serotonin
  + Microbiota
  + Gut brain axis
  + Irritable bowel syndrome
  + Stress

## Network Pharmacology-Based Strategy for Predicting Active Ingredients and Potential Targets of Gegen Qinlian Decoction for Rotavirus Enteritis.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Peicheng Zhong |
| **Author** | Lijun Song |
| **Author** | Mengyue Gao |
| **Author** | Xiaotong Wang |
| **Author** | Wenpan Tan |
| **Author** | Huanqian Lu |
| **Author** | Qian Lan |
| **Author** | Zuyi Zhao |
| **Author** | Wenchang Zhao |
| **Abstract** | MATERIALS AND METHODS: In this study, a network pharmacology-based strategy was used to elucidate the mechanism of GGQLD for the treatment of RVE. Oral bioavailability and drug-likeness were taken as the judgment criteria to search the active ingredients of GGQLD in traditional Chinese medicine systems pharmacology database and analysis platform (TCMSP). The affinity between protein and ingredients was further determined using the similarity ensemble approach to find the corresponding targets. According to the genes related to enteritis in GeneCards database, the key targets were screened by intersections between drug and disease targets. And the therapeutic mechanism was predicted using the protein-protein interactions (PPIs), the Gene Ontology (GO), and the Kyoto Encyclopedia of Genes and Genomes (KEGG) database, which was verified by detecting calcium ion concentration with the fluorescent probe. RESULT: 130 active ingredients were screened from GGQLD, including (R)-canadine, moupinamide, formononetin, and other flavonoids. They act on a total of 366 targets, which is mainly distributed in the biological process of hormone binding or signaling pathways of neuroactive ligand receptor interaction, serotonergic synapse, and calcium signaling pathway. Furthermore, serotonin receptors, adrenergic receptors, cholinergic receptors, and dopamine receptors in the enteric nervous system may be the key targets of RVE treatment by GGQLD. CONCLUSION: This study demonstrated that the potential mechanism that GGQLD can effectively improve the symptoms of RVE may depend on the regulation of calcium ions, serotonin, and gastrointestinal hormone ion that could mutually affect the intestinal nervous system. |
| **Date** | 2020 |
| **Language** | eng |
| **Rights** | Copyright © 2020 Peicheng Zhong et al. |
| **Extra** | Place: United States PMID: 32802121 PMCID: PMC7414372 |
| **Volume** | 2020 |
| **Pages** | 2957567 |
| **Publication** | Evidence-based complementary and alternative medicine : eCAM |
| **DOI** | [10.1155/2020/2957567](http://doi.org/10.1155/2020/2957567) |
| **Journal Abbr** | Evid Based Complement Alternat Med |
| **ISSN** | 1741-427X 1741-4288 |
| **Date Added** | 6/11/2025, 2:32:27 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

## Neuroimmunophysiology of the gut: advances and emerging concepts focusing on the epithelium.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Keith A. Sharkey |
| **Author** | Paul L. Beck |
| **Author** | Derek M. McKay |
| **Abstract** | The epithelial lining of the gastrointestinal tract serves as the interface for digestion and absorption of nutrients and water and as a defensive barrier. The defensive functions of the intestinal epithelium are remarkable considering that the gut lumen is home to trillions of resident bacteria, fungi and protozoa (collectively, the intestinal microbiota) that must be prevented from translocation across the epithelial barrier. Imbalances in the relationship between the intestinal microbiota and the host lead to the manifestation of diseases that range from disorders of motility and sensation (IBS) and intestinal inflammation (IBD) to behavioural and metabolic disorders, including autism and obesity. The latest discoveries shed light on the sophisticated intracellular, intercellular and interkingdom signalling mechanisms of host defence that involve epithelial and enteroendocrine cells, the enteric nervous system and the immune system. Together, they maintain homeostasis by integrating luminal signals, including those derived from the microbiota, to regulate the physiology of the gastrointestinal tract in health and disease. Therapeutic strategies are being developed that target these signalling systems to improve the resilience of the gut and treat the symptoms of gastrointestinal disease. |
| **Date** | 2018 Dec |
| **Language** | eng |
| **Extra** | Place: England PMID: 30069036 |
| **Volume** | 15 |
| **Pages** | 765-784 |
| **Publication** | Nature reviews. Gastroenterology & hepatology |
| **DOI** | [10.1038/s41575-018-0051-4](http://doi.org/10.1038/s41575-018-0051-4) |
| **Issue** | 12 |
| **Journal Abbr** | Nat Rev Gastroenterol Hepatol |
| **ISSN** | 1759-5053 1759-5045 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Animals
  + Gastrointestinal Microbiome/physiology
  + Intestinal Diseases/physiopathology
  + Intestinal Mucosa/cytology/\*physiology/physiopathology
  + Neuroimmunomodulation/\*physiology

