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See editorial on page 1053.

In achalasia, patients with persistent or recurrent symptoms after laparoscopic Heller myotomy, per-oral endoscopic myotomy resulted in a significantly higher success rate than pneumatic dilation, with a numerically higher incidence of grade A-B reflux esophagitis.

Stomach**1119 SOX9 Modulates the Transformation of Gastric Stem Cells Through Biased Symmetric Cell Division***Q. Chen, K. Weng, M. Lin, M. Jiang, Y. Fang, S. S. W. Chung, X. Huang, Q. Zhong, Z. Liu, Z. Huang, J. Lin, P. Li, W. El-Rifai, A. Zaika, H. Li, A. K. Rustgi, H. Nakagawa, J. A. Abrams, T. C. Wang, C. Lu, C. Huang, and J. Que*

See editorial on page 1052.

This study used a novel mouse model to define a key factor and the underlying mechanism that modulates the transformation of gastric progenitor cells to promote gastric tumorigenesis.

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Intestinal tissue stiffening, due to fibrosis, in inflammatory bowel disease reduces the population and stemness of the intestinal stem cells and promotes their differentiation toward goblet cells.

GI Cancer

1152 **Comparing Time to Diagnosis and Treatment Between Younger and Older Adults With Colorectal Cancer: A Population-Based Study**

M. Castelo, L. Paszat, B. E. Hansen, A. S. Scheer, N. Faught, L. Nguyen, and N. N. Baxter

In a population-based study including 90,225 patients with colorectal cancer in Ontario, Canada, between 2003 and 2018, adults aged younger than 50 years had overall similar times from presentation to treatment start compared with older adults.

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Tyrosine released by colorectal cancers deficient of ubiquitously transcribed tetratricopeptide repeat on chromosome X maintains the survival and immunosuppressive ability of intratumoral myeloid-derived suppressor cells.

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A newly developed artificial intelligence system was able to accurately distinguish remission from inflammation in biopsies of ulcerative colitis and predict prognosis.

1189 **Host Sorbitol and Bacterial Sorbitol Utilization Promote *Clostridioides difficile* Infection in Inflammatory Bowel Disease**

Z. Yang, J. Qin, L. Zhao, T. Chen, Q. Huang, Y. Jian, Q. Zhao, S. Yang, Q. Li, Q. Liu, M. Otto, and M. Li

Patients with inflammatory bowel disease are at higher risk of *Clostridioides difficile* infection because these bacteria can use a specific sugar that is more abundant in patients with inflammatory bowel disease.

Functional GI Disease

1202 **Randomized Placebo-Controlled Phase 3 Trial of Vibrating Capsule for Chronic Constipation**

S. S. C. Rao, E. M. M. Quigley, W. D. Chey, A. Sharma, and A. J. Lembo

The vibrating capsule is a novel, drug-free capsule device that significantly improved bowel symptoms and quality of life in patients with chronic constipation and was safe, in a randomized clinical trial.

1211 **Factor Analysis of the Rome IV Criteria for Major Disorders of Gut-Brain Interaction (DGBI) Globally and Across Geographical, Sex, and Age Groups**

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Factor analysis on a global sample of patients validates major disorders of the gut-brain interaction (DGBI). This was true for sub-analyses by geographical regions, sex, and age groups.

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1223 Surveillance for Pancreatic Cancer in High-Risk Individuals Leads to Improved Outcomes: A Propensity Score-Matched Analysis

D. C. F. Klatte, B. Boekstijn, A. M. Onnekink, F. W. Dekker, L. G. van der Geest, M. N. J. M. Wasser, S. Feshtali, J. S. D. Mieog, S. A. C. Luelmo, H. Morreau, T. P. Potjer, A. Inderson, J. J. Boonstra, H. F. A. Vasen, J. E. van Hooft, B. A. Bonsing, and M. E. van Leerdam, on behalf of the Dutch Pancreatic Cancer Group

Patients at high risk of pancreatic cancer who were diagnosed in a screening program had a notably better survival than patients diagnosed in the general population.

1232 Targeting UBE2T Potentiates Gemcitabine Efficacy in Pancreatic Cancer by Regulating Pyrimidine Metabolism and Replication Stress

X. Jiang, Y. Ma, T. Wang, H. Zhou, K. Wang, W. Shi, L. Qin, J. Guan, L. Li, B. Long, J. Wang, X. Guan, H. Ye, J. Yang, Z. Yu, and Z. Jiao

Ubiquitin-conjugating enzyme E2T is a driver of gemcitabine resistance that modulates pyrimidine metabolism remodeling and replication stress response, thereby providing a new strategy to combat pancreatic cancer with gemcitabine resistance.

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1248 Sphingolipids Are Depleted in Alcohol-Related Liver Fibrosis

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The abnormal composition of 18 types of lipid classes in the liver and blood in people with early alcohol-related liver disease is specific to the type of liver damage and has implications on the risk of developing symptomatic liver disease.

1261 Disruption of SLFN11 Deficiency-Induced CCL2 Signaling and Macrophage M2 Polarization Potentiates Anti-PD-1 Therapy Efficacy in Hepatocellular Carcinoma

C. Zhou, J. Weng, C. Liu, S. Liu, Z. Hu, X. Xie, D. Gao, Q. Zhou, J. Sun, R. Xu, H. Li, Y. Shen, Y. Yi, Y. Shi, X. Sheng, Q. Dong, M.-C. Hung, and N. Ren

Disruption of C-C motif chemokine ligand 2 signaling and infiltration of immunosuppressive macrophages induced by Schlafen family 11 deficiency potentiates anti-PD-1 therapy efficacy in hepatocellular carcinoma.

1279 A Therapeutically Targetable TAZ-TEAD2 Pathway Drives the Growth of Hepatocellular Carcinoma via ANLN and KIF23

Y. Saito, D. Yin, N. Kubota, X. Wang, A. Filliol, H. Remotti, A. Nair, L. Fazlollahi, Y. Hoshida, I. Tabas, K. J. Wangenstein, and R. F. Schwabe

A tumor-promoting TAZ-TEAD2-ANLN/KIF23 pathway in hepatocellular carcinoma was identified. Targeting this pathway in tumor cells (eg, by TEAD inhibitors or statins) showed therapeutic effects and can potentially be combined with already approved hepatocellular carcinoma therapies that target nontumor cells.

1293 Refining Classification of Cholangiocarcinoma Subtypes via Proteogenomic Integration Reveals New Therapeutic Prospects

S. Y. Cho, H. Hwang, Y.-H. Kim, B. C. Yoo, N. Han, S.-Y. Kong, M.-J. Baek, K.-H. Kim, M. R. Lee, J. G. Park, S.-S. Han, W. J. Lee, C. Park, J. B. Park, J. Y. Kim, S.-J. Park, and S. M. Woo

Multomics characterization of intrahepatic cholangiocarcinoma is reported, and the subtypes show molecular heterogeneity and mixed metabolism features. A novel stem-like molecular subtype was identified. Aldehyde dehydrogenase 1 family member A1, an oncogene suppressor, is a potential therapeutic target for intrahepatic cholangiocarcinoma.

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