### Contents

**Highlights of This Issue**  5831

**SPECIAL FEATURES**

**Editorial**  5833

*Gauging Progress in a Decades-Old Fight*

Jesse Potash and Kenneth C. Anderson

**CCR Translations**  5834

*Model T Muscle CARs Can Treat Brain Tumors*

Laura A. Johnson

See article p. 5949

**CCR New Strategies**  5837

*New Strategies in Sarcoma Therapy: Linking Biology and Novel Agents*

Katherine A. Janeway and Robert G. Maki

**CCR Perspectives in Drug Approval**  5845

*U.S. Food and Drug Administration Approval Summary: Brentuximab Vedotin for the Treatment of Relapsed Hodgkin Lymphoma or Relapsed Systemic Anaplastic Large-Cell Lymphoma*


**Molecular Pathways**  5850

*Molecular Pathways: Tumor Cells Co-opt the Brain-Specific Metabolism Gene CPT1C to Promote Survival*

Patrick T. Reilly and Tak W. Mak

**Review**  5856

*The PI3K/AKT/mTOR Pathway as a Therapeutic Target in Endometrial Cancer*

Brian M. Slomovitz and Robert L. Coleman

**HUMAN CANCER BIOLOGY**  5865

*Novel Tumor Subgroups of Urothelial Carcinoma of the Bladder Defined by Integrated Genomic Analysis*

Carolyn D. Hurst, Fiona M. Platt, Claire F. Taylor, and Margaret A. Knowles

*Functional, Genetic, and Epigenetic Aspects of Base and Nucleotide Excision Repair in Colorectal Carcinomas*


**Clinical Cancer Research**

The Journal of Clinical and Translational Research

November 1, 2012 • Volume 18 • Number 21

www.aacrjournals.org
CANCER THERAPY: PRECLINICAL

5911 Src Inhibition with Saracatinib Reverses Fulvestrant Resistance in ER-Positive Ovarian Cancer Models In Vitro and In Vivo
Fiona Simpkins, Pedro Hevia-Paez, Jun Sun, Wendy Ullmer, Candace A. Gilbert, Thiago da Silva, Ali Pedram, Ellis R. Levin, Isildinha M. Reis, Brian Rabinovich, Diana Azzam, Xiang-Xi Xu, Tan A. Ince, Ji-Yeon Yang, Roel G.W. Verhaak, Yiling Lu, Gordon B. Mills, and Joyce M. Slingerland

5924 Differential Gene Expression Profile Associated to Apoptosis Induced by Dexamethasone in CLL Cells According to IGHV/ZAP-70 Status
Maria Joao Baptista, Ana Muntañola, Eva Calpe, Pau Abrissquet, Olga Salamero, Eva Fernández, Carles Codony, Eva Giné, Susana G. Kalko, Marta Crespo, and Francesc Bosch

5934 Stichoposide C Induces Apoptosis through the Generation of Ceramide in Leukemia and Colorectal Cancer Cells and Shows In Vivo Antitumor Activity
Seong-Hoon Yun, Eun-Seon Park, Sung-Won Shin, Yong-Woo Na, Jin-Young Han, Jin-Sook Jeong, Valeria V. Shastina, Valentin A. Stonik, Joo-In Park, and Jong-Young Kwak

5949 Suppression of Human Glioma Xenografts with Second-Generation IL13R-Specific Chimeric Antigen Receptor–Modified T Cells
See commentary p. 5834

CANCER THERAPY: CLINICAL

5961 FoxM1 Inhibition Sensitizes Resistant Glioblastoma Cells to Temozolomide by Downregulating the Expression of DNA-Repair Gene Rad51
Nu Zhang, Xinjian Wu, Lixuan Yang, Feihe Xiao, Heng Zhang, Aidong Zhou, Zhengong Huang, and Suyun Huang

IMAGING, DIAGNOSIS, PROGNOSIS

5972 Circulating miRNAs as Surrogate Markers for Circulating Tumor Cells and Prognostic Markers in Metastatic Breast Cancer
Dharamia Madhavan, Manuela Zacknick, Markus Wallwiener, Katarina Cuk, Caroline Modugno, Martina Scharpf, Sarah Schott, Jörg Heil, Andrey Turchinovich, Rongxi Yang, Axel Benner, Sabine Rietdorf, Andreas Trumpp, Christof Söhn, Klaus Pantel, Andreas Schneeweiss, and Barbara Burwinkel

5983 Predictors of Survival in Never-Smokers with Non-Small Cell Lung Cancer: A Large-Scale, Two-Phase Genetic Study
Xia Pu, Yuanqing Ye, Margaret R. Spitz, Liang Wang, Jian Gu, Scott M. Lippman, Michelle A.T. Hildebrandt, Waun Ki Hong, John D. Minna, Jack A. Roth, Ping Yang, and Xifeng Wu

