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 *K. Gottlieb, J. Requa, W. Karnes, R. Chandra Gudivada, J. Shen, E. Rael, V. Arora, T. Dao, A. Ninh, and J. McGill*

Machine reading of endoscopic videos in an ulcerative colitis clinical trial shows promise in replacing central readers with excellent machine-to-human interobserver agreement for UCEIS and endoscopic Mayo score

- 720 Evaluating Responses to Gluten Challenge: A Randomized, Double-Blind, 2-Dose Gluten Challenge Trial**

 *M. M. Leonard, J. A. Silvester, D. Leffler, A. Fasano, C. P. Kelly, S. K. Lewis, J. D. Goldsmith, E. Greenblatt, W. W. Kwok, W. J. McAuliffe, K. Galinsky, J. Siegelman, I.-T. Chow, J. A. Wagner, A. Sapone, and G. Smithson*

We explored the many ways to diagnose or to measure treatment impact in CeD. We found that IL-2 was best for measuring immediate reaction to gluten in patients with CeD on a gluten-free diet.

Clinical—Liver

- 734 Fibrates for Itch (FITCH) in Fibrosing Cholangiopathies: A Double-Blind, Randomized, Placebo-Controlled Trial**

 *E. de Vries, R. Bolier, J. Goet, A. Parés, J. Verbeek, M. de Vree, J. Drenth, K. van Erpecum, K. van Nieuwkerk, F. van der Heide, N. Mostafavi, J. Helder, C. Ponsioen, R. Oude Elferink, H. van Buuren, and U. Beuers, for the Netherlands Association for the Study of the Liver-Cholestasis Working Group*

See editorial on page 649.

Treatment of severe or moderate itch with bezafibrate over three weeks in patients with primary sclerosing cholangitis and primary biliary cholangitis was effective and safe.

Clinical—Pancreas

- 744 Worldwide Burden of, Risk Factors for, and Trends in Pancreatic Cancer**

 *J. Huang, V. Lok, C. H. Ngai, L. Zhang, J. Yuan, X. Q. Lao, K. Ng, C. Chong, Z.-J. Zheng, and M. C. S. Wong*

This study analyzed data from 48 countries and found an increasing incidence from pancreatic cancer worldwide, especially among women and people 50 years and older, but also among younger individuals.

Basic and Translational—Alimentary Tract

- 755 Combinatorial Transcriptional Profiling of Mouse and Human Enteric Neurons Identifies Shared and Disparate Subtypes In Situ**

 *A. A. May-Zhang, E. Tycksen, A. N. Southard-Smith, K. K. Deal, J. T. Benthal, D. P. Buehler, M. Adam, A. J. Simmons, J. R. Monaghan, B. K. Matlock, D. K. Flaherty, S. S. Potter, K. S. Lau, and E. M. Southard-Smith*

See editorial on page 651.

We generated a comprehensive transcriptional atlas of healthy, adult enteric neurons for humans and mice, discovered new neuron subtype markers, identified sex differences, and mapped regional variation of some neuron types in the intestine.

771 Prevalence and Effect of Genetic Risk of Thromboembolic Disease in Inflammatory Bowel Disease

T. Naito, G. J. Botwin, T. Haritunians, D. Li, S. Yang, M. Khrom, J. Braun, L. Abbou, E. Mengesha, C. Stevens, A. Masamune, M. Daly, and D. P. B. McGovern, and NIDDK IBD Genetics Consortium

Our analyses demonstrated that approximately 1 in 7 inflammatory bowel disease patients are at around 2.5 times higher risk of developing Thrombo-embolic disease.

781 PD-1 Signaling Promotes Tumor-Infiltrating Myeloid-Derived Suppressor Cells and Gastric Tumorigenesis in Mice

W. Kim, T. H. Chu, H. Nienhüser, Z. Jiang, A. Del Portillo, H. E. Remotti, R. A. White, Y. Hayakawa, H. Tomita, J. G. Fox, C. G. Drake, and T. C. Wang

This study identified mechanisms by which gastric tumors in mice escape the effects of a class of anti-tumor drugs called immune checkpoint inhibitors. The study identified cell types that can be depleted from tumors to increase the efficacy of these drugs.

797 Epithelial TLR4 Signaling Activates DUOX2 to Induce Microbiota-Driven Tumorigenesis

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809 Altered Intestinal ACE2 Levels Are Associated With Inflammation, Severe Disease, and Response to Anti-Cytokine Therapy in Inflammatory Bowel Disease

A. A. Potdar, S. Dube, T. Naito, K. Li, G. Botwin, T. Haritunians, D. Li, D. Casero, S. Yang, J. Bilsborough, J. G. Perrigoue, L. A. Denson, M. Daly, S. R. Targan, P. Fleshner, J. Braun, S. Kugathasan, T. S. Stappenbeck, and D. P. B. McGovern

Reduced SB, but elevated colonic ACE2 expression in IBD are associated with inflammation and severe disease but normalized following anti-cytokine therapy suggesting compartmentalization of ACE2-related biology in SB and colonic inflammation.

823 Wnt Signaling Shapes the Histologic Variation in Diffuse Gastric Cancer

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See editorial on page 653.

Human liver organoid (HLO) based screening system, termed LoT assay, will offer an opportunity to analyze cholestatic pathology specific to developing drugs and genetic susceptibility otherwise inaccessible at preclinical stage.

847 Regeneration Defects in Yap and Taz Mutant Mouse Livers Are Caused by Bile Duct Disruption and Cholestasis

E. Verboven, I. M. Moya, L. Sansores-Garcia, J. Xie, H. Hillen, W. Kowalczyk, G. Vella, S. Verhulst, S. A. Castaldo, A. Algueró-Nadal, L. Romanelli, C. Mercader-Celma, N. A. Souza, S. Soheily, L. Van Huffel, T. Van Brussel, D. Lambrechts, T. Roskams, F. P. Lemaigre, G. Bergers, L. A. van Grunsven, and G. Halder

Our study revealed that a major organ growth control pathway is not directly required for liver regeneration but identified a clinically important process that impairs liver regeneration.

CRIg⁺ Macrophages Prevent Gut Microbial DNA-Containing Extracellular Vesicle-Induced Tissue Inflammation and Insulin Resistance

Z. Luo, Y. Ji, H. Gao, F. C. Gomes Dos Reis, G. Bandyopadhyay, Z. Jin, C. Ly, Y.-j. Chang, D. Zhang, D. Kumar, and W. Ying

Gut microbiota extracellular vesicles can translocate through obese disrupted gut barrier. Liver CRIg⁺ macrophages can clear circulating microbiota-derived extracellular vesicles that exacerbate tissue inflammation and insulin resistance in obesity.

Basic and Translational—Pancreas

875 Pancreatic β -Cells Communicate With Vagal Sensory Neurons



M. Makhmutova, J. Weitz, A. Tamayo, E. Pereira, M. Boulina, J. Almaça, R. Rodriguez-Diaz, and A. Caicedo

Our study established that insulin secreting beta cell of the pancreas communicate with sensory neurons of the vagus nerve, which in turns relay this information to the brain.

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S. O. Aseem, N. Jalan-Sakrikar, C. Chi, A. Navarro-Corcuera, T. M. De Assuncao, F. H. Hamdan, S. Chowdhury, J. M. Banales, S. A. Johnsen, V. H. Shah, and R. C. Huebert

Using combined epigenomic and transcriptomic approaches, this study defines an epigenetic mechanism downstream of TGF β that mediates the transcription of a fibrogenic gene network in cholangiocytes.

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