

Gastroenterology

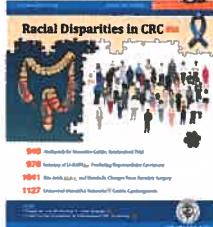
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ORIGINAL RESEARCH**Full Reports****Clinical—Alimentary Tract****918 Risk of Postpolypectomy Bleeding With Uninterrupted Clopidogrel Therapy in an Industry-Independent, Double-Blind, Randomized Trial**

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Continuing clopidogrel around the time of colonoscopy did not increase the risk of bleeding if a polyp needed to be removed.

926 Dexlansoprazole and Esomeprazole Do Not Affect Bone Homeostasis in Healthy Postmenopausal Women

K. E. Hansen, J. W. Nieves, S. Nudurupati, D. C. Metz, and M. C. Perez

PPI therapy increased bone turnover but did not alter mineral homeostasis, calcium absorption, or bone mineral density. The mechanism by which PPI therapy might cause skeletal harm remains unclear.

935 Acceptance and Commitment Therapy Reduces Psychological Stress in Patients With Inflammatory Bowel Diseases

B. Wynne, L. McHugh, W. Gao, D. Keegan, K. Byrne, C. Rowan, K. Hartery, C. Kirschbaum, G. Doherty, G. Cullen, B. Dooley, and H. E. Mulcahy

See editorial on page 856.

This randomized controlled trial demonstrates that a psychological treatment, Acceptance and Commitment Therapy, is effective in reducing stress and depression in patients with IBD.

946 Efficacy and Safety of Abrilumab in a Randomized, Placebo-Controlled Trial for Moderate-to-Severe Ulcerative Colitis

W. J. Sandborn, M. Cyrille, M. B. Hansen, B. G. Feagan, E. V. Loftus Jr, G. Rogler, S. Vermeire, M. L. Cruz, J. Yang, M. J. Boedigheimer, L. Abuqayyas, C. M. Evangelista, B. A. Sullivan, and W. Reinisch

Abrikumab (anti- $\alpha_4\beta_7$ antibody) treatment for 8 weeks in patients with ulcerative colitis resulted in significantly greater remission, response, and mucosal healing rates versus placebo.

958 Racial Disparities in Incidence of Young-Onset Colorectal Cancer and Patient Survival*C. C. Murphy, K. Wallace, R. S. Sandler, and J. A. Baron***See editorial on page 858.**

The dominant factor driving increases in CRC among younger adults has been increasing rates of rectal cancer, more prominent among whites. These findings provide clues for understanding reasons why incidence has increased.

Clinical—Liver**966 Propensity for Intra-abdominal and Hepatic Adiposity Varies Among Ethnic Groups***U. Lim, K. R. Monroe, S. Buchthal, B. Fan, I. Cheng, B. S. Kristal, J. W. Lampe, M. A. Hullar, A. A. Franke, D. O. Stram, L. R. Wilkens, J. Shepherd, T. Ernst, and L. Le Marchand*

Differences in how body fat is distributed may partially explain ethnic/racial disparities in important metabolic diseases such as fatty liver disease, diabetes and others.

976 Accuracy of the Liver Imaging Reporting and Data System in Computed Tomography and Magnetic Resonance Image Analysis of Hepatocellular Carcinoma or Overall Malignancy—A Systematic Review*C. B. van der Pol, C. S. Lim, C. B. Sirlin, T. A. McGrath, J.-P. Salameh, M. R. Bashir, A. Tang, A. G. Singal, A. F. Costa, K. Fowler, and M. D. F. McInnes***See editorial on page 860.**

A radiologic method successfully predicts cancer risk among different liver lesions, to inform decisions regarding follow-up and treatment.

987 Direct-Acting Antiviral Therapy for HCV Infection Is Associated With a Reduced Risk of Cardiovascular Disease Events*A. A. Butt, P. Yan, A. Shuaib, A.-B. Abou-Samra, O. S. Shaikh, and M. S. Freiberg***See editorial on page 862.**

Treatment with newer all-oral agents against hepatitis C virus is associated with a significant reduction in risk of future cardiovascular disease events.

997 Validation of Baveno VI Criteria for Screening and Surveillance of Esophageal Varices in Patients With Compensated Cirrhosis and a Sustained Response to Antiviral Therapy*D. Thabut, C. Bureau, R. Layese, V. Bourcier, M. Hammouche, C. Cagnot, P. Marcellin, D. Guyader, S. Pol, D. Larrey, V. De Lédinghen, D. Ouzan, F. Zoulim, D. Roulot, A. Tran, J.-P. Bronowicki, J.-P. Zarski, O. Goria, P. Calès, J.-M. Péron, L. Alric, M. Bourlière, P. Mathurin, J.-F. Blanc, A. Abergel, L. Serfaty, A. Mallat, J.-D. Grangé, P. Attali, Y. Bacq, C. Wartelle-Bladou, T. Dao, C. Pilette, C. Silvain, C. Christidis, D. Capron, B. Bernard-Chabert, S. Hillaire, V. Di Martino, A. Sutton, E. Audureau, F. Roudot-Thoraval, and P. Nahon, for the ANRS CO12 CirVir group***See editorial on page 864.**

Screening and surveillance of esophageal varices in cirrhotic patients may not be needed as frequently, in patients successfully treated for viral hepatitis. Progression of portal hypertension is mainly dependent upon viral suppression and Baveno VI criteria.