## Neuropharmacology of purinergic receptors in human submucous plexus: Involvement of P2X₁, P2X₂, P2X₃ channels, P2Y and A₃ metabotropic receptors in neurotransmission.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | A. Liñán-Rico |
| **Author** | J. E. Wunderlich |
| **Author** | J. T. Enneking |
| **Author** | D. R. Tso |
| **Author** | I. Grants |
| **Author** | K. C. Williams |
| **Author** | A. Otey |
| **Author** | K. Michel |
| **Author** | M. Schemann |
| **Author** | B. Needleman |
| **Author** | A. Harzman |
| **Author** | F. L. Christofi |
| **Abstract** | RATIONALE: The role of purinergic signaling in human ENS is not well understood. We sought to further characterize the neuropharmacology of purinergic receptors in human ENS and test the hypothesis that endogenous purines are critical regulators of neurotransmission. EXPERIMENTAL APPROACH: LSCM-Fluo-4/(Ca(2+))-imaging of postsynaptic Ca(2+) transients (PSCaTs) was used as a reporter of synaptic transmission evoked by fiber tract electrical stimulation in human SMP surgical preparations. Pharmacological analysis of purinergic signaling was done in 1,556 neurons (identified by HuC/D-immunoreactivity) in 235 ganglia from 107 patients; P2XR-immunoreactivity was evaluated in 19 patients. Real-time MSORT (Di-8-ANEPPS) imaging tested effects of adenosine on fast excitatory synaptic potentials (fEPSPs). RESULTS: Synaptic transmission is sensitive to pharmacological manipulations that alter accumulation of extracellular purines: Apyrase blocks PSCaTs in a majority of neurons. An ecto-NTPDase-inhibitor 6-N,N-diethyl-D-β,γ-dibromomethyleneATP or adenosine deaminase augments PSCaTs. Blockade of reuptake/deamination of eADO inhibits PSCaTs. Adenosine inhibits fEPSPs and PSCaTs (IC50 = 25 µM), sensitive to MRS1220-antagonism (A3AR). A P2Y agonist ADPβS inhibits PSCaTs (IC50 = 111 nM) in neurons without stimulatory ADPbS responses (EC50 = 960 nM). ATP or a P2X1,2,2/3 (α,β-MeATP) agonist evokes fast, slow, biphasic Ca(2+) transients or Ca(2+) oscillations (ATP,EC50 = 400 mM). PSCaTs are sensitive to P2X1 antagonist NF279. Low (20 nM) or high (5 µM) concentrations of P2X antagonist TNP-ATP block PSCaTs in different neurons; proportions of neurons with P2XR-immunoreactivity follow the order P2X2 > P2X1 >> P2X3; P2X1 + P2X2 and P2X3 + P2X2 are co-localized. RT-PCR identified mRNA-transcripts for P2X1-7, P2Y1,2,12-14R. CONCLUSIONS: Purines are critical regulators of neurotransmission in human ENS. Purinergic signaling involves P2X1, P2X2, P2X3 channels, P2X1 + P2X2 co-localization and inhibitory P2Y or A3 receptors. These are potential novel therapeutic targets for neurogastroenterology. |
| **Date** | 2015 Aug |
| **Language** | eng |
| **Rights** | Published by Elsevier Ltd. |
| **Extra** | Place: England PMID: 25724083 PMCID: PMC4466061 |
| **Volume** | 95 |
| **Pages** | 83-99 |
| **Publication** | Neuropharmacology |
| **DOI** | [10.1016/j.neuropharm.2015.02.014](http://doi.org/10.1016/j.neuropharm.2015.02.014) |
| **Journal Abbr** | Neuropharmacology |
| **ISSN** | 1873-7064 0028-3908 |
| **Date Added** | 6/11/2025, 2:32:27 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Calcium/metabolism
  + A(3) inhibitory receptors
  + Adenosine Triphosphate/metabolism
  + ATP
  + Colectomy
  + Electric Stimulation
  + Endogenous adenosine
  + Excitatory Postsynaptic Potentials/physiology
  + Human enteric nervous system
  + Immunohistochemistry
  + Inhibitory P2Y receptors
  + Neurons/\*drug effects/\*physiology
  + P2X channels
  + Purinergic Agents/pharmacology
  + Purinergic synaptic transmission
  + Receptors, Purinergic/\*metabolism
  + Submucous plexus
  + Submucous Plexus/\*drug effects/\*physiology
  + Synaptic Transmission/drug effects/physiology
  + Voltage-Sensitive Dye Imaging

