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TABLE OF  
CONTENTS

## Contents

### ON THE COVER



See Editorial by Aghemo and Buti on page 795; and articles by Lawitz et al on page 893 and Gane et al on page 902 for more information.

### COVERING THE COVER

777 A. T. Chan and C. S. Williams

### COMMENTARIES

780 Focal and Local: Ectopic Lymphoid Structures and Aggregates of Myeloid and Other Immune Cells in Liver

E. Pikarsky and M. Heikenwalder

784 What Is A Normal Intestinal Mucosa?

M. N. Marsh and K. Rostami

### MENTORING, EDUCATION, AND TRAINING CORNER

789 How to Effectively Use High-Resolution Esophageal Manometry

D. A. Carlson and P. J. Kahrilas

### EDITORIALS

793 Understanding Postcolonoscopy Colorectal Cancers: The Next Frontier

N. N. Baxter

See Stoffel EM et al on page 870.

795 Hepatitis C Therapy: Game Over!

COV

A. Aghemo and M. Buti

See Lawitz E et al on page 893; and See Gane EJ et al on page 902.

798 Mitochondrial Amino Acid Metabolism Provides Vulnerabilities in Mutant KRAS-Driven Cancers

Y. M. Shah and C. A. Lyssiotis

See Wong CC et al on page 945.

V Video CCH Related article in CGH

CME CME quiz E Editorial accompanies this article WWW Additional online content available COV Cover

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**801 The Concept of Immune Tolerance in Chronic Hepatitis B Virus Infection Is Alive and Well***D. R. Milich*

See Mason WS et al on page 986.

**805 "To Be or Not to Be": Immune Tolerance in Chronic Hepatitis B***U. Protzer and P. Knolle*

See Mason WS et al on page 986.

**807 TIMPing Fate: Why Pancreatic Cancer Cells Sojourn in the Liver***A. Torres-Hernandez and G. Miller*

See Grünwald B et al on page 1011.

**GASTROENTEROLOGY IN MOTION****809 EUS-Guided Methylene Blue Injection to Facilitate Pancreatic Duct Access**V CME **After Unsuccessful ERCP***B. J. Elmunzer and C. R. Piraka***CLINICAL CHALLENGES AND IMAGES IN GI****811 An Unusual Cause of Persistent Abdominal Pain***T. Iida, A. Goto, and H. Nakase***813 A Huge Abdominal Mass***G. C. Sotiropoulos, S. Karatapanis, and G. Kouraklis***815 An Unusual Cause of Rectal Invasion***H. S. Y. Chang, J. J. H. Low, and C. S. Chong***817 An Exceptional Cause of Abdominal Pain***M. Ronot, W. Allaham, and M. Lagadec***ELECTRONIC CLINICAL CHALLENGES AND IMAGES IN GI**For a full list, please see the table of contents online at [www.gastrojournal.org](http://www.gastrojournal.org).**PRACTICAL TEACHING CASE****819 An Unusual Cause of Recurrent Severe Abdominal Colic**CME *K. Deng, R. Hu, and Y. Zhang***AGA CLINICAL PRACTICE UPDATE: EXPERT REVIEW****822 Diagnosis and Management of Low-Grade Dysplasia in Barrett's Esophagus:**WWW **Expert Review From the Clinical Practice Updates Committee of the American Gastroenterological Association***S. Wani, J. H. Rubenstein, M. Vieth, and J. Bergman***REVIEWS AND PERSPECTIVES****Brief Review****836 The Effect of Microbiota and the Immune System on the Development and Organization of the Enteric Nervous System***Y. Obata and V. Pachnis***Reviews in Basic and Clinical Gastroenterology and Hepatology****845 An Intestinal Microbiota-Farnesoid X Receptor Axis Modulates Metabolic Disease***F. J. Gonzalez, C. Jiang, and A. D. Patterson*

## ORIGINAL RESEARCH

## Full Reports

## Clinical—Alimentary Tract

**860 Alcohol Consumption and Multiple Dysplastic Lesions Increase Risk of Squamous Cell Carcinoma in the Esophagus, Head, and Neck**

