REVIEWS

5945 DNA Damage Response and Growth Factor Signaling Pathways in Gliomagenesis and Therapeutic Resistance
Massimo Squatrito and Eric C. Holland

5950 MicroRNA Regulation of Cancer Stem Cells
Can Liu and Dean G. Tang

MEETING REPORTS

5955 Circulating Tumor Cell Isolation and Diagnostics: Toward Routine Clinical Use
Anja van de Stolpe, Klaus Pantel, Stefan Sleijfer, Leon W. Terstappen, and Jaap M.J. den Toonder

5961 Systems Biology: Confronting the Complexity of Cancer
Andrew J. Gentles and Daniel Gallahan

INTEGRATED SYSTEMS AND TECHNOLOGIES

5965 Using Tandem Mass Spectrometry in Targeted Mode to Identify Activators of Class IA PI3K in Cancer
Xuemei Yang, Alexa B. Turke, Jie Qi, Youngchul Song, Brent N. Bexer, Todd W. Miller, Pasi A. Jänne, Carlos L. Arteaga, Lewis C. Cantley, Jeffrey A. Engelman, and John M. Asara

Précis: Defining the upstream acting tyrosine kinase pathways that activate PI3K signaling in different tumors may help inform clinical decisions about personalized strategies for cancer treatment.

MOLECULAR AND CELLULAR PATHOBIOLOGY

6010 Activated Notch1 Induces Lung Adenomas in Mice and Cooperates with Myc in the Generation of Lung Adenocarcinoma
Thaddeus D. Allen, Elena M. Rodriguez, Kirk D. Jones, and J. Michael Bishop

Précis: This study offers a preclinical genetic proof-of-concept that targeted inhibitors of the Notch pathway should be useful to treat lung adenocarcinomas and other solid tumors driven by oncogenic Myc.

Blocking Hypoxia-Induced Autophagy in Tumors Restores Cytotoxic T-Cell Activity and Promotes Regression
Muhammad Zaeem Noman, Bassam Janji, Bozena Kaminska, Kris Van Moer, Sandrine Pierson, Piotr Przanowski, Stéphanie Buart, Guy Berchem, Pedro Romero, Fatihia Mami-Chouaib, and Salem Chouaib

Précis: This study establishes a crucial causal link between hypoxia-induced autophagy in tumor cells and their resistance to killing by antigen-specific cytotoxic T cells, revealing a major role for autophagy in mediating immune escape in cancer.

Précis: Findings demonstrate a dual role for mast cells in the progression of prostate cancer, arguing that therapeutic targeting of mast cells may be beneficial in early but not late stages of this disease.

Précis: Findings show how p53 mediates an important aspect of its tumor suppressor function by stimulating natural killer cells, a powerful arm of the innate immune system that can destroy tumor cells.
**Taxane-Induced Blockade to Nuclear Accumulation of the Androgen Receptor Predicts Clinical Responses in Metastatic Prostate Cancer**


*Précis: This study suggests a histochemical test in circulating cancer cells that could predict therapeutic responses to taxanes used to treat advanced prostate cancer.*

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**Biological Roles of the Delta Family Notch Ligand Dll4 in Tumor and Endothelial Cells in Ovarian Cancer**


*Précis: Findings define a functionally important role for a Notch receptor ligand of the Delta family in both the tumor and endothelial compartments of ovarian cancer, with potential implications to leverage outcomes of anti-VEGF treatment.*

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**Vitamin D3 Enhances the Apoptotic Response of Epithelial Tumors to Aminolevulinate-Based Photodynamic Therapy**

Sanjay Anand, Clara Wilson, Tayyaba Hasan, and Edward V. Maytin

*Précis: This important study shows how vitamin D3 can be used as a simple, nontoxic, and highly effective preconditioning regimen to enhance the response of epithelial tumors to a combination drug phototherapy, perhaps broadening its clinical applications.*

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**Endothelial Cells Create a Stem Cell Niche in Glioblastoma by Providing NOTCH Ligands That Nurture Self-Renewal of Cancer Stem-Like Cells**

Thant S. Zhu, Mark A. Costello, Caroline E. Talsma, Callie G. Flack, Jessica G. Crowley, Jie Wang, Xiaming He, Shawn L. Hervey-Jumper, Jason A. Heth, Karin M. Mura, Francesco DiMeco, Angelo L. Vescovi, and Xing Fan

*Précis: This important human study expands concepts of how the tumor endothelium supports cancer growth, in providing not only a blood supply but also a niche to feed self-renewal of cancer stem-like cells.*

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**A Novel ALK Secondary Mutation and EGFR Signaling Cause Resistance to ALK Kinase Inhibitors**


*Précis: Identifying mechanisms of resistance to targeted inhibitors represents a first step in developing second generation drugs and/or rationale combination therapies as potential clinical therapies for cancer patients.*
ABOUT THE COVER

Mast cells are best known for their primary involvement in allergic reactions, but have recently been reappraised as important players in either cancer promotion or inhibition. Pittoni and colleagues report that mast cells are enriched and degranulated in areas of adenocarcinoma in prostate tumor-bearing mice and patients, and foster tumor growth through MMP-9 provision. However, mast cell–targeted therapy in this setting has a dark side, originating from the previously unrecognized capacity of mast cells to control neuroendocrine prostate tumor variants. For details, see the article by Pittoni and colleagues on page 5987 of this issue.
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