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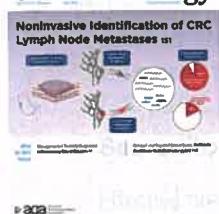
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CME quiz



Editorial accompanies this article



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ORIGINAL RESEARCH**Full Reports****Clinical—Alimentary Tract**

- 66** **TAK-101 Nanoparticles Induce Gluten-Specific Tolerance in Celiac Disease: A Randomized, Double-Blind, Placebo-Controlled Study**

C. P. Kelly, J. A. Murray, D. A. Leffler, D. R. Getts, A. C. Bledsoe, G. Smithson, M. R. First, A. Morris, M. Boyne, A. Elhofy, T.-T. Wu, J. R. Podojil, and S. D. Miller, on behalf of the TAK-101 Study Group

See editorial on page 21.

TAK-101 is a novel therapy that reduced immune activation and intestinal damage induced by oral gluten exposure in patients with celiac disease.

- 81** **Gluten Degradation, Pharmacokinetics, Safety, and Tolerability of TAK-062, an Engineered Enzyme to Treat Celiac Disease**

I. S. Pultz, M. Hill, J. M. Vitanza, C. Wolf, L. Saaby, T. Liu, P. Winkle, and D. A. Leffler

See editorial on page 21.

Effective break down of gluten in the stomach by TAK-062 offers the potential to reduce the toxicity of accidental gluten ingestion and improve disease control in patients with celiac disease on a gluten free diet.

- 94** **Ethnicity Associations With Food Sensitization Are Mediated by Gut Microbiota Development in the First Year of Life**

H. M. Tun, Y. Peng, B. Chen, T. B. Konya, N. P. Morales-Lizcano, R. Chari, C. J. Field, D. S. Guttman, A. B. Becker, P. J. Mandhane, T. J. Moraes, M. R. Sears, S. E. Turvey, P. Subbarao, E. Simons, J. A. Scott, and A. L. Kozyrskyj

Development of gut flora in the first year of life orchestrates risk of food allergy in children, and a higher risk was observed among Asian-Canadian children.

- 107** **Paternal Exposure to Immunosuppressive and/or Biologic Agents and Birth Outcomes in Patients With Immune-Mediated Inflammatory Diseases**

J. Meserve, J. Luo, W. Zhu, N. Veeravalli, G. Bandoli, C. D. Chambers, A. G. Singh, B. S. Boland, W. J. Sandborn, U. Mahadevan, and S. Singh

See editorial on page 24.

Exposure to immunosuppressive and/or biologic therapies around conception in expectant fathers does not negatively impact neonatal outcomes, and are safe to use in men planning conception.

- 116** **Global Patterns and Trends in Gastric Cancer Incidence Rates (1988–2012) and Predictions to 2030**

Y. Lin, Y. Zheng, H.-l. Wang, and J. Wu

Although gastric cancer incidence rates in most countries will decrease or remain stable by 2030, Ecuador and Lithuania will experience substantially increasing trends.

- 128** **Simple Sugar and Sugar-Sweetened Beverage Intake During Adolescence and Risk of Colorectal Cancer Precursors**

H.-K. Joh, D. H. Lee, J. Hur, K. Nimptsch, Y. Chang, H. Joung, X. Zhang, L. F. M. Rezende, J. E. Lee, K. Ng, C. Yuan, F. K. Tabung, J. A. Meyerhardt, A. T. Chan, T. Pischon, M. Song, C. S. Fuchs, W. C. Willett, Y. Cao, S. Ogino, E. Giovannucci, and K. Wu

See editorial on page 27.

High intake of simple sugars and sugar-sweetened beverages during adolescence was significantly associated with increased risk of colorectal adenoma, especially rectal adenoma.

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**Familial Burden and Other Clinical Factors Associated With Various Types of Cancer in Individuals With Lynch Syndrome***L. H. Biller, M. Horiguchi, H. Uno, C. Ukaegbu, S. Syngal, and M. B. Yurgelun*

Among individuals with Lynch syndrome, having first- and/or second-degree relatives with specific cancer types was associated with an increased likelihood of having that same type of cancer.

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**A Liquid Biopsy Assay for Noninvasive Identification of Lymph Node Metastases in T1 Colorectal Cancer***Y. Wada, M. Shimada, T. Murano, H. Takamaru, Y. Morine, T. Ikemoto, Y. Saito, F. Balaguer, L. Bujanda, M. Pellise, K. Kato, Y. Saito, H. Ikematsu, and A. Goel***See editorial on page 29.**

This study reports a novel biomarker signature that can distinguish high-risk T1 CRCs patients with lymph node metastasis from those who do not.

