

Contents

Molecular Cancer Therapeutics

The Cancer Drug Development Journal: From Concept to Clinic

August 2011 • Volume 10 • Number 8

Highlights of This Issue 1309

SPOTLIGHT ON CLINICAL RESPONSE

1311

A Pilot Clinical Study of Treatment Guided by Personalized Tumorgrafts in Patients with Advanced Cancer

Manuel Hidalgo, Elizabeth Bruckheimer, N.V. Rajeshkumar, Ignacio Garrido-Laguna, Elizabeth De Oliveira, Belen Rubio-Viqueira, Steven Strawn, Michael J. Wick, James Martell, and David Sidransky

1357

High-Risk Endometrial Carcinoma Profiling Identifies TGF- β 1 as a Key Factor in the Initiation of Tumor Invasion

Laura Muinelo-Romay, Eva Colas, Jorge Barbazan, Lorena Alonso-Alconada, Marta Alonso-Nocelo, Marta Bouso, Teresa Curiel, Juan Cueva, Urbano Anido, Jeronimo Forteza, Antonio Gil-Moreno, Jaume Reventos, Rafael Lopez-Lopez, and Miguel Abal

1367

Truncated ErbB2 Expressed in Tumor Cell Nuclei Contributes to Acquired Therapeutic Resistance to ErbB2 Kinase Inhibitors

Wenle Xia, Zuguo Liu, Rongrong Zong, Leihua Liu, Sumin Zhao, Sarah S. Bacus, Yubin Mao, Jia He, Julia D. Wulfkuhle, Emanuel F. Petricoin III, Takuwa Osada, Xiao-Yi Yang, Zachary C. Hartman, Timothy M. Clay, Kimberly L. Blackwell, Herbert K. Lyerly, and Neil L. Spector

THERAPEUTIC DISCOVERY

1317

Phenotypic Reversion of Invasive Neurofibromin-Deficient Schwannoma by FTS: Ras Inhibition Reduces BMP4/Erk/Smad Signaling

Batya Barkan, Yoel Kloog, and Marcelo Ehrlich

1327

Dual Targeting of Tumor Angiogenesis and Chemotherapy by Endostatin-Cytosine Deaminase-Uracil Phosphoribosyltransferase

Chun-Te Chen, Hirohito Yamaguchi, Hong-Jen Lee, Yi Du, Heng-Huan Lee, Weiya Xia, Wen-Hsuan Yu, Jennifer L. Hsu, Chia-Jui Yen, Hui-Lung Sun, Yan Wang, Edward T. H. Yeh, Gabriel N. Hortobagyi, and Mien-Chie Hung

1375

Enhanced Antitumor Effects by Chemical Modified IGB3 Analogues

Zhixia Zhou, Cai Zhang, Chengfeng Xia, Wenlan Chen, Huawei Zhu, Pingping Shang, Fang Ma, Peng George Wang, Jian Zhang, Wenfang Xu, and Zhigang Tian

1337

MicroRNA-199a-3p Is Downregulated in Human Osteosarcoma and Regulates Cell Proliferation and Migration

Zhenfeng Duan, Edwin Choy, David Harmon, Xianzhe Liu, Michiro Susa, Henry Mankin, and Francis Hornicek

1385

Targeting the Mitochondria Activates Two Independent Cell Death Pathways in Ovarian Cancer Stem Cells

Ayesha B. Alvero, Michele K. Montagna, Jennie C. Holmberg, Vinicius Craveiro, David Brown, and Gil Mor

1346

Berberine Suppresses Androgen Receptor Signaling in Prostate Cancer

Jing Li, Bo Cao, Xichun Liu, Xueqi Fu, Zhenggang Xiong, Li Chen, Oliver Sartor, Yan Dong, and Haitao Zhang

1394

Preclinical Characterization of OSI-027, a Potent and Selective Inhibitor of mTORC1 and mTORC2: Distinct from Rapamycin

Shripad V. Bhagwat, Prafulla C. Gokhale, Andrew P. Crew, Andy Cooke, Yan Yao, Christine Mantis, Jennifer Kahler, Jennifer Workman, Mark Bittner, Lorina Dudkin, David M. Epstein, Neil W. Gibson, Robert Wild, Lee D. Arnold, Peter J. Houghton, and Jonathan A. Pachter

