Contents

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

Molecular Pathways

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
Maria Dolores Giráldez, Francesc Balaguer, Luis Bujanda, Miriam Cuatrecasas, Jenifer Muñoz, Virginia Alonso-Espinaco, Mikel Larzabal, Anna Petit, Victoria Gonzalo, Teresa Ocaña, Letícia Moreira, José María Enríquez-Navascués, C. Richard Boland, Ajay Goel, Antoni Castells, and Sergi Castellví-Bel

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

CANCER THERAPY: PRECLINICAL

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, Alexa S. Green, Christine Vignon, Valerie Bardet, Aymeric Neyret, Melanie Pannetier, Lise Willems, Sophie Park, Alexandre Macone, Sauver-Michel Maïra, 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

The Journal of Clinical and Translational Research

November 15, 2010 • Volume 16 • Number 22
5458 Transduction of Tumor-Specific T Cells with CXCR2 Chemokine Receptor Improves Migration to Tumor and Antitumor Immune Responses
Weiyi Peng, Yang Ye, Brian A. Rabinovich, Chengwen Liu, Yanyan Lou, Minying Zhang, Mayra Whittington, Yan Yang, Willem W. Overwijk, Gregory Lizee, and Patrick Hvu

5469 Atu027 Prevents Pulmonary Metastasis in Experimental and Spontaneous Mouse Metastasis Models
Ansgar Santel, Manuela Aleku, Nadine Röder, Kristin Möpert, Birgit Durieux, Oliver Janké, Oliver Keil, Jens Endruschat, Sibylle Dames, Christian Lange, Mona Eisermann, Kathrin Löffler, Melanie Fechner, Gerald Fisch, Christiane Vank, Ute Schaeper, Klaus Giese, and Jörg Kaufmann

5481 Eradication of Medullary Multiple Myeloma by CD4+ Cytotoxic Human T Lymphocytes Directed at a Single Minor Histocompatibility Antigen
Robbert M. Spaapen, Richard W.J. Groen, Kelly van den Oudenedal, Teun Guichelaar, Maureen van Elk, Tineke Aarts-Riemens, Andries C. Bloem, Gert Storm, Anton C. Martens, Henk M. Lokhorst, and Tuna Mutis

5489 Reciprocal and Complementary Role of MET Amplification and EGFR T790M Mutation in Acquired Resistance to Kinase Inhibitors in Lung Cancer
Kenichi Suda, Isao Murakami, Tatsuya Katayama, Kenji Tomizawa, Hirotaka Osada, Yosihata Sekido, Yoshihiko Maehara, Yasushi Yatabe, and Tetsuya Mitsudomi
See commentary p. 5371

5499 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

IMAGING, DIAGNOSIS, PROGNOSIS

5511 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

5522 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

5529 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 Hermet, Antonia Rizzani, Christiane J. Bruns, Frank T. Kolligs, Thomas Kirchner, Burkhard Göke, and Enrico N. De Toni

CANCER THERAPY: CLINICAL

5539 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

5548 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
Richard J. Barth, Jr., Dawn A. Fisher, Paul K. Wallace, Jacqueline Y. Channon, Randolph J. Noelle, Jiang GUI, and Marc S. Ernstoff
A Sense of Urgency: Evaluating the Link between Clinical Trial Development Time and the Accrual Performance of Cancer Therapy Evaluation Program (NCI-CTEP) Sponsored Studies
Steven K. Cheng, Mary S. Dietrich, and David M. Dilts
See commentary p. 5381

REO-10: A Phase I Study of Intravenous Reovirus and Docetaxel in Patients with Advanced Cancer
Charles Comins, James Spicer, Andrew Protheroe, Victoria Roulstone, Katie Twigger, Christine M. White, Richard Vile, Alan Melcher, Matt C. Coffey, Karl L. Mettinger, Gerard Nuovo, David E. Cohn, Mitch Phelps, Kevin J. Harrington, and Hardev S. Pandha

Combination of Temsirolimus (CCI-779) with Chemoradiation in Newly Diagnosed Glioblastoma Multiforme (GBM) (NCCTG trial N027D) Is Associated with Increased Infectious Risks

Optimizing the Detection of Lung Cancer Patients Harboring Anaplastic Lymphoma Kinase (ALK) Gene Rearrangements Potentially Suitable for ALK Inhibitor Treatment
D. Ross Camidge, Scott A. Kono, Antonella Flacco, Aik-Choon Tan, Robert C. Doebele, Qing Zhou, Lucio Crino, Wilbur A. Franklin, and Marielle Varella-Garcia

Germline Polymorphisms in Genes Involved in the IGF1 Pathway Predict Efficacy of Cetuximab in Wild-type KRAS mCRC Patients
Thomas Winder, Wu Zhang, Dongyun Yang, Yan Ning, Pierre Bohanes, Armin Gerger, Peter M. Wilson, Alexandra Pohl, David J. Mauro, Christiane Langer, Eric K. Rowinsky, and Heinz-Josef Lenz

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.