Molecular Cancer Therapeutics
The Journal of Cancer Drug Discovery & Preclinical Development
July 2013 • Volume 12 • Number 7

Contents

Highlights of This Issue 1151

REVIEW

1153  The Potential Role of miR-451 in Cancer Diagnosis, Prognosis, and Therapy
  Xuan Pan, Rui Wang, and Zhao-Xia Wang

CHEMICAL THERAPEUTICS

1163  CXCR4-Targeted Therapy Inhibits VEGF Expression and Chondrosarcoma Angiogenesis and Metastasis
  Xiaojuan Sun, Cherie Charbonneau, Lei Wei, Wentian Yang, Qian Chen, and Richard M. Terek

1171  CRM1 and BRAF Inhibition Synergize and Induce Tumor Regression in BRAF-Mutant Melanoma
  Roberto A. Salas Fragomeni, Hye Won Chung, Yosef Landesman, William Senapedis, Jean-Richard Saint-Martin, Hensin Tsao, Keith T. Flaherty, Sharon Shacham, Michael Kauffman, and James C. Cusack

1180  Identification and Characterization of a Small-Molecule Inhibitor of Wnt Signaling in Glioblastoma Cells
  Alessandra De Robertis, Silvia Valensin, Marco Rossi, Patrizia Tunicci, Margherita Verani, Antonella De Rosa, Cinzia Giordano, Maurizio Varrone, Arianna Nencini, Carmela Pratelli, Tiziana Benicchi, Annette Bakker, Jeffrey Hill, Kanda Sanghongsitak, Vishal Pendlharkar, Boping Liu, Fui Mee Ng, Siew Wen Then, Shi Jing Tai, Seong-Moon Cheong, Xi He, Andrea Caricasole, and Massimiliano Salerno

LARGE MOLECULE THERAPEUTICS

1202  MPT0B098, a Novel Microtubule Inhibitor That Destabilizes the Hypoxia-Inducible Factor-1α mRNA through Decreasing Nuclear–Cytoplasmic Translocation of RNA-Binding Protein HuR

1213  IGF-1R Targeting Increases the Antitumor Effects of DNA-Damaging Agents in SCLC Model: An Opportunity to Increase the Efficacy of Standard Therapy
  Charles Ferté, Yohann Loriot, Céline Clémenson, Frederic Commo, Andrea Gombos, Jean-Emmanuel Bibault, Ingrid Fumagalli, Saad Hamama, Nathalie Auger, Benoit Lahon, Cyrus Chargari, Julien Calderaro, Jean-Charles Soria, and Eric Deutsch

1223  Human Anti-Macrophage Migration Inhibitory Factor Antibodies Inhibit Growth of Human Prostate Cancer Cells In Vitro and In Vivo
  Filza Hussain, Michael Freissmuth, Dirk Volkel, Michael Thiele, Patrice Douillard, Gerhard Antoine, Patrick Thurner, Hartmut Ehrlich, Hans-Peter Schwarz, Friedrich Scheiflinger, and Randolph J. Kerschbaumer

1235  Multivalent Scaffold Proteins as Superagonists of TRAIL Receptor 2–Induced Apoptosis
  Jeffery S. Swers, Luba Grinberg, Lin Wang, Hui Feng, Kristen Lekstrom, Rosa Carrasco, Zhan Xiao, Ivan Inigo, Ching Ching Leow, Herren Wu, David A. Tice, and Manuel Baca

1245  Fibroblast Growth Factor Receptor 3 Is a Rational Therapeutic Target in Bladder Cancer
  Kilian M. Gust, David J. McConkey, Shannon Aueray, Paul K. Hegarty, Jing Qing, Jolanta Bondaruk, Avi Ashkenazi, Bogdan Czerniak, Colin P. Dinney, and Peter C. Black
DCDT2980S, an Anti-CD22-Monomethyl Auristatin E Antibody–Drug Conjugate, Is a Potential Treatment for Non-Hodgkin Lymphoma


Triptolide Induces the Expression of miR-142-3p: A Negative Regulator of Heat Shock Protein 70 and Pancreatic Cancer Cell Proliferation


