

World Journal of *Gastroenterology*

Weekly Volume 32 Number 6 February 14, 2026



World Journal of *Gastroenterology*

Editorial Board

2026-2029

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
<https://www.wjgnet.com>

The *World Journal of Gastroenterology* Editorial Board Members are composed of 352 distinguished experts active in the relevant field, distributed in 46 countries/regions, including Italy (66), Japan (53), China (29), United States (29), South Korea (16), Spain (15), Australia (13), Greece (12), Brazil (11), Germany (7), India (7), Romania (7), Taiwan (7), Türkiye (7), United Kingdom (7), Russia (5), Hungary (5), Mexico (4), New Zealand (3), Poland (3), France (3), Canada (3), Austria (3), Belgium (3), Croatia (3), Egypt (3), Thailand (3), Sweden (3), Pakistan (2), Argentina (2), Israel (2), Netherlands (2), Moldova (1), Morocco (1), Jordan (1), Kazakhstan (1), Lebanon (1), Portugal (1), Norway (1), Singapore (1), Slovenia (1), Albania (1), Estonia (1), Ireland (1), United Arab Emirates (1), and Trinidad and Tobago (1).

Editor-in-Chief

Andrzej S Tarnawski, MD, PhD, Professor, (Email: atarnawski@yahoo.com) Department of Gastroenterology Research, University of California Irvine and The Veterans Administration Long Beach Healthcare System, Long Beach, CA 90822, United States

Executive Associate Editor-in-Chief

Jian-Gao Fan, MD, PhD, Professor, Department of Gastroenterology, Shanghai Key Laboratory of Children's Digestion and Nutrition, Xinhua Hospital, Shanghai Jiaotong University School of Medicine, Shanghai 200092, China

Hou-Bao Liu, PhD, Chief Physician, Professor, Department of General Surgery, Biliary Tract Disease Center of Zhongshan Hospital Zhongshan Hospital, Fudan University, Shanghai 200032, China

Naohisa Yoshida, MD, PhD, Assistant Professor, Department of Molecular Gastroenterology and Hepatology, Kyoto Prefectural University of Medicine, Kyoto 602-8566, Japan

Xian-Jun Yu, MD, PhD, Professor, Department of Oncology, Shanghai Medical College, Fudan University, Shanghai 200032, China

Associate Editor

Antonio Facciorusso, MD, PhD, Full Professor, Director, Gastroenterology Unit, Department of Experimental Medicine, Università del Salento, Lecce 73100, Italy

Maria Gazouli, PhD, Professor, Basic Medical Sciences, Athens Medical School, Athens 11527, Greece

Zhen-Dong Jin, MD, PhD, Director, Professor, Department of Gastroenterology, Changhai Hospital, Second Military Medical University, Shanghai 200433, China

Tatsuo Kanda, MD, PhD, Professor, Division of Gastroenterology and Hepatology, Uonuma Institute of Community Medicine, Niigata University Medical and Dental Hospital, Minamiuonuma 949-7302, Japan; Department of General Medicine, Uonuma Kikan Hospital, Minamiuonuma 949-7302, Japan

Peter Laszlo Lakatos, MD, PhD, Professor, Division of Gastroenterology, McGill University Health Center, Montreal, QC H3G 1A4, Canada

Nahum Mendez-Sanchez, MD, PhD, Professor, Liver Research Unit, Medica Sur Clinic and Foundation, Mexico City 14050, Mexico

Takeshi Suda, MD, PhD, Professor, Department of Gastroenterology and Hepatology, Uonuma Institute of Community Medicine, Niigata University Medical and Dental Hospital, Minami Uonuma, Niigata 949-7302, Japan

Editorial Board

Zaigham Abbas, Professor, Hepatogastroenterology and Liver Transplantation, Dr. Ziauddin University Hospital, Karachi, Sindh 75600, Pakistan

Sherief Abd-Elsalam, MD, PhD, Associate Professor, Tropical Medicine and Infectious Diseases Department, Faculty of Medicine, Tanta University, Tanta 35127, Egypt

Shahab Abid, MD, PhD, Professor, Section of Gastroenterology at Department of Medicine, Aga Khan University, Karachi 74800, Pakistan

Yasushi Adachi, MD, PhD, Professor, Department of Gastroenterology, Sapporo Medical University, Sapporo 060-8543, Japan

Samir Ahboucha, PhD, Associate Professor, Faculty of Khouribga, Sultan Moulay Slimane University, Khouribga, Settat 25000, Morocco

Yoshio Aizawa, MD, PhD, Professor, Division of Gastroenterology and Hepatology, Department of Internal Medicine, The Jikei University Katsushika Medical Center, Katsushika-ku, Tokyo 1258506, Japan

Amedeo Amedei, Associate Professor, Department of Clinical and Experimental Medicine, University of Florence, Florence, Tuscany 50135, Italy

Pietro Andreone, MD, Associate Professor, Professor, Dipartimento di Scienze Mediche e Chirurgiche, University of Bologna, Policlinico Sant'Orsola-Malpighi, Bologna 40138, Italy

Francesco Angelico, MD, Associate Professor, Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome 00161, Italy

Vito Annese, MD, PhD, Professor, Department of Gastroenterology, Valiant Clinici, City Walk, Dubai, United Arab Emirates

Bruno Annibale, MD, Professor, Medical-Surgical Department of Clinical Sciences and Translational Medicine, Sapienza University of Rome, Rome 00189, Italy

Minoti V Apte, PhD, Professor, Pancreatic Research Group, South Western Sydney Clinical School, University of New South Wales, Sydney, New South Wales 2050, Australia

Makoto Arai, MD, PhD, Professor, Department of Gastroenterology, Tokyo Women's Medical University Yachiyo Medical Center, Yachiyo 276-8524, Japan

Takaaki Arigami, MD, PhD, Department of Digestive Surgery, Breast and Thyroid Surgery, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima 890-8520, Japan

Naoki Asano, MD, PhD, Professor, Division of Carcinogenesis and Senescence Biology, Tohoku University Graduate School of Medicine, 47-1 Nodayama, Natori 981-1293, Miyagi, Japan

Paolo Aurello, MD, PhD, Assistant Professor, Dipartimento di Scienze Medico-Chirurgiche e di Medicina Traslazionale, University of Rome "La Sapienza", Rome 00189, Italy

Gian Luca Baiocchi, MD, Associate Professor, Department of Clinical and Experimental Sciences, University of Brescia, Brescia 25127, Italy

Yasemin Hatice Balaban, MD, Professor, Department of Gastroenterology, Hacettepe University, Ankara 06100, Türkiye

Giorgos Bamias, MD, PhD, Associate Professor, GI Unit, 3rd Academic Department of Internal Medicine, National and Kapodistrian University of Athens, Sotiria Hospital, Athens 11526, Greece

Yung-Jue Bang, MD, PhD, Professor, Department of Internal Medicine, Seoul National University College of Medicine, Seoul 110-744, South Korea

Donatella Barisani, MD, Associate Professor, School of Medicine and Surgery, University of Milano-Bicocca, Monza 20900, Italy

Michele Barone, MD, PhD, Section of Gastroenterology, Department of Regenerative and Precision Medicine-Jonian Area, University of Bari, Bari 70124, Italy

Gabrio Bassotti, MD, PhD, Associate Professor, Department of Medicine, Gastroenterology and Hepatology Section, University of Perugia Medical School, San Sisto 06156, Italy

Ian Beales, MD, Assistant Professor, Department of Gastroenterology, Norfolk and Norwich University Hospital, Norwich, Norfolk NR4 7UY, United Kingdom

Trond Berg, PhD, Professor, Department of Biosciences, University of Oslo, Oslo N316, Norway

Madhav Bhatia, PhD, Emeritus Professor, Department of Pathology and Molecular Medicine, University of Otago, Christchurch 8140, New Zealand

Josep M Bordas, MD, PhD, Department of Gastroenterology, Hospital Clinic, Barcelona 08022, Spain

Dmitry S Bordin, MD, PhD, Professor, Department of Pancreatic, Biliary and Upper GI Tract Diseases, A.S. Loginov Moscow Clinical Scientific Center, Moscow 111123, Russia

Lisardo Boscá, PhD, Senior Researcher, Department of Metabolism and Immunology, Instituto de Investigaciones Biomédicas Sols-Morreale (Spanish Research Council and Autonomous University of Madrid), Madrid 28029, Spain

Barbara Braden, PhD, Professor, Translational Gastroenterology Unit, Oxford University Hospitals NHS Foundation Trust, Oxford OX3 9DU, United Kingdom

Luis Bujanda, MD, PhD, Professor, Department of Gastroenterology, Biodonostia Health Research Institute, San Sebastian 33490, Spain

Octavio Caba, PhD, Professor, Department of Human Anatomy and Embriology, University of Granada, Granada 18016, Spain

Giuseppe Maurizio Campo, PhD, Professor, Department of Clinical and Experimental Medicine, University of Messina, Messina 98125, Italy

Guray Can, MD, Associate Professor, Department of Gastroenterology, Bolu Abant İzzet Baysal University, Bolu TR-14280, Türkiye

Claudia Cardoso, PhD, Associate Professor, Professor, Department of Internal Medicine, Federal University of Rio de Janeiro - Universidade Federal do Rio de Janeiro, Rio de Janeiro 22750240, Brazil

Andres F Carrion, MD, Assistant Professor, Postdoctoral Fellow, Division of Gastroenterology and Hepatology, University of Miami Miller School of Medicine, Miami, FL 33136, United States

Lucia Carulli, MD, PhD, Associate Professor, Department of Medicine, Endocrinology, Metabolism and Geriatrics, University of Modena and Reggio Emilia, Modena 41124, Italy

- Roberto J Carvalho-Filho, MD, PhD**, Division of Gastroenterology, Hepatology Section, Federal University of Sao Paulo, Sao Paulo 04023-060, Brazil
- Fernando J Castro, MD**, Digestive Disease Center, Cleveland Clinic Florida, Weston, FL 33331, United States
- Herwig Cerwenka, MD, Professor**, Department of Surgery, Medical University of Graz, Graz A-8036, Austria
- Soo-Cheon Chae, PhD, Professor**, Department of Pathology, School of Medicine, Wonkwang University, Iksan, Chonbuk 570-749, South Korea
- Antonios Chatzigeorgiou, MD, PhD, Assistant Professor**, Department of Experimental Physiology, Medical School, National and Kapodistrian University of Athens, Athens 11527, Greece
- Júlio Maria Fonseca Chebli, MD, PhD, Associate Professor, Professor**, Department of Medicine, Universidade Federal de Juiz de Fora, Juiz de Fora, Minas Gerais 36036-247, Brazil
- Adam S Cheifetz, MD, Associate Professor, Assistant Professor**, Department of Medicine, Beth Israel Deaconess Medical Center, Boston, MA 02215, United States
- Isabelle Andrée Chemin, Professor**, Department of Hepatocarcinogenesis and Viral Infection, Centre de Recherche en Cancérologie de Lyon Inserm U1052, Lyon 69003, France
- Xiaoxin Chen, MD, PhD, Professor**, Cancer Research Program, Julius L Chambers Biomedical Biotechnology Research Institute, North Carolina Central University, Durham, NC 27707, United States
- Giuseppe Chiarioni, MD**, Division of Gastroenterology, University of Verona, Verona 37122, Italy
- Hideyuki Chiba, MD, PhD**, Department of Gastroenterology, Omori Red Cross Hospital, Tokyo 143-8527, Japan
- King-Wah Chiu, MD, Professor**, Division of Hepato-Gastroenterology, Department of Internal Medicine, Chang Gung Memorial Hospital-Kaohsiung Medical Center, Chang Gung University College of Medicine, Kaohsiung 83305, Taiwan
- Byung-Ho Choe, MD, PhD, Professor**, Department of Pediatrics, School of Medicine, Kyungpook National University, Daegu 41404, South Korea
- Kenneth Siu-Ho Chok, MD, Associate Professor**, Department of Surgery, Queen Mary Hospital, The University of Hong Kong, Hong Kong 999077, China
- Grigorios Christodoulidis, MD, PhD**, Department of General Surgery, University Hospital of Larissa, Larissa 41110, Greece
- Wan-Long Chuang, MD, PhD, Professor**, Hepatobiliary Division, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung 807, Taiwan
- Halina Cichoż-Lach, MD, Professor**, Department of Gastroenterology with Endoscopy Unit, Medical Univeristy of Lublin, Lublin 20-954, Poland
- Pilar Codoñer-Franch, PhD, Professor**, Department of Pediatrics, Dr. Peset University Hospital, Valencia 46017, Spain
- Helen G Coleman, PhD, Professor**, Centre for Public Health, Queen's University Belfast, Belfast BT12 6BJ, United Kingdom
- Sandro Contini, MD, Associate Professor**, Department of Surgical Sciences, Faculty of Medicine, University of Parma, Parma 43126, Italy
- Elena Corradini, MD, Associate Professor**, Department of Medical and Surgical Sciences for Children and Adults, University of Modena and Reggio Emilia, Modena 41124, Italy

Fernando J Corrales, PhD, Professor, Functional Proteomics Laboratory, National Biotechnology Center (CNB-CSIC), Madrid 28049, Spain

Gaetano Corso, MD, PhD, Professor, Dipartimento di Medicina Clinica e Sperimentale, Università di Foggia, Foggia I-71122, Italy

José Cotter, MD, PhD, Professor, Department of Gastroenterology, Hospital da Senhora da Oliveira, Guimarães 4835-044, Portugal

Bo-Ta Cui, MD, Associate Professor, Department of Microbiota Medicine and Medical Center for Digestive Diseases, The Second Affiliated Hospital of Nanjing Medical University, No. 121 Jiangjiayuan, Nanjing 210011, Jiangsu Province, China

Zhi-Jun Dai, MD, PhD, Professor, Department of Breast Cancer, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou 310003, Zhejiang Province, China

Andrew S Day, MD, Professor, Department of Paediatrics and Child Health, University of Otago Christchurch, Christchurch 8041, New Zealand

Ângelo Zambam de Mattos, MD, PhD, Graduate Program in Medicine: Hepatology, Federal University of Health Sciences of Porto Alegre, Porto Alegre, Rio Grande do Sul 90020-090, Brazil

Paola De Nardi, MD, Associate Professor, Colorectal Surgical Oncology, Department of Abdominal Oncology, Fondazione Giovanni Pascale IRCCS, Naples 34105, Italy

Cláudia P de Oliveira, MD, PhD, Professor, Department of Gastroenterology, Faculdade de Medicina da Universidade de São Paulo, São Paulo 04126000, Brazil