## Pediatric Neurogastroenterology and Motility: Moving Rapidly Into the Future.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Atchariya Chanpong |
| **Author** | Nikhil Thapar |
| **Abstract** | The field of pediatric neurogastroenterology and motility encompasses some of the most common and severe gastrointestinal (GI) disorders that affect children. GI motility disorders remain, in general, poorly understood, variably diagnosed, and inadequately treated. Although the field progressed relatively slowly over the last decades, the coming years will, no doubt, see it move into a prolific and dynamic era. With this review, we look forward to this brighter future for the field and highlight emerging areas that show promise and deserve focus in the coming years. This includes the role of early life programming and insult of the enteric neuromusculature as a key determinant of motility diseases and factors that are likely to be relevant in disease etiopathogenesis. We discuss several recent and futuristic developments and advancements in investigative and diagnostic tools as well as novel approaches that have been introduced in the management of GI motility disorders. These include targeted and personalized medicine in both pharmacological and multidisciplinary approaches as well as the emerging therapeutic options such as bioelectrical neuromodulation and regenerative medicine. |
| **Date** | 2023 May 1 |
| **Language** | eng |
| **Rights** | Copyright © 2023 by European Society for European Society for Pediatric Gastroenterology, Hepatology, and Nutrition and North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition. |
| **Extra** | Place: United States PMID: 36705671 |
| **Volume** | 76 |
| **Pages** | 547-552 |
| **Publication** | Journal of pediatric gastroenterology and nutrition |
| **DOI** | [10.1097/MPG.0000000000003721](http://doi.org/10.1097/MPG.0000000000003721) |
| **Issue** | 5 |
| **Journal Abbr** | J Pediatr Gastroenterol Nutr |
| **ISSN** | 1536-4801 0277-2116 |
| **Date Added** | 6/11/2025, 2:32:25 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Precision Medicine
  + Child
  + \*Enteric Nervous System/pathology
  + \*Gastrointestinal Diseases/diagnosis/therapy/pathology
  + Cognition
  + Gastrointestinal Motility

