

# Gastroenterology

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- 980 **Rifaximin Reduces the Number and Severity of Intestinal Lesions Associated With Use of Nonsteroidal Anti-Inflammatory Drugs in Humans**  
 *C. Scarpignato, W. Dolak, A. Lanas, P. Matzneller, C. Renzulli, M. Grimaldi, M. Zeitlinger, and I. Bjarnason*

A poorly absorbed antibiotic, rifaximin, can prevent NSAID-induced damage, indicating that enteric bacteria may play an important role in injury responses to these drugs.

**983 Germline Mutations in *PALB2*, *BRCA1*, and *RAD51C*, Which Regulate DNA Recombination Repair, in Patients With Gastric Cancer**

*R. Sahasrabudhe, P. Lott, M. Bohorquez, T. Toal, A. P. Estrada, J. J. Suarez, A. Brea-Fernández, J. Cameselle-Teijeiro, C. Pinto, I. Ramos, A. Mantilla, R. Prieto, A. Corvalan, E. Norero, C. Alvarez, T. Tapia, P. Carvallo, L. M. Gonzalez, A. Cock-Rada, A. Solano, F. Neffa, A. Della Valle, C. Yau, G. Soares, A. Borowsky, N. Hu, L.-J. He, X.-Y. Han, Latin American Gastric Cancer Genetics Collaborative Group, P. R. Taylor, A. M. Goldstein, J. Torres, M. Echeverry, C. Ruiz-Ponte, M. R. Teixeira, and L. G. Carvajal-Carmona*

**See editorial on page 926.**

Mutations in the *PALB2*, *BRCA1* and *RAD51C* genes are found in a subset of patients with gastric cancers. Tumors from these patients were heterogeneous based on histology but harbored a homologous recombination deficient mutation signature.

**Full Reports**

**Clinical—Alimentary Tract**

**987 Low Risk of High-Grade Dysplasia or Esophageal Adenocarcinoma Among Patients With Barrett's Esophagus Less Than 1 cm (Irregular Z Line) Within 5 Years of Index Endoscopy**

*P. N. Thota, P. Vennelaganti, S. Vennelaganti, P. Young, S. Gaddam, N. Gupta, D. Lieberman, R. Sampliner, G. W. Falk, S. Mathur, K. Kennedy, B. D. Cash, F. Moawad, A. Bansal, M. C. Spaander, M. J. Bruno, J. Vargo, and P. Sharma*

In this multicenter cohort study of 1791 patients with Barrett's esophagus, no patients with an irregular Z line developed high-grade dysplasia or cancer over a median follow up period of approximately 6 years.

**993 Patients With Barrett's Esophagus and Confirmed Persistent Low-Grade Dysplasia Are at Increased Risk for Progression to Neoplasia**

*L. C. Duits, M. J. van der Wel, C. C. Cotton, K. N. Phoa, F. J. W. ten Kate, C. A. Seldenrijk, G. J. A. Offerhaus, M. Visser, S. L. Meijer, R. C. Mallant-Hent, K. K. Krishnadath, R. E. Pouw, J. G. P. Tijssen, N. J. Shaheen, and J. J. G. H. M. Bergman*

**See editorial on page 928.**

The risk of neoplastic progression in Barrett's patients with low-grade dysplasia increases dramatically if expert pathologists confirm the diagnosis, or if dysplasia is confirmed at 2 independent endoscopies.

**1002 Detection of Sessile Serrated Adenomas in the Proximal Colon Using Wide-Field Fluorescence Endoscopy**

*B. P. Joshi, Z. Dai, Z. Gao, J. H. Lee, N. Ghimire, J. Chen, A. Prabhu, E. J. Wamsteker, R. S. Kwon, G. H. Elta, E. M. Stoffel, A. Pant, T. Kaltenbach, R. M. Soetikno, H. D. Appelman, R. Kuick, D. K. Turgeon, and T. D. Wang*

Sessile serrated adenomas (SSA) can cause colorectal cancer, but are difficult to visualize endoscopically. This study demonstrates the clinical utility of a fluorescently-labeled peptide to enhance visualization of these pre-malignant lesions.

**1014 Gastrointestinal Safety of Direct Oral Anticoagulants: A Large Population-Based Study**

*E N. S. Abraham, P. A. Noseworthy, X. Yao, L. R. Sangaralingham, and N. D. Shah*

**See editorial on page 932.**

Among all age groups, apixaban may be the preferred direct oral anticoagulant agent to minimize GI bleeding; especially among patients over the age of 75, for whom GI bleeding risk is much higher.

**1023 Western Dietary Pattern Increases, and Prudent Dietary Pattern Decreases, Risk of Incident Diverticulitis in a Prospective Cohort Study**

*L. L. Strate, B. R. Keeley, Y. Cao, K. Wu, E. L. Giovannucci, and A. T. Chan*

**See editorial on page 934.**

A dietary pattern high in red meat, refined grains and high-fat dairy (Western) was associated with an increased risk of developing diverticulitis, whereas a diet high in fruits, vegetables and whole grains (Prudent) was associated with decreased risk.