CME WWW

*C. Katada, T. Yokoyama, T. Yano, K. Kaneko, I. Oda, Y. Shimizu, H. Doyama, T. Koike, K. Takizawa, M. Hirao, H. Okada, T. Yoshii, K. Konishi, T. Yamanouchi, T. Tsuda, T. Omori, N. Kobayashi, T. Shimoda, A. Ochiai, Y. Amanuma, S. Ohashi, T. Matsuda, H. Ishikawa, A. Yokoyama, and M. Muto*

Multiple dysplastic lesions in the esophagus increase risk of multiple squamous cell carcinomas (SCCs). Alcohol abstinence decreased the risk of multiple SCCs of the esophagus whereas smoking abstinence did not.

**870 Clinical and Molecular Characteristics of Post-Colonoscopy Colorectal Cancer: A Population-based Study**

E WWW

*E. M. Stoffel, R. Erichsen, T. Frøslev, L. Pedersen, M. Vyberg, E. Koeppe, S. D. Crockett, S. R. Hamilton, H. T. Sørensen, and J. A. Baron*

**See editorial on page 793.**

Tumors found in colorectal cancer (CRC) patients who have undergone colonoscopy are more often proximal and have DNA mismatch repair deficiency, compared to CRCs detected in patients without previous colonoscopies.

**879 Regular Aspirin Use Associates With Lower Risk of Colorectal Cancers With Low Numbers of Tumor-Infiltrating Lymphocytes**

CME WWW

*Y. Cao, R. Nishihara, Z. R. Qian, M. Song, K. Mima, K. Inamura, J. A. Nowak, D. A. Drew, P. Lochhead, K. Nosh, T. Morikawa, X. Zhang, K. Wu, M. Wang, W. S. Garrett, E. L. Giovannucci, C. S. Fuchs, A. T. Chan, and S. Ogino*

The immune response in the tumor microenvironment could be involved in the effects of aspirin in colorectal cancer chemoprevention.

## Clinical—Liver

**893 Efficacy of Sofosbuvir, Velpatasvir, and GS-9857 in Patients With Genotype 1 Hepatitis C Virus Infection in an Open-Label, Phase 2 Trial**E WWW  
COV

*E. Lawitz, N. Reau, F. Hineostrova, M. Rabinovitz, E. Schiff, A. Sheikh, Z. Younes, R. Herring Jr, K. R. Reddy, T. Tran, M. Bennett, R. Nahass, J. C. Yang, S. Lu, H. Dvory-Sobol, L. M. Stamm, D. M. Brainard, J. G. McHutchison, B. Pearlman, M. Shiffman, T. Hawkins, M. Curry, and I. Jacobson*

**See editorial on page 795.**

Sofosbuvir-velpatasvir plus GS-9857 (8 weeks in treatment-naïve patients or 12 weeks in treatment-experienced patients) was safe and effective in patients previously treated with direct-acting antivirals, with or without compensated cirrhosis.

**902 Efficacy of Sofosbuvir, Velpatasvir, and GS-9857 in Patients With Hepatitis C Virus Genotype 2, 3, 4, or 6 Infections in an Open-Label, Phase 2 Trial**E WWW  
COV

*E. J. Gane, K. V. Kowdley, D. Pound, C. A. M. Stedman, M. Davis, K. Etzkorn, S. C. Gordon, D. Bernstein, G. Everson, M. Rodriguez-Torres, N. Tsai, O. Khalid, J. C. Yang, S. Lu, H. Dvory-Sobol, L. M. Stamm, D. M. Brainard, J. G. McHutchison, M. Tong, R. T. Chung, K. Beavers, J. E. Poulos, P. Y. Kwo, and M. H. Nguyen*

**See editorial on page 795.**

Sofosbuvir-velpatasvir plus GS-9857 (8 weeks in treatment-naïve patients or 12 weeks in treatment-experienced patients) was safe and effective for patients with HCV genotype 2, 3, 4, or 6 infections, with or without compensated cirrhosis.

