Highlights of This Issue 2183

REVIEW
2185  Cabozantinib in Combination with Immunotherapy for Advanced Renal Cell Carcinoma and Urothelial Carcinoma: Rationale and Clinical Evidence
Paulo Bergerot, Peter Lamb, Evelyn Wang, and Sumanta K. Pal

SMALL MOLECULE THERAPEUTICS
2194  FGF401, A First-In-Class Highly Selective and Potent FGFR4 Inhibitor for the Treatment of FGFR19-Driven Hepatocellular Cancer
Andreas Weiss, Flavia Adler, Alexandra Buhles, Christelle Stamm, Robin A. Fairhurst, Michael Kiffer, Dario Sterker, Mario Centeleghe, Markus Wattmann, Jacqueline Kinyamu-Akunda, Heiko S. Schadt, Philippe Coutet, Armin Wolf, Youzhen Wang, Patrizia Barzaghi-Rinaudo, Masato Muzakami, Audrey Kauffmann, Thomas Knoepfel, Nicole Buschmann, Catherine Leblanc, Robert Mah, Pascal Furet, Jutta Blank, Francesco Hofmann, William R. Sellers, and Diana Graus Porta

Aurora A–Selective Inhibitor LY3295668 Leads to Dominant Mitotic Arrest, Apoptosis in Cancer Cells, and Shows Potent Preclinical Antitumor Efficacy

2207  Short- and Long-Term Effects of CDK4/6 Inhibition on Early-Stage Breast Cancer

2233  Ovarian Primary and Metastatic Tumors Suppressed by Survivin Knockout or a Novel Survivin Inhibitor
Guannan Zhao, Qinghui Wang, Zhongzhi Wu, Xinchun Tian, Huan Yan, Baojin Wang, Peixin Dong, Hidemichi Watari, Lawrence M. Pfeffer, Yuqi Guo, Wei Li, and Junming Yue

2246  Anti–B-cell Maturation Antigen Chimeric Antigen Receptor T cell Function against Multiple Myeloma Is Enhanced in the Presence of Lenalidomide
Melissa Works, Neha Soni, Collin Hauskins, Catherine Sierra, Alex Baturevych, Ian C. Jones, Wendy Curtis, Patrick Carlson, Timothy G. Johnstone, David Kugler, Ronald J. Hause, Yue Jiang, Lindsey Wimberly, Christopher R. Clouser, Heidi K. Jessup, Blythe Sather, Ruth A. Salmon, and Michael O. Potts

2258  Lenalidomide Augments the Antitumor Activities of Eps8 Peptide-Specific Cytotoxic T Lymphocytes against Multiple Myeloma
Xiaoling Xie, Yiran Chen, YuXing Hu, Yanjie He, Honghao Zhang, and Yuhua Li

2270  Fenretinide via NOXA Induction, Enhanced Activity of the BCL-2 Inhibitor Venetoclax in High BCL-2–Expressing Neuroblastoma Preclinical Models
Thinh H. Nguyen, Balakrishna Koneru, Sung-Jen Wei, Wan Hsi Chen, Monish Ram Makena, Eduardo Urias, Min H. Kang, and C. Patrick Reynolds

2283  CNDAC-Induced DNA Double-Strand Breaks Cause Aberrant Mitosis Prior to Cell Death
Xiaojun Liu, Yingjun Jiang, Kei-ichi Takata, Billie Nowak, Chaomei Liu, Richard D. Wood, Walter N. Hittelman, and William Plunkett

2296  Morin Inhibits Proliferation and Induces Apoptosis by Modulating the miR-188-5p/PTEN/AKT Regulatory Pathway in CML Cells
Zi-Yuan Nie, Lin Yang, Xiao-Jun Liu, Zhan Yang, Gao-Shan Yang, Jing Zhou, Yan Qin, Jing Yu, Ling-Ling Jiang, Jian-Kun Wen, and Jian-Min Luo

2308  Fenretinide, Tocilizumab, and Reparixin Provide Multifaceted Disruption of Oral Squamous Cell Carcinoma Stem Cell Properties: Implications for Tertiary Chemoprevention
Susan R. Mallery, Daren Wang, Brian Santiago, Ping Pei, Caroline Bissonnette, Jhaneyti Asiri Jayawardena, Steven P. Schwendeman, Richard Spinney, and James Lang
Ketotifen Modulates Mast Cell Chemotaxis to Kit-Ligand, but Does Not Impact Mast Cell Numbers, Degranulation, or Tumor Behavior in Neurofibromas of Nf1-Deficient Mice

