Contents

Highlights of This Issue 5915

SPECIAL FEATURES

CCR Translations

5917  Braking Bad: Blockade of Inhibitory Pathways Improves Interleukin-15 Therapy
William E. Carson III

5920  Toward a Better Understanding of Race and Cancer
Otis W. Brawley

CCR Drug Updates

5923  Pazopanib in Renal Cell Carcinoma
James E. Ward and Walter M. Stadler

Molecular Pathways

5928  Hypoxia and Hypoxia-Inducible Factors: Master Regulators of Metastasis
Xin Lu and Yibin Kang

5936  Targeting RET Receptor Tyrosine Kinase Activation in Cancer
John E. Phay and Manisha H. Shah

Review

5942  Resveratrol: Challenges in Translation to the Clinic — A Critical Discussion
Lalita Subramanian, Sherry Youssef, Saswati Bhattacharya, Jason Kenealey, Arthur S. Polans and Paul R. van Ginkel

CCR Focus

5950  Striving to Improve Outcomes in Oncology: Unmet Expectations in a Complex Disease
Susan E. Bates

5951  Translating Clinical Trials into Meaningful Outcomes
Patricia M. LoRusso, Lowell E. Schnipper, David J. Stewart, Scott A. Boerner, Steven D. Averbuch and Walter Wolf

5956  Making the Investigational Oncology Pipeline More Efficient and Effective: Are We Headed In the Right Direction?
Patricia M. LoRusso, Aparna B. Anderson, Scott A. Boerner and Steven D. Averbuch

5963  Evaluating Patient-Centered Outcomes in the Randomized Controlled Trial and Beyond: Informing the Future with Lessons from the Past
Christopher M. Booth

5972  Biologically Targeted Cancer Therapy and Marginal Benefits: Are We Making Too Much of Too Little or Are We Achieving Too Little by Giving Too Much?
Tito Fojo and David R. Parkinson

5981  Explaining Marginal Benefits to Patients, When "Marginal" Means Additional but Not Necessarily Small
Thomas J. Smith and Bruce E. Hillner

5987  The 2010 Health Care Reform Act: A Potential Opportunity to Advance Cancer Research by Taking Cancer Personally
William S. Dalton, Daniel M. Sullivan, Timothy J. Yeatman and David A. Fenstermacher

5997  The Impact of Insurance on Access to Cancer Clinical Trials at a Comprehensive Cancer Center
Justin F. Klamerus, Suanna S. Bruinooge, Xiaobu Ye, Mandi L. Klamers, Dorothy Damron, Dina Lansey, John C. Lowery, Luis A. Diaz Jr., Jean G. Ford, Norma Kanarek and Charles M. Rudin

6004  Value and Cancer Care: Toward an Equitable Future
Lowell E. Schnipper, Neal J. Meropol and Dan W. Brock
HUMAN CANCER BIOLOGY

6009 IQGAP1 Plays an Important Role in the Invasiveness of Thyroid Cancer
Zhi Liu, Dingxie Liu, Ermal Bojdani, Adel K. El-Naggar, Vasily Vasko and Mingzhao Xing

6019 Simultaneous Blockade of Multiple Immune System Inhibitory Checkpoints Enhances Antitumor Activity Mediated by Interleukin-15 in a Murine Metastatic Colon Carcinoma Model
Ping Yu, Jason C. Steel, Meili Zhang, John C. Morris and Thomas A. Waldmann

6029 Vertical Targeting of the Phosphatidylinositol-3 Kinase Pathway as a Strategy for Treating Melanoma
Saadia A. Aziz, Lucia B. Jilaveanu, Christopher Zito, Robert L. Camp, David L. Rimm, Patricia Conrad and Harriet M. Kluger

6040 The Oncogenic BRAF Kinase Inhibitor PLX4032/RG7204 Does Not Affect the Viability or Function of Human Lymphocytes across a Wide Range of Concentrations

6049 Microenvironmental Regulation of Glioblastoma Radioreponse
Muhammad Jamal, Barbara H. Rath, Eli S. Williams, Kevin Camphausen and Philip J. Toftilon

6060 The Notch Target Hes1 Directly Modulates Gli1 Expression and Hedgehog Signaling: A Potential Mechanism of Therapeutic Resistance
Karisa C. Schreck, Pete Taylor, Luigi Marchionni, Vidya Gopalakrishnan, Eli E. Bar, Nicholas Gaiano and Charles G. Eberhart

6071 A Hypoxia- and α-Fetoprotein-Dependent Oncolytic Adenovirus Exhibits Specific Killing of Hepatocellular Carcinomas
Oh-Joon Kwon, Pyung-Hwan Kim, Steven Huyn, Lily Wu, Minjung Kim and Chae-Ok Yun

IMAGING, DIAGNOSIS, PROGNOSIS

6083 Genotypic Profiling of 452 Choroidal Melanomas with Multiplex Ligation-Dependent Probe Amplification
Bertil Damato, Justyna A. Dopierala, Sarah E. Coupland

