


BREAKING ADVANCES

- 781 Highlights from Recent Cancer Literature


REVIEWS

- 783 Signaling-Mediated Regulation of MicroRNA Processing
Jia Shen and Mien-Chie Hung
- 792 Fearful Symmetry: Subversion of Asymmetric Division in Cancer Development and Progression
Jeevisha Bajaj, Bryan Zimdahl, and Tannishtha Reya
- 798 The Emerging Protumor Role of $\gamma\delta$ T Lymphocytes: Implications for Cancer Immunotherapy
Margarida Rei, Daniel J. Pennington, and Bruno Silva-Santos

PERSPECTIVES

- 803 Breast Cancer Prevention: Lessons to be Learned from Mechanisms of Early Pregnancy-Mediated Breast Cancer Protection
 Fabienne Meier-Abt, Mohamed Bentires-Alj, and Christoph Rochlitz
- 808 Redundancy: A Critical Obstacle to Improving Cancer Therapy
Orit Lavi

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, Toyooki Murohara, and Masahide Takahashi

Précis: Tumor pathogenesis relies upon PI3K/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 Romania, Michela Falco, Silvia Lorenzi, Raffaella Meazza, Stefania Petrini, 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 Hébuterne, 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 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.

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858 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.

PREVENTION AND EPIDEMIOLOGY

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

Nadia M. Bastide, Fatima Chenni, Marc Audebert, Raphaëlle L. Santarelli, Sylviane Taché, Nathalie Naud, Maryse Baradat, Isabelle Jouanin, Reggie Surya, Ditte A. Hobbs, Gunter G. Kuhnle, Isabelle Raymond-Letron, Françoise Gueraud, Denis E. Corpet, and Fabrice H.F. Pierre

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.

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

880 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.

TUMOR AND STEM CELL BIOLOGY

892 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-Panabières

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.

CORRECTIONS

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

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

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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.

