## Highlights of This Issue

1689

### REVIEW

1691

**BH3 Mimetics: Status of the Field and New Developments**
Christian Billard

1693

**S49076 Is a Novel Kinase Inhibitor of MET, AXL, and FGFR with Strong Preclinical Activity Alone and in Association with Bevacizumab**
Mike F. Burbridge, Céline J. Bossard, Carine Saunier, Imre Fejes, Alain Bruno, Stéphane Léonce, Gilles Ferry, Georges Da Violaete, François Bouzoz, Valérie Cattan, Anne Jacobet-Bescod, Paolo M. Comoglio, Brian P. Lockhart, Jean A. Boutin, Alex Cordi, Jean-Claude Ortuno, Alain Pierred, John A. Hickman, Francisco H. Cruzaleguit, and Stéphane Depil

### SMALL MOLECULE THERAPEUTICS

1701

**Pharmacologic Inhibition of MEK Signaling Prevents Growth of Canine Hemangiosarcoma**
Nicholas J. Andersen, Brian J. Nickoloff, Karl J. Dykema, Elissa A. Boguslawski, Roman I. Krivocheitser, Roe E. Froman, Michelle J. Dawes, Laurence H. Baker, Dafydd G. Thomas, Debra A. Kamstock, Barbara E. Kitchell, Kyle A. Furge, and Nicholas S. Duesbery

1703

**Synergistic Induction of Apoptosis in Multiple Myeloma Cells by Bortezomib and Hypoxia-Activated Prodrug TH-302, In Vivo and In Vitro**
Jinsong Hu, Els Van Valkenborgh, Dehui Xu, Eline Menu, Hendrik De Raeeve, Elke De Bryune, Song Xu, Ben Van Camp, Damian Handsides, Charles P. Hart, and Karin Vanderkerken

1715

**AZD3514: A Small Molecule That Modulates Androgen Receptor Signaling and Function In Vitro and In Vivo**

1728

**Smac Mimetics in Combination with TRAIL Selectively Target Cancer Stem Cells in Nasopharyngeal Carcinoma**
Man-si Wu, Guang-feng Wang, Zhi-qiang Zhao, Yi Liang, Heng-bang Wang, Miao-yi Wu, Ping Min, Li-zhen Chen, Qi-sheng Feng, Jin-xin Bei, Yi-xin Zeng, and Dajun Yang

1738

**Targeting Protein Tyrosine Phosphatase SHP2 for the Treatment of PTPN11-Associated Malignancies**
Bing Yu, Wei Liu, Wen-Mei Yu, Mignon L. Loh, Shawn Alter, Olgun Guvenç, Alexander D. MacKerell Jr, Li-Da Tang, and Cheng-Kui Qu

1749

**S49076 Is a Novel Kinase Inhibitor of MET, AXL, and FGFR with Strong Preclinical Activity Alone and in Association with Bevacizumab**
Mike F. Burbridge, Céline J. Bossard, Carine Saunier, Imre Fejes, Alain Bruno, Stéphane Léonce, Gilles Ferry, Georges Da Violaete, François Bouzoz, Valérie Cattan, Anne Jacobet-Bescod, Paolo M. Comoglio, Brian P. Lockhart, Jean A. Boutin, Alex Cordi, Jean-Claude Ortuno, Alain Pierred, John A. Hickman, Francisco H. Cruzaleguit, and Stéphane Depil

### LARGE MOLECULE THERAPEUTICS

1774

**Targeted Cytolysins Synergistically Potentiate Cytoplasmic Delivery of Gelonin Immunotoxin**
Christopher M. Pirie, David V. Liu, and K. Dane Wittrup

### CANCER THERAPEUTICS INSIGHTS

1783

**Combined Inhibition of HER1/EGFR and RAC1 Results in a Synergistic Antiproliferative Effect on Established and Primary Cultured Human Glioblastoma Cells**

