

Gastroenterology

www.gastrojournal.org

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May 2018

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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. 2018 US subscription rates: individual, \$711.00; student and resident, \$271.00. 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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G. F. Brady, R. Kwan, J. Bragazzi Cunha, J. S. Elenbaas, and M. B. Omary

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ORIGINAL RESEARCH

Brief Reports

1620 Mutations in Mitochondrial DNA From Pancreatic Ductal Adenocarcinomas Associate

With Survival Times of Patients and Accumulate as Tumors Progress

J. F. Hopkins, R. E. Denroche, J. A. Aguiar, F. Notta, A. A. Connor, J. M. Wilson, L. D. Stein, S. Gallinger, and P. C. Boutros

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The authors identified 304 mutations in the mitochondrial genomes of 268 pancreatic cancer patients and found that mutations in two complex I genes were associated with worse overall survival.

1625 Lamin A/C Maintains Exocrine Pancreas Homeostasis by Regulating Stability of RB and Activity of E2F

J. S. Elenbaas, J. Bragazzi Cunha, R. Azuero-Dajud, B. Nelson, E. A. Oral, J. A. Williams, C. L. Stewart, and M. B. Omary

The nuclear intermediate filament protein lamin A/C maintains pancreatic homeostasis by enhancing RB protein stability and inhibiting E2F transcriptional activity.

1630 HIF1-alpha Regulates Acinar Cell Function and Response to Injury in Mouse Pancreas

M.-J. Park, S. Iyer, X. Xue, J. Bragazzi Cunha, S. Gu, D. Moons, S. W. Pipe, J. A. Williams, D. M. Simeone, Y. M. Shah, and M. B. Omary

HIF1-alpha exerts dual roles in the regulation of exocrine pancreas homeostasis and in the progression of acute pancreatitis that is promoted by intra-pancreatic coagulation.

Full Reports

Clinical—Alimentary Tract

1635 Bi-directionality of Brain-Gut Interactions in Patients With Inflammatory Bowel Disease

D. J. Gracie, E. A. Guthrie, P. J. Hamlin, and A. C. Ford

A bi-directional relationship is present between psychological disorders and disease activity, suggesting that IBD patients should be monitored for the presence of psychological co-morbidity, and that evidence-based management strategies for treatment of mood disorders in IBD are needed.

1647 Histologic Factors Associated With Need for Surgery in Patients With Pedunculated T1 Colorectal Carcinomas

Y. Backes, S. G. Elias, J. N. Groen, M. P. Schwartz, F. H. J. Wolfhagen, J. M. J. Geesing, F. ter Borg, J. van Bergeijk, B. W. M. Spanier, W. H. de Vos tot Nederveen Cappel, K. Kessels, C. A. Seldenrijk, M. G. Raicu, P. Drillenburg, A. N. Milne, M. Kerkhof, T. C. J. Seerden, P. D. Siersema, F. P. Vleggaar, G. J. A. Offerhaus, M. M. Lacle, and L. M. G. Moons, on behalf of the Dutch T1 CRC Working Group

The authors identified histologic features of tumors that stratify patients with pedunculated T1 colorectal carcinomas into those who require surgery (due to high risk of metastasis) with greater accuracy than previous models.

1660 Pharmacokinetics and Exposure Response Relationships of Ustekinumab in Patients With Crohn's Disease

O. J. Adedokun, Z. Xu, C. Gasink, D. Jacobstein, P. Szapary, J. Johanns, L.-L. Gao, H. M. Davis, S. B. Hanauer, B. G. Feagan, S. Ghosh, and W. J. Sandborn

For patients with Crohn's disease, higher ustekinumab concentrations correlated with better efficacy and maintenance trough concentrations between 0.8 -1.4 $\mu\text{g/ml}$ or greater appear optimal.

1672 Prevalence of and Factors Associated With Fecal Incontinence: Results From a Population-Based Survey

S. B. Menees, C. V. Almario, B. M. R. Spiegel, and W. D. Chey

In a survey of 71,000 Americans, 1 in 7 reported prior fecal incontinence. Importantly, incontinence was more common and more severe in patients with inflammatory bowel disease, celiac disease, irritable bowel syndrome, and diabetes.

1682 Effects of Training and Feedback on Accuracy of Predicting Rectosigmoid Neoplastic Lesions and Selection of Surveillance Intervals by Endoscopists Performing Optical Diagnosis of Diminutive Polyps

J. L. A. Vleugels, M. G. W. Dijkgraaf, Y. Hazewinkel, L. K. Wanders, P. Fockens, and E. Dekker, on behalf of the DISCOUNT study group

The diagnosis of diminutive polyps with Narrow Band Imaging can replace histology in clinical practice if endoscopists are trained in a validated program and their performance is measured prior to implementation.

Clinical—Liver**1694 Association Between Portosystemic Shunts and Increased Complications and Mortality in Patients With Cirrhosis**

M. Simón-Talero, D. Roccarina, J. Martínez, K. Lampichler, A. Baiges, G. Low, E. Llop, M. Praktijnjo, M. H. Maurer, A. Zipprich, M. Triolo, G. Vangrinsven, R. García-Martínez, A. Dam, A. Majumdar, C. Picón, D. Toth, A. Darnell, J. G. Abrales, M. Lopez, G. Kukuk, A. Krag, R. Bañares, W. Laleman, V. La Mura, C. Ripoll, A. Berzigotti, J. Trebicka, J. L. Calleja, P. Tandon, V. Hernandez-Gea, T. Reiberger, A. Albillos, E. A. Tsochatzis, S. Augustin, and J. Genescà, for the Baveno VI-SPSS group from the Baveno Cooperation

See editorial on page 1569.

