

## MOLECULAR CANCER THERAPEUTICS

## TABLE OF CONTENTS

## HIGHLIGHTS

- 1 Selected Articles from This Issue**

## REVIEW

- 3 The Ongoing Search for Biomarkers of CDK4/6 Inhibitor Responsiveness in Breast Cancer**  
Scott F. Schoninger and Stacy W. Blain

## SMALL MOLECULE THERAPEUTICS

- 13 Pharmacology of the ATM Inhibitor AZD0156: Potentiation of Irradiation and Olaparib Responses Preclinically**

**AC** Lucy C. Riches, Antonio G. Trinidad, Gareth Hughes, Gemma N. Jones, Adina M. Hughes, Andrew G. Thomason, Paul Gavine, Andy Cui, Stephanie Ling, Jonathan Stott, Roger Clark, Samantha Peel, Pendeep Gill, Louise M. Goodwin, Aaron Smith, Kurt G. Pike, Bernard Barlaam, Martin Pass, Mark J. O'Connor, Graeme Smith, and Elaine B. Cadogan

- 26 The Novel ATR Inhibitor BAY 1895344 Is Efficacious as Monotherapy and Combined with DNA Damage-Inducing or Repair-Compromising Therapies in Preclinical Cancer Models**

**AC** Antje M. Wengner, Gerhard Siemeister, Ulrich Lücking, Julien Lefranc, Lars Wortmann, Philip Lienau, Benjamin Bader, Ulf Bömer, Dieter Moosmayer, Uwe Eberspächer, Sven Golfier, Christoph A. Schatz, Simon J. Baumgart, Bernard Haendler, Pascale Lejeune, Andreas Schlicker, Franz von Nussbaum, Michael Brands, Karl Ziegelbauer, and Dominik Mumberg

- 39 A Multifunctional Therapy Approach for Cancer: Targeting Raf1-Mediated Inhibition of Cell Motility, Growth, and Interaction with the Microenvironment**

**AC** Limin Zhang, Abhinandan Pattanayak, Wenqi Li, Hyun-Kyung Ko, Graham Fowler, Ryan Gordon, and Raymond Bergan

- 52 Quantitative High-Throughput Screening Using an Organotypic Model Identifies Compounds that Inhibit Ovarian Cancer Metastasis**

Hilary A. Kenny, Madhu Lal-Nag, Min Shen, Betul Kara, Dominik A. Nahotko, Kristen Wroblewski, Sarah Fazal, Siquan Chen, Chun-Yi Chiang, Yen-Ju Chen, Kyle R. Brimacombe, Juan Marugan, Marc Ferrer, and Ernst Lengyel

- 63 Inhibition of Autotaxin with GLPG1690 Increases the Efficacy of Radiotherapy and Chemotherapy in a Mouse Model of Breast Cancer**

Xiaoyun Tang, Melinda Wuest, Matthew G.K. Benesch, Jennifer Dufour, YuanYuan Zhao, Jonathan M. Curtis, Alain Monjardet, Bertrand Heckmann, David Murray, Frank Wuest, and David N. Brindley

- 75 A Novel Small Molecule Targets Androgen Receptor and Its Splice Variants in Castration-Resistant Prostate Cancer**

Zhenyu Yang, Dan Wang, James K. Johnson, Laura E. Pascal, Keita Takubo, Raghunandan Avula, Anish Bhaswanth Chakka, Jianhua Zhou, Wei Chen, Mingming Zhong, Qiong Song, Hui Ding, Zeyu Wu, Uma R. Chandran, Taber S. Maskrey, Joel B. Nelson, Peter Wipf, and Zhou Wang

- 89 Verticillin A Causes Apoptosis and Reduces Tumor Burden in High-Grade Serous Ovarian Cancer by Inducing DNA Damage**

Amrita Salvi, Chiraz Soumia M. Amrine, Julia R. Austin, KiAundra Kilpatrick, Angela Russo, Daniel Lantvit, Esther Calderon-Gierszal, Zachary Mattes, Cedric J. Pearce, Mark W. Grinstaff, Aaron H. Colby, Nicholas H. Oberlies, and Joanna E. Burdette

- 101 A Novel Salicylanilide Derivative Induces Autophagy Cell Death in Castration-Resistant Prostate Cancer via ER Stress-Activated PERK Signaling Pathway**

Chia-Ling Hsieh, Hsu-Shan Huang, Kuan-Chou Chen, Teigi Saka, Chih-Ying Chiang, Leland W.K. Chung, and Shian-Ying Sung

