

Gastroenterology

Volume 159 / Number 2

August 2020

www.gastrojournal.org

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Publisher: *Gastroenterology* (ISSN 0016-5085) is published monthly (semi monthly in January and May) in two indexed volumes by Elsevier Inc, 230 Park Avenue, New York, NY 10169-0901, USA. Periodicals postage paid at New York, NY and additional mailing offices. POSTMASTER: Send address changes to Elsevier, Journal Returns, 1799 Highway 50 East, Linn, MO 65051, USA. 2020 US subscription rates: individual, \$739.00; student and resident, \$282.00. Outside of the U.S. and possessions: individual, \$968.00; student and resident, \$562.00; surface delivery, no additional charge; air mail delivery, add \$78.00. Prices subject to change without notice.

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Clinical—Alimentary Tract

- 467 **Probiotics Reduce Mortality and Morbidity in Preterm, Low-Birth-Weight Infants: A Systematic Review and Network Meta-analysis of Randomized Trials**
R. L. Morgan, G. A. Preidis, P. C. Kashyap, A. V. Weizman, and B. Sadeghirad, and the McMaster Probiotic, Prebiotic, and Synbiotic Work Group

A comparison of different probiotic combinations identified a few single- and multiple-strain probiotics demonstrating efficacy for the prevention of mortality and morbidity in preterm infants.

481 **Corticosteroids, But Not TNF Antagonists, Are Associated With Adverse COVID-19 Outcomes in Patients With Inflammatory Bowel Diseases: Results From an International Registry**

E. J. Brenner, R. C. Ungaro, R. B. Gearry, G. G. Kaplan, M. Kissous-Hunt, J. D. Lewis, S. C. Ng, J.-F. Rahier, W. Reinisch, F. M. Ruemmele, F. Steinwurz, F. E. Underwood, X. Zhang, J.-F. Colombel, and M. D. Kappelman

We created an international registry of IBD patients who developed COVID-19. Corticosteroids, but not TNF antagonists, were associated with adverse outcomes. Other risk factors were similar to the general population.

492 **Risk Factors for Early-Onset Colorectal Cancer**

E. E. Low, J. Demb, L. Liu, A. Earles, R. Bustamante, C. D. Williams, D. Provenzale, T. Kaltenbach, A. J. Gawron, M. E. Martinez, and S. Gupta

In an analysis of veterans, we found that weight loss is an early sign of colorectal cancer in persons younger than 50 years, and that aspirin can decrease risk.

502 **Increased Risk of Colorectal Cancer in Individuals With a History of Serrated Polyps**

D. Li, L. Liu, H. B. Fevrier, S. E. Alexeeff, A. R. Doherty, M. Raju, L. B. Amsden, J. K. Lee, T. R. Levin, D. A. Corley, and L. J. Herrinton

Persons found to have a serrated polyp during colonoscopy are at increased risk for cancer and should be carefully monitored by surveillance colonoscopy.

512 **Efficacy of Real-Time Computer-Aided Detection of Colorectal Neoplasia in a Randomized Trial**

A. Repici, M. Badalamenti, R. Maselli, L. Correale, F. Radaelli, E. Rondonotti, E. Ferrara, M. Spadaccini, A. Alkandari, A. Fugazza, A. Anderloni, P. A. Galtieri, G. Pellegatta, S. Carrara, M. Di Leo, V. Craviotto, L. Lamonaca, R. Lorenzetti, A. Andrealli, G. Antonelli, M. Wallace, P. Sharma, T. Rosch, and C. Hassan

Including real-time, computer-aided detection of polyps in colonoscopy examination increases rates of adenoma detection by 30%.

Clinical—Liver

521 **JNJ-56136379, an HBV Capsid Assembly Modulator, Is Well-Tolerated and Has Antiviral Activity in a Phase 1 Study of Patients With Chronic Infection**

F. Zoulim, O. Lenz, J. J. Vandenbossche, W. Talloen, T. Verbinnen, I. Moscalu, A. Streinu-Cercel, S. Bourgeois, M. Buti, J. Crespo, J. Manuel Pascasio, C. Sarrazin, T. Vanwolleghem, U. Shukla, J. Fry, and J. Z. Yogarntnam

Researchers have discovered a therapeutic agent that has few side effects and appears to be effective in limiting replication of HBV in patients with chronic infections.

