SMALL MOLECULE THERAPEUTICS

Identification of Preferred Chemotherapeutics for Combining with a CHK1 Inhibitor
Yang Xiao, Judi Ramiscal, Kaska Kowanetz, Christopher Del Nagro, Shiva Malek, Marie Evangelista, Elizabeth Blackwood, Peter K. Jackson, and Thomas O’Brien

Gramicidin A Induces Metabolic Dysfunction and Energy Depletion Leading to Cell Death in Renal Cell Carcinoma Cells
Justin M. David, Tori A. Owens, Sonali P. Barwe, and Ayyappan K. Rajasekaran

Developing Lipid Nanoparticle-Based siRNA Therapeutics for Hepatocellular Carcinoma Using an Integrated Approach
Leiming Li, Rongqi Wang, Denise Wilcox, Aparna Sarthy, Xiaoyu Lin, Xiaoli Huang, Lu Tian, Prasad Dane, Robert D. Hubbard, Todd M. Hansen, Carol Wada, Xinli Liu, Shuang Liu, and Douglas K. Graham

BAY 80-6946 Is a Highly Selective Intravenous PI3K Inhibitor with Potent p110α and p110δ Activities in Tumor Cell Lines and Xenograft Models
Ningshu Liu, Bruce R. Rowley, Cathy O. Bull, Claudia Schneider, Andrea Haegerbarth, Christoph A. Schatz, Paul R. Fracasso, Dean P. Wilkie, Martin Hentemann, Scott M. Wilhelm, William J. Scott, Dominik Mumberg, and Karl Ziegelbauer

PRIMA-1Met/PR-246 Displays High Antitumor Activity in Multiple Myeloma By Induction of p73 and Noxa
Manujendra N. Saha, Hua Jiang, Yijun Yang, Donna Reeco, and Hong Chang

Synergistic Targeting of PI3K/AKT Pathway and Androgen Receptor Axis Significantly Delays Castration-Resistant Prostate Cancer Progression In Vivo
Christian Thomas, Francois Lamoureux, Claire Crafter, Barry R. Davies, Eliana Beraldi, Ladan Fazli, Soojin Kim, Daksh Thaper, Martin E. Gleave, and Amina Zoubeidi

AMG 900, a Small-Molecule Inhibitor of Aurora Kinases, Potentiates the Activity of Microtubule-Targeting Agents in Human Metastatic Breast Cancer Models

UNC569, a Novel Small-Molecule Mer Inhibitor with Efficacy against Acute Lymphoblastic Leukemia In Vitro and In Vivo
Sandra Christoph, Deborah DeRyckere, Jennifer Schlegel, J. Kimble Frazer, Lance A. Batchelor, Alesia Y. Trakhimets, Susan Sather, Debra M. Hunter, Christopher T. Cummings, Jing Liu, Chao Yang, Dmitri Kireev, Catherine Simpson, Jacqueline Norris-Drouin, Emily A. Hull-Ryde, William P. Janzen, Gary L. Johnson, Xiaodong Wang, Stephen V. Frye, H. Shelton Earp III, and Douglas K. Graham

SK-216, an Inhibitor of Plasminogen Activator Inhibitor-1, Limits Tumor Progression and Angiogenesis
Takeshi Masuda, Noboru Hattori, Tadashi Senoo, Shin Akita, Nobuhisa Ishikawa, Kazunori Fujita, Yoshiyuki Haruta, Hiroshi Murai, and Nobuo Kono

Paclitaxel–Hyaluronic NanoConjugates Prolong Overall Survival in a Preclinical Brain Metastases of Breast Cancer Model
Rajender K. Mittapalli, Xintao Liu, Chris E. Adkins, Mohamed I. Nounou, Kaci A. Bohn, Tori B. Terrell, Hussain Al-Shatallah, Werner J. Geldenhuys, Diane Palmieri, Patricia S. Steeg, Quentin R. Smith, and Paul R. Lockman

Isolation of a Novel Thioflavin S–Derived Compound That Inhibits BAG-1–Mediated Protein Interactions and Targets BRAF Inhibitor-Resistant Cell Lines
Marion Enthammer, Emmanouil S. Papadakis, Maria Salome Gachet, Martin Deutsch, Stefan Schweiger, Katarzyna Koziel, Muhammad Imtiaz Ashraf, Sana Khalid, Gerhard Wolber, Graham Packham, Ramsey I. Cutress, Hermann Stuppner, and Jakob Troppmair
The Novel ATP-Competitive Inhibitor of the MET Hepatocyte Growth Factor Receptor EMD1214063 Displays Inhibitory Activity against Selected MET-Mutated Variants
Michaela Medová, Benoît Pochon, Bruno Streit, Wiesława Blank-Liss, Paola Francica, Deborah Stroka, Adrian Keogh, Daniel M. Aebersold, Andree Blaukat, Friedhelm Bladt, and Yitzhak Zimmer

Characterization of a New Class of Androgen Receptor Antagonists with Potential Therapeutic Application in Advanced Prostate Cancer
Huifang Li, Mohamed D.H. Hassona, Nathan A. Lack, Peter Averio-Ciliaes, Eric Leblanc, Peyman Tavassoli, Natalia Kanaan, Kate Frewin, Kriti Singh, Hans Adomat, Konrad J. Böhm, Helge Prinz, Emma Tomlinson Guns, Paul S. Rennie, and Artem Cherkasov