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**Outcomes of Thermal Ablation of the Mucosal Defect Margin After Endoscopic Mucosal Resection: A Prospective, International, Multicenter Trial of 1000 Large Nonpedunculated Colorectal Polyps***M. Sidhu, N. Shahidi, S. Gupta, L. Desomer, S. Vosko, W. Arnout van Hattem, L. F. Hourigan, E. Y. T. Lee, A. Moss, S. Raftopoulos, S. J. Heitman, S. J. Williams, S. Zanati, D. J. Tate, N. Burgess, and M. J. Bourke*

In this study prospective study, 1037 LNPCPs that underwent successful EMR with complete EMT-T were enrolled. Recurrence at SC1 occurred in 10/707 cases (1.4%). In an international multicentre cohort of over 1000 LNPCPs, EMR-T significantly reduces the frequency of recurrence at SC1.

Clinical—Liver

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**Bariatric Surgery Reduces Cancer Risk in Adults With Nonalcoholic Fatty Liver Disease and Severe Obesity***V. K. Rustgi, Y. Li, K. Gupta, C. D. Minacapelli, A. Bhurwal, C. Catalano, and M. I. Elsaid*

In this study of privately insured patients, we found that bariatric surgery may reduce the risk of cancer and specifically obesity-related cancer in individuals with severe obesity and NAFLD.

Clinical—Biliary

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**Fully Covered Self-Expanding Metal Stent vs Multiple Plastic Stents to Treat Benign Biliary Strictures Secondary to Chronic Pancreatitis: A Multicenter Randomized Trial***M. Ramchandani, S. Lakhtakia, G. Costamagna, A. Tringali, A. Püspöek, B. Tribl, W. Dolak, J. Devière, M. Arvanitakis, S. van der Merwe, W. Laleman, T. Ponchon, V. Lepilliez, A. Gabrielli, L. Bernardoni, M. J. Bruno, J.-W. Poley, U. Arnelo, J. Lau, A. Roy, M. Bourke, A. Kaffes, H. Neuhaus, J. Peetermans, M. Rousseau, and D. N. Reddy***See editorial on page 31.**

For benign biliary stricture secondary to chronic pancreatitis, 12-month endotherapy using a single fully covered self-expandable metal stent has similar efficacy and safety and requires fewer procedural interventions than multiple plastic stents.

Basic and Translational—Alimentary Tract

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**Sequential Administration of XPO1 and ATR Inhibitors Enhances Therapeutic Response in TP53-mutated Colorectal Cancer***A. Inoue, F. S. Robinson, R. Minelli, H. Tomihara, B. S. Rizi, J. L. Rose, T. Kodama, S. Srinivasan, A. L. Harris, A. M. Zuniga, R. A. Mullinax, X. Ma, S. Seth, J. R. Daniele, M. D. Peoples, S. Loponte, K. C. Akdemir, T. O. Khor, N. Feng, J. Roszik, M. M. Sobieski, D. Brunell, C. Stephan, V. Giuliani, A. K. Deem, T. Shingu, Y. L. Deribe, D. G. Menter, T. P. Heffernan, A. Viale, C. A. Bristow, S. Kopetz, G. F. Draetta, G. Genovese, and A. Carugo***See editorial on page 33.**

Developing an approach that combines functional genomics, drug screening and patient-derived xenograft models, we uncovered novel rational drug combinations in colorectal cancer based on TP53 mutational status.

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Bacterial Swarmers Enriched During Intestinal Stress Ameliorate Damage

A. De, W. Chen, H. Li, J. R. Wright, R. Lamendella, D. J. Lukin, W. A. Szymczak, K. Sun, L. Kelly, S. Ghosh, D. B. Kearns, Z. He, C. Jobin, X. Luo, A. Byju, S. Chatterjee, B. San Yeoh, M. Vijay-Kumar, J. X. Tang, M. Prajapati, T. B. Bartnikas, and S. Mani

Bacterial swarmers are a feature of a stressed intestine, and when present in high abundance protect from intestinal inflammation in a microbiome dependent manner, facilitated by its distinct form of motility.

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Neutrophils Alter DNA Repair Landscape to Impact Survival and Shape Distinct Therapeutic Phenotypes of Colorectal Cancer

T. M. Bui, V. Butin-Israeli, H. L. Wiesolek, M. Zhou, J. F. Rehring, L. Wiesmüller, J. D. Wu, G.-Y. Yang, S. B. Hanauer, J. A. Sebag, and R. Sumagin

This work identified new mechanisms by which neutrophils aberrantly alter DNA repair pathways in tumor cells and delineate translatable therapies to target early versus advanced sporadic colorectal cancer.

