

# Gastroenterology

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Tridipitant, an NK1R antagonist, was found to be safe and effective in reducing nausea, vomiting and overall gastroparesis symptoms in patients with idiopathic and diabetic gastroparesis.

**Epidemiologic Burden and Treatment of Chronic Symptomatic Functional Bowel Disorders in the United States: A Nationwide Analysis***C. Ma, S. E. Congly, K. L. Novak, P. J. Bellettrutti, M. Raman, M. Woo, C. N. Andrews, and Y. Nasser*

This analysis of national-level survey data (2007-2015) identified over 4 million ambulatory encounters accounting for over \$350 million USD annually in clinic visits for chronic symptomatic functional bowel disorders. <20% of these visits were associated with non-pharmacological management strategies.

**Worldwide Prevalence and Burden of Functional Gastrointestinal Disorders, Results of Rome Foundation Global Study**

*A. D. Sperber, S. I. Bangdiwala, D. A. Drossman, U. C. Ghoshal, M. Simren, J. Tack, W. E. Whitehead, D. L. Dumitrescu, X. Fang, S. Fukudo, J. Kellow, E. Okeke, E. M. M. Quigley, M. Schmulson, P. Whorwell, T. Archampong, P. Adibi, V. Andresen, M. A. Benninga, B. Bonaz, S. Bor, L. B. Fernandez, S. C. Choi, E. S. Corazziari, C. Francisconi, A. Hani, L. Lazebnik, Y. Y. Lee, A. Mulak, M. M. Rahman, J. Santos, M. Setschedi, A. F. Syam, S. Vanner, R. K. Wong, A. Lopez-Colombo, V. Costa, R. Dickman, M. Kanazawa, A. H. Keshteli, R. Khatun, I. Maleki, P. Poitras, N. Pratap, O. Stefanyuk, S. Thomson, J. Zeevenhooven, and O. S. Palsson*

Functional gastrointestinal disorders, such as irritable bowel syndrome, are common worldwide, have negative effects on quality of life, and are a substantial economic burden; further research and new treatment strategies are needed.

**A Phase 1b Safety Study of SER-287, a Spore-Based Microbiome Therapeutic, for Active Mild to Moderate Ulcerative Colitis**

*M. R. Henn, E. J. O'Brien, L. Diao, B. G. Feagan, W. J. Sandborn, C. Huttenhower, J. R. Wortman, B. H. McGovern, S. Wang-Weigand, D. I. Lichter, M. Chafee, C. B. Ford, P. Bernardo, P. Zhao, S. Simmons, A. D. Tomlinson, D. N. Cook, R. J. Pomerantz, B. K. Misra, J. G. Auninš, and M. Trucksis*

The authors identified a community of bacteria that are reduced in the intestinal microbiomes of patients with UC but when given orally (in spore form) induces remission in about 40% of patients.

**From Birth to Overweight and Atopic Disease: Multiple and Common Pathways of the Infant Gut Microbiome**

*K. Vu, W. Lou, H. M. Tun, T. B. Konya, N. Morales-Lizcano, R. S. Chari, C. J. Field, D. S. Guttman, R. Mandal, D. S. Wishart, M. B. Azad, A. B. Becker, P. J. Mandhane, T. J. Moraes, D. L. Lefebvre, M. R. Sears, S. E. Turvey, P. Subbarao, J. A. Scott, and A. L. Kozyrskyj*

Being born by cesarean section or after prolonged labour increases the chance of developing allergies or obesity. Abnormalities in gut bacteria of babies, including finding *C difficile*, could be the reason for this.

**Fecal Microbiota Transplantation Reduces Symptoms in Some Patients With Irritable Bowel Syndrome With Predominant Abdominal Bloating: Short- and Long-term Results From a Placebo-Controlled Randomized Trial**

*T. Holvoet, M. Joossens, J. F. Vázquez-Castellanos, E. Christiaens, L. Heyerick, J. Boelens, B. Verhasselt, H. van Vlierberghe, M. De Vos, J. Raes, and D. De Looze*

**See editorial on page 15.**

FMT reduces symptoms in some patients with IBS, but effects decrease with time. Studies are needed to identify which patients are most likely to respond and which components of the fecal material are responsible for the therapeutic effects.

