Highlights of This Issue 1

SPECIAL FEATURES

CCR 20th Anniversary Commentary

3 Clinical Cancer Research: The 20th Anniversary

CCR Translations

4 Bromodomain Inhibition in Diffuse Large B-cell Lymphoma—Giving MYC a Brake
   Anja Mottok and Randy D. Gascoyne
   See related article, p. 113

7 New, Tolerable γ-Secretase Inhibitor Takes Desmoid Down a Notch
   Dennis P.M. Hughes, Shivaani Kummar, and Alexander J. Lazar
   See related article, p. 60

CCR New Strategies

10 New Strategies in Renal Cell Carcinoma: Targeting the Genetic and Metabolic Basis of Disease
   Ramaprasad Srinivasan, Christopher J. Ricketts, Carole Sourbier, and W. Marston Linehan

Molecular Pathways

18 Molecular Pathways: Not a Simple Tube—The Many Functions of Blood Vessels
   Brent A. Orr and Charles G. Eberhart

24 Molecular Pathways: Targeting the Kinase Effectors of Rho-Family GTPases
   Tatiana Y. Prudnikova, Sonali J. Rawat, and Jonathan Chernoff

CANCER THERAPY: CLINICAL

30 Tadalafil Augments Tumor Specific Immunity in Patients with Head and Neck Squamous Cell Carcinoma
   Joseph A. Califano, Zubair Khan, Kimberly A. Noonan, Lakshmi Rudraraju, Zhe Zhang, Hao Wang,
   Steven Goodman, Christine G. Gourin, Patrick K. Ha, Carole Fakhry, John Saunders, Marshall Levine, Mei Tang,
   Geoffrey Neuner, Jeremy D. Richmon, Ray Blanco, Nishant Agrawal, Wayne M. Koch, Shanthi Marur,
   Donald T. Weed, Paolo Serafini, and Ivan Borrello

39 Tadalafil Reduces Myeloid-Derived Suppressor Cells and Regulatory T Cells and Promotes Tumor Immunity in Patients with Head and Neck Squamous Cell Carcinoma
   Donald T. Weed, Jennifer L. Vella, Isidirinha M. Reis, Adriana C. De la fuente, Carmen Gomez, Zoukaa Sargi,
   Ronen Nazarian, Joseph Califano, Ivan Borrello, and Paolo Serafini

49 Combination of the mTOR Inhibitor Ridaforolimus and the Anti-IGF1R Monoclonal Antibody Dalotuzumab: Preclinical Characterization and Phase I Clinical Trial
   Serena Di Cosimo, Siriam Sadhunanayanan, Johanna C. Bendell, Andrés Cervantes, Mark N. Stein,
   Irene Braña, Desamparados Roda, Brian B. Haines, Theresa Zhang, Christopher G. Winter, Sharda Iha,
   Youyuan Xu, Jason Frazier, Richard A. Klinghofer, Ann Leighton-Swayne, Yang Song, Scot Ebbinghaus, and José Baselga

60 A Phase I, Dose-Finding Study in Patients with Advanced Solid Malignancies of the Oral γ-Secretase Inhibitor PF-03084014
   Wells A. Messersmith, Geoffrey I. Shapiro, James M. Cleary, Antonio Iimeno, Arvind Dasari,
   Bo Huang, M. Naveed Shaik, Rossano Cesari, Xianxian Zheng, Jennifer M. Reynolds,
   See related commentary, p. 7

68 A Phase I Study of Veliparib (ABT-888) in Combination with Low-Dose Fractionated Whole Abdominal Radiation Therapy in Patients with Advanced Solid Malignancies and Peritoneal Carcinomatosis
   Kim A. Reiss, Joseph M. Herman, Marianna Zahrulak, Anthony Brade, Laura A. Dawson, Angela Scardina,
   Caitlin Jaffe, Emily Petit, Amy Hacker-Prietz, Robert J. Kinders, Lihua Wang, Alice Chen,
   Sarah Temkin, Naomí Hotúa, Lillian L. Siu, and Nilofer S. Azad

77 First-in-Human Phase I Study of Pictilisib (GDC-0941), a Potent Pan–Class I Phosphatidylinositol-3-Kinase (PI3K) Inhibitor, in Patients with Advanced Solid Tumors
   Debasish Sarker, Joo Eun Ang, Richard Baird, Rebecca Kristeleit, Krunal Shah, Victor Moreno,
   Paul A. Clarke, Florence J. Reynaud, Gallia Levy, Joseph A. Ware, Kathlyn Mazina, Ray Lin, Jenny Wu,
   Jill Fединский, Jill M. Sporke, Mark R. Lackner, Yihing Yan, Lori S. Friedman, Stan B. Kaye,
   Mika K. Derynck, Paul Workman, and Johann S. de Bono
First-in-Human Phase I Dose Escalation Study of a Second-Generation Non-Ansamycin HSP90 Inhibitor, AT13387, in Patients with Advanced Solid Tumors
Geoffrey I. Shapiro, Eunice Kwak, Bruce J. Dezube, Murray Yule, John Aytton, John Lyons, and Danuka Mahadevan

PERSONALIZED MEDICINE AND IMAGING

Preexisting MEK1P124 Mutations Diminish Response to BRAF Inhibitors in Metastatic Melanoma Patients

Dynamic Contrast-Enhanced Magnetic Resonance Imaging for Assessment of Antiangiogenic Treatment Effects in Multiple Myeloma
Maximilian Mez, Judith Ritsch, Christina Kunz, Barbara Wagner, Sandra Sauer, Dirk Hose, Thomas Moehler, Stefan Delorme, Hartmut Goldschmidt, Christian Zechmann, and Jens Hillengass