## Recent drug delivery systems targeting the gut-brain-microbiome axis for the management of chronic diseases.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Debjani Ray |
| **Author** | Piyas Bose |
| **Author** | Saptarshi Mukherjee |
| **Author** | Subhadeep Roy |
| **Author** | Santanu Kaity |
| **Abstract** | In recent years, the study of microorganisms and the brain has become increasingly connected. The gut-brain-microbiome axis (GBMA), a bi-directional communication system, is the key part of how the body's bacteria and the brain interact. This system can influence the brain and behaviour. Changes in this relationship have been linked to various mental and physical health conditions. The immune system, tryptophan metabolism, the vagus nerve, and the enteric nervous system all facilitate connections between the gut and brain. Microbes produce Peptidoglycans, branched-chain amino acids, and short-chain fatty acids, which are involved in this communication. Studies suggest the gut microbiome may be involved in conditions like autism, anxiety, obesity, schizophrenia, Parkinson's disease, and Alzheimer's disease. Researchers are exploring the gut-brain connection to cure a variety of disorders, such as neurological disorders, cancers, metabolic problems, and liver diseases. Developing novel drug delivery systems is a key focus in GBMA for therapeutic targeting at various disease pathways. Notable platforms attracting significant interest include silica nanoparticle-based delivery systems for probiotic spores, composite hydrogels formulated from protein isolates and citrus pectin, and biomimetic nanosystems designed for targeted therapeutic delivery. This review summarizes different methods of delivering drugs and using dietary interventions to target the GBMA and treat these conditions in a less invasive way. By understanding how the gut and brain communicate, scientists aim to develop new and more effective therapies for these complex chronic diseases. |
| **Date** | 2025 May 25 |
| **Language** | eng |
| **Rights** | Copyright © 2025 Elsevier B.V. All rights reserved. |
| **Extra** | Place: Netherlands PMID: 40425058 |
| **Volume** | 680 |
| **Pages** | 125776 |
| **Publication** | International journal of pharmaceutics |
| **DOI** | [10.1016/j.ijpharm.2025.125776](http://doi.org/10.1016/j.ijpharm.2025.125776) |
| **Journal Abbr** | Int J Pharm |
| **ISSN** | 1873-3476 0378-5173 |
| **Date Added** | 6/11/2025, 2:32:26 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Drug Delivery Systems
  + Dysbiosis
  + Gut-Brain-Microbiome-Axis
  + Microbiota
  + Signalling

## Secretion of Acid Sphingomyelinase and Ceramide by Endothelial Cells Contributes to Radiation-Induced Intestinal Toxicity.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Daniela Leonetti |
| **Author** | Hala Estéphan |
| **Author** | Natacha Ripoche |
| **Author** | Nolwenn Dubois |
| **Author** | Audrey Aguesse |
| **Author** | Sébastien Gouard |
| **Author** | Lisa Brossard |
| **Author** | Sophie Chiavassa |
| **Author** | Isabelle Corre |
| **Author** | Claire Pecqueur |
| **Author** | Michel Neunlist |
| **Author** | Elie Hadchity |
| **Author** | Marie-Hélène Gaugler |
| **Author** | Maxime M. Mahé |
| **Author** | François Paris |
| **Abstract** | Ceramide-induced endothelial cell apoptosis boosts intestinal stem cell radiosensitivity. However, the molecular connection between these two cellular compartments has not been clearly elucidated. Here we report that ceramide and its related enzyme acid sphingomyelinase (ASM) are secreted by irradiated endothelial cells and act as bystander factors to enhance the radiotoxicity of intestinal epithelium. Ceramide and the two isoforms of ASM were acutely secreted in the blood serum of wild-type mice after 15 Gy radiation dose, inducing a gastrointestinal syndrome. Interestingly, serum ceramide was not enhanced in irradiated ASMKO mice, which are unable to develop intestinal failure injury. Because ASM/ceramide were secreted by primary endothelial cells, their contribution was studied in intestinal epithelium dysfunction using coculture of primary endothelial cells and intestinal T84 cells. Adding exogenous ASM or ceramide enhanced epithelial cell growth arrest and death. Conversely, blocking their secretion by endothelial cells using genetic, pharmacologic, or immunologic approaches abolished intestinal T84 cell radiosensitivity. Use of enteroid models revealed ASM and ceramide-mediated deleterious mode-of-action: when ceramide reduced the number of intestinal crypt-forming enteroids without affecting their structure, ASM induced a significant decrease of enteroid growth without affecting their number. Identification of specific and different roles for ceramide and ASM secreted by irradiated endothelial cells opens new perspectives in the understanding of intestinal epithelial dysfunction after radiation and defines a new class of potential therapeutic radiomitigators. SIGNIFICANCE: This study identifies secreted ASM and ceramide as paracrine factors enhancing intestinal epithelial dysfunction, revealing a previously unknown class of mediators of radiosensitivity. |
| **Date** | 2020 Jun 15 |
| **Language** | eng |
| **Rights** | ©2020 American Association for Cancer Research. |
| **Extra** | Place: United States PMID: 32291318 |
| **Volume** | 80 |
| **Pages** | 2651-2662 |
| **Publication** | Cancer research |
| **DOI** | [10.1158/0008-5472.CAN-19-1527](http://doi.org/10.1158/0008-5472.CAN-19-1527) |
| **Issue** | 12 |
| **Journal Abbr** | Cancer Res |
| **ISSN** | 1538-7445 0008-5472 |
| **Date Added** | 6/11/2025, 2:32:27 PM |
| **Modified** | 6/16/2025, 1:11:48 PM |

