

Highlights of This Issue 233

SMALL MOLECULE THERAPEUTICS

- 235** Induction of MNK Kinase-dependent eIF4E Phosphorylation by Inhibitors Targeting BET Proteins Limits Efficacy of BET Inhibitors
Thao N.D. Pham, Krishan Kumar, Brian T. DeCant, Meng Shang, Samad Z. Munshi, Maria Matsangou, Kazumi Ebine, and Hidayatullah G. Munshi
- 245** Necuparanib, A Multitargeting Heparan Sulfate Mimetic, Targets Tumor and Stromal Compartments in Pancreatic Cancer
Amanda MacDonald, Michelle Priess, Jennifer Curran, Jamey Guess, Victor Farutin, Ilse Oosterom, Chia Lin Chu, Edward Cochran, Lynn Zhang, Kristen Getchell, Martijn Lolkema, Birgit C. Schultes, and Silva Krause
- 257** Intestinal Toxicity in Rats Following Administration of CDK4/6 Inhibitors Is Independent of Primary Pharmacology
Stephane Thibault, Wenyue Hu, Brad Hirakawa, Dalia Kalabat, Tania Franks, Tae Sung, Su Khoh-Reiter, Shuyan Lu, Martin Finkelstein, Bart Jessen, and Aida Sacaan
- 267** Pleiotropic Action of Novel Bruton's Tyrosine Kinase Inhibitor BGB-3111 in Mantle Cell Lymphoma
Carrie J. Li, Changying Jiang, Yang Liu, Taylor Bell, Wencai Ma, Yin Ye, Shengjian Huang, Hui Guo, Hui Zhang, Lai Wang, Jing Wang, Krystle Nomie, Liang Zhang, and Michael Wang
- 278** Inhibition of MERTK Promotes Suppression of Tumor Growth in BRAF Mutant and BRAF Wild-Type Melanoma
Lenka Sinik, Katherine A. Minson, John J. Tentler, Jacqueline Carrico, Stacey M. Bagby, William A. Robinson, Rotem Kami, Tal Burstyn-Cohen, S. Gail Eckhardt, Xiaodong Wang, Stephen V. Frye, H. Shelton Earp, Deborah DeRyckere, and Douglas K. Graham
- 289** Targeting the Sphingosine 1-Phosphate Axis Exerts Potent Antitumor Activity in BRAF-Resistant Melanomas
David Garandau, Justine Noujarède, Justine Leclerc, Caroline Imbert, Virginie Garcia, Marie-Lise Bats, Florian Rambow, Julia Gilhodes, Thomas Filleron, Nicolas Meyer, Stéphanie Brayer, Silvia Arcucci, Sophie Tartare-Deckert, Bruno Ségui, Jean-Christophe Marine, Thierry Levade, Corine Bertolotto, and Nathalie Andrieu-Abadie

- 301** Urolithin A, a Novel Natural Compound to Target PI3K/AKT/mTOR Pathway in Pancreatic Cancer
Tulasigeri M. Totiger, Supriya Srinivasan, Venkatakrishna R. Jala, Purushottam Lamichhane, Austin R. Dosch, Alexander A. Gaidarski III, Chandrashekhar Joshi, Shobith Rangappa, Jason Castellanos, Praveen Kumar Vemula, Xi Chen, Deukwoo Kwon, Nilesh Kashikar, Michael VanSaun, Nipun B. Merchant, and Nagaraj S. Nagathihalli

LARGE MOLECULE THERAPEUTICS

- 312** CD3-Bispecific Antibody Therapy Turns Solid Tumors into Inflammatory Sites but Does Not Install Protective Memory
 Hreinn Benonisson, Işıl Altıntaş, Marjolein Sluiter, Sandra Verploegen, Aran F. Labrijn, Danita H. Schuurhuis, Mischa A. Houtkamp, J. Sjeff Verbeek, Janine Schuurman, and Thorbald van Hall
- 323** Combining DNA Vaccine and AIM2 in H1 Nanoparticles Exert Anti-Renal Carcinoma Effects via Enhancing Tumor-Specific Multi-functional CD8⁺ T-cell Responses
Dafei Chai, Hongjian Shan, Gang Wang, Qing Zhang, Huizhong Li, Lin Fang, Jingyuan Song, Nianli Liu, Qian Zhang, Hong Yao, and Junnian Zheng
- 335** APOMAB Antibody-Drug Conjugates Targeting Dead Tumor Cells are Effective *In Vivo*
Alexander H. Staudacher, Yanrui Li, Vasilios Liapis, Jeff Jia Cheng Hou, David Chin, Olan Dolezal, Timothy E. Adams, Patrick H. van Berkel, and Michael P. Brown

