Highlights of This Issue 2475

REVIEW

2477 Suppression of Feedback Loops Mediated by PI3K/mTOR Induces Multiple Overactivation of Compensatory Pathways: An Unintended Consequence Leading to Drug Resistance
Enrique Rozengurt, Heloisa P. Soares, and James Sinnet-Smith

SMALL MOLECULE THERAPEUTICS

2489 Delineating the mTOR Kinase Pathway Using a Dual TORC1/2 Inhibitor, AZD8055, in Multiple Myeloma
Diana Cirstea, Loredana Santo, Teru Hideshima, Homare Eda, Yuko Mishima, Neeharika Nemani, Anuj Mahindra, Andrew Yee, Gullu Gorgun, Yiguo Hu, Hiroto Ohguchi, Rikio Suzuki, Francesca Cottini, Sylvie M. Guichard, Kenneth C. Anderson, and Noopur Raje

2501 Dual Targeting of Hypoxia and Homologous Recombination Repair Dysfunction in Triple-Negative Breast Cancer
Francis W. Hunter, Huai-Ling Hsu, Jiechuang Su, Susan M. Pullen, William R. Wilson, and Jingli Wang

2515 Novel Selective Estrogen Mimics for the Treatment of Tamoxifen-Resistant Breast Cancer
Mary Ellen Molloy, Bethany E. Perez White, Teshome Gherezghiher, Bradley T. Michalsen, Rui Xiong, Hitisha Patel, Huiping Zhao, Philipp Y. Maximov, V. Craig Jordan, Gregory R.J. Thatcher, and Debra A. Tonetti

2527 Pazopanib, a Novel Multitargeted Kinase Inhibitor, Shows Potent In Vitro Antitumor Activity in Gastric Cancer Cell Lines with FGFR2 Amplification
Seung Tae Kim, Hye-Lim Jang, Su Jin Lee, Jeeyun Lee, Yoon-La Choi, Kyoungh-Mee Kim, Jeonghee Cho, Se Hoon Park, Young Suk Park, Ho Yeong Lim, Masakazu Yashiro, Won Ki Kang, and Joon Oh Park

2537 Small Molecule BMH-Compounds That Inhibit RNA Polymerase I and Cause Nucleolar Stress
Karita Peltonen, Laureen Colis, Hester Liu, Sari Jałam, Zhewei Zhang, Taija af Hallström, Henna M. Moore, Paul Sirajuddin, and Marikki Laiho

2547 The Fibroblast Growth Factor Receptor Genetic Status as a Potential Predictor of the Sensitivity to CH5183284/Debio 1347, a Novel Selective FGFR Inhibitor
Yoshito Nakanishi, Nukinori Akiyama, Toshiyuki Tsukaguchi, Toshikiko Fujii, Kiyosaki Sakata, Hitoshi Sase, Takehito Isobe, Kenji Morikami, Hidetoshi Shindoh, Toshiyuki Mio, Hirotsuo Ebiike, Naoki Taka, Yuko Arki, and Nobuya Ishii

2559 Monensin Inhibits Epidermal Growth Factor Receptor Trafficking and Activation: Synergistic Cytotoxicity in Combination with EGFR Inhibitors
Khalil Dayekh, Stephanie Johnson-Obaseki, Martin Corsten, Patrick J. Villeneuve, Harmanjotinder S. Sekhon, Johanne L. Weberpals, and Jim Dimitroulakos

2572 Targeted Silencing of MLL5 Inhibits Tumor Growth and Promotes Gamma-Irradiation Sensitization in HPV16/18-Associated Cervical Cancers
Dawn Sijin Nin, Chow Wenn Yew, Sun Kuie Tay, and Lih-Wen Deng

2583 Bisphosphonates Inhibit Stellate Cell Activity and Enhance Antitumor Effects of Nanoparticle Albumin–Bound Paclitaxel in Pancreatic Ductal Adenocarcinoma

2595 Development of Targeted Near-Infrared Imaging Agents for Prostate Cancer
Xinning Wang, Steve S. Huang, Warren D.W. Heston, Hong Guo, Bing-Cheng Wang, and James P. Basilion
Table of Contents

LARGE MOLECULE THERAPEUTICS

2607 Anti-MET ImmunoPET for Non–Small Cell Lung Cancer Using Novel Fully Human Antibody Fragments
Keyu Li, Richard Tavare, Kirstin A. Zettlitz, Shannon M. Mumenthaler, Parag Mallick, Yu Zhou, James D. Marks, and Anna M. Wu

2618 Preclinical Profile of the HER2-Targeting ADC SYD983/SYD985: Introduction of a New Duocarmycin-Based Linker-Drug Platform
Wim Dokter, Ruud Ubink, Miranda van der Lee, Monique van der Vleuten, Tanja van Achterberg, Danielle Jacobs, Eline Loosveld, Diels van den Dobbeleer, David Egging, Ellen Mattaart, Patrick Groothuis, Patrick Beusker, Ruud Coumans, Ronald Elgersma, Wiro Menge, John Joosten, Henri Spijker, Tijl Huijbregts, Vincent de Groot, Michel Eppink, Guy de Roo, Gijs Verheijden, and Marco Timmers