**Effects of Diet-Modulated Autologous Fecal Microbiota Transplantation on Weight Regain**

*E. Rinott, I. Youngster, A. Yaskolka Meir, G. Tsaban, H. Zelicha, A. Kaplan, D. Knights, K. Tuohy, F. Fava, M. U. Scholz, O. Ziv, E. Reuven, A. Tirosh, A. Rudich, M. Blüher, M. Stumvoll, U. Ceglarek, K. Clement, O. Koren, D. D. Wang, F. B. Hu, M. J. Stampfer, and I. Shai*

**See editorial on page 17.**

This study found that participants who lost weight on a healthy diet and were then fed capsules containing fecal material collected during the diet period for months after the maximal weight loss, regained less weight than participants given placebo tablets, by modulating the intestinal microbiota. A plant-based diet (in participants) or Mankai diet (in mice) produced the optimal fecal microbiome for preventing weight regain and for retaining glycemic control.

**174 Ambulatory Reflux Monitoring Guides Proton Pump Inhibitor Discontinuation in Patients****With Gastroesophageal Reflux Symptoms: A Clinical Trial**

R. Yadlapati, M. Masihi, C. P. Gyawali, D. A. Carlson, P. J. Kahrilas, B. D. Nix, A. Jain, J. R. Triggs, M. F. Vaezi, L. Kia, A. Kaizer, and J. E. Pandolino

See editorial on page 19.

Many patients with symptoms of heartburn and regurgitation will not find symptom relief with proton pump inhibitor therapy. Ambulatory reflux monitoring identifies patients that do not require ongoing therapy.

**183 Fecal Microbiota Transplantation Is Highly Effective in Real-World Practice: Initial Results****From the FMT National Registry**

C. R. Kelly, E. F. Yen, A. M. Grinspan, S. A. Kahn, A. Atreja, J. D. Lewis, T. A. Moore, D. T. Rubin, A. M. Kim, S. Serra, Y. Nersesova, L. Fredell, D. Hunsicker, D. McDonald, R. Knight, J. R. Allegretti, J. Pekow, I. Absah, R. Hsu, J. Vincent, S. Khanna, L. Tangen, C. V. Crawford, M. C. Mattar, L. A. Chen, M. Fischer, R. I. Arsenescu, P. Feuerstadt, J. Goldstein, D. Kerman, A. C. Ehrlich, G. D. Wu, and L. Laine

Approximately 90% of patients who undergo FMT for *C. difficile* infection can expect to be cured of the infection with few serious side effects due to FMT.

**Clinical—Liver****193 Effects of Early Placement of Transjugular Portosystemic Shunts in Patients With High-Risk****Acute Variceal Bleeding: a Meta-analysis of Individual Patient Data**

O. Nicoară-Farcău, G. Han, M. Rudler, D. Angrisani, A. Monescillo, F. Torres, G. Casanovas, J. Bosch, Y. Lv, D. Thabut, D. Fan, V. Hernández-Gea, and J. C. García-Pagán, on behalf of the Preemptive TIPS Individual Data Metanalysis, International Variceal Bleeding Study and Baveno Cooperation Study groups

This study analyzed data from 7 studies of high-risk patients with cirrhosis and acute variceal bleeding and found that preemptive placement of TIPS reduces the risk of death and controls bleeding and ascites better than treatment with drugs and endoscopy.

**206 Alterations in Gut Microbiome in Cirrhosis as Assessed by Quantitative Metagenomics:****Relationship With Acute-on-Chronic Liver Failure and Prognosis**

C. Solé, S. Guilly, K. Da Silva, M. Llopis, E. Le-Chatelier, P. Huelin, M. Carol, R. Moreira, N. Fabrellas, G. De Prada, L. Napoleone, I. Graupera, E. Pose, A. Juanola, N. Borruel, M. Berland, D. Toapanta, F. Casellas, F. Guarner, J. Doré, E. Solà, S. D. Ehrlich, and P. Ginès

Using metagenomics, we demonstrated that progression of cirrhosis, from compensated to decompensated cirrhosis and ACLF, is associated with parallel remarkable changes in gut-microbiome. Microbiome findings correlated with clinical outcomes, survival and functional changes.

