

## Highlights of This Issue 765

## REVIEWS

- 767** **Strategic Combinations: The Future of Oncolytic Virotherapy with Reovirus**  
Xing Zhao, Cariad Chester, Narendiran Rajasekaran, ZhiXu He, and Holbrook E. Kohrt
- 774** **The Role of PGC1 $\alpha$  in Cancer Metabolism and its Therapeutic Implications**  
Zheqiong Tan, Xiangjian Luo, Lanbo Xiao, Min Tang, Ann M. Bode, Zigang Dong, and Ya Cao

## SMALL MOLECULE THERAPEUTICS

- 783** **Preclinical Characterization of G1T28: A Novel CDK4/6 Inhibitor for Reduction of Chemotherapy-Induced Myelosuppression**  
 John E. Bisi, Jessica A. Sorrentino, Patrick J. Roberts, Francis X. Tavares, and Jay C. Strum
- 794** **Applying Small Molecule Signal Transducer and Activator of Transcription-3 (STAT3) Protein Inhibitors as Pancreatic Cancer Therapeutics**  
Carolyn C. Arpin, Stephen Mac, Yanlin Jiang, Huiwen Cheng, Michelle Grimard, Brent D.G. Page, Malgorzata M. Kamocka, Sina Haftchenary, Han Su, Daniel P. Ball, David A. Rosa, Ping-Shan Lai, Rodolfo F. Gómez-Biagi, Ahmed M. Ali, Rahul Rana, Helmut Hanenberg, Kagan Kerman, Kyle C. McElyea, George E. Sandusky, Patrick T. Gunning, and Melissa L. Fishel
- 806** **EC-70124, a Novel Glycosylated Indolocarbazole Multikinase Inhibitor, Reverts Tumorigenic and Stem Cell Properties in Prostate Cancer by Inhibiting STAT3 and NF- $\kappa$ B**  
Gianluca Civenni, Nicole Longoni, Paula Costales, Cecilia Dallavalle, Cristina García Inclán, Domenico Albino, Luz Elena Nuñez, Francisco Morís, Giuseppina M. Carbone, and Carlo V. Catapano
- 819** **ABCG2 and ABCB1 Limit the Efficacy of Dasatinib in a PDGF-B–Driven Brainstem Glioma Model**  
Rajendar K. Mittapalli, Alexander H. Chung, Karen E. Parrish, Donna Crabtree, Kyle G. Halvorson, Guo Hu, William F. Elmquist, and Oren J. Becher
- 830** **Histone Deacetylase Inhibitors Enhance the Therapeutic Potential of Reovirus in Multiple Myeloma**  
Andrew Stiff, Enrico Caserta, Douglas W. Sborov, Gerard J. Nuovo, Xiaokui Mo, Sarah Y. Schlotter, Alessandro Canella, Emily Smith, Joseph Badway, Matthew Old, Alena Cristina Jaime-Ramirez, Pearly Yan, Don M. Benson, John C. Byrd, Robert Baiocchi, Balveen Kaur, Craig C. Hofmeister, and Flavia Pichiorri
- 842** **Combined Effects of Suberoylanilide Hydroxamic Acid and Cisplatin on Radiation Sensitivity and Cancer Cell Invasion in Non–Small Cell Lung Cancer**  
Jianguo Feng, Shirong Zhang, Kan Wu, Bing Wang, Jeffrey Y.C. Wong, Hong Jiang, Rujun Xu, Lisha Ying, Haixiu Huang, Xiaoliang Zheng, Xufeng Chen, and Shenglin Ma
- 854** **Bortezomib Inhibits Giant Cell Tumor of Bone through Induction of Cell Apoptosis and Inhibition of Osteoclast Recruitment, Giant Cell Formation, and Bone Resorption**  
Leqin Xu, Jian Luo, Rongrong Jin, Zhiying Yue, Peng Sun, Zhengfeng Yang, Xinghai Yang, Wei Wan, Jishen Zhang, Shichang Li, Mingyao Liu, and Jianru Xiao
- 866** **Posaconazole, a Second-Generation Triazole Antifungal Drug, Inhibits the Hedgehog Signaling Pathway and Progression of Basal Cell Carcinoma**  
Baozhi Chen, Vinh Trang, Alex Lee, Noelle S. Williams, Alexandra N. Wilson, Ervin H. Epstein Jr, Jean Y. Tang, and James Kim
- 877** **Intermittent High-Dose Scheduling of AZD8835, a Novel Selective Inhibitor of PI3K $\alpha$  and PI3K $\delta$ , Demonstrates Treatment Strategies for PIK3CA-Dependent Breast Cancers**  
 Kevin Hudson, Urs J. Hancox, Cath Trigwell, Robert McEwen, Urszula M. Polanska, Myria Nikolaou, Pablo Morentin Gutierrez, Alvaro Avivar-Valderas, Oona Delpuech, Philippa Dudley, Lyndsey Hanson, Rebecca Ellston, Alys Jones, Marie Cumberbatch, Sabina C. Cosulich, Lara Ward, Francisco Cruzalegui, and Stephen Green
- 890** **Addition of DHA Synergistically Enhances the Efficacy of Regorafenib for Kidney Cancer Therapy**  
Jeffrey Kim, Arzu Ulu, Debin Wan, Jun Yang, Bruce D. Hammock, and Robert H. Weiss

