

Highlights of This Issue 273

REVIEW

- 275 Targeting Microtubules by Natural Agents for Cancer Therapy**
Eiman Mukhtar, Vaqar Mustafa Adhami, and Hasan Mukhtar

SMALL MOLECULE THERAPEUTICS

- 285 Inhibition of GSK-3 Induces Differentiation and Impaired Glucose Metabolism in Renal Cancer**
Krishnendu Pal, Ying Cao, Irina N. Gaisina, Santanu Bhattacharya, Shamit K. Dutta, Enfeng Wang, Hendra Gunosewoyo, Alan P. Kozikowski, Daniel D. Billadeau, and Debabrata Mukhopadhyay

- 297 Bisphosphonamidate Clodronate Prodrug Exhibits Selective Cytotoxic Activity against Melanoma Cell Lines**
Marie R. Webster, Chandrashekhar Kamat, Nick Connis, Ming Zhao, Ashani T. Weeraratna, Michelle A. Rudek, Christine L. Hann, and Caren L. Freel Meyers

- 307 Selective Inhibition of Pancreatic Ductal Adenocarcinoma Cell Growth by the Mitotic MPS1 Kinase Inhibitor NMS-P715**
Roger B. Slee, Brenda R. Grimes, Ruchi Bansal, Jesse Gore, Corinne Blackburn, Lyndsey Brown, Rachel Gasaway, Jaesik Jeong, Jose Victorino, Keith L. March, Riccardo Colombo, Brittney-Shea Herbert, and Murray Korc

- 316 Inhibition of Insulin-like Growth Factor-Binding Protein-3 Signaling through Sphingosine Kinase-1 Sensitizes Triple-Negative Breast Cancer Cells to EGF Receptor Blockade**
Janet L. Martin, Hasanthi C. de Silva, Mike Z. Lin, Carolyn D. Scott, and Robert C. Baxter

- 329 The Selective Anaplastic Lymphoma Receptor Tyrosine Kinase Inhibitor ASP3026 Induces Tumor Regression and Prolongs Survival in Non-Small Cell Lung Cancer Model Mice**
Masamichi Mori, Yoko Ueno, Satoshi Konagai, Hiroshi Fushiki, Itsuro Shimada, Yutaka Kondoh, Rika Saito, Kenichi Mori, Nobuaki Shindou, Takatoshi Soga, Hideki Sakagami, Takashi Furutani, Hitoshi Doihara, Masafumi Kudoh, and Sadao Kuromitsu

- 341 A Naturally Derived Small Molecule Disrupts Ligand-Dependent and Ligand-Independent Androgen Receptor Signaling in Human Prostate Cancer Cells**
Karishma S. Amin, Shankar Jagadeesh, Gakul Baishya, Paruchuri G. Rao, Nabin C. Barua, Samir Bhattacharya, and Partha P. Banerjee

- 353 Overcoming Acquired BRAF Inhibitor Resistance in Melanoma via Targeted Inhibition of Hsp90 with Ganetespib**
Jaime Acquaviva, Donald L. Smith, John-Paul Jimenez, Chaohua Zhang, Manuel Sequeira, Suqin He, Jim Sang, Richard C. Bates, and David A. Proia

- 364 Characterization of LY2228820 Dimesylate, a Potent and Selective Inhibitor of p38 MAPK with Antitumor Activity**
Robert M. Campbell, Bryan D. Anderson, Nathan A. Brooks, Harold B. Brooks, Edward M. Chan, Alfonso De Dios, Raymond Gilmour, Jeremy R. Graff, Enrique Jambriña, Mary Mader, Denis McCann, Songqing Na, Stephen H. Parsons, Susan E. Pratt, Chuan Shih, Louis F. Stancato, James J. Starling, Courtney Tate, Juan A. Velasco, Yong Wang, and Xiang S. Ye

LARGE MOLECULE THERAPEUTICS

- 375 Increasing the Antitumor Effect of an EpCAM-Targeting Fusion Toxin by Facile Click PEGylation**
Manuel Simon, Nikolas Stefan, Lubor Borsig, Andreas Plückthun, and Uwe Zangemeister-Wittke