5992 Impact of Expression of Human Epidermal Growth Factor Receptors EGFR and ERBB2 on Survival in Stage II/III Gastric Cancer
Masanori Terashima, Koji Kitada, Atsushi Ochiai, Wataru Ichikawa, Isssei Kuruhashi, Shinichi Sakuramoto, Hitoshi Katai, Takeshi Sano, Hiroshi Imamura, and Mitsuhiro Sasaki; for the ACTS-GC Group

6001 ColoGuidePro: A Prognostic 7-Gene Expression Signature for Stage III Colorectal Cancer Patients
Anita Sveen, Trude H. Aagesen, Arild Nesbakken, Gunn Iren Meling, Torleiv O. Rognum, Knut Liestøl, Rolf I. Skotheim, and Ragnhild A. Lothe

6011 A Phase I Trial and Pharmacokinetic Study of Sorafenib in Children with Refractory Solid Tumors or Leukemias: A Children’s Oncology Group Phase I Consortium Report
Brigitte C. Widemann, AeRang Kim, Elizabeth Fox, Sylvain Baruchel, Peter C. Adamson, Ashish M. Ingle, Julia Glade Bender, Michael Burke, Brenda Weigel, Diana Stempak, Frank M. Balis, and Susan M. Blaney
Phase II Clinical and Pharmacokinetic Study of Aflibercept in Patients with Previously Treated Metastatic Colorectal Cancer

Phase I Study of Vorinostat in Combination with Temozolomide in Patients with High-Grade Gliomas: North American Brain Tumor Consortium Study 04-03

Pharmacokinetic and Pharmacodynamic Analysis of Circulating Biomarkers of Anti-NRP1, a Novel Antiangiogenesis Agent, in Two Phase I Trials in Patients with Advanced Solid Tumors
Yan Xin, Jessica Li, Jenny Wu, Rashell Kinard, Colin D. Weekes, Amita Patnaik, Patricia LoRusso, Rainer Brachmann, Raymond K. Tong, Yibing Yan, Ryan Watts, Shuang Bai, and Priti S. Hegde

Efficacy of Cetuximab in Metastatic Castration-Resistant Prostate Cancer Might Depend on EGFR and PTEN Expression: Results from a Phase II Trial (SAKK 08/07)
Richard Cathomas, Christian Rothermundt, Dirk Klingbiel, Lukas Bubendorf, Rolf Jaggi, Daniel C. Betticher, Peter Brauchli, Denise Cotting, Cornelia Droegge, Ralph Winterhalder, Daniele Siciliano, Dominik R. Berthold, Miklos Pless, Ralph Schiess, Roger von Moos, and Silke Gillessen; for the Swiss Group for Clinical Cancer Research (SAKK)

Pediatric Phase I Trial and Pharmacokinetic Study of MLN8237, an Investigational Oral Selective Small-Molecule Inhibitor of Aurora Kinase A: A Children’s Oncology Group Phase I Consortium Study
Yael P. Mossé, Emily Lipsitz, Elizabeth Fox, David T. Teachey, John M. Maris, Brenda Weigel, Peter C. Adamson, Mark A. Ingle, Charlotte H. Ahern, and Susan M. Blaney

Developing and Validating Continuous Genomic Signatures in Randomized Clinical Trials for Predictive Medicine
Shigeyuki Matsui, Richard Simon, Pingping Qu, John D. Shaughnessy Jr, Bart Barlogie, and John Crowley

Spleen Cells from Young Donors Eradicate Large Tumors–Letter
Laszlo Radvanyi

Spleen Cells from Young Donors Eradicate Large Tumors–Response
Donald A. Rowley, Karin Schreiber, and Hans Schreiber

Bioluminescence Imaging of Prenylation Inhibition–Letter
Philippe Clezardin

Bioluminescence Imaging of Prenylation Inhibition–Response
Kendall J. Blumer, Katherine Weilbaecher, and David Piwnica-Worms

Correction: The Use of Quantitative Real-Time Reverse-Transcriptase PCR for 5' and 3' Portions of ALK Transcripts to Detect ALK Rearrangements in Lung Cancers
Richard Cathomas, Christian Rothermundt, Dirk Klingbiel, Lukas Bubendorf, Rolf Jaggi, Daniel C. Betticher, Peter Brauchli, Denise Cotting, Cornelia Droegge, Ralph Winterhalder, Daniele Siciliano, Dominik R. Berthold, Miklos Pless, Ralph Schiess, Roger von Moos, and Silke Gillessen; for the Swiss Group for Clinical Cancer Research (SAKK)
ABOUT THE COVER

Serotonin receptors are expressed in the liver and human hepatocellular cancer (HCC). The cover shows the immunohistochemical staining of the serotonin receptor 1B (HTR1B) in a specimen of human HCC. In a subset of tumors, the expression of HTR1B was significantly increased compared with corresponding nontumor liver tissue of the same patient. The expression of the receptor correlated with a higher proliferation rate and tumor size, suggesting an involvement of serotonin receptors in tumor growth of human HCC. For details, see the article by Soll and colleagues on page 5902 of this issue.