BREAKING ADVANCES

5943 Highlights from Recent Cancer Literature

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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. Janne, 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.
**THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY**

**6030** 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.

**6040** 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 pre-conditioning regimen to enhance the response of epithelial tumors to a combination drug phototherapy, perhaps broadening its clinical applications.

**TUMOR AND STEM CELL BIOLOGY**

**6051** 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.

**6061** 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. Taloma, Callie G. Flack, Jessica G. Crowley, Lisa L. Ham, Xiaobing He, Shawn L. Hervey-Jumper, Jason A. Heth, Karin M. Muraszko, 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.

**6073** DLL4-Notch Signaling Mediates Tumor Resistance to Anti-VEGF Therapy In Vivo

Ji-Liang Li, Richard C.A. Sainson, Chern Ein Oon, Helen Turley, Russell Leek, Helen Sheldon, Esther Bridges, Wen Shi, Cameron Snell, Emma T. Bowden, Herren Wu, Partha S. Chowdhury, Angela J. Russell, Craig P. Montgomery, Richard Poulsom, and Adrian L. Harris

**Précis:** Findings implicate the DLL4-Notch signaling pathway in mediating resistance to the widely administered angiogenic drug bevacizumab, suggesting that a combined blockade could enhance its efficacy.
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.