Regorafenib Inhibits Growth, Angiogenesis, and Metastasis in a Highly Aggressive, Orthotopic Colon Cancer Model

Lotfi Abou-Elkacem, Susanne Arns, Gunnar Brix, Felix Gremse, Dieter Zopf, Fabian Kiessling, and Wiltrud Lederle

Antiproliferative Effects of Continued Mitogen-Activated Protein Kinase Pathway Inhibition following Acquired Resistance to BRAF and/or MEK Inhibition in Melanoma

Matteo S. Carlino, Kavitha Gowrishankar, Catherine A.B. Saunders, Giulietta M. Pupo, Stephanie Snuyman, Xu Dong Zhang, Robyn Saw, Therese M. Becker, Richard F. Kefferd, Georgina V. Long, and Helen Rizos

Overlapping Functions of ABC Transporters in Topotecan Disposition as Determined in Gene Knockout Mouse Models

Amrit K. Tiwari, Rong Zhang, and James M. Gallo

Zoledronic Acid Reverses the Epithelial–Mesenchymal Transition and Inhibits Self-Renewal of Breast Cancer Cells through Inactivation of NF-κB

Amanda J. Schech, Armina A. Kazi, Rabia A. Gilani, and Angela H. Brodie

Overlapping Functions of ABC Transporters in Topotecan Disposition as Determined in Gene Knockout Mouse Models

Amit K. Tiwari, Rong Zhang, and James M. Gallo

Zoledronic Acid Reverses the Epithelial–Mesenchymal Transition and Inhibits Self-Renewal of Breast Cancer Cells through Inactivation of NF-κB

Amanda J. Schech, Armina A. Kazi, Rabia A. Gilani, and Angela H. Brodie

REGULAR FEATURES

Drug Repurposing for Gastrointestinal Stromal Tumor

Ziyan Y. Pessetto, Scott J. Weir, Geetika Sethi, Melinda A. Broward, and Andrew K. Godwin

Potential Role of mTORC2 as a Therapeutic Target in Clear Cell Carcinoma of the Ovary

Takeshi Hisamatsu, Seiji Mabuchi, Yuki Matsumoto, Mahiru Kawano, Tomoyuki Sasano, Ryoko Takahashi, Kenjiro Sawada, Kimihiko Ito, Hirohisa Kurachi, Russell J. Schilder, Joseph R. Testa, and Tadashi Kimura

Metabolomics Identifies Pyrimidine Starvation as the Mechanism of 5-Aminomimidazole-4-Carboxamide-1-β-Riboside-Induced Apoptosis in Multiple Myeloma Cells

Carolyne Bardeleben, Sanjai Sharma, Joseph R. Reeve, Sara Bassilian, Patrick Frost, Bao Hoang, Yijiang Shi, and Alan Lichtenstein

COMPANION DIAGNOSTICS AND CANCER BIOMARKERS

Potential Role of mTORC2 as a Therapeutic Target in Clear Cell Carcinoma of the Ovary

Takeshi Hisamatsu, Seiji Mabuchi, Yuki Matsumoto, Mahiru Kawano, Tomoyuki Sasano, Ryoko Takahashi, Kenjiro Sawada, Kimihiko Ito, Hirohisa Kurachi, Russell J. Schilder, Joseph R. Testa, and Tadashi Kimura

Metabolomics Identifies Pyrimidine Starvation as the Mechanism of 5-Aminomimidazole-4-Carboxamide-1-β-Riboside-Induced Apoptosis in Multiple Myeloma Cells

Carolyne Bardeleben, Sanjai Sharma, Joseph R. Reeve, Sara Bassilian, Patrick Frost, Bao Hoang, Yijiang Shi, and Alan Lichtenstein

COMPANION DIAGNOSTICS AND CANCER BIOMARKERS

Potential Role of mTORC2 as a Therapeutic Target in Clear Cell Carcinoma of the Ovary

