SMALL MOLECULE THERAPEUTICS

2409 Highlights of This Issue

2411 Targeting Ribonucleotide Reductase M2 and NF-κB Activation with Didox to Circumvent Tamoxifen Resistance in Breast Cancer
Khyati N. Shah, Elizabeth A. Wilson, Ritu Malla, Howard L. Ellord, and Jesika S. Faridi

2422 HSP90 Inhibitor–SN-38 Conjugate Strategy for Targeted Delivery of Topoisomerase I Inhibitor to Tumors
David A. Proia, Donald L. Smith, Junyi Zhang, John-Paul Jimenez, Jim Sang, Luisa Shin Ogawa, Manuel Sequeira, Noriaki Tatsuta, Sami Osman, Richard C. Bates, Dinesh Chimmanamada, and Weiren Ying

2433 Inhibition of ABCB1 Overcomes Cancer Stem Cell–like Properties and Acquired Resistance to MET Inhibitors in Non–Small Cell Lung Cancer
Teppei Sugano, Masahiro Seike, Rintaro Noro, Chie Soeno, Mika Chiba, Fenfei Zou, Shinijs Nakamichi, Nobuhiko Nishiijima, Masaru Matsumoto, Akihiko Miyanaga, Kaoru Kubota, and Akihiko Gemma

2441 Tumors with AKT1E17K Mutations Are Rational Targets for Single Agent or Combination Therapy with AKT Inhibitors
Barry R. Davies, Nin Guan, Armelle Logie, Claire Crafter, Lyndsey Hanson, Vivien Jacobs, Neil James, Philippa Dudley, Kelly Jacques, Brendon Ladd, Celina M. D’Cruz, Michael Zinda, Justin Lindemann, Makoto Kodaia, Kenji Tamura, and Emma L. Jenkins

2452 Sarcoma Cell Line Screen of Oncology Drugs and Investigational Agents Identifies Patterns Associated with Gene and microRNA Expression
Beverly A. Teicher, Eric Polley, Mark Kunkel, David Evans, Thomas Silvers, Rene Delosh, Julie Lauteman, Chad Ogle, Russell Reinhart, Michael Selby, John Connelly, Erik Harris, Anne Monks, and Joel Morris

2463 A Novel Eg5 Inhibitor (LY2523355) Causes Mitotic Arrest and Apoptosis in Cancer Cells and Shows Potent Antitumor Activity in Xenograft Tumor Models
Xiang S. Ye, Li Fan, Robert D. Van Horn, Ryuichiro Nakai, Yoshihisa Ohta, Shino Akinaga, Chikara Murakata, Yoshinori Yamashita, Tingguyin Yin, Kelly M. Credille, Gregory P. Donoho, Farhana F. Merzouq, Heng Li, Amit Aggarwal, Kerry Blanchard, and Eric H. Westin

2473 CXCR4 Protein Epitope Mimetic Antagonist POL5551 Disrupts Metastasis and Enhances Chemotherapy Effect in Triple-Negative Breast Cancer
Jingyu Xiang, Michelle A. Hurchla, Francesca Fontana, Xinming Su, Sarah R. Amend, Alison K. Isser, Garry J. Douglas, Chidananda Mudalagiriyyappa, Kathryn E. Luker, Timothy Pluurd, Fosuso A. Ademuyiwa, Barbara Romagnoli, Gérald Tuffin, Eric Chevalier, Gary D. Luker, Michael Bauer, Johann Zimmermann, Rebecca L. Afi, Klaus Dembowsky, and Katherine N. Weibach

2486 A Novel Inhibitor of AKT1–PDPK1 Interaction Efficiently Suppresses the Activity of AKT Pathway and Restricts Tumor Growth In Vivo
Kristina Maemets-Allas, Janeli Viil, and Viljar Jaks

2497 Identification of Novel Ezrin Inhibitors Targeting Metastatic Osteosarcoma by Screening Open Access Malaria Box
Haydar Çelik, Sung-Hyeok Hong, Daisy D. Colón-López, Jenny Han, Yasemin Saygideger Kont, Tszon Z. Minas, Matthew Swift, Mikell Paige, Eric Glasgow, Jeffrey A. Toretsky, Jürgen Bosch, and Aykut Üren

2508 AZD2014, an Inhibitor of mTORC1 and mTORC2, Is Highly Effective in ER+ Breast Cancer When Administered Using Intermittent or Continuous Schedules
Table of Contents

2519  Dual HER2/PIK3CA Targeting Overcomes Single-Agent Acquired Resistance in HER2-Amplified Uterine Serous Carcinoma Cell Lines In Vitro and In Vivo
Salvatore Lopez, Emiliano Cocco, Jonathan Black, Stefania Bellone, Elena Bonazzoli, Federica Predolini, Francesca Ferrari, Carlton L. Schwaab, Diana P. English, Elena Ratner, Dan-Arin Silasi, Masoud Azodi, Peter E. Schwartz, Corrado Terranova, Roberto Angioli, and Alessandro D. Santin

2527  Effective Inhibition of Bone Morphogenetic Protein Function by Highly Specific Llama-Derived Antibodies
Silvia Calpe, Koen Wagner, Mohamed El Khattabi, Lucy Rutten, Cheryl Zimberlin, Edward Dolk, C. Theo Verrips, Jan Paul Medema, Hergen Spits, and Kausilia K. Krishnadath