### Tags:

* + Humans
  + Male
  + Animals
  + Disease Models, Animal
  + Mice
  + Coculture Techniques
  + Cells, Cultured
  + Mice, Knockout
  + Primary Cell Culture
  + Bystander Effect/radiation effects
  + Ceramides/blood/\*metabolism
  + Desipramine/pharmacology
  + Endothelial Cells/drug effects/\*metabolism/radiation effects
  + Epithelial Cells/drug effects/pathology/radiation effects
  + Intestinal Mucosa/cytology/drug effects/\*pathology/radiation effects
  + Paracrine Communication/genetics/radiation effects
  + Radiation Injuries/blood/etiology/\*pathology/prevention & control
  + Radiation Tolerance/drug effects/genetics
  + RNA, Small Interfering/metabolism
  + Sphingomyelin Phosphodiesterase/antagonists & inhibitors/blood/genetics/\*metabolism

## Study of the roles of caspase-3 and nuclear factor kappa B in myenteric neurons in a P2X7 receptor knockout mouse model of ulcerative colitis.

|  |  |
| --- | --- |
| **Item Type** | Journal Article |
| **Author** | Henrique Inhauser Riceti Magalhães |
| **Author** | Felipe Alexandre Machado |
| **Author** | Roberta Figueiroa Souza |
| **Author** | Marcos Antônio Ferreira Caetano |
| **Author** | Vanessa Ribeiro Figliuolo |
| **Author** | Robson Coutinho-Silva |
| **Author** | Patricia Castelucci |
| **Abstract** | BACKGROUND: The literature indicates that the enteric nervous system is affected in inflammatory bowel diseases (IBDs) and that the P2X7 receptor triggers neuronal death. However, the mechanism by which enteric neurons are lost in IBDs is unknown. AIM: To study the role of the caspase-3 and nuclear factor kappa B (NF-κB) pathways in myenteric neurons in a P2X7 receptor knockout (KO) mouse model of IBDs. METHODS: Forty male wild-type (WT) C57BL/6 and P2X7 receptor KO mice were euthanized 24 h or 4 d after colitis induction by 2,4,6-trinitrobenzene sulfonic acid (colitis group). Mice in the sham groups were injected with vehicle. The mice were divided into eight groups (n = 5): The WT sham 24 h and 4 d groups, the WT colitis 24 h and 4 d groups, the KO sham 24 h and 4 d groups, and the KO colitis 24 h and 4 d groups. The disease activity index (DAI) was analyzed, the distal colon was collected for immunohistochemistry analyses, and immunofluorescence was performed to identify neurons immunoreactive (ir) for calretinin, P2X7 receptor, cleaved caspase-3, total caspase-3, phospho-NF-κB, and total NF-κB. We analyzed the number of calretinin-ir and P2X7 receptor-ir neurons per ganglion, the neuronal profile area (µm²), and corrected total cell fluorescence (CTCF). RESULTS: Cells double labeled for calretinin and P2X7 receptor, cleaved caspase-3, total caspase-3, phospho-NF-κB, or total NF-κB were observed in the WT colitis 24 h and 4 d groups. The number of calretinin-ir neurons per ganglion was decreased in the WT colitis 24 h and 4 d groups compared to the WT sham 24 h and 4 d groups, respectively (2.10 ± 0.13 vs 3.33 ± 0.17, P < 0.001; 2.92 ± 0.12 vs 3.70 ± 0.11, P < 0.05), but was not significantly different between the KO groups. The calretinin-ir neuronal profile area was increased in the WT colitis 24 h group compared to the WT sham 24 h group (312.60 ± 7.85 vs 278.41 ± 6.65, P < 0.05), and the nuclear profile area was decreased in the WT colitis 4 d group compared to the WT sham 4 d group (104.63 ± 2.49 vs 117.41 ± 1.14, P < 0.01). The number of P2X7 receptor-ir neurons per ganglion was decreased in the WT colitis 24 h and 4 d groups compared