

## Highlights of This Issue 1727

## SMALL MOLECULE THERAPEUTICS

- 1729** **Cotargeting of MEK and PDGFR/STAT3 Pathways to Treat Pancreatic Ductal Adenocarcinoma**  
Nisebita Sahu, Emily Chan, Felix Chu, Thinkh Pham, Hartmut Koeppen, William Forrest, Mark Merchant, and Jeff Settleman

- 1739** **Preclinical Efficacy and Molecular Mechanism of Targeting CDK7-Dependent Transcriptional Addiction in Ovarian Cancer**  
Zhenfeng Zhang, Huixin Peng, Xiaojie Wang, Xia Yin, Pengfei Ma, Ying Jing, Mei-Chun Cai, Jin Liu, Meiyang Zhang, Shengzhe Zhang, Kaixuan Shi, Wei-Qiang Gao, Wen Di, and Guanglei Zhuang

- 1751** **CDK4/6 Inhibitors Sensitize Rb-positive Sarcoma Cells to Wee1 Kinase Inhibition through Reversible Cell-Cycle Arrest**  
Ashleigh M. Francis, Angela Alexander, Yanna Liu, Smruthi Vijayaraghavan, Kwang Hui Low, Dong Yang, Tuyen Bui, Neeta Somaiah, Vinod Ravi, Khandan Keyomarsi, and Kelly K. Hunt

- 1765**  **$\beta$ -Catenin Inhibitor BC2059 Is Efficacious as Monotherapy or in Combination with Proteasome Inhibitor Bortezomib in Multiple Myeloma**  
Ioanna Savvidou, Tiffany Khong, Andrew Cuddihy, Catriona McLean, Stephen Horrigan, and Andrew Spencer

- 1779** **Inhibition of Hsp90 Suppresses PI3K/AKT/mTOR Signaling and Has Antitumor Activity in Burkitt Lymphoma**  
Lisa Giulino-Roth, Herman J. van Besien, Tanner Dalton, Jennifer E. Totonchy, Anna Rodina, Tony Taldone, Alexander Bolaender, Hediye Erdjument-Bromage, Jouliana Sadek, Amy Chadburn, Matthew J. Barth, Filemon S. Dela Cruz, Allison Rainey, Andrew L. Kung, Gabriela Chiosis, and Ethel Cesarman

- 1791** **Discovery of a Novel Small-Molecule Inhibitor that Targets PP2A- $\beta$ -Catenin Signaling and Restricts Tumor Growth and Metastasis**  
Shrankhla Maheshwari, Srinivasa R. Avula, Akhilesh Singh, L. Ravithej Singh, Gopala R. Palnati, Rakesh K. Arya, Srikanth H. Cheruvu, Sudhir Shahi, Tanuj Sharma, Sanjeev Meena, Anup K. Singh, Ruchir Kant, Mohammed Riyazuddin, Himangsu K. Bora, Mohammad I. Siddiqi, Jiaur R. Gayen, Koneni V. Sashidhara, and Dipak Datta

- 1806** **Metformin Synergizes with BCL-XL/BCL-2 Inhibitor ABT-263 to Induce Apoptosis Specifically in p53-Defective Cancer Cells**

Xinzhe Li, Bo Li, Zhenhong Ni, Peng Zhou, Bin Wang, Jintao He, Haojun Xiong, Fan Yang, Yaran Wu, Xilin Lyu, Yan Zhang, Yijun Zeng, Jiqin Lian, and Fengtian He

- 1819** **Combination Treatment with Orlistat-Containing Nanoparticles and Taxanes Is Synergistic and Enhances Microtubule Stability in Taxane-Resistant Prostate Cancer Cells**

Joshua J. Soucek, Amanda L. Davis, Tanner K. Hill, Megan B. Holmes, Bowen Qi, Pankaj K. Singh, Steven J. Kridel, and Aaron M. Mohs

- 1831** **Synthesis and Profiling of a Novel Potent Selective Inhibitor of CHK1 Kinase Possessing Unusual N-trifluoromethylpyrazole Pharmacophore Resistant to Metabolic N-dealkylation**

Pounami Samadder, Tereza Suchánková, Ondřej Hylse, Prashant Khirsariya, Fedor Nikulenkov, Stanislav Drápela, Nicol Straková, Petr Vanhara, Kateřina Vašíčková, Hana Kolářová, Lucia Binó, Miroslava Bittová, Petra Ovesná, Peter Kollár, Radek Fedr, Milan Ešner, Josef Jaroš, Aleš Hampl, Lumír Krejčí, Kamil Paruch, and Karel Souček

- 1843** **ADA-07 Suppresses Solar Ultraviolet-Induced Skin Carcinogenesis by Directly Inhibiting TOPK**

Ge Gao, Tianshun Zhang, Qiushi Wang, Kanamata Reddy, Hanyong Chen, Ke Yao, Keke Wang, Eunmiri Roh, Tatyana Zykova, Weiya Ma, Joohyun Ryu, Clara Curiel-Lewandrowski, David Alberts, Sally E. Dickinson, Ann M. Bode, Ying Xing, and Zigang Dong

## LARGE MOLECULE THERAPEUTICS

- 1855** **Antitumor Synergism and Enhanced Survival with a Tumor Vasculature-Targeted Enzyme Prodrug System, Rapamycin, and Cyclophosphamide**

John J. Kraus, Needa Virani, Patrick H. McKernan, Quang Nguyen, Kar-Ming Fung, Vassilios I. Sikavitsas, Carla Kurkjian, and Roger G. Harrison

- 1866** **A Potential Mechanism for ADC-Induced Neutropenia: Role of Neutrophils in Their Own Demise**


Hui Zhao, Sara Gulesserian, Maria Christina Malinao, Sathish Kumar Ganesan, James Song, Mi Sook Chang, Melissa M. Williams, Zhilan Zeng, Michael Mattie, Brian A. Mendelsohn, David R. Stover, and Fernando Doñate

See related article, p. 1877

# Table of Contents

**1877** Inhibition of Megakaryocyte Differentiation by Antibody–Drug Conjugates (ADCs) is Mediated by Macropinocytosis: Implications for ADC-induced Thrombocytopenia

Hui Zhao, Sara Gulesserian, Sathish Kumar Ganesan, Jimmy Ou, Karen Morrison, Zhilan Zeng, Veronica Robles, Josh Snyder, Lisa Do, Hector Aviña, Sher Karki, David R. Stover, and Fernando Doñate  
*See related article, p. 1866*

**1887**  Enzymatic Inactivation of Endogenous IgG by IdeS Enhances Therapeutic Antibody Efficacy

Sofia Järnum, Anna Runström, Robert Bockermann, Lena Winstedt, Max Crispin, and Christian Kjellman

**1898** IL6 Receptor Blockade Enhances Chemotherapy Efficacy in Pancreatic Ductal Adenocarcinoma

Kristen B. Long, Graham Tooker, Evan Tooker, Santiago Lombo Luque, Jae W. Lee, Xiaoqing Pan, and Gregory L. Beatty

**1909** A Novel Theranostic Strategy for MMP-14–Expressing Glioblastomas Impacts Survival

Suchismita Mohanty, Zixin Chen, Kai Li, Goreti Ribeiro Morais, Jessica Klockow, Ketan Yerneni, Laura Pisani, Frederick T. Chin, Siddharta Mitra, Samuel Cheshier, Edwin Chang, Sanjiv Sam Gambhir, Jianghong Rao, Paul M. Loadman, Robert A. Falconer, and Heike E. Daldrop-Link

**1922** Herpes Simplex Virus Glycoprotein D Targets a Specific Dendritic Cell Subset and Improves the Performance of Vaccines to Human Papillomavirus-Associated Tumors

Bruna F.M.M. Porchia, Ana Carolina R. Moreno, Rodrigo N. Ramos, Mariana O. Diniz, Laís Helena T.M. de Andrade, Daniela S. Rosa, José Alexandre M. Barbuto, Silvia B. Boscardin, and Luís Carlos S. Ferreira

## CANCER BIOLOGY AND SIGNAL TRANSDUCTION

**1934** Inhibition of Aurora A and Aurora B Is Required for the Sensitivity of HPV-Driven Cervical Cancers to Aurora Kinase Inhibitors


David Martin, Sora Fallaha, Martina Proctor, Alexander Stevenson, Lewis Perrin, Nigel McMillan, and Brian Gabrielli

**1942** mTORC1 Inhibition Induces Resistance to Methotrexate and 6-Mercaptopurine in Ph<sup>+</sup> and Ph-like B-ALL

Thanh-Trang T. Vo, J. Scott Lee, Duc Nguyen, Brandon Lui, William Pandori, Andrew Khaw, Sharmila Mallya, Mengrou Lu, Markus Müschen, Marina Konopleva, and David A. Fruman

**1954** Wnt/ $\beta$ -catenin Signaling Contributes to Tumor Malignancy and Is Targetable in Gastrointestinal Stromal Tumor

Shan Zeng, Adrian M. Seifert, Jennifer Q. Zhang, Michael J. Cavnar, Teresa S. Kim, Vinod P. Balachandran, Juan A. Santamaria-Barria, Noah A. Cohen, Michael J. Beckman, Benjamin D. Medina, Ferdinand Rossi, Megan H. Crawley, Jennifer K. Loo, Joanna H. Maltbaek, Peter Besmer, Cristina R. Antonescu, and Ronald P. DeMatteo

**1967**  An *In Vivo* Functional Screen Identifies JNK Signaling As a Modulator of Chemotherapeutic Response in Breast Cancer

Matthew Ashenden, Antoinette van Weverwijk, Nirupa Murugaesu, Antony Fearn, James Campbell, Qiong Gao, Marjan Irvani, and Clare M. Isacke