The prevalence of spontaneous portosystemic shunts (SPSS) in patients with cirrhosis increases as liver function deteriorates. Patients with adequate liver function and SPSS develop more complications and mortality compared to those without SPSS.

1706 Surveillance Imaging and Alpha Fetoprotein for Early Detection of Hepatocellular Carcinoma in Patients With Cirrhosis: A Meta-analysis

K. Tzartzeva, J. Obi, N. E. Rich, N. D. Parikh, J. A. Marrero, A. Yopp, A. K. Waljee, and A. G. Singal

See editorial on page 1572.

Ultrasound alone has poor sensitivity to detect hepatocellular carcinoma at an early stage in patients with cirrhosis; however, using a blood-based biomarker, alpha fetoprotein (AFP), in conjunction with ultrasound can significantly increase early detection of hepatocellular carcinoma.

1719 Patterns and Trends of Liver Cancer Incidence Rates in Eastern and Southeastern Asian Countries (1983-2007) and Predictions to 2030

J. Wu, S. Yang, K. Xu, C. Ding, Y. Zhou, X. Fu, Y. Li, M. Deng, C. Wang, X. Liu, and L. Li

In this study, the authors report that by year 2030, liver cancer incidence rates in most Eastern and Southeastern Asian countries will decrease significantly.

Clinical—Pancreas**1729 Acute Pancreatitis and Pancreatic Cancer Risk: A Nationwide Matched-Cohort Study in Denmark**

J. Kirkegård, D. Cronin-Fenton, U. Heide-Jørgensen, and F. V. Mortensen

The authors demonstrate that patients who develop acute pancreatitis harbor an increased risk of pancreatic cancer in subsequent years.

Basic and Translational—Alimentary Tract**1737 Ceragenin CSA13 Reduces *Clostridium difficile* Infection in Mice by Modulating the Intestinal Microbiome and Metabolites**

J. Wang, S. Ghali, C. Xu, C. C. Mussatto, C. Ortiz, E. C. Lee, D. H. Tran, J. P. Jacobs, V. Lagishetty, K. F. Faull, T. Moller, M. Rossetti, X. Chen, and H. W. Koon

See editorial on page 1573.

This report demonstrated the efficacy of a novel drug, CSA13, in inhibiting *C difficile* infection in mice and further showed that the intestinal microbiota and novel metabolites are involved in the protective effect.

1751 Microbiota-Derived Metabolic Factors Reduce *Campylobacteriosis* in Mice

X. Sun, K. Winglee, R. Z. Gharaibeh, J. Gauthier, Z. He, P. Tripathi, D. Avram, S. Bruner, A. Fodor, and C. Jobin

Bacterial deoxycholic acids derived from anaerobic bacteria protect the host against *Campylobacter jejuni*-induced colitis. The mechanism by which this occurs involves blockade of mTOR signaling.

Basic and Translational—Liver

1764 **TLR7 Agonist Increases Responses of Hepatitis B Virus-Specific T Cells and Natural Killer Cells in Patients With Chronic Hepatitis B Treated With Nucleos(T)ide Analogues**

C. Boni, A. Vecchi, M. Rossi, D. Laccabue, T. Giuberti, A. Alfieri, P. Lampertico, G. Grossi, F. Facchetti, M. R. Brunetto, B. Coco, D. Cavallone, A. Mangia, R. Santoro, V. Piazzolla, A. Lau, A. Gagar, G. M. Subramanian, and C. Ferrari

The TLR-7 agonist GS-9620 improves T and NK cell responses and reduces NK cell suppression of T cells in patients with chronic hepatitis B. This suggests that GS-9620 might be considered as a component of combination therapies directed against HBV.

1778 **Hepatitis B Virus Does Not Interfere With Innate Immune Responses in the Human Liver**

A. Suslov, T. Boldanova, X. Wang, S. Wieland, and M. H. Heim

Lack of an interferon-gamma response to hepatitis B virus infection is likely due to evasion as opposed to immune suppression.

1791 **HBV Bypasses the Innate Immune Response and Does Not Protect HCV From Antiviral Activity of Interferon**

P. Mutz, P. Metz, F. A. Lempp, S. Bender, B. Qu, K. Schöneweis, S. Seitz, T. Tu, A. Restuccia, J. Frankish, C. Dächert, B. Schusser, R. Koschny, G. Polychronidis, P. Schemmer, K. Hoffmann, T. F. Baumert, M. Binder, S. Urban, and R. Bartenschlager

In this study, the authors demonstrate that Hepatitis B virus fails to activate or inhibit the interferon system and is insensitive to interferon-induced antiviral effects.

Basic and Translational—Pancreas

1805 **Pancreatitis-Induced Depletion of Syntaxin 2 Promotes Autophagy and Increases Basolateral Exocytosis**

S. Dolai, T. Liang, A. I. Orabi, D. Holmyard, L. Xie, D. Greitzer-Antes, Y. Kang, H. Xie, T. A. Javed, P. P. Lam, D. C. Rubin, P. Thorn, and H. Y. Gaisano

In the exocrine pancreas, secretory granule trafficking and exit (exocytosis) and autophagy are accelerated by depletion of syntaxin-2, which accentuates cell-damaging events.

1822 **STING Signaling Promotes Inflammation in Experimental Acute Pancreatitis**

Q. Zhao, Y. Wei, S. J. Pandol, L. Li, and A. Habtezion

The mechanisms that initiate inflammation in acute pancreatitis remain poorly understood. In this study, the authors demonstrate that activation of the intracellular receptor STING ignites inflammation within pancreatic cells.

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- 1845 Could Fecal Transplantation Become Part of PD-1-Based Immunotherapy, Due to Effects of the Intestinal Microbiome?**
P. Biancheri, D. Divekar, and A. J. M. Watson

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L. Hao, Z. Liao, and L.-H. Hu
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