

October 15, 2015 • Volume 21 • Number 20

Highlights of This Issue 4497**SPECIAL FEATURES****CCR 20th Anniversary Commentary**

- 4499** CCR 20th Anniversary Commentary: Prospects and Challenges of Therapeutic Nanoparticles in Cancer
Mohammad Aminur Rahman and Dong M. Shin


CCR Translations

- 4502** Imaging Tumor Acidity: pH-Low Insertion Peptide Probe for Optoacoustic Tomography
Yana K. Reshetnyak
See related article, p. 4576
- 4505** Docetaxel Resistance in Prostate Cancer: Taking It Up a Notch
Tian Zhang and Andrew J. Armstrong
See related article, p. 4619

Molecular Pathways

- 4508** Molecular Pathways: Anticancer Activity by Inhibition of Nucleocytoplasmic Shuttling
Fabio Conforti, Yisong Wang, Jose A. Rodriguez, Anna Teresa Alberobello, Yu-Wen Zhang, and Giuseppe Giaccone

Review

- 4514** Invasive Bladder Cancer: Genomic Insights and Therapeutic Promise
 Jaegil Kim, Rehan Akbani, Chad J. Creighton, Seth P. Lerner, John N. Weinstein, Gad Getz, and David J. Kwiatkowski

CCR Focus

- 4526** On Innovating and Inspiring the Clinical Trial Enterprise
Susan E. Bates
- 4527** Advancing Clinical Trials to Streamline Drug Development
Susan E. Bates, Donald A. Berry, Sanjeeve Balasubramaniam, Stuart Bailey, Patricia M. LoRusso, and Eric H. Rubin

- 4536** Next-Generation Sequencing to Guide Clinical Trials

Lillian L. Siu, Barbara A. Conley, Scott Boerner, and Patricia M. LoRusso

- 4545** Expansion Cohorts in First-in-Human Solid Tumor Oncology Trials

Marc R. Theoret, Lee H. Pai-Scherf, Meredith K. Chuk, Tatiana M. Prowell, Sanjeeve Balasubramaniam, Tamy Kim, Geoffrey Kim, Paul G. Kluetz, Patricia Keegan, and Richard Pazdur

- 4552** Failures in Phase III: Causes and Consequences

Bostjan Seruga, Alberto Ocana, Eitan Amir, and Ian F. Tannock

- 4561** The Urgent Need for Clinical Research Reform to Permit Faster, Less Expensive Access to New Therapies for Lethal Diseases



David J. Stewart, Gerald Batist, Hagop M. Kantarjian, John-Peter Bradford, Joan H. Schiller, and Razelle Kurzrock

CANCER THERAPY: CLINICAL

- 4569** Phase I Clinical Trial to Determine the Feasibility and Maximum Tolerated Dose of Panitumumab to Standard Gemcitabine-Based Chemoradiation in Locally Advanced Pancreatic Cancer

Annette A. van Zweeden, Hans J. van der Vliet, Johanna W. Wilmink, Martijn R. Meijerink, Otto W.M. Meijer, Anna M.E. Bruynzeel, Geertjan van Tienhoven, Elisa Giovannetti, Geert Kazemier, Maarten A.J.M. Jacobs, and Henk M.W. Verheul

PERSONALIZED MEDICINE AND IMAGING

- 4576** Targeting Acidity in Pancreatic Adenocarcinoma: Multispectral Optoacoustic Tomography Detects pH-Low Insertion Peptide Probes *In Vivo*

Charles W. Kimbrough, Anil Khanal, Matthew Zeiderman, Bigya R. Khanal, Neal C. Burton, Kelly M. McMasters, Selwyn M. Vickers, William E. Grizzle, and Lacey R. McNally
See related commentary, p. 4502

Table of Contents

4586 Serial Next-Generation Sequencing of Circulating Cell-Free DNA Evaluating Tumor Clone Response To Molecularly Targeted Drug Administration

Jean Sebastien Frenel, Suzanne Carreira, Jane Goodall, Desam Roda, Raquel Perez-Lopez, Nina Tunariu, Ruth Riisnaes, Susana Miranda, Ines Figueiredo, Daniel Nava-Rodrigues, Alan Smith, Christophe Leux, Isaac Garcia-Murillas, Roberta Ferraldeschi, David Lorente, Joaquin Mateo, Michael Ong, Timothy A. Yap, Udai Banerji, Delila Gasi Tandefelt, Nick Turner, Gerhardt Attard, and Johann S. de Bono