177Lu-EC0800 Combined with the Antifolate Pemetrexed: Preclinical Pilot Study of Folate Receptor Targeted Radionuclide Tumor Therapy
Josefine Reber, Stephanie Haller, Christopher P. Leamon, and Cristina Müller

MTI-101 (Cyclized HYD1) Binds a CD44 Containing Complex and Induces Necrotic Cell Death in Multiple Myeloma
Anthony W. Gebhard, Priyesh Jain, Rajesh R. Nair, Michael F. Emmons, Raúl F. Argilagos, John M. Koomen, Mark L. McLaughlin, and Lori A. Hazlehurst

A Highly Potent and Specific MET Therapeutic Protein Antagonist with Both Ligand-Dependent and Ligand-Independent Activity

Molecular Radiotherapy Using Cleavable Radioimmunoconjugates That Target EGFR and γH2AX
Bart Cornelissen, Andrew Waller, Sarah Able, and Katherine A. Vallis

The Cannabinoid WIN 55,212-2 Decreases Specificity Protein Transcription Factors and the Oncogenic Cap Protein eIF4E in Colon Cancer Cells
Sandip Sreevalsan and Stephen Safe

In Vitro and In Vivo Therapeutic Efficacy of Carfilzomib in Mantle Cell Lymphoma: Targeting the Immunoproteasome
Liang Zhang, Lan V. Pham, Kate J. Newberry, Zhishuo Ou, Rong Liang, Jianfei Qian, Luhong Sun, Marzena Blonska, Yun You, Jing Yang, Xin Lin, Alex Rollo, Archito T. Tamayo, John Lee, Richard J. Ford, Xiurong Zhao, Larry W. Kwak, Qing Yi, and Michael Wang

Attenuation of Argininosuccinate Lyase Inhibits Cancer Growth via Cyclin A2 and Nitric Oxide
Hau-Lun Huang, Hui-Ping Hsu, Shu-Chu Shieh, Yang-Sheng Chang, Wei-Ching Chen, Chien-Yu Cho, Chiao-Fang Teng, Il-Jen Su, Wen-Chun Hung, and Ming-Derg Lai

PARP1 Is Overexpressed in Nasopharyngeal Carcinoma and Its Inhibition Enhances Radiotherapy
Jeremy P.H. Chow, Wing Yu Man, Mao Mao, Han Chen, Florence Cheung, John Nicholls, Sai Wah Tsao, Maria Li Lung, and Randy Y.C. Poon

Contribution of ATM and ATR to the Resistance of Glioblastoma and Malignant Melanoma Cells to the Methylating Anticancer Drug Temozolomide
Marcus Eich, Wynand Paul Roos, Teodora Nikolova, and Bernd Kaina

Axl Mediates Acquired Resistance of Head and Neck Cancer Cells to the Epidermal Growth Factor Receptor Inhibitor Erlotinib
Keith M. Giles, Felicity C. Kalinowska, Patrick A. Candy, Michael R. Epis, Priscilla M. Zhang, Andrew D. Redfern, Lisa M. Stuart, Gregory J. Goodall, and Peter J. Leedman

Hsp90 Inhibitors Promote p53-Dependent Apoptosis through PUMA and Bax
Kan He, Xingnan Zheng, Lin Zhang, and Jian Yu
miRNA-141, Downregulated in Pancreatic Cancer, Inhibits Cell Proliferation and Invasion by Directly Targeting MAP4K4

Gang Zhao, Bo Wang, Yang Liu, Jun-gang Zhang, Shi-chang Deng, Qi Qin, Kui Tian, Xiang Li, Shuai Zhu, Yi Niu, Qiong Gong, and Chun-you Wang

Arginine Deiminase Resistance in Melanoma Cells Is Associated with Metabolic Reprogramming, Glucose Dependence, and Glutamine Addiction

Yan Long, Wen-Bin Tsai, Medhi Wangpaichitr, Takashi Tsukamoto, Niramol Savaraj, Lynn G. Feun, and Macus Tien Kuo

Combining PARP-1 Inhibition and Radiation in Ewing Sarcoma Results in Lethal DNA Damage

Hae-June Lee, Changhwan Yoon, Benjamin Schmidt, Do Joong Park, Alexia Y. Zhang, Hayriye V. Erkizan, Jeffrey A. Toretsky, David G. Kirsch, and Sam S. Yoon

Tools and Technologies

Capillary Isoelectric-Focusing Immunoassays to Study Dynamic Oncoprotein Phosphorylation and Drug Response to Targeted Therapies in Non-Small Cell Lung Cancer


Letter to the Editor

EGFR Exon 20 Insertion A763-Y764insFQEA and Response to Erlotinib—Letter

Pei Jye Voon, Dana Wai Yi Tsui, Nitzan Rosenfeld, and Tan Min Chin

About the Cover

Ribbon representation of a homology model of the c-Met specific Anticalin PRS-110. Anticalins are engineered human lipocalins that represent a next generation class of drug molecules. The lipocalins have a structurally conserved β-barrel architecture that forms a cup-shaped ligand binding pocket that can accommodate small and large ligands. The β strands (blue) of the lipocalin form the base of the ligand-binding pocket and the entry of the pocket is comprised of four loops connecting the β strands. Novel, target-specific Anticalins are generated by engineering mutations (pink regions, PRS-110 mutations) within these four loops and then selecting variants with the desired binding activity. For details, see article by Olwill and colleagues on page 2459.