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Clinical—Alimentary Tract

- 924 **Accuracy in Diagnosis of Celiac Disease Without Biopsies in Clinical Practice**
K. J. Werkstetter, I. R. Korponay-Szabó, A. Popp, V. Villanacci, M. Salemme, G. Heilig, S. T. Lillevang, M. L. Mearin, C. Ribes-Koninckx, A. Thomas, R. Troncone, B. Filipiak, M. Mäki, J. Gyimesi, M. Najafi, J. Dolinšek, S. Dydensborg Sander, R. Auricchio, A. Papadopoulou, A. Vécsei, P. Szitanyi, E. Donat, R. Nenna, P. Alliet, F. Penagini, H. Garnier-Lengliné, G. Castillejo, K. Kurppa, R. Shamir, A. C. Hauer, F. Smets, S. Corujeira, M. van Winckel, S. Buderus, S. Chong, S. Husby, and S. Koletzko, on behalf of the ProCeDE study group

In children and adolescents with symptoms of celiac disease and high levels of tissue-transglutaminase IgA autoantibodies, diagnosis of celiac disease can be made safely with a confirmatory test in a second blood sample, without the need for upper endoscopy with biopsies.

936 **A Diet Low in FODMAPs Reduces Symptoms in Patients With Irritable Bowel Syndrome and A Probiotic Restores Bifidobacterium Species: A Randomized Controlled Trial**

H. M. Staudacher, M. C. E. Lomer, F. M. Farquharson, P. Louis, F. Fava, E. Franciosi, M. Scholz, K. M. Tuohy, J. O. Lindsay, P. M. Irving, and K. Whelan

See editorial on page 886.

This study confirms that a low FODMAP diet is effective in improving IBS symptoms but also provides evidence that probiotics could be used in conjunction with a low FODMAP diet to restore gut *Bifidobacteria* species.

948 **Vasoactive Intestinal Polypeptide and Mast Cells Regulate Increased Passage of Colonic Bacteria in Patients With Irritable Bowel Syndrome**

O. Bednarska, S. A. Walter, M. Casado-Bedmar, M. Ström, E. Salvo-Romero, M. Vicario, E. A. Mayer, and Å. V. Keita

This study demonstrates increased translocation of both commensal and pathogenic viable bacteria through the colonic mucosa of patients with irritable bowel syndrome, which is dependent upon mast cells and vasoactive intestinal polypeptide.

961 **Avoidance of Cow's Milk–Based Formula for At-Risk Infants Does Not Reduce Development of Celiac Disease: A Randomized Controlled Trial**

M. Hyytinen, E. Savilahti, S. M. Virtanen, T. Härkönen, J. Ilonen, K. Luopajarvi, R. Uibo, O. Vaarala, H. K. Åkerblom, and M. Knip, for the Finnish TRIGR Pilot Study Group

Avoidance of cow's milk formula did not reduce the risk for celiac disease later in childhood. Increased titers of antibodies directed against cow's milk early in life may indicate abnormal intestinal permeability.

971 **Association Between Proton Pump Inhibitor Use and Cognitive Function in Women**

P. Lochhead, K. Hagan, A. D. Joshi, H. Khalili, L. H. Nguyen, F. Grodstein, and A. T. Chan

In this analysis involving 13,864 participants in the Nurses' Health Study II, no convincing association was observed between long-term use of proton pump inhibitors and cognitive function.

980 **Association Between Natural Killer Cell Activity and Colorectal Cancer in High-Risk Subjects Undergoing Colonoscopy**

G. Jobin, R. Rodriguez-Suarez, and K. Betito

Measurement of the function of a specific subset of immune cells, natural killer cells, using a simple blood test, may be a useful new way to augment the yield of finding colorectal cancer on colonoscopy.

Clinical—Liver

988 **Analysis of Liver Offers to Pediatric Candidates on the Transplant Wait List**

E. K. Hsu, M. L. Shaffer, L. Gao, C. Sonnenday, M. L. Volk, J. Bucuvalas, and J. C. Lai

See editorial on page 888.

