

## 普拉梭菌与肠道疾病关系的研究进展

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### 背景资料

正常人体胃肠道细菌微生态处于一种平衡状态, 若这种平衡被破坏将会引起许多相关疾病, 目前菌群失调越来越受到人们的重视。普拉梭菌(*Faecalibacterium prausnitzii*, *F. prausnitzii*)是人类肠道共生菌的一个重要组成部分, 对人类的健康发挥着重要的作用。最近研究发现一些肠道疾病肠内*F. prausnitzii*数量的发生了很大的变化。

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### Abstract

Recently, the relationship between intestinal dysbacteriosis and intestinal disease has become a hot research topic. As one of the most abundant symbiotic bacteria in the human gut, *Faecalibacterium prausnitzii* plays an important role in intestinal disease and has received more and more attention. This article reviews the advances in the understanding of the mechanism of action and active ingredients of this bacterium as well as its relationship with intestinal disease.

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Key Words: *Faecalibacterium prausnitzii*; Gut microbial communities; Intestinal disease

### Advances in understanding relationship between *Faecalibacterium prausnitzii* and intestinal disease

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### 摘要

肠道菌群失调与肠道疾病的关系一直是当前研究的热点。普拉梭菌作为人类最丰富的肠道共生菌之一, 其在肠道疾病中所起的作用越来越引起人们的重视。本文就此菌的作用机制、抗炎有效成分以及与肠道疾病的关系的研究进展作一综述。

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关键词: 普拉梭菌; 肠道微生物; 肠道疾病

**核心提要:** 普拉梭菌(*Faecalibacterium prausnitzii*, *F. prausnitzii*)是存在于健康人群肠道中最丰富的肠道微生物之一, 其数量的变化与肠道疾病的发生发展有着重要的联系. 本文综述当前的研究进展, 探讨肠道*F. prausnitzii*数量与肠道疾病发生的关系.

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## 0 引言

普拉梭菌(*Faecalibacterium prausnitzii*, *F. prausnitzii*)是存在于健康人群肠道中最丰富的肠道微生物之一, 约占肠道粪便细菌总数的5%<sup>[1]</sup>. *F. prausnitzii*作为健康人类肠道共生菌的一个重要组成部分对人类的健康发挥着重要的作用, 目前越来越多的研究发现肠内*F. prausnitzii*改变导致的微生态失衡与一些肠道疾病的发病密切相关. 研究认为*F. prausnitzii*和其上清具有抗炎效应, 可明显改善肠道炎症<sup>[2]</sup>. 本文综合最近发表的文献, 对*F. prausnitzii*的特性、作用机制及与肠道疾病的相关性作一综述.

## 1 *F. prausnitzii*的命名来历和生物特性

1922年, Prausnitz从一例患者的胸腔脓肿中分离出来一种棒状杆菌, 最初被归为梭菌*Fusobacterium*属, 直到1996年此菌的不同人类菌株的完整的16s rRNA基因序列被构建后, 才发现他与梭状芽孢杆菌属结构更接近<sup>[3,4]</sup>. 2002年Duncan等<sup>[5]</sup>建议将其归属为一个新的菌种*Faecalibacterium*属, 定义为不产芽孢厌氧菌和不动革兰氏阳性杆菌, 并将此菌更名*Faecalibacterium prausnitzii*, 简称*F. prausnitzii*. *F. prausnitzii*归属于厚壁菌门(*Firmicutes*)柔嫩梭菌属(*Clostridium leptum*), 有多个亚种A2-165、SL3/3、L2/6、M21/2、HTF-F和KLE1255, 其中A2-165是最常见且研究得最多的一种. 现代的种系遗传学分析显示*F. prausnitzii*具有两种不同的种系: I型和II型,

其中II型对区别炎症性肠病(inflammatory bowel disease, IBD)亚型有一定帮助. *F. prausnitzii*是一种厌氧菌, 对氧极度敏感, 即使在厌氧环境下也很难培养, 但在培养基中加上黄素、半胱氨酸或谷胱甘肽可使其在微需氧环境下生长. *F. prausnitzii*酵解葡萄糖后能够产生大量的丁酸盐、甲酸盐和少量D-乳酸盐.

