




Highlights of This Issue 1793

REVIEWS

- 1795** Strategies to Address Chimeric Antigen Receptor Tonic Signaling
Adam Ajina and John Maher
- 1816** Shedding Light on the Dark Cancer Genomes: Long Noncoding RNAs as Novel Biomarkers and Potential Therapeutic Targets for Cancer
Lin Zhang, Dan Peng, Anil K. Sood, Chi V. Dang, and Xiaomin Zhong
- 1824** We're Not "DON" Yet: Optimal Dosing and Prodrug Delivery of 6-Diazo-5-oxo-L-norleucine
Kathryn M. Lemberg, James J. Vornov, Rana Rais, and Barbara S. Slusher

SMALL MOLECULE THERAPEUTICS

- 1833** AKR1C3 Inhibitor KV-37 Exhibits Antineoplastic Effects and Potentiates Enzalutamide in Combination Therapy in Prostate Adenocarcinoma Cells
Kshitij Verma, Nehal Gupta, Tianzhu Zang, Phumvadee Wangtrakuldee, Sanjay K. Srivastava, Trevor M. Penning, and Paul C. Trippier
- 1846** Novel Trifluoromethylated Enobosarm Analogues with Potent Antiandrogenic Activity *In Vitro* and Tissue Selectivity *In Vivo*
D. Alwyn Dart, Sahar Kandil, Serena Tommasini-Ghelfi, Gilberto Serrano de Almeida, Charlotte L. Bevan, Wenguo Jiang, and Andrew D. Westwell
- 1859** Repositioning Dopamine D2 Receptor Agonist Bromocriptine to Enhance Docetaxel Chemotherapy and Treat Bone Metastatic Prostate Cancer
Yang Yang, Kenza Mamouni, Xin Li, Yanhua Chen, Sravan Kavuri, Yuhong Du, Haiyan Fu, Omer Kucuk, and Daqing Wu
- 1871** Arsenic Trioxide and Sorafenib Induce Synthetic Lethality of FLT3-ITD Acute Myeloid Leukemia Cells
Rui Wang, Ying Li, Ping Gong, Janice Gabrielove, Samuel Waxman, and Yongkui Jing

- 1881** A Quinoline-Based DNA Methyltransferase Inhibitor as a Possible Adjuvant in Osteosarcoma Therapy
Maria Cristina Manara, Sergio Valente, Camilla Cristalli, Giordano Nicoletti, Lorena Landuzzi, Clemens Zwergel, Roberta Mazzone, Giulia Stazi, Paola B. Arimondo, Michela Pasello, Clara Guerzoni, Piero Picci, Patrizia Nanni, Pier-Luigi Lollini, Antonello Mai, and Katia Scotlandi
- 1893** Efficacy of the MDM2 Inhibitor SAR405838 in Glioblastoma Is Limited by Poor Distribution Across the Blood–Brain Barrier
Minjee Kim, Daniel J. Ma, David Calligaris, Shuangling Zhang, Ryan W. Feathers, Rachael A. Vaubel, Isabelle Meaux, Ann C. Mladek, Karen E. Parrish, Fang Jin, Cedric Barriere, Laurent Debussche, James Watters, Shulan Tian, Paul A Decker, Jeanette E. Eckel-Passow, Gaspar J. Kitange, Aaron J. Johnson, Ian F. Parney, Panos Z. Anastasiadis, Nathalie Y.R. Agar, William F. Elmquist, and Jann N. Sarkaria
- 1902** Therapeutic Targeting of KDM1A/LSD1 in Ewing Sarcoma with SP-2509 Engages the Endoplasmic Reticulum Stress Response 
Kathleen I. Pishas, Christina D. Drenberg, Cenny Taslim, Emily R. Theisen, Kirsten M. Johnson, Ranajeet S. Saund, Ioana L. Pop, Brian D. Crompton, Elizabeth R. Lawlor, Franck Tirode, Jaume Mora, Olivier Delattre, Mary C. Beckerle, David F. Callen, Sunil Sharma, and Stephen L. Lessnick
- 1917** STAT3 Cyclic Decoy Demonstrates Robust Antitumor Effects in Non–Small Cell Lung Cancer 
Christian Njatcha, Mariya Farooqui, Adam Kornberg, Daniel E. Johnson, Jennifer R. Grandis, and Jill M. Siegfried
- 1927** Anti-PSMA/CD3 Bispecific Antibody Delivery and Antitumor Activity Using a Polymeric Depot Formulation 
Wilhem Leconet, He Liu, Ming Guo, Sophie Le Lamer-Déchamps, Charlotte Molinier, Sae Kim, Tjasa Vrlinic, Murielle Oster, Fang Liu, Vicente Navarro, Jaspreet S. Batra, Adolfo Lopez Noriega, Sylvestre Grizot, and Neil H. Bander

LARGE MOLECULE THERAPEUTICS

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1941 Intratumoral Delivery of an Adenoviral Vector Carrying the *SOCS-1* Gene Enhances T-Cell-Mediated Antitumor Immunity By Suppressing PD-L1
Satoshi Nakagawa, Satoshi Serada, Reisa Kakubari, Kosuke Hiramatsu, Takahito Sugase, Shinya Matsuzaki, Satoko Matsuzaki, Yutaka Ueda, Kiyoshi Yoshino, Tomoharu Ohkawara, Minoru Fujimoto, Tadimitsu Kishimoto, Tadashi Kimura, and Tetsuji Naka

1951 Recombinant MDA-7/IL24 Suppresses Prostate Cancer Bone Metastasis through Downregulation of the Akt/Mcl-1 Pathway
Anjan K. Pradhan, Praveen Bhoopathi, Sarmistha Talukdar, Xue-Ning Shen, Luni Emdad, Swadesh K. Das, Devanand Sarkar, and Paul B. Fisher

1961 Leukocyte Differentiation by Histidine-Rich Glycoprotein/Stanniocalcin-2 Complex Regulates Murine Glioma Growth through Modulation of Antitumor Immunity
Francis P. Roche, Ilkka Pietilä, Hiroshi Kaito, Elisabet O. Sjöström, Nadine Sobotzki, Oriol Noguera, Tor Persson Skare, Magnus Essand, Bernd Wollscheid, Michael Welsh, and Lena Claesson-Welsh

CANCER BIOLOGY AND TRANSLATIONAL STUDIES

1973 KDM6B Counteracts EZH2-Mediated Suppression of *IGFBP5* to Confer Resistance to PI3K/AKT Inhibitor Treatment in Breast Cancer
Wenyu Wang, Keng Gat Lim, Min Feng, Yi Bao, Puay Leng Lee, Yu Cai, Yufeng Chen, Hao Zhang, Diego Marzese, Dave S.B. Hoon, and Qiang Yu

1984 Identification of FDA-Approved Oncology Drugs with Selective Potency in High-Risk Childhood Ependymoma
Andrew M. Donson, Vladimir Amani, Elliot A. Warner, Andrea M. Griesinger, Davis A. Witt, Jean M. Mulcahy Levy, Lindsey M. Hoffman, Todd C. Hankinson, Michael H. Handler, Rajeev Vibhakar, Kathleen Dorris, and Nicholas K. Foreman

1995 Nuclear PTEN Localization Contributes to DNA Damage Response in Endometrial Adenocarcinoma and Could Have a Diagnostic Benefit for Therapeutic Management of the Disease
Ananda Mukherjee, Amanda L. Patterson, Jitu W. George, Tyler J. Carpenter, Zachary B. Madaj, Galen Hostetter, John I. Risinger, and Jose M. Teixeira

2004 The Role of Pyruvate Dehydrogenase Kinase-4 (PDK4) in Bladder Cancer and Chemoresistance
Benjamin L. Woolbright, Dharamainder Choudhary, Andrew Mikhalyuk, Cassandra Trammel, Sambantham Shanmugam, Erika Abbott, Carol C. Pilbeam, and John A. Taylor III