**1979** FBW7-Dependent Mcl-1 Degradation Mediates the Anticancer Effect of Hsp90 Inhibitors

Jingshan Tong, Shuai Tan, Zaneta Nikolovska-Coleska, Jian Yu, Fangdong Zou, and Lin Zhang

**1989** Tyrosine Kinase Inhibitors Protect the Salivary Gland from Radiation Damage by Inhibiting Activation of Protein Kinase C- $\delta$

Sten M. Wie, Elizabeth Wellberg, Sana D. Karam, and Mary E. Reyland

## COMPANION DIAGNOSTICS AND CANCER BIOMARKERS

**1999** Optimization of *RAS/BRAF* Mutational Analysis Confirms Improvement in Patient Selection for Clinical Benefit to Anti-EGFR Treatment in Metastatic Colorectal Cancer

Cristina Santos, Daniel Azuara, Rocio Garcia-Carbonero, Pilar Garcia Alfonso, Alfredo Carrato, M<sup>a</sup> Elena Elez, Auxiliadora Gomez, Ferran Losa, Clara Montagut, Bartomeu Massuti, Valenti Navarro, Mar Varela, Adriana Lopez-Doriga, Victor Moreno, Manuel Valladares, Jose Luis Manzano, Jose Maria Vieitez, Enrique Aranda, Xavier Sanjuan, Josep Tabernero, Gabriel Capella, and Ramon Salazar

**2008** Cooperative Targets of Combined mTOR/HDAC Inhibition Promote MYC Degradation

John K. Simmons, Aleksandra M. Michalowski, Benjamin J. Gamache, Wendy DuBois, Jyoti Patel, Ke Zhang, Joy Gary, Shuling Zhang, Snehal Gaikwad, Daniel Connors, Nicholas Watson, Elena Leon, Jin-Qiu Chen, W. Michael Kuehl, Maxwell P. Lee, Adriana Zingone, Ola Landgren, Peter Ordentlich, Jing Huang, and Beverly A. Mock



# Table of Contents

## MODELS AND TECHNOLOGIES

- 2022** **Modeling Therapy Resistance in *BRCA1/2*-Mutant Cancers**  
Amy Dréan, Chris T. Williamson, Rachel Brough, Inger Brandsma, Malini Menon, Asha Konde, Isaac Garcia-Murillas, Helen N. Pemberton, Jessica Frankum, Rumana Rafiq, Nicholas Badham, James Campbell, Aditi Gulati, Nicholas C. Turner, Stephen J. Pettitt, Alan Ashworth, and Christopher J. Lord

- 2035** **Metformin Inhibits Cellular Proliferation and Bioenergetics in Colorectal Cancer Patient-Derived Xenografts**  
Nur-Afidah Mohamed Suhaimi, Wai Min Phyoo, Hao Yun Yap, Sharon Heng Yee Choy, Xiaona Wei, Yukti Choudhury, Wai Jin Tan, Luke Anthony Peng Yee Tan, Roger Sik Yin Foo, Suzanne Hui San Tan, Zenia Tiang, Chin Fong Wong, Poh Koon Koh, and Min-Han Tan

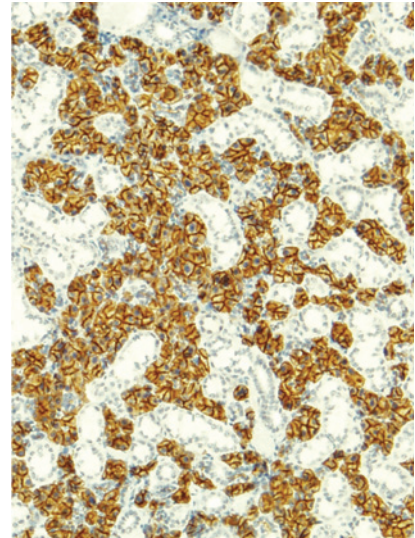


AC icon indicates AuthorChoice

For more information please visit [www.aacrjournals.org](http://www.aacrjournals.org)

## ABOUT THE COVER

Irradiation therapy for head and neck cancer frequently damages normal oral tissues including the salivary glands, resulting in loss of saliva producing acinar cells and reduced saliva production. Tyrosine kinase inhibitors (TKIs) provide robust radioprotection of salivary gland function, which is associated with salivary acinar cell regeneration. The cover shows aquaporin 5 stained acinar cells in the submandibular gland of mice treated with dasatinib in conjunction with irradiation. For more details, see article by Wie and colleagues on page 1989.



# Molecular Cancer Therapeutics

**16 (9)**

*Mol Cancer Ther* 2017;16:1727-2044.

**Updated version** Access the most recent version of this article at:  
<http://mct.aacrjournals.org/content/16/9>

**E-mail alerts** [Sign up to receive free email-alerts](#) related to this article or journal.

**Reprints and Subscriptions** To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at [pubs@aacr.org](mailto:pubs@aacr.org).

**Permissions** To request permission to re-use all or part of this article, use this link <http://mct.aacrjournals.org/content/16/9>. Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.