## 2 肠内*F. prausnitzii*的影响因素

*F. prausnitzii*在健康人类肠道含量丰富, 在粪便中微生物的5%, 甚至在有些人群中可高达15%<sup>[6]</sup>. 此菌也广泛分布在一些动物胃肠道, 如哺乳动物猪、牛、小鼠和家禽类鸡<sup>[7,8]</sup>. *F. prausnitzii*在肠道菌群中的比例受到结肠环境的影响, 肠道中pH值、胆酸盐和氧含量均可影响*F. prausnitzii*的生长<sup>[5,9]</sup>. 吸烟和要素饮食可降低其在肠道中的含量<sup>[10]</sup>, 肠镜检查前服用聚乙二醇400清肠后肠黏膜相关*F. prausnitzii*也会降低. 一些药物的使用也会影响*F. prausnitzii*在肠道中的含量, 利福昔明可以提高肠道*F. prausnitzii*含量<sup>[11]</sup>, 英夫利昔和大剂量的皮质醇激素也可逆转活动性克罗恩病(Crohn's disease, CD)患者粪便中降低的*F. prausnitzii*<sup>[12]</sup>. 某些基因的缺失也可影响肠道菌群的变化, 动物实验显示NOD<sub>2</sub>基因敲除小鼠的回肠和盲肠中黏膜相关*F. prausnitzii*的数量明显减少<sup>[13]</sup>.

## 3 *F. prausnitzii*的抗炎机制

*F. prausnitzii*及其培养上清能够减轻三硝基苯磺酸(trinitro-benzene-sulfonic acid, TNBS)诱导的肠道炎症<sup>[1]</sup>, 具有明确的抗炎效应, 其抗炎效应与调节机体免疫有关. 一个可能的机制是抑制机体核因子- $\kappa$ B(nuclear factor- $\kappa$ B, NF- $\kappa$ B)的活性, NF- $\kappa$ B是参与免疫和炎症的重要转录因子, 其激活后可促进促炎介质的表达. Sokol等<sup>[2]</sup>发现*F. prausnitzii*培养上清可抑制Caco-2细胞白介素(interleukin, IL)-1 $\beta$ 诱导的NF- $\kappa$ B的活性和IL-8的分泌; 另一个免疫因素是*F. prausnitzii*能够诱导外周血单个核细胞生成大量抗炎因子IL-10, 维持肠道的生态稳定, IL-10可抑制干扰素- $\gamma$ (interferon- $\gamma$ , IFN- $\gamma$ )、肿瘤坏死因子- $\alpha$ (tumour necrosis factor- $\alpha$ , TNF- $\alpha$ )、IL-6、IL-12炎症因子的产生, 诱导肠黏膜Treg细胞的生成和抑制炎症的作用. Rossi等<sup>[14]</sup>也通过体内外研究证实*F. prausnitzii* A2-165能促进

## ■ 研发前沿

*F. prausnitzii*是新近发现的一种肠道益生菌, 与肠道疾病, 尤其是炎症性肠病的发病密切相关, 但是其作用的有效成分和其作用的机制目前还未完全阐明, 是目前研究的热点.

## ■ 相关报道

Sokol等认为*F. prausnitzii*培养上清可抑制白介素(interleukin, IL)-1 $\beta$ 诱导的NF- $\kappa$ B的活性和促炎因子IL-8的分泌, 且能够诱导外周血单个核细胞生成大量抗炎因子IL-10, 诱导肠黏膜Treg细胞的生成和抑制炎症的作用, 维持肠道的生态稳定.

## ■ 创新盘点

以前有关此类文章多是研究类的文献, 本文将目前的最新研究成果进行了分析总结, 综述了*F. prausnitzii*的抗炎有效成分及发病机制, 及其在几种肠道疾病的作用机制。

T细胞的增殖和IL-10的分泌, 抑制IFN- $\gamma$ <sup>+</sup> T细胞的分化。近来研究表明*F. prausnitzii*还可以通过临床研究发现人类肠道中树突状细胞(dendritic cell, DC)细胞表达Toll样受体4(Toll-like receptor 4, TLR4)的数量与水平呈负相关, 提示肠道DC的功能可能受此菌的影响<sup>[15]</sup>。

*F. prausnitzii*还可以提高肠黏膜屏障功能。Carlsson等<sup>[16]</sup>研究认为*F. prausnitzii*上清还可以通过影响肠上皮细胞通透性来增强肠道黏膜屏障功能, 减轻DSS诱导的小鼠结肠和回肠的炎症。Laval等<sup>[17]</sup>体内外研究也发现*F. prausnitzii*能够提高紧密连接蛋白闭合蛋白和E-钙黏蛋白来减轻TNF- $\alpha$ 诱导的肠黏膜高渗状态。

