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# Cancer Research

September 15, 2011 • Volume 71 • Number 18

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## INTEGRATED SYSTEMS AND TECHNOLOGIES

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*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.*

## MICROENVIRONMENT AND IMMUNOLOGY

- 5976 | **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, Fathia 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.*

- 5987 | **Mast Cell Targeting Hampers Prostate Adenocarcinoma Development but Promotes the Occurrence of Highly Malignant Neuroendocrine Cancers**  
Paola Pittoni, Claudio Tripodo, Silvia Piconese, Giorgio Mauri, Mariella Parenza, Alice Rigoni, Sabina Sangaletti, and Mario P. Colombo

*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.*

- 5998 | **Human NK Cells Are Alerted to Induction of p53 in Cancer Cells by Upregulation of the NKG2D Ligands ULBP1 and ULBP2**  
Sonja Textor, Nathalie Fiegler, Annette Arnold, Angel Porgador, Thomas G. Hofmann, and Adelheid Cerwenka

*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.*

## 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.*

6019

**Taxane-Induced Blockade to Nuclear Accumulation of the Androgen Receptor Predicts Clinical Responses in Metastatic Prostate Cancer**

Medha S. Darshan, Matthew S. Loftus, Maria Thadani-Mulero, Benjamin P. Levy, Daniel Escuin, Xi Kathy Zhou, Ada Gjyrezi, Chantal Chanel-Vos, Ruoqian Shen, Scott T. Tagawa, Neil H. Bander, David M. Nanus, and Paraskevi Giannakakou

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

6051

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

Takaaki Sasaki, Jussi Koivunen, Atsuko Ogino, Masahiko Yanagita, Sarah Nikiforow, Wei Zheng, Christopher Lathan, J. Paul Marcoux, Jinyan Du, Katsuhiko Okuda, Marzia Capelletti, Takeshi Shimamura, Dalia Ercan, Magda Stumpfova, Yun Xiao, Stanislaw Weremowicz, Mohit Butaney, Stephanie Heon, Keith Wilner, James G. Christensen, Michel J. Eck, Kwok-Kin Wong, Neal Lindeman, Nathanael S. Gray, Scott J. Rodig, and Pasi A. Jänne

*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.

**THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY**

6030

**Biological Roles of the Delta Family Notch Ligand DLL4 in Tumor and Endothelial Cells in Ovarian Cancer**

Wei Hu, Chunhua Lu, Hee Dong Han, Jie Huang, De-yu Shen, Rebecca L. Stone, Alpa M. Nick, Mian M.K. Shahzad, Edna Mora, Nicholas B. Jennings, Sun Joo Lee, Ju-Won Roh, Koji Matsuo, Masato Nishimura, Blake W. Goodman, Robert B. Jaffe, Robert R. Langley, Michael T. Deavers, Gabriel Lopez-Berestein, Robert L. Coleman, and Anil K. Sood

*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 Aminolevulinic Acid-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.

**TUMOR AND STEM CELL BIOLOGY**

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. Talsma, Callie G. Flack, Jessica G. Crowley, Lisa L. Hamm, 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 Poulosom, and Adrian L. Harris

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

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## CORRECTIONS

6084 **Correction: Aggressive Fibromatosis (Desmoid Tumor) Is Derived from Mesenchymal Progenitor Cells**

6085 **Correction: ID4 Imparts Chemoresistance and Cancer Stemness to Glioma Cells by Derepressing miR-9\*-Mediated Suppression of SOX2**

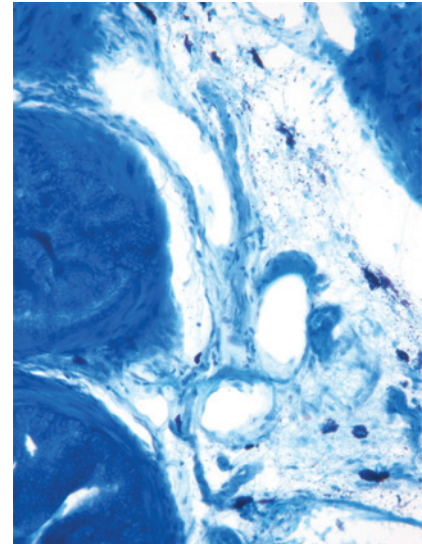
6086 **Correction: Effect of ON 01910.Na, an Anticancer Mitotic Inhibitor, on Cell-Cycle Progression Correlates with RanGAP1 Hyperphosphorylation**

6087 **Correction: Hedgehog Fights Back: Mechanisms of Acquired Resistance against Smoothed Antagonists**

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## 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.



# Cancer Research

The Journal of Cancer Research (1916–1930) | The American Journal of Cancer (1931–1940)

## 71 (18)

*Cancer Res* 2011;71:5943-6087.

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