


## Highlights of This Issue 1897

## REVIEWS

- 1899**  **ATM Dysfunction in Pancreatic Adenocarcinoma and Associated Therapeutic Implications**  
Samantha A. Armstrong, Christopher W. Shultz, Ariana Azimi-Sadjadi, Jonathan R. Brody, and Michael J. Pishvaian
- 1909** **Targeting the EGFR and Immune Pathways in Squamous Cell Carcinoma of the Head and Neck (SCCHN): Forging a New Alliance**  
Nabil F. Saba, Zhuo Gerogia Chen, Missak Haigentz, Paolo Bossi, Alessandra Rinaldo, Juan P. Rodrigo, Antti A. Mäkitie, Robert P. Takes, Primož Stojan, Jan B. Vermorken, and Alfio Ferlito

## SMALL MOLECULE THERAPEUTICS

- 1916** **First-in-Class Phosphorylated-p68 Inhibitor RX-5902 Inhibits  $\beta$ -Catenin Signaling and Demonstrates Antitumor Activity in Triple-Negative Breast Cancer**  
Anna Capasso, Stacey M. Bagby, Kyrie L. Dailey, Naomi Currimjee, Betelehem W. Yacob, Anastasia Ionkina, Julie G. Frank, Deog Joong Kim, Christina George, Young B. Lee, Ely Benaim, Brian Gittleman, Sarah J. Hartman, Aik Choon Tan, Jihye Kim, Todd M. Pitts, S. Gail Eckhardt, John J. Tentler, and Jennifer R. Diamond
- 1926**  **Targeting the Somatostatin Receptor 2 with the Miniaturized Drug Conjugate, PEN-221: A Potent and Novel Therapeutic for the Treatment of Small Cell Lung Cancer**  
Kerry A. Whalen, Brian H. White, James M. Quinn, Kristina Kriksciukaite, Rossitza Alargova, Tsun P. Au Yeung, Patrick Bazinet, Adam Brockman, Michelle M. DuPont, Haley Oller, James Gifford, Charles-Andre Lemelin, Patrick Lim Soo, Samantha Perino, Benoît Moreau, Gitanjali Sharma, Rajesh Shinde, Beata Sweryda-Krawiec, Mark T. Bilodeau, and Richard Wooster
- 1937** **Assessing Metabolic Intervention with a Glutaminase Inhibitor in Real-Time by Hyperpolarized Magnetic Resonance in Acute Myeloid Leukemia**  
Niki M. Zacharias, Natalia Baran, Sriram S. Shanmugavelandy, Jaehyuk Lee, Juliana Velez Lujan, Prasanta Dutta, Steven W. Millward, Tianyu Cai, Christopher G. Wood, David Piwnica-Worms, Marina Konopleva, and Pratip K. Bhattacharya

- 1947** **Antitumor Activity and Mechanistic Characterization of APE1/Ref-1 Inhibitors in Bladder Cancer**  
Melissa L. Fishel, Hanyu Xia, Jack McGeown, David W. McIlwain, May Elbanna, Ariel A. Craft, Hristos Z. Kaimakliotis, George E. Sandusky, Chi Zhang, Roberto Pili, Mark R. Kelley, and Travis J. Jerde
- 1961** **DHA-SBT-1214 Taxoid Nanoemulsion and Anti-PD-L1 Antibody Combination Therapy Enhances Antitumor Efficacy in a Syngeneic Pancreatic Adenocarcinoma Model**  
Gulzar Ahmad, Gerardo G. Mackenzie, James Egan, and Mansoor M. Amiji
- 1973** **The Novel Small-Molecule SR18662 Efficiently Inhibits the Growth of Colorectal Cancer *In Vitro* and *In Vivo***  
Julie Kim, Chao Wang, Ainara Ruiz de Sabando, Hannah L. Cole, Timothy J. Huang, Jie Yang, Thomas D. Bannister, Vincent W. Yang, and Agnieszka B. Bialkowska
- 1985** **KIT-Dependent and KIT-Independent Genomic Heterogeneity of Resistance in Gastrointestinal Stromal Tumors — TORC1/2 Inhibition as Salvage Strategy**  
Thomas Mühlenberg, Julia Ketzer, Michael C. Heinrich, Susanne Grunewald, Adrian Marino-Enriquez, Marcel Trautmann, Wolfgang Hartmann, Eva Wardelmann, Jürgen Treckmann, Karl Worm, Stefanie Bertram, Thomas Herold, Hans-Ulrich Schildhaus, Hanno Glimm, Albrecht Stenzinger, Benedikt Brors, Peter Horak, Peter Hohenberger, Stefan Fröhling, Jonathan A. Fletcher, and Sebastian Bauer
- 1997** **Suppression of Prostate Cancer Pathogenesis Using an MDA-9/Syntenin (SDCBP) PDZ1 Small-Molecule Inhibitor**  
Swadesh K. Das, Timothy P. Kegelman, Anjan K. Pradhan, Xue-Ning Shen, Praveen Bhoopathi, Sarmistha Talukdar, Santanu Maji, Devanand Sarkar, Luni Emdad, and Paul B. Fisher