## 4 *F. prausnitzii*抗炎有效成分

*F. prausnitzii*与其培养上清具有抗炎效应虽然已得到公认, 但是何种物质直接影响机体免疫以及确切的作用机制目前还未阐明。很多研究认为*F. prausnitzii*是通过其主要分解产物-丁酸盐起作用的, *F. prausnitzii*能够通过发酵葡萄糖产生大量的丁酸盐, *F. prausnitzii*培养上清中含有大量的丁酸盐<sup>[18]</sup>。丁酸盐可为肠上皮细胞提供能量, 通过增加紧密蛋白的合成增强肠道黏膜屏障功能, 对保持肠道健康起着重要作用<sup>[1]</sup>。丁酸盐还可通过抑制乙酰化酶的活性, 使组蛋白高乙酰化, 从而抑制NF- $\kappa$ B的活性, 减少IL-8的生成, 调节机体免疫; 可通过促进组蛋白乙酰化影响基因表达, 诱导肿瘤细胞大量凋亡, 可以抑制亚硝酸铵和过氧化氢对机体的毒性作用, 具有抗肿瘤作用。但有研究显示与*F. prausnitzii*上清中含量相当的丁酸盐并不能完全替代*F. prausnitzii*上清发挥其抗炎作用<sup>[1]</sup>, 提示*F. prausnitzii*上清中可能存在其他代谢产物发挥着重要的作用。Rossi等<sup>[19]</sup>从HTF-F菌株提取的胞外聚合物基体(extracellular polymeric matrix, EPM)具有抗炎效应, 能够通过调节TLR<sub>2</sub>依赖的调节抗原递呈细胞IL-12和IL-10细胞因子的释放, 来达到抗炎作用。Miquel等<sup>[20]</sup>研究认为水杨酸作为*F. prausnitzii*代谢产物之一能够抑制IL-8细胞因子的释放, 发挥与*F. prausnitzii*上清和丁酸盐相似的抗炎作用, 而*F. prausnitzii*的其他代谢产物莽草酸、棉子糖和 $\alpha$ -酮戊二酸均无明显抗炎作用。Quévrain<sup>[21]</sup>最近成功从*F. prausnitzii*上清中分离出一种15 kDa的蛋白, 将其命名为微生物抗炎分子(microbial anti-

inflammatory molecule, MAM), 能够抑制肠上皮细胞中NF- $\kappa$ B通路, DNBS诱导的小鼠肠道炎症。

## 5 *F. prausnitzii*与肠道疾病的关系

5.1 炎症性肠病 *F. prausnitzii*的数量在IBD患者肠道中数量较健康人群明显降低, 且与疾病的活动性有关。成人克罗恩病(Crohn's disease, CD)的粪便和回肠黏膜中*F. prausnitzii*的数量较健康人群明显减少, 活动期CD患者*F. prausnitzii*数量较缓解期明显降低<sup>[22]</sup>。同样, Machiels等<sup>[23]</sup>分析了127例溃疡性结肠炎(ulcerative colitis, UC)患者和87例对照组人群, 发现活动性UC患者肠道中*F. prausnitzii*菌数量明显低于正常对照人群, 且疾病的活动性与*F. prausnitzii*数量呈负相关。也有研究发现UC患者及其一级亲戚的粪便中*F. prausnitzii*数量较对照人群明显降低<sup>[24]</sup>。最近一项关于*F. prausnitzii*和IBD的Meta分析也显示IBD患者粪便和肠道中*F. prausnitzii*均降低, 特别是回肠病变的CD患者最为明显<sup>[25]</sup>。有研究认为儿童CD患者粪便中*F. prausnitzii*是升高而不是降低的, 很可能与儿童的肠道微生态与成人不同有关<sup>[26]</sup>。也提示炎症性肠病是一种多因素病变, 不同的病变部位、不同发病年龄和严重程度的不同, 其发病原因均不尽相同。

*F. prausnitzii*在IBD患者肠道中数量与病变严重程度、治疗和预后也有明显的相关性。Sokol等<sup>[2]</sup>研究发现CD经手术治疗患者中, 术后6 mo内复发者术前和术后6 mo肠道黏膜相关*F. prausnitzii*数量均较术后6 mo内未复发的患者明显降低。Varela等<sup>[24]</sup>的一项横断面研究发现UC患者给5-ASA治疗后病情得到稳定缓解的患者肠道中*F. prausnitzii*数量逐渐增加, 那些肠道中*F. prausnitzii*数量不能增高的患者存在着较高疾病复发风险, 多见于病情严重的、病变范围广泛、缓解期短暂、有频繁复发史者。*F. prausnitzii*在肠道的高定植可阻止疾病的复发, 改善疾病的预后。

