# MOLECULAR CANCER THERAPEUTICS

## TABLE OF CONTENTS

### HIGHLIGHTS

2233  Selected Articles from This Issue

### MCT FIRST DISCLOSURES

2235  Preclinical Development of MGC018, a Duocarmycin-based Antibody-drug Conjugate Targeting B7-H3 for Solid Cancer

#### A C
Juniper A. Scribner, Jennifer G. Brown, Thomas Son, Michael Chiechi, Pam Li, Sharad Sharma, Hua Li, Anushka De Costa, Ying Li, Yan Chen, Ann Easton, Nicholas C. Yee-Toy, Francine Z. Chen, Sergey Gorlatov, Bhaswati Barat, Ling Huang, Christina R. Wolff, Jeff Hooley, Tim E. Hotaling, Timur Gaynutdinov, Valentina Ciccarone, James Tamura, Scott Koenig, Paul A. Moore, Ezio Bonvini, and Deryk Loo

### REVIEW

2245  Therapeutic Targeting of Mitochondrial One-Carbon Metabolism in Cancer

#### A C
Aamod S. Dekhne, Zhanjun Hou, Aleem Gangjee, and Larry H. Matherly

### SMALL MOLECULE THERAPEUTICS

2256  The Dual Androgen Receptor and Glucocorticoid Receptor Antagonist CB-03-10 as Potential Treatment for Tumors that have Acquired GR-mediated Resistance to AR Blockade

Caridad Rosette, Frances J. Agan, Niccolette Rosette, Alessandro Mazzetti, Luigi Moro, and Mara Gerloni

2267  An RNA-Binding Protein, Hu-antigen R, in Pancreatic Cancer Epithelial to Mesenchymal Transition, Metastasis, and Cancer Stem Cells

Ruochen Dong, Ping Chen, Kishore Polireddy, Xiaoqing Wu, Tao Wang, Remya Ramesh, Dan A. Dixon, Liang Xu, Jeffrey Aub, and Qi Chen

2278  Synthetic Lethal Metabolic Targeting of Androgen-Deprived Prostate Cancer Cells with Metformin

Ring Yang, Shivashankar Damodaran, Tariq A. Kheenees, Mikołaj J. Filon, Adam Schultz, Joseph Gawdzik, Tyler Etheridge, Dmitry Malin, Kyle A. Richards, Vincent L. Cryns, and David F. Jarrard

### LARGE MOLECULE THERAPEUTICS

2288  CH7233163 Overcomes Osimertinib-Resistant EGFR-Del19/T790M/C797S Mutation

#### A C
Kenji Kashima, Hiroki Kawauchi, Hiromi Tanimura, Yukako Tachibana, Takashi Chiba, Takuya Torizawa, and Hiroshi Sakamoto

2298  Osimertinib, an Irreversible Next-Generation EGFR Tyrosine Kinase Inhibitor, Exerts Antitumor Activity in Various Preclinical NSCLC Models Harboring the Uncommon EGFR Mutations G719X or L861Q or S768I

Nicolas Flor’c’h, Sangbin Lim, Sue Bickerton, Afshan Ahmed, Jonathan Orme, Jelena Urosevic, Matthew J. Martin, Darren A.E. Cross, Byoung Chul Cho, and Paul D. Smith

2308  Efficacy, Tolerability, and Pharmacokinetics of Combined Targeted MEK and Dual mTORC1/2 Inhibition in a Preclinical Model of Mucosal Melanoma

Bih-Rong Wei, Shelley B. Hoover, Cody J. Peer, Jennifer E. Dwyer, Hibret A. Adisu, Priya Shankarappa, Howard Yang, Maxwell Lee, Tyler J. Peat, William D. Figg, and R. Mark Simpson

2319  Menin-mediated Repression of Glycolysis in Combination with Autophagy Protects Colon Cancer Against Small-molecule EGFR Inhibitors

Bryson W. Katona, Taylor Hojnacki, Rebecca A. Glynn, Kayla E. Paulosky, Katherine M. Szigety, Yan Cao, Xuyao Zhang, Zijie Feng, Xin He, Jian Ma, and Xianxin Hua

2330  LILRB4-targeting Antibody-Drug Conjugates for the Treatment of Acute Myeloid Leukemia

Yasuaki Anami, Mi Deng, Xun Gui, Aiko Yamaguchi, Chisato M. Yamazaki, Ningyan Zhang, Cheng Cheng Zhang, Zhiqiang An, and Kyoji Tsuchikama

2340  Dual Mechanisms of Novel CD73-Targeted Antibody and Antibody-Drug Conjugate in Inhibiting Lung Tumor Growth and Promoting Antitumor Immune-Effector Function

Rui Jin, Liang Liu, Yun Xing, Tao Meng, Lanping Ma, Jinpeng Pei, Ying Cong, Xuesai Zhang, Zhiqiang Ren, Xin Wang, Jingkang Shen, and Ker Yu
<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>2371</td>
<td>Calcium Channel Blockers Impair the Antitumor Activity of Anti-CD20 Monoclonal Antibodies by Blocking EGR-1 Induction</td>
<td>Ivana Spasevska, Eva Laure Matera, Kamel Chettab, Jade Ville, Marie Potier-Cartereau, Lars Petter Jordheim, Catherine Thieblemont, Denis Sahin, Christian Klein, and Charles Dumontet</td>
</tr>
<tr>
<td>2382</td>
<td>Nf1-Mutant Tumors Undergo Transcriptome and Kinome Remodeling after Inhibition of either mTOR or MEK</td>
<td>Daniela Pucciarelli, Steven P. Angus, Benjamin Huang, Chi Zhang, Hiroki J. Nakaoka, Ganesh Krishnamurthi, Sourav Bandyopadhyay, D. Wade Clapp, Kevin Shannon, Gary L. Johnson, and Jean L. Nakamura</td>
</tr>
<tr>
<td>2396</td>
<td>Enhanced Immunotherapy with LHHR-R Targeted Lytic Peptide in Ovarian Cancer</td>
<td>Mark Seungwook Kim, Shaolin Ma, Anca Chelaru-Raicu, Carola Leuschner, Hector W. Allá, Sanghoon Lee, Robert L. Coleman, and Anil K. Sood</td>
</tr>
</tbody>
</table>

**CANCER BIOLOGY AND TRANSLATIONAL STUDIES**

**ABOUT THE COVER**

In this issue of Molecular Cancer Therapeutics, Jin and colleagues describe the discovery and mechanism of novel anti-CD73 antibody (Hu001) and CD73-ADC (Hu001-MMAE). High CD73 staining was found in lung cancer epithelial tumor cells and stromal cells in tumor microenvironment, pictured on our cover. The anti-tumor efficacy of Hu001 required both the Fc-dependent cell-mediated cytotoxicity and a multifaceted remodeling in the tumor immune microenvironment. The novel Hu001-MMAE elicited dramatic dual benefits in killing CD73-high tumors while simultaneously promoting the effector function in T lymphocytes and dendritic cells. Read the full article on page 2340.