

## Highlights of This Issue 1877

## SPECIAL FEATURES

## CCR Translations

**1879** Can an Immune Checkpoint Inhibitor (Sometimes) Make Things Worse?

Elad Sharon

*See related article, p. 1920*

## CCR Perspectives in Regulatory Science and Policy

**1882** FDA's Approach to Regulating Biosimilars

Steven J. Lemery, M. Stacey Ricci, Patricia Keegan, Amy E. McKee, and Richard Pazdur

## CCR Drug Updates

**1886** Atezolizumab: A PD-L1–Blocking Antibody for Bladder Cancer

Brant A. Inman, Thomas A. Longo, Sundhar Ramalingam, and Michael R. Harrison

## Molecular Pathways

**1891** Molecular Pathways: Revisiting Glycogen Synthase Kinase-3 $\beta$  as a Target for the Treatment of Cancer

Amy Walz, Andrey Ugolkov, Sunandana Chandra, Alan Kozikowski, Benedito A. Carneiro, Thomas V. O'Halloran, Francis J. Giles, Daniel D. Billadeau, and Andrew P. Mazar

## CANCER THERAPY: CLINICAL

**1898** Long-term Survival in Glioblastoma with Cytomegalovirus pp65-Targeted Vaccination

Kristen A. Batich, Elizabeth A. Reap, Gary E. Archer, Luis Sanchez-Perez, Smita K. Nair, Robert J. Schmittling, Pam Norberg, Weihua Xie, James E. Herndon II, Patrick Healy, Roger E. McLendon, Allan H. Friedman, Henry S. Friedman, Darell Bigner, Gordana Vlahovic, Duane A. Mitchell, and John H. Sampson

**1910** A First-in-Human Phase I Study of a Bivalent MET Antibody, Emibetuzumab (LY2875358), as Monotherapy and in Combination with Erlotinib in Advanced Cancer

Lee S. Rosen, Jonathan W. Goldman, Alain P. Algazi, P. Kellie Turner, Brian Moser, Tianle Hu, Xuejing Aimee Wang, Jay Tuttle, Volker Wacheck, James E. Wooldridge, and Michaela Banck

**1920** Hyperprogressive Disease Is a New Pattern of Progression in Cancer Patients Treated by Anti-PD-1/PD-L1

Stéphane Champiat, Laurent Derle, Samy Ammari, Christophe Massard, Antoine Hollebecque, Sophie Postel-Vinay, Nathalie Chaput, Alexander Eggermont, Aurélien Marabelle, Jean-Charles Soria, and Charles Ferte

*See related commentary, p. 1879***1929** Results from an Integrated Safety Analysis of Urelumab, an Agonist Anti-CD137 Monoclonal Antibody

Neil H. Segal, Theodore F. Logan, F. Stephen Hodi, David McDermott, Ignacio Melero, Omid Hamid, Henrik Schmidt, Caroline Robert, Vanna Chiarion-Sileni, Paolo A. Ascierto, Michele Maio, Walter J. Urba, Tara C. Gangadhar, Satyendra Suryawanshi, Jaclyn Neely, Maria Jure-Kunkel, Suba Krishnan, Holbrook Kohrt, Mario Sznol, and Ronald Levy

**1937** Randomized, Placebo-Controlled, Phase II Study of Veliparib in Combination with Carboplatin and Paclitaxel for Advanced/Metastatic Non–Small Cell Lung Cancer

Suresh S. Ramalingam, Normand Blais, Julien Mazieres, Martin Reck, C. Michael Jones, Erzsebet Juhasz, Laszlo Urban, Sergey Orlov, Fabrice Barlesi, Ebenezer Kio, Ulrich Keiholz, Qin Qin, Jiang Qian, Caroline Nickner, Juliann Dziubinski, Hao Xiong, Peter Ansell, Mark McKee, Vincent Giranda, and Vera Gorbunova

**1945** A Novel Compound ARN-3236 Inhibits Salt-Inducible Kinase 2 and Sensitizes Ovarian Cancer Cell Lines and Xenografts to Paclitaxel

Jinhua Zhou, Albandri Alfraidi, Shu Zhang,

Janice M. Santiago-O'Farrill,

Venkata Krishna Yerramreddy Reddy, Abdulkhaliq Alsaadi,

Ahmed A. Ahmed, Hailing Yang, Jinsong Liu, Weiqun Mao,

Yan Wang, Hiroshi Takemori, Hariprasad Vankayalapati,

Zhen Lu, and Robert C. Bast Jr

# Table of Contents

## 1955 Integrative Development of a TLR8 Agonist for Ovarian Cancer Chemoimmunotherapy

Bradley J. Monk, Andrea Facciabene, William E. Brady, Carol A. Aghajanian, Paula M. Fracasso, Joan L. Walker, Heather A. Lankes, Kristi L. Manjarrez, Gwenn-ael H. Danet-Desnoyers, Katherine M. Bell-McGuinn, Carolyn K. McCourt, Alexander Malykhin, Robert M. Hershberg, and George Coukos