Clinical—Pancreas**1010 Impaired Exocrine Pancreatic Function Associates With Changes in Intestinal Microbiota Composition and Diversity***F. Frost, T. Kacprowski, M. Rühlemann, R. Bülow, J.-P. Kühn, A. Franke, F.-A. Heinsen, M. Pietzner, M. Nauck, U. Völker, H. Völzke, A. A. Aghdassi, M. Sendler, J. Mayerle, F. U. Weiss, G. Homuth, and M. M. Lerch*

The body's pancreatic enzyme functions influence the intestine's microbiome as much or more than other commonly known factors, such as age, body-mass-index, sex, smoking, alcohol consumption, or dietary factors.

1016 Superiority of Step-up Approach vs Open Necrosectomy in Long-term Follow-up of Patients With Necrotizing Pancreatitis

R. A. Hollemans, O. J. Bakker, M. A. Boermeester, T. L. Bollen, K. Bosscha, M. J. Bruno, E. Buskens, C. H. Dejong, P. van Duijvendijk, C. H. van Eijck, P. Fockens, H. van Goor, W. M. van Grevenstein, E. van der Harst, J. Heisterkamp, E. J. Hesselink, S. Hofker, A. P. Houdijk, T. Karsten, P. M. Kruyt, C. J. van Laarhoven, J. S. Laméris, M. S. van Leeuwen, E. R. Manusama, I. Q. Molenaar, V. B. Nieuwenhuijs, B. van Ramshorst, D. Roos, C. Rosman, A. F. Schaapherder, G. P. van der Schelling, R. Timmer, R. C. Verdonk, R. J. de Wit, H. G. Gooszen, M. G. Besselink, and H. C. van Santvoort, for the Dutch Pancreatitis Study Group

See editorial on page 867.

Patients with infected necrotizing pancreatitis should undergo radiological or endoscopic drainage as the first step in invasive treatment, instead of a major abdominal operation.

1027 An Endoscopic Transluminal Approach, Compared With Minimally Invasive Surgery, Reduces Complications and Costs for Patients With Necrotizing Pancreatitis

J. Y. Bang, J. P. Arnoletti, B. A. Holt, B. Sutton, M. K. Hasan, U. Navaneethan, N. Feranec, C. M. Wilcox, B. Tharian, R. H. Hawes, and S. Varadarajulu

See editorial on page 867.

For patients with severe pancreatitis, treatment of some complications with endoscopy, rather than minimally invasive surgery, had better patient outcomes and fewer complications.

Basic and Translational—Alimentary Tract

1041 Role of Bile Acids and GLP-1 in Mediating the Metabolic Improvements of Bariatric Surgery

V. L. Albaugh, B. Banan, J. Antoun, Y. Xiong, Y. Guo, J. Ping, M. Alikhan, B. A. Clements, N. N. Abumrad, and C. R. Flynn

Bile diversion to the ileum augments bile acid synthesis and leads to rapid resolution of diabetes/obesity. Even in the absence of obesity or high fat feeding, however, bile diversion improves glucose homeostasis and modifies the gut microbiome.

1052 Small Heterodimer Partner and Fibroblast Growth Factor 19 Inhibit Expression of NPC1L1 in Mouse Intestine and Cholesterol Absorption

Y.-C. Kim, S. Byun, S. Seok, G. Guo, H. E. Xu, B. Kemper, and J. K. Kemper

A study in mice found that certain genes impact the absorption of cholesterol and change bile made by the liver; this information may provide new strategies for treating high cholesterol in humans.

1066 BHLHA15-Positive Secretory Precursor Cells Can Give Rise to Tumors in Intestine and Colon in Mice

Y. Hayakawa, M. Tsuboi, S. Asfaha, H. Kinoshita, R. Niikura, M. Konishi, M. Hata, Y. Oya, W. Kim, M. Middelhoff, Y. Hikiba, N. Higashijima, S. Ihara, T. Ushiku, M. Fukayama, Y. Tailor, Y. Hirata, C. Guha, K. S. Yan, K. Koike, and T. C. Wang

Notch and YAP pathways are a critical regulator of interconversion from intestinal secretory precursors, and that secretory precursors can act as a cellular origin of cancer after converting to long-lived stem-like cells.

1082 Inhibiting Interleukin 36 Receptor Signaling Reduces Fibrosis in Mice With Chronic Intestinal Inflammation

K. Scheibe, C. Kersten, A. Schmied, M. Vieth, T. Prims, B. Carlé, F. Knieling, J. Claussen, A. C. Klimowicz, J. Zheng, P. Baum, S. Meyer, S. Schürmann, O. Friedrich, M. J. Waldner, T. Rath, S. Wirtz, G. Kollias, A. B. Ekici, R. Atreya, E. L. Raymond, M. L. Mbow, M. F. Neurath, and C. Neufert

See editorial on page 871.

