Highlights of This Issue 3103

SPOTLIGHT ON MOLECULAR PROFILING

3105 Genome-Wide mRNA and microRNA Profiling of the NCI 60 Cell-Line Screen and Comparison of FdUMP[10] with Fluorouracil, Flouxuridine, and Topoisomerase 1 Poisons
William H. Gmeiner, William C. Reinhold, and Yves Pommier

REVIEWS

3115 Breaking through a Plateau in Renal Cell Carcinoma Therapeutics: Development and Incorporation of Biomarkers
Sumanta Kumar Pal, Marcin Kortylewski, Hua Yu, and Robert A. Figlin

3126 Resistance May Not Be Futile: microRNA Biomarkers for Chemoresistance and Potential Therapeutics
Kristi E. Allen and Glen J. Weiss

3137 Proof of Concept: Network and Systems Biology Approaches Aid in the Discovery of Potent Anticancer Drug Combinations
Asfar S. Azmi, Zhiwei Wang, Philip A. Philip, Ramzi M. Mohammad, and Fazlul H. Sarkar

THERAPEUTIC DISCOVERY

3145 The Quassinoid Derivative NBT-272 Targets Both the AKT and ERK Signaling Pathways in Embryonal Tumors
Deborah Castelletti, Giulio Fiaschetti, Valeria Di Dato, Urs Ziegler, Candy Kumps, Katelyn De Preter, Tarek Shalaby, Daniela De Martino, Thorsten Berg, Angelika Eggert, Alexandre Arcaro, and Michael A. Grotzer

3158 Modulation of 4E-BP1 Function as a Critical Determinant of Enzastaurin-Induced Apoptosis
Chad A. Dumstorf, Bruce W. Konicek, Ann M. McNulty, Stephen H. Parsons, Luc Furic, Nahum Sonenberg, and Jeremy R. Graff

3164 Antagonism of Cytotoxic Chemotherapy in Neuroblastoma Cell Lines by 13-cis-Retinoic Acid Is Mediated by the Antiapoptotic Bcl-2 Family Proteins
Michael D. Hadjidaniel and C. Patrick Reynolds

3175 Menonisin Is a Potent Inducer of Oxidative Stress and Inhibitor of Androgen Signaling Leading to Apoptosis in Prostate Cancer Cells
Kirsti Ketola, Paula Vainio, Vidal Fey, Olli Kallioniemi, and Kristiina Iljin

3186 Targeting Aldehyde Dehydrogenase Cancer Stem Cells in Ovarian Cancer

3200 Combined Inhibition of Notch Signaling and Bcl-2/Bcl-xL Results in Synergistic Antimyeloma Effect
Ming Li, Feng Chen, Nicholas Clifton, Daniel M. Sullivan, William S. Dalton, Dmitry I. Gabrilovich, and Yulia Nefedova

3210 The Histone Deacetylase Inhibitor, Vorinostat, Reduces Tumor Growth at the Metastatic Bone Site and Associated Osteolysis, but Promotes Normal Bone Loss
Jitesh Pratap, Jacqueline Akech, John J. Wixted, Gabriela Szabo, Sadiq Hussain, Meghan E. Mcgee-Lawrence, Xiaodong Li, Krystin Bedard, Robinder J. Dhillon, Andre J. Van Wijnen, Janet J. Stein, Gary S. Stein, Jennifer J. Westendorf, and Jane B. Lian
Peroxisome Proliferator-Activated Receptor-γ Activation Inhibits Tumor Metastasis by Antagonizing Smad3-Mediated Epithelial-Mesenchymal Transition
Ajaya Kumar Reka, Himabindu Kurapati, Venkata R. Narala, Guido Bommer, Jun Chen, Theodore J. Standiford, and Venkateshwar G. Keshamouni

Combined Treatment with Silibinin and Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitors Overcomes Drug Resistance Caused by T790M Mutation
Jin Kyung Rho, Yun Jung Choi, Byung-Suk Jeon, Su Jin Choi, Gi Jeong Cheon, Sang-Keun Woo, Hye-Ryoun Kim, Cheol Hyeon Kim, Chang-Min Choi, and Jae Cheol Lee

Antiangiogenic Activity of a Neutralizing Human Single-Chain Antibody Fragment against Fibroblast Growth Factor Receptor 1
Roberto Ronca, Patrizia Benzoni, Daria Leali, Chiara Urbinati, Michela Belleri, Michela Corsini, Patrizia Alessi, Daniela Coltrini, Stefano Calza, Marco Presta, and Patrizia Dell’Era

MS-275 Sensitizes TRAIL-Resistant Breast Cancer Cells, Inhibits Angiogenesis and Metastasis, and Reverses Epithelial-Mesenchymal Transition In vivo
Rakesh K. Srivastava, Razelle Kurzrock, and Sharmila Shankar

Chemoprevention of Chemically Induced Skin Tumorigenesis by Ligand Activation of Peroxisome Proliferator–Activated Receptor–β/δ and Inhibition of Cyclooxygenase 2
Bokai Zhu, Robert Bai, Mary J. Kennett, Boo-Hyon Kang, Frank J. Gonzalez, and Jeffrey M. Peters

