

Highlights of This Issue 3207

SPECIAL FEATURES

CCR Translations

- 3209 | **BEAMing Up Personalized Medicine: Mutation Detection in Blood**
Andrea L. Richardson and J. Dirk Iglehart
See article p. 3462

CCR Perspectives in Drug Approval

- 3212 | **U.S. Food and Drug Administration Approval: Ruxolitinib for the Treatment of Patients with Intermediate and High-Risk Myelofibrosis**
Albert Deisseroth, Edvardas Kaminskas, Joseph Grillo, Wei Chen, Haleh Saber, Hong L. Lu, Mark D. Rothmann, Satjit Brar, Jian Wang, Christine Garnett, Julie Bullock, Laurie B. Burke, Atiqur Rahman, Rajeshwari Sridhara, Ann Farrell, and Richard Pazdur

CCR Drug Updates

- 3218 | **Vismodegib**
Charles M. Rudin

Molecular Pathways

- 3223 | **Molecular Pathways: The Role of NR4A Orphan Nuclear Receptors in Cancer**
Helen M. Mohan, Carol M. Aherne, Ailin C. Rogers, Alan W. Baird, Des C. Winter, and Evelyn P. Murphy

Review

- 3229 | **Best Practices in Cancer Nanotechnology: Perspective from NCI Nanotechnology Alliance**
William C. Zamboni, Vladimir Torchilin, Anil K. Patri, Jeff Hrkach, Stephen Stern, Robert Lee, Andre Nel, Nicholas J. Panaro, and Piotr Grodzinski

HUMAN CANCER BIOLOGY

- 3242 | **Distinguishing Clinicopathologic Features of Patients with V600E and V600K BRAF-Mutant Metastatic Melanoma**
Alexander M. Menzies, Lauren E. Haydu, Lydia Visintin, Matteo S. Carlino, Julie R. Howle, John F. Thompson, Richard F. Kefford, Richard A. Scolyer, and Georgina V. Long
- 3250 | **Regional Cell Proliferation in Microdissected Human Prostate Specimens after Heavy Water Labeling *In Vivo*: Correlation with Prostate Epithelial Cells Isolated from Seminal Fluid**
Gregory M. Hayes, Jeff Simko, Daniel Holochwost, Kyle Kuchinsky, Robert Busch, Lisa Misell, Elizabeth J. Murphy, Peter Carroll, June Chan, Katsuto Shinohara, and Marc K. Hellerstein
- 3261 | **Changes in Gene Transcription Underlying the Aberrant Citrate and Choline Metabolism in Human Prostate Cancer Samples**
Helena Bertilsson, May-Britt Tessem, Arnar Flatberg, Trond Viset, Ingrid Gribbestad, Anders Angelsen, and Jostein Halgunset
- 3270 | **Chemokine (C-X-C Motif) Ligand 12 Is Associated with Gallbladder Carcinoma Progression and Is a Novel Independent Poor Prognostic Factor**
Hyun Jung Lee, Kyungmin Lee, Dong Gwang Lee, Kwang-Hee Bae, Jang-Seong Kim, Zhe Long Liang, Song Mei Huang, Yoon Suk Oh, Ha Yon Kim, Deog Yeon Jo, Jeong-Ki Min, Jin-Man Kim, and Hyo Jin Lee
- 3281 | **CD20⁺ Tumor-Infiltrating Lymphocytes Have an Atypical CD27⁻ Memory Phenotype and Together with CD8⁺ T Cells Promote Favorable Prognosis in Ovarian Cancer**
Julie S. Nielsen, Rob A. Sahota, Katy Milne, Sara E. Kost, Nancy J. Nesslinger, Peter H. Watson, and Brad H. Nelson

3293 **Profiling Three-Dimensional Nuclear Telomeric Architecture of Myelodysplastic Syndrome and Acute Myeloid Leukemia Defines Patient Subgroups**

Macoura Gadji, Julius Adebayo Awe, Prerana Rodrigues, Rajat Kumar, Donald S. Houston, Ludger Klewes, Tandakha Ndiaye Dièye, Eduardo Magalhães Rego, Roberto Falcão Passetto, Fábio Morato de Oliveira, and Sabine Mai

3305 **AIB1:ER α Transcriptional Activity Is Selectively Enhanced in Aromatase Inhibitor-Resistant Breast Cancer Cells**

Jane O'Hara, Damir Vareslija, Jean McBryan, Fiona Bane, Paul Tibbitts, Christopher Byrne, Ronán M. Conroy, Yuan Hao, Peadar Ó Gaora, Arnold D.K. Hill, Marie McIlroy, and Leonie S. Young

CANCER THERAPY: PRECLINICAL

3316 **Role of Apollon in Human Melanoma Resistance to Antitumor Agents That Activate the Intrinsic or the Extrinsic Apoptosis Pathways**

Elena Tassi, Marina Zanon, Claudia Vegetti, Alessandra Molla, Ilaria Bersani, Valentina Perotti, Marzia Pennati, Nadia Zaffaroni, