Table of Contents

May 2014 • Volume 13 • Number 5

Molecular Cancer Therapeutics

Highlights of This Issue 1019

REVIEW

1021 Picking the Point of Inhibition: A Comparative Review of PI3K/AKT/mTOR Pathway Inhibitors
   Rodrigo Dienstmann, Jordi Rodon, Violeta Serra, and Josep Tabernero

SMALL MOLECULE THERAPEUTICS

1032 Enhancement of Nab-Paclitaxel Antitumor Activity through Addition of Multitargeting Antiangiogenic Agents in Experimental Pancreatic Cancer
   Niranjan Awasthi, Changhua Zhang, Anna M. Schwarz, Stefan Hinz, Margaret A. Schwarz, and Roderich E. Schwarz

1044 The Phosphoinositide 3-Kinase α Selective Inhibitor BYL719 Enhances the Effect of the Protein Kinase C Inhibitor AEB071 in GNAQ/GNA11-Mutant Uveal Melanoma Cells
   Elgilda Musi, Grazia Ambrosini, Elisa de Stanchina, and Gary K. Schwartz

1054 Centmitor-1, a Novel Acridinyl-Acetohydrazide, Possesses Similar Molecular Interaction Field and Antimitotic Cellular Phenotype as Rigosertib, ON 01910.Na

1067 Preclinical Evaluation of the Supercritical Extract of Azadirachta Indica (Neem) Leaves In Vitro and In Vivo on Inhibition of Prostate Cancer Tumor Growth
   Qiang Wu, Manish Kohli, H. Robert. Bergen III, John C. Cheville, R. Jeffrey Karnes, Hong Cao, Charles Y.F. Young, Donald J. Tindall, Mark A. McNiven, and Krishna Vanaja Donkena

1078 Characterization of the Activity of the PI3K/mTOR Inhibitor XL765 (SAR245409) in Tumor Models with Diverse Genetic Alterations Affecting the PI3K Pathway

1092 UPARANT: A Urokinase Receptor–Derived Peptide Inhibitor of VEGF-Driven Angiogenesis with Enhanced Stability and In Vitro and In Vivo Potency
   Maria Vincenza Carriero, Katia Bifulco, Michele Minopoli, Liliana Lista, Ornela Maglio, Luigi Mele, Gioconda Di Carluccio, Mario De Rosa, and Vincenzo Pavone

1092 Preclinical Pharmacological Evaluation of a Novel Multiple Kinase Inhibitor, ON123300, in Brain Tumor Models
   Xiaoping Zhang, Hua Lv, Qingyu Zhou, Rana Elkholy, Jerry E. Chipuk, M.V. Ramana Reddy, E. Premkumar Reddy, and James M. Gallo

1105 Characterization of the Novel and Specific PI3Kα Inhibitor NVP-BYL719 and Development of the Patient Stratification Strategy for Clinical Trials

1130 Protein Kinase D as a Potential Chemotherapeutic Target for Colorectal Cancer
   Ning Wei, Edward Chu, Peter Wipf, and John C. Schmitz
1142 Highly Active Combination of BRD4 Antagonist and Histone Deacetylase Inhibitor against Human Acute Myelogenous Leukemia Cells
See related article, p. 1194

1155 Combination of Imatinib with CXCR4 Antagonist BKT140 Overcomes the Protective Effect of Stroma and Targets CML In Vitro and In Vivo
Katia Beider, Merav Darash-Yahana, Orly Blaier, Maya Koren-Michowitz, Michal Abraham, Hanna Wald, Ori Wald, Eithan Galun, Orly Eizenberg, Amnon Peled, and Arnon Nagler

1170 The Use of Olaparib (AZD2281) Potentiates SN-38 Cytotoxicity in Colon Cancer Cells by Indirect Inhibition of Rad51-Mediated Repair of DNA Double-Strand Breaks
Makiko Tahara, Takeshi Inoue, Futoshi Sato, Yasuyuki Miyakura, Hisanaga Horie, Yoshikazu Yasuda, Hirofumi Fujii, Kenjiro Kotake, and Kokichi Sugano

1181 A Novel Temozolomide–Perillyl Alcohol Conjugate Exhibits Superior Activity against Breast Cancer Cells In Vitro and Intracranial Triple-Negative Tumor Growth In Vivo
Thomas C. Chen, Hee-Yeon Cho, Weijun Wang, Manasi Barath, Natasha Sharma, Florence M. Hofman, and Axel H. Schonthal

CANCER BIOLOGY AND SIGNAL TRANSDUCTION

1194 Targeting STAT5 in Hematologic Malignancies through Inhibition of the Bromodomain and Extra-Terminal (BET) Bromodomain Protein BRD2
Suhu Liu, Sarah R. Walker, Erik A. Nelson, Robert Cerulli, Michael Xiang, Patricia A. Toniolo, Jun Qi, Richard M. Stone, Martha Wadleigh, James E. Bradner, and David A. Frank
See related article, p. 1142

1206 Embelin Reduces Colitis-Associated Tumorigenesis through Limiting IL-6/STAT3 Signaling
Yun Dai, Hongmei Jiao, Guigen Teng, Weihong Wang, Rongxing Zhang, Yunhong Wang, Lionel Hebbard, Jacob George, and Liang Qiao

