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- 990** **Gastrointestinal and Extra-Intestinal Manifestations of IgG4-Related Disease**  
 (www) *K. Miyabe, Y. Zen, L. D. Cornell, G. Rajagopalan, V. R. Chowdhary, L. R. Roberts, and S. T. Chari*

## ORIGINAL RESEARCH

### Brief Reports

- 1004** **Effects of Prebiotics vs a Diet Low in FODMAPs in Patients With Functional Gut Disorders**  
 (E) (www) *J.-W. Huaman, M. Mego, C. Manichanh, N. Cañellas, D. Cañueto, H. Segurola, M. Jansana, C. Malagelada, A. Accarino, J. Vulevic, G. Tzortzis, G. Gibson, E. Saperas, F. Guarner, and F. Azpiroz*  
 See editorial on page 960.

A low FODMAP diet improved functional gut symptoms but the symptoms reappeared soon after discontinuation. A prebiotic supplementation produced similar reduction in symptoms but this persisted after discontinuation.

- 1008** **Gene Expression Signature for Prediction of Golimumab Response in a Phase 2a Open-Label Trial of Patients With Ulcerative Colitis**  
 (E) (www) *S. E. Telesco, C. Brodmerkel, H. Zhang, L. (Lee-Lian) Kim, J. Johanns, A. Mazumder, K. Li, F. Baribaud, M. Curran, R. Strauss, B. Paxson, S. Plevy, T. Davison, L. Knight, S. Dibben, S. Schreiber, W. Sandborn, P. Rutgeerts, C. A. Siegel, W. Reinisch, and L. E. Greenbaum*  
 See editorial on page 963.

This study prospectively evaluated a gene expression biomarker for prediction of golimumab response in a phase 2a open-label trial of ulcerative colitis patients, revealing several challenges to advancing precision medicine in IBD.

- 1012** **An FXR Agonist Reduces Bile Acid Synthesis Independently of Increases in FGF19 in Healthy Volunteers**  
 (www) *A. Al-Khaifi, M. Rudling, and B. Angelin*

Treating humans with the synthetic FXR agonist Px-102 demonstrates that suppression of BA synthesis is primarily induced by hepatic FXR activation, independent of circulating FGF19.

- 1017** **Chymotrypsin Reduces the Severity of Secretagogue-Induced Pancreatitis in Mice**  
 (www) *Z. Jancsó, E. Hegyi, and M. Sahin-Tóth*

The digestive enzyme chymotrypsin protects against the development of pancreatitis by reducing levels of the harmful digestive enzyme trypsin, which causes pancreatitis when activated inside the pancreas.

### Full Reports

#### Clinical—Alimentary Tract

- 1022** **Updated International Consensus Diagnostic Criteria for Eosinophilic Esophagitis: Proceedings of the AGREE Conference**  
 (www) *E. S. Dellon, C. A. Liacouras, J. Molina-Infante, G. T. Furuta, J. M. Spergel, N. Zevit, S. J. Spechler, S. E. Attwood, A. Straumann, S. S. Aceves, J. A. Alexander, D. Atkins, N. C. Arva, C. Blanchard, P. A. Bonis, W. M. Book, K. E. Capocelli, M. Chehade, E. Cheng, M. H. Collins, C. M. Davis, J. A. Dias, C. Di Lorenzo, R. Dohil, C. Dupont, G. W. Falk, C. T. Ferreira, A. Fox, N. P. Gonsalves, S. K. Gupta, D. A. Katzka, Y. Kinoshita, C. Menard-Katcher, E. Kodroff, D. C. Metz, S. Miehlke, A. B. Muir, V. A. Mukkada, S. Murch, S. Nurko, Y. Ohtsuka, R. Orel, A. Papadopoulou, K. A. Peterson, H. Philpott, P. E. Putnam, J. E. Richter, R. Rosen, M. E. Rothenberg, A. Schoepfer, M. M. Scott, N. Shah, J. Sheikh, R. F. Souza, M. J. Strobel, N. J. Talley, M. F. Vaezi, Y. Vandenplas, M. C. Vieira, M. M. Walker, J. B. Wechsler, B. K. Wershil, T. Wen, G.-Y. Yang, I. Hirano, and A. J. Bredenoord*

Proton pump inhibitor medications can be used as a treatment for esophageal eosinophilia due to EoE rather than as a requirement for diagnosis.