**1031 Asymptomatic Carriers Contribute to Nosocomial *Clostridium difficile* Infection:  
A Cohort Study of 4508 Patients**

T. Blixt, K. O. Gradel, C. Homann, J. B. Seidelin, K. Schønning, A. Lester, J. Houlind, M. Stangerup, M. Gottlieb, and J. D. Knudsen

During hospitalization, *C difficile* can be transmitted effectively by asymptomatic carriers.

**1042 Prevalence, Risk Factors, and Outcomes of Irritable Bowel Syndrome After Infectious  
Enteritis: A Systematic Review and Meta-analysis**

F. Klem, A. Wadhwa, L. J. Prokop, W. J. Sundt, G. Farrugia, M. Camilleri, S. Singh, and M. Grover

See editorial on page 936.

Eleven percent of individuals develop post-infectious IBS following a gastrointestinal infection. Female gender, underlying psychological distress, and more severe symptoms during infection are associated with a higher risk for this condition.

**1055 Steatorrhea and Hyperoxaluria in Severely Obese Patients Before and After Roux-en-Y  
Gastric Bypass**

A. M. Moreland, C. A. Santa Ana, J. R. Asplin, J. A. Kuhn, R. P. Holmes, J. A. Cole, E. A. Odstrcil, T. G. Van Dinter Jr, J. G. Martinez, and J. S. Fordtran

Urine oxalate excretion was abnormally high in severely obese patients prior to gastric bypass, unrelated to steatorrhea. Hyperoxaluria after bypass was equally severe, but, in contrast, was associated with the presence of steatorrhea.

**Clinical—Liver****1068 In Patients With Severe Alcoholic Hepatitis, Prednisolone Increases Susceptibility to  
Infection and Infection-Related Mortality, and Is Associated With High Circulating Levels of  
Bacterial DNA**

N. Vergis, S. R. Atkinson, S. Knapp, J. Maurice, M. Allison, A. Austin, E. H. Forrest, S. Masson, A. McCune, D. Patch, P. Richardson, D. Gleeson, S. D. Ryder, M. Wright, and M. R. Thursz

See editorial on page 938.

Patients with alcoholic hepatitis who are at risk of developing steroid-induced infections can be identified through measurement of circulating bacterial DNA before administering prednisolone.

**1078 Association of Liver Injury From Specific Drugs, or Groups of Drugs, With Polymorphisms  
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P. Nicoletti, G. P. Athal, E. S. Björnsson, R. J. Andrade, A. Sawle, M. Arrese, H. X. Barnhart, E. Bondon-Guitton, P. H. Hayashi, F. Bessone, A. Carvajal, I. Cascorbi, E. T. Cirulli, N. Chalasani, A. Conforti, S. A. Coulthard, M. J. Daly, C. P. Day, J. F. Dillon, R. J. Fontana, J. I. Grove, P. Hallberg, N. Hernández, L. Ibáñez, G. A. Kullak-Ublick, T. Laitinen, D. Larrey, M. I. Lucena, A. H. Maitland-van der Zee, J. H. Martin, M. Molokhia, M. Pirmohamed, E. E. Powell, S. Qin, J. Serrano, C. Stephens, A. Stolz, M. Wadelius, P. B. Watkins, A. Floratos, Y. Shen, M. R. Nelson, T. J. Urban, and A. K. Daly; on behalf of International Drug-Induced Liver Injury Consortium, Drug-Induced Liver Injury Network Investigators, and International Serious Adverse Events Consortium

The rare HLA-A\*33:01 allele increases the risk of terbinafine DILI as well as DILI from other unrelated drugs.

**1090 Changes in the Prevalence of Hepatitis C Virus Infection, Nonalcoholic Steatohepatitis, and  
Alcoholic Liver Disease Among Patients With Cirrhosis or Liver Failure on the Waitlist for  
Liver Transplantation**

D. Goldberg, I. C. Ditah, K. Saeian, M. Lalehzari, A. Aronsohn, E. C. Gorospe, and M. Charlton

Decreased HCV prevalence has led to fewer cases of HCV-related chronic liver failure, but within the context of a continued burden of HCC. In contrast, NASH is increasing across the entire spectrum from cirrhosis->chronic liver failure and HCC.

**Basic and Translational—Alimentary Tract****1100 Nutritional Wheat Amylase-Trypsin Inhibitors Promote Intestinal Inflammation via Activation of Myeloid Cells**

*V. F. Zevallos, V. Raker, S. Tenzer, C. Jimenez-Calvente, M. Ashfaq-Khan, N. Rüssel, G. Pickert, H. Schild, K. Steinbrink, and D. Schuppan*

Nutritional amylase trypsin inhibitors in wheat products activate innate immune cells in the gut and surrounding lymph nodes, thereby exacerbating intestinal inflammation.