1217 Ponatinib Induces Apoptosis in Imatinib-Resistant Human Mast Cells by Dephosphorylating Mutant D816V KIT and Silencing β-Catenin Signaling
Bei Jin, Ke Ding, and Jingxuan Pan

1231 PIM Kinases Are Essential for Chronic Lymphocytic Leukemia Cell Survival (PIM2/3) and CXCR4-Mediated Microenvironmental Interactions (PIM1)

1246 Pharmacologic Suppression of JAK1/2 by JAK1/2 Inhibitor AZD1480 Potently Inhibits IL-6–Induced Experimental Prostate Cancer Metastases Formation
Lei Gu, Pooja Talati, Paraskevi Vogiatzi, Ana L. Romero-Weaver, Junaid Abdulghani, Zhuyong Liao, Benjamin Leiby, David T. Hoang, Tuomas Mirtti, Kalle Alonen, Michael Zinda, Dennis Huszar, and Marja T. Nevalainen

1259 Hedgehog Pathway Inhibition in Chondrosarcoma Using the Smoothened Inhibitor IPI-926 Directly Inhibits Sarcoma Cell Growth

1270 Epithelial-to-Mesenchymal Transition Mediates Docetaxel Resistance and High Risk of Relapse in Prostate Cancer
Mercedes Marı´n-Aguilera, Jordi Codony-Servat, Oскаr Reig, Juan José Lozano, Pedro Luis Fernández, María Verónica Pereira, Natalia Jiménez, Michael Donovan, Pere Puig, Lourdes Menguial, Raquel Bermudo, Albert Font, Enrique Gallardo, María José Ribal, Antonio Alcaraz, Pere Gasco´n, and Begon´a Mellado

1285 Identification of Transmembrane Protein 98 as a Novel Chemoresistance-Conferring Gene in Hepatocellular Carcinoma
Kevin Tak-Pan Ng, Chung Mau Lo, Dong Yong Guo, Xiang Qi, Chang Xian Li, Wei Geng, Xiao Bing Liu, Chang Chun Ling, Yuen Yuen Ma, Wai Ho Yeueng, Yan Shao, Ronnie Tung-Ping Poon, Sheung Tat Fan, and Kwan Man
<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1298</td>
<td>Aurora Kinase Inhibition Induces PUMA via NF-κB to Kill Colon Cancer Cells</td>
<td>Jing Sun, Kyle Knickelbein, Kan He, Dongshi Chen, Crissy Dudgeon, Yongqian Shu, Jian Yu, and Lin Zhang</td>
</tr>
<tr>
<td>1309</td>
<td>Nuclear Translocation of Hand-1 Acts as a Molecular Switch to Regulate Vascular Radiosensitivity in Medulloblastoma Tumors: The Protein uPAR Is a Cytoplasmic Sequestration Factor for Hand-1</td>
<td>Swapna Asuthkar, Venkateswara Rao Gogineni, Jasti S. Rao, and Kiran Kumar Velpula</td>
</tr>
<tr>
<td>1323</td>
<td>The G Protein–Coupled Receptor GALR2 Promotes Angiogenesis in Head and Neck Cancer</td>
<td>Rajat Banerjee, Elizabeth A. Van Tubergen, Christina S. Scanlon, Robert Vander Broek, Joel P. Lints, Min Liu, Nickole Russo, Ronald C. Inglehart, Yugang Wang, Peter J. Polverini, Keith L. Kirkwood, and Nisha J. D'Silva</td>
</tr>
<tr>
<td>1334</td>
<td>The Role of Gene Body Cytosine Modifications in MGMT Expression and Sensitivity to Temozolomide</td>
<td>Erika L. Moen, Amy L. Stark, Wei Zhang, M. Eileen Dolan, and Lucy A. Godley</td>
</tr>
<tr>
<td>1345</td>
<td>ERBB3/HER2 Signaling Promotes Resistance to EGFR Blockade in Head and Neck and Colorectal Cancer Models</td>
<td>Li Zhang, Carla Castanaro, Bo Luan, Katie Yang, Liangfen Fan, Jeanette L. Fairhurst, Ashique Rafique, Terra B. Potocky, Jing Shan, Frank J. Dellino, Ergang Shi, Tammy Huang, Joel H. Martin, Gang Chen, Douglas MacDonald, John S. Rudge, Gavin Thurston, and Christopher Daly</td>
</tr>
<tr>
<td>1369</td>
<td>Metallothionein 1G and Zinc Sensitize Human Colorectal Cancer Cells to Chemotherapy</td>
<td>Juan M. Arriaga, Angela Greco, José Mordoh, and Michele Bianchini</td>
</tr>
</tbody>
</table>

**COMPANION DIAGNOSTICS AND CANCER BIOMARKERS**

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
</table>
ABOUT THE COVER

Angiogenesis is important for tumor progression. In squamous cell carcinoma of the head and neck (SCCHN), angiogenesis is activated by cytokines including IL-6 and VEGF. Galanin receptor 2 (GALR2) is a G protein-coupled receptor that induces aggressive growth in SCCHN. GALR2 stimulates tumor angiogenesis in SCCHN via p38-mediated inhibition of tristetraprolin (TTP) with resultant enhanced cytokine secretion. Given that p38 inhibitors are in clinical use for inflammatory disorders, GALR2/p38-mediated cytokine secretion may be an excellent target for new adjuvant therapy in SCCHN. For details, see article by Banerjee, Van Tubergen, and colleagues on page 1323.