# Table of Contents

## LARGE MOLECULE THERAPEUTICS

- 2008** **Preclinical Efficacy and Safety Comparison of CD3 Bispecific and ADC Modalities Targeting BCMA for the Treatment of Multiple Myeloma**  
Siler H. Panowski, Tracy C. Kuo, Yi Zhang, Amy Chen, Tao Geng, Laura Aschenbrenner, Cris Kamperschroer, Edward Pascua, Wei Chen, Kathy Delaria, Santiago Farias, Marjorie Bateman, Russell G. Dushin, Sherman M. Chin, Thomas J. Van Blarcom, Yik Andy Yeung, Kevin C. Lindquist, Allison G. Chunyk, Bing Kuang, Bora Han, Michael Mirsky, Ingrid Pardo, Bernard Buetow, Thomas G. Martin, Jeffrey L. Wolf, David Shelton, Arvind Rajpal, Pavel Strop, Javier Chaparro-Riggers, and Barbra J. Sasu
- 2021** **Anti-miRNA Oligonucleotide Therapy for Chondrosarcoma**  
Xiaojuan Sun, Yupeng Chen, Hongchuan Yu, Jason T. Machan, Ashna Alladin, Jose Ramirez, Ross Taliano, Jesse Hart, Qian Chen, and Richard M. Terek
- 2030** **Development of Therapeutic Anti-JAGGED1 Antibodies for Cancer Therapy**  
Massimo Masiero, Demin Li, Pat Whiteman, Carol Bentley, Jenny Greig, Tasneem Hassanali, Sarah Watts, Stephen Stribbling, Jenna Yates, Ellen Bealing, Ji-Liang Li, Chandramouli Chillakuri, Devon Sheppard, Sébastien Serres, Manuel Sarmiento-Soto, James Larkin, Nicola R. Sibson, Penny A. Handford, Adrian L. Harris, and Alison H. Banham
- 2043** **U3-1402, a Novel HER3-Targeting Antibody-Drug Conjugate, for the Treatment of Colorectal Cancer**  
Shigehiro Koganemaru, Yasutoshi Kuboki, Yoshikatsu Koga, Takashi Kojima, Mayumi Yamauchi, Naoyuki Maeda, Takashi Kagari, Kenji Hirotani, Masahiro Yasunaga, Yasuhiro Matsumura, and Toshihiko Doi
- 2051** **Preclinical Development of the Anti-LAG-3 Antibody REGN3767: Characterization and Activity in Combination with the Anti-PD-1 Antibody Cemiplimab in Human PD-1xLAG-3-Knockin Mice**  
Elena Burova, Aynur Hermann, Jie Dai, Erica Ullman, Gabor Halasz, Terra Potocky, Seongwon Hong, Matt Liu, Omaira Allbritton, Amy Woodruff, Jerry Pei, Ashique Rafique, William Poueymirou, Joel Martin, Douglas MacDonald, William C. Olson, Andrew Murphy, Ella Ioffe, Gavin Thurston, and Markus Mohrs

## CANCER BIOLOGY AND TRANSLATIONAL STUDIES

- 2063** **PARP1 Inhibition Radiosensitizes Models of Inflammatory Breast Cancer to Ionizing Radiation**  
Anna R. Michmerhuizen, Andrea M. Pesch, Leah Moubadder, Benjamin C. Chandler, Kari Wilder-Romans, Meleah Cameron, Eric Olsen, Dafydd G. Thomas, Amanda Zhang, Nicole Hirsh, Cassandra L. Ritter, Meilan Liu, Shyam Nyati, Lori J. Pierce, Reshma Jaggi, and Corey Speers
- 2074** **Tumor Priming by SMO Inhibition Enhances Antibody Delivery and Efficacy in a Pancreatic Ductal Adenocarcinoma Model**  
Jun Wang, Darren K.W. Chan, Arindam Sen, Wen Wee Ma, and Robert M. Straubinger
- 2085** **Glibenclamide Targets Sulfonylurea Receptor 1 to Inhibit p70S6K Activity and Upregulate KLF4 Expression to Suppress Non-Small Cell Lung Carcinoma**  
Kexin Xu, Geng Sun, Min Li, Hongling Chen, Zuhao Zhang, Xixi Qian, Ping Li, Lin Xu, Wenbin Huang, and Xuerong Wang
- 2097** **Target Deconvolution of a Multikinase Inhibitor with Antimetastatic Properties Identifies TAOK3 as a Key Contributor to a Cancer Stem Cell-Like Phenotype**  
Yansong Bian, Yaroslav Teper, Lesley A. Mathews Griner, Taylor J. Aiken, Vivek Shukla, Rajarshi Guha, Paul Shinn, Hong-Wu Xin, Holger Pflücke, Astin S. Powers, Dandan Li, Jian-kang Jiang, Paresma Patel, Steven A. Rogers, Jeffrey Aubé, Marc Ferrer, Craig J. Thomas, and Udo Rudloff
- 2111** **COMMD3:BMI1 Fusion and COMMD3 Protein Regulate C-MYC Transcription: Novel Therapeutic Target for Metastatic Prostate Cancer**  
Syed Umbreen, Mudassir Meraj Bandy, Anmbreen Jamroze, Adrian P. Mansini, Arsheed A. Ganaie, Marina G. Ferrari, Raihana Maqbool, Firdous H. Beigh, Paari Murugan, Colm Morrissey, Eva Corey, Badrinath R. Konety, and Mohammad Saleem
- 2124** **Neuregulin Signaling Is a Mechanism of Therapeutic Resistance in Head and Neck Squamous Cell Carcinoma**  
Marta Baro, Cecilia Lopez Sambrooks, Barbara A. Burtness, Mark A. Lemmon, and Joseph N. Contessa