534 **Liver Phenotypes of European Adults Heterozygous or Homozygous for Pi*Z Variant of AAT (Pi*MZ vs Pi*ZZ genotype) and Noncarriers**

C. V. Schneider, K. Hamesch, A. Gross, M. Mandorfer, L. S. Moeller, V. Pereira, M. Pons, P. Kuca, M. C. Reichert, F. Benini, B. Burbaum, J. Voss, M. Gutberlet, V. Woditsch, C. Lindhauer, M. Fromme, J. Kümpers, L. Bewersdorf, B. Schaefer, M. Eslam, R. Bals, S. Janciauskiene, J. Carvão, D. Neureiter, B. Zhou, K. Wöran, H. Bantel, A. Geier, T. Dirrichs, F. Stickel, A. Teumer, J. Verbeek, F. Nevens, O. Govaere, M. Krawczyk, T. Roskams, J. Haybaeck, G. Lurje, J. Chorostowska-Wynimko, J. Genesca, T. Reiberger, F. Lammert, A. Krag, J. George, Q. M. Anstee, M. Trauner, C. Datz, N. T. Gaisa, H. Denk, C. Trautwein, E. Aigner, and P. Strnad, on behalf of the European Alpha-1 Liver Study Group

See editorial on page 433.

Adults heterozygous for (who have 1 gene copy of) the genetic alteration that causes alpha-1 antitrypsin deficiency develop less severe liver disease than adults who are homozygous for (have 2 gene copies of) the variant, but have more evidence of liver disease than individuals without this genetic variant.

549 Collagenous Colitis Is Associated With HLA Signature and Shares Genetic Risks With Other Immune-Mediated Diseases

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E. Stahl, G. Roda, A. Dobbyn, J. Hu, Z. Zhang, H. Westerlind, F. Bonfiglio, T. Raj, J. Torres, A. Chen, R. Petras, D. S. Pardi, A. C. Iuga, G. S. Levi, W. Cao, P. Jain, F. Rieder, I. O. Gordon, J. H. Cho, M. D'Amato, N. Harpaz, K. Hao, J. F. Colombel, and I. Peter

A genetic study of collagenous colitis detected independent risk and protective human leukocyte antigen (HLA) loci associated with disease risk and identified a complex pattern of polygenic pleiotropy between collagenous colitis and other immune-mediated diseases.

Clinical—Pancreas**562 A MicroRNA Signature Identifies Pancreatic Ductal Adenocarcinoma Patients at Risk for Lymph Node Metastases**

www

S. Nishiwada, M. Sho, J. K. Banwait, K. Yamamura, T. Akahori, K. Nakamura, H. Baba, and A. Goel

The authors identified genes that are expressed at higher levels in pancreatic tumors from patients with vs without metastases. This pattern of gene expression might be used to identify patients at higher risk for pancreatic tumor metastasis.

Basic and Translational—Alimentary Tract**575 Notch Signaling Mediates Differentiation in Barrett's Esophagus and Promotes Progression to Adenocarcinoma**

www

B. Kunze, F. Wein, H.-Y. Fang, A. Anand, T. Baumeister, J. Strangmann, S. Gerland, J. Ingermann, N. S. Münch, M. Wiethaler, V. Sahm, A. Hidalgo-Sastre, S. Lange, C. J. Lightdale, A. Bokhari, G. W. Falk, R. A. Friedman, G. G. Ginsberg, P. G. Iyer, Z. Jin, H. Nakagawa, C. J. Shawber, T. Nguyen, W. J. Raab, P. Dalerba, A. K. Rustgi, A. R. Sepulveda, K. K. Wang, R. M. Schmid, T. C. Wang, J. A. Abrams, and M. Quante

We identified a pathway in esophageal tissues of patients with BE that mediates cell differentiation and promotes progression to EAC.