Takeshi Hisamatsu, Seiji Mabuchi, Yuki Matsumoto, Mahiru Kawano, Tomoyuki Sasano, Ryoko Takahashi, Kenjiro Sawada, Kimihiko Ito, Hirohisa Kurachi, Russell J. Schilder, Joseph R. Testa, and Tadashi Kimura

Metabolomics Identifies Pyrimidine Starvation as the Mechanism of 5-Aminomimidazole-4-Carboxamide-1-β-Riboside-Induced Apoptosis in Multiple Myeloma Cells

Carolyne Bardeleben, Sanjai Sharma, Joseph R. Reeve, Sara Bassilian, Patrick Frost, Bao Hoang, Yijiang Shi, and Alan Lichtenstein

COMPANION DIAGNOSTICS AND CANCER BIOMARKERS

Potential Role of mTORC2 as a Therapeutic Target in Clear Cell Carcinoma of the Ovary

Takeshi Hisamatsu, Seiji Mabuchi, Yuki Matsumoto, Mahiru Kawano, Tomoyuki Sasano, Ryoko Takahashi, Kenjiro Sawada, Kimihiko Ito, Hirohisa Kurachi, Russell J. Schilder, Joseph R. Testa, and Tadashi Kimura

Metabolomics Identifies Pyrimidine Starvation as the Mechanism of 5-Aminomimidazole-4-Carboxamide-1-β-Riboside-Induced Apoptosis in Multiple Myeloma Cells

Carolyne Bardeleben, Sanjai Sharma, Joseph R. Reeve, Sara Bassilian, Patrick Frost, Bao Hoang, Yijiang Shi, and Alan Lichtenstein

Metabolomics Identifies Pyrimidine Starvation as the Mechanism of 5-Aminomimidazole-4-Carboxamide-1-β-Riboside-Induced Apoptosis in Multiple Myeloma Cells

Carolyne Bardeleben, Sanjai Sharma, Joseph R. Reeve, Sara Bassilian, Patrick Frost, Bao Hoang, Yijiang Shi, and Alan Lichtenstein

COMPANION DIAGNOSTICS AND CANCER BIOMARKERS

Potential Role of mTORC2 as a Therapeutic Target in Clear Cell Carcinoma of the Ovary

Takeshi Hisamatsu, Seiji Mabuchi, Yuki Matsumoto, Mahiru Kawano, Tomoyuki Sasano, Ryoko Takahashi, Kenjiro Sawada, Kimihiko Ito, Hirohisa Kurachi, Russell J. Schilder, Joseph R. Testa, and Tadashi Kimura

Metabolomics Identifies Pyrimidine Starvation as the Mechanism of 5-Aminomimidazole-4-Carboxamide-1-β-Riboside-Induced Apoptosis in Multiple Myeloma Cells

Carolyne Bardeleben, Sanjai Sharma, Joseph R. Reeve, Sara Bassilian, Patrick Frost, Bao Hoang, Yijiang Shi, and Alan Lichtenstein

COMPANION DIAGNOSTICS AND CANCER BIOMARKERS

Potential Role of mTORC2 as a Therapeutic Target in Clear Cell Carcinoma of the Ovary

Takeshi Hisamatsu, Seiji Mabuchi, Yuki Matsumoto, Mahiru Kawano, Tomoyuki Sasano, Ryoko Takahashi, Kenjiro Sawada, Kimihiko Ito, Hirohisa Kurachi, Russell J. Schilder, Joseph R. Testa, and Tadashi Kimura
ABOUT THE COVER

Hypoxia can drive loss of tumor cell differentiation and elevate metastatic potential in pancreatic cancer. Inhibition of heparanase with PG545 reduced vascular function and increased hypoxia in a GEMM of pancreatic cancer; however, PG545 treatment did not enhance tumor cell EMT. Immunofluorescence was used to show that tumors from PG545-treated animals express elevated levels of membrane-associated β-catenin, a characteristic of epithelial cells. These data are consistent with observed changes in E-cadherin and other EMT-associated proteins and suggest that the proinvasive effects of hypoxia can be abrogated by inhibition of heparanase. For details, see article by Ostapoff and colleagues on page 1190.