- 386 Novel Neutralizing Hedgehog Antibody MEDI-5304 Exhibits Antitumor Activity by Inhibiting Paracrine Hedgehog Signaling**
Neil R. Michaud, Youzhen Wang, Kristen A. McEachern, Jerold J. Jordan, Anne Marie Mazzola, Axel Hernandez, Sanjoo Jalla, Jon W. Chesebrough, Mark J. Hynes, Matthew A. Belmonte, Lidong Wang, Jaspal S. Kang, Jelena Jovanović, Naomi Laing, David W. Jenkins, Elaine Hurt, Meina Liang, Christopher Frantz, Robert E. Hollingsworth, Diane M. Simeone, David C. Blakey, and Vahe Bedian

Table of Contents

- 399** Pharmacodynamic and Antineoplastic Activity of BI 836845, a Fully Human IGF Ligand-Neutralizing Antibody, and Mechanistic Rationale for Combination with Rapamycin



Katrin Friedbichler, Marco H. Hofmann, Monika Kroez, Elinborg Ostermann, Herbert R. Lamche, Christian Koessl, Eric Borges, Michael N. Pollak, Günther Adolf, and Paul J. Adam

- 410** MM-141, an IGF-IR- and ErbB3-Directed Bispecific Antibody, Overcomes Network Adaptations That Limit Activity of IGF-IR Inhibitors



Jonathan B. Fitzgerald, Bryan W. Johnson, Jason Baum, Sharlene Adams, Sergio Iadevaia, Jian Tang, Victoria Rimkunas, Lihui Xu, Neeraj Kohli, Rachel Rennard, Maja Razlog, Yang Jiao, Brian D. Harms, Kenneth J. Olivier Jr, Birgit Schoeberl, Ulrik B. Nielsen, and Alexey A. Lugovskoy

- 426** The Effect of Photoimmunotherapy Followed by Liposomal Daunorubicin in a Mixed Tumor Model: A Demonstration of the Super-Enhanced Permeability and Retention Effect after Photoimmunotherapy

Kohei Sano, Takahito Nakajima, Peter L. Choyke, and Hisataka Kobayashi

CANCER BIOLOGY AND SIGNAL TRANSDUCTION

- 433** Stereospecific PARP Trapping by BMN 673 and Comparison with Olaparib and Rucaparib

Junko Murai, Shar-Yin N. Huang, Amèlie Renaud, Yiping Zhang, Jiuping Ji, Shunichi Takeda, Joel Morris, Beverly Teicher, James H. Doroshow, and Yves Pommier

- 444** MiR-134/487b/655 Cluster Regulates TGF- β -Induced Epithelial-Mesenchymal Transition and Drug Resistance to Gefitinib by Targeting *MAGI2* in Lung Adenocarcinoma Cells

Kazuhiro Kitamura, Masahiro Seike, Tetsuya Okano, Kuniko Matsuda, Akihiko Miyanaga, Hideaki Mizutani, Rintaro Noro, Yuji Minegishi, Kaoru Kubota, and Akihiko Gemma

- 454** GSK3 Inhibitors Regulate *MYCN* mRNA Levels and Reduce Neuroblastoma Cell Viability through Multiple Mechanisms, Including p53 and Wnt Signaling

David J. Duffy, Aleksandar Krstic, Thomas Schwarzl, Desmond G. Higgins, and Walter Kolch

- 468** Therapeutic Inhibition of Jak Activity Inhibits Progression of Gastrointestinal Tumors in Mice



Emma Stuart, Michael Buchert, Tracy Putoczki, Stefan Thiem, Ryan Farid, Joachim Elzer, Dennis Huszar, Paul M. Waring, Toby J. Phesse, and Matthias Ernst

- 475** Acquired Resistance to Dasatinib in Lung Cancer Cell Lines Conferred by *DDR2* Gatekeeper Mutation and *NF1* Loss

Ellen M. Beauchamp, Brittany A. Woods, Austin M. Dulak, Li Tan, Chunxiao Xu, Nathanael S. Gray, Adam J. Bass, Kwok-kin Wong, Matthew Meyerson, and Peter S. Hammerman

- 483** Blocking SDF-1 α /CXCR4 Downregulates PDGF-B and Inhibits Bone Marrow-Derived Pericyte Differentiation and Tumor Vascular Expansion in Ewing Tumors

