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## BREAKING ADVANCES

**824** ERAP1 Regulates Natural Killer Cell Function by Controlling the Engagement of Inhibitory Receptors  
Loredana Cifaldi, Paolo Romania, Michela Falco, Silvia Lorenzi, Raffaella Meaza, Stefania Petrimi, Marco Andreani, Daniela Pende, Franco Locatelli, and Doriana Fruci  
*Précis: This study identifies a protease responsible for trimming MHC class I-bound peptides in cancer cells as a target for regulating NK-cell immunity, with implications for improving outcomes of NK cell–based immunotherapeutic strategies.*

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**783** Signaling-Mediated Regulation of MicroRNA Processing  
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*Précis: This study identifies a protease responsible for trimming MHC class I-bound peptides in cancer cells as a target for regulating NK-cell immunity, with implications for improving outcomes of NK cell–based immunotherapeutic strategies.*

**792** Fearful Symmetry: Subversion of Asymmetric Division in Cancer Development and Progression  
Jeevisha Bajaj, Bryan Zimdahl, and Tannishtha Reya  
*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.*

**798** The Emerging Protumor Role of γδ T Lymphocytes: Implications for Cancer Immunotherapy  
Margarida Rei, Daniel J. Pennington, and Bruno Silva-Santos  
*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.*

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**803** Breast Cancer Prevention: Lessons to be Learned from Mechanisms of Early Pregnancy–Mediated Breast Cancer Protection  
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*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.*

**808** Redundancy: A Critical Obstacle to Improving Cancer Therapy  
Orit Lavi  
*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.*

## MICROENVIRONMENT AND IMMUNOLOGY

**813** Akt–Girdin Signaling in Cancer-Associated Fibroblasts Contributes to Tumor Progression  
Yumiko Yamamura, Naoya Asai, Atsushi Enomoto, Takuya Kato, Shinji Mii, Yuji Kondo, Kaori Ushida, Kaoru Niimi, Nobuyuki Tsunoda, Masato Nagino, Shu Ichihara, Koichi Furukawa, Kengo Maeda, Toyoaki Murohara, and Masahide Takahashi  
*Précis: These results elucidate a long noncoding RNA–facilitated pathway of aberrant lipid metabolism that contributes to the development of liver cancer, with potential clinical implications for its prevention and management.*

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Loredana Cifaldi, Paolo Romania, Michela Falco, Silvia Lorenzi, Raffaella Meaza, Stefania Petrimi, Marco Andreani, Daniela Pende, Franco Locatelli, and Doriana Fruci  
*Précis: This study identifies a protease responsible for trimming MHC class I-bound peptides in cancer cells as a target for regulating NK-cell immunity, with implications for improving outcomes of NK cell–based immunotherapeutic strategies.*

**835** Genetic and Pharmacological Inactivation of the Purinergic P2RX7 Receptor Dampens Inflammation but Increases Tumor Incidence in a Mouse Model of Colitis-Associated Cancer  
Paul Hofman, Julien Cherfils-Vicini, Marie Baniz, Marius Ilie, Thierry Juhel, Xavier Héburene, Eric Gilson, Annie Schmid-Alliana, Olivier Boyer, Sahil Adriouch, and Valérie Vouret-Craviari  
*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.*

## 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 Cai, Zelin Xiao, Yue Wang, Mimiying Zheng, Tianqiang Song, Xiaoli Cai, Baodi Sun, Lihong Ye, and Xiaodong Zhang  
*Précis: These results elucidate a long noncoding RNA–facilitated pathway of aberrant lipid metabolism that contributes to the development of liver cancer, with potential clinical implications for its prevention and management.*
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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.