CANCER THERAPY: PRECLINICAL

Inhibition of Bromodomain Proteins for the Treatment of Human Diffuse Large B-cell Lymphoma
Sally E. Trabucco, Rachel M. Gerstein, Andrew M. Evens, James E. Bradner, Leonard D. Shultz, Dale L. Geerter, and Hong Zhang
See related commentary, p. 4

Potential Mechanisms for Thrombocytopenia Development with Trastuzumab Emtansine (T-DM1)
Hirdesh Uppal, Estelle Doudeament, Kaushiki Mahapatra, Walter C. Darbonne, Daniela Bumbaca, Ben-Quan Shen, Xiaoyan Du, Ola Saad, Kristin Bowles, Steve Olsen, Gail D. Lewis Phillips, Dylan Hartley, Mark X. Li, Sandhya Barabas, and Vanitha Ramakrishnan

The Novel IKK2 Inhibitor LY2409881 Potently Synergizes with Histone Deacetylase Inhibitors in Preclinical Models of Lymphoma through the Downregulation of NF-κB
Changchun Deng, Mark Lipstein, Richard Rodriguez, Xavier O. Jirau Serrano, Christine McIntosh, Wei-Yun Tsch, Andrew S. Wasmuth, Susan Jaken, and Owen A. O’Connor

CD99 Triggering in Ewing Sarcoma Delivers a Lethal Signal through p53 Pathway Reactivation and Cooperates with Doxorubicin
Clara Guerzoni, Valentina Fiori, Mario Terracciano, Maria Cristina Manara, Diego Moricoli, Michela Pasello, Marika Sciandra, Giordano Nicoletti, Mara Gellini, Sabrina Dominici, Claudia Chiodoni, Pier Maria Formanari, Pier-Luigi Lollini, Mario P. Colombo, Piero Pici, Maurizio Cianfriglia, Mauro Magnani, and Katia Scioletti

Low Expression of the E3 Ubiquitin Ligase CBL Confers Chemoresistance in Human Pancreatic Cancer and Is Targeted by Epidermal Growth Factor Receptor Inhibition
Brian E. Kadera, Paul A. Toste, Nanping Wu, Luyi Li, Andrew H. Nguyen, David W. Dawson, and Timothy R. Donahue

Cabozaontinib Overcomes Crizotinib Resistance in ROS1 Fusion–Positive Cancer
Ryohei Katayama, Yuka Kobayashi, Luc Fribo, Elizabeth L. Lockerman, Sumie Koike, Alice T. Shaw, Jeffrey A. Engelman, and Naoya Fujita

BIOLGY OF HUMAN TUMORS

Development of a Prognostic Genetic Signature to Predict the Metastatic Risk Associated with Cutaneous Melanoma

Molecular Characterization of Choroid Plexus Tumors Reveals Novel Clinically Relevant Subgroups
Diana M. Merino, Adam Shlien, Anita Villani, Malgorzata Pienkowski, Stephen Mack, Vijay Ramaswamy, David Shih, Ruth Tatevossian, Ana Novokmet, Sanza Choufani, Rina Dvir, Myran Ben-Arush, Brent T. Harris, Eugene I. Hwang, Rishi Lulla, Stefan M. Pfister, Maria Isabel Achatz, Nada Jabado, Jonathan L. Finlay, Rosanna Weksberg, Cynthia Hawkins, Michael D. Taylor, Uri Tabori, David W. Ellison, Richard J. Gilbertson, and David Malkin
Table of Contents

193 The Ability of Bilirubin in Identifying Smokers with Higher Risk of Lung Cancer: A Large Cohort Study in Conjunction with Global Metabolomic Profiling
Chi-Pang Wen, Fanmao Zhang, Dong Liang, Christopher Wen, Jian Gu, Heath Skinner, Wong-Ho Chow, Yuanqing Ye, Xia Pu, Michelle A.T. Hildebrandt, Maosheng Huang, Chien-Hua Chen, Chao Agnes Hsiung, Min Kuang Tsai, Chwen Keng Tsao, Scott M. Lippman, and XiFeng Wu

201 Activation of IL6/IGFIR Confers Poor Prognosis of HBV-Related Hepatocellular Carcinoma through Induction of OCT4/NANOG Expression
Te-Sheng Chang, Yu-Chih Wu, Ching-Chi Chi, Wei-Chi Su, Pey-Jium Chang, Kam-Fai Lee, Tao-Hsin Tung, Jui Wang, Jun-Jen Liu, Shui-Yi Tung, Liang-Mou Kuo, Hong-Nerng Ho, Thai-Yen Ling, and Yen-Hua Huang

211 Effects of BRCA1- and BRCA2-Related Mutations on Ovarian and Breast Cancer Survival: A Meta-analysis
Qian Zhong, Hong-Ling Peng, Xia Zhao, Lin Zhang, and Wei-Ting Hwang

LETTERS TO THE EDITOR

221 Diffusion-Weighted MRI for Lymphoma Staging—Letter
Hugo J.A. Adams and Thomas C. Kwee

222 Diffusion-Weighted MRI for Lymphoma Staging—Response
Marius E. Mayerhoefer and Markus Raderer

ABOUT THE COVER

The cover shows the results of an unsupervised two-dimensional hierarchical clustering analysis of the 5,000 most variable genes classifying breast tumors into ER⁺, HER2⁺, or triple-negative (ER⁻, PR⁻, HER2⁻) subtypes. The analysis was performed on 800 breast tumors obtained from the Karolinska Institutet, Sweden. The RAS gene expression signature was high in the triple-negative subtype and low in the ER⁺ subtype. For details, see the article by Di Cosimo and colleagues on page 49 of this issue.