## 1967 The Added Value of Circulating Tumor Cell Enumeration to Standard Markers in Assessing Prognosis in a Metastatic Castration-Resistant Prostate Cancer Population

Glenn Heller, Karim Fizazi, Robert McCormack, Arturo Molina, David MacLean, Iain J. Webb, Fred Saad, Johann S. de Bono, and Howard I. Scher

## 1974 A Phase II, Randomized, Open-Label Study of Neoadjuvant Degarelix versus LHRH Agonist in Prostate Cancer Patients Prior to Radical Prostatectomy

Rashid K. Sayyid, Andrew Evans, Karen Hersey, Ranjena Maloni, Antonio Hurtado-Coll, Girish Kulkarni, Antonio Finelli, Alexandre R. Zlotta, Robert Hamilton, Martin Gleave, and Neil E. Fleshner

## 2006 A Four-Gene Promoter Methylation Marker Panel Consisting of *GREM1*, *NEURL*, *LAD1*, and *NEFH* Predicts Survival of Clear Cell Renal Cell Cancer Patients

Iris J.H. van Vlodrop, Sophie C. Joosten, Tim De Meyer, Kim M. Smits, Leander Van Neste, Veerle Melotte, Marcella M.L.L. Baldewijns, Leo J. Schouten, Piet A. van den Brandt, Jana Jeschke, Joo Mi Yi, Kornel E. Schuebel, Nita Ahuja, James G. Herman, Maureen J. Aarts, Fred T. Bosman, Wim Van Criekinge, and Manon van Engeland

## 2019 Significant Effect of Polymorphisms in *CYP2D6* on Response to Tamoxifen Therapy for Breast Cancer: A Prospective Multicenter Study



Hitoshi Zembutsu, Seigo Nakamura, Sadako Akashi-Tanaka, Takashi Kuwayama, Chie Watanabe, Tomoko Takamaru, Hiroyuki Takei, Takashi Ishikawa, Kana Miyahara, Hiroshi Matsumoto, Yoshie Hasegawa, Goro Kutomi, Hiroaki Shima, Fukino Satomi, Minoru Okazaki, Hisamitsu Zaha, Mai Onomura, Ayami Matsukata, Yasuaki Sagara, Shinichi Baba, Akimitsu Yamada, Kazuhiro Shimada, Daisuke Shimizu, Koichiro Tsugawa, Arata Shimo, Ern Yu Tan, Mikael Hartman, Ching-Wan Chan, Soo Chin Lee, and Yusuke Nakamura

## PERSONALIZED MEDICINE AND IMAGING

### 1981 Assessment of Total Lesion Glycolysis by <sup>18</sup>F FDG PET/CT Significantly Improves Prognostic Value of GEP and ISS in Myeloma



James E. McDonald, Marcus M. Kessler, Michael W. Gardner, Amy F. Buros, James A. Ntambi, Sarah Waheed, Frits van Rhee, Maurizio Zangari, Christoph J. Heuck, Nathan Petty, Carolina Schinke, Sharmilan Thanendrarajan, Alan Mitchell, Antje Hoering, Bart Barlogie, Gareth J. Morgan, and Faith E. Davies

### 1988 *RET* Aberrations in Diverse Cancers: Next-Generation Sequencing of 4,871 Patients



Shumei Kato, Vivek Subbiah, Erica Marchlik, Sheryl K. Elkin, Jennifer L. Carter, and Razelle Kurzrock

### 1998 Early Detection of Lung Cancer Using DNA Promoter Hypermethylation in Plasma and Sputum

Alicia Hulbert, Ignacio Jusue-Torres, Alejandro Stark, Chen Chen, Kristen Rodgers, Beverly Lee, Candace Griffin, Andrew Yang, Peng Huang, John Wrangle, Steven A. Belinsky, Tza-Huei Wang, Stephen C. Yang, Stephen B. Baylin, Malcolm V. Brock, and James G. Herman

## CANCER THERAPY: PRECLINICAL

### 2027 The MAPK Pathway Regulates Intrinsic Resistance to BET Inhibitors in Colorectal Cancer

Yufang Ma, Lihong Wang, Leif R. Neitzel, Sudan N. Loganathan, Nan Tang, Lili Qin, Emily E. Crispi, Yan Guo, Stefan Knapp, R. Daniel Beauchamp, Ethan Lee, and Jialiang Wang

### 2038 A Potent *In Vivo* Antitumor Efficacy of Novel Recombinant Type I Interferon


Kang-Jian Zhang, Xiao-Fei Yin, Yuan-Qin Yang, Hui-Ling Li, Yan-Ni Xu, Lie-Yang Chen, Xi-Jun Liu, Su-Jing Yuan, Xian-Long Fang, Jing Xiao, Shuai Wu, Hai-Neng Xu, Liang Chu, Kanstantsin V. Katlinski, Yuliya V. Katlinskaya, Rong-Bing Guo, Guang-Wen Wei, Da-Cheng Wang, Xin-Yuan Liu, and Serge Y. Fuchs