PRECLINICAL DEVELOPMENT

<p>1407</p> <p>Enhanced Efficacy of IGF1R Inhibition in Pediatric Glioblastoma by Combinatorial Targeting of PDGFRα/β Aleksandra Bielen, Lara Perryman, Gary M. Box, Melanie Valenti, Alexis de Haven Brandon, Vanessa Martins, Alexa Jury, Sergey Popov, Sharon Gowan, Sébastien Jeay, Florence I. Raynaud, Francesco Hofmann, Darren Hargrave, Suzanne A. Eccles, and Chris Jones</p>	<p>1481</p> <p>Trabectedin and Its C Subunit Modified Analogue PM01183 Attenuate Nucleotide Excision Repair and Show Activity toward Platinum-Resistant Cells Daniele G. Soares, Miriana S. Machado, Céline J. Rocca, Virginie Poindessous, Djamilia Ouaret, Alain Sarasin, Carlos M. Galmarini, João A. P. Henriques, Alexandre E. Escargueil, and Annette K. Larsen</p>
<p>1419</p> <p>Peloruside- and Laulimalide-Resistant Human Ovarian Carcinoma Cells Have βI-Tubulin Mutations and Altered Expression of βII- and βIII-Tubulin Isotypes Arun Kanakkanthara, Anja Wilmes, Aurora O'Brate, Daniel Escuin, Ariane Chan, Ada Gjyrezi, Janet Crawford, Pisana Rawson, Bronwyn Kivell, Peter T. Northcote, Ernest Hamel, Paraskevi Giannakakou, and John H. Miller</p>	<p>1490</p> <p>Molecular and Cellular Pharmacology of the Novel Noncamptothecin Topoisomerase I Inhibitor Genz-644282 Dhriti Sooryakumar, Thomas S. Dexheimer, Beverly A. Teicher, and Yves Pommier</p>
<p>1430</p> <p>Sodium Butyrate Inhibits the Self-Renewal Capacity of Endometrial Tumor Side-Population Cells by Inducing a DNA Damage Response Kiyoko Kato, Aya Kuhara, Tomoko Yoneda, Takafumi Inoue, Tomoka Takao, Tatsuhiro Ohgami, Li Dan, Ayumi Kuboyama, Soshi Kusunoki, Satoru Takeda, and Norio Wake</p>	<p>1500</p> <p>Neutralizing Monoclonal Antibody to Periostin Inhibits Ovarian Tumor Growth and Metastasis Min Zhu, Romaine E. Saxton, Lillian Ramos, David D. Chang, Beth Y. Karlan, Judith C. Gasson, and Dennis J. Slamon</p>
MOLECULAR MEDICINE IN PRACTICE	
<p>1440</p> <p>In Vivo Activity of Combined PI3K/mTOR and MEK Inhibition in a <i>Kras^{G12D};Pten</i> Deletion Mouse Model of Ovarian Cancer Kathryn M. Kinross, Daniel V. Brown, Margarete Kleinschmidt, Susan Jackson, James Christensen, Carleen Cullinane, Rodney J. Hicks, Ricky W. Johnstone, and Grant A. McArthur</p>	<p>1509</p> <p>Rationally Designed Treatment for Solid Tumors with MAPK Pathway Activation: A Phase I Study of Paclitaxel and Bortezomib Using an Adaptive Dose-Finding Approach Janice M. Mehnert, Antoinette R. Tan, Rebecca Moss, Elizabeth Poplin, Mark N. Stein, Mika Sovak, Kelly Levinson, Hongxia Lin, Michael Kane, Murugesan Gounder, Yong Lin, Weichung Joe Shih, Eileen White, Eric H. Rubin, and Vassiliki Karantza</p>
<p>1450</p> <p>Levels of p27 Sensitize to Dual PI3K/mTOR Inhibition Misu Lee, Marily Theodoropoulou, Jochen Graw, Federico Roncaroli, Maria Chiara Zatelli, and Natalia S. Pellegata</p>	<p>1520</p> <p>Melanoma Prognosis: A REMARK-Based Systematic Review and Bioinformatic Analysis of Immunohistochemical and Gene Microarray Studies Sarah-Jane Schramm and Graham J. Mann</p>
CORRECTION	
<p>1460</p> <p>Combinatorial Effects of Lapatinib and Rapamycin in Triple-Negative Breast Cancer Cells Tongrui Liu, Rami Yacoub, LaTonia D. Taliaferro-Smith, Shi-Yong Sun, Tisheeka R. Graham, Ryan Dolan, Christine Lobo, Mourad Tighiouart, Lily Yang, Amy Adams, and Ruth M. O'Regan</p>	<p>1529</p> <p>Correction: Targeting Oncogenic ALK: A Promising Strategy for Cancer Treatment</p>
<p>1470</p> <p>Restitution of Tumor Suppressor MicroRNAs Using a Systemic Nanovector Inhibits Pancreatic Cancer Growth in Mice Dipankar Pramanik, Nathaniel R. Campbell, Collins Karikari, Raghu Chivukula, Oliver A. Kent, Joshua T. Mendell, and Anirban Maitra</p>	

ABOUT THE COVER

Modification of the glycolipid ligands for natural killer T (NKT) cells might be an efficient approach to improve their stimulatory activity or to shift the proportional release of Th1 and Th2 cytokines. The chemical modified iGb3 analogue, 4'''-dh-iGb3, made by introducing a hydroxyl group at C4 of iGb3 and removing the 4''' hydroxyl group of the terminal galactose, could increase the stability of the CD1d/antigen/TCR ternary complex and IFN- γ signaling of NKT cells, and thus stimulate more IFN- γ production by NKT cells. 4'''-dh-iGb3-loaded dendritic cells significantly inhibit growth of subcutaneous melanoma and suppress lung metastasis in C57BL/6 mice. The 4'''-dh-iGb3-loaded dendritic cell vaccine may serve as a potent new NKT-based therapy against tumors. For details, see article by Zhou and colleagues on page 1375.