5.2 肠易激综合征 肠易激综合征(irritable bowel syndrome, IBS)是以慢性复发性腹痛、腹泻、排便习惯和大便性状异常为主要临床表现的功能性肠道疾病。目前有研究认为肠道菌群失调与IBS的发生及临床症状密切相关<sup>[27]</sup>。IBS患者肠道中厚壁菌门和拟杆菌比例较健康人群



升高了2倍<sup>[28]</sup>。有研究认为IBD的不同类型也与*F. prausnitzii*相关, 腹泻便秘相交替的IBS中*F. prausnitzii*的数量明显下降, 而腹泻型和便秘型IBS未见减少<sup>[29]</sup>。Lopez-Siles等<sup>[30]</sup>用qPCR方法检测了45例CD患者、28例UC、10例IBS及28例对照组人群黏膜相关*F. prausnitzii*和大肠杆菌, 发现IBD患者*F. prausnitzii*明显低于IBS, 而大肠杆菌高于IBS。Soldi等<sup>[31]</sup>用RT-PCR、变性梯度凝胶电泳技术和新一代测序技术检测了15例非便秘型IBS和健康人群患者粪便中微生物群的组成和差异, 发现IBS患者粪便中*Faecalibacterium*菌属的比例高于健康人群(4.42% vs 5.66%), 使用利福昔明治疗14 d后, 腹泻症状缓解, *Faecalibacterium*比例明显升高( $T_{14}$ : 8.50% vs  $T_0$ : 5.58%)。 *F. prausnitzii*还可通过增强肠道上皮屏障功能, 降低由于压力所致的IBS肠道高敏性, 从而缓解IBS小鼠内脏疼痛, 但上清无镇痛作用<sup>[32]</sup>。

**5.3 结直肠癌** *F. prausnitzii*在肠癌患者的肠道分布较健康人群存在差异。Lopez-Siles等<sup>[33]</sup>用qPCR方法检测了20例结直肠癌患者肠黏膜相关*F. prausnitzii*含量, 发现肠癌的肠道黏膜组织*F. prausnitzii*的含量较健康对照组明显降低。Balamurugan等<sup>[34]</sup>用16SrRNA测序技术检测了20例结直肠癌、9例上消化道肿瘤和17例健康自愿者粪便中细菌的种类, 结果发现结直肠癌患者粪便中产丁酸盐的直肠真杆菌(*Eubacterium rectale*)和*F. prausnitzii*的含量较健康自愿者明显减少。*F. prausnitzii*的重要产物之一丁酸盐除了抗炎作用外, 还可通过促进组蛋白乙酰化影响基因表达, 诱导肿瘤细胞大量凋亡, 并抑制亚硝酸铵和过氧化氢对结肠细胞的毒性作用, 具有抗肿瘤作用, 故肠道*F. prausnitzii*的减少与结直肠癌的发病存在一定的相关性。但也有研究发现结直肠癌及腺瘤性息肉病患者肠道柔嫩梭菌和球形梭菌明显增加<sup>[35]</sup>。Sobhani等<sup>[36]</sup>检测了60例肠癌患者和119例正常人群的粪便微生物DNA, 认为肠癌患者中*F. prausnitzii*属与正常患者之间无明显统计学差异, 而拟杆菌和普氏杆菌在肠癌人群中明显升高。*F. prausnitzii*在肠癌患者肠道中的分布还有一定的争议, 造成各研究结果差异的原因不明, 临床均为小样本研究, 有待大样本研究进一步明确。

**5.4 *F. prausnitzii*与其他肠道疾病的关系** *F. prausnitzii*在其他肠道疾病中也有改变, 乳糜

泄<sup>[37]</sup>、慢性自发性腹泻<sup>[38]</sup>、急性阑尾炎<sup>[39]</sup>、肠道神经内分泌肿瘤<sup>[41]</sup>的患者肠道或粪便中*F. prausnitzii*含量较健康人群均有明显下降。

## 6 讨论

*F. prausnitzii*是肠道中不可缺少的一种潜在益生菌, 其细菌本身和培养上清均具有抗炎作用。随着对其研究的深入, 抗炎有效成分的不断发现, 相信不久的将来补充*F. prausnitzii*的某种有效代谢产物将会成为治疗肠道病变, 尤其是炎症性肠病的重要手段。

