

Gastroenterology

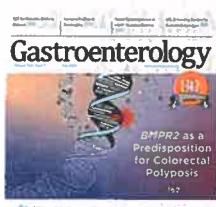
Volume 165 / Issue 1

July 2023

www.gastrojournal.org

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Publisher: *Gastroenterology* (ISSN 0016-5085) is published monthly (semi-monthly in April) in two indexed volumes by Elsevier Inc, 230 Park Avenue, New York, NY 10169-0901, USA. Periodicals postage paid at New York, NY and additional mailing offices. POSTMASTER: Send address changes to Elsevier, Journal Returns, 1799 Highway 50 East, Linn, MO 65051, USA. 2023 US subscription rates: individual, \$848.00; student and resident, \$323.00. Outside of the U.S. and possessions: individual, \$1026.00; student and resident, \$596.00; surface delivery, no additional charge; air mail delivery, add \$78.00. Prices subject to change without notice.

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D. Sun, C. Liu, Y. Zhu, C. Yu, Y. Guo, D. Sun, Y. Pang, P. Pei, H. Du, L. Yang, Y. Chen, X. Meng, Y. Liu, J. Zhang, D. Schmidt, D. Avery, J. Chen, Z. Chen, J. Lv, H. Kan, and L. Li, for the China Kadoorie Biobank Collaborative Group

Long-term exposure to high levels of fine ($\leq 2.5 \mu\text{m}$) particulate matter is associated with an increased risk of esophageal cancer.

Small Bowel

- 71 **The Long Noncoding RNA Cardiac Mesoderm Enhancer-Associated Noncoding RNA (*Carmn*) Is a Critical Regulator of Gastrointestinal Smooth Muscle Contractile Function and Motility**
X. He, K. Dong, J. Shen, G. Hu, J. D. Mintz, R. T. Atawia, J. Zhao, X. Chen, R. W. Caldwell, M. Xiang, D. W. Stepp, D. J. Fulton, and J. Zhou

See editorial on page 27.

The muscle cells of the gastrointestinal tract provide the force to move food. Our understanding of muscle cell function has been based on the actions of proteins, but the current study found that *Carmn*, a special type of long noncoding RNAs found in muscle cells, is critical for muscle contraction, gastrointestinal movement, and survival.

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Single-Cell Profiling of Tumor Immune Microenvironment Reveals Immune Irresponsiveness in Gastric Signet-Ring Cell Carcinoma*J. Chen, K. Liu, Y. Luo, M. Kang, J. Wang, G. Chen, J. Qi, W. Wu, B. Wang, Y. Han, L. Shi, K. Wang, X. Han, X. Ma, W. Liu, Y. Ding, L. Wang, H. Liang, L. Wang, and J. Chen*

Gastric signet-ring cell adenocarcinoma is a rare gastric cancer subtype associated with poor patient survival. We provide the first molecular portrayal of immune components in this disease through integrative single-cell transcriptomic and proteomic profiling.

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Oncomicrobial Community Profiling Identifies Clinicomolecular and Prognostic Subtypes of Colorectal Cancer*D. Mouradov, P. Greenfield, S. Li, E.-J. In, C. Storey, A. Sakthianandeswaren, P. Georgeson, D. D. Buchanan, R. L. Ward, N. J. Hawkins, I. Skinner, I. T. Jones, P. Gibbs, C. Ma, Y. J. Liew, K. Y. C. Fung, and O. M. Sieber*

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This study describes a gut bacteria-based classification system for bowel cancer that delineates 3 distinct subtypes that differ in tumor features and patient outcomes.

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Proteomic Profiling of Colorectal Adenomas Identifies a Predictive Risk Signature for Development of Metachronous Advanced Colorectal Neoplasia*J. M. Bech, T. Terkelsen, A. S. Bartels, F. Coscia, S. Doll, S. Zhao, Z. Zhang, N. Brünner, J. Lindebjerg, G. I. Madsen, X. Fang, M. Mann, and J. M. Afonso Moreira*

Colon polyps are mostly harmless but, over time, some can develop into colon cancer. This study showed that the protein content of polyps could predict events several years in advance.

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A TEAD2-Driven Endothelial-Like Program Shapes Basal-Like Differentiation and Metastasis of Pancreatic Cancer*H.-B. Yoo, J. W. Moon, H.-R. Kim, H. S. Lee, K. Miyabayashi, C. H. Park, S. Ge, A. Zhang, Y. K. Tae, Y. Sub, H.-W. Park, H. Y. Gee, F. Notta, D. A. Tuveson, S. Bang, M.-Y. Kim, and J.-S. Roe*

TEAD2 expression is increased in basal-like pancreatic cancer cells and activates endothelial-like enhancers. Hence, inhibition of TEAD2 activity is sufficient to repress basal-like subtype differentiation and its associated phenotypes.