2541  Targeting G-Quadruplex DNA Structures by EMICORON Has a Strong Antitumor Efficacy against Advanced Models of Human Colon Cancer
Manuela Porru, Simona Artuso, Erica Salvati, Armandodoriano Bianco, Marco Franceschin, Maria Grazia Diodoro, Daniela Passeri, Augusto Orlandi, Francesco Savorani, Maurizio D’Incalci, Annamaria Biroccio, and Carlo Leonetti

2552  Single-Molecule Supercoil Relaxation Assay as a Screening Tool to Determine the Mechanism and Efficacy of Human Topoisomerase IB Inhibitors
Yonnee Seol, Hongliang Zhang, Keli Agama, Nicholas Lorenzo, Yves Pommier, and Keir C. Neuman

2560  Poly-ADP-Ribose Polymerase as a Therapeutic Target in Pediatric Diffuse Intrinsic Pontine Glioma and Pediatric High-Grade Astrocytoma
Yevgen Chornenkyy, Sameer Agnihotri, Man Yu, Pawel Buzkowicz, Patricia Rakopoulos, Brian Golbourn, Livia Garzia, Robert Siddaway, Stephanie Leung, James T. Rutka, Michael D. Taylor, Peter B. Dirks, and Cynthia Hawkins

2569  A Phase I Study of the SMAC-Mimetic Birinapant in Adults with Refractory Solid Tumors or Lymphoma
Ravi K. Amaravadi, Russell J. Schilder, Lainie P. Martin, Myron Levin, Martin A. Graham, David E. Weng, and Alex A. Adjei

2576  Specific CP110 Phosphorylation Sites Mediate Anaphase Catastrophe after CDK2 Inhibition: Evidence for Cooperation with USP33 Knockdown
Shanhu Hu, Yun Lu, Bernardo Ortiz, Cristina Godek, Lisa Maria Mustachio, Mananori Kawakami, David Sekula, Duane A. Compton, Sarah Freemantle, and Ethan Dmitrovsky

2586  Antiandrogen Therapy with Hydroxyflutamide or Androgen Receptor Degradation Enhancer ASC-J9 Enhances BCG Efficacy to Better Suppress Bladder Cancer Progression
Zhiqun Shang, Yanjun Li, Minghao Zhang, Jing Tian, RuiFa Han, Chih-Rong Shyr, Edward Messing, Shuyuan Yeh, Yuanjie Niu, and Chawshang Chang

LARGE MOLECULE THERAPEUTICS

2595  Neutralization of KIT Oncogenic Signaling in Leukemia with Antibodies Targeting KIT Membrane Proximal Domain 5
Marianne Le Gall, Ronan Grépin, Madeline Neiveyans, Christian Audrai, Yongfeng Fan, Yu Zhou, James D. Marks, André Pélegrin, and Marie-Alis Poul

2606  Antibody Format and Drug Release Rate Determine the Therapeutic Activity of Noninternalizing Antibody–Drug Conjugates
Rémy Gébleux, Sarah Wulfhaf, Giulio Casi, and Dario Neri

CANCER BIOLOGY AND SIGNAL TRANSDUCTION

2613  Targeting FGFR Pathway in Human Hepatocellular Carcinoma: Expressing pFGFR and pMET for Antitumor Activity

2623  HMDB and 5-AzadC Combination Reverses Tumor Suppressor CCAAT/Enhancer-Binding Protein Delta to Strengthen the Death of Liver Cancer Cells
Chien-Feng Li, Hsin-Hwa Tsai, Chiung-Yuan Ko, Yen-Chen Pan, Chia-Jui Yen, Hong-Yue Lai, Chiou-Hwa Yuh, Wan-Chen Wu, and Ju-Ming Wang
Tumor MET Expression and Gene Amplification in Chinese Patients with Locally Advanced or Metastatic Gastric or Gastroesophageal Junction Cancer
Zhi Peng, Zhongwu Li, Jing Gao, Ming Lu, Jifang Gong, En-Tzu Tang, Kelly S. Oliner, Yong-Jiang Hei, Hui Zhou, and Lin Shen

Seribantumab, an Anti-ERBB3 Antibody, Delays the Onset of Resistance and Restores Sensitivity to Letrozole in an Estrogen Receptor–Positive Breast Cancer Model

MiRNA-203 Reduces Nasopharyngeal Carcinoma Radioresistance by Targeting IL8/AKT Signaling
Jia-Quan Qu, Hong-Mei Yi, Xue Ye, Jin-Feng Zhu, Hong Yi, Li-Na Li, Ta Xiao, Li Yuan, Jiao-Yang Li, Yuan-Yuan Wang, Juan Feng, Qu-Yan He, Shan-Shan Lu, and Zhi-Qiang Xiao

A Novel Fully Humanized 3D Skin Equivalent to Model Early Melanoma Invasion

Early-stage cutaneous melanoma development is characterized by uncontrolled proliferation and invasion of melanoma cells from the epidermis into the dermis through the basement membrane. This process is modeled using a novel full-thickness human melanoma skin equivalent in which melanoma cells form nests at the epidermal/dermal junction, as seen in this image, the basement membrane component type IV collagen, before disrupting the basement membrane structure as they invade at later time points. For full details of this model and its use for the investigation of early melanoma invasion, see the article by Hill and colleagues on page 2665.