Preclinical Development

Detection of Tumor Response to a Vascular Disrupting Agent by Hyperpolarized 13C Magnetic Resonance Spectroscopy
Sarah E. Bohndiek, Mikko I. Kettunen, De-en Hu, Timothy H. Witney, Brett W.C. Kennedy, Ferdia A. Gallagher, and Kevin M. Brindle

Combination of Vorinostat and Flavopiridol Is Selectively Cytotoxic to Multidrug-Resistant Neuroblastoma Cell Lines with Mutant TP53
Jen-Ming Huang, Michael A. Sheard, Lingyun Ji, Richard Sposto, and Nino Keshelava

Inhibition of Constitutive Activation of STAT3 by Curcurbitacin-I (JSI-124) Sensitized Human B-Leukemia Cells to Apoptosis
Ganchimeg Ishdorj, John R. Johnston, and Spencer B. Gibson

Cytochrome P450 1B1 Gene Polymorphisms as Predictors of Anticancer Drug Activity: Studies with In vitro Models
Audrey Laroche-Clary, Valerie Le Morvan, Takao Yamori, and Jacques Robert

Rb–Raf-1 Interaction Disruptor RRD-251 Induces Apoptosis in Metastatic Melanoma Cells and Synergizes with Dacarbazine
Sandeep Singh, Rebecca Davis, Vignesh Alamanda, Roberta Pireddu, Daniel Pernazza, Said Sebti, Nicholas Lawrence, and Srikumar Chellappan

Cyclin G–Associated Kinase Is Necessary for Osteosarcoma Cell Proliferation and Receptor Trafficking
Michiro Susa, Edwin Choy, Jianzhe Liu, Joseph Schwab, Francis J. Hornicek, Henry Mankin, and Zhenfeng Duan

Identification of Predictive Markers of Response to the MEKfs1/2 Inhibitor Selumetinib (AZD6244) in K-ras–Mutated Colorectal Cancer
John J. Tentler, Sujatha Nallapareddy, Aik Choon Tan, Anna Spreatoc, Todd M. Pitts, M. Pia Morelli, Heather M. Selby, Maria I. Kachera, Sara A. Flanigan, Gillian N. Kulkowski, Stephen Leong, John J. Arcaroli, Wells A. Messersmith, and S. Gail Eckhardt
Contrasting Effects of Nutlin-3 on TRAIL- and Docetaxel-Induced Apoptosis Due to Upregulation of TRAIL-R2 and Mcl-1 in Human Melanoma Cells
Hsin-Yi Tseng, Chen Chen Jiang, Amanda Croft, Kwang Hong Tay, Rick Francis Thorne, Fan Yang, Hao Liu, Peter Hersey, and Xu Dong Zhang

Nakiterpiosin Targets Tubulin and Triggers Mitotic Catastrophe in Human Cancer Cells
Jen-Hsuan Wei and Joachim Seemann

AZ960, a Novel Jak2 Inhibitor, Induces Growth Arrest and Apoptosis in Adult T-Cell Leukemia Cells
Jing Yang, Takayuki Ikezoe, Chie Nishioka, Mutsuo Furihata, and Akihito Yokoyama

Specific Alterations of MicroRNA Transcriptome and Global Network Structure in Colorectal Carcinoma after Cetuximab Treatment
Marco Ragusa, Alessandra Majorana, Luisa Statello, Marco Maugeri, Loredana Salito, Davide Barbagallo, Maria Rosa Guglielmino, Laura R. Duro, Rosario Angelica, Rosario Caltabiano, Antonio Biondi, Maria Di Vita, Giuseppe Privitera, Marina Scalia, Alessandro Cappellani, Enrico Vasquez, Salvatore Lanzafame, Francesco Basile, Cinzia Di Pietro, and Michele Purrello

Phase I Clinical Trial of MPC-6827 (Azixa), a Microtubule Destabilizing Agent, in Patients with Advanced Cancer
Apostolia-Maria Tsimeridou, Wallace Akerley, Matthias C. Schabel, David S. Hong, Cynthia Uehara, Anil Chhabra, Terri Warren, Gary G. Mather, Brent A. Evans, Deane P. Woodland, Edward A. Swabb, and Razelle Kurzrock

About the Cover
Aldehyde dehydrogenase-1A1 (ALDH1A1) is heterogeneously expressed in multiple tumors. Cells with ALDH1A1 activity have been shown to have increased tumorigenicity, differentiation capacity, and chemoresistance. To confirm that the spotty heterogeneous expression of ALDH1A1 was not being visualized in tumor-infiltrating macrophages, frozen patient samples were subjected to dual immunohistochemistry against ALDH1A1 (DAB/brown) and CD68 (a pan-macrophage marker, Ferangi Blue), where distinct populations are noted. Landen and colleagues show that increased ALDH1A1 expression was associated with poor survival and is a viable target for therapy in preclinical models of ovarian cancer. For details, see article by Landen and colleagues on page 3186.