Giovanni Domenico De Palma, MD, Department of Clinical Medicine and Surgery, "Federico II" University of Naples, Naples 80131, Italy

Emilio De Raffe, MD, PhD, Assistant Professor, Dipartimento dell'Apparato Digerente, Policlinico S.Orsola-Malpighi, University of Bologna, Bologna 40138, Italy

Heitor Siffert Pereira de Souza, MD, PhD, Department of Clinical Medicine, School of Medicine, Federal University of Rio de Janeiro, Rio de Janeiro 21941-913, Brazil

Benedicte Yvonne De Winter, MD, PhD, Professor, Faculty of Medicine and Health Sciences, Laboratory of Experimental Medicine and Pediatrics, University of Antwerp, Antwerp 2610, Belgium

Gian Luigi de'Angelis, MD, PhD, Gastroenterology and Endoscopy Unit, University of Parma, University Hospital of Parma, Parma 43126, Italy

Giuliana Decorti, MD, Associate Professor, Department of Medical, Surgical and Health Sciences, University of Trieste, Institute for Maternal and Child Health - IRCCS "Burlo Garofolo", Trieste 34127, Italy

Francesco Di Mario, MD, Department of Medicine and Surgery, University of Parma, Parma 43126, Italy

Vincent Di Martino, MD, PhD, Professor, Department of Hepatology, Jean Minjoz University Hospital, Besançon 25030, France

Zhi Du, PhD, Professor, Department of Hepatobiliary Surgery, Third Central Hospital of Tianjin, Tianjin 300170, China

Dan Lucian Dumitrascu, MD, PhD, Professor, 2nd Medical Department Cluj County Emergency Clinical Hospital Romania, University of Medicine and Pharmacy Iuliu Hatieganu Cluj-Napoca, Cluj-Napoca, Cluj RO 400006, Romania

Nageshwar Reddy Duvvuru, MD, Department of Medical Gastroenterology, Asian Institute of Gastroenterology, Hyderabad, Telangana 500082, India

Cumali Efe, MD, Associate Professor, Department of Gastroenterology, Harran University, Şanlıurfa 06100, Türkiye

Eli D Ehrenpreis, MD, Professor, Department of Medicine, Rosalind Franklin University Medical School, Chicago, IL 60064, United States

Nikolas Eleftheriadis, MD, Euromedica Kyanous Stauros, Thessaloniki 50200, Greece

Gulsum Ozlem Elpek, MD, Professor, Department of Pathology, Akdeniz University Medical School, Dumlupinar Bulvari, Antalya 07070, Türkiye

Mortada H F El-Shabrawi, MD, Professor, Department of Paediatrics, Kasr Alainy School of Medicine, Cairo University, Cairo 11562, Egypt

Hirayuki Enomoto, MD, PhD, Professor, Division of Hepatobiliary and Pancreatic Diseases, Department of Gastroenterology, Hyogo Medical University, Nishinomiya, Hyogo 663-8501, Japan

Atilla Ertan, MD, Professor, Department of Internal Medicine, Division of Gastroenterology, Hepatology and Nutrition Ertan Digestive Disease Center of Excellence, University of Texas Health McGovern Medical School, Houston, TX 77030, United States

Guy D Eslick, PhD, Professor, Centre for Digestive Health, The University of Newcastle, Newcastle, NSW 2300, Australia

Serag M Esmat, MD, Professor, Department of Internal Medicine, Faculty of Medicine, Cairo University, Cairo 11562, Egypt

Massimiliano Fabozzi, MD, PhD, FACS, Department of Oncological Surgery, Arcispedale Santa Maria Nuova - IRCCS, Oncological Centre of Reggio Emilia, Reggio Emilia, Emilia Romagna 42123, Italy

Daniel T Farkas, MD, Associate Professor, Department of Surgery, BronxCare Health System, Bronx, NY 10457, United States

Matteo Fassan, MD, PhD, Department of Medicine, Surgical Pathology Unit, University of Padua, Padua 35121, Italy

Peter Ferenci, MD, Professor, Internal Medicine III, Gastroenterology and Hepatology, Medical University of Vienna, Wien A-1090, Austria

Conrado M Fernandez-Rodriguez, MD, PhD, Associate Professor, Department of Gastroenterology and Hepatology, Hospital Universitario Fundacion Alcorcon, Service of Gastroenterology, Alcorcon, Madrid 28922, Spain

Giovanna Ferraioli, MD, Department of Clinical, Surgical, Diagnostic and Pediatric Sciences, Medical School University of Pavia, Pavia 27100, Italy

Mirella Fraquelli, MD, PhD, Internal Medicine, Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico, Milano 20122, Italy

De-Liang Fu, MD, PhD, Professor, Department of Pancreatic Surgery, Pancreatic Disease Institute, Huashan Hospital, Shanghai 200040, China

Pietro Fusaroli, MD, Associate Professor, Department of Medical and Surgical Sciences, University of Bologna/Hospital of Imola, Bologna 40121, Italy

Alfred Gangl, MD, Professor, Department of Medicine 3, Division of Gastroenterology and Hepatology, Medical University of Vienna, Allgemeines Krankenhaus, Vienna A-1090, Austria

Diego García-Compeán, MD, Professor, Gastroenterology Service and Department of Internal Medicine, Faculty of Medicine, University Hospital "Dr. José E. González", Universidad Autónoma de Nuevo León, Monterrey, Nuevo León 64700, Mexico

Matteo Garcovich, MD, PhD, Internal Medicine, Gastroenterology and Hepatology, Fondazione IRCCS Agostino Gemelli Hospital, Università Cattolica del Sacro Cuore, Rome 00168, Italy

Pankaj Garg, MD, Department of Colorectal Surgery, Garg Fistula Research Institute, Panchkula, Haryana 134113, India

Nikolaus Gassler, MD, Professor, Institute of Pathology, RWTH Aachen University, Braunschweig 38114, Germany

Tom Johannes Gerardus Gevers, MD, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Maastricht University Medical Center, Maastricht, Limburg 6202 AZ, Netherlands

Paola Ghiorzo, PhD, Assistant Professor, Department of Internal Medicine and Medical Specialties, University of Genoa, Genoa 16132, Italy

Luca Vittorio Gianotti, MD, PhD, Professor, School of Medicine and Surgery, University of Milano-Bicocca, Department of Surgery, San Gerardo Hospital, Monza 20900, Italy

Wataru Gonoi, MD, PhD, Assistant Professor, Department of Radiology, Graduate School of Medicine, The University of Tokyo, Tokyo 1138655, Japan

Mark Gorrell, PhD, Professor, Liver Enzymes in Metabolism and Inflammation Program, Centenary Institute and University of Sydney, Sydney, NSW 2006, Australia

Alberto Grassi, MD, PhD, Department of Internal Medicine and Hepatology, Infermi Hospital, Rimini 47921, Italy

Gabriele Grassi, MD, PhD, Associate Professor, Department of Life Sciences, University Hospital of Cattinara, Trieste 34149, Italy

Michał Grąt, MD, PhD, Department of General, Transplant and Liver Surgery, Medical University of Warsaw, Warsaw 02-097, Poland

Antonietta Gerarda Gravina, PhD, MD, Associate Professor, Department of Precision Medicine, Gastroenterology Unit, University of Campania "Luigi Vanvitelli", Naples 80138, Italy

Antonio Grieco, MD, Associate Professor, Liver Transplant Medicine, Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica del Sacro Cuore, Roma, Institute of Internal Medicine, Rome 00168, Italy

Fabio Grizzi, PhD, Department of Immunology and Inflammation, Humanitas Clinical and Research Hospital, Rozzano 20089, Italy

Samir C Grover, MD, Assistant Professor, Division of Gastroenterology, St. Michael's Hospital, University of Toronto, Toronto, Ontario M5B1W8, Canada

Sushovan Guha, MD, PhD, Professor, Department of Internal Medicine, University of Texas Health Science Center, Houston, TX 77030, United States

Chisato Hamashima, MD, PhD, Professor, Faculty of Medical Technology, Teikyo University, Tokyo 1738605, Japan

Ken Haruma, MD, PhD, Professor, Department of Internal Medicine 2, Kawasaki Medical School Kawasaki Hospital, Okayama 701-0192, Japan

Naoki Hashimoto, MD, PhD, Professor, Department of Surgery, Kindai University, Osaka 577-8502, Japan

Goran Hauser, MD, PhD, Associate Professor, Department of Internal Medicine, Division of Gastroenterology, Clinical Hospital Centre, Medical Faculty, Faculty of Health Studies, University of Rijeka, Rijeka 51000, Croatia

Koichi Hayano, MD, PhD, Associate Professor, Department of Frontier Surgery, Chiba University Graduate School of Medicine, Chiba-shi 260-8677, Japan

Paul Henderson, PhD, Child Life and Health, University of Edinburgh, Edinburgh EH16 4TJ, United Kingdom

Harald Peter Hoensch, MD, Professor, Marien Hospital Medical Department, Private Practice in Internal Medicine and Gastroenterology, Darmstadt D-64285, Germany

Gordon Stanley Howarth, PhD, Professor, School of Animal and Veterinary Sciences, University of Adelaide, Roseworthy, South Australia 5371, Australia

Ping-I Hsu, MD, Professor, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Kaohsiung Veterans General Hospital, Kaohsiung 813, Taiwan

Jun-Te Hsu, MD, Professor, Department of Surgery, Chang Gung Memorial Hospital, Taoyuan County and Chang Gung Medicine Colledge, Taoyuan 333, Taiwan

Bing-Sheng Huang, PhD, Associate Professor, Medical AI Lab, School of Biomedical Engineering, Health Science Centre, Shenzhen University, Shenzhen 518000, Guangdong Province, China

Chang-Ming Huang, MD, PhD, Professor, Department of Gastric Surgery, Fujian Medical University Union Hospital, Fuzhou 350001, Fujian Province, China

Jia-Ling Huang, MD, PhD, Assistant Professor, Department of Pathology, Geisinger Medical Center, Geisinger Commonwealth School of Medicine, 100 N Academy Ave, Danville, PA 17822, United States

Calogero Iacono, MD, Associate Professor, Department of Surgical Sciences, Dentistry, Gynecology and Pediatrics, Division of General and Hepatobiliary Surgery, University of Verona, Verona 37134, Italy

Mostafa Ibrahim, MD, Assistant Professor, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, Erasme Hospital, Brussels B-1070, Belgium

Enzo Ierardi, MD, Associate Professor, Section of Gastroenterology, Department of Emergency and Organ Transplantation, University of Bari, Bari, BA 70124, Italy

Masahiro Iizuka, MD, PhD, Akita Health Care Center, Akita Red Cross Hospital, Akita City, Akita 010-0001, Japan

Yoshihiro Ikura, MD, Professor, Department of Pathology, Takatsuki General Hospital, Takatsuki, Osaka Prefecture 569-1192, Japan

Hiroyuki Imaeda, MD, Professor, Department of Gastroenterology, Saitama Medical University, Iruma-gun, Saitama 350-0495, Japan

Kazuaki Inoue, MD, PhD, Associate Professor, Department of Internal Medicine, Division of Gastroenterology, Showa University Fujigaoka Hospital, Yokohama 227-8501, Japan

Raffaele Iorio, MD, Associate Professor, Department of Translational Medical Science, Section of Pediatrics, University Federico II, Naples 80131, Italy

Paola Iovino, MD, Associate Professor, Department of Medicine, Surgery and Dentistry, Scuola Medica Salernitana, University of Salerno, Baronissi, Salerno 84081, Italy

Shuji Isaji, MD, PhD, Professor, Department of Hepatobiliary Pancreatic and Transplant Surgery, Mie University Graduate School of Medicine, Tsu, Mie 514-8507, Japan

Vasily Isakov, MD, PhD, Professor, Department of Gastroenterology and Hepatology, Federal Research Center of Nutrition, Biotechnology and Food Safety, Moscow 115446, Russia

Toru Ishikawa, MD, Department of Gastroenterology and Hepatology, Saiseikai Niigata Hospital, Niigata 950-1104, Japan

Masaya Iwamuro, MD, PhD, Assistant Professor, Department of Gastroenterology and Hepatology, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, Okayama 700-8558, Japan

Yoshiaki Iwasaki, MD, PhD, Professor, Health Service Center, Okayama University, Okayama 700-8530, Japan

Khaled Ali Jadallah, MD, Associate Professor, Department of Internal Medicine, King Abdullah University Hospital, Faculty of Medicine, Jordan University of Science and Technology, Irbid 22110, Jordan

Jeong Won Jang, MD, PhD, Associate Professor, Department of Internal Medicine, The Catholic University of Korea, Seoul 06591, South Korea

Kalpesh Jani, MD, Department of Gastrointestinal and Minimal Access Surgery, Vadodara Institute of Gastrointestinal and Obesity Surgery, Vadodara, Gujarat 390011, India

Harindra Jayasekara, MD, PhD, Melbourne School of Population and Global Health, The University of Melbourne, Melbourne, Victoria 3010, Australia

Robert Thomas Jensen, MD, Digestive Diseases Branch, National Institutes of Health, Bethesda, CA 20892, United States

Guang Ji, MD, PhD, Professor, Institute of Digestive Diseases, Longhua Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai 200032, China

Wei Jiang, MD, PhD, Professor, Department of Gastroenterology, Zhongshan Hospital, Fudan University, Shanghai 200032, China

Miguel Jiménez Pérez, MD, PhD, Assistant Professor, UGC de Aparato Digestivo, Unidad de Hepatología-Trasplante Hepático, Hospital Regional Universitario de Málaga, Málaga 29010, Spain

Young Do Jung, MD, PhD, Professor, Department of Biochemistry, Chonnam National University Medical School, Jeonnam 58138, South Korea

Satoru Kakizaki, MD, PhD, Assistant Professor, Associate Professor, Department of Internal Medicine, Division of Gastroenterology and Hepatology, Gunma University Graduate School of Medicine, Maebashi 3718511, Japan

Hiroteru Kamimura, MD, PhD, Assistant Professor, Division of Gastroenterology and Hepatology, Niigata University Graduate School of Medical and Dental Sciences, Chuo-ku, Niigata 951-8510, Japan

Georgios Karamanolis, MD, PhD, Associate Professor, Department of Gastroenterology, Medical School, National and Kapodistrian University of Athens, Athens 11527, Greece

Rashmi Kaul, PhD, Professor, Department of Biochemistry and Microbiology, Oklahoma State University-Center for Health Sciences, Tulsa, OK 74107, United States