Randala Hamdan, Zhichao Zhou, and Eugenie S. Kleinerman

- 492** OATP1A/1B Transporters Affect Irinotecan and SN-38 Pharmacokinetics and Carboxylesterase Expression in Knockout and Humanized Transgenic Mice

Dilek Iusuf, Marion Ludwig, Ahmed Elbatsh, Anita van Esch, Evita van de Steeg, Els Wagenaar, Martin van der Valk, Fan Lin, Olaf van Tellingen, and Alfred H. Schinkel

- 504** Genetic and Pharmacologic Evidence That mTOR Targeting Outweighs mTORC1 Inhibition as an Antimyeloma Strategy

Xi Chen, Elena Díaz-Rodríguez, Enrique M. Ocio, Bruno Paiva, Deborah S. Mortensen, Antonia Lopez-Girona, Rajesh Chopra, Jesús San Miguel, and Atanasio Pandiella

COMPANION DIAGNOSTICS AND CANCER BIOMARKERS

- 517** Activation of AR Sensitizes Breast Carcinomas to NVP-BEZ235's Therapeutic Effect Mediated by PTEN and KLLN Upregulation



Yu Wang, Qi Yu, Xin He, Todd Romigh, Jessica Altemus, and Charis Eng

- 528** Platin Polymorphisms Predict Gender- and Stage-Specific Colon Cancer Recurrence after Adjuvant Chemotherapy

Yan Ning, Armin Gerger, Wu Zhang, Diana L. Hanna, Dongyun Yang, Thomas Winder, Takeru Wakatsuki, Melissa J. Labonte, Sebastian Stintzing, Nico Volz, Yu Sunakawa, Stefan Stremtizer, Rita El-Khoueiry, and Heinz-Josef Lenz



Table of Contents

- 540** **Nonclinical Evaluation of the Serum Pharmacodynamic Biomarkers HGF and Shed MET following Dosing with the Anti-MET Monovalent Monoclonal Antibody Onartuzumab**
Elaine Mai, Zhong Zheng, Youjun Chen, Jing Peng, Christophe Severin, Ellen Filvaroff, Mally Romero, William Mallet, Surinder Kaur, Thomas Gelzleichter, Ihsan Nijem, Mark Merchant, and Judy C. Young

CORRECTION

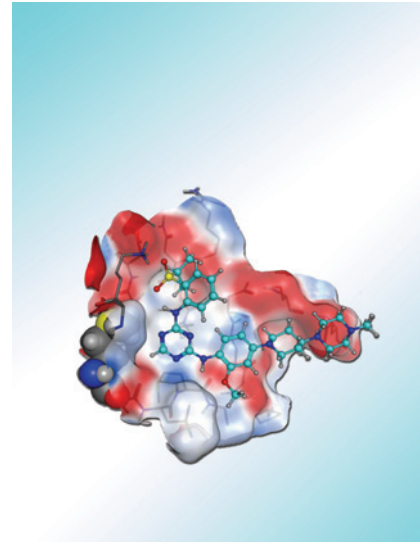
- 553** **Correction: Aerosol Delivery of Urocanic Acid-Modified Chitosan/Programmed Cell Death 4 Complex Regulated Apoptosis, Cell Cycle, and Angiogenesis in Lungs of *K-ras* Null Mice**

 AC icon indicates Author Choice

For more information please visit www.aacrjournals.org

ABOUT THE COVER

The ALK/MET inhibitor crizotinib has already shown efficacy in ALK-driven non-small cell lung cancer patients, but the treatment is not curative with rapid acquisition of resistance, which is partly attributable to the gatekeeper-residue mutation L1196M of ALK. Computational modeling suggested that ASP3026, a novel small molecule ALK inhibitor, is well docked with both wild-type and L1196M ALK, and fits more deeply within the ATP-binding pocket of the L1196M form, with the larger side-chain of methionine compared to leucine, than crizotinib. This might explain why ASP3026 showed more potent efficacy against the L1196M mutant within the therapeutic margin compared with crizotinib. For details, see article by Mori and colleagues, on page 329.



Molecular Cancer Therapeutics

13 (2)

Mol Cancer Ther 2014;13:273-553.

Updated version Access the most recent version of this article at:
<http://mct.aacrjournals.org/content/13/2>

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.

Permissions To request permission to re-use all or part of this article, use this link <http://mct.aacrjournals.org/content/13/2>.
Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.