### 2050 Ovarian Cancers Harbor Defects in Nonhomologous End Joining Resulting in Resistance to Rucaparib

Aiste McCormick, Peter Donoghue, Michelle Dixon, Richard O'Sullivan, Rachel L. O'Donnell, James Murray, Angelika Kaufmann, Nicola J. Curtin, and Richard J. Edmondson

# Table of Contents

## BIOLOGY OF HUMAN TUMORS

- 2061**  **Fecal Bacteria Act as Novel Biomarkers for Noninvasive Diagnosis of Colorectal Cancer**  
Qiaoyi Liang, Jonathan Chiu, Yingxuan Chen, Yanqin Huang, Akira Higashimori, Jingyuan Fang, Hassan Brim, Hassan Ashktorab, Siew Chien Ng, Simon Siu Man Ng, Shu Zheng, Francis Ka Leung Chan, Joseph Jao Yiu Sung, and Jun Yu
- 2071** **A Positive Feedback Loop of lncRNA-PVT1 and FOXM1 Facilitates Gastric Cancer Growth and Invasion**  
Mi-die Xu, Yiqin Wang, Weiwei Weng, Ping Wei, Peng Qi, Qiongyan Zhang, Cong Tan, Shu-juan Ni, Lei Dong, Yusi Yang, Wanrun Lin, Qinghua Xu, Dan Huang, Zhaohui Huang, Yuqing Ma, Wei Zhang, Weiqi Sheng, and Xiang Du
- 2081** **Integrative Systemic and Local Metabolomics with Impact on Survival in High-Grade Serous Ovarian Cancer**  
Anna Bachmayr-Heyda, Stefanie Aust, Katharina Auer, Samuel M. Meier, Klaus G. Schmetterer, Sabine Dekan, Christopher Gerner, and Dietmar Pils
- 2093** **Tumor Thickness and Mitotic Rate Robustly Predict Melanoma-Specific Survival in Patients with Primary Vulvar Melanoma: A Retrospective Review of 100 Cases**  
Priyadharsini Nagarajan, Jonathan L. Curry, Jing Ning, Jin Piao, Carlos A. Torres-Cabala, Phyu P. Aung, Doina Ivan, Merrick I. Ross, Charles F. Levenback, Michael Frumovitz, Jeffrey E. Gershenwald, Michael A. Davies, Anais Malpica, Victor G. Prieto, and Michael T. Tetzlaff

- 2105** **Overexpression of Functional SLC6A3 in Clear Cell Renal Cell Carcinoma**  
Jennifer Hansson, David Lindgren, Helén Nilsson, Elinn Johansson, Martin Johansson, Lena Gustavsson, and Håkan Axelsson
- 2116** **Cytidine Deaminase Deficiency Reveals New Therapeutic Opportunities against Cancer**  
Hamza Mameri, Ivan Bièche, Didier Meseure, Elisabetta Marangoni, Géraldine Buhagiar-Labarchède, André Nicolas, Sophie Vacher, Rosine Onclercq-Delic, Vinodh Rajapakse, Sudhir Varma, William C. Reinhold, Yves Pommier, and Mounira Amor-Guélet

## CORRECTION

- 2127** **Correction: Inhibition of SOAT1 Suppresses Glioblastoma Growth via Blocking SREBP-1-Mediated Lipogenesis**

 **AC icon indicates Author Choice**

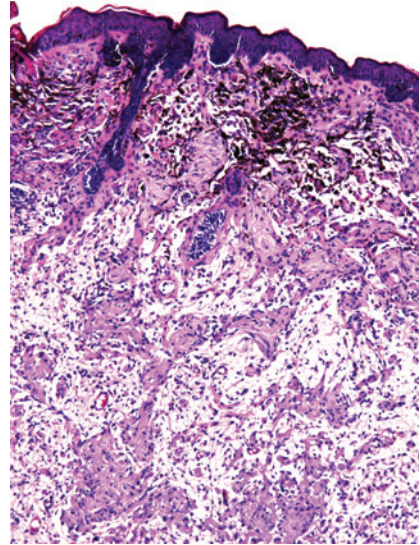
For more information please visit [www.aacrjournals.org](http://www.aacrjournals.org)



# Table of Contents

## ABOUT THE COVER

The cover shows a section of a primary tumor from mice harboring activated *Braf* and inactivated *Pten* in melanocytes that developed a genetically induced melanoma tumor. The staining shows aggressive tumor growth in animals treated with vehicle (as opposed to those treated with novel recombinant sIFN-1 interferon). For details, see the article by Zhang and colleagues on page 2038 of this issue.



# Clinical Cancer Research

**23 (8)**

*Clin Cancer Res* 2017;23:1877-2127.

**Updated version** Access the most recent version of this article at:  
<http://clincancerres.aacrjournals.org/content/23/8>

**E-mail alerts** [Sign up to receive free email-alerts](#) related to this article or journal.

**Reprints and Subscriptions** To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at [pubs@aacr.org](mailto:pubs@aacr.org).

**Permissions** To request permission to re-use all or part of this article, use this link <http://clincancerres.aacrjournals.org/content/23/8>. Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.