## 7 参考文献

- Arumugam M, Raes J, Pelletier E, Le Paslier D, Yamada T, Mende DR, Fernandes GR, Tap J, Bruls T, Batto JM, Bertalan M, Borruel N, Casellas F, Fernandez L, Gautier L, Hansen T, Hattori M, Hayashi T, Kleerebezem M, Kurokawa K, Leclerc M, Levenez F, Manichanh C, Nielsen HB, Nielsen T, Pons N, Poulain J, Qin J, Sicheritz-Ponten T, Tims S, Torrents D, Ugarte E, Zoetendal EG, Wang J, Guarner F, Pedersen O, de Vos WM, Brunak S, Doré J, Antolín M, Artiguenave F, Blottiere HM, Almeida M, Brechot C, Cara C, Chervaux C, Cultrone A, Delorme C, Denariáz G, Dervyn R, Foerstner KU, Friss C, van de Guchte M, Guedon E, Haimet F, Huber W, van Hylckama-Vlieg J, Jamet A, Juste C, Kaci G, Knol J, Lakhdari O, Layec S, Le Roux K, Maguin E, Mérieux A, Melo Minardi R, M'rimini C, Muller J, Oozeer R, Parkhill J, Renault P, Rescigno M, Sanchez N, Sunagawa S, Torrejon A, Turner K, Vandemeulebrouck G, Varela E, Winogradsky Y, Zeller G, Weissenbach J, Ehrlich SD, Bork P. Enterotypes of the human gut microbiome. *Nature* 2011; 473: 174-180 [PMID: 21508958 DOI: 10.1038/nature09944]
- Sokol H, Pigneur B, Watterlot L, Lakhdari O, Bermúdez-Humarán LG, Gratadoux JJ, Blugeon S, Bridonneau C, Furet JP, Corthier G, Grangette C, Vasquez N, Pochart P, Trugnan G, Thomas G, Blottière HM, Doré J, Marteau P, Seksik P, Langella P. *Faecalibacterium prausnitzii* is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. *Proc Natl Acad Sci USA* 2008; 105: 16731-16736 [PMID: 18936492 DOI: 10.1073/pnas.0804812105]
- Wang RF, Cao WW, Cerniglia CE. Phylogenetic analysis of *Fusobacterium prausnitzii* based upon the 16S rRNA gene sequence and PCR confirmation. *Int J Syst Bacteriol* 1996; 46: 341-343 [PMID: 8573517 DOI: 10.1099/00207713-46-1-341]
- Suau A, Bonnet R, Sutren M, Godon JJ, Gibson GR, Collins MD, Doré J. Direct analysis of genes encoding 16S rRNA from complex communities reveals many novel molecular species within the human gut. *Appl Environ Microbiol* 1999; 65: 4799-4807 [PMID: 10543789]
- Duncan SH, Hold GL, Harmsen HJ, Stewart CS, Flint HJ. Growth requirements and fermentation

## 应用要点

本文总结了近几年*F. prausnitzii*与肠道疾病发生的相关性, 分析了其抗炎机制、作用有效成分。相信不久的将来,*F. prausnitzii*或将成为治疗肠道病变, 尤其是炎症性疾病的重要手段。

## ■ 名词解释

微生态失衡: 肠道菌群紊乱, 指人体肠道内致病菌和益生菌的比例失调, 致病菌、条件致病菌的数量增多, 而益生菌数量减少;  
肠黏膜屏障: 指肠道能够防止肠内的有害物质如细菌和毒素穿过肠黏膜进入人体内其他组织、器官和血液循环的结构和功能的总和。