This study used national transplant registry databases to examine deceased donor liver offer acceptance patterns and their contributions to pediatric liver wait-list mortality.

996 **Risk of Hepatocellular Cancer in HCV Patients Treated With Direct-Acting Antiviral Agents**

F. Kanwal, J. Kramer, S. M. Asch, M. Chayanupatkul, Y. Cao, and H. B. El-Serag

See editorial on page 890.

This study demonstrated that patients with HCV cured by DAAs are dramatically less likely to develop HCC; however, HCV-cured patients with cirrhosis should still be screened for HCC.

1006 **Influence of Metabolic Risk Factors on Risk of Hepatocellular Carcinoma and Liver-Related Death in Men With Chronic Hepatitis B: A Large Cohort Study**

M.-W. Yu, C.-L. Lin, C.-J. Liu, S.-H. Yang, Y.-L. Tseng, and C.-F. Wu

This study investigated determinants that increase the risk of hepatocellular carcinoma and liver-related death in male hepatitis B virus carriers with higher burden of metabolic risk factors.

1018 Randomized Comparison of 3 High-Level Disinfection and Sterilization Procedures for Duodenoscopes

G. M. Snyder, S. B. Wright, A. Smithey, M. Mizrahi, M. Sheppard, E. B. Hirsch, R. Chuttani, R. Heroux, D. S. Yassa, L. B. Olafsdottir, R. B. Davis, J. Anastasiou, V. Bapat, K. Bidari, D. K. Pleskow, D. Leffler, B. Lane, A. Chen, H. S. Gold, A. Bartley, A. D. King, and M. S. Sawhney

See editorial on page 892.

Duodenoscopes have been implicated in the transmission of bacterial infections. This randomized trial compared 3 different methods of reprocessing duodenoscopes, finding that they were all similarly effective.

Basic and Translational—Alimentary Tract

1026 Intestinal Fungal Dysbiosis Is Associated With Visceral Hypersensitivity in Patients With Irritable Bowel Syndrome and Rats

S. Botschuijver, G. Roeselers, E. Levin, D. M. Jonkers, O. Welting, S. E. M. Heinsbroek, H. H. de Weerd, T. Boekhout, M. Fornai, A. A. Masclee, F. H. J. Schuren, W. J. de Jonge, J. Seppen, and R. M. van den Wijngaard

Fungal gut dysbiosis was demonstrated in IBS patients and in a rat model of IBS. Fungicides and inhibition of fungal recognition by the immune system reversed visceral hypersensitivity in rats.

1040 MET Signaling Mediates Intestinal Crypt-Villus Development, Regeneration, and Adenoma Formation and Is Promoted by Stem Cell CD44 Isoforms

S. P. J. Joosten, J. Zeilstra, H. van Andel, R. C. Mijns, J. Zaunbrecher, A. A. M. Duivenvoorden, M. van de Wetering, H. Clevers, M. Spaargaren, and S. T. Pals

MET and CD44 are regulators of intestinal homeostasis, regeneration, and adenoma formation. These molecules represent potential therapeutic targets in colorectal cancer patients receiving anti-EGFR receptor treatment or in patients resistant to EGFR inhibitors.

1054 Treatment of Intestinal Fibrosis in Experimental Inflammatory Bowel Disease by the Pleiotropic Actions of a Local Rho Kinase Inhibitor

T. Holvoet, S. Devriese, K. Castermans, S. Boland, D. Leysen, Y.-P. Vandewynckel, L. Devisscher, L. Van den Bossche, S. Van Welden, M. Dullaers, R. E. Vandenbroucke, R. De Rycke, K. Geboes, A. Bourin, O. Defert, P. Hindryckx, M. De Vos, and D. Laukens

See editorial on page 895.

Intestinal fibrosis resulting in partial obstruction is a common, and frequently untreatable complication of Crohn's disease. This study shows that local inhibition of rho kinases represents a safe strategy to control intestinal fibrosis.

1068 Enteric Glia Regulate Gastrointestinal Motility but Are Not Required for Maintenance of the Epithelium in Mice

M. Rao, D. Rastelli, L. Dong, S. Chiu, W. Setlik, M. D. Gershon, and G. Corfas

Contrary to current dogma, this study demonstrates that glial cells are not required for maintaining integrity of the intestinal epithelium, but they do regulate gut motility in a sex-dependent manner.