to the WT sham 24 h and 4 d groups, respectively (19.49 ± 0.35 vs 22.21 ± 0.18, P < 0.001; 20.35 ± 0.14 vs 22.75 ± 0.51, P < 0.001), and no P2X7 receptor-ir neurons were observed in the KO groups. Myenteric neurons showed ultrastructural changes in the WT colitis 24 h and 4 d groups and in the KO colitis 24 h group. The cleaved caspase-3 CTCF was increased in the WT colitis 24 h and 4 d groups compared to the WT sham 24 h and 4 d groups, respectively (485949 ± 14140 vs 371371 ± 16426, P < 0.001; 480381 ± 11336 vs 378365 ± 4053, P < 0.001), but was not significantly different between the KO groups. The total caspase-3 CTCF, phospho-NF-κB CTCF, and total NF-κB CTCF were not significantly different among the groups. The DAI was recovered in the KO groups. Furthermore, we demonstrated that the absence of the P2X7 receptor attenuated inflammatory infiltration, tissue damage, collagen deposition, and the decrease in the number of goblet cells in the distal colon. CONCLUSION: Ulcerative colitis affects myenteric neurons in WT mice but has a weaker effect in P2X7 receptor KO mice, and neuronal death may be associated with P2X7 receptor-mediated caspase-3 activation. The P2X7 receptor can be a therapeutic target for IBDs. |
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## Transplanted ENSCs form functional connections with intestinal smooth muscle and restore colonic motility in nNOS-deficient mice.

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| **Item Type** | Journal Article |
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| **Abstract** | BACKGROUND: Enteric neuropathies, which result from abnormalities of the enteric nervous system, are associated with significant morbidity and high health-care costs, but current treatments are unsatisfactory. Cell-based therapy offers an innovative approach to replace the absent or abnormal enteric neurons and thereby restore gut function. METHODS: Enteric neuronal stem cells (ENSCs) were isolated from the gastrointestinal tract of Wnt1-Cre;R26tdTomato mice and generated neurospheres (NS). NS transplants were performed via injection into the mid-colon mesenchyme of nNOS(-/-) mouse, a model of colonic dysmotility, using either 1 (n = 12) or 3 (n = 12) injections (30 NS per injection) targeted longitudinally 1-2 mm apart. Functional outcomes were assessed up to 6 weeks later using electromyography (EMG), electrical field stimulation (EFS), optogenetics, and by measuring colorectal motility. RESULTS: Transplanted ENSCs formed nitrergic neurons in the nNOS(-/-) recipient colon. Multiple injections of ENSCs resulted in a significantly larger area of coverage compared to single injection alone and were associated with a marked improvement in colonic function, demonstrated by (1) increased colonic muscle activity by EMG recording, (2) faster rectal bead expulsion, and (3) increased fecal pellet output in vivo. Organ bath studies revealed direct neuromuscular communication by optogenetic stimulation of channelrhodopsin-expressing ENSCs and restoration of smooth muscle relaxation in response to EFS. CONCLUSIONS: These results demonstrate that transplanted ENSCs can form effective neuromuscular connections and improve colonic motor function in a model of colonic dysmotility, and additionally reveal that multiple sites of cell delivery led to an improved response, paving the way for optimized clinical trial design. |
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