REVIEW

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

SMALL MOLECULE THERAPEUTICS

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

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

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, Ricardo Colombo, Brittney-Shea Herbert, and Murray Korc

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

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

LARGE MOLECULE THERAPEUTICS

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

Novel Neutralizing Hedgehog Antibody MEDI-5304 Exhibits Antitumor Activity by Inhibiting Paracrine Hedgehog Signaling
Pharmacodynamic and Antineoplastic Activity of BI 836845, a Fully Human IGF Ligand-Neutralizing Antibody, and Mechanistic Rationale for Combination with Rapamycin

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

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

Stereospecific PARP Trapping by BMN 673 and Comparison with Olaparib and Rucarib
Junko Murai, Shar-Yin N. Huang, Amelie Renaud, Yiping Zhang, Jiuping Ji, Shunichi Takeda, Joel Morris, Beverly Teicher, James H. Doroshow, and Yves Pommier

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 Miyazaki, Hideo Mizutani, Rintaro Noro, Yuji Minegishi, Kaoru Kubota, and Akihiko Gemma

GSK3 Inhibitors Regulate MYCN mRNA Levels and Reduce Neuroblastoma Cell Viability through Multiple Mechanisms, Including p53 and Wnt Signaling
David J. Duffy, Aleksandar Kesic, Thomas Schwarzl, Desmond G. Higgins, and Walter Kolch

Therapeutic Inhibition of Jak Activity Inhibits Progression of Gastrointestinal Tumors in Mice
Emma Stuart, Michael Buchert, Tracy Putoczki, Stefan Thienn, Ryan Farid, Joachim Elzer, Dennis Huszar, Paul M. Waring, Toby J. Phesse, and Matthias Ernst

Acquired Resistance to Dasatinib in Lung Cancer Cell Lines Conferred by DDR2 Gatekeeper Mutation and NFI 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

Blocking SDF-1α/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

OATP1A/IB Transporters Affect Irinotecan and SN-38 Pharmacokinetics and Carboxylesterase Expression in Knockout and Humanized Transgenic Mice
Dilek Iusuf, Marion Ludwig, Ahmed Elbabsh, Anita van Esch, Evita van de Steeg, Els Wagenaar, Martin van der Valk, Fan Lin, Olaf van Tellingen, and Alfred H. Schinkel

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, Antonio Lopez-Girona, Rajesh Chopra, Jesús San Miguel, and Atanasio Pandiella

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

Plastin 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, Takeku Wakatsuki, Melissa J. Labonte, Sebastian Stintzing, Nico Volz, Yu Sunakawa, Stefan Stremitzer, Rita El-Khoueiry, and Heinz-Josef Lenz
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: 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

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.