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Bone Morphogenetic Protein Pathway Antagonism by *Grem1* Regulates Epithelial Cell Fate in Intestinal Regeneration

M. A. J. Koppens, H. Davis, G. N. Valbuena, E. J. Mulholland, N. Nasreddin, M. Colombe, A. Antanaviciute, S. Biswas, M. Friedrich, L. Lee, Oxford IBD Cohort Investigators, L. M. Wang, V. H. Koelzer, J. E. East, A. Simmons, D. J. Winton, and S. J. Leedham

Koppens et al investigate the role of a key intestinal signalling pathway, Bone Morphogenetic Protein (BMP), in homeostasis, inflammation and intestinal wounding, and show that signalling attenuation through physiological expression of a key pathway antagonist Grem1 is required for successful regeneration.

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Fecal Microbiota Transplantation for Recurrent *Clostridioides difficile* Infection Associates With Functional Alterations in Circulating microRNAs

T. M. Monaghan, A. M. Seekatz, N. O. Markham, T. O. Yau, M. Hatziapostolou, T. Jilani, N. Christodoulou, B. Roach, E. Birli, O. Pomenya, T. Louie, D. B. Lacy, P. Kim, C. Lee, D. Kao, and C. Polytarchou

Successful fecal microbiota transplantation for recurrent *Clostridioides difficile* infection associates with increased expression of specific microRNAs in blood and colonic tissues. These microRNAs target inflammatory proteins and can protect gut barrier from damage from *C. difficile* toxins.

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Intestinal Sulfation Is Essential to Protect Against Colitis and Colonic Carcinogenesis

P. Xu, Y. Xi, J. Zhu, M. Zhang, Z. Luka, D. B. Stolz, X. Cai, Y. Xie, M. Xu, S. Ren, Z. Huang, D. Yang, J. D. York, X. Ma, and W. Xie

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Basic and Translational—Liver

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Deleterious Variants in *ABCC12* are Detected in Idiopathic Chronic Cholestasis and Cause Intrahepatic Bile Duct Loss in Model Organisms

D.-H. Pham, R. Kudira, L. Xu, C. A. Valencia, J. L. Ellis, T. Shi, K. J. Evasion, I. Osuji, N. Matuschek, L. Pfuhler, M. Mullen, S. K. Mohanty, A. Husami, L. N. Bull, K. Zhang, S. Wali, C. Yin, and A. Miethke

See editorial on page 35.

ABCC12 encodes MRP9 protein that is important for maintaining cholangiocyte health in zebrafish and mice. Pathogenic variants in this gene are associated with intrahepatic bile duct loss in patients with chronic cholestasis.

- 301**   **Epithelia-Sensory Neuron Cross Talk Underlies Cholestatic Itch Induced by Lysophosphatidylcholine**
Y. Chen, Z.-L. Wang, M. Yeo, Q.-J. Zhang, A. E. López-Romero, H.-P. Ding, X. Zhang, Q. Zeng, S. L. Morales-Lázaro, C. Moore, Y.-A. Jin, H.-H. Yang, J. Morstein, A. Bortsov, M. Krawczyk, F. Lammert, M. Abdelmalek, A. M. Diehl, P. Milkiewicz, A. E. Kremer, J. Y. Zhang, A. Nackley, T. E. Reeves, M.-C. Ko, R.-R. Ji, T. Rosenbaum, and W. Liedtke

Identification of lysophosphatidylcholine as a novel itch-causing endogenous phospholipid with potential key impact on itch of chronic liver disease. We also uncovered lysophosphatidylcholine's cognate receptor in skin, calcium-permeable TRPV4 channels.

Basic and Translational—Pancreas

- 318** **Bcl3 Couples Cancer Stem Cell Enrichment With Pancreatic Cancer Molecular Subtypes**
 *J. Ai, S. M. Wörmann, K. Görgülü, M. Vallespinos, S. Zagorac, S. Alcalá, N. Wu, D. Kabacaoglu, A. Berninger, D. Navarro, E. Kaya-Aksoy, D. A. Ruess, K. J. Ciecielski, M. Kowalska, I. E. Demir, G. O. Ceyhan, I. Heid, R. Braren, M. Riemann, S. Schreiner, S. Hofmann, M. Kutschke, M. Jastroch, J. Slotta-Huspenina, A. Muckenhuber, A. M. Schlitter, R. M. Schmid, K. Steiger, K. N. Diakopoulos, M. Lesina, B. Sainz Jr., and H. Algül*

BCL3 may serve as a putative stratification marker for PDAC subtypes and tumor aggressiveness guiding individualized diagnostics and therapy.

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