Kazumichi Kawakubo, MD, PhD, Assistant Professor, Department of Gastroenterology and Hepatology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo 0608638, Japan

Sahil Khanna, MD, Assistant Professor, Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN 55905, United States

In Hee Kim, MD, PhD, Professor, Department of Internal Medicine, Chonbuk National University Hospital, Jeonju, Jeonbuk 561-712, South Korea

Seung Up Kim, MD, PhD, Associate Professor, Department of Internal Medicine, Yonsei University College of Medicine, Seoul 03722, South Korea

Byung Joo Kim, PhD, Professor, School of Korean Medicine, Pusan National University, Yangsan 50612, South Korea

Dong Joon Kim, MD, PhD, Professor, Department of Internal Medicine, Hallym University College of Medicine Institute for Liver and Digestive Diseases, Hallym University, Hallym University Chuncheon Sacred Heart Hospital, Gangwon-do 24253, South Korea

Donghee Kim, MD, PhD, Associate Professor, Division of Gastroenterology and Hepatology, Stanford University School of Medicine, Stanford, CA 94304, United States

Gwang Ha Kim, MD, PhD, Professor, Division of Gastroenterology, Department of Internal Medicine and Biomedical Research Institute, Pusan National University Hospital, Busan 49241, South Korea

Hideaki Kinugasa, MD, PhD, Assistant Professor, Department of Gastroenterology and Hepatology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama 700-8558, Japan

Yasuhiro Koga, MD, PhD, Professor, Department of Gastroenterology, Tokai University School of Medicine, Isehara, Kanagawa 259-1193, Japan

Bledar Kraja, MD, PhD, Professor, Department of Biomedical Sciences, Physiology Section, Faculty of Medicine, University Hospital Center Mother Teresa, University Clinic of Gastrohepatology, Tirana 1001, Albania

Wolfgang Kreisel, MD, Department of Medicine II, Gastroenterology, Hepatology, Endocrinology, and Infectious Diseases, Faculty of Medicine, Medical Center - University of Freiburg, Freiburg 79106, Germany

Somashekar G Krishna, MD, Professor, FACC, FASGE, AGAF, Division of Gastroenterology, Hepatology, and Nutrition, The Ohio State University Wexner Medical Center, Columbus, OH 43210, United States

Veerapol Kukongviriyapan, PhD, Associate Professor, Department of Pharmacology, Faculty of Medicine, Khon Kaen University, Muang, Khon Kaen 40002, Thailand

Vincenzo La Mura, MD, PhD, Associate Professor, Department of Pathophysiology and Transplantation, University of Milan, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico-University of Milan, Milan 20122, Italy

Quirino Lai, MD, PhD, Transplant Unit, Sapienza University of Rome, Rome 00161, Italy

Daniela Cornelia Lazăr, PhD, Associate Professor, Department of Internal Medicine I, The University of Medicine and Pharmacy "Victor Babes" Timisoara, Timisoara 300041, Romania

Vijitra Leardkamolkarn, PhD, Professor, Associate Professor, Department of Anatomy, Mahidol University, Bangkok 10400, Thailand

Kyu Taek Lee, MD, PhD, Professor, Department of Gastroenterology, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Ilwon-Dong, Seoul 135710, South Korea

Soo-Youn Lee, MD, PhD, Professor, Department of Laboratory Medicine and Genetics, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Ilwon-Dong, Gangnam-gu, Seoul 135-710, South Korea

Sung-Chul Lim, PhD, MD, Professor, Department of Pathology, Chosun University Hospital, Gwangju 501-717, South Korea

Alexander Link, MD, PhD, Associate Professor, Professor, Department of Gastroenterology, Hepatology and Infectious Diseases, Otto-von-Guericke University Hospital Magdeburg, Magdeburg 39120, Germany

Zheng-Wen Liu, MD, PhD, Professor, Department of Infectious Diseases, First Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710061, Shaanxi Province, China

Hui-Kang Liu, PhD, Division of Basic Chinese Medicine, National Research Institute of Chinese Medicine, Taipei 112, Taiwan

Ana Lleo, MD, PhD, Associate Professor, Department of Biomedical Science, Humanitas University, Pieve Emanuele, Milan 20090, Italy

Johannes-Matthias Lühr, MD, Professor, Department of Clinical Science, Intervention, and Technology, Karolinska University Hospital, Stockholm 14186, Sweden

Amedeo Lonardo, MD, Professor, Department of Internal Medicine, Azienda Ospedaliero-Universitaria di Modena, Modena 41126, Italy

- Xi-Dai Long, MD, PhD, Professor**, Department of Pathology, The Affiliated Hospital of Youjiang Medical University for Nationalities, Baise 533000, Guangxi Zhuang Autonomous Region, China
- Misha D P Luyer, MD, PhD**, Department of Surgery, Catharina Hospital, Eindhoven 5623 EJ, Netherlands
- Ming-Zhe Ma, MD, Assistant Professor**, Department of Gastric Surgery, Fudan University Shanghai Cancer Center, Shanghai 200032, China
- Tomasz Hubert Mach, MD, PhD, Professor**, Department of Gastroenterology and Hepatology, Jagiellonian University Medical College, University Hospital, Cracow 31-531, Poland
- Govind K Makharia, MD, Professor**, Department of Gastroenterology and Human Nutrition, All India Institute of Medical Sciences, New Delhi, Delhi 110029, India
- Emanuel K Manesis, MD, Professor**, Department of Internal Medicine, Athens University School of Medicine, Athens 104 34, Greece
- Francesco Manguso, MD, PhD**, Department of Gastroenterology, Azienda Ospedaliera Di Rilievo Nazionale Antonio Cardarelli, Napoli 80131, Italy
- Lorenzo Mannelli, MD, PhD, Assistant Professor**, Department of Radiology, SDN, Naples 80143, Italy
- Ivana Maric, MD, PhD, Professor**, Department of Anatomy, Faculty of Medicine, University of Rijeka, Rijeka 51000, Croatia
- José Manuel Martín-Villa, PhD, Professor**, Departamento de Inmunología, Oftalmología y ORL, Facultad de Medicina, Universidad Complutense de Madrid, Madrid 28040, Spain
- Luca Mastracci, MD, Full Professor**, Department of Surgical Sciences and Integrated Diagnostics, University of Genoa and Ospedale Policlinico San Martino, Genoa 16132, Italy
- Yoichi Matsuo, MD, PhD, Professor**, Department of Gastroenterological Surgery, Nagoya City University Graduate School of Medical Sciences, Nagoya 4678601, Japan
- Mark C Mattar, MD, Associate Professor**, Department of Gastroenterology, MedStar Georgetown University Hospital, Washington, DC 20007, United States
- Julio Mayol, MD, PhD, Professor**, Department of Surgery, Universidad Complutense de Madrid Medical School, Hospital Clinico San Carlos, Madrid 28040, Spain
- Giuseppe Mazzarella, PhD**, Unit of Immunobiology, Laboratory of Immunomorphology, Institute of Food Sciences, National Council Research, Avellino 83100, Italy
- Neil Donald Merrett, MD, Professor**, Department of Surgery, University of Western Sydney, Penrith, NSW 2571, Australia
- Pal Miheller, MD, PhD, Professor**, Department of Surgery, Transplantation and Gastroenterology, Semmelweis University, Budapest, Pest H-1088, Hungary
- Marco Milone, MD, PhD, Associate Professor**, Clinical Medicine and Surgery, "Federico II" University of Naples, Naples 80131, Italy
- Eiji Miyoshi, MD, PhD, Professor**, Department of Molecular Biochemistry and Clinical Investigation, Osaka University Graduate School of Medicine, Suita, Osaka 565-0871, Japan
- Toru Mizuguchi, MD, PhD, Professor**, Department of Nursing and Surgical Science, Sapporo Medical University Postgraduate School of Health Science, Sapporo, Hokkaido 0608556, Japan

Dimitrios-Paraskevas Moris, MD, PhD, Department of Surgery, Duke University Medical Center, Durham, NC 27710, United States

Sergey Morozov, PhD, MD, Department of Gastroenterology, Hepatology and Nutrition, Federal Research Center of Nutrition and Biotechnology, 21 Kashirskoye Shosse, Moscow 115446, Russia

David L Morris, MD, FRCS (Ed), Professor, Department of Surgery, University of New South Wales, Sydney, New South Wales 2217, Australia

Naofumi Mukaida, MD, PhD, Professor, Division of Molecular Bioregulation, Cancer Research Institute, Kanazawa University, Kanazawa, Ishikawa 920-1192, Japan

Sandeep Mukherjee, Professor, Department of Internal Medicine, Creighton University Medical Center, Omaha, NE 68124, United States

Atsuhiko Murata, MD, PhD, Chief Physician, Department of Preventive Medicine and Community Health, School of Medicine, University of Occupational and Environmental Health, Fukuoka 8078555, Japan

Hikaru Nagahara, MD, PhD, Professor, Department of Gastroenterology, Saiseikai Kurihashi Hospital, Kuki-shi, Saitama-ken 349-1105, Japan

Masaki Nagaya, MD, PhD, Professor, Meiji University International Institute for Bio-Resource Research, Meiji University, Kawasaki 214-8571, Japan

Hiroshi Nakano, MD, PhD, Associate Professor, Department of Gastroenterological Surgery, St. Marianna University Hospital, Kawasaki, Kanagawa 216-8511, Japan

Shivananda Nayak, PhD, Professor, Department of Preclinical Sciences, Faculty of Medical Sciences, The University of The West Indies, Mount Hope, Trinidad and Tobago

Lucian Negreanu, MD, PhD, Associate Professor, Department of Internal Medicine II, Internal Medicine II Gastroenterology, University Hospital Bucharest, Bucharest 050098, Romania

Matthias Ocker, MD, Professor, Department of Medical, Division of Hematology, Oncology, and Cancer Immunology, Campus Charité Mitte, Charité University Medicine Berlin, Berlin 10117, Germany

Shogo Ohkoshi, MD, PhD, Professor, Department of Internal Medicine, School of Life Dentistry at Niigata, The Nippon Dental University, Niigata 951-8580, Japan

Satoshi Ono, MD, PhD, Department of Gastroenterology and Gastrointestinal Endoscopy, Tokyo Metropolitan Institute for Geriatrics and Gerontology, Tokyo 173-0015, Japan

Shozo Osera, MD, PhD, Chief Physician, Department of Gastroenterology, Saku Central Hospital Advanced Care Center, Saku, Nagano 385-0051, Japan

Motoyuki Otsuka, MD, Assistant Professor, Department of Gastroenterology, Graduate School of Medicine, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan

Hasan Ozen, MD, Professor, Department of Pediatrics, Division of Gastroenterology, Hepatology and Nutrition, Hacettepe University School of Medicine, Ankara 06100, Türkiye

Salvatore Paiella, MD, Assistant Professor, General and Pancreatic Surgery Unit, Pancreas Institute, University of Verona Hospital Trust, GB Rossi Hospital, Verona 37129, Italy

Arturo Panduro, MD, PhD, Department of Molecular Biology in Medicine, Civil Hospital of Guadalajara Fray Antonio Alcalde/University of Guadalajara, Guadalajara, Jalisco 44280, Mexico

Won Sang Park, MD, PhD, Professor, Department of Pathology, College of Medicine, The Catholic University of Korea, Seoul 137-701, South Korea

Kwan-Kyu Park, MD, PhD, Professor, Department of Pathology, Catholic University of Daegu, Daegu 42472, South Korea

Rinaldo Pellicano, MD, Professor, Gastroenterology Unit, AOU Città della Salute e della Scienza, Turin 10100, Italy

Gianluca Pellino, MD, PhD, Associate Professor, Colorectal Unit, Department of General and Digestive Surgery, Vall d'Hebron University Hospital, Universitat Autònoma de Barcelona (UAB), Barcelona 08035, Spain

Angela Peltec, MD, PhD, Associate Professor, Department of Internal Medicine, Discipline of Gastroenterology, State University of Medicine and Pharmacy "Nicolae Testemitanu", Chisinau 2019, Moldova

Enrique Perez-Cuadrado-Robles, MD, PhD, Department of Gastroenterology, Cliniques Universitaires Saint-Luc., Bruxelles 1200, Belgium

Marcos V Perini, MD, PhD, Associate Professor, Department of Surgery, The University of Melbourne, Melbourne, Victoria 3084, Australia

Martina Perse, PhD, Institute of Pathology, Medical Experimental Centre, University of Ljubljana, Faculty of Medicine, Ljubljana 1000, Slovenia

Antonio Picardi, MD, PhD, Associate Professor, Professor, Unit of Internal Medicine and Hepatology, Department of Medicine, University Campus Bio-Medico, Rome 00128, Italy

Federico Piñero, MD, Hepatology and Liver Transplant Unit, Hospital Universitario Austral, Buenos Aires B1629HJ, Argentina

Dimitri Poddighe, MD, PhD, Associate Professor, Department of Medicine, Nazarbayev University School of Medicine, Astana 010000, Kazakhstan

Piero Portincasa, MD, PhD, Department of Biomedical Sciences and Human Oncology, University of Bari Medical School, Bari 70124, Italy

Bogdan Procopet, MD, PhD, Assistant Professor, 3rd Medical Department, "Iuliu Hațieganu" University of Medicine and Pharmacy, Institute for Gastroenterology and Hepatology "Prof. Dr. O. Fodor", Cluj-Napoca 400126, Romania

Chun-Feng Qu, MD, PhD, Professor, Department of Immunology, National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China

Zoltán Rakonczay Jr, MD, PhD, Professor, Department of Pathophysiology, University of Szeged, Szeged 6701, Hungary

José M Ramia, MD, PhD, Associate Professor, Department of Surgery, University General Hospital of Alicante, Alicante 03010, Spain

Timo Rath, MD, PhD, Department of Internal Medicine 1, Division of Gastroenterology, Ludwig Demling Endoscopy Center of Excellence, Friedrich-Alexander-University, Erlangen Nuernberg, Erlangen 91054, Germany

Pradip Raychaudhuri, PhD, Professor, Department of Biochemistry and Molecular Genetics (M/C 669), University of Illinois, College of Medicine, 900S. Ashland Ave., Chicago, IL 60607, United States; Jesse Brown VA Medical Center, 820S. Damen Ave., Chicago, IL 60612, United States

Zhi-Gang Ren, MD, PhD, Associate Chief Physician, Chief Physician, Postdoctoral Fellow, Department of Infectious Diseases, State Key Laboratory of Antiviral Drugs, Pingyuan Laboratory, The First Affiliated Hospital of Zhengzhou University, Jianshe East Road, Zhengzhou 450052, Henan Province, China

