Highlights of This Issue 5369

SPECIAL FEATURES

5371 Highly Active Antitumor Therapy (HAATT) for Epidermal Growth Factor Receptor–Mutant Lung Cancer
Juliann Chmielecki and William Pao
See article p. 5489

5374 Target of Rapamycin Signaling in Leukemia and Lymphoma
Collin Vu and David A. Fruman

5381 Phase III Clinical Trial Development: A Process of Chutes and Ladders
David M. Dilts, Steven K. Cheng, Joshua S. Crites, Alan B. Sandler, and James H. Doroshow
See article p. 5557

5390 Hypoexpression and Epigenetic Regulation of Candidate Tumor Suppressor Gene CADM-2 in Human Prostate Cancer
Guimin Chang, Shuping Xu, Rajiv Dhir, Uma Chandran, Denise S. O’Keefe, Norman M. Greenberg, and Jeffrey R. Gingrich

5402 MSH6 and MUTYH Deficiency Is a Frequent Event in Early-Onset Colorectal Cancer

5414 Differential Gene Expression in Benign Prostate Epithelium of Men with and without Prostate Cancer: Evidence for a Prostate Cancer Field Effect

5424 Dual Inhibition of PI3K and mTORC1/2 Signaling by NVP-BEZ235 as a New Therapeutic Strategy for Acute Myeloid Leukemia
Nicolas Chapuis, Jerome Tamburini, Alexia S. Green, Christine Vignon, Valerie Bardet, Aymeric Neyret, Melanie Pannetier, Lise Willems, Sophie Park, Alexandre Macone, Sauveur-Michel Maira, Norbert Ifrah, François Dreyfus, Olivier Herault, Catherine Lacombe, Patrick Mayeux, and Didier Bouscary

5436 The Insulin-like Growth Factor I Receptor/Insulin Receptor Tyrosine Kinase Inhibitor PQIP Exhibits Enhanced Antitumor Effects in Combination with Chemotherapy Against Colorectal Cancer Models
Sara A. Flanigan, Todd M. Pitts, S. Gail Eckhardt, John J. Tentler, Aik Choon Tan, Andrew Thorburn, and Stephen Leong

5447 Development of a Validated Immunofluorescence Assay for γH2AX as a Pharmacodynamic Marker of Topoisomerase I Inhibitor Activity
Robert J. Kinders, Melinda Hollingshead, Scott Lawrence, Jiuping Ji, Brian Tabb, William M. Bonner, Yves Pommier, Larry Rubinstein, Yvonne A. Evrard, Ralph E. Parchment, Joseph Tomaszewski, and James H. Doroshow; for the National Cancer Institute Phase 0 Clinical Trials Team
IMAGING, DIAGNOSIS, PROGNOSIS

**Overexpression of High-Mobility Group Box 2 Is Associated with Tumor Aggressiveness and Prognosis of Hepatocellular Carcinoma**
Jung-Hee Kwon, Jongmin Kim, Jin Young Park, Sun Mi Hong, Chang Wook Park, Seok Joo Hong, Sun Young Park, Yoon Jung Choi, In-Gu Do, Jae-Won Joh, Dae Shick Kim, and Kwan Yong Choi

**Prognostic Significance of RNA-Dependent Protein Kinase on Non–Small Cell Lung Cancer Patients**
Abujiang Pataer, Maria Gabriela Raso, Arlene M. Correa, Carmen Behrens, Koji Tsuta, Luisa Solis, Bingliang Fang, Jack A. Roth, Ignacio I. Wistuba, and Stephen G. Swisher

**Expression, Cellular Distribution, and Prognostic Relevance of TRAIL Receptors in Hepatocellular Carcinoma**
Lydia Kriegl, Andreas Jung, Jutta Engel, Rene Jackstadt, Alexander L. Gerbes, Eike Gallmeier, Jana A. Reiche, Heiko Hermeking, Antonia Rizzani, Christine Brun, Frank T. Kolligs, Thomas Kirchner, Burkhard Göke, and Enrico N. De Toni

CANCER THERAPY: CLINICAL

**Vaccination of Metastatic Renal Cancer Patients with MVA-5T4: A Randomized, Double-Blind, Placebo-Controlled Phase III Study**
Robert J. Amato, Robert E. Hawkins, Howard L. Kaufman, John A. Thompson, Piotr Tomczak, Cezary Szczylik, Mike McDonald, Sarah Eastty, William H. Shingler, Jackie de Belin, Madusha Goonewardena, Stuart Naylor, and Richard Harrop

**Mechanisms of Synergistic Antileukemic Interactions between Valproic Acid and Cytarabine in Pediatric Acute Myeloid Leukemia**
Chengzhi Xie, Holly Edwards, Xuelian Xu, Hui Zhou, Steven A. Buck, Mark L. Stout, Qun Yu, Jeffrey E. Rubnitz, Larry H. Matherly, Jeffrey W. Taub, and Yubin Ge

**A Randomized Trial of Ex vivo CD40L Activation of a Dendritic Cell Vaccine in Colorectal Cancer Patients: Tumor-Specific Immune Responses Are Associated with Improved Survival**
ABOUT THE COVER

Atu027, a liposomal siRNA, is a novel RNAi therapeutic for cancer therapy suppressing PKN3 gene expression in endothelial cells of the vasculature. In cultured human endothelial cells (HUVEC), Atu027 mediated downregulation of PKN3 led to increased levels of the adhesion protein vascular endothelial (VE)-cadherin. The different levels of VE-cadherin protein are depicted in this image in a color-coded manner reflecting highest VE-cadherin levels as red colored membrane staining. The authors show that Atu027 treatment modulates the vascular endothelium in a way that metastasis through the blood vessels to the lung is effectively inhibited. For further details, please see Santel and colleagues on page 5469 in this issue.