1796

**Cyclin G1 Expands Liver Tumor-Initiating Cells by Sox2 Induction via Akt/mTOR Signaling**
Wen Wen, Tao Han, Cheng Chen, Lei Huang, Wen Sun, Xue Wang, Shu-Zhen Chen, Dai-Min Xiang, Liang Tang, Dan Cao, Gen-Sheng Feng, Meng-Chao Wu, Jin Ding, and Hong-Yang Wang
An Autocrine Loop between TGF-β1 and the Transcription Factor Brachyury Controls the Transition of Human Carcinoma Cells into a Mesenchymal Phenotype
Cecilia Larocca, Joseph R. Cohen, Romaine I. Fernando, Bruce Huang, Duane H. Hamilton, and Claudia Palena

Impact of Tumor HER2/ERBB2 Expression Level on HER2-Targeted Liposomal Doxorubicin-Mediated Drug Delivery: Multiple Low-Affinity Interactions Lead to a Threshold Effect
Bart S. Hendriks, Stephan G. Klinz, Joseph G. Reynolds, Christopher W. Espelin, Daniel F. Gaddy, and Thomas J. Wickham

Inhibition of ABCB1 Expression Overcomes Acquired Docetaxel Resistance in Prostate Cancer
Yezi Zhu, Chengfei Liu, Nagalakshmi Nadiminty, Wei Lou, Ramakumar Tummala, Christopher P. Evans, and Allen C. Gao

Ethacrynic Acid Oxadiazole Analogs Induce Apoptosis in Malignant Hematologic Cells through Downregulation of Mcl-1 and c-FLIP, Which Was Attenuated by GSTP1-1
Guyue Liu, Rui Wang, Yuetong Wang, Pengzhan Li, Guisen Zhao, Linxiang Zhao, and Yongkui Jing

Sulindac Selectively Inhibits Colon Tumor Cell Growth by Activating the cGMP/PKG Pathway to Suppress Wnt/β-Catenin Signaling

Chk1/2 Inhibition Overcomes the Cisplatin Resistance of Head and Neck Cancer Cells Secondary to the Loss of Functional p53
Mayur A. Gadhikar, Maria Rita Sciuto, Marcus Vinicius Ortega Alves, Curtis R. Pickering, Abdulllah A. Osman, David M. Neskey, Mei Zhao, Alison L. Fitzgerald, Jeffrey N. Myers, and Mitchell J. Frederick

BCL-2 Hypermethylation Is a Potential Biomarker of Sensitivity to Antimitotic Chemotherapy in Endocrine-Resistant Breast Cancer

Apoptotic Circulating Tumor Cells in Early and Metastatic Breast Cancer Patients
Galatea Kallergi, Georgios Konstantinidis, Harris Markomanolaki, Maria A. Papadaki, Dimitris Mavroidis, Christos Stournaras, Vassilis Georgoulis, and Sofia Agelaki

A c-Myc Activation Sensor-Based High-Throughput Drug Screening Identifies an Antineoplastic Effect of Nitazoxanide
Hua Fan-Minogue, Sandhya Bodapati, David Solow-Cordero, Alice Fan, Ramasamy Paulmurugan, Tarik F. Massoud, Dean W. Felsher, and Sanjiv S. Gambhir

NF1 Deletion Generates Multiple Subtypes of Soft-Tissue Sarcoma That Respond to MEK Inhibition
Rebecca D. Dodd, Jeffrey K. Mito, William C. Eward, Rhea Chitalia, Mohit Sachdeva, Yan Ma, Jordi Barretina, Leslie Dodd, and David G. Kirsch

Correction: MPT0B098, a Novel Microtubule Inhibitor That Destabilizes the Hypoxia-Inducible Factor-1α mRNA through Decreasing Nuclear–Cytoplasmic Translocation of RNA-Binding Protein HuR

Obituary
O. Michael Colvin, MD: In Memoriam (1936–2013)
Correction: Dual Programmed Cell Death Pathways Induced by p53 Transactivation Overcome Resistance to Oncolytic Adenovirus in Human Osteosarcoma Cells

AC icon indicates Author Choice
For more information please visit www.aacrjournals.org

ABOUT THE COVER

Continued androgen receptor (AR) expression and signaling is a key driver in castration-resistant prostate cancer (CRPC). AZD3514 is an orally bioavailable drug that inhibits androgen-dependent and -independent AR signalling \textit{in vitro} and \textit{in vivo}. Using immunohistochemistry, R3327H prostate tumors were scored for intensity of nuclear AR to assess the impact of AZD3514 on AR. For more details, see article by Loddick and colleagues on page 1715.