**1034 Fermentable Sugar Ingestion, Gas Production, and Gastrointestinal and Central Nervous System Symptoms in Patients With Functional Disorders**

*C. H. Wilder-Smith, S. S. Olesen, A. Materna, and A. M. Drewes*

Consuming sugars can cause gastrointestinal and central nervous system symptoms in patients with functional gastrointestinal disorders. Differing aspects of gut bacterial metabolism may underlie these groups of symptoms.

**1045 Efficacy of Ustekinumab for Inducing Endoscopic Healing in Patients With Crohn's Disease**

*P. Rutgeerts, C. Gasink, D. Chan, Y. Lang, P. Pollack, J.-F. Colombel, D. C. Wolf, D. Jacobstein, J. Johanns, P. Szapary, O. J. Adedokun, B. G. Feagan, and W. J. Sandborn*

Significant reductions in endoscopic disease activity were induced at week 8 with IV ustekinumab compared to placebo. Endoscopic improvement and reduction in endoscopic inflammation was better maintained at week 44 with SC ustekinumab than placebo.

**1059 Number of Adenomas Removed and Colorectal Cancers Prevented in Randomized Trials of Flexible Sigmoidoscopy Screening**

*P. F. Pinsky, M. Loberg, C. Senore, K. Wooldrage, W. Atkin, M. Bretthauer, A. J. Cross, G. Hoff, O. Holme, M. Kalager, N. Segnan, and R. E. Schoen*

Number Needed to Remove (NNR) is a proposed metric for assessing efficiency of adenoma removal in preventing colorectal cancer (CRC). An NNR of approximately 50 adenomas removed per CRC case prevented was estimated using data from 4 sigmoidoscopy screening trials.

**1069 Deep Learning Localizes and Identifies Polyps in Real Time With 96% Accuracy in Screening Colonoscopy**

*G. Urban, P. Tripathi, T. Alkayali, M. Mittal, F. Jalali, W. Karnes, and P. Baldi*

Deep Learning, a form of artificial intelligence, can be used to assist in screening colonoscopy procedures to assist in finding precancerous polyps in real-time and with high accuracy.

**1079 Sex-Based Differences in Incidence of Inflammatory Bowel Diseases—Pooled Analysis of Population-Based Studies From Western Countries**

*S. C. Shah, H. Khalili, C. Gower-Rousseau, O. Olen, E. I. Benchimol, E. Lyng, K. R. Nielsen, P. Brassard, M. Vutcovici, A. Bitton, C. N. Bernstein, D. Leddin, H. Tamim, T. Stefanesson, E. V. Loftus Jr, B. Moum, W. Tang, S. C. Ng, R. Gearry, B. Sincic, S. Bell, B. E. Sands, P. L. Lakatos, Z. Végh, C. Ott, G. G. Kaplan, J. Burisch, and J.-F. Colombel*

Using robust and comprehensive population data from Western countries, this study found clear sex-based differences in the incidence of Crohn's disease and ulcerative colitis according to the age of disease onset.

**1090 Misoprostol Heals Small Bowel Ulcers in Aspirin Users With Small Bowel Bleeding**

*M. H. Kyaw, K. Otani, J. Y. L. Ching, A. Higashimori, K. M. Kee, T. Watanabe, Y. K. Tse, V. Lee, T. Tanigawa, P. K. Cheong, B. Y. Suen, Y. Fujiwara, K. Lam, T. Arakawa, and F. K. L. Chan*

**See editorial on page 965.**

Misoprostol has been identified as a drug treatment for healing of small bowel ulcers in aspirin users complicated by small bowel bleeding.

**1098 Methotrexate Is Not Superior to Placebo in Maintaining Steroid-Free Response or Remission in Ulcerative Colitis**

*H. Herfarth, E. L. Barnes, J. F. Valentine, J. Hanson, P. D. R. Higgins, K. L. Isaacs, S. Jackson, M. T. Osterman, K. Anton, A. Ivanova, M. D. Long, C. Martin, R. S. Sandler, B. Abraham, R. K. Cross, G. Dryden, M. Fischer, W. Harlan, C. Levy, R. McCabe, S. Polyak, S. Saha, E. Williams, V. Yajnik, J. Serrano, B. E. Sands, and J. D. Lewis for the Clinical Research Alliance of the Crohn's and Colitis Foundation*

**See editorial on page 967.**

MTX may have limited efficacy to induce steroid-free response or remission in combination with a standardized steroid taper, but MTX was not better than placebo in preventing relapse in patients with UC.