## Basic and Translational—Alimentary Tract

**910 Increased Activation of the TRESK K<sup>+</sup> Mediates Vago-Vagal Reflex Malfunction in Diabetic Rats**

WWW

*G. Grabauskas, X. Wu, I. Song, S.-Y. Zhou, T. Lanigan, and C. Owyang*

Activation of the TRESK K<sup>+</sup> channel reduced nodose ganglia excitability and disrupted gastrointestinal functions.

- 923 Antibiotics Suppress Activation of Intestinal Mucosal Mast Cells and Reduce Dietary Lipid Absorption in Sprague-Dawley Rats**  
*H. Sato, L. S. Zhang, K. Martinez, E. B. Chang, Q. Yang, F. Wang, P. N. Howles, R. Hokari, S. Miura, and P. Tso*

Intestinal microbiota is a key player in the activation of mucosal mast cells by dietary lipid, which may lead to increased gut permeability. Gut bacteria also has a novel role in facilitating the absorption of dietary lipids.

- 933 Protective Actions of Epithelial 5-Hydroxytryptamine 4 Receptors in Normal and Inflamed Colon**

*S. N. Spohn, F. Bianco, R. B. Scott, C. M. Keenan, A. A. Linton, C. H. O'Neill, E. Bonora, M. Dickey, B. Lavoie, R. L. Wilcox, W. K. MacNaughton, R. De Giorgio, K. A. Sharkey, and G. M. Mawe*

5-HT<sub>4</sub>R activation maintains motility in healthy colons of mice and guinea pigs, and reduces inflammation in colons of mice with colitis. Agonists might be developed as treatments for patients with inflammatory bowel disease.

- 945 SLC25A22 Promotes Proliferation and Survival of Colorectal Cancer Cells With KRAS Mutations and Xenograft Tumor Progression in Mice via Intracellular Synthesis of Aspartate**

*C. C. Wong, Y. Qian, X. Li, J. Xu, W. Kang, J. H. Tong, K.-F. To, Y. Jin, W. Li, H. Chen, M. Y. Y. Go, J.-L. Wu, K. W. Cheng, S. S. M. Ng, J. J. Y. Sung, Z. Cai, and J. Yu*

See editorial on page 798.

Patients with colorectal tumors that express increased levels of SLC25A22 have shorter survival times than patients whose tumors have lower levels. SLC25A22 induces intracellular synthesis of aspartate, activation of MEK and ERK signaling, and reduces oxidative stress.

- 961 Epigenetic Homogeneity Within Colorectal Tumors Predicts Shorter Relapse-Free and Overall Survival Times for Patients With Locoregional Cancer**

*A. Martínez-Cardús, S. Moran, E. Musulen, C. Moutinho, J. L. Manzano, E. Martínez-Balibrea, M. Tierno, E. Élez, S. Landolfi, P. Lorden, C. Arribas, F. Müller, C. Bock, J. Tabernero, and M. Esteller*

Significant heterogeneity was found in patterns of DNA methylation within each one of 79 colorectal tumors. The level of heterogeneity correlates with times of relapse-free and overall survival.

## Basic and Translational—Liver

- 973 Robust HCV Genotype 3a Infectious Cell Culture System Permits Identification of Escape Variants With Resistance to Sofosbuvir**

*S. Ramirez, L. S. Mikkelsen, J. M. Gottwein, and J. Bukh*

Sofosbuvir escape variants could compromise the effectiveness of nucleotide analogs against hepatitis C virus infection.

- 986 HBV DNA Integration and Clonal Hepatocyte Expansion in Chronic Hepatitis B Patients Considered Immune Tolerant**

*W. S. Mason, U. S. Gill, S. Litwin, Y. Zhou, S. Peri, O. Pop, M. L. W. Hong, S. Naik, A. Quaglia, A. Bertoletti, and P. T. F. Kennedy*

See editorials on pages 801 and 805.

A high level of HBV DNA integration and clonal hepatocyte expansion in patients considered immune tolerant indicated that hepatocarcinogenesis could be underway – even in patients with early-stage chronic HBV infection.