# TABLE OF CONTENTS

**112 Molecular Inhibitor of QSOX1 Suppresses Tumor Growth *In Vivo***

Amber L. Fifield, Paul D. Hanavan, Douglas O. Faigel, Eduard Sergienko, Andrey Bobkov, Nathalie Meurice, Joachim L. Petit, Alysia Polito, Thomas R. Caulfield, Erik P. Castle, John A. Copland, Debabrata Mukhopadhyay, Krishnendu Pal, Shomit K. Dutta, Huijun Luo, Thai H. Ho, and Douglas F. Lake

**123 Synergism between ATM and PARP1 Inhibition Involves DNA Damage and Abrogating the G<sub>2</sub> DNA Damage Checkpoint**

Joyce P.Y. Mak, Hoi Tang Ma, and Randy Y.C. Poon

**135 Dipyridamole Enhances the Cytotoxicities of Trametinib against Colon Cancer Cells through Combined Targeting of HMGCS1 and MEK Pathway**

Sheng Zhou, Huanji Xu, Qiulin Tang, Hongwei Xia, and Feng Bi

**147 Dual Inhibition of Angiopoietin-TIE2 and MET Alters the Tumor Microenvironment and Prolongs Survival in a Metastatic Model of Renal Cell Carcinoma**

May Elbanna, Ashley R. Orillion, Nur P. Damayanti, Remi Adelaiye-Ogala, Li Shen, Kiersten Marie Miles, Sreenivasulu Chintala, Eric Ciamporcerio, Swathi Ramakrishnan, Sheng-yu Ku, Karen Rex, Sean Caenepeel, Angela Coxon, and Roberto Pili

## LARGE MOLECULE THERAPEUTICS

**157 Precision Chemoradiotherapy for HER2 Tumors Using Antibody Conjugates of an Auristatin Derivative with Reduced Cell Permeability**

**AC** Dina V. Hingorani, Matthew K. Doan, Maria F. Camargo, Joseph Aguilera, Seung M. Song, Donald Pizzo, Daniel J. Scanderbeg, Ezra E.W. Cohen, Andrew M. Lowy, Stephen R. Adams, and Sunil J. Advani

**168 Efficacy of the Antibody-Drug Conjugate W0101 in Preclinical Models of IGF-1 Receptor Overexpressing Solid Tumors**

Barbara Akla, Matthieu Broussas, Noureddine Loukili, Alain Robert, Charlotte Beau-Larvor, Martine Malissard, Nicolas Boute, Thierry Champion, Jean-Francois Haeuw, Alain Beck, Michel Perez, Cyrille Dreyfus, Mariya Pavlyuk, Eric Chetaille, and Nathalie Corvaia

**178 Minicircle DNA-Engineered CAR T Cells Suppressed Tumor Growth in Mice**

Jinsheng Han, Fei Gao, Songsong Geng, Xueshuai Ye, Tie Wang, Pingping Du, Ziqi Cai, Zexian Fu, Zhilong Zhao, Long Shi, Qingxia Li, and Jianhui Cai

**187 Role of Dimerized C16orf74 in Aggressive Pancreatic Cancer: A Novel Therapeutic Target**

Toshihiro Kushibiki, Toru Nakamura, Masumi Tsuda, Takahiro Tsuchikawa, Koji Hontani, Kazuho Inoko, Mizuna Takahashi, Toshimichi Asano, Keisuke Okamura, Soichi Murakami, Yo Kurashima, Yuma Ebihara, Takehiro Noji, Yoshitsugu Nakanishi, Kimitaka Tanaka, Nako Maishi, Katsunori Sasaki, Woong-Ryeon Park, Toshiaki Shichinohe, Kyoko Hida, Shinya Tanaka, and Satoshi Hirano

## CANCER BIOLOGY AND TRANSLATIONAL STUDIES

**199 ALDH1A1 Contributes to PARP Inhibitor Resistance via Enhancing DNA Repair in BRCA2<sup>-/-</sup> Ovarian Cancer Cells**

Lu Liu, Shurui Cai, Chunhua Han, Ananya Banerjee, Dayong Wu, Tiantian Cui, Guozhen Xie, Junran Zhang, Xiaoli Zhang, Eric McLaughlin, Ming Yin, Floor J. Backes, Arnab Chakravarti, Yanfang Zheng, and Qi-En Wang

**211 PD-1/PD-L1 Immune Checkpoint Inhibition with Radiation in Bladder Cancer: *In Situ* and Abscopal Effects**

Alexis Rompré-Brodeur, Surashri Shinde-Jadhav, Mina Ayoub, Ciriaco A. Piccirillo, Jan Seuntjens, Fadi Brimo, Jose Joao Mansure, and Wassim Kassouf