4597 Increased Expression of HER2, HER3, and HER2:HER3 Heterodimers in HPV-Positive HNSCC Using a Novel Proximity-Based Assay: Implications for Targeted Therapies

Netanya I. Pollock, Lin Wang, Gerald Wallweber, William E. Gooding, Weidong Huang, Ahmed Chenna, John Winslow, Malabika Sen, Kara A. DeGrave, Hua Li, Yan Zeng, and Jennifer R. Grandis

CANCER THERAPY: PRECLINICAL

4607 Lenalidomide Enhances Immune Checkpoint Blockade-Induced Immune Response in Multiple Myeloma

Güllü Görgün, Mehmet K. Samur, Kristen B. Cowens, Steven Paula, Giada Bianchi, Julie E. Anderson, Randie E. White, Ahaana Singh, Hiroto Ohguchi, Rikio Suzuki, Shohei Kikuchi, Takeshi Harada, Teru Hideshima, Yu-Tzu Tai, Jacob P. Laubach, Noopur Rajee, Florence Magrangeas, Stephane Minvielle, Herve Avet-Loiseau, Nikhil C. Munshi, David M. Dorfman, Paul G. Richardson, and Kenneth C. Anderson

4619 Notch Pathway Inhibition Using PF-03084014, a γ -Secretase Inhibitor (GSI), Enhances the Antitumor Effect of Docetaxel in Prostate Cancer

Di Cui, Jinlu Dai, Jill M. Keller, Atsushi Mizokami, Shujie Xia, and Evan T. Keller
See related commentary, p. 4505

4630 Macitentan, a Dual Endothelin Receptor Antagonist, in Combination with Temozolomide Leads to Glioblastoma Regression and

 Long-term Survival in Mice

Sun-Jin Kim, Ho Jeong Lee, Mark Seungwook Kim, Hyun Jin Choi, Junqin He, Qiuyu Wu, Kenneth Aldape, Jeffrey S. Weinberg, W.K. Alfred Yung, Charles A. Conrad, Robert R. Langley, François Lehenbre, Urs Regenass, and Isaiah J. Fidler

4642 Treatment with Ibrutinib Inhibits BTK- and VLA-4-Dependent Adhesion of Chronic Lymphocytic Leukemia Cells *In Vivo*

Sarah E.M. Herman, Rashida Z. Mustafa, Jade Jones, Deanna H. Wong, Mohammed Farooqui, and Adrian Wiestner

4652 Mevalonate Pathway Antagonist Suppresses Formation of Serous Tubal Intraepithelial Carcinoma and Ovarian Carcinoma in Mouse Models

Yusuke Kobayashi, Hiroyasu Kashima, Ren-Chin Wu, Jin-Gyoung Jung, Jen-Chun Kuan, Jinghua Gu, Jianhua Xuan, Lori Sokoll, Kala Visvanathan, Ie-Ming Shih, and Tian-Li Wang

4663 Dual Targeting of Protein Degradation Pathways with the Selective HDAC6 Inhibitor ACY-1215 and Bortezomib Is Synergistic in Lymphoma

Jennifer E. Amengual, Paul Johannet, Maximilian Lombardo, Kelly Zullo, Daniela Hoehn, Govind Bhagat, Luigi Scotto, Xavier Jirau-Serrano, Dejan Radeski, Jennifer Heinen, Hongfeng Jiang, Serge Cremers, Yuan Zhang, Simon Jones, and Owen A. O'Connor

BIOLOGY OF HUMAN TUMORS

4676 Autocrine Activation of CHRM3 Promotes Prostate Cancer Growth and Castration Resistance via CaM/CaMKK-Mediated Phosphorylation of Akt

Naitao Wang, Ming Yao, Jin Xu, Yizhou Quan, Kaiqing Zhang, Ru Yang, and Wei-Qiang Gao

4686 SMO Gene Amplification and Activation of the Hedgehog Pathway as Novel Mechanisms of Resistance to Anti-Epidermal Growth Factor Receptor Drugs in Human Lung Cancer