- 999 Inflammation-Induced Expression and Secretion of MicroRNA 122 Leads to Reduced Blood Levels of Kidney-Derived Erythropoietin and Anemia**

*M. Rivkin, A. Simerzin, E. Zorde-Khvalevsky, C. Chai, J. B. Yuval, N. Rosenberg, R. Harari-Steinfeld, R. Schneider, G. Amir, R. Condiotti, M. Heikenwalder, A. Weber, C. Schramm, H. Wege, J. Kluwe, E. Galun, and H. Giladi*

In mice, lipopolysaccharide-induced inflammation increases blood levels of MicroRNA 122, which reduces expression of erythropoietin in the kidney. Blocking MicroRNA 122 in patients with inflammation could reduce development or progression of anemia.

**1011** **Pancreatic Premalignant Lesions Secrete Tissue Inhibitor of Metalloproteinases-1, Which Activates Hepatic Stellate Cells Via CD63 Signaling to Create a Premetastatic Niche in the Liver**

*B. Grünwald, V. Harant, S. Schaten, M. Frühschütz, R. Spallek, B. Höchst, K. Stutzer, S. Berchtold, M. Erkan, O. Prokopchuk, M. Martignoni, I. Esposito, M. Heikenwalder, A. Gupta, J. Siveke, P. Saftig, P. Knolle, D. Wöhlleber, and A. Krüger*

See editorial on page 807.

Strategies to block TIMP1 signaling via CD63 might prevent pancreatic ductal adenocarcinoma metastasis to the liver.

**CONTINUING MEDICAL EDUCATION (CME)/MOC ACTIVITIES**

- e13 Exam 1: EUS-Guided Methylene Blue Injection to Facilitate Pancreatic Duct Access After Unsuccessful ERCP**
- e15 Exam 2: An Unusual Cause of Recurrent Severe Abdominal Colic**
- e16 Exam 3: Alcohol Consumption and Multiple Dysplastic Lesions Increase Risk of Squamous Cell Carcinoma in the Esophagus, Head, and Neck**
- e17 Exam 4: Regular Aspirin Use Associates With Lower Risk of Colorectal Cancers With Low Numbers of Tumor-Infiltrating Lymphocytes**

**SELECTED SUMMARIES**

- 1025 Targeting S1P Receptors, A New Mechanism of Action for Inflammatory Bowel Disease Therapy**  
*G. Bamias and J. Rivera-Nieves*
- 1027 Nonsteroidal Anti-inflammatory Drugs for Prevention of Post-ERCP Pancreatitis: Sooner Rather Than Later during ERCP?**  
*G. A. Coté and B. J. Elmunzer*
- 1029 Operate or Medicate: Understanding Surgical Risks in the Elderly with Inflammatory Bowel Disease**  
*M. S. Piper, A. K. Waljee, and R. W. Stidham*
- 1030 Treatment Targets in Ulcerative Colitis**  
*R. Khanna and V. Jairath*

**CORRESPONDENCE**

- 1033 The Exact Mechanism by Which Hepatic Transmembrane 6 Superfamily Member 2 Modulates Triglyceride Metabolism Is Still Uncertain**  
*S. Sookoian and C. J. Pirola*
- 1034 Reply**  
*Y. Fan, C. J. Willer, and Y. E. Chen*
- 1035 Uncertain Benefits of Simvastatin in the Treatment of Patients With Variceal Hemorrhage**  
*T. Chaudhry, A. Dillon, and I. A. Rowe*
- 1036 Altered Pharmacokinetics of Statins Explain Increased Risk of Rhabdomyolysis in Advanced Cirrhosis**  
*R. A. Weersink, J. P. H. Drenth, and S. D. Borgsteede*

- 1037 Did Statins Really Improve Survival in Cirrhotic Patients With a History of Variceal Bleeding?**  
*G.-H. Lo*
- 1037 Reply**  
*J. G. Abraldes, F. Torres, and J. Bosch, on behalf of the BLEPS study group*
- 1038 Oral Contraceptive Use and Crohn's Disease Complications**  
*L. Gawron and S. Kane*
- 1039 Reply**  
*H. Khalili and O. Olén*
- 1040 Is Early Endoscopy-Based Therapy the Best Strategy to Prevent All Crohn's Disease Postoperative Recurrence?**  
*A. Sartini, E. Scaiola, and A. Belluzzi*
- 1041 Reply**  
*M. D. Regueiro and B. G. Feagan*

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