Vasiliy Ivanovich Reshetnyak, MD, Full Professor, Department of Propaedeutics of Internal Diseases and Gastroenterology, Russian University of Medicine, Moscow 127473, Russian

J Marc Rhoads, MD, Professor, Department of Pediatrics, Division of Gastroenterology, Hepatology, and Nutrition, McGovern Medical School, The University of Texas Health Science Center at Houston, Houston, TX 77030, United States

Luciana Rigoli, MD, Professor, Department of Human Pathology in Adult and Developmental Age "G. Barresi", University of Messina, Messina 98125, Italy

Seungil Ro, PhD, Associate Professor, Department of Physiology and Cell Biology, Reno School of Medicine, University of Nevada, Reno, NV 89557, United States

Ricardo Robles, PhD, MD, Professor, Department of Surgery and Organ Transplantation, Virgen de la Arrixaca University Hospital, Murcia 30120, Spain

Raquel Rocha, PhD, Professor, Department of Sciences of Nutrition, School of Nutrition, Federal University of Bahia, Rua Basilio da Gama, 200-Canela, Salvador, BA 40110-040, Brazil

Francisco Rodriguez-Frias, PhD, Associate Professor, Senior Researcher, Liver Pathology Unit, Biochemistry and Microbiology Departments, Hospital Universitari Vall d'Hebron, Barcelona 08035, Spain

Udo Rolle, MD, PhD, Professor, Department of Pediatric Surgery and Pediatric Urology, University Hospital, Goethe University Frankfurt/M, Frankfurt 60590, Germany

Luca Roncucci, MD, PhD, Associate Professor, Assistant Professor, Department of Diagnostic and Clinical Medicine, and Public Health, University of Modena and Reggio Emilia, Policlinico, Modena 41125, Italy

Joan Rosello-Catafau, PhD, Professor, Department of Experimental Pathology, Institute of Biomedical Research of Barcelona, Barcelona, Catalunya 08036, Spain

Kamran Rostami, MD, PhD, Department of Gastroenterology, MidCentral DHB Palmerston Hospital, Palmerston North 4472, New Zealand

Takao Sakai, MD, PhD, Professor, Department of Diagnostic Pathology, Fujita Health University, Toyoake, Aichi 4701192, Japan

Madhusudana Girija Sanal, PhD, Associate Professor, Department of Molecular and Cellular Medicine, Institute of Liver and Biliary Sciences, New Delhi, Delhi 110070, India

Ken Sato, MD, PhD, Professor, Department of Healthcare Informatics, Takasaki University of Health and Welfare, 37-1 Nakaorui-machi, Takasaki, Gunma 370-0033, Japan

Hildegard M Schuller, PhD, Professor, Department of Biomedical and Diagnostic Sciences, College of Veterinary Medicine, University of Tennessee Knoxville, Knoxville, TN 37996, United States

Annalucia Serafino, PhD, Senior Researcher, Institute of Translational Pharmacology, National Research Council of Italy, Rome 00133, Italy

Neal Shahidi, MD, PhD, Assistant Professor, Department of Medicine, St Paul's Hospital, Division of Gastroenterology, Vancouver, British Columbia V6Z 1Y6, Canada

Ala I Sharara, MD, Professor, Division of Gastroenterology, Department of Internal Medicine, American University of Beirut Medical Center, Beirut 1107 2020, Lebanon

Vishal Sharma, MD, Associate Professor, Department of Gastroenterology, Postgraduate Institute of Medical Education and Research, Chandigarh 160012, India

Sunil G Sheth, MD, Associate Professor, Department of Medicine, Division of Gastroenterology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA 02215, United States

Rui-Hua Shi, MD, PhD, Professor, Department of Gastroenterology, Southeast University, Zhongda Hospital, Nanjing 210009, Jiangsu Province, China

Qiang Shi, PhD, Associate Professor, Endoscopy Center, Zhongshan Hospital of Fudan University, Shanghai 200032, China

Yukihiro Shimizu, MD, PhD, Gastroenterology Center, Nanto Municipal Hospital, Nanto, Toyama 932-0211, Japan

Noam Shussman, MD, Department of General Surgery, Hadassah Hebrew University Medical Center, Jerusalem 91120, Israel

Giuseppe Sica, MD, PhD, Associate Professor, Department of Surgery, Tor Vergata University Hospital, Rome 00133, Italy

Predrag Sikiric, MD, PhD, Department of Pharmacology, School of Medicine, University of Zagreb, Zagreb 10000, Croatia

Aytan Sipahi, PhD, Assistant Professor, Department of Gastroenterology and Hepatology, University of São Paulo School of Medicine - LIM 07, São Paulo, SP 01246-903, Brazil

Ferenc Sipos, MD, PhD, Department of Hematology and Internal Medicine, Semmelweis University, Budapest 1088, Hungary

Stanislav Sitkin, MD, PhD, Associate Professor, Senior Researcher, Department of Internal Diseases, Gastroenterology and Dietetics, North-Western State Medical University named after I.I. Mechnikov, St. Petersburg 190000, Russia

Sinead M Smith, PhD, Assistant Professor, Department of Clinical Medicine, Trinity College Dublin, Dublin D24, Ireland

Ross Cyril Smith, MD, Professor, Division of Surgery, Head of the Cancer Surgery Research Laboratory, Kolling Institute, University of Sydney, StLeonards, NSW 2065, Australia

Rosa Leonôra Salerno Soares, MD, PhD, Professor, Department of Internal Medicine, Faculty of Medicine, Federal Fluminense University, Niterói, Rio de Janeiro 24030210, Brazil

Myeong Jun Song, PhD, Associate Professor, Department of Internal Medicine, Daejeon St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Daejeon 301-723, South Korea

Maurizio Soresi, MD, Associate Professor, Department of Health Promotion Sciences, Maternal and Infant Care, Internal Medicine and Medical Specialties (PROMISE), University of Palermo, Palermo 90127, Italy

Cosimo Sperti, MD, Associate Professor, Professor, Department of Surgery, Oncology and Gastroenterology, 1st General Surgery, University of Padua, Padua 35128, Italy

Giovanni Squadrito, MD, Professor, Clinical and Molecular Hepatology Unit, Department of Internal Medicine, University of Messina, Messina 98124, Italy

Carol Stanciu, Professor, Department of Gastroenterology, "Grigore T. Popa" University of Medicine and Pharmacy, "St. Spiridon" University Hospital, Institute of Gastroenterology and Hepatology, Iasi 700111, Romania

Adrian John Stanley, MD, Professor, Department of Gastroenterology, Glasgow Royal Infirmary, Glasgow G4 0SF, United Kingdom

Gabriele Stocco, PhD, PharmD, Associate Professor, Department of Medical, Surgical and Health Sciences, University of Trieste/Institute for Maternal and Child Health IRCCS Burlo Garofolo, Trieste 34127, Italy

Letitia Adela Maria Streba, MD, PhD, Professor, Department of Internal Medicine 1, Filantropia University Hospital, Craiova 200349, Romania

Koichi Suda, Professor, Department of Surgery, Fujita Health University, Toyoake, Aichi 470-1192, Japan

Mitsushige Sugimoto, MD, PhD, AGAF, Professor, Division of Genome-Wide Infectious Microbiology, Research Center for GLOBAL and LOCAL Infectious Disease, Oita University, 1-1 Idaigaoka, Hasama, Yufu, Oita 879-5593, Japan

Haruhiko Sugimura, MD, PhD, Professor, Department of Tumor Pathology, Hamamatsu University School of Medicine, Hamamatsu 431-3192, Japan

Keith Sultan, MD, Assistant Professor, Division of Gastroenterology, Northwell Health, North Shore University Hospital and Long Island Jewish Medical Center, Great Neck, NY 10021, United States

Si-Yu Sun, MD, PhD, Professor, Department of Gastroenterology, Shengjing Hospital of China Medical University, Shenyang 110004, Liaoning Province, China

Veysel Tahan, MD, Associate Professor, Department of Internal Medicine, Division of Gastroenterology and Hepatology, University of Missouri, Columbia, Missouri 65212, United States

Akihiro Tamori, MD, PhD, Professor, Department of Hepatology, Osaka City University Graduate School of Medicine, Osaka 5458585, Japan

Kok Yang Tan, Associate Professor, Department of Surgery, Khoo Teck Puat Hospital, Singapore 768828, Singapore

Yasuhito Tanaka, MD, PhD, Professor, Department of Gastroenterology and Hepatology, Faculty of Life Sciences, Kumamoto University, Kumamoto 860-0862, Japan

Naoki Tanaka, MD, PhD, Professor, Department of Global Medical Research Promotion, Shinshu University School of Medicine, Matsumoto, Nagano 390-8621, Japan

Giovanni Tarantino, MD, Professor, Senior Researcher, Department of Clinical Medicine and Surgery, Federico II University Medical School, Naples 80131, Italy

Oscar Tatsuya Teramoto-Matsubara, MD, Department of Gastroenterology and Endoscopy, ABC Medical Center, Mexico City 11000, Mexico

Ragesh Babu Thandassery, MD, Assistant Professor, Department of Medicine, Central Arkansas Veterans Healthcare System, Little Rock, AR 72205, United States

Konstantinos Thomopoulos, MD, Professor, Division of Gastroenterology, Department of Internal Medicine, University Hospital of Patras, Patras 26504, Greece

Guido Alberto Massimo Tiberio, MD, Professor, Surgical Clinic, Department of Clinical and Experimental Sciences, University of Brescia, Brescia 25100, Italy

Minoru Tomizawa, MD, PhD, Department of Gastroenterology, National Hospital Organization Shimoshizu Hospital, Yotsukaido City, Chiba 284-0003, Japan

Maria Lina Tornesello, PhD, Department of Research, Istituto Nazionale Tumori IRCCS Fond Pascale, Napoli 80131, Italy

Ervin Toth, MD, PhD, Endoscopy Unit, Department of Gastroenterology, Skåne University Hospital, Malmö 20502, Sweden

David Tougeron, MD, PhD, Full Professor, Department of Gastroenterology, Poitiers University Hospital, Poitiers 86000, France

Cristiane Valle Tovo, MD, PhD, Associate Professor, Department of Gastroenterology and Hepatology, Universidade Federal de Ciências da Saúde de Porto Alegre, Porto Alegre, RS 90050-170, Brazil

Osamu Toyoshima, MD, PhD, Professor, Department of Gastroenterology, Toyoshima Endoscopy Clinic, Tokyo 157-0066, Japan

Sombat Treeprasertsuk, MD, PhD, Professor, Department of Medicine, Division of Gastroenterology, Faculty of Medicine, Chulalongkorn University, and Thai Red Cross, Bangkok 10330, Thailand

John K Triantafyllidis, MD, PhD, Associate Professor, Inflammatory Bowel Disease Unit, "Metropolitan General" Hospital, Holargos "Mediterraneo First Care" Glyfada, Holargos, Attica 15562, Greece

Konstantinos Triantafyllou, MD, PhD, Professor, Hepatogastroenterology Unit, Second Department of Internal Medicine – Propaedeutic, Medical School, National and Kapodistrian University of Athens, "Attikon" University General Hospital, Athens 12462, Greece

Anca Trifan, MD, Professor, Department of Gastroenterology and Internal Medicine, "Grigore T. Popa" University of Medicine and Pharmacy, "St. Spiridon" University Hospital, Institute of Gastroenterology and Hepatology, Iasi 700111, Romania

Dhiraj Tripathi, MD, Professor, Liver Unit, Queen Elizabeth Hospital, Birmingham B15 2TH, United Kingdom

Maria Fernanda Troncoso, PhD, Assistant Professor, Department of Biological Chemistry and Institute of Biochemistry and Biophysics, School of Pharmacy and Biochemistry, University of Buenos Aires and National Research Council of Argentina, Buenos Aires C1113AAD, Argentina

Apostolos Tsolakis, MD, PhD, Department of Oncology and Pathology, Karolinska Institutet, Stockholm 171 76, Sweden

Georgios Tsoulfas, MD, PhD, Professor, Department of Transplant Surgery, Aristotle University of Thessaloniki School of Medicine, Thessaloniki 54124, Greece

Yosuke Tsuji, MD, PhD, Assistant Professor, Department of Gastroenterology, Graduate School of Medicine, The University of Tokyo, Tokyo 113-8655, Japan

Hong Tu, MD, PhD, Professor, State Key Laboratory of Oncogenes and Related Genes, Shanghai Cancer Institute, Renji Hospital, Shanghai Jiao-Tong University School of Medicine, Shanghai 200032, China

Zsolt Tulassay, MD, Molecular Medicine Research Group, Hungarian Academy of Sciences, Budapest 1088, Hungary

Gokhan Tumgor, MD, PhD, Professor, Pediatric Gastroenterology, Cukurova University Medical Faculty, Adana 01380, Türkiye

Balasubramaniyan Vairappan, PhD, Associate Professor, Professor, Liver Diseases Research Lab, Department of Biochemistry, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry 605006, India

Abhinav Vasudevan, PhD, Adjunct Associate Professor, Department of Gastroenterology and Hepatology, Eastern Health, Box Hill 3128, Australia

Gilberto Vaughan, PhD, Division of Viral Hepatitis, Centers for Disease Control and Prevention, Atlanta, GA 30329, United States

Umberto Vespasiani-Gentilucci, PhD, Associate Professor, Unit of Internal Medicine and Hepatology, Department of Medicine, University Campus Bio-Medico, Rome 00128, Italy

Silvia Vidal, PhD, Assistant Professor, Immunology, Institut Investigacions Biomediques-Institut Recerca Hospital Sant Pau, Barcelona 08025, Spain

Yirupaiahgar K S Viswanath, Professor, Department of Upper GI Surgery Endoscopy and Laparoscopic Surgery, James Cook University Hospital, Middlesbrough, Cleveland TS4 3BW, United Kingdom

Marco Vivarelli, MD, Professor, Department of Experimental and Clinical Medicine, Polytechnic University of Marche, Hepatobiliary, Pancreatic and Abdominal Transplantation Surgery, Ospedali Riuniti delle Marche, via Conca 71, Ancona 60126, Italy

Tamara Vorobjova, MD, PhD, Associate Professor, Department of Immunology, Institute of Biomedicine and Translational Medicine, University of Tartu, Tartu 51014, Estonia

Yu-Gang Wang, MD, Professor, Department of Gastroenterology, Tongren Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200336, China

Yuan-Hung Wang, PhD, Associate Professor, Graduate Institute of Clinical Medicine, Taipei Medical University, Taipei 110, Taiwan