- products of *Fusobacterium prausnitzii*, and a proposal to reclassify it as *Faecalibacterium prausnitzii* gen. nov., comb. nov. *Int J Syst Evol Microbiol* 2002; 52: 2141-2146 [PMID: 12508881 DOI: 10.1099/00207713-52-6-2141]
- 6 Hold GL, Schwiertz A, Aminov RI, Blaut M, Flint HJ. Oligonucleotide probes that detect quantitatively significant groups of butyrate-producing bacteria in human feces. *Appl Environ Microbiol* 2003; 69: 4320-4324 [PMID: 12839823]
- 7 Nava GM, Stappenbeck TS. Diversity of the autochthonous colonic microbiota. *Gut Microbes* 2011; 2: [PMID: 21637026]
- 8 Oikonomou G, Teixeira AG, Foditsch C, Bicalho ML, Machado VS, Bicalho RC. Fecal microbial diversity in pre-weaned dairy calves as described by pyrosequencing of metagenomic 16S rDNA. Associations of *Faecalibacterium* species with health and growth. *PLoS One* 2013; 8: e63157 [PMID: 23646192 DOI: 10.1371/journal.pone.0063157]
- 9 Lopez-Siles M, Khan TM, Duncan SH, Harmsen HJ, Garcia-Gil LJ, Flint HJ. Cultured representatives of two major phylogroups of human colonic *Faecalibacterium prausnitzii* can utilize pectin, uronic acids, and host-derived substrates for growth. *Appl Environ Microbiol* 2012; 78: 420-428 [PMID: 22101049 DOI: 10.1128/AEM.06858-11]
- 10 Benus RF, van der Werf TS, Welling GW, Judd PA, Taylor MA, Harmsen HJ, Whelan K. Association between *Faecalibacterium prausnitzii* and dietary fibre in colonic fermentation in healthy human subjects. *Br J Nutr* 2010; 104: 693-700 [PMID: 20346190 DOI: 10.1017/S0007114510001030]
- 11 Dörffel Y, Swidsinski A, Loening-Baucke V, Wiedenmann B, Pavel M. Common biostructure of the colonic microbiota in neuroendocrine tumors and Crohn's disease and the effect of therapy. *Inflamm Bowel Dis* 2012; 18: 1663-1671 [PMID: 22113988 DOI: 10.1002/ibd.21923]
- 12 Swidsinski A, Loening-Baucke V, Vaneechoutte M, Doerffel Y. Active Crohn's disease and ulcerative colitis can be specifically diagnosed and monitored based on the biostructure of the fecal flora. *Inflamm Bowel Dis* 2008; 14: 147-161 [PMID: 18050295 DOI: 10.1002/ibd.20330]
- 13 Li E, Hamm CM, Gulati AS, Sartor RB, Chen H, Wu X, Zhang T, Rohlf FJ, Zhu W, Gu C, Robertson CE, Pace NR, Boedeker EC, Harpaz N, Yuan J, Weinstock GM, Sodergren E, Frank DN. Inflammatory bowel diseases phenotype, *C. difficile* and NOD2 genotype are associated with shifts in human ileum associated microbial composition. *PLoS One* 2012; 7: e26284 [PMID: 22719818 DOI: 10.1371/journal.pone.0026284]
- 14 Rossi O, van Berkel LA, Chain F, Tanweer Khan M, Taverne N, Sokol H, Duncan SH, Flint HJ, Harmsen HJ, Langella P, Samsom JN, Wells JM. *Faecalibacterium prausnitzii* A2-165 has a high capacity to induce IL-10 in human and murine dendritic cells and modulates T cell responses. *Sci Rep* 2016; 6: 18507 [PMID: 26725514 DOI: 10.1038/srep18507]