Inflammatory Bowel Disease

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Comparative Effectiveness of Anti-TNF in Combination With Low-Dose Methotrexate vs Anti-TNF Monotherapy in Pediatric Crohn's Disease: A Pragmatic Randomized Trial*M. D. Kappelman, D. A. Wohl, H. H. Herfarth, A. M. Firestone, J. Adler, R. F. Amoury, J. E. Aronow, D. M. Bass, J. A. Bass, K. Benkov, C. B. Tobi, M. E. Boccieri, B. M. Boyle, W. B. Brinkman, J. M. Cabera, K. Chun, R. B. Colletti, C. M. Dodds, J. M. Dorsey, D. R. Ebach, E. Entrena, C. B. Forrest, J. A. Galanko, J. E. Grunow, A. S. Gulati, A. Ivanova, T. W. Jester, J. L. Kaplan, S. Kugathasan, M. E. Kusek, I. H. Leibowitz, T. M. Linville, E. A. Lipstein, P. A. Margolis, P. Minar, Z. Molle-Rios, J. Moses, K. K. Olano, L. Osaba, P. J. Palomo, H. Pappa, K. T. Park, D. S. Pashankar, L. Pitch, M. Robinson, C. M. Samson, K. C. Sandberg, J. R. Schuchard, M. Seid, K. A. Shelly, S. J. Steiner, J. A. Strople, J. S. Sullivan, J. Tung, P. Wali, M. Zikry, M. Weinberger, S. A. Saeed, and A. Bousvaros*

Tumor necrosis factor inhibitors, including infliximab and adalimumab, are a mainstay of pediatric Crohn's disease therapy; however, nonresponse and loss of response is common. Combination therapy with methotrexate may improve response. This randomized clinical trial compared tumor necrosis factor inhibitor combination therapy with methotrexate to tumor necrosis factor inhibitor alone. Combination therapy outperformed monotherapy for patients starting adalimumab, but not infliximab.

Colon

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BMPR2 as a Novel Predisposition Gene for Hereditary Colorectal Polyposis*L. Bonjoch, C. Fernandez-Rozadilla, M. Alvarez-Barona, A. Lopez-Novo, C. Herrera-Pariente, J. Amigo, L. Bujanda, D. Remedios, A. Dacal, J. Cubilla, F. Balaguer, F. Fernández-Bañares, A. Carracedo, R. Jover, S. Castellvi-Bel, and C. Ruiz-Ponte*

Variants in the BMPR2 gene affect molecular processes that could increase the risk of developing colonic polyposis and colorectal cancer.

Pancreas

- 173** **Distinct Serum Immune Profiles Define the Spectrum of Acute and Chronic Pancreatitis From the Multicenter Prospective Evaluation of Chronic Pancreatitis for Epidemiologic and Translational Studies (PROCEED) Study**
B. Lee, E. K. Jones, M. Manohar, L. Li, D. Yadav, D. L. Conwell, P. A. Hart, S. S. Vege, E. L. Fogel, J. Serrano, D. Andersen, M. D. Bellin, M. D. Topazian, S. K. Van Den Eeden, S. J. Pandol, C. E. Forsmark, W. E. Fisher, W. G. Park, S. Z. Husain, and A. Habtezion, on behalf of the Consortium for the Study of Chronic Pancreatitis, Diabetes, and Pancreatic Cancer (CPDPC)

Analysis of serum immune markers in a large cohort of pancreatitis allowed the identification of distinct immune markers that could serve as potential biomarkers providing mechanistic insights into pancreatitis progression.

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In an animal model for Wilson's disease, the peptide ARBM101 drains excess liver copper down to normal levels within days, plausibly suggesting new treatment concepts for this disease.

- 201** **Macrophage-derived Osteopontin (SPP1) Protects From Nonalcoholic Steatohepatitis**
H. Han, X. Ge, S. S. B. Komakula, R. Desert, S. Das, Z. Song, W. Chen, D. Athavale, H. Gaskell, D. Lantvit, G. Guzman, and N. Nieto

Currently, there are no approved treatments for nonalcoholic steatohepatitis, making this a major unmet clinical need. Although dynamic changes in liver macrophage subsets during the pathogenesis of nonalcoholic steatohepatitis link these shifts to pathologic tissue remodeling, macrophages also have potential to reduce steatosis and fibrosis, an aspect of macrophage function that has been understudied. Thus, the significance of this proposal lies in the delineation of the not previously known, protective role of osteopontin in macrophages in nonalcoholic steatohepatitis.

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E. Kharazmi, D. Scherer, F. Boekstegers, Q. Liang, K. Sundquist, J. Sundquist, M. Fallah, and J. Lorenzo Bermejo

The number of gallbladder operations to treat gallstones continues to rise. Patients with gallstone disease have an increased risk of kidney cancer shortly after and even many years after gallbladder surgery.

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J.-H. Kang, P. L. Splinter, C. E. Trussoni, N. E. Piriis, G. J. Gores, N. F. LaRusso, and S. P. O'Hara

The "epigenetic reader" bromodomain and extraterminal domain proteins drive cholangiocyte senescence, a pathologic feature of primary sclerosing cholangitis; targeting bromodomain and extraterminal domain proteins represents a novel treatment for primary sclerosing cholangitis.

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Fecal-based colorectal cancer screening is effective when there is adherence to the program of sequential (annual) testing. In circumstances when the uptake of fecal-based tests is suboptimal, colonoscopy should be considered in order to obtain maximum benefit.

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