Highlights of This Issue 2409

SMALL MOLECULE THERAPEUTICS

2411 Targeting Ribonucleotide Reductase M2 and NF-xB 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, Jaimei Acquaviva, Suqin He, Chaohua Zhang, Vladimir Khazak, Igor Astsaturov, Takayo Inoue, Noriaki Tatsuta, Sami Osman, Richard C. Bates, Dinesh Chimmanamada, and Weiwen 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, Shinji Nakamin, Nobuhiko Nishijima, Masaru Matsumoto, 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, Lynsey Hanson, Vivien Jacobs, Neil James, Philippa Dudley, Kelly Jacques, Brendon Ladd, Celina M. D’Cruz, Zhi Xu, Justin Lindemann, Makoto Koidzma, 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 Lauter, 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, Tingguy Qin, Kelly M. Credille, Gregory P. Donoho, Farhana F. Mezroug, Heng Li, Amit Aggarwal, Kelly 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, Ximing Su, Sarah R. Amend, Alison K. Isser, Garry J. Douglas, Chidambara Mudalagiriyyappa, Kathryn E. Luker, Timothy Pluard, Foluso O. Ademuyiwa, Barbara Romagnoli, Gerald Tuffin, Eric Chevalier, Gary D. Luker, Michael Bauer, Johann Zimmermann, Rebecca L. Afi, Klaus Dembowsky, and Katherine N. Weilbacher

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

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

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 Coco, Jonathan Black, Stefania Bellone, Elena Bonazzoli, Federica Predolini, Francesca Ferrari, Carlton L. Schwab, 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 Portu, 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
Yoneee Seol, Hongliang Zhang, Keli Agama, Nicholas Lorence, 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

2569 A Phase I Study of the SMAC-Mimetic Birinapant in Adults with Refractory Solid Tumors or Lymphoma
Ravi K. Amravadi, Russell J. Schleder, 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, Remardo Orz, Kristina Godek, Lisa Maria Mustachio, Masanori 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, Shusuyan Yeh, Yuanjie Niu, and Chawmshang Chang

LARGE MOLECULE THERAPEUTICS

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

2606 Antibody Format and Drug Release Rate Determine the Therapeutic Activity of Noninternalizing Antibody–Drug Conjugates
Rémy Gébéaux, Sarah Wulfhaid, 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-Chun Pan, Chia-Jui Yen, Hong-Yue Lai, Chiou-Hwa Yuh, Wan-Chen Wu, and Ju-Ming Wang
2634 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

2642 Seribantumab, an Anti-ERBB3 Antibody, Delays the Onset of Resistance and Restores Sensitivity to Letrozole in an Estrogen Receptor–Positive Breast Cancer Model

COMPANION DIAGNOSTICS AND CANCER BIOMARKERS
2653 MiRNA-203 Reduces Nasopharyngeal Carcinoma Radioresistance by Targeting IL8/AKT Signaling
Jia-Quan Qu, Hong-Mei Yi, Xu 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

MODELS AND TECHNOLOGIES
2665 A Novel Fully Humanized 3D Skin Equivalent to Model Early Melanoma Invasion

ABOUT THE COVER
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.