Nir Wasserberg, MD, Associate Professor, Professor, Department of Surgery, Rabin Medical Center, Petach Tiqwa 49100, Israel

David I Watson, MD, PhD, Professor, Flinders University Discipline of Surgery, Flinders University, Flinders Medical Centre, Adelaide, South Australia 5042, Australia

Charles Melbern Wilcox, MD, Professor, Medicine, Division of Gastroenterology and Hepatology, University of Alabama at Birmingham, Birmingham, AL 35294, United States

Tibor Wittmann, MD, PhD, Professor, First Department of Medicine, University of Szeged, Szeged H-6720, Hungary

Qi Xie, MD, PhD, Professor, Department of Medical Imaging, Nansha Hospital, Guangzhou First People's Hospital, School of Medicine, South China University of Technology, Guangzhou 511457, Guangdong Province, China

Cheng-Fu Xu, MD, Chief Physician, Professor, Department of Gastroenterology, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou 310003, Zhejiang Province, China

Feng Yang, MD, PhD, Associate Professor, Department of Pancreatic Surgery, Huashan Hospital, Shanghai Medical College, Fudan University, Shanghai 200040, China

Tzung-Hai Yen, MD, PhD, Professor, Department of Nephrology, Chang Gung Memorial Hospital, No. 5 Fu-Hsing Street, Kweishan, Taoyuan City 333, Taiwan

Desmond Yip, MD, Professor, Department of Medical Oncology, The Canberra Hospital, Garran, ACT 2606, Australia

Michele Yip-Schneider, PhD, Professor, Department of Surgery, Indiana University School of Medicine, Indianapolis, IN 46202, United States

Kentaro Yoshioka, MD, PhD, Center for Liver Diseases, Meijo Hospital, Nagoya, Aichi 460-0001, Japan

Yan-Bo Yu, MD, Professor, Department of Gastroenterology, Laboratory of Translational Gastroenterology, Qilu Hospital, Shandong University, Jinan 250012, Shandong Province, China

Chao-Hui Yu, MD, PhD, Professor, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou 310003, Zhejiang Province, China

Ilhami Yuksel, MD, Professor, Department of Gastroenterology, Ankara Bilkent City Hospital, Ankara 06800, Türkiye; Department of Gastroenterology, Ankara Yildirim Beyazıt University, School of Medicine, Ankara 06300, Türkiye

Cyrla Zaltman, MD, PhD, Associate Professor, Department of Internal Medicine, Federal University of Rio de Janeiro, Rio de Janeiro 21941-913, Brazil

Li Zhang, MD, PhD, School of Biotechnology and Biomolecular Sciences, University of New South Wales, Sydney, NSW 2052, Australia

Ce-Fan Zhou, PhD, Professor, School of Life and Health Sciences, Institute of Biomedical Research, National "111" Center for Cellular Regulation and Molecular Pharmaceutics, Key Laboratory of Fermentation Engineering (Ministry of Education), Hubei University of Technology, Wuhan 430068, Hubei Province, China

Demosthenes E Ziogas, MD, PhD, Assistant Professor, Department of Surgery, University of Ioannina, Ioannina GR 45110, Greece

EDITORIAL

Lu JG, Gao YZ. Dyspepsia following *Helicobacter pylori* eradication: Shifts in etiology and clinical challenges. *World J Gastroenterol* 2026; 32(6): 115699 [DOI: [10.3748/wjg.v32.i6.115699](https://doi.org/10.3748/wjg.v32.i6.115699)]

Xu JJ, Ni CX, Xu JJ. Emerging role of DNA polymerase epsilon non-exonuclease domain mutations in colorectal cancer: From sequence variants to clinical implications. *World J Gastroenterol* 2026; 32(6): 116028 [DOI: [10.3748/wjg.v32.i6.116028](https://doi.org/10.3748/wjg.v32.i6.116028)]

REVIEW

Yin HY, You QH, Zhang WJ, Ji G, Dang YQ. High-protein diets and metabolic dysfunction-associated steatotic liver disease: A double-edged sword in liver health. *World J Gastroenterol* 2026; 32(6): 113804 [DOI: [10.3748/wjg.v32.i6.113804](https://doi.org/10.3748/wjg.v32.i6.113804)]

ORIGINAL ARTICLE**Retrospective Cohort Study**

Lian WL, Cai LS, Lian MQ, Lian MJ, Sun YQ, Lv CB, Huang GP, Huang RJ, Zhang YB, Zeng WM, Xu QH, Zhu QJ, Chen QX. Efficacy and safety of sequential hyperthermic intraperitoneal chemotherapy following surgery for pathological T staging 4 gastric cancer. *World J Gastroenterol* 2026; 32(6): 115556 [DOI: [10.3748/wjg.v32.i6.115556](https://doi.org/10.3748/wjg.v32.i6.115556)]

Retrospective Study

Feng W, Ye QW, Wang QL, Chen SY, Ma Y, Meng FL. Predictors of one-year adverse outcomes after laparoscopic resection for hepatocellular carcinoma: Development and validation of an early-warning model. *World J Gastroenterol* 2026; 32(6): 113195 [DOI: [10.3748/wjg.v32.i6.113195](https://doi.org/10.3748/wjg.v32.i6.113195)]

Clinical Trials Study

Park SB, Kang SB, Seo GS, Eun CS, Choi CH, Yang DH, Park JJ, Moon CM, Jung SH, Park H, Park MH, Yoo HK, Kim J, Heo JA, Park DI. Efficacy and safety of a novel sodium picosulfate oral tablet in a randomized controlled trial for bowel preparation. *World J Gastroenterol* 2026; 32(6): 113880 [DOI: [10.3748/wjg.v32.i6.113880](https://doi.org/10.3748/wjg.v32.i6.113880)]

Observational Study

Caballero-Mateos AM, Trigo-Salado C, Suárez-Toribio Á, Martín-Rodríguez MDM, Rodríguez-González FJ, Valdés-Delgado T, Pallarés-Manrique H, Trapero-Martínez AM, Olmedo-Martín R, Bailón-Gaona C, Benítez Cantero JM, Gros B, Sáez-Díaz A, Hernández-Martínez Á. Long-term clinical outcomes with filgotinib in ulcerative colitis: 12-month results from the FILGUITO study. *World J Gastroenterol* 2026; 32(6): 115941 [DOI: [10.3748/wjg.v32.i6.115941](https://doi.org/10.3748/wjg.v32.i6.115941)]

Basic Study

Yang PC, Xiao CY, Wang J, Yan CH, Li QY, Li SY, Li J, Zhang LJ, Dai CB. Effects and mechanism of *Bifidobacterium* on intestinal inflammation resulting from deoxycholic acid-induced M1 polarization of macrophages. *World J Gastroenterol* 2026; 32(6): 113010 [DOI: [10.3748/wjg.v32.i6.113010](https://doi.org/10.3748/wjg.v32.i6.113010)]

Zhang MY, Sun RQ, Min Q, Zhu YQ, Qin SK, Guo QL. Synergistic antitumor effect of oroxylin A and donafenib in hepatocellular carcinoma through tumor protein p53 signaling pathway activation. *World J Gastroenterol* 2026; 32(6): 113529 [DOI: [10.3748/wjg.v32.i6.113529](https://doi.org/10.3748/wjg.v32.i6.113529)]

META-ANALYSIS

Xing Y, Yan WM, Bai RX. Effects of bariatric surgery on obesity associated gastroesophageal reflux disease: Insights from a systematic review and network meta-analysis. *World J Gastroenterol* 2026; 32(6): 114600 [DOI: 10.3748/wjg.v32.i6.114600]

LETTER TO THE EDITOR

Wang YP, Dai JL, Li L, Wen B. Insights into the influencing factors of fecal gut microbiota in hepatocellular carcinoma. *World J Gastroenterol* 2026; 32(6): 115217 [DOI: 10.3748/wjg.v32.i6.115217]

Wan KR, Qian C, Liu LM. Bidirectional regulation between the endocrine system and liver: From mechanisms to multidisciplinary clinical care. *World J Gastroenterol* 2026; 32(6): 115232 [DOI: 10.3748/wjg.v32.i6.115232]

ABOUT COVER

Editorial Board Member of *World Journal of Gastroenterology*, Ken Sato, MD, PhD, Professor, Department of Healthcare Informatics, Takasaki University of Health and Welfare, 37-1 Nakaorui-machi, Takasaki, Gunma 370-0033, Japan. satoken@gunma-u.ac.jp

AIMS AND SCOPE

The primary aim of *World Journal of Gastroenterology* (*WJG, World J Gastroenterol*) is to provide scholars and readers from various fields of gastroenterology and hepatology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online. *WJG* mainly publishes articles reporting research results and findings obtained in the field of gastroenterology and hepatology and covering a wide range of topics including gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, gastrointestinal oncology, and pediatric gastroenterology.

INDEXING/ABSTRACTING

The *WJG* is now abstracted and indexed in Science Citation Index Expanded (SCIE), MEDLINE, PubMed, PubMed Central, Scopus, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2025 edition of Journal Citation Reports® cites the 2024 journal impact factor (JIF) for *WJG* as 5.4; Quartile: Q1. The *WJG*'s CiteScore for 2024 is 8.1.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Yu-Qing Zhao*; Production Department Director: *Xiao-Mei Zheng*; Cover Editor: *Jia-Ru Fan*.

NAME OF JOURNAL

World Journal of Gastroenterology

ISSN

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

LAUNCH DATE

October 1, 1995

FREQUENCY

Weekly

EDITORS-IN-CHIEF

Andrzej S Tarnawski

EXECUTIVE ASSOCIATE EDITORS-IN-CHIEF

Xian-Jun Yu, Jian-Gao Fan, Hou-Bao Liu

EDITORIAL BOARD MEMBERS

<http://www.wjgnet.com/1007-9327/editorialboard.htm>

PUBLICATION DATE

February 14, 2026

COPYRIGHT

© 2026 Baishideng Publishing Group Inc

PUBLISHING PARTNER

Shanghai Pancreatic Cancer Institute and Pancreatic Cancer Institute, Fudan University
Biliary Tract Disease Institute, Fudan University

INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

POLICY OF CO-AUTHORS

<https://www.wjgnet.com/bpg/GerInfo/310>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>

PUBLISHING PARTNER'S OFFICIAL WEBSITE

<https://www.shca.org.cn>
<https://www.zs-hospital.sh.cn>

Emerging role of DNA polymerase epsilon non-exonuclease domain mutations in colorectal cancer: From sequence variants to clinical implications

Jia-Ju Xu, Chun-Xiao Ni, Jia-Ju Xu

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade A, Grade B

Novelty: Grade B, Grade B

Creativity or Innovation: Grade B, Grade C

Scientific Significance: Grade B, Grade C

P-Reviewer: Sheng JP, Professor, China; Xu M, PhD, China

Received: November 2, 2025

Revised: December 19, 2025

Accepted: December 25, 2025

Published online: February 14, 2026

Processing time: 94 Days and 0.5 Hours



Jia-Ju Xu, Department of Pediatrics, Yantai Yuhuangding Hospital, Yantai 264000, Shandong Province, China

Chun-Xiao Ni, Department of Minimally Invasive Oncology, Tai'an City Central Hospital, Tai'an 271000, Shandong Province, China

Jia-Ju Xu, Department of Medical Oncology, Tai'an City Central Hospital, Tai'an 271000, Shandong Province, China

Co-first authors: Jia-Ju Xu and Chun-Xiao Ni.

Corresponding author: Jia-Ju Xu, MD, Doctor, Department of Medical Oncology, Tai'an City Central Hospital, No. 29 Longtan Road, Tai'an 271000, Shandong Province, China.

jiajuxu1101@163.com

Abstract

This editorial highlights the emerging significance of non-exonuclease domain mutations (non-EDMs) in DNA polymerase epsilon (POLE) in colorectal cancer (CRC), inspired by the recent study by Taskiran *et al.* Their study revealed an exceptionally high frequency of POLE mutations (53.65%) in a Turkish CRC cohort, primarily attributed to a specific frameshift variant (p.V1446fs3) with undetermined pathogenic significance. Notably, the non-EDMs showed significant co-occurrence with mutations in critical genes, such as *MLH3*, *MSH3*, *KRAS*, *PIK3CA*, and *BRAF*, implying a potential synergistic interaction between impaired DNA repair mechanisms and activation of oncogenic pathways. Although POLE-mutant tumors rarely display high microsatellite instability, their hypermutator phenotype may make them more responsive to immunotherapy. This commentary underscores the need for functional assays and validation through multi-center studies to establish the pathogenicity and clinical relevance of non-EDMs. Furthermore, it advocates for the incorporation of comprehensive POLE sequencing, including non-EDM regions, into standard molecular subtyping frameworks for CRC to refine personalized treatment strategies.

Key Words: DNA polymerase epsilon; Colorectal cancer; Non-exonuclease domain mutations; Co-mutation; Tumor mutational burden

Core Tip: Building on Taskiran *et al*'s findings of a high frequency of non-exonuclease domain mutations (non-EDMs) in polymerase epsilon (POLE), particularly the p.V1446fs3 variant, this editorial highlights their potential clinical significance in colorectal cancer. These non-EDMs, often co-occurring with mutations in DNA repair and oncogenic signaling genes, may define a distinct subgroup of tumors. The editorial advocates for functional validation and the integration of comprehensive POLE sequencing into molecular subtyping to unlock their potential as biomarkers for guiding immunotherapy and personalized treatment strategies.

Citation: Xu JJ, Ni CX, Xu JJ. Emerging role of DNA polymerase epsilon non-exonuclease domain mutations in colorectal cancer: From sequence variants to clinical implications. *World J Gastroenterol* 2026; 32(6): 116028

URL: <https://www.wjgnet.com/1007-9327/full/v32/i6/116028.htm>

DOI: <https://dx.doi.org/10.3748/wjg.v32.i6.116028>

INTRODUCTION

Colorectal cancer (CRC) is a malignancy with high global incidence and mortality rates[1,2]. The significant genetic heterogeneity of CRC remains a central focus and challenge in oncology research. Within the complex molecular landscape of CRC, mutations affecting the DNA polymerase epsilon (POLE) gene, particularly those affecting its exonuclease domain [exonuclease domain mutations (EDMs)], have gained increasing attention due to their association with hypermutator phenotypes and potential favorable responses to immune checkpoint inhibitors (ICIs)[3,4]. Compared to EDMs, the biological role, clinical significance, and relationships with microsatellite instability (MSI) status and co-mutation profiles of POLE non-EDMs (non-EDMs) in CRC remain largely unexplored and need further studies[5].