## 1109 Efficacies of Genotypic Resistance-Guided vs Empirical Therapy for Refractory *Helicobacter pylori* Infection

J.-M. Liou, P.-Y. Chen, J.-C. Luo, J.-Y. Lee, C.-C. Chen, Y.-J. Fang, T.-H. Yang, C.-Y. Chang, M.-J. Bair, M.-J. Chen, Y.-C. Hsu, W.-F. Hsu, C.-C. Chang, J.-T. Lin, C.-T. Shun, E. M. El-Omar, and M.-S. Wu, on behalf of the Taiwan Gastrointestinal Disease and *Helicobacter* Consortium

Properly designed empirical therapy, based on medication history, is an acceptable alternative to genotypic resistance-guided therapy for eradication of refractory *H pylori* infection after consideration of accessibility, cost, and patient preference.

### Clinical—Liver

## 1120 Efficacy of Sofosbuvir and Velpatasvir, With and Without Ribavirin, in Patients With Hepatitis C Virus Genotype 3 Infection and Cirrhosis

R. Esteban, J. A. Pineda, J. L. Calleja, M. Casado, M. Rodríguez, J. Turnes, L. E. Morano Amado, R. M. Morillas, X. Fornis, J. M. Pascasio Acevedo, R. J. Andrade, A. Rivero, J. A. Carrión, S. Lens, M. Riveiro-Barciela, B. McNabb, G. Zhang, G. Camus, L. M. Stamm, D. M. Brainard, G. M. Subramanian, and M. Buti

See editorial on page 969.

After 12 weeks of treatment with sofosbuvir/velpatasvir with or without ribavirin, a high rate of patients with genotype 3 and compensated cirrhosis achieved an SVR12.

## 1128 No Association Between Screening for Hepatocellular Carcinoma and Reduced Cancer-Related Mortality in Patients With Cirrhosis

A. M. Moon, N. S. Weiss, L. A. Beste, F. Su, S. B. Ho, G.-Y. Jin, E. Lowy, K. Berry, and G. N. Ioannou

See editorial on page 972.

In a matched case-control study, HCC screening in cirrhotic patients with ultrasonography, AFP, or both was not associated with decreased HCC-related mortality.

## 1140 Simtuzumab Is Ineffective for Patients With Bridging Fibrosis or Compensated Cirrhosis Caused by Nonalcoholic Steatohepatitis

S. A. Harrison, M. F. Abdelmalek, S. Caldwell, M. L. Shiffman, A. M. Diehl, R. Ghalib, E. J. Lawitz, D. C. Rockey, R. A. Schall, C. Jia, B. J. McColgan, J. G. McHutchison, G. M. Subramanian, R. P. Myers, Z. Younossi, V. Ratziu, A. J. Muir, N. H. Afdhal, Z. Goodman, J. Bosch, and A. J. Sanyal, for the GS-US-321-0105 and GS-US-321-0106 Investigators

Patients with nonalcoholic steatohepatitis (NASH) develop liver fibrosis (scarring) that can lead to cirrhosis and liver failure. Simtuzumab did not reduce fibrosis in patients with NASH.

## 1154 Changing Trends in Etiology-Based Annual Mortality From Chronic Liver Disease, From 2007 Through 2016

D. Kim, A. A. Li, C. Gadiparthi, M. A. Khan, G. Cholankeril, J. S. Glenn, and A. Ahmed

A marked decline in hepatitis C virus infection-related national mortality was found following the introduction of direct-acting antiviral therapies in the United States. However, the mortality for alcoholic liver disease continues to rise in the time period from 2007-2016.

### Basic and Translational—Alimentary Tract

## 1164 Inhibiting RHOA Signaling in Mice Increases Glucose Tolerance and Numbers of Enteroendocrine and Other Secretory Cells in the Intestine

N. Petersen, T. M. Frimurer, M. Terndrup Pedersen, K. L. Egerod, N. J. Wewer Albrechtsen, J. J. Holst, A. Grapin-Botton, K. B. Jensen, and T. W. Schwartz

See editorial on page 974.

