# Table of Contents

## April 2015 • Volume 14 • Number 4

### Highlights of This Issue

845

### REVIEW

847  
PD-L1 Expression as a Predictive Biomarker in Cancer Immunotherapy  
Sandip Pravin Patel and Razelle Kurzrock

### SMALL MOLECULE THERAPEUTICS

857  
Preclinical Pharmacological Evaluation of Letrozole as a Novel Treatment for Gliomas  
Nimita Dave, Lionel M.L. Chow, Gary A. Gudelsky, Kathleen L’Ainsc, Xiaoyang Qi, and Pankaj B. Desai

865  
Functional Genetic Screen Identifies Increased Sensitivity to WEE1 Inhibition in Cells with Defects in Fanconi Anemia and HR Pathways  
Marieke Aarts, Ilirjana Bajrami, Maria T. Herrera-Abreu, Richard Elliott, Rachel Brough, Alan Ashworth, Christopher J. Lord, and Nicholas C. Turner

877  
ATF4 Gene Network Mediates Cellular Response to the Anticancer PAD Inhibitor YW3-56 in Triple-Negative Breast Cancer Cells  
Shu Wang, Xiayun Amy Chen, Jing Hu, Jian-kang Jiang, Yunfei Li, Ka Yim Chan-Sal, Ying Gu, Gong Chen, Craig Thomas, B. Franklin Pugh, and Yannmg Wang

889  
The Combination of the PARP Inhibitor Rucaparib and 5FU Is an Effective Strategy for Treating Acute Leukemias  
Maria Vittoria Verga Falzappa, Chiara Ronchini, Mario Farettta, Ilaria Iacobucci, Andrea Ghelli Lusena Di Rorà, Giovanni Martinelli, Ludger Hinrich Meyer, Klaus-Michael Debatin, Stefania Orecchioni, Francesco Bertolini, and Pier Giuseppe Pellici

899  
Magnetic Resonance Spectroscopy for Detection of Choline Kinase Inhibition in the Treatment of Brain Tumors  
Manoj Kumar, Sean P. Areluckas, Sona Sakse, Gaurav Verma, Ranit Jnye, Stephen Pickup, Anatoliy V. Popov, Edward J. Delikatny, and Harish Poptani

909  
IKKβ Regulates VEGF Expression and Is a Potential Therapeutic Target for Ovarian Cancer as an Antiangiogenic Treatment  

920  
Efficacy of Carboplatin Alone and in Combination with ABT888 in Intracranial Murine Models of BRCA-Mutated and BRCA–Wild-Type Triple-Negative Breast Cancer  

931  
The Selective PI3K Inhibitor XL147 (SAR245408) Inhibits Tumor Growth and Survival and Potentiates the Activity of Chemotherapeutic Agents in Preclinical Tumor Models  

### LARGE MOLECULE THERAPEUTICS

941  
New Blocking Antibodies against Novel AGR2–C4.4A Pathway Reduce Growth and Metastasis of Pancreatic Tumors and Increase Survival in Mice  
Thinhvengadam Arumugam, Deleng Deng, Laura Bover, Huamin Wang, Craig D. Logsdon, and Vijaya Ramachandran
952 Tumor Cells Chronically Treated with a Trastuzumab–Maytansinoid Antibody–Drug Conjugate Develop Varied Resistance Mechanisms but Respond to Alternate Treatments

964 Nonclinical Safety Evaluation of VX15/2503, a Humanized IgG4 Anti-SEMA4D Antibody
John E. Leonard, Terrence L. Fisher, Laurie A. Winter, Chad A. Cornelius, Christine Reilly, Ernest S. Smith, and Maurice Zauderer

973 A Novel Neutralizing Antibody Targeting Pregnancy-Associated Plasma Protein-A Inhibits Ovarian Cancer Growth and Ascites Accumulation in Patient Mouse Tumorgrafts
Marc A. Becker, Paul Haluska Jr, Laurie K. Bale, Claus Oxvig, and Cheryl A. Conover

982 The IGF-Trap: Novel Inhibitor of Carcinoma Growth and Metastasis
Ni Wang, Roni F. Rayes, Seyed Mehdy Elahi, Yifan Lu, Mark A. Hancock, Bernard Massie, Gerald E. Rowe, Hafida Aomari, Sazzad Hossain, Yves Durocher, Maxime Pinard, Sébastien Tabaries, Peter M. Siegel, and Pnina Brodt