2630 An Antimesothelin-Monomethyl Auristatin E Conjugate with Potent Antitumor Activity in Ovarian, Pancreatic, and Mesothelioma Models
Suzie J. Scales, Nidhi Gupta, Glenn Pacheco, Ron Firestein, Dorothy M. French, Hartmut Koeppen, Linda Rangell, Vivian Barry-Hamilton, Elizabeth Luis, Josefa Chuh, Yin Zhang, Gladyis S. Ingle, Aimee Fourie-O'Donohue, Katherine R. Kozak, Sarajane Ross, Mark S. Dennis, and Susan D. Spencer

2641 A Chemically Defined Trifunctional Antibody–Cytokine–Drug Conjugate with Potent Antitumor Activity
Thomas List, Giulio Casi, and Dario Neri

2653 Efficacy of RG7787, a Next-Generation Mesothelin-Targeted Immunotoxin, against Triple-Negative Breast and Gastric Cancers
Christine Alewine, Laiman Xiang, Takao Yamori, Gerhard Niederfellner, Klaus Bosslet, and Ira Pastan

2662 MEDI-573, Alone or in Combination with Mammalian Target of Rapamycin Inhibitors, Targets the Insulin-like Growth Factor Pathway in Sarcomas
Haihong Zhong, Christine Fazenbaker, Shannon Breen, Cui Chen, Jiaqi Huang, Christopher Morehouse, Yihong Yao, and Robert E. Hollingsworth

2674 Therapeutic Targeting of Angiogenesis with a Recombinant CTT Peptide–Endostatin Mimic–Kringle 5 Protein
Houbin Wang, Zhigang Yang, and Jun Gu

2688 Development of Human Serine Protease-Based Therapeutics Targeting Fn14 and Identification of Fn14 as a New Target Overexpressed in TNBC
Hong Zhou, Khalid A. Mohamedali, Ana Maria Gonzalez-Angulo, Yu Cao, Mary Migliorini, Lawrence H. Cheung, Janine LoBello, Xiudong Lei, Yuan Qi, Walter N. Hittelman, Jeffrey A. Winkles, Nhan L. Tran, and Michael G. Rosenblum

CANCER BIOLOGY AND SIGNAL TRANSDUCTION

2706 Longitudinal Time-Dependent Effects of Irradiation on Multidrug Resistance in a Non–Small Lung Cancer Cell Line
Yumiko Kono, Keita Utsunomiya, Shohei Kanno, and Noboru Tanigawa

2713 SNAI2 Modulates Colorectal Cancer 5-Fluorouracil Sensitivity through miR145 Repression
Victoria J. Findlay, Cindy Wang, Lourdes M. Nogueira, Katie Hurst, Daniel Quirk, Stephen P. Ethier, Kevin F. Staveley O’Carroll, Dennis K. Watson, and E. Ramsay Camp

2727 Tissue Penetration and Activity of Camptothecins in Solid Tumor Xenografts
Alastair H. Kyle, Jennifer H.E. Baker, Maria-Jose Gandolfi, Stefan A. Reinsberg, and Andrew I. Minchinton

COMPANION DIAGNOSTICS AND CANCER BIOMARKERS

2738 A Comprehensive Evaluation of Biomarkers Predictive of Response to PI3K Inhibitors and of Resistance Mechanisms in Head and Neck Squamous Cell Carcinoma
Tuhina Mazumdar, Lauren A. Byers, Patrick Kwok Shing Ng, Gordon B. Mills, Shaohua Peng, Lixia Diao, You-Hong Fan, Katherine Stemke-Hale, John V. Heymach, Jeffrey N. Myers, Bonnie S. Glisson, and Faye M. Johnson
MODELS AND TECHNOLOGIES

Identification of Kinase Inhibitor Targets in the Lung Cancer Microenvironment by Chemical and Phosphoproteomics
Manuela Gridling, Scott B. Ficarro, Florian P. Breitwieser, Lanxi Song, Katja Parapatics, Jacques Colinge, Eric B. Haura, Jarrod A. Marto, Giulio Superti-Furga, Keiryn L. Bennett, and Uwe Rix

LETTERS TO THE EDITOR

PDT with a Glucose-Conjugated Chlorin for GIST—Letter
Mark Linch and Andrew J. Hayes

CORRECTION

Correction: The Aurora Kinase A Inhibitor MLN8237 Enhances Cisplatin-Induced Cell Death in Esophageal Adenocarcinoma Cells

ABOUT THE COVER

Interrelation between vasculature, blood flow, proliferation, and hypoxia is shown in an HCT116 tumor xenograft 24 hours following irinotecan treatment. Irinotecan initially halts proliferation throughout the tissue but by 24 hours the S-phase fraction returns to near-control levels. The image was produced using multiplexed immunohistochemistry to illustrate the effects of drugs in the context of the tumor microenvironment. Greyscale images of the individual staining patterns were coregistered to produce the composite image shown here. HCT116 xenografts exhibit a corded architecture, where sheaths of tumor cells can be seen to surround individual vessels. Cells can survive to ~150 m away from the blood vessels but become increasingly oxygen-deprived and eventually necrose. For details, see the article by Kyle and colleagues on page 2727.