Ciersten A. Burks, Steven D. Rhodes, Waylan K. Bessler, Shi Chen, Abhi Smith, Jeffrey R. Gehlhausen, Eric T. Hawley, Li Jiang, Xiaohong Li, Jin Yuan, Qingbo Lu, Max Jacobsen, George E. Sandusky, David R. Jones, D. Wade Clapp, and Jaishri O. Blakeley

Microvesicle-Mediated Delivery of Minicircle DNA Results in Effective Gene-Directed Enzyme Prodrug Cancer Therapy


Utility of the RIG-I Agonist Triphosphate RNA for Melanoma Therapy

Mike W. Helms, Kerstin Jahn-Hofmann, Felix Gnerlich, Christiane Metz-Weidmann, Monika Braun, Gabriele Dietert, Petra Scheer, Kai Grandier, Joachim Thielhaber, Hui Cao, Timothy R. Wagenaar, Max M. Schnurr, Stefan Endres, Dmitri Wiederschain, Sabine Scheidler, Simon Rothenfußer, Bodo Brunner, and Lars M. König

Acquired Resistance to EGFR TKIs Mediated by TGFβ/Integrin β3 Signaling in EGFR-Mutant Lung Cancer

Caiyun Wang, Tao Wang, Dacheng Lv, Ling Li, Jinnan Yue, Hong-Zhuang Chen, and Lu Xu

Tumor Intrinsic Efficacy by SHP2 and RTK Inhibitors in KRAS-Mutant Cancers


Exploiting Arginine Auxotrophy with Pegylated Arginine Deiminase (ADI-PEG20) to Sensitize Pancreatic Cancer to Radiotherapy via Metabolic Dysregulation

Pankaj K. Singh, Amit A. Deorukhkar, Bhanu P. Venkatesulu, Xiaolin Li, Ramesh Tailor, John S. Bomalaski, and Sunil Krishnan

Is the Fate of Clinical Candidate Arry-520 Already Sealed? Predicting Resistance in Eg5-Inhibitor Complexes

Rose-Laure Indorato, Sandeep K. Talapatra, Fangzhu Lin, Shozeb Haider, Simon P. Mackay, Frank Kozielski, and Dimitrios A. Skoufias

Inhibition of AKT Sensitizes Cancer Cells to Antineoplastic Drugs by Downregulating Flap Endonuclease 1

Hong Zhu, Congyu Wu, Tinger Wu, Wen Xia, Shusheng Ci, Weiru He, Yilan Zhang, Lulu Li, Shiyong Zhou, Jing Zhang, Ashlin M. Edick, Anna Zhang, Fei-Yan Pan, Zhigang Hu, Lingfeng He, and Zhigang Guo

Distinct Transcriptional Programming Drive Response to MAPK Inhibition in BRAFV600E-Mutant Melanoma Patient-Derived Xenografts

Tianshu Feng, Javad Golji, Ailing Li, Xiamei Zhang, David A. Ruddy, Daniel P. Rakie, Felipe C. Geyer, Jane Gu, Hui Gao, Juliet A. Williams, Darrin D. Stuart, and Matthew J. Meyer

Transcription Factor SOX18 Promotes Clear Cell Renal Cell Carcinoma Progression and Alleviates Cabozantinib-Mediated Inhibitory Effects

Yun Huaqi, Qin Caipeng, Wang Qiang, Du Yiqing, Dai Xiang, Tang Xu, Zhang Xiaowei, Li Qing, Liu Shijun, and Xu Tao

Hyaluronic Acid Binding to TLR4 Promotes Proliferation and Blocks Apoptosis in Colon Cancer

Sarbeet Makkar, Terrence E. Riehl, Baosheng Chen, Yan Yan, David M. Alvarado, Matthew A. Gioorba, and William F. Stenson

Transgelin 2 Promotes Paclitaxel Resistance, Migration, and Invasion of Breast Cancer by Directly Interacting with PTEN and Activating PI3K/Akt/GSK-3β Pathway

Leichao Liu, Ti Meng, Xiaowei Zheng, Yang Liu, Ruifang Hao, Yan Yan, Siying Chen, Haisheng You, Jianfeng Xing, and Yalin Dong
Pancreatic cancer is notoriously difficult to treat. One potential opportunity for targeting pancreatic cancer is through its modified amino acid metabolism. Specifically, depriving arginine-dependent tumor cells of arginine can lead to cell death. To achieve this, a polyethylene glycol (PEG)-conjugated arginine deiminase construct (ADI-PEG20) was previously designed and tested as a monotherapy in clinical studies with limited success. In the cover image, adapted from Figure 3 of the associated manuscript, Singh and colleagues demonstrate ADI-PEG20 radiosensitized pancreatic cancer cells by inducing ER stress (red fluorescence, BIP). Therefore, ADI-PEG20 could be combined with radiation therapy in patients whose tumors are arginine-dependent. Read the full study on page 2381.