# Table of Contents



**899** Effective Concentration of a Multikinase Inhibitor within Bone Marrow Correlates with *In Vitro* Cell Killing in Therapy-Resistant Chronic Myeloid Leukemia

Chaofeng Mu, Xiaoyan Wu, Helen Ma, Wenjing Tao, Guodong Zhang, Xiaojun Xia, Jianliang Shen, Junhua Mai, Tong Sun, Xiaoping Sun, Ralph B. Arlinghaus, and Haifa Shen

**911** Preclinical Evaluation of UAB30 in Pediatric Renal and Hepatic Malignancies

Alicia M. Waters, Jerry E. Stewart, Venkatram R. Atigadda, Elizabeth Mroczek-Musulman, Donald D. Muccio, Clinton J. Grubbs, and Elizabeth A. Beierle

**922** 7-(2-Thienyl)-7-Deazaadenosine (AB61), a New Potent Nucleoside Cytostatic with a Complex Mode of Action



Pavla Perlíková, Gabriela Rylová, Petr Nauš, Tomáš Elbert, Eva Tloušťová, Aurelie Bourderieux, Lenka Poštová Slavětínská, Kamil Motyka, Dalibor Doležal, Pawel Znojek, Alice Nová, Monika Harvanová, Petr Džubák, Michal Šiller, Jan Hlaváč, Marián Hajdúch, and Michal Hocek

## LARGE MOLECULE THERAPEUTICS

**938** Development of Novel Quaternary Ammonium Linkers for Antibody–Drug Conjugates



Patrick J. Burke, Joseph Z. Hamilton, Thomas A. Pires, Jocelyn R. Setter, Joshua H. Hunter, Julia H. Cochran, Andrew B. Waight, Kristine A. Gordon, Brian E. Toki, Kim K. Emmerton, Weiping Zeng, Ivan J. Stone, Peter D. Senter, Robert P. Lyon, and Scott C. Jeffrey

**946** RG7386, a Novel Tetravalent FAP-DR5 Antibody, Effectively Triggers FAP-Dependent, Avidity-Driven DR5 Hyperclustering and Tumor Cell Apoptosis



Peter Brünker, Katharina Wartha, Thomas Friess, Sandra Grau-Richards, Inja Waldhauer, Claudia Ferrara Koller, Barbara Weiser, Meher Majety, Valeria Runza, Huifeng Niu, Kathryn Packman, Ningping Feng, Sherif Daouti, Ralf J. Hosse, Ekkehard Mössner, Thomas G. Weber, Frank Herting, Werner Scheuer, Hadassah Sade, Cuiying Shao, Bin Liu, Peng Wang, Gary Xu, Suzana Vega-Harring, Christian Klein, Klaus Bosslet, and Pablo Umaña

**958** Molecular Basis of Valine-Citrulline-PABC Linker Instability in Site-Specific ADCs and Its Mitigation by Linker Design

Magdalena Dorywalska, Russell Dushin, Ludivine Moine, Santiago E. Farias, Dahui Zhou, Thayalan Navaratnam, Victor Lui, Adela Hasa-Moreno, Meritxell Galindo Casas, Thomas-Toan Tran, Kathy Delaria, Shu-Hui Liu, Davide Foletti, Christopher J. O'Donnell, Jaume Pons, David L. Shelton, Arvind Rajpal, and Pavel Strop

**971** A Novel Recombinant Anti-CD22 Immunokinase Delivers Proapoptotic Activity of Death-Associated Protein Kinase (DAPK) and Mediates Cytotoxicity in Neoplastic B Cells