Interleukin 36A expression is associated with intestinal fibrosis in IBD patients and targeting of Interleukin 36 receptor signaling suppresses fibrosis in models chronic intestinal inflammation.

1098 ATF4 Deficiency Promotes Intestinal Inflammation in Mice by Reducing Uptake of Glutamine and Expression of Antimicrobial Peptides

X. Hu, J. Deng, T. Yu, S. Chen, Y. Ge, Z. Zhou, Y. Guo, H. Ying, Q. Zhai, Y. Chen, F. Yuan, Y. Niu, W. Shu, H. Chen, C. Ma, Z. Liu, and F. Guo

A compound the body makes that is related to the body's stress response plays an important role in regulating the intestine; changing this compound may help in treating inflammatory bowel disease.

1112 Histone Demethylase JMJD2D Interacts With β -Catenin to Induce Transcription and Activate Colorectal Cancer Cell Proliferation and Tumor Growth in Mice

K. Peng, L. Kou, L. Yu, C. Bai, M. Li, P. Mo, W. Li, and C. Yu

JMJD2D promotes colorectal cancer (CRC) progression through enhancing Wnt signaling, suggesting JMJD2D is a potent molecular target for CRC treatment.

1127 Integrated Analysis of Mouse and Human Gastric Neoplasms Identifies Conserved microRNA Networks in Gastric Carcinogenesis

Z. Chen, Z. Li, M. Soutto, W. Wang, M. B. Piazuelo, S. Zhu, Y. Guo, M. J. Maturana, A. H. Corvalan, X. Chen, Z. Xu, and W. M. El-Rifai

This study identified conserved miRNA signatures and predicted signaling networks that are associated with early stages of gastric tumorigenesis. Strategies to restore MIR143-3p or inhibit BRD2 might be developed further for treatment of gastric cancer.

1140 Interleukin 1 Up-regulates MicroRNA 135b to Promote Inflammation-Associated Gastric Carcinogenesis in Mice

T.-S. Han, D. C.-C. Voon, H. Oshima, M. Nakayama, K. Echizen, E. Sakai, Z. W. E. Yong, K. Murakami, L. Yu, T. Minamoto, C.-Y. Ock, B. J. Jenkins, S.-J. Kim, H.-K. Yang, and M. Oshima

MicroRNA-135b is strongly induced in gastritis and early gastric carcinogenesis. It functionally links inflammation and pre-neoplastic hyperplasia. This insight could help with the early intervention and diagnosis of gastric cancer.

Basic and Translational—Liver**1156 NADPH Oxidase 1 in Liver Macrophages Promotes Inflammation and Tumor Development in Mice**

S. Liang, H.-Y. Ma, Z. Zhong, D. Dhar, X. Liu, J. Xu, Y. Koyama, T. Nishio, D. Karin, G. Karin, R. Mccubbin, C. Zhang, R. Hu, G. Yang, L. Chen, S. Ganguly, T. Lan, M. Karin, T. Kisileva, and D. A. Brenner

NOX1 in macrophages drives liver inflammation, thereby promoting HCC development. Targeting NOX1 thus may represent a new therapeutic approach to treat HCC.

1173 Activation of Autophagy, Observed in Liver Tissues From Patients With Wilson Disease and From ATP7B-Deficient Animals, Protects Hepatocytes From Copper-Induced Apoptosis

E. V. Polishchuk, A. Merolla, J. Lichtmannegger, A. Romano, A. Indrieri, E. Y. Ilyecheva, M. Concilli, R. De Cegli, R. Crispino, M. Mariniello, R. Petruzzelli, G. Ranucci, R. Iorio, F. Pietrocola, C. Einer, S. Borchard, A. Zibert, H. H. Schmidt, E. Di Schiavi, L. V. Puchkova, B. Franco, G. Kroemer, H. Zischka, and R. S. Polishchuk

Autophagic sequestration of damaged cellular components helps hepatocytes to combat copper toxicity in Wilson disease.

Basic and Translational—Biliary**1190 Nuclear Translocation of RELB Is Increased in Diseased Human Liver and Promotes Ductular Reaction and Biliary Fibrosis in Mice**

C. Elßner, B. Goeppert, T. Longerich, A.-L. Scherr, J. Stindt, L. K. Nanduri, C. Rupp, J. N. Kather, N. Schmitt, N. Kautz, K. Breuhahn, L. Ismail, D. Heide, J. Hetzer, M. García-Beccaria, N. Hövelmeyer, A. Waisman, T. Urbanik, S. Mueller, G. Gdynia, J. M. Banales, S. Roessler, P. Schirmacher, D. Jäger, S. Schölch, V. Keitel, M. Heikenwalder, H. Schulze-Bergkamen, and B. C. Köhler

RELB drives cholangiocyte proliferation, ductular reaction and biliary fibrosis in liver diseases. Lymphotxin beta acts as responsible cytokine activating non-canonical NF- κ B signaling in biliary epithelial cells. Thereby, cholangiocytes are activated into a secretory active and proliferative state.

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