


Highlights of This Issue 1779
REVIEWS

- 1781**  **ATM Mutations in Cancer: Therapeutic Implications**
Michael Choi, Thomas Kipps, and Razelle Kurzrock
- 1792** **Concepts to Target MYC in Pancreatic Cancer**
Matthias Wirth, Siavosh Mahboobi, Oliver H. Krämer, and Günter Schneider

SMALL MOLECULE THERAPEUTICS

- 1799**  **Pharmacological Inhibition of the Protein Kinase MRK/ZAK Radiosensitizes Medulloblastoma**
Daniel Markowitz, Caitlin Powell, Nhan L. Tran, Michael E. Berens, Timothy C. Ryken, Magimairajan Vanan, Lisa Rosen, Mingzhu He, Shan Sun, Marc Symons, Yousef Al-Abed, and Rosamaria Ruggieri
- 1809** **Combination of Eribulin and Aurora A Inhibitor MLN8237 Prevents Metastatic Colonization and Induces Cytotoxic Autophagy in Breast Cancer**
Varvara K. Kozyreva, Anna A. Kiseleva, Ryan J. Ice, Brandon C. Jones, Yuriy V. Loskutov, Fatimah Matalkah, Matthew B. Smolkin, Kristina Marinak, Ryan H. Livengood, Mohamad A. Salkeni, Sijin Wen, Hannah W. Hazard, Ginger P. Layne, Callee M. Walsh, Pamela S. Cantrell, Greg W. Kilby, Sricharan Mahavadi, Neal Shah, and Elena N. Pugacheva
- 1823** ***In Silico* Analysis Guides Selection of BET Inhibitors for Triple-Negative Breast Cancer Treatment**
Javier Pérez-Peña, Gemma Serrano-Heras, Juan Carlos Montero, Verónica Corrales-Sánchez, Atanasio Pandiella, and Alberto Ocaña
- 1834** **Theranostic Agents for Photodynamic Therapy of Prostate Cancer by Targeting Prostate-Specific Membrane Antigen**
Xinning Wang, Brian Tsui, Gopalkrishnan Ramamurthy, Ping Zhang, Joseph Meyers, Malcolm E. Kenney, Jonathan Kiechle, Lee Ponsky, and James P. Basilion
- 1845** **Osimertinib (AZD9291) Enhanced the Efficacy of Chemotherapeutic Agents in ABCB1- and ABCG2-Overexpressing Cells *In Vitro*, *In Vivo*, and *Ex Vivo***
Zhen Chen, Yifan Chen, Meng Xu, Likun Chen, Xu Zhang, Kenneth Kin Wah To, Hongyun Zhao, Fang Wang, Zhongjun Xia, Xiaoqin Chen, and Liwu Fu

- 1859** **The Combination of Vemurafenib and Pro-caspase-3 Activation Is Synergistic in Mutant BRAF Melanomas**
Jessie Peh, Timothy M. Fan, Kathryn L. Wycislo, Howard S. Roth, and Paul J. Hergenrother

LARGE MOLECULE THERAPEUTICS

- 1870**  **A New Class of Antibody–Drug Conjugates with Potent DNA Alkylating Activity**
Michael L. Miller, Nathan E. Fishkin, Wei Li, Kathleen R. Whiteman, Yelena Kovtun, Emily E. Reid, Katie E. Archer, Erin K. Maloney, Charlene A. Audette, Michele F. Mayo, Alan Wilhelm, Holly A. Modafferi, Rajeeva Singh, Jan Pinkas, Victor Goldmacher, John M. Lambert, and Ravi V.J. Chari
- 1879**  **Macrophage-Mediated Trogocytosis Leads to Death of Antibody-Opsonized Tumor Cells**
Ramraj Velmurugan, Dilip K. Challa, Sripad Ram, Raimund J. Ober, and E. Sally Ward
- 1890** **A New Anti-CXCR4 Antibody That Blocks the CXCR4/SDF-1 Axis and Mobilizes Effector Cells**
Matthieu Broussas, Nicolas Boute, Barbara Akla, Sven Berger, Charlotte Beau-Larvor, Thierry Champion, Alain Robert, Alain Beck, Jean-François Haeuw, Liliane Goetsch, Christian Bailly, Charles Dumontet, Thomas Matthes, Nathalie Corvaia, and Christine Klinguer-Hamour
- 1900**  **SYD985, a Novel Duocarmycin-Based HER2-Targeting Antibody–Drug Conjugate, Shows Antitumor Activity in Uterine Serous Carcinoma with HER2/Neu Expression**
Jonathan Black, Gulden Menderes, Stefania Bellone, Carlton L. Schwab, Elena Bonazzoli, Francesca Ferrari, Federica Predolini, Christopher De Haydu, Emiliano Cocco, Natalia Buza, Pei Hui, Serena Wong, Salvatore Lopez, Elena Ratner, Dan-Arin Silasi, Masoud Azodi, Babak Litkouhi, Peter E. Schwartz, Peter Goedings, Patrick H. Beusker, Miranda M.C. van der Lee, C. Marco Timmers, Wim H.A. Dokter, and Alessandro D. Santin
- 1910** **Combining ABCG2 Inhibitors with IMMU-132, an Anti-Trop-2 Antibody Conjugate of SN-38, Overcomes Resistance to SN-38 in Breast and Gastric Cancers**
Chien-Hsing Chang, Yang Wang, Maria Zalath, Donglin Liu, Thomas M. Cardillo, and David M. Goldenberg