Nils Lilienthal, Gregor Lohmann, Giuliano Crispantu, Elena Vasyutina, Stefan Zittrich, Petra Mayer, Carmen Diana Herling, Mehmet Kemal Tur, Michael Hallek, Gabriele Pfitzer, Stefan Barth, and Marco Herling

**985** Novel Anti-CRR9/CLPTM1L Antibodies with Antitumorigenic Activity Inhibit Cell Surface Accumulation, PI3K Interaction, and Survival Signaling

László G. Puskás, Imola Mán, Gabor Szebeni, László Tiszlavicz, Susan Tsai, and Michael A. James

**998** Improved Tumor-Specific Drug Accumulation by Polymer Therapeutics with pH-Sensitive Drug Release Overcomes Chemotherapy Resistance

Anne-Kathrin Heinrich, Henrike Lucas, Lucie Schindler, Petr Chytil, Tomáš Etrych, Karsten Mäder, and Thomas Mueller

**1008** Gastric Adenocarcinomas Express the Glycosphingolipid Gb<sub>3</sub>/CD77: Targeting of Gastric Cancer Cells with Shiga Toxin B-Subunit

Philipp Emanuel Geyer, Matthias Maak, Ulrich Nitsche, Markus Perl, Alexander Novotny, Julia Slotta-Huspenina, Estelle Dransart, Anne Holtorf, Ludger Johannes, and Klaus-Peter Janssen

## CANCER BIOLOGY AND SIGNAL TRANSDUCTION

**1018** The Bromodomain BET Inhibitor JQ1 Suppresses Tumor Angiogenesis in Models of Childhood Sarcoma

Hemant K. Bid, Doris A. Phelps, Linlin Xaio, Denis C. Guttridge, Jiayuh Lin, Cheryl London, Laurence H. Baker, Xiaokui Mo, and Peter J. Houghton

**1029** BRD4 Regulates EZH2 Transcription through Upregulation of C-MYC and Represents a Novel Therapeutic Target in Bladder Cancer

Xinchao Wu, Dong Liu, Dan Tao, Wei Xiang, Xingyuan Xiao, Miao Wang, Liang Wang, Gang Luo, Yawei Li, Fuqing Zeng, and Guosong Jiang

**1043** Expression of GRP78, Master Regulator of the Unfolded Protein Response, Increases Chemoresistance in Pancreatic Ductal Adenocarcinoma

Jenifer B. Gifford, Wei Huang, Ann E. Zeleniak, Antreas Hindoyan, Hong Wu, Timothy R. Donahue, and Reginald Hill



# Table of Contents


- 1053** Protein Kinase Inhibitor H89 Enhances the Activity of *Pseudomonas* Exotoxin A–Based Immunotoxins  
Xiufen Liu, Fabian Müller, Alan S. Wayne, and Ira Pastan
- 1063** Recombinant Arabidopsis HSP70 Sustains Cell Survival and Metastatic Potential of Breast Cancer Cells  
Alessandra Nigro, Loredana Mauro, Francesca Giordano, Salvatore Panza, Rina Iannacone, Grazia Maria Liuzzi, Saveria Aquila, Francesca De Amicis, Francesco Cellini, Cesare Indiveri, and Maria Luisa Panno
- 1074** CD20-Targeting Immunotherapy Promotes Cellular Senescence in B-Cell Lymphoma  
J. Henry M. Däbritz, Yong Yu, Maja Milanovic, Martin Schönlein, Mathias T. Rosenfeldt, Jan R. Dörr, Andreas M. Kaufmann, Bernd Dörken, and Clemens A. Schmitt
- 1082** Long Noncoding RNA *PVT1* Promotes Non-Small Cell Lung Cancer Cell Proliferation through Epigenetically Regulating LATS2 Expression  
Li Wan, Ming Sun, Guo-Jian Liu, Chen-Chen Wei, Er-Bao Zhang, Rong Kong, Tong-Peng Xu, Ming-De Huang, and Zhao-Xia Wang
- 1095** Antagonizing the Hedgehog Pathway with Vismodegib Impairs Malignant Pleural Mesothelioma Growth *In Vivo* by Affecting Stroma  
Mayura Meerang, Karima Bérard, Emanuela Felley-Bosco, Olivia Lauk, Bart Vrugt, Andreas Boss, David Kenkel, Angela Broggin-Tenzer, Rolf A. Stahel, Stephan Ami, Walter Weder, and Isabelle Opitz
- 1113** MR Studies of Glioblastoma Models Treated with Dual PI3K/mTOR Inhibitor and Temozolomide: Metabolic Changes Are Associated with Enhanced Survival  
Marina Radoul, Myriam M. Chaumeil, Pia Eriksson, Alan S. Wang, Joanna J. Phillips, and Sabrina M. Ronen
- 1123** High Expression of miR-532-5p, a Tumor Suppressor, Leads to Better Prognosis in Ovarian Cancer Both *In Vivo* and *In Vitro*  
Fan Wang, Jeremy T.-H. Chang, Chester Jingshiu Kao, and R. Stephanie Huang
- 1132** Expression Profile of BCL-2, BCL-X<sub>L</sub>, and MCL-1 Predicts Pharmacological Response to the BCL-2 Selective Antagonist Venetoclax in Multiple Myeloma Models  
 Elizabeth A. Punnoose, Joel D. Levenson, Franklin Peale, Erwin R. Boghaert, Lisa D. Belmont, Nguyen Tan, Amy Young, Michael Mitten, Ellen Ingalla, Walter C. Darbonne, Anatol Oleksijew, Paul Tapang, Peng Yue, Jason Oeh, Leslie Lee, Sophie Maiga, Wayne J. Fairbrother, Martine Amiot, Andrew J. Souers, and Deepak Sampath