591 Single-Cell Analyses of Colon and Blood Reveal Distinct Immune Cell Signatures of Ulcerative Colitis and Crohn's Disease

www

V. Mitsialis, S. Wall, P. Liu, J. Ordovas-Montanes, T. Parmet, M. Vukovic, D. Spencer, M. Field, C. McCourt, J. Toothaker, A. Bousvaros, Boston Children's Hospital Inflammatory Bowel Disease Center, Brigham and Women's Hospital Crohn's and Colitis Center, A. K. Shalek, L. Kean, B. Horwitz, J. Goldsmith, G. Tseng, S. B. Snapper, and L. Konnikova

The authors analyzed immune cells in colon tissues and blood samples from patients with IBD and found that samples from patients with CD vs UC contain different types of immune cells.

Basic and Translational—Liver**609 Hepatocellular Carcinoma Cells Up-regulate PVRL1, Stabilizing PVR and Inhibiting the Cytotoxic T-Cell Response via TIGIT to Mediate Tumor Resistance to PD1 Inhibitors in Mice**

E www

D. K.-C. Chiu, V. W.-H. Yuen, J. W.-S. Cheu, L. L. Wei, V. Ting, M. Fehlings, H. Sumatoh, A. Nardin, E. W. Newell, I. O.-L. Ng, T. C.-C. Yau, C.-M. Wong, and C. C.-L. Wong

See editorial on page 434.

We identified a protein on liver cancer cells that suppresses the anti-tumor immune response. Strategies to block this protein might be used to increase anti-tumor immunity.

624 **Hedgehog Signaling Demarcates a Niche of Fibrogenic Peribiliary Mesenchymal Cells**

V. Gupta, I. Gupta, J. Park, Y. Bram, and R. E. Schwartz

The authors identified a population of liver cells that proliferate and promote development of fibrosis in mice with liver injuries.

639 ***Lactococcus lactis* Subspecies *cremoris* Elicits Protection Against Metabolic Changes Induced by a Western-Style Diet**

C. R. Naudin, K. Maner-Smith, J. A. Owens, G. M. Wynn, B. S. Robinson, J. D. Matthews, A. R. Reedy, L. Luo, A. A. Wolfarth, T. M. Darby, E. A. Ortlund, and R. M. Jones

Dietary supplementation with a novel beneficial bacterium, namely *L. lactis* sp. *Cremoris* lowered Western-style diet-induced weight gain, body mass index, cholesterol levels, and hepatic steatosis and inflammation.

652 **Effects of Hepatitis B Surface Antigen on Virus-Specific and Global T Cells in Patients With Chronic Hepatitis B Virus Infection**

N. Le Bert, U. S. Gill, M. Hong, K. Kunasegaran, D. Z. M. Tan, R. Ahmad, Y. Cheng, C. -A. Dutertre, A. Heinecke, L. Rivino, A. Tan, N. K. Hansi, M. Zhang, S. Xi, Y. Chong, S. Pflanz, E. W. Newell, P. T. F. Kennedy, and A. Bertoletti

In patients with chronic HBV infection, the length of time they are infected, rather than the level of HBV proteins secreted by liver cells, determines whether patients will have an immune response to the virus.

Basic and Translational—Pancreas

665 **CXCL10 and CCL21 Promote Migration of Pancreatic Cancer Cells Toward Sensory Neurons and Neural Remodeling in Tumors in Mice, Associated With Pain in Patients**

M. Hirth, J. Gandla, C. Höper, M. M. Gaida, N. Agarwal, M. Simonetti, A. Demir, Y. Xie, C. Weiss, C. W. Michalski, T. Hackert, M. P. Ebert, and R. Kuner

The authors identified molecules produced by neurons that attract cancer cells to neurons and cause pain.

682 **SETDB1 Inhibits p53-Mediated Apoptosis and Is Required for Formation of Pancreatic Ductal Adenocarcinomas in Mice**

S. Ogawa, A. Fukuda, Y. Matsumoto, Y. Hanyu, M. Sono, Y. Fukunaga, T. Masuda, O. Araki, M. Nagao, T. Yoshikawa, N. Goto, Y. Hiramatsu, M. Tsuda, T. Maruno, Y. Nakanishi, M. S. Hussein, T. Tsuruyama, K. Takaori, S. Uemoto, and H. Seno

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The authors identified a protein in pancreatic cancer cells that promotes their survival and development of pancreatic tumors in mice.

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