## Table of Contents

**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 LaSance, 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, Xiangyun Amy Chen, Jing Hu, Jian-kang Jiang, Yunfei Li, Ka Yim Chan-Salis, Ying Gu, Gong Chen, Craig Thomas, B. Franklin Pugh, and Yanning Wang  

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

899  
**Magnetic Resonance Spectroscopy for Detection of Choline Kinase Inhibition in the Treatment of Brain Tumors**  
Manoj Kumar, Sean P. Arlauckas, Sona Saksena, Gaurav Verma, Ranjit Iyengar, Stephen Pickup, Anatoliy V. Popov, Edward J. Delikatny, and Harish Poptani  

**LARGE MOLECULE THERAPEUTICS**  
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**  

**NEW BLOCKING ANTIBODIES AGAINST NOVEL AGR2–C4.4A PATHWAY REDUCE GROWTH AND METASTASIS OF PANCREATIC TUMORS AND INCREASE SURVIVAL IN MICE**  
Thiruvengadam Arumugam, Deleng Deng, Laura Bover, Huamin Wang, Craig D. Logsdon, and Vijaya Ramachandran
Tumor Cells Chronically Treated with a Trastuzumab–Maytansinoid Antibody–Drug Conjugate Develop Varied Resistance Mechanisms but Respond to Alternate Treatments
Frank Loganzo, Xingzhi Tan, Matthew Sung, Guixian Jin, Jeremy S. Myers, Eugene Melamud, Steven H. Young, Liang Han, James Sinnet-Smith, and Enrique Rozengurt

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

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

The IGF-Trap: Novel Inhibitor of Carcinoma Growth and Metastasis
Ni Wang, Roni F. Rates, Seyyed 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

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

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

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 Litwin, Siddharth Balachandran, Luis J. Sigal, Dennis Huszar, and Denise C. Conolly

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 Altmare, Hope E. Utomun, Herbert I. Hurwitz, and Andrew B. Nixon

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, Alaa T. Alshawareda, Emad A. Rakha, Stephen Y.T. Chan, Ian O. Ellis, and Srinivasan Madhusudan
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

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.