- 15 Ramirez-Farias C, Slezak K, Fuller Z, Duncan A, Holtrop G, Louis P. Effect of inulin on the human gut microbiota: stimulation of *Bifidobacterium adolescentis* and *Faecalibacterium prausnitzii*. *Br J Nutr* 2009; 101: 541-550 [PMID: 18590586 DOI: 10.1017/S0007114508019880]
- 16 Carlsson AH, Yakymenko O, Olivier I, Håkansson F, Postma E, Keita AV, Söderholm JD. *Faecalibacterium prausnitzii* supernatant improves intestinal barrier function in mice DSS colitis. *Scand J Gastroenterol* 2013; 48: 1136-1144 [PMID: 23971882 DOI: 10.3109/00365521.2013.828773]
- 17 Laval L, Martin R, Natividad JN, Chain F, Miquel S, Desclée de Maredsous C, Capronnier S, Sokol H, Verdu EF, van Hylckama Vlieg JE, Bermúdez-Humarán LG, Smokvina T, Langella P. *Lactobacillus rhamnosus* CNCM I-3690 and the commensal bacterium *Faecalibacterium prausnitzii* A2-165 exhibit similar protective effects to induced barrier hyper-permeability in mice. *Gut Microbes* 2015; 6: 1-9 [PMID: 25517879 DOI: 10.4161/19490976.2014.990784]
- 18 Louis P, Flint HJ. Diversity, metabolism and microbial ecology of butyrate-producing bacteria from the human large intestine. *FEMS Microbiol Lett* 2009; 294: 1-8 [PMID: 19222573 DOI: 10.1111/j.1574-6968.2009.01514.x]
- 19 Rossi O, Khan MT, Schwarzer M, Hudcovic T, Srutkova D, Duncan SH, Stolte EH, Kozakova H, Flint HJ, Samsom JN, Harmsen HJ, Wells JM. *Faecalibacterium prausnitzii* Strain HTF-F and Its Extracellular Polymeric Matrix Attenuate Clinical Parameters in DSS-Induced Colitis. *PLoS One* 2015; 10: e0123013 [PMID: 25910186 DOI: 10.1371/journal.pone.0123013]
- 20 Miquel S, Leclerc M, Martin R, Chain F, Lenoir M, Raguideau S, Hudault S, Bridonneau C, Northen T, Bowen B, Bermúdez-Humarán LG, Sokol H, Thomas M, Langella P. Identification of metabolic signatures linked to anti-inflammatory effects of *Faecalibacterium prausnitzii*. *MBio* 2015; 6: pii e00300-15 [PMID: 25900655 DOI: 10.1128/mBio.00300-15]
- 21 Quévrain E, Maubert MA, Michon C, Chain F, Marquant R, Tailhades J, Miquel S, Carlier L, Bermúdez-Humarán LG, Pigneur B, Lequin O, Kharrat P, Thomas G, Rainteau D, Aubry C, Breyner N, Afonso C, Lavielle S, Grill JP, Chassaing G, Chatel JM, Trugnan G, Xavier R, Langella P, Sokol H, Seksik P. Identification of an anti-inflammatory protein from *Faecalibacterium prausnitzii*, a commensal bacterium deficient in Crohn's disease. *Gut* 2016; 65: 415-425 [PMID: 26045134 DOI: 10.1136/gutjnl-2014-307649]
- 22 Martinez-Medina M, Aldeguez X, Gonzalez-Huix F, Acero D, Garcia-Gil LJ. Abnormal microbiota composition in the ileocolonic mucosa of Crohn's disease patients as revealed by polymerase chain reaction-denaturing gradient gel electrophoresis. *Inflamm Bowel Dis* 2006; 12: 1136-1145 [PMID: 17119388 DOI: 10.1097/01.mib.0000235828.09305.0c]
- 23 Machiels K, Joossens M, Sabino J, De Preter V, Arijis I, Eeckhaut V, Ballet V, Claes K, Van Immerseel F, Verbeke K, Ferrante M, Verhaegen J, Rutgeerts P, Vermeire S. A decrease of the butyrate-producing species *Roseburia hominis* and *Faecalibacterium prausnitzii* defines