2013 Induction of Thioredoxin-Interacting Protein by a Histone Deacetylase Inhibitor, Entinostat, Is Associated with DNA Damage and Apoptosis in Esophageal Adenocarcinoma
Paul L. Feingold, Deborah R. Surman, Kate Brown, Yuan Xu, Lucas A. McDuffie, Vivek Shukla, Emily S. Reardon, Daniel R. Crooks, Jane B. Trepel, Sunmin Lee, Min-Jung Lee, Shaojian Gao, Sichuan Xi, Kaitlin C. McLoughlin, Laurence P. Diggs, David G. Beer, Derek J. Nancarrow, Leonard M. Neckers, Jeremy L. Davis, Chuong D. Hoang, Jonathan M. Hernandez, David S. Schrupp, and R. Taylor Ripley

2024 Dual Targeting of ERBB2/ERBB3 for the Treatment of SLC3A2-NRG1-Mediated Lung Cancer
Dong Hoon Shin, Jeong Yeon Jo, and Ji-Youn Han

2034 Targeting Notch1 and *IKK α* Enhanced NF- κ B Activation in CD133⁺ Skin Cancer Stem Cells
Xin Xin Quan, Nga Voong Hawk, Weiping Chen, Jamie Coupar, Steven K. Lee, David W. Petersen, Paul S. Meltzer, Andrew Montemarano, Martin Braun, Zhong Chen, and Carter Van Waes

2049 Role of EphB3 Receptor in Mediating Head and Neck Tumor Growth, Cell Migration, and Response to PI3K Inhibitor
Shilpa Bhatia, Anastacia Griego, Shelby Lennon, Ayman Oweida, Jaspreet Sharma, Christina Rohmer, Nomin Uyanga, Sanjana Bukkapatnam, Benjamin Van Court, David Raben, Christian Young, Lynn Heasley, and Sana D. Karam

COMPANION DIAGNOSTIC, PHARMACOGENOMIC, AND CANCER BIOMARKERS

2060 Drug-Sensitivity Screening and Genomic Characterization of 45 HPV-Negative Head and Neck Carcinoma Cell Lines for Novel Biomarkers of Drug Efficacy
Tatiana Lepikhova, Piia-Riitta Karhemo, Riku Louhimo, Bhagwan Yadav, Astrid Murumägi, Evgeny Kuleskiy, Mikko Kivento, Harri Sihto, Reidar Grénman, Stina M. Syrjänen, Olli Kallioniemi, Tero Aittokallio, Krister Wennerberg, Heikki Joensuu, and Outi Monni

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2073 Retraction: Garcinol Potentiates TRAIL-Induced Apoptosis through Modulation of Death Receptors and Antiapoptotic Proteins

2074 Retraction: Coronarin D, a Labdane Diterpene, Inhibits both Constitutive and Inducible Nuclear Factor- κ B Pathway Activation, Leading to Potentiation of Apoptosis, Inhibition of Invasion, and Suppression of Osteoclastogenesis

2075 Retraction: Potentiation of Paclitaxel Activity by the HSP90 Inhibitor 17-allylamino-17-demethoxygeldanamycin in Human Ovarian Carcinoma Cell Lines with High Levels of Activated AKT



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ABOUT THE COVER

Chimeric antigen receptors (CARs) are synthetic proteins in which an extracellular antigen-targeting moiety is fused to a bespoke intracellular signalling domain. The adoptive transfer of autologous CAR T-cells targeting B-cell tumor-associated antigens is now commonplace in the clinic. However, emerging evidence indicates that these receptors may sometimes signal in a tonic, ligand-independent fashion. This diagram highlights several potential strategies to prevent unintended CAR activation and thereby address the negative consequences of unconstrained tonic signalling upon CAR T-cell efficacy and persistence.