CANCER BIOLOGY AND TRANSLATIONAL STUDIES

- 346** MTORC1/2 Inhibition as a Therapeutic Strategy for PIK3CA Mutant Cancers
Stephanie L. Fricke, Susan N. Payne, Peter F. Favreau, Jeremy D. Kratz, Cheri A. Pasch, Tyler M. Foley, Alexander E. Yueh, Dana R. Van De Hey, Mitchell G. Depke, Demetra P. Korkos, Gioia Chengcheng Sha, Rebecca A. DeStefanis, Linda Clipson, Mark E. Burkard, Kayla K. Lemmon, Benjamin M. Parsons, Paraic A. Kenny, Kristina A. Matkowskyj, Michael A. Newton, Melissa C. Skala, and Dustin A. Deming

Table of Contents

356 AKT Inhibition Modulates H3K4 Demethylase Levels in PTEN-Null Prostate Cancer

Mohammad Imran Khan, Abid Hamid, Suvasmita Rath, Bushra Ateeq, Qateeb Khan, Imtiaz A. Siddiqui, Vaqar Mustafa Adhami, Hani Choudhry, Mazin A. Zamzami, and Hasan Mukhtar

364 Combined PPAR γ Activation and XIAP Inhibition as a Potential Therapeutic Strategy for Ovarian Granulosa Cell Tumors

Dilys T.H. Leung, Trang Nguyen, Edwina May Oliver, Juliana Matti, Maria Alexiadis, John Silke, Thomas W. Jobling, Peter J. Fuller, and Simon Chu

376 3D Growth of Cancer Cells Elicits Sensitivity to Kinase Inhibitors but Not Lipid Metabolism Modifiers



Dylan T. Jones, Alessandro Valli, Syed Haider, Qifeng Zhang, Elizabeth A. Smethurst, Zachary T. Schug, Barrie Peck, Eric O. Aboagye, Susan E. Critchlow, Almut Schulze, Eyal Gottlieb, Michael J.O. Wakelam, and Adrian L. Harris

389 Therapeutic Inhibition of the Receptor Tyrosine Kinase AXL Improves Sensitivity to Platinum and Taxane in Ovarian Cancer

Jeanne M. Quinn, Molly M. Greenwade, Marguerite L. Palisoul, Gregory Opara, Katina Massad, Lei Guo, Peinan Zhao, Hollie Beck-Noia, Ian S. Hagemann, Andrea R. Hagemann, Carolyn K. McCourt, Premal H. Thaker, Matthew A. Powell, David G. Mutch, and Katherine C. Fuh

399 Cooperative Effect of Oncogenic *MET* and *PIK3CA* in an HGF-Dominant Environment in Breast Cancer



Shuying Liu, Shunqiang Li, Bailiang Wang, Wenbin Liu, Mihai Gagea, Huiqin Chen, Joohyuk Sohn, Napa Parinyanitikul, Tina Primeau, Kim-Anh Do, George F. Vande Woude, John Mendelsohn, Naoto T. Ueno, Gordon B. Mills, Debu Tripathy, and Ana M. Gonzalez-Angulo

413 Glycoprotein-130 Expression Is Associated with Aggressive Bladder Cancer and Is a Potential Therapeutic Target

Darryl T. Martin, Hongliang Shen, Jill M. Steinbach-Rankins, Xi Zhu, Katelyn K. Johnson, Jamil Syed, W. Mark Saltzman, and Robert M. Weiss

421 Predicting Novel Therapies and Targets: Regulation of Notch3 by the Bromodomain Protein BRD4

Alejandro Villar-Prados, Sherry Y. Wu, Karem A. Court, Shaolin Ma, Christopher LaFargue, Mamur A. Chowdhury, Margaret I. Engelhardt, Cristina Ivan, Prahlad T. Ram, Ying Wang, Keith Baggerly, Cristian Rodriguez-Aguayo, Gabriel Lopez-Berestein, Shyh-Ming Yang, David J. Maloney, Makoto Yoshioka, Jeffrey W. Strovel, Jason Roszik, and Anil K. Sood