The recent work by Taskiran *et al*[6], which was published in the *World J Gastroenterol*, directly addresses this unmet need. Their retrospective analysis of 356 Turkish patients with CRC identified 191 patients with POLE mutations, enabling a systematic characterization of these mutations. The study specifically focused on non-EDMs, detailing their distribution, correlation with MSI status, and co-mutation landscapes. The research expands our understanding of the POLE mutation spectrum, effectively redirecting attention from the established EDMs to the overlooked non-EDMs. It also highlights the high frequency of non-EDMs in populations such as the Turkish cohort and emphasizes their potential as biomarkers and active players in tumorigenesis.

This editorial aims to provide an in-depth analysis and forward-looking perspective based on the key findings by Taskiran *et al*[6], integrating current knowledge on POLE mutations in CRC. We also discuss the potential functional impact of POLE non-EDMs, explain their clinical relevance, and illuminate future research directions, inspiring new viewpoints for precision medicine in CRC.

REVISING THE POLE GENE IN CRC: FROM CLASSICAL EDMS TO NEGLECTED NON-EDMS

The POLE protein primarily comprises two core functional domains: The C-terminal 3'-5' exonuclease domain (EDM, responsible for proofreading function) and the N-terminal DNA polymerase domain (non-EDM, responsible for DNA synthesis)[7]. Highly expressed during the S phase of the cell cycle, POLE is crucial for maintaining genomic stability and fidelity. "Hotspot" mutations within the EDM (typically referring to the exon 9 to 14 region), such as *P286R*, *V411 L*, and *S459F*, impair the proofreading function of the polymerase and lead to the accumulation of errors during DNA replication, triggering an ultra-hypermutated phenotype[8]. Studies have shown that compared to common hypermutated and non-hypermutated tumors, POLE-class tumors possess a higher number of nonsynonymous single-nucleotide variants (SNVs) and elevated expression levels of programmed cell death 1, programmed cell death ligand 1, and *CD8A*. Patients in this category are generally younger at disease onset, a finding corroborated by contemporary molecular profiling studies of early-onset CRC cohorts[9]. All early-onset cases carry the *P286R* mutation, a feature associated with POLE EDM variants like *P286R*[10]. These hypermutated tumors typically exhibit an exceptionally high tumor mutational burden (TMB), generating a large number of neoantigens, which may enhance sensitivity to ICIs[11]. Despite the low overall incidence of POLE EDMs in CRC (approximately 1%-2% in previous studies[12-15]), their clinical significance is considerable. Recent analyses have shown that POLE-mutant CRCs, including those with non-EDMs, are characterized by distinct clinicopathological features, most notably a high TMB and younger age, and can occur in both right- and left-sided colons[16]. More importantly, several studies and clinical cases have indicated that patients with metastatic CRC with pathogenic POLE EDMs may benefit significantly from ICIs, regardless of the MSI status[17-19]. A global study also showed that compared to patients with deficient mismatch repair (dMMR)/MSI-high (MSI-H) metastatic CRC, patients with metastatic CRC and POLE/*POLD1* proofreading deficiency achieve a superior objective response rate and progression-free survival after receiving ICIs[20]. These findings establish POLE EDMs as highly promising predictive biomarkers for immunotherapy in CRC.

Compared to the well-characterized EDMs, there are relatively few studies on POLE non-EDMs, and their functional and clinical significance remain largely unknown. Non-EDMs are distributed within the polymerase domain or other regions of the POLE gene and may indirectly affect DNA replication fidelity by modulating the stability of the POLE protein and its interactions with other proteins and controlling the activity of DNA polymerase or the overall function of the replication complex[21]. Although previous studies have reported the presence of POLE non-EDMs in CRC, their precise role remains unclear[5,17]. Notably, some of the previous studies have found that a synergistic effect occurs when POLE EDMs coexist with specific non-EDMs (*e.g.*, AA 1906, 1826-7), resulting in a significantly higher TMB than either variant type alone[5]. The study by Taskiran *et al*[6] reported the opposite results. Their analysis of a Turkish CRC cohort revealed an overall POLE mutation frequency of 53.65% (191/356), substantially higher than the previously reported range of 1%-12.3%. However, further analysis showed that this high prevalence was primarily driven by a specific non-EDM variant-exon 34 c.4337 4338delTG p.V1446fs3, which was detected in 182 patients (95.29% of POLE-mutant cases). After excluding this high-frequency variant, the POLE mutation rate dropped to 2.53%, aligning with the mutation rates reported in other studies[12-15]. This finding highlights the need for careful interpretation of the p.V1446fs3 variant, whose high frequency suggests potential population-specific effects or functional relevance, despite conflicting classifications of the pathogenesis. The high prevalence of the p.V1446fs3 variant in this cohort underscores a pressing need for its functional characterization. Future studies should employ *in vitro* assays to assess its impact on DNA polymerase fidelity and replication rates, and utilize cellular models (*e.g.*, clustered regularly interspaced short palindromic repeats-edited organoids or isogenic cell lines) to determine its effects on mutation rates, genomic stability, and cellular proliferation. *In vivo* models should also evaluate their tumorigenic potential and effects on the tumor microenvironment.

The study also identified various other non-EDMs, including p.D612N, p.R1909, p.N518fs10, p.Q1774, p.Q911, p.A1885T, and p.L1171fs6. Additionally, two EDM variants, namely p.Y458F and p.Y468N, were detected, each accounting for 0.52% of cases. p.Y458F has been confirmed as a pathogenic variant, whereas the significance of p.Y468N remains uncertain. Consistent with previous studies, these findings suggest a more complex and comprehensive perspective of the POLE mutational landscape in CRC and underscore the importance of systematically screening the entire POLE coding region, beyond classical EDMs[22].

In summary, Taskiran *et al*[6] not only revealed the high frequency of POLE non-EDMs in specific populations but also challenged the traditional understanding of POLE mutations in CRC.

ROLE OF MUTATIONS, MSI, AND CO-MUTATION PROFILES IN CRC

Studies have confirmed that MSI is frequently observed in non-EDM high-TMB tumors, whereas EDM tumors display a distinct pattern of MSI[5]. Taskiran *et al*[6] not only delineated the distribution profile of POLE mutations in a Turkish CRC cohort but also provided valuable insights into the complex relationships between these mutations, MSI status, and co-occurring somatic mutations, explaining how POLE mutations shape the molecular landscape and clinical behavior of CRC. In their study, the vast majority (87.96%) of patients with CRC and POLE mutations exhibited proficient mismatch repair (pMMR) [*i.e.*, MSI-low (MSI-L) or microsatellite stable (MSS)], while only 12.04% of patients with CRC and POLE mutations revealed dMMR (MSI-H). This finding indicates that non-EDMs represent the predominant form of POLE mutations in the Turkish population, occurring more frequently in MSS/MSI-L tumors. This observation partly aligns with previous studies suggesting that POLE EDMs are primarily found in MSS tumors and may confer a hypermutated phenotype, potentially enhancing the response to immunotherapy, similar to that observed in MSI-H tumors[23]. Consistent with prior studies[24], the strong association between POLE mutations and MSI-L/MSS status reported by Taskiran *et al*[6] suggests the need for re-evaluating the interaction between different POLE mutation types (EDMs *vs* non-EDMs) and the MMR system. This association is particularly driven by the high frequency of non-EDMs in this context.

The observation that most POLE-mutant tumors in this cohort were MSS/MSI-L strongly suggests that predominant non-EDMs (especially the high-frequency p.V1446fs3 variant) are not sufficient to drive the ultra-hypermutated phenotype classically associated with pathogenic EDMs. It is crucial to clarify that the MSI status and TMB are distinct biomarkers for immunotherapy, albeit sometimes overlapping. The response to immunotherapy in MSS/MSI-L tumors relies on whether the specific POLE mutation confers a sufficiently high TMB, not on MSI-H. Taskiran *et al*[6] did not report TMB data, which is a limitation. Previous studies have reported a spectrum of functional consequences for non-EDMs. For instance, some studies indicated that certain non-EDMs are associated with an intermediate or high TMB[25], potentially activating immune responses in an MSS background[24]. In contrast, other non-EDMs, like the majority of those reported by Taskiran *et al*[6], may not drive hypermutation as strongly as EDMs, and their effects may be contingent on the MMR context[24,26]. A study found that most non-EDMs were not associated with the characteristic genomic alterations of pathogenic POLE mutations[26]. Therefore, the potential for immunotherapy responsiveness is likely not a class effect of all non-EDMs but relies on the specific mutation and its functional impact, which must be empirically determined through TMB measurement and functional studies.

In terms of concomitant mutations, Taskiran *et al*[6] revealed specific co-mutation patterns in POLE-mutant CRC. *MLH3* (72.25%) and *MSH3* (72.25%) were the genes most frequently co-mutated with POLE mutations (especially non-EDMs), followed by *KRAS* (41.36%), *PIK3CA* (14.66%), *BRAF* (6.81%), *etc.* Among these, the functional relevance of co-mutations in MMR genes (*MLH3/MSH3*) and their potential synergistic effects with POLE deserve particular attention. The high co-occurrence of POLE mutations with *MLH3/MSH3* mutations suggests a potential "double-hit" or synergistic effect, where decreased DNA replication fidelity (due to POLE mutation) and impaired DNA mismatch repair capacity (due to *MLH3/MSH3* mutations) act together. This may further increase genomic instability and elevate TMB, potentially

affecting the biological behavior of the tumor and its response to treatment. One study indicated that the co-occurrence of POLE EDMs with mutations in MMR genes, including *MLH3* and *MSH3*, may be associated with higher TMB and an MSI-H phenotype[27]. Other studies have indicated that the POLE mutation spectrum is modulated by the properties of the mutant allele, its abundance, and MMR status, suggesting an interactive mechanism between POLE and the MMR system[28]. Furthermore, studies have confirmed the association of *MSH4* mutations with the MSI-H phenotype[29], supporting the notion that mutations in non-core MMR genes can also lead to MSI.

Equally critical are co-mutations in oncogenic drivers (*KRAS*, *PIK3CA*, and *BRAF*), which directly affect signaling pathways and therapeutic targeting. *KRAS*, *PIK3CA*, and *BRAF* are common oncogenic drivers of CRC. They regulate the mitogen-activated protein kinase and phosphatidylinositol 3-kinase (PI3K) and protein kinase B (AKT) signaling pathways, respectively, which play central roles in cell proliferation, differentiation, survival, and metabolism[30,31]. Studies have confirmed that significantly more MSI-H or TMB-high samples are found in subgroups with *RAS/BRAF* alterations[32]. The co-occurrence of POLE mutations with mutations in these key signaling genes suggests that POLE-mutant tumors might be driven by both DNA repair defects and the activation of oncogenic signaling pathways. This complex molecular background not only affects tumor aggressiveness and metastatic potential but also has complex implications for responses to targeted therapy and immunotherapy. For instance, *KRAS* mutations typically predict resistance to epidermal growth factor receptor (EGFR) inhibitors, while the *BRAF* V600E mutation is associated with poor prognosis. Here, specific combinations (e.g., *BRAF* inhibitor + EGFR inhibitor ± mitogen-activated extracellular signal-regulated kinase inhibitor) have shown clinical application potential[33]. *PIK3CA* mutations may suggest sensitivity to PI3K/AKT/mammalian target of rapamycin pathway inhibitors. Therefore, understanding the presence of these concomitant mutations in the context of the POLE mutation is crucial for developing individualized treatment strategies.

Finally, other notable co-mutations (e.g., *TP53*) add further complexity to the molecular landscape. The co-mutation analysis by Taskiran *et al*[6] revealed mutations in several other genes beyond the core MMR and signaling pathways, including *PMS2*, *MSH6*, *ERCC5*, *TCF7 L2*, and the critical tumor suppressor *TP53*. For instance, inactivation of *TP53* is a well-established driver that can accelerate tumor progression[34]. To succinctly summarize the key co-mutation patterns and their implications, we have compiled them in Table 1. Collectively, the combination of multiple gene mutations detailed in Table 1 suggests that POLE-mutant CRC is not driven by a single genetic event but is regulated by a complex molecular network, where defects in DNA replication and repair (POLE, MMR genes) may establish genomic instability, which then cooperates with activated oncogenic pathways (*KRAS*, *PIK3CA*, *BRAF*) and loss of tumor suppressors (*TP53*) to drive tumorigenesis and shape clinical behavior. Insights from tumor evolution studies indicate that defects in DNA replication and repair (e.g., POLE and MMR genes) may establish a permissive genomic landscape that precedes and facilitates the acquisition of driver alterations in signaling pathways[35]. Future work involving functional experiments and larger clinical cohorts is needed to decipher the interplay between these co-mutation events and their overall impact on clinical outcomes.

A notable limitation of the study by Taskiran *et al*[6], which compared POLE mutation subtypes, is the limited number of EDM cases (only 2), hindering a meaningful comparison of MSI status distribution or co-mutation patterns between EDMs and non-EDMs. Therefore, future studies with larger sample sizes, particularly those including sufficient EDM cases, are needed to clarify the precise relationship between POLE mutation types and MSI status.

THE POTENTIAL AND CHALLENGES OF POLE NON-EXONUCLEASES DOMAIN MUTATIONS IN THE PRECISION DIAGNOSIS AND TREATMENT OF CRC

Taskiran *et al*[6] provided an in-depth analysis of POLE mutations in a Turkish CRC cohort, with a particular focus on understudied non-EDMs. This work advances the field of precision oncology in CRC by highlighting novel research avenues. A key implication is that POLE non-EDMs, especially variants like p.V1446fs3, may be present at remarkably high frequencies in specific populations. It is important to note that a high TMB, which can be driven by DNA replication repair deficiencies, has been established as a predictive biomarker for response to immunotherapy independent of the MSI status. This provides a mechanistic rationale for exploring immunotherapy in MSS/MSI-L CRCs harboring specific, functionally impactful POLE mutations. These mutations often co-occur with specific MSI statuses (predominantly MSI-L or MSS) and distinct co-mutation profiles involving genes such as *MLH3*, *MSH3*, *KRAS*, *PIK3CA*, and *BRAF*. Collectively, these findings make POLE non-EDMs potential biomarkers with an active role in the pathogenesis of CRC, moving beyond the concept of mere “bystander” mutations.