**1114 Heterotrimeric G Stimulatory Protein  $\alpha$  Subunit Is Required for Intestinal Smooth Muscle Contraction in Mice**

*X. Qin, S. Liu, Q. Lu, M. Zhang, X. Jiang, S. Hu, J. Li, C. Zhang, J. Gao, M.-S. Zhu, R. Feil, H. Li, M. Chen, L. S. Weinstein, Y. Zhang, and W. Zhang*

Heterotrimeric G stimulatory protein alpha subunit (Gsa) is required for intestinal smooth muscle contraction, and genetic deficiency of Gsa in smooth muscle cells of mice results in intestinal dysmotility.

**1126 Intestinal Farnesoid X Receptor Controls Transintestinal Cholesterol Excretion in Mice**

*J. F. de Boer, M. Schonewille, M. Boesjes, H. Wolters, V. W. Bloks, T. Bos, T. H. van Dijk, A. Jurdzinski, R. Boverhof, J. C. Wolters, J. A. Kuivenhoven, J. M. van Deursen, R. P. J. Oude Elferink, A. Moschetta, C. Kremoser, H. J. Verkade, F. Kuipers, and A. K. Groen*

The recently discovered transintestinal pathway for cholesterol removal, termed TICE, can be stimulated to the point that mice can excrete 60% of their total body cholesterol content each day.

**1139 Differentiation of Mouse Enteric Nervous System Progenitor Cells Is Controlled by Endothelin 3 and Requires Regulation of *Ednrb* by SOX10 and ZEB2**

*Y. Watanabe, L. Stanchina, L. Lecerf, N. Gacem, A. Conidi, V. Baral, V. Pingault, D. Huylebroeck, and N. Bondurand*

Using in vivo and in vitro approaches in mice, coordinated actions of endothelin-3, Sox10 and Zeb2 were shown to control neuronal differentiation of enteric nervous system progenitors. The underlying mechanism involves cooperative direct activation of the *Ednrb* promoter by these transcription factors.

**1151 Ultrasound-Mediated Delivery of RNA to Colonic Mucosa of Live Mice**

*C. M. Schoellhammer, G. Y. Lauwers, J. A. Goettel, M. A. Oberli, C. Cleveland, J. Y. Park, D. Minahan, Y. Chen, D. G. Anderson, A. Jaklenec, S. B. Snapper, R. Langer, and G. Traverso*

Delivery of unformulated anti-Tnf- $\alpha$  siRNA to the colon using low-frequency ultrasound, results in reduced TNF levels in murine colitis.

**Basic and Translational—Liver****1161 Genome-Wide CRISPR Screen Identifies Regulators of Mitogen-Activated Protein Kinase as Suppressors of Liver Tumors in Mice**

*C.-Q. Song, Y. Li, H. Mou, J. Moore, A. Park, Y. Pomyen, S. Hough, Z. Kennedy, A. Fischer, H. Yin, D. G. Anderson, D. Conte Jr, L. Zender, X. W. Wang, S. Thorgeirsson, Z. Weng, and W. Xue*

**See editorial on page 941.**

A genome-wide CRISPR genetic screen in mice identified new genes, such as *Ras*, that suppress the development of liver cancer.

**1174 Milk Fat Globule-EGF Factor 8, Secreted by Mesenchymal Stem Cells, Protects Against Liver Fibrosis in Mice**

*S. Y. An, Y. J. Jang, H.-J. Lim, J. Han, J. Lee, G. Lee, J. Y. Park, S.-Y. Park, J. H. Kim, B.-R. Do, C. Han, H.-K. Park, O.-H. Kim, M. J. Song, S.-J. Kim, and J.-H. Kim*

**See editorial on page 943.**

Mesenchymal stem cells obtained from the human placenta released proteins that attenuated liver fibrosis. Specifically, MGF8 was identified as a critical anti-fibrotic factor.

- 1187**  **Choline Kinase  $\alpha$  Mediates Interactions Between the Epidermal Growth Factor Receptor and Mechanistic Target of Rapamycin Complex 2 in Hepatocellular Carcinoma Cells to Promote Drug Resistance and Xenograft Tumor Progression**  
*X.-M. Lin, L. Hu, J. Gu, R.-Y. Wang, L. Li, J. Tang, B.-H. Zhang, X.-Z. Yan, Y.-J. Zhu, C.-L. Hu, W.-P. Zhou, S. Li, J.-F. Liu, F. J. Gonzalez, M.-C. Wu, H.-Y. Wang, and L. Chen*

Choline kinase alpha served as an adaptor molecule tethering EGFR and mTORC2, which was critical for AKT activation and HCC progression, and which renders cells more resistant to EGFR targeted therapy

- 1203**  **X-box Binding Protein 1 Regulates Unfolded Protein, Acute-Phase, and DNA Damage Responses During Regeneration of Mouse Liver**  
*J. Argemí, T. R. Kress, H. C. Y. Chang, R. Ferrero, C. Bértolo, H. Moreno, M. González-Aparicio, I. Uriarte, L. Guembe, V. Segura, R. Hernández-Alcoceba, M. A. Ávila, B. Amati, J. Prieto, and T. Aragón*

During liver regeneration, hepatic cells produce increased amounts of XBP1 which activates a multifaceted gene expression program that enhances protein folding and secretion, and subsequently attenuates tissue damage and ensures DNA integrity in proliferating cells.

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