6093 Prognostic Value of Baseline [18F] Fluorodeoxyglucose Positron Emission Tomography and 99mTc-MDP Bone Scan in Progressing Metastatic Prostate Cancer

6100 Intrinsic Breast Tumor Subtypes, Race, and Long-Term Survival in the Carolina Breast Cancer Study

6111 A Combination of Serum Markers for the Early Detection of Colorectal Cancer
Norbert Wild, Herbert Andres, Wolfgang Rollinger, Friedemann Krause, Peter Dilba, Michael Tacke and Johann Karl

CANCER THERAPY: PRECLINICAL

6122 CD8+ Enriched “Young” Tumor Infiltrating Lymphocytes Can Mediate Regression of Metastatic Melanoma
Mark E. Dudley, Colin A. Gross, Michelle M. Langhan, Marcos R. Garcia, Richard M. Sherry, James C. Yang, Giao Q. Phan, Udai S. Kammula, Marybeth S. Hughes, Deborah E. Citrin, Nicholas P. Restifo, John R. Wunderlich, Peter A. Priesto, Jenny J. Hong, Russell C. Langan, Daniel A. Zlott, Kathleen E. Morton, Donald E. White, Carolyn M. Laurencot and Steven A. Rosenberg

6132 Phase I Clinical Trial of the Chimeric Anti-Mesothelin Monoclonal Antibody MORAb-009 in Patients with Mesothelin-Expressing Cancers
Raffit Hassan, Steven J. Cohen, Martin Phillips, Ira Pastan, Elad Sharon, Ronan J. Kelly, Charles Schweizer, Susan Weil and Daniel Laheru
Phase I and Pharmacokinetic Studies of CYT-6091, a Novel PEGylated Colloidal Gold-rhTNF Nanomedicine

Tumor Survivin Is Downregulated by the Antisense Oligonucleotide LY2181308: A Proof-of-Concept, First-in-Human Dose Study
Denis C. Talbot, Malcolm Ranson, Joanna Davies, Michael Lahn, Sophie Callies, Valérie André, Sunil Kadam, Michael Burgess, Christopher Slapak, Anna L. Olsen, Peter I. McHugh, Johann S. de Bono, Julian Matthews, Azeem Saleem and Patricia Price

PREDICTIVE BIOMARKERS AND PERSONALIZED MEDICINE

A Marker of Homologous Recombination Predicts Pathologic Complete Response to Neoadjuvant Chemotherapy in Primary Breast Cancer
Monika Graeser, Afshan McCarthy, Christopher J. Lord, Kay Savage, Margaret Hills, Janine Salter, Nicholas Orr, Marina Parton, Ian E. Smith, Jorge S. Reis-Filho, Mitch Dowsett, Alan Ashworth and Nicholas Turner

Gene Polymorphisms in Cyclophosphamide Metabolism Pathway, Treatment-Related Toxicity, and Disease-Free Survival in SWOG 8897 Clinical Trial for Breast Cancer
Song Yao, William E. Barlow, Kathy S. Albain, Ji-Youb Choi, Hua Zhao, Robert B. Livingston, Warren Davis, James M. Rae, J-Tien Yeh, Laura F. Hutchins, Peter M. Ravdin, Silvana Martino, Alan P. Lyss, C. Kent Osborne, Martin Abeloff, Gabriel N. Hortobagyi, Daniel F. Hayes and Christine B. Ambrosone

LETTERS TO THE EDITOR

Chromosome 17 Polysomy without HER2 Amplification Does Not Predict Response to Lapatinib in Metastatic Breast Cancer—Letter
Cathy B. Moelans, Roel A. de Weger and Paul J. van Diest

Chromosome 17 Polysomy without HER2 Amplification Does Not Predict Response to Lapatinib in Metastatic Breast Cancer—Response
Leona Downey and Robert Livingston

Do Rectal Cancer Patients with PIK3CA Mutations Benefit from Preoperative Radiotherapy with Regard to Local Recurrences?
Youji He, Laura J. Van’t Veer, Marta Lopez-Yurda, Cornelis J.H. van de Velde and Corrie A.M. Marijnen

Clinical Usefulness of Microarrays for Cancer Prognosis in 2010—Letter
Serge Koscielny and Stefan Michiels

Statistical Evaluation of Clinical Usefulness of Microarrays for Cancer Prognosis Needs to be Placed in the Context of Clinical Reality—Response
Weida Tong and Xiaohui Fan

Acknowledgment to Reviewers
ABOUT THE COVER

Intracerebral xenograft initiated from the CD133+ glioblastoma stem-like cell line GBMJ1. At the initial signs of morbidity (94 days after implantation) a representative mouse was euthanized and the brain tumor prepared for histological analyses. This figure shows the immunofluorescent analyses of GFAP (red) and III tubulin (green) with nuclei counterstained with DAPI (blue) at 20x magnification. For details, see the article by Jamal and colleagues on page 6049 of this issue.