**219 Efficacy and Safety of Aldafermin, an Engineered FGF19 Analog, in a Randomized, Double-Blind, Placebo-Controlled Trial of Patients With Nonalcoholic Steatohepatitis**

S. A. Harrison, G. Neff, C. D. Guy, M. R. Bashir, A. H. Paredes, J. P. Frias, Z. Younes, J. F. Trotter, N. T. Gunn, S. E. Moussa, A. Kohli, K. Nelson, M. Gottwald, W. C. G. Chang, A. Z. Yan, A. M. DePaoli, L. Ling, and H. D. Lieu

In this clinical trial, a drug called aldafermin reduced liver fat and markers of disease progression in patients with NASH, with no adverse side effects.

**Basic and Translational—Alimentary Tract****232 Transcription and DNA Methylation Patterns of Blood-Derived CD8<sup>+</sup> T Cells Are Associated With Age and Inflammatory Bowel Disease But Do Not Predict Prognosis**

M. Gasparetto, F. Payne, K. Nayak, J. Kraiczy, C. Glemas, Y. Philip-McKenzie, A. Ross, R. D. Edgar, D. R. Zerbino, C. Salvestrini, F. Torrente, N. T. Ventham, R. Kalla, J. Satsangi, P. Sarkies, R. Heuschkel, and M. Zilbauer

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The authors found that gene expression and DNA methylation patterns in immune cells do not correlate with outcomes of children and adults with IBD, and therefore do not currently support their use to determine prognosis.

**245 Expression of R-Spondin 1 in *Apc<sup>Min/+</sup>* Mice Suppresses Growth of Intestinal Adenomas by Altering Wnt and Transforming Growth Factor Beta Signaling**

*M. Lähde, S. Heino, J. Högström, S. Kaijalainen, A. Anisimov, D. Flanagan, P. Kallio, V.-M. Leppänen, A. Ristimäki, O. Ritvos, K. Wu, T. Tammela, M. Hodder, O. J. Sansom, and K. Alitalo*

RSPO1 protein reduces activity of a pathway that contributes to colorectal tumorigenesis. Administration of RSPO1 might slow or prevent intestinal adenoma development.

**260 DDIT4 Licenses Only Healthy Cells to Proliferate During Injury-induced Metaplasia**

*Z.-F. Miao, J.-X. Sun, M. Adkins-Threats, M.-J. Pang, J.-H. Zhao, X. Wang, K.-W. Tang, Z.-N. Wang, and J. C. Mills*

Regulation of the key cell energy protein complex, mTORC1, may be critical in understanding how mature cells that become temporary stem cells to repair injury (a process called metaplasia) can sometimes mutate to become tumor cells.

**272 Population-Level Configurations of Gut Mycobiome Across 6 Ethnicities in Urban and Rural China**

*Y. Sun, T. Zuo, C. P. Cheung, W. Gu, Y. Wan, F. Zhang, N. Chen, H. Zhan, Y. K. Yeoh, J. Niu, Y. Du, F. Zhang, Y. Wen, J. Yu, J. J. Y. Sung, P. K. S. Chan, F. K. L. Chan, K. Wang, S. C. Ng, and Y. Miao*

The human gut fungal composition is greatly individual-specific and varies across populations. Urbanization could shift the gut fungal structure.

**287 Intestinal Inflammation Modulates the Expression of ACE2 and TMPRSS2 and Potentially Overlaps With the Pathogenesis of SARS-CoV-2-related Disease**

*M. Suárez-Fariñas, M. Tokuyama, G. Wei, R. Huang, A. Livanos, D. Jha, A. Levescot, H. Irizar, R. Kosoy, S. Cording, W. Wang, B. Losic, R. C. Ungaro, A. Di'Narzo, G. Martínez-Delgado, M. Suprun, M. J. Corley, A. Stojmirovic, S. M. Houten, L. Peters, M. Curran, C. Brodmerek, J. Perrigoue, J. R. Friedman, K. Hao, E. E. Schadt, J. Zhu, H. M. Ko, J. Cho, M. C. Dubinsky, B. E. Sands, L. Ndhlovu, N. Cerf-Bensussan, A. Kasarskis, J.-F. Colombel, N. Harpaz, C. Argmann, and S. Mehandru*

Common IBD medications have complex and region-specific effect on SARS-CoV-2 receptors, ACE2 and TMPRSS2, in the intestines. Overlapping immune response signatures in COVID-19 patients and IBD patients indicate a potential role for IBD medications in the treatment of COVID-19.

