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### MICROENVIRONMENT AND IMMUNOLOGY

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**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:** Tumor pathogenesis relies upon P38/Akt signaling not only in tumor cells but also in cells of the tumor microenvironment, as shown here in cancer-associated fibroblasts through a mechanism involving activation of an actin-binding protein that drives the invasive behavior of nearby cancer cells.

824  
**ERAP1 Regulates Natural Killer Cell Function by Controlling the Engagement of Inhibitory Receptors**

Loredana Cifaldi, Paolo Romana, Michela Falco, Silvia Lorenzi, Raffaella Meazza, Stefania Petriti, 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 Bazin, Marius Ilie, Thierry Juhel, Xavier Hébuneer, 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.

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, Minying 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.
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, Anu 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 multikinase 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.

Establishment and Characterization of a Cell Line from Human Circulating Colon Cancer Cells

Laure Cayrefourcq, Thibault Mazard, Simon Joosse, Jérôme Solassol, Jeanne Ramos, Eric Assenat, Udo Schumacher, Valérie Costes, Thierry Maudelonde, Klaus Pantel, and Catherine Alix-Panabière

Précis: The analysis of circulating tumor cells will contribute to personalized medicine by tailoring anticancer therapies to the genetic and phenotypic characteristics of metastatic cells in individual cancer patients.

Correction: Peptides and Aptamers Targeting HSP70: A Novel Approach for Anticancer Chemotherapy

Correction: Macrophage Inflammatory Protein Derivative ECI301 Enhances the Alarmin-Associated Abscopal Benefits of Tumor Radiotherapy
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.