**221 Blockade of Glutathione Metabolism in IDH1-Mutated Glioma**

Xiaoying Tang, Xiao Fu, Yang Liu, Di Yu, Sabrina J. Cai, and Chunzhang Yang

**231 Enzalutamide-Induced Feed-Forward Signaling Loop Promotes Therapy-Resistant Prostate Cancer Growth Providing an Exploitable Molecular Target for Jak2 Inhibitors**

Vindhya Udhane, Cristina Maranto, David T. Hoang, Lei Gu, Andrew Erickson, Savita Devi, Pooja G. Talati, Anjishnu Banerjee, Kenneth A. Iczkowski, Kenneth Jacobsohn, William A. See, Tuomas Mirtti, Deepak Kilari, and Marja T. Nevalainen

**247 Modulating TAK1 Expression Inhibits YAP and TAZ Oncogenic Functions in Pancreatic Cancer**

**AC** Raffaella Santoro, Marco Zanotto, Francesca Simionato, Camilla Zecchetto, Valeria Merz, Chiara Cavallini, Geny Piro, Fabio Sabbadini, Federico Boschi, Aldo Scarpa, and Davide Melisi

**258 Targeting Histone Chaperone FACT Complex Overcomes 5-Fluorouracil Resistance in Colon Cancer**

Heyu Song, Jiping Zeng, Shrabasti Roychoudhury, Pranjali Biswas, Bhopal Mohapatra, Sutapa Ray, Kayvon Dowlatshahi, Jing Wang, Vimla Band, Geoffrey Talmon, and Kishor K. Bhakat

# TABLE OF CONTENTS

**270 Synergy between EphA2-ILs-DTXp, a Novel EphA2-Targeted Nanoliposomal Taxane, and PD-1 Inhibitors in Preclinical Tumor Models**

Walid S. Kamoun, Anne-Sophie Dugast, James J. Suchy, Stephanie Grabow, Ross B. Fulton, James F. Sampson, Lia Luus, Michael Santiago, Alexander Koshkaryev, Gang Sun, Vasileios Askoxyllakis, Eric Tam, Zhaohua Richard Huang, Daryl C. Drummond, and Andrew J. Sawyer

## COMPANION DIAGNOSTIC, PHARMACOGENOMIC, AND CANCER BIOMARKERS

**282 ADP-Ribosylation Levels and Patterns Correlate with Gene Expression and Clinical Outcomes in Ovarian Cancers**

Lesley B. Conrad, Ken Y. Lin, Tulip Nandu, Bryan A. Gibson, Jayanthi S. Lea, and W. Lee Kraus

**292 Predictive and Pharmacodynamic Biomarkers of Response to the Phosphatidylinositol 3-Kinase Inhibitor Taselisib in Breast Cancer Preclinical Models**

Heather M. Moore, Heidi M. Savage, Carol O'Brien, Wei Zhou, Ethan S. Sokol, Michael E. Goldberg, Ciara Metcalfe, Lori S. Friedman, Mark R. Lackner, and Timothy R. Wilson

**304 Pralatrexate in Combination with Oxaliplatin in Advanced Esophagogastric Cancer: A Phase II Trial with Predictive Molecular Correlates**

Usha Malhotra, Sarbajit Mukherjee, Christos Fountzilias, Patrick Boland, Austin Miller, Santosh Patnaik, Kristopher Attwood, Sai Yendamuri, Araba Adjei, Eric Kannisto, Mateusz Opyrchal, Peter Bushunow, Peter Loud, Renuka Iyer, and Nikhil Khushalani

**312 Identification of Expression Profiles Defining Distinct Prognostic Subsets of Radioactive-Iodine Refractory Differentiated Thyroid Cancer from the DECISION Trial**

Jaume Capdevila, Ignacio Matos, Francesco M. Mancuso, Carmela Iglesias, Paolo Nuciforo, Carles Zafon, Hector G. Palmer, Zighereda Ogbah, Laura Muiños, Jorge Hernando, Guillermo Villacampa, Carol E. Peña, Josep Taberner, Marcia S. Brose, Martin Schlumberger, and Ana Vivancos

**318 Acknowledgment to Reviewers**

**AC** icon indicates AuthorChoice

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

## ABOUT THE COVER

Chimeric antigen receptor T (CAR T) cells represent a new paradigm in cancer therapy. However, viral-based production of these CAR T cells is laborious and comes at a high cost. Therefore, Cai and colleagues sought to utilize minicircle DNA (mcDNA) to produce CAR T cells without the need for viruses. In the cover image, the authors demonstrate strong expression of PSCA on a prostate xenograft. CAR T cells derived using mcDNA targeted at this PSCA infiltrated the tumor and increased cytokine secretion. Read the article on page 178.