**302 Interleukin 33 Triggers Early Eosinophil-Dependent Events Leading to Metaplasia in a Chronic Model of Gastritis-Prone Mice**

*C. De Salvo, L. Pastorelli, C. P. Petersen, L. F. Buttò, K.-A. Buela, S. Omenetti, S. A. Locovei, S. Ray, H. R. Friedman, J. Duijser, W. Xin, A. Osme, F. Cominelli, G. H. Mahabeleshwar, J. C. Mills, J. R. Goldenring, and T. T. Pizarro*

IL-33-activated eosinophils are important in the early cascade of events leading to intestinalized metaplasia in gastritis-prone mice, and represents a potential mechanism that promotes the inflammation-metaplasia-dysplasia-carcinoma sequelae.

**317 Elucidation of *Proteus mirabilis* as a Key Bacterium in Crohn's Disease Inflammation**

*J. Zhang, E. C. Hoedt, Q. Liu, E. Berendsen, J. J. Teh, A. Hamilton, A. W. O'Brien, J. Y. L. Ching, H. Wei, K. Yang, Z. Xu, S. H. Wong, J. W. Y. Mak, J. J. Y. Sung, M. Morrison, J. Yu, M. A. Kamm, and S. C. Ng*

*P. mirabilis* in the gut is associated with CD and can induce inflammation in cells and animal models of colitis. *P. mirabilis* may act as a pathobiont and play a crucial role in the pathogenesis of CD.

**Basic and Translational—Liver****331 Steatohepatitis Impairs T-cell-Directed Immunotherapies Against Liver Tumors in Mice**

*B. Heinrich, Z. J. Brown, L. P. Diggs, M. Vormehr, C. Ma, V. Subramanyam, U. Rosato, B. Ruf, J. S. Walz, J. C. McVey, S. Wabitsch, Q. Fu, S. J. Yu, Q. Zhang, C. W. Lai, U. Sahin, and T. F. Greten*

The authors found that fatty liver reduces the efficacy of immunotherapy against liver cancer, but that restoring immune cells to the liver can increase the efficacy of this treatment.

**Basic and Translational—Pancreas****346****Mesenchymal Plasticity Regulated by Prrx1 Drives Aggressive Pancreatic Cancer Biology**

*K. Feldmann, C. Maurer, K. Peschke, S. Teller, K. Schuck, K. Steiger, T. Engleitner, R. Öllinger, A. Nomura, N. Wirges, A. Papargyriou, R. S. Jahan Sarker, R. A. Ranjan, Z. Dantes, W. Weichert, A. K. Rustgi, R. M. Schmid, R. Rad, G. Schneider, D. Saur, and M. Reichert*

Prrx1 regulates dynamic changes in cell differentiation, so called plasticity, in cancer-associated fibroblasts (CAFs). By manipulating Prrx1-driven plasticity in CAFs pancreatic cancer biology is altered identifying CAF plasticity as potential therapeutic target.

**362****Targeting DNA Damage Response and Replication Stress in Pancreatic Cancer**

*S. B. Dreyer, R. Upstill-Goddard, V. Paulus-Hock, C. Paris, E.-M. Lampraki, E. Dray, B. Serrels, G. Caligiuri, S. Rebus, D. Plenker, Z. Galluzzo, H. Brunton, R. Cunningham, M. Tesson, C. Nourse, U.-M. Bailey, M. Jones, K. Moran-Jones, D. W. Wright, F. Duthie, K. Oien, L. Evers, C. J. McKay, G. A. McGregor, A. Gulati, R. Brough, I. Bajrami, S. Pettitt, M. L. Dziubinski, J. Candido, F. Balkwill, S. T. Barry, R. Grützmann, L. Rahib, Glasgow Precision Oncology Laboratory, Australian Pancreatic Cancer Genome Initiative, A. Johns, M. Pajic, F. E. M. Froeling, P. Beer, E. A. Musgrove, G. M. Petersen, A. Ashworth, M. C. Frame, H. C. Crawford, D. M. Simeone, C. Lord, D. Mukhopadhyay, C. Pilarsky, D. A. Tuveson, S. L. Cooke, N. B. Jamieson, J. P. Morton, O. J. Sansom, P. J. Bailey, A. V. Biankin, and D. K. Chang*

Some patients with pancreatic cancer cannot repair damaged DNA in the tumor, and we target this vulnerability using new therapies using new markers that predict response.

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*M. M. Leonard, B. Lebwohl, A. Rubio-Tapia, and F. Biagi*

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