This perspective is gaining formal recognition in the field. A recent comprehensive review on predictive biomarkers for immunotherapy in CRC explicitly categorized POLE/*POLD1* mutations alongside dMMR as one of the few currently established biomarkers[36]. From a biomarker perspective, if validated, POLE non-EDMs that are correlated with specific clinicopathological features, prognosis, or treatment responses (such as to immunotherapy), particularly variants with functional impact, hold significant clinical value. While POLE EDMs are well-established biomarkers for high TMB and sensitivity to ICIs[17,20], it remains crucial to determine whether non-EDMs confer similar or distinct immunomodulatory effects. Emerging clinical evidence supports this potential. For instance, a recent study on neoadjuvant immunotherapy in locally advanced CRC reported that patients with POLE mutations achieved pathological complete response or clinical complete response[37]. Though preliminary, this finding provides direct clinical support for the immunogenicity of POLE-mutant tumors, including those with non-EDMs. In the study conducted by Taskiran *et al*[6], most POLE-mutant cases were pMMR/MSI-L, a subgroup that typically responds well to conventional chemotherapy but gains limited benefit from ICI monotherapy. Using POLE non-EDMs to identify an ICI-benefitting subset in this population can markedly expand the application of immunotherapy in CRC. Moreover, the frequent co-occurrence of

Table 1 Key co-mutation partners in polymerase epsilon-mutant colorectal cancer and their potential clinical relevance

Co-mutated gene	Functional category	Potential biological consequence	Potential clinical relevance
<i>MLH3/MSH3</i>	DNA mismatch repair (accessory proteins)	Potential synergistic (“double-hit”) effect on genomic instability with POLE mutations; may further elevate tumor mutational burden[27,35]	Requires validation; may identify a subset with enhanced response to ICIs[27]
<i>KRAS</i>	Oncogenic signaling (MAPK pathway)	Constitutive activation of proliferation/survival signals[30]	Suggests resistance to anti-EGFR therapy[30]; may necessitate <i>KRAS</i> -targeted strategies (e.g., <i>KRAS</i> G12C inhibitors)
<i>PIK3CA</i>	Oncogenic signaling (PI3K/AKT pathway)	Activation of growth and metabolic pathways[31]	Potential sensitivity to PI3K/AKT/mTOR pathway inhibitors (in research settings)[31]
<i>BRAF</i>	Oncogenic signaling (MAPK pathway)	Constitutive MAPK pathway activation; often associated with specific subtypes[30,32]	<i>BRAF</i> V600E mutation confers poor prognosis; may guide use of <i>BRAF</i> /EGFR/MEK inhibitor combinations[33]
<i>TP53</i>	Tumor suppressor	Loss of cell cycle control and apoptosis; promotes genomic instability[34]	Associated with tumor progression and worse prognosis; a common event in advanced CRC[34]

The clinical relevance summarized here is primarily hypothetical and based on the established roles of these genes in colorectal cancer biology and general therapeutic principles. Prospective clinical validation is required to confirm these associations in the specific context of polymerase epsilon-mutant colorectal cancer. MAPK: Mitogen-activated protein kinase; PI3K: Phosphatidylinositol 3-kinase; AKT: Protein kinase B; POLE: Polymerase epsilon; ICI: Immune checkpoint inhibitor; EGFR: Epidermal growth factor receptor; mTOR: Mammalian target of rapamycin; MEK: Mitogen-activated extracellular signal-regulated kinase; CRC: Colorectal cancer.

POLE mutations, including non-EDMs, with driver mutations in genes such as *KRAS*, *PIK3CA*, and *BRAF* strengthens the rationale for combination therapies. The combination of ICIs may target neoantigens arising from POLE-driven genomic instability, with targeted agents against coexisting driver alterations. This strategy may yield synergistic antitumor effects and help overcome treatment resistance. However, it is crucial to emphasize that clinical evidence supporting the use of non-EDMs to guide therapy, particularly immunotherapy, is currently limited and largely hypothetical. Therefore, our conclusions regarding personalized treatment must be tempered. Prospective clinical trials that stratify patients based on specific, functionally validated POLE non-EDMs are unequivocally needed to definitively establish their predictive value for treatment outcomes, especially for immunotherapy.

However, several challenges impede the translation of POLE non-EDMs, as biomarkers, into clinical practice. Specifically, functional validation is necessary to distinguish driver mutations from passive bystanders. Although Taskiran *et al*[6] reported a high frequency of non-EDMs, it did not provide direct evidence of their functional impact. Future studies should adopt a multi-locus molecular profiling approach, as exemplified by a recent study of a *POLD1* variant carrier. In that work, sequencing multiple independent tumors and polyps from affected individuals consistently revealed hypermutation and specific mutational signatures, providing compelling evidence for the variant’s pathogenicity[38]. This model underscores the need for applying similar and rigorous molecular analyses to prevalent non-EDMs like p.V1446fs3. The frameshift mutation p.V1446fs3 is expected to result in a truncated protein and loss of function; however, its precise molecular mechanisms and biological impacts necessitate further *in vitro* and *in vivo* functional experiments. Second, issues of population specificity and generalizability remain considerable, and the high frequency of p.V1446fs3 observed in this Turkish cohort may not be replicated in other ethnic or geographic populations. Large-scale, multi-center, prospective studies are needed to validate these findings and determine which non-EDMs represent genuine, recurrent driver mutations. Third, standardized detection methods are essential. To ensure accurate identification of all types of POLE mutations, including non-EDMs, we recommend the use of high-quality, comprehensive next-generation sequencing panels that cover the entire coding region of the POLE gene. Wet-lab protocols must ensure sufficiently high and uniform coverage depth to reliably call mutations[39]. Bioinformatic pipelines rely on rigorous benchmarking and calibration to ensure robust detection of SNVs, with particular emphasis on insertion/deletion (indel) mutations (e.g., p.V1446fs3), which are known to be error-prone in standard variant-calling workflows[40, 41]. Integrating cost-effective, standardized POLE testing into existing CRC molecular diagnostic workflows represents an important future step. Notably, ongoing research into deep learning models that predict the MSI status and POLE mutations based on routine histological slides[42] offers a novel and promising screening approach. Finally, clinical interpretation and decision-making present a major hurdle. Even after confirming the functional and predictive value of non-EDMs, interpreting their significance in complex clinical contexts and formulating optimal treatment strategies necessitates extensive real-world data, potentially supported by multi-omics integration and artificial intelligence-driven decision support systems.

Future studies on POLE non-EDMs should focus on several key areas. First, using molecular, cellular, and animal models, functional and mechanistic studies are needed to systematically evaluate how various non-EDM variants affect POLE protein function, cellular phenotype, and tumorigenesis. Second, large-scale clinical cohort studies that integrate comprehensive clinical, pathological, treatment response, and survival data from diverse patients with POLE-mutant CRC are pivotal to definitively establish the prognostic and predictive value of non-EDMs. Third, it is critical to explore novel therapeutic strategies by identifying synthetic lethal interactions for POLE-deficient tumors and optimizing combination regimens of ICIs with chemotherapy, targeted therapy, or radiotherapy. Finally, by determining their

correlation with CRC risk, researchers should investigate the role of specific POLE mutation signatures in early detection and prevention, which may improve early warning and risk stratification. Notably, the updated Chinese Society of Clinical Oncology guidelines have strengthened the recommendation for POLE testing, underscoring its growing clinical relevance[43]. This shift highlights the need for integrating comprehensive POLE sequencing, including non-EDM regions, into standard molecular diagnostics to guide personalized therapy in CRC.

CONCLUSION

The study by Taskiran *et al*[6] opened a window into the complexity and potential significance of POLE non-EDMs in CRC. Despite the considerable challenges ahead, continued exploration in this field promises to advance precision diagnosis and treatment for patients with CRC. As the study itself emphasizes, functional validation and multi-center collaboration are essential in the next step.

FOOTNOTES

Author contributions: Xu JJ, Ni CX and Xu JJ (corresponding author) contributed to this paper; Xu JJ (corresponding author) was responsible for the manuscript's intellectual direction, from the initial overall concept and outline to the specific discussion; Xu JJ and Ni CX contributed to the writing, editing the manuscript, and review of literature.

Supported by the Scientific Research Fund of Tai'an Science and Technology Agency, No. 2019NS180.

Conflict-of-interest statement: The authors declare that they have no conflict of interest.

Open Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

Country of origin: China

ORCID number: Jia-Ju Xu 0009-0000-4128-1003; Chun-Xiao Ni 0009-0000-0185-1534; Jia-Ju Xu 0000-0002-3633-0920.

S-Editor: Fan M

L-Editor: A

P-Editor: Wang CH

REFERENCES

- 1 Wu Q, Luo Y, Zhang S, Xie X. The Clinicopathological Characteristics of POLE-mutated Colorectal Cancer and the Prognostic Value of POLE Status. *Clin Oncol (R Coll Radiol)* 2023; **35**: e563-e565 [RCA] [PMID: 37286436 DOI: 10.1016/j.clon.2023.05.015] [FullText]
- 2 Sameer AS. Colorectal cancer: molecular mutations and polymorphisms. *Front Oncol* 2013; **3**: 114 [RCA] [PMID: 23717813 DOI: 10.3389/fonc.2013.00114] [FullText] [Full Text(PDF)]
- 3 Forgó E, Gomez AJ, Steiner D, Zehnder J, Longacre TA. Morphological, immunophenotypical and molecular features of hypermutation in colorectal carcinomas with mutations in DNA polymerase ε (POLE). *Histopathology* 2020; **76**: 366-374 [RCA] [PMID: 31479159 DOI: 10.1111/his.13984] [FullText]
- 4 Favre L, Cohen J, Calderaro J, Pécriaux A, Nguyen CT, Bourgoin R, Larnaudie L, Dupuy A, Ollier M, Lechapt E, Sloma I, Tournigand C, Rousseau B, Pujals A. High prevalence of unusual KRAS, NRAS, and BRAF mutations in POLE-hypermutated colorectal cancers. *Mol Oncol* 2022; **16**: 3055-3065 [RCA] [PMID: 35624529 DOI: 10.1002/1878-0261.13257] [FullText] [Full Text(PDF)]
- 5 Arora S, Xiu J, Sohal D, Lou E, Goldberg RM, Weinberg BA, Grothey A, Korn WM, Khushman M, Shields AF, Marshall J, Hall MJ. The landscape of POLE variants in colorectal and endometrial tumors: Correlation with microsatellite instability (MSI) and tumor mutation burden (TMB). *J Clin Oncol* 2020; **38**: e13538 [RCA] [DOI: 10.1200/jco.2020.38.15_suppl.e13538] [FullText]
- 6 Taskiran I, Orenay-Boyacioglu S, Boyacioglu O, Erdogdu IH, Culhaci N, Meteoglu I. DNA polymerase epsilon-mutant colorectal cancers: Insights into non-exonuclease domain mutation variants, microsatellite instability status, and co-mutation profiles. *World J Gastroenterol* 2025; **31**: 112524 [RCA] [PMID: 41356525 DOI: 10.3748/wjg.v31.i44.112524] [FullText] [Full Text(PDF)]
- 7 Chaabouni N, Vroobel K, Attygalle A, Proszek P, Johnson L, Smalley M, Shaikh R, Lalondrelle S, Taylor A, George AJ. Pole mutated endometrial carcinoma: Clinical and genomic characteristics from a real-world UK cohort. *J Clin Oncol* 2024; **42**: e17600 [DOI: 10.1200/jco.2024.42.16_suppl.e17600] [FullText]
- 8 Fang H, Barbour JA, Poulos RC, Katainen R, Aaltonen LA, Wong JWH. Mutational processes of distinct POLE exonuclease domain mutants drive an enrichment of a specific TP53 mutation in colorectal cancer. *PLoS Genet* 2020; **16**: e1008572 [RCA] [PMID: 32012149 DOI: 10.1371/journal.pgen.1008572] [FullText] [Full Text(PDF)]
- 9 Nasrollahi E, Wang S, Yanes R, Gonzalez Gomez C, Magge T, Overacre A, Hsieh R, Mcfarquhar A, Tatsuoka C, Singhi A, Saeed A, Sahin IH. A Comprehensive Molecular and Clinical Study of Patients with Young-Onset Colorectal Cancer. *Cancers (Basel)* 2025; **17**: 2763 [RCA] [PMID: 40940860 DOI: 10.3390/cancers17172763] [FullText] [Full Text(PDF)]