COMPANION DIAGNOSTIC, PHARMACOGENOMIC, AND CANCER BIOMARKERS

437 Circulating Tumor Cells with Stemness and Epithelial-to-Mesenchymal Transition Features Are Chemoresistant and Predictive of Poor Outcome in Metastatic Breast Cancer

Maria A. Papadaki, Giannis Stoupis, Panayiotis A. Theodoropoulos, Dimitris Mavroudis, Vassilis Georgoulas, and Sofia Agelaki

448 Genome-Wide Sequencing of Cell-Free DNA Identifies Copy-Number Alterations That Can Be Used for Monitoring Response to Immunotherapy in Cancer Patients



Taylor J. Jensen, Aaron M. Goodman, Shumei Kato, Christopher K. Ellison, Gregory A. Daniels, Lisa Kim, Prachi Nakashe, Erin McCarthy, Amin R. Mazloom, Graham McLennan, Daniel S. Grosu, Mathias Ehrich, and Razelle Kurzrock

459 miR-454-3p Is an Exosomal Biomarker and Functions as a Tumor Suppressor in Glioma

Naiyuan Shao, Lian Xue, Rong Wang, Kaiming Luo, Feng Zhi, and Qing Lan

470 Combined Cellular and Biochemical Profiling to Identify Predictive Drug Response Biomarkers for Kinase Inhibitors Approved for Clinical Use between 2013 and 2017

Joost C.M. Uitdehaag, Jeffrey J. Kooijman, Jeroen A.D.M. de Roos, Martine B.W. Prinsen, Jelle Dylus, Nicole Willemsen-Seegers, Yusuke Kawase, Masaaki Sawa, Jos de Man, Suzanne J.C. van Gerwen, Rogier C. Buijsman, and Guido J.R. Zaman

MODELS AND TECHNOLOGIES

482 The T197A Knock-in Model of *Cdkn1b* Gene to Study the Effects of p27 Restoration *In Vivo*

Carmela De Marco, Nicola Rinaldo, Fernanda De Vita, Floriana Forzati, Elvira Caira, Valentina Iovane, Orlando Paciello, Donatella Montanaro, Sara D'Andrea, Gustavo Baldassarre, Serenella Papparella, Donatella Malanga, Alfonso Baldi, and Giuseppe Viglietto



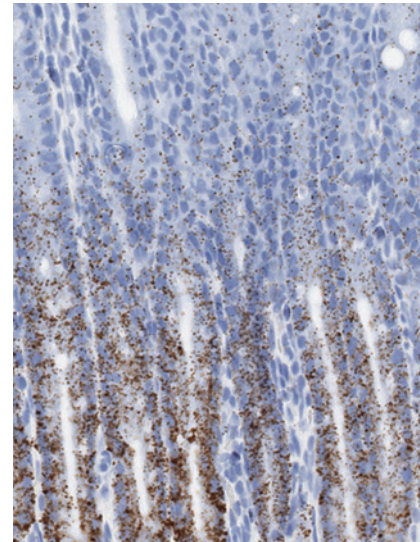
AC icon indicates AuthorChoice

For more information please visit www.aacrjournals.org

Table of Contents

ABOUT THE COVER

Abemaciclib, a cyclin-dependent kinase 4 and 6 dual inhibitor, was recently approved for the treatment of breast cancer. However, diarrhea is a common adverse event observed in patients treated with abemaciclib. Therefore, Thibault and colleagues sought to determine if toxicity was due to CDK4/6 inhibition or instead due to secondary pharmacological targets. Shown is an image of *in situ* hybridization (ISH) of rats administered 120 mg/kg abemaciclib using brown reagent with hematoxylin (blue) background. The representative section demonstrated an increased number of crypt cells staining for Smoc2, consistent and proportional to the elongation of the crypts in rats administered abemaciclib. For details, see article on page 257.



Molecular Cancer Therapeutics

18 (2)

Mol Cancer Ther 2019;18:233-493.

Updated version Access the most recent version of this article at:
<http://mct.aacrjournals.org/content/18/2>

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.

Permissions To request permission to re-use all or part of this article, use this link <http://mct.aacrjournals.org/content/18/2>.
Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.