Carminia Maria Della Corte, Claudio Bellevedere, Giovanni Vicidomini, Donata Vitagliano, Umberto Malapelle, Marina Accardo, Alessio Fabozzi, Alfonso Fiorelli, Morena Fasano, Federica Papaccio, Erika Martinelli, Teresa Troiani, Giancarlo Troncone, Mario Santini, Roberto Bianco, Fortunato Ciardiello, and Floriana Morgillo

4698 SRRM4 Expression and the Loss of REST Activity May Promote the Emergence of the Neuroendocrine Phenotype in Castration-Resistant Prostate Cancer

Xiaotun Zhang, Ilsa M. Coleman, Lisha G. Brown, Lawrence D. True, Lori Kollath, Jared M. Lucas, Hung-Ming Lam, Ruth Dumpit, Eva Corey, Lisly Chéry, Bryce Lakely, Celestia S. Higano, Bruce Montgomery, Martine Roudier, Paul H. Lange, Peter S. Nelson, Robert L. Vessella, and Colm Morrissey

Table of Contents

4709 Exome Sequencing Reveals *AMER1* as a Frequently Mutated Gene in Colorectal Cancer

Rebeca Sanz-Pamplona, Adriana Lopez-Doriga, Laia Paré-Brunet, Kira Lázaro, Fernando Bellido, M. Henar Alonso, Susanna Aussó, Elisabet Guinó, Sergi Beltrán, Francesc Castro-Giner, Marta Gut, Xavier Sanjuan, Adria Closa, David Cordero, Francisco D. Morón-Duran, Antonio Soriano, Ramón Salazar, Laura Valle, and Victor Moreno

4719 Keap1–Nrf2 Interaction Suppresses Cell Motility in Lung Adenocarcinomas by Targeting the S100P Protein

Ming-Hsien Chien, Wei-Jiunn Lee, Feng-Koo Hsieh, Chia-Feng Li, Tsu-Yao Cheng, Ming-Yang Wang, Jin-Shing Chen, Jyh-Ming Chow, Yi-Hua Jan, Michael Hsiao, Kuo-Tai Hua, and Min-Liang Kuo

4733 Clinical Application of Prognostic Gene Expression Signature in Fusion Gene–Negative Rhabdomyosarcoma: A Report from the Children’s Oncology Group

Pooja Hingorani, Edoardo Missiaglia, Janet Shipley, James R. Anderson, Timothy J. Triche, Mauro Delorenzi, Julie Gastier-Foster, Michele Wing, Douglas S. Hawkins, and Stephen X. Skapek

LETTER TO THE EDITOR

4740 Siltuximab for Multicentric Castleman Disease—Letter

Raphael Teipel, Rainer Ordemann, Ulrike Proske, Frank Dietrich, Marika Mende, Gerhard Ehninger, Frank Kroschinsky, and Uwe Platzbecker

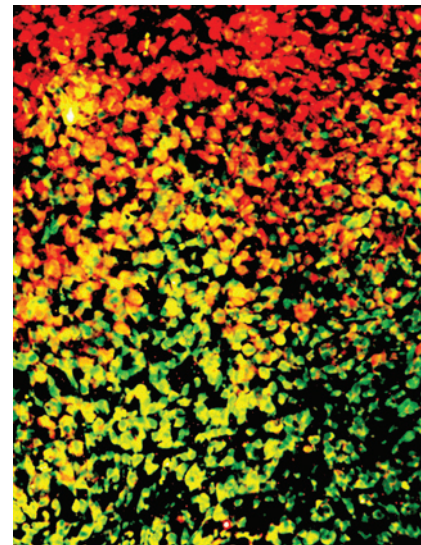
 AC icon indicates Author Choice

 CME icon indicates that this article is available for continuing medical education credit at <http://cme.aacrjournals.org>

For more information please visit www.aacrjournals.org

ABOUT THE COVER

This is a section of human LN-229 glioblastoma growing in the brain of nude mice. Immunohistochemical staining shows heterogeneous expression of endothelin receptors ET_{AR} depicted in green and ET_{BR} depicted in red. For details see the article by Kim and colleagues on page 4630 of this issue.



Clinical Cancer Research

21 (20)

Clin Cancer Res 2015;21:00-4740.

Updated version Access the most recent version of this article at:
<http://clincancerres.aacrjournals.org/content/21/20>

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.

Permissions To request permission to re-use all or part of this article, use this link <http://clincancerres.aacrjournals.org/content/21/20>.
Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.