## MODELS AND TECHNOLOGIES

- 1145** Modeling Therapy Response and Spatial Tissue Distribution of Erlotinib in Pancreatic Cancer  
Barbara M. Grüner, Isabel Winkelmann, Annette Feuchtinger, Na Sun, Benjamin Balluff, Nicole Teichmann, Alexander Herner, Evdokia Kalideris, Katja Steiger, Rickmer Braren, Michaela Aichler, Irene Esposito, Roland M. Schmid, Axel Walch, and Jens T. Siveke

## COMPANION DIAGNOSTICS AND CANCER BIOMARKERS

- 1106** Nanofluidic Digital PCR and Extended Genotyping of *RAS* and *BRAF* for Improved Selection of Metastatic Colorectal Cancer Patients for Anti-EGFR Therapies  
Daniel Azuara, Cristina Santos, Adriana Lopez-Doriga, Julieta Grasselli, Marga Nadal, Xavier Sanjuan, Fátima Marin, Joana Vidal, Robert Montal, Victor Moreno, Beatriz Bellosillo, Guillem Argiles, Elena Elez, Rodrigo Dienstmann, Clara Montagut, Josep Taberner, Gabriel Capellá, and Ramon Salazar

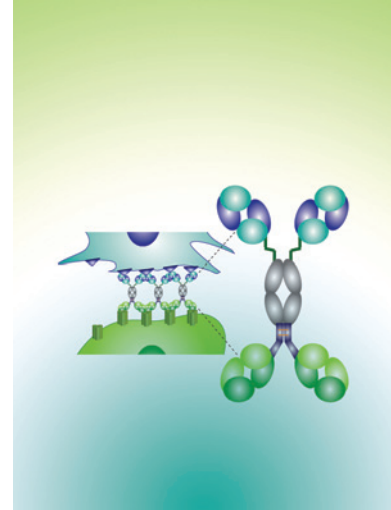
 AC icon indicates Author Choice  
For more information please visit [www.aacrjournals.org](http://www.aacrjournals.org)

# Table of Contents



## ABOUT THE COVER

The tetravalent FAP-DR5 bispecific antibody (RG7386) is rationally designed to exhibit bivalent binding to FAP and DR5. By simultaneous binding to both targets, the death receptor on tumor cells is being hyper-cross-linked, resulting in strictly target-dependent apoptosis induction of cancer cells. For details, see the article by Brünker, Wartha, and colleagues beginning on page 946.



# Molecular Cancer Therapeutics

**15 (5)**

*Mol Cancer Ther* 2016;15:765-1152.

**Updated version** Access the most recent version of this article at:  
<http://mct.aacrjournals.org/content/15/5>

**E-mail alerts** [Sign up to receive free email-alerts](#) related to this article or journal.

**Reprints and Subscriptions** To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at [pubs@aacr.org](mailto:pubs@aacr.org).

**Permissions** To request permission to re-use all or part of this article, use this link <http://mct.aacrjournals.org/content/15/5>. Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.