1082 Colorectal Cancer Cell Line Proteomes Are Representative of Primary Tumors and Predict Drug Sensitivity

J. Wang, D. Mouradov, X. Wang, R. N. Jorissen, M. C. Chambers, L. J. Zimmerman, S. Vasaiakar, C. G. Love, S. Li, K. Lowes, K.-J. Leuchowius, H. Jousset, J. Weinstock, C. Yau, J. Mariadason, Z. Shi, Y. Ban, X. Chen, R. J. C. Coffey, R. J. C. Slebos, A. W. Burgess, D. C. Liebler, B. Zhang, and O. M. Sieber

Colorectal cancer cell lines, an important preclinical model of cancer, are representative of patient tumors at the global protein level. Protein profiling has potential utility for predicting therapeutic responses.

Basic and Translational—Liver

1096 **Epigenome-Wide Association Study Identifies Methylation Sites Associated With Liver Enzymes and Hepatic Steatosis**

J. Nano, M. Ghanbari, W. Wang, P. S. de Vries, K. Dhana, T. Muka, A. G. Uitterlinden, J. B. J. van Meurs, A. Hofman, BIOS consortium, O. H. Franco, Q. Pan, S. Darwish Murad, and A. Dehghan

DNA methylation might play a role in liver function. New differentially methylated genes were discovered associated with liver function and further experimental evidence suggested a potential involvement in lipid metabolism.

1107 **Antibodies Against Immune Checkpoint Molecules Restore Functions of Tumor-Infiltrating T Cells in Hepatocellular Carcinomas**

G. Zhou, D. Sprengers, P. P. C. Boor, M. Doukas, H. Schutz, S. Mancham, A. Pedroza-Gonzalez, W. G. Polak, J. de Jonge, M. Gaspersz, H. Dong, K. Thielemans, Q. Pan, J. N. M. Ijzermans, M. J. Bruno, and J. Kwekkeboom

Inhibitory immune checkpoint molecules PD-1, TIM3, LAG3 and CTLA4 are up-regulated on T cells in tumors of HCC patients. Targeting these molecules by blocking antibodies can restore anti-tumor functions of tumor-infiltrating T cells.

1120 **MAN2A1-FER Fusion Gene Is Expressed by Human Liver and Other Tumor Types and Has Oncogenic Activity in Mice**

Z.-H. Chen, Y. P. Yu, J. Tao, S. Liu, G. Tseng, M. Nalesnik, R. Hamilton, R. Bhargava, J. B. Nelson, A. Pennathur, S. P. Monga, J. D. Luketich, G. K. Michalopoulos, and J.-H. Luo

Chromosome breaking and rejoining results in production of a new protein that transforms normal cells into cancer cells.

1133 **Dynamics of Proliferative and Quiescent Stem Cells in Liver Homeostasis and Injury**

W. Cao, K. Chen, M. Bolkestein, Y. Yin, M. M. A. Versteegen, M. J. C. Bijvelds, W. Wang, N. Tuysuz, D. ten Berge, D. Sprengers, H. J. Metselaar, L. J. W. van der Laan, J. Kwekkeboom, R. Smits, M. P. Peppelenbosch, and Q. Pan

This study reports that quiescent cells are *bona fide* stem cells in the mouse liver. They respond to tissue injury and give rise to proliferative stem cells, including LGR5-expressing cells.

Basic and Translational—Pancreas

1148 **Restoration of CFTR Activity in Ducts Rescues Acinar Cell Function and Reduces Inflammation in Pancreatic and Salivary Glands of Mice**

M. Zeng, M. Szymczak, M. Ahuja, C. Zheng, H. Yin, W. Swaim, J. A. Chiorini, R. J. Bridges, and S. Muallem

Autoimmune diseases that attack the pancreas and salivary glands compromise their functions. Correcting ductal secretion in mouse models of these diseases corrected acinar cell secretion function and repaired the glands.

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