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824 ERAP1 Regulates Natural Killer Cell Function by Controlling the Engagement of Inhibitory Receptors  
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846 Long Noncoding RNA HULC Modulates Abnormal Lipid Metabolism in Hepatoma Cells through an miR-9–Mediated RXRA Signaling Pathway  
Ming Cui, Zelin Xiao, Yue Wang, Mingsing Zheng, Tianqiang Song, Xiaoli Cai, Baodi Sun, Lihong Ye, and Xiaodong Zhang

#### MOLECULAR AND CELLULAR PATHOBIOLOGY

846 Long Noncoding RNA HULC Modulates Abnormal Lipid Metabolism in Hepatoma Cells through an miR-9–Mediated RXRA Signaling Pathway  
Ming Cui, Zelin Xiao, Yue Wang, Mingsing Zheng, Tianqiang Song, Xiaoli Cai, Baodi Sun, Lihong Ye, and Xiaodong Zhang

**Précis:** These timely and provocative findings suggest cautions in the clinical development of P2RX7 antagonists to treat inflammatory bowel disease, highlighting a need for additional investigations to gain a more complete understanding of how P2RX7 may influence risks in the development of inflammation-associated colon cancer.
Single-Strand DNA-Binding Protein SSB1 Facilitates TERT Recruitment to Telomeres and Maintains Telomere G-Overhangs
Raj K. Pandita, Tracy T. Chow, Durga Udayakumar, Amanda L. Bain, Liza Cubeddu, Clayton R. Hunt, Wei Shi, Nobuo Horikoshi, Yong Zhao, Woodring E. Wright, Kum Kum Khanna, Jerry W. Shay, and Tej K. Pandita

Précis: These findings offer an explanation for how telomerase is recruited to telomeres, a critical step in maintaining telomere ends and cell viability in all cancer cells.

A Central Role for Heme Iron in Colon Carcinogenesis Associated with Red Meat Intake

Précis: Elevated risk of colon cancer associated with red meat consumption is linked to heme iron, which may initiate carcinogenesis by enabling lipid peroxidation, providing a possible etiologic basis to understand this connection.

Crosstalk between KIT and FGFR3 Promotes Gastrointestinal Stromal Tumor Cell Growth and Drug Resistance
Nathalie Javidi-Sharifi, Elie Traer, Jacqueline Martinez, Aru Gupta, Takehiro Taguchi, Jennifer Dunlap, Michael C. Heinrich, Christopher L. Corless, Brian P. Rubin, Brian J. Druker, and Jeffrey W. Tyner

Précis: These findings provide a mechanistic rationale for use of existing FGFR inhibitors and multitarget inhibitors that target FGFR3 as strategies to improve treatment of gastrointestinal stromal tumors that exhibit resistance to imatinib mesylate, with immediate implications for clinical evaluation.

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ABOUT THE COVER

The high concentration of extracellular ATP in inflammatory lesions activates the purinergic P2RX7 receptor, which is expressed on immune and nonimmune cells of the gastrointestinal tract. The P2RX7 receptor participates in the initiation as well as the regulation of the inflammatory response and consequently can favor colon carcinogenesis. Using both genetic and pharmacological models of P2RX7 inactivation, we found that P2RX7 acted at an early stage to suppress the development of colitis-associated cancer. For details, see the article by Hofman and colleagues on page 835.