# Table of Contents

**2135** HER-Family Ligands Promote Acquired Resistance to Trastuzumab in Gastric Cancer

Aida Sampera, Francisco Javier Sánchez-Martín, Oriol Arpí, Laura Visa, Mar Iglesias, Sílvia Menéndez, Élisabeth Gaye, Alba Dalmases, Sergi Clavé, Mariona Gelabert-Baldrich, Thomas Tuxen Poulsen, Michael Kragh, Beatriz Bellosillo, Joan Albanell, Ana Rovira, and Clara Montagut

**2146** Targeting PI3K/Akt/mTOR Pathway Identifies Differential Expression and Functional Role of IL8 in Liver Cancer Stem Cell Enrichment

Deniz Cansen Kahraman, Tamer Kahraman, and Rengul Cetin-Atalay

**2158** eIF4A Inhibitors Suppress Cell-Cycle Feedback Response and Acquired Resistance to CDK4/6 Inhibition in Cancer

Tim Kong, Yibo Xue, Regina Cencic, Xianbing Zhu, Anie Monast, Zheng Fu, Virginie Pilon, Veena Sangwan, Marie-Christine Guiot, William D. Foulkes, John A. Porco Jr, Morag Park, Jerry Pelletier, and Sidong Huang

## CORRECTION

**2182** Correction: An Anti-GDNF Family Receptor Alpha 1 (GFRA1) Antibody–Drug Conjugate for the Treatment of Hormone Receptor–Positive Breast Cancer

Sunil Bhakta, Lisa M. Crocker, Yvonne Chen, Meredith Hazen, Melissa M. Schutten, Dongwei Li, Coenraad Kuijl, Rachana Ohri, Fiona Zhong, Kirsten A. Poon, Mary Ann T. Go, Eric Cheng, Robert Piskol, Ron Firestein, Aimee Fourie-O'Donohue, Katherine R. Kozak, Helga Raab, Jo-Anne Hongo, Deepak Sampath, Mark S. Dennis, Richard H. Scheller, Paul Polakis, and Jagath R. Junutula

## MODELS AND TECHNOLOGIES

**2171** Improved Drug Delivery to Brain Metastases by Peptide-Mediated Permeabilization of the Blood–Brain Barrier

Synnøve Nymark Aasen, Heidi Espedal, Christopher Florian Holte, Olivier Keunen, Tine Veronika Karlsen, Olav Tenstad, Zaynah Maheraly, Hrvoje Miletic, Tuyen Hoang, Anne Vaag Eikeland, Habib Baghirov, Dag Erlend Olberg, Geoffrey John Pilkington, Gobinda Sarkar, Robert B. Jenkins, Terje Sundstrøm, Rolf Bjerkvig, and Frits Thorsen



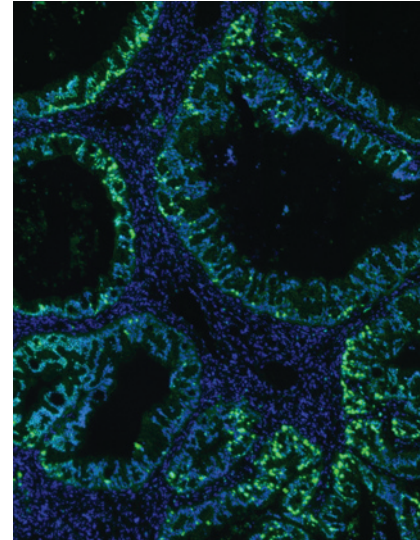
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# Table of Contents

## ABOUT THE COVER

Desmoplasia, hypovascularity, and hypoperfusion work in tandem to prevent antibody therapy of pancreatic adenocarcinoma. In order to disrupt the tumor-stroma interaction and alleviate these factors, Wang and colleagues designed a smoothed inhibitor of sonic hedgehog signaling (NVP-LDE225). In the patient-derived xenograft shown on the cover, NVP-LDE225 reduced the number of Ki67<sup>+</sup> tumor cells (shown in green). Cell nuclei are counterstained in blue. Taken together, their results demonstrate that NVP-LDE225 dosage for five to ten days primes tumors for treatment with therapeutic antibodies such as cetuximab. Their results rationalize future clinical study of NVP-LDE225 in solid tumors. Read the full article on page 2074.



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