1004 Trifluridine Induces p53-Dependent Sustained G2 Phase Arrest with Its Massive Misincorporation into DNA and Few DNA Strand Breaks
Kazuaki Matsuoka, Makoto Iimori, Shinichiro Niimi, Hiroshi Tsukihara, Sugiko Watanabe, Shinichi Kiyonari, Mamoru Kiniwa, Koji Ando, Eriko Tokunaga, Hiroshi Saeki, Eiji Oki, Yoshihiro Maehara, and Hiroyuki Kitao

1014 Dual PI3K/mTOR Inhibitors Induce Rapid Overactivation of the MEK/ERK Pathway in Human Pancreatic Cancer Cells through Suppression of mTORC2
Helena P. Soares, Ming Ming, Michelle Mellon, Steven H. Young, Liang Han, James Sinnet-Smith, and Enrique Rozengurt

1024 Targeting Integrin-Linked Kinase Suppresses Invasion and Metastasis through Downregulation of Epithelial-to-Mesenchymal Transition in Renal Cell Carcinoma
Kyung Seok Han, Na Li, Peter A. Raven, Ladan Fazli, Susan Ettinger, Sung Joon Hong, Martin E. Gleave, and Alan I. So

1035 Targeted Blockade of JAK/STAT3 Signaling Inhibits Ovarian Carcinoma Growth
Galina Gritsina, Fang Xiao, Shane W. O’Brien, Rashid Gabbasov, Marisa A. Maglaty, Ren-Huan Xu, Roshan J. Thapa, Yan Zhou, Emmanuelle Nicolas, Samuel Littwin, Siddharth Balachandran, Luis J. Sigal, Dennis Huszar, and Denise C. Connolly

COMPANION DIAGNOSTICS AND CANCER BIOMARKERS

1048 Biomarker Signatures Correlate with Clinical Outcome in Refractory Metastatic Colorectal Cancer Patients Receiving Bevacizumab and Everolimus
Yingmiao Liu, Mark D. Starr, John C. Brady, Christel Rushing, Anuradha Bulusu, Herbert Pang, Wanda Honeycutt, Anthony Amara, Ivy Altimore, Hope E. Uronis, Herbert I. Hurwitz, and Andrew B. Nixon

1057 Transcriptomic and Protein Expression Analysis Reveals Clinicopathological Significance of Bloom Syndrome Helicase (BLM) in Breast Cancer
Arvind Arora, Tarek M.A. Abdel-Fatah, Devika Agarwal, Rachel Doherty, Paul M. Moseley, Mohammed A. Aleskandary, Andrew R. Green, Graham Ball, Ala’a T. Alshareda, Emad A. Rakha, Stephen Y.T. Chan, Ian O. Ellis, and Srinivasan Madhusudan
Table of Contents

1066 Polymorphic CAG Repeat and Protein Expression of Androgen Receptor Gene in Colorectal Cancer
Rui Huang, Guiyu Wang, Yanni Song, Feng Wang, Bing Zhu, Qingchao Tang, Zheng Liu, Yinggang Chen, Qian Zhang, Shan Muhammad, and Xishan Wang

MODELS AND TECHNOLOGIES
1075 Multifunctional Polymeric Micelles Co-loaded with Anti-Survivin siRNA and Paclitaxel Overcome Drug Resistance in an Animal Model of Ovarian Cancer
Giuseppina Salzano, Gemma Navarro, Malav S. Trivedi, Giuseppe De Rosa, and Vladimir P. Torchilin

ABOUT THE COVER
Deregulation of cell-cycle checkpoints is a feature of many different cancer types. WEE1 kinase plays an important role in the maintenance of these cell-cycle checkpoints by inhibiting cyclin-dependent kinase (CDK) activity. Through siRNA screening, it was found that cancer cells with defects in Fanconi Anemia (FA) and homologous recombination pathways were more sensitive to WEE1 inhibition. The cover image shows that WEE1 inhibition in cells depleted of FA protein FANCM resulted in increased replication stress (pan-nuclear γH2AX staining in green) and premature entry into mitosis (yellow). Phospho-histone H3 staining (red) was used to identify mitotic cells. DNA was counterstained with DAPI (blue). For details, see the article by Aarts and colleagues on page 865.