Inhibition of RhoA/ROCK increases L cell numbers and GLP1 secretion *in vitro* in intestinal organoids and in mice. A ROCK inhibitor increased glucose tolerance in insulin-resistant mice, demonstrating potential benefits in type 2 diabetes.

**1177 Diet Modifies Colonic Microbiota and CD4<sup>+</sup> T-Cell Repertoire to Induce Flares of Colitis in Mice With Myeloid-Cell Expression of Interleukin 23**

www

L. Chen, Z. He, A. C. Iuga, S. N. Martins Filho, J. J. Faith, J. C. Clemente, M. Deshpande, A. Jayaprakash, J.-F. Colombel, J. J. Laffaille, R. Sachidanandam, G. C. Furtado, and S. A. Lira

This study shows that alterations in the diet, intestinal microbiota, and IL23 signaling can contribute to pathogenesis of inflammatory bowel disease.

**1192 Vitamin D Regulation of the Uridine Phosphorylase 1 Gene and Uridine-Induced DNA Damage in Colon in African Americans and European Americans**

www

N. Bhasin, D. Alleyne, O. A. Gray, and S. S. Kupfer

This research identified decreased protective effect of vitamin D through actions on DNA repair in the colon in African Americans that could contribute to increased risk of colorectal cancer in this population.

**1205 Expression of CCR6 and CXCR6 by Gut-Derived CD4<sup>+</sup>/CD8 $\alpha$ <sup>+</sup> T-Regulatory Cells, Which Are Decreased in Blood Samples From Patients With Inflammatory Bowel Diseases**

www

E. Godefroy, J. Alameddine, E. Montassier, J. Mathé, J. Desfrancois-Noël, N. Marec, C. Bossard, A. Jarry, C. Bridonneau, A. Le Roy, G. Sarabayrouse, E. Kerdreux, A. Bourreille, H. Sokol, F. Jotereau, and F. Altare

CCR6 and CXCR6 co-expression by blood CD4<sup>+</sup>/CD8 $\alpha$ <sup>+</sup> T cells identifies *Faecalibacterium prausnitzii*-specific Treg cells of colon origin, which are markedly decreased in IBD.

**Basic and Translational—Liver****1218 Dysregulated Bile Transporters and Impaired Tight Junctions During Chronic Liver Injury in Mice**

v

www

T. Pradhan-Sundd, R. Vats, J. O. Russell, S. Singh, A. A. Michael, L. Molina, S. Kakar, P. Cornuet, M. Poddar, S. C. Watkins, K. N. Nejak-Bowen, S. P. Monga, and P. Sundd

Physical breach of blood-bile-barrier and impairment of bile transport in the liver contributes to chronic liver injury. Reestablishing the integrity of tight junctions and rescuing the expression of bile transporters attenuates liver injury.

**1233 Overexpression of Rac GTPase Activating Protein 1 Contributes to Proliferation of Cancer Cells by Reducing Hippo Signaling to Promote Cytokinesis**

e

www

X.-M. Yang, X.-Y. Cao, P. He, J. Li, M.-X. Feng, Y.-L. Zhang, X.-L. Zhang, Y.-H. Wang, Q. Yang, L. Zhu, H.-Z. Nie, S.-H. Jiang, G.-A. Tian, X.-X. Zhang, Q. Liu, J. Ji, X. Zhu, Q. Xia, and Z.-G. Zhang

See editorial on page 976.

RACGAP1 and the Hippo pathway displayed a novel interplay in promoting cytokinesis of HCC cells. RACGAP1 may be a potential tolerable and effective target for HCC therapy.

**Basic and Translational—Pancreas****1250 Transient High Pressure in Pancreatic Ducts Promotes Inflammation and Alters Tight Junctions via Calcineurin Signaling in Mice**

www

L. Wen, T. A. Javed, D. Yimlamai, A. Mukherjee, X. Xiao, and S. Z. Husain

Transiently high intraductal pressure causes pancreatitis by increasing inflammatory genes and disrupting tight junctions. An important mediator of pressure-induced pancreatitis is a calcium target molecule called calcineurin.

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