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CANCER BIOLOGY AND SIGNAL TRANSDUCTION

- 1920** Protection against HPV-16–Associated Tumors Requires the Activation of CD8⁺ Effector Memory T Cells and the Control of Myeloid-Derived Suppressor Cells
Mariana O. Diniz, Natiely S. Sales, Jamile R. Silva, and Luis Carlos S. Ferreira
- 1931** Emodin Inhibits Breast Cancer Growth by Blocking the Tumor-Promoting Feedforward Loop between Cancer Cells and Macrophages
Stephen Iwanowycz, Junfeng Wang, Johnie Hodge, Yuzhen Wang, Fang Yu, and Daping Fan
- 1943** Infiltrating T Cells Promote Bladder Cancer Progression via Increasing IL1→Androgen Receptor→HIF1 α →VEGF α Signals
Le Tao, Jianxin Qiu, Ming Jiang, Wenbin Song, Shuyuan Yeh, Hong Yu, Lijuan Zang, Shujie Xia, and Chawnshang Chang
- 1952** The Mitogen-Activated Protein Kinase Pathway Facilitates Resistance to the Src Inhibitor Dasatinib in Thyroid Cancer
Thomas C. Beadnell, Katie M. Mishall, Qiong Zhou, Stephen M. Riffert, Kelsey E. Wuensch, Brittelle E. Kessler, Maia L. Corpuz, Xia Jing, Jihye Kim, Guoliang Wang, Aik Choon Tan, and Rebecca E. Schweppe

- 1964** Upregulation of AKT3 Confers Resistance to the AKT Inhibitor MK2206 in Breast Cancer
Casey Stottrup, Tiffany Tsang, and Y. Rebecca Chin
- 1975** ERK1 as a Therapeutic Target for Dendritic Cell Vaccination against High-Grade Gliomas
Min-Chi Ku, Inan Edes, Ivo Bendix, Andreas Pohlmann, Helmar Waiczies, Tim Prozorovski, Martin Günther, Conrad Martin, Gilles Pagès, Susanne A. Wolf, Helmut Kettenmann, Wolfgang Uckert, Thoralf Niendorf, and Sonia Waiczies

COMPANION DIAGNOSTICS AND CANCER BIOMARKERS

- 1988** Afatinib against Esophageal or Head-and-Neck Squamous Cell Carcinoma: Significance of Activating Oncogenic *HER4* Mutations in HNSCC
Yu Nakamura, Yosuke Togashi, Hirokazu Nakahara, Shuta Tomida, Eri Banno, Masato Terashima, Hidetoshi Hayashi, Marco A. de Velasco, Kazuko Sakai, Yoshihiko Fujita, Takatsugu Okegawa, Kikuo Nutahara, Suguru Hamada, and Kazuto Nishio
- 1998** High Levels of Expression of P-glycoprotein/Multidrug Resistance Protein Result in Resistance to Vintafolide
Amy D. Guertin, Jennifer O'Neil, Alexander Stoeck, Joseph A. Reddy, Razvan Cristescu, Brian B. Haines, Marlene C. Hinton, Ryan Dorton, Alicia Bloomfield, Melissa Nelson, Marilyn Vetzal, Serguei Lejnine, Michael Nebozhyn, Theresa Zhang, Andrey Loboda, Kristen L. Picard, Emmett V. Schmidt, Isabelle Dussault, and Christopher P. Leamon



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ABOUT THE COVER

The cover shows a schematic of the mechanism of action of an antibody–drug conjugate (ADC) utilizing a new class of DNA alkylating agent as the cytotoxic payload (shown as a red circle). Its antibody component enables the ADC to bind specifically to cancer cells expressing its antigen target. Once bound, the conjugate is internalized and the cytotoxic payload is released. For ADCs with a cleavable linker, this release can be through linker cleavage, as shown, as well as through lysosomal degradation of the antibody component. The released DNA alkylating agent can disrupt the DNA in its cell of release, causing cell death. With a cleavable linker, it can also enter an adjacent cancer cell and kill it. For details, see the article by Miller and colleagues beginning on page 1870.



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