




## 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 $\alpha$*  Enhanced NF- $\kappa$ B Activation in CD133<sup>+</sup> 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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**2072** Retraction:  $\gamma$ -Tocotrienol Promotes TRAIL-Induced Apoptosis through Reactive Oxygen Species/Extracellular Signal-Regulated Kinase/p53-Mediated Upregulation of Death Receptors

**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- $\kappa$ 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.



# Molecular Cancer Therapeutics

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