- 10 **Hino H**, Shiomi A, Kusuhara M, Kagawa H, Yamakawa Y, Hatakeyama K, Kawabata T, Oishi T, Urakami K, Nagashima T, Kinugasa Y, Yamaguchi K. Clinicopathological and mutational analyses of colorectal cancer with mutations in the POLE gene. *Cancer Med* 2019; **8**: 4587-4597 [RCA] [PMID: 31240875 DOI: 10.1002/cam4.2344] [FullText] [Full Text(PDF)]
- 11 **Le DT**, Durham JN, Smith KN, Wang H, Bartlett BR, Aulakh LK, Lu S, Kemberling H, Wilt C, Luber BS, Wong F, Azad NS, Rucki AA, Laheru D, Donehower R, Zaheer A, Fisher GA, Crocenzi TS, Lee JJ, Greten TF, Duffy AG, Ciombor KK, Eyring AD, Lam BH, Joe A, Kang SP, Holdhoff M, Danilova L, Cope L, Meyer C, Zhou S, Goldberg RM, Armstrong DK, Bever KM, Fader AN, Taube J, Housseau F, Spetzler D, Xiao N, Pardoll DM, Papadopoulos N, Kinzler KW, Eshleman JR, Vogelstein B, Anders RA, Diaz LA Jr. Mismatch repair deficiency predicts response of solid tumors to PD-1 blockade. *Science* 2017; **357**: 409-413 [RCA] [PMID: 28596308 DOI: 10.1126/science.aan6733] [FullText]
- 12 **Stenzinger A**, Pfarr N, Endris V, Penzel R, Jansen L, Wolf T, Herpel E, Warth A, Klauschen F, Kloor M, Roth W, Bläker H, Chang-Claude J, Brenner H, Hoffmeister M, Weichert W. Mutations in POLE and survival of colorectal cancer patients--link to disease stage and treatment. *Cancer Med* 2014; **3**: 1527-1538 [RCA] [PMID: 25124163 DOI: 10.1002/cam4.305] [FullText] [Full Text(PDF)]
- 13 **Guo Y**, Guo XL, Wang S, Chen X, Shi J, Wang J, Wang K, Klempner SJ, Wang W, Xiao M. Genomic Alterations of NTRK, POLE, ERBB2, and Microsatellite Instability Status in Chinese Patients with Colorectal Cancer. *Oncologist* 2020; **25**: e1671-e1680 [RCA] [PMID: 32627883 DOI: 10.1634/theoncologist.2020-0356] [FullText] [Full Text(PDF)]
- 14 **Zhang X**, Wang X, Xin Y, Bai Y, Li J, Shen L. Clinicopathological and genomic characteristics of POLE-mutated colorectal cancer in a Chinese population. *J Clin Oncol* 2021; **39**: e15531 [RCA] [DOI: 10.1200/jco.2021.39.15_suppl.e15531] [FullText]
- 15 **Domingo E**, Freeman-Mills L, Rayner E, Glaire M, Briggs S, Vermeulen L, Fessler E, Medema JP, Boot A, Morreau H, van Wezel T, Liefers GJ, Lothe RA, Danielsen SA, Sveen A, Nesbakken A, Zlobec I, Lugli A, Koelzer VH, Berger MD, Castellví-Bel S, Muñoz J; Epicolon consortium, de Bruyn M, Nijman HW, Novelli M, Lawson K, Oukrif D, Frangou E, Dutton P, Tejpar S, Delorenzi M, Kerr R, Kerr D, Tomlinson I, Church DN. Somatic POLE proofreading domain mutation, immune response, and prognosis in colorectal cancer: a retrospective, pooled biomarker study. *Lancet Gastroenterol Hepatol* 2016; **1**: 207-216 [RCA] [PMID: 28404093 DOI: 10.1016/S2468-1253(16)30014-0] [FullText]
- 16 **Oh H**, Jang I, Hwang J, Lee S, An J, Sim J. Clinicopathologic Analysis of Five Patients with POLE-Mutated Colorectal Cancer in a Single Korean Institute. *Diagnostics (Basel)* 2025; **15**: 972 [RCA] [PMID: 40310397 DOI: 10.3390/diagnostics15080972] [FullText]
- 17 **Oh CR**, Kim JE, Hong YS, Kim SY, Ahn JB, Baek JY, Lee MA, Kang MJ, Cho SH, Beom SH, Kim TW. Phase II study of durvalumab monotherapy in patients with previously treated microsatellite instability-high/mismatch repair-deficient or POLE-mutated metastatic or unresectable colorectal cancer. *Int J Cancer* 2022; **150**: 2038-2045 [RCA] [PMID: 35179785 DOI: 10.1002/ijc.33966] [FullText]
- 18 **Kawai T**, Nyuya A, Mori Y, Tanaka T, Tanioka H, Yasui K, Toshima T, Taniguchi F, Shigeyasu K, Umeda Y, Fujiwara T, Okawaki M, Yamaguchi Y, Goel A, Nagasaka T. Clinical and epigenetic features of colorectal cancer patients with somatic POLE proofreading mutations. *Clin Epigenetics* 2021; **13**: 117 [RCA] [PMID: 34034807 DOI: 10.1186/s13148-021-01104-7] [FullText] [Full Text(PDF)]
- 19 **Li X**, Tang C, Zhang H, Zhou Z, Ma J, Yuan X, Zhong Z, Chen J, Peng H, Zhang C. Ultra-Hypermutation Driven by POLE Mutation in Metastatic Colorectal Cancer: A Case for Immunotherapy Without dMMR. 2024 Preprint [DOI: 10.21203/rs.3.rs-5450020/v1] [FullText]
- 20 **Ambrosini M**, Rousseau B, Manca P, Artz O, Marabelle A, André T, Maddalena G, Mazzoli G, Intini R, Cohen R, Cercek A, Segal NH, Saltz L, Varghese AM, Yaeger R, Nusrat M, Goldberg Z, Ku GY, El Dika I, Margalit O, Grinshpun A, Murtaza Kasi P, Schilsky R, Lutfi A, Shacham-Shmueli E, Khan Afghan M, Weiss L, Westphalen CB, Conca V, Decker B, Randon G, Elez E, Fakih M, Schrock AB, Cremolini C, Jayachandran P, Overman MJ, Lonardi S, Pietrantonio F. Immune checkpoint inhibitors for POLE or POLD1 proofreading-deficient metastatic colorectal cancer. *Ann Oncol* 2024; **35**: 643-655 [RCA] [PMID: 38777726 DOI: 10.1016/j.annonc.2024.03.009] [FullText]
- 21 **Meng X**, Wei L, Devbandari S, Zhang T, Xiang J, Remus D, Zhao X. DNA polymerase ϵ relies on a unique domain for efficient replisome assembly and strand synthesis. *Nat Commun* 2020; **11**: 2437 [RCA] [PMID: 32415104 DOI: 10.1038/s41467-020-16095-x] [FullText] [Full Text(PDF)]
- 22 **Jiang M**, Jia Y, Han J, Shi J, Su C, Zhang R, Xing M, Jin S, Zong H. Distinct clinical pattern of colorectal cancer patients with POLE mutations: A retrospective study on real-world data. *Front Genet* 2022; **13**: 963964 [RCA] [PMID: 36479248 DOI: 10.3389/fgene.2022.963964] [FullText]
- 23 **Wen L**, Chen Z, Ji X, Fong WP, Shao Q, Ren C, Cai Y, Li B, Yuan Y, Wang D, Li Y. Pathological complete response to immune checkpoint inhibitor in patients with colorectal cancer liver metastases harboring POLE exonuclease domain mutation. *J Immunother Cancer* 2022; **10**: e004487 [RCA] [PMID: 35793867 DOI: 10.1136/jitc-2022-004487] [FullText] [Full Text(PDF)]
- 24 **Chen YX**, Wang ZX, Yuan SQ, Jiang TJ, Huang YS, Xu RH, Wang F, Zhao Q. POLE/POLD1 mutation in non-exonuclease domain matters for predicting efficacy of immune-checkpoint-inhibitor therapy. *Clin Transl Med* 2021; **11**: e524 [RCA] [PMID: 34586735 DOI: 10.1002/ctm2.524] [FullText] [Full Text(PDF)]
- 25 **Gong J**, Wang C, Lee PP, Chu P, Fakih M. Response to PD-1 Blockade in Microsatellite Stable Metastatic Colorectal Cancer Harboring a POLE Mutation. *J Natl Compr Canc Netw* 2017; **15**: 142-147 [RCA] [PMID: 28188185 DOI: 10.6004/jnccn.2017.0016] [FullText]
- 26 **León-Castillo A**, Britton H, McConechy MK, McAlpine JN, Nout R, Kommos S, Brucker SY, Carlson JW, Epstein E, Rau TT, Bosse T, Church DN, Gilks CB. Interpretation of somatic POLE mutations in endometrial carcinoma. *J Pathol* 2020; **250**: 323-335 [RCA] [PMID: 31829442 DOI: 10.1002/path.5372] [FullText] [Full Text(PDF)]
- 27 **Ding J**, Patel N. 740 Biomarkers diverging between tumor mutation burden and microsatellite instability. *J Immunother Cancer* 2020; **8**: A786-787 [DOI: 10.1136/jitc-2020-site2020.0740] [FullText]
- 28 **Hodel KP**, Sun MJS, Ungerleider N, Park VS, Williams LG, Bauer DL, Immethun VE, Wang J, Suo Z, Lu H, McLachlan JB, Pursell ZF. POLE Mutation Spectra Are Shaped by the Mutant Allele Identity, Its Abundance, and Mismatch Repair Status. *Mol Cell* 2020; **78**: 1166-1177.e6 [RCA] [PMID: 32497495 DOI: 10.1016/j.molcel.2020.05.012] [FullText]
- 29 **Yang Y**, Jain RK, Glenn ST, Xu B, Singh PK, Wei L, Hu Q, Long M, Hutson N, Wang J, Battaglia S, George S. Complete response to anti-PD-L1 antibody in a metastatic bladder cancer associated with novel MSH4 mutation and microsatellite instability. *J Immunother Cancer* 2020; **8**: e000128 [RCA] [PMID: 32221012 DOI: 10.1136/jitc-2019-000128] [FullText] [Full Text(PDF)]
- 30 **Wang C**, Pan D. Mutation patterns and prognostic analysis of BRAF/KRAS/PIK3CA in colorectal cancer. *J Clin Lab Anal* 2022; **36**: e24444 [RCA] [PMID: 35435290 DOI: 10.1002/jcla.24444] [FullText] [Full Text(PDF)]
- 31 **Brinzan CS**, Aschie M, Cozaru GC, Deacu M, Dumitru E, Burlacu I, Mitroi A. KRAS, NRAS, BRAF, PIK3CA, and AKT1 signatures in colorectal cancer patients in south-eastern Romania. *Medicine (Baltimore)* 2022; **101**: e30979 [RCA] [PMID: 36221415 DOI: 10.1097/MD.00000000000030979] [FullText] [Full Text(PDF)]

- 32 **Schulze M**, Wang X, Hamad J, Hopkins JF, Hopkins JF, Scheuenpflug J, Feng Z. Abstract 2120: Exploring the genomic landscape of colorectal cancer for enabling clinical genomics informed and real-world data based clinical development. *Cancer Res* 2023; **83**: 2120 [DOI: 10.1158/1538-7445.AM2023-2120] [FullText]
- 33 **Fox DA**, Bhamidipati D, Kopetz S, Hong DS. Durable Remission After Targeted Therapy in BRAF V600E-Mutant Metastatic Colorectal Cancer: Case Report. *J Immunother Precis Oncol* 2025; **8**: 11-14 [RCA] [PMID: 39811421 DOI: 10.36401/JIPO-24-16] [FullText]
- 34 **Sclafani F**, Wilson SH, Cunningham D, Gonzalez De Castro D, Kalaitzaki E, Begum R, Wotherspoon A, Capdevila J, Glimelius B, Roselló S, Thomas J, Tait D, Brown G, Oates J, Chau I. Analysis of KRAS, NRAS, BRAF, PIK3CA and TP53 mutations in a large prospective series of locally advanced rectal cancer patients. *Int J Cancer* 2020; **146**: 94-102 [RCA] [PMID: 31199501 DOI: 10.1002/ijc.32507] [FullText]
- 35 **Chikaishi Y**, Matsuoka H, Sugihara E, Takeda M, Sumitomo M, Yamada S, Inaguma G, Omura Y, Cheong Y, Kobayashi Y, Nakauchi M, Hiro J, Masumori K, Otsuka K, Nishihara H, Suda K, Saya H, Takimoto T. Mutation Analysis of TMB-High Colorectal Cancer: Insights Into Molecular Pathways and Clinical Implications. *Cancer Sci* 2025; **116**: 1082-1093 [RCA] [PMID: 39822019 DOI: 10.1111/cas.16455] [Full Text] [Full Text(PDF)]
- 36 **Sahin IH**, Saridogan T, Kim R. Predictive biomarkers for immune checkpoint inhibition for patients with colorectal cancer: a comprehensive review. *Immunotherapy* 2025; **17**: 727-734 [RCA] [PMID: 40652318 DOI: 10.1080/1750743X.2025.2530853] [FullText] [Full Text(PDF)]
- 37 **Li Y**, Liang F, Li Z, Zhang X, Wu A. Neoadjuvant Immunotherapy for Patients With Microsatellite Instability-High or POLE-Mutated Locally Advanced Colorectal Cancer With Bulky Tumors: New Optimization Strategy. *Clin Colorectal Cancer* 2025; **24**: 18-31.e2 [RCA] [PMID: 39095269 DOI: 10.1016/j.clcc.2024.07.001] [FullText]
- 38 **Buchanan DD**, Georgeson P, Walker R, Joo JE, Clendenning M, Como J, O'Keeffe R, Prisc A, Chu YL, Jenkins MA, Rosty C, Winship IM, Macrae FA, Ip E, Harris R, Goodwin A, Mahmood K. The germline POLD1 c.1420 C > A (p.Leu474Ile) variant segregates with endometrial cancer, colorectal cancer and colonic polyps demonstrating hypermutation and defective POLD1 mutational signatures. *Fam Cancer* 2025; **24**: 82 [RCA] [PMID: 41212251 DOI: 10.1007/s10689-025-00506-3] [FullText]
- 39 **Choate LA**, Koleilat A, Harris K, Vidal-Folch N, Guenzel A, Newman J, Peterson BJ, Peterson SE, Rice CS, Train LJ, Hasadsri L, Marcou CA, Moyer AM, Baudhuin LM. Confirmation of Insertion, Deletion, and Deletion-Insertion Variants Detected by Next-Generation Sequencing. *Clin Chem* 2023; **69**: 1155-1162 [RCA] [PMID: 37566393 DOI: 10.1093/clinchem/hvad110] [FullText]
- 40 **SoRelle JA**, Wachsmann M, Cantarel BL. Assembling and Validating Bioinformatic Pipelines for Next-Generation Sequencing Clinical Assays. *Arch Pathol Lab Med* 2020; **144**: 1118-1130 [RCA] [PMID: 32045276 DOI: 10.5858/arpa.2019-0476-RA] [FullText]
- 41 **Wang N**, Lysenkov V, Orte K, Kairisto V, Aakko J, Khan S, Elo LL. Tool evaluation for the detection of variably sized indels from next generation whole genome and targeted sequencing data. *PLoS Comput Biol* 2022; **18**: e1009269 [RCA] [PMID: 35176018 DOI: 10.1371/journal.pcbi.1009269] [FullText] [Full Text(PDF)]
- 42 **Gustav M**, Reitsam NG, Carrero ZI, Loeffler CML, van Treeck M, Yuan T, West NP, Quirke P, Brinker TJ, Brenner H, Favre L, Märkl B, Stenzinger A, Brobeil A, Hoffmeister M, Calderaro J, Pujals A, Kather JN. Deep learning for dual detection of microsatellite instability and POLE mutations in colorectal cancer histopathology. *NPJ Precis Oncol* 2024; **8**: 115 [RCA] [PMID: 38783059 DOI: 10.1038/s41698-024-00592-z] [FullText]
- 43 **Wang F**, Chen G, Zhang Z, Yuan Y, Wang Y, Gao YH, Sheng W, Wang Z, Li X, Yuan X, Cai S, Ren L, Liu Y, Xu J, Zhang Y, Liang H, Wang X, Zhou A, Ying J, Li G, Cai M, Ji G, Li T, Wang J, Hu H, Nan K, Wang L, Zhang S, Li J, Xu RH. The Chinese Society of Clinical Oncology (CSCO): Clinical guidelines for the diagnosis and treatment of colorectal cancer, 2024 update. *Cancer Commun (Lond)* 2025; **45**: 332-379 [RCA] [PMID: 39739441 DOI: 10.1002/cac2.12639] [FullText] [Full Text(PDF)]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: <https://www.f6publishing.com/helpdesk>
<https://www.wjgnet.com>