- dysbiosis in patients with ulcerative colitis. *Gut* 2014; 63: 1275-1283 [PMID: 24021287 DOI: 10.1136/gutjnl-2013-304833]
- 24 Varela E, Manichanh C, Gallart M, Torrejón A, Borrueal N, Casellas F, Guarner F, Antolin M. Colonisation by *Faecalibacterium prausnitzii* and maintenance of clinical remission in patients with ulcerative colitis. *Aliment Pharmacol Ther* 2013; 38: 151-161 [PMID: 23725320 DOI: 10.1111/apt.12365]
  - 25 Cao Y, Shen J, Ran ZH. Association between *Faecalibacterium prausnitzii* Reduction and Inflammatory Bowel Disease: A Meta-Analysis and Systematic Review of the Literature. *Gastroenterol Res Pract* 2014; 2014: 872725 [PMID: 24799893 DOI: 10.1155/2014/872725]
  - 26 Hansen R, Russell RK, Reiff C, Louis P, McIntosh F, Berry SH, Mukhopadhyay I, Bisset WM, Barclay AR, Bishop J, Flynn DM, McGrogan P, Loganathan S, Mahdi G, Flint HJ, El-Omar EM, Hold GL. Microbiota of de-novo pediatric IBD: increased *Faecalibacterium prausnitzii* and reduced bacterial diversity in Crohn's but not in ulcerative colitis. *Am J Gastroenterol* 2012; 107: 1913-1922 [PMID: 23044767 DOI: 10.1038/ajg.2012.335]
  - 27 Yang J, Lee HR, Low K, Chatterjee S, Pimentel M. Rifaximin versus other antibiotics in the primary treatment and retreatment of bacterial overgrowth in IBS. *Dig Dis Sci* 2008; 53: 169-174 [PMID: 17520365 DOI: 10.1007/s10620-007-9839-8]
  - 28 Rajilić-Stojanović M, Biagi E, Heilig HG, Kajander K, Kekkonen RA, Tims S, de Vos WM. Global and deep molecular analysis of microbiota signatures in fecal samples from patients with irritable bowel syndrome. *Gastroenterology* 2011; 141: 1792-1801 [PMID: 21820992 DOI: 10.1053/j.gastro.2011.07.043]
  - 29 Duboc H, Rainteau D, Rajca S, Humbert L, Farabos D, Maubert M, Grondin V, Jouet P, Bouhassira D, Seksik P, Sokol H, Coffin B, Sabaté JM. Increase in fecal primary bile acids and dysbiosis in patients with diarrhea-predominant irritable bowel syndrome. *Neurogastroenterol Motil* 2012; 24: 513-520, e246-e247 [PMID: 22356587 DOI: 10.1111/j.1365-2982.2012.01893.x]
  - 30 Lopez-Siles M, Martinez-Medina M, Busquets D, Sabat-Mir M, Duncan SH, Flint HJ, Aldeguer X, Garcia-Gil LJ. Mucosa-associated *Faecalibacterium prausnitzii* and *Escherichia coli* co-abundance can distinguish Irritable Bowel Syndrome and Inflammatory Bowel Disease phenotypes. *Int J Med Microbiol* 2014; 304: 464-475 [PMID: 24713205 DOI: 10.1016/j.ijmm.2014.02.009]
  - 31 Soldi S, Vasileiadis S, Uggeri F, Campanale M, Morelli L, Fogli MV, Calanni F, Grimaldi M, Gasbarrini A. Modulation of the gut microbiota composition by rifaximin in non-constipated irritable bowel syndrome patients: a molecular approach. *Clin Exp Gastroenterol* 2015; 8: 309-325 [PMID: 26673000 DOI: 10.2147/CEG.S89999]
  - 32 Miquel S, Martín R, Lashermes A, Gillet M, Meleine M, Gelot A, Eschalier A, Ardid D, Bermúdez-Humarán LG, Sokol H, Thomas M, Theodorou V, Langella P, Carvalho FA. Antinociceptive effect of *Faecalibacterium prausnitzii* in non-inflammatory IBS-like models. *Sci Rep* 2016; 6: 19399 [PMID: 26775847 DOI: 10.1038/srep19399]
  - 33 Lopez-Siles M, Martinez-Medina M, Surís-Valls R, Aldeguer X, Sabat-Mir M, Duncan SH, Flint HJ, Garcia-Gil LJ. Changes in the Abundance of *Faecalibacterium prausnitzii* Phylogroups I and II in the Intestinal Mucosa of Inflammatory Bowel Disease and Patients with Colorectal Cancer. *Inflamm Bowel Dis* 2016; 22: 28-41 [PMID: 26595550 DOI: 10.1097/MIB.0000000000000590]
  - 34 Balamurugan R, Rajendiran E, George S, Samuel GV, Ramakrishna BS. Real-time polymerase chain reaction quantification of specific butyrate-producing bacteria, *Desulfovibrio* and *Enterococcus faecalis* in the feces of patients with colorectal cancer. *J Gastroenterol Hepatol* 2008; 23: 1298-1303 [PMID: 18624900 DOI: 10.1111/j.1440-1746.2008.05490.x]
  - 35 Scanlan PD, Shanahan F, Clune Y, Collins JK, O'Sullivan GC, O'Riordan M, Holmes E, Wang Y, Marchesi JR. Culture-independent analysis of the gut microbiota in colorectal cancer and polyposis. *Environ Microbiol* 2008; 10: 789-798 [PMID: 18237311 DOI: 10.1111/j.1462-2920.2007.01503.x]
  - 36 Sobhani I, Tap J, Roudot-Thoraval F, Roperch JP, Letulle S, Langella P, Corthier G, Tran Van Nhieu J, Furet JP. Microbial dysbiosis in colorectal cancer (CRC) patients. *PLoS One* 2011; 6: e16393 [PMID: 21297998 DOI: 10.1371/journal.pone.0016393]
  - 37 De Palma G, Nadal I, Medina M, Donat E, Ribes-Koninckx C, Calabuig M, Sanz Y. Intestinal dysbiosis and reduced immunoglobulin-coated bacteria associated with coeliac disease in children. *BMC Microbiol* 2010; 10: 63 [PMID: 20181275 DOI: 10.1186/1471-2180-10-63]
  - 38 Swidsinski A, Loening-Baucke V, Verstraelen H, Osowska S, Doerffel Y. Biostructure of fecal microbiota in healthy subjects and patients with chronic idiopathic diarrhea. *Gastroenterology* 2008; 135: 568-579 [PMID: 18570896 DOI: 10.1053/j.gastro.2008.04.017]
  - 39 Swidsinski A, Dörffel Y, Loening-Baucke V, Theissig F, Rückert JC, Ismail M, Rau WA, Gaschler D, Weizenegger M, Kühn S, Schilling J, Dörffel WV. Acute appendicitis is characterised by local invasion with *Fusobacterium nucleatum*/necrophorum. *Gut* 2011; 60: 34-40 [PMID: 19926616 DOI: 10.1136/gut.2009.191320]

## 同符评价

*F. prausnitzii* 作为人类最丰富的肠道共生菌之一, 其在肠道疾病中所起的作用越来越引起人们的重视。本文对 *F. prausnitzii* 的作用机制、抗炎有效成分以及与肠道疾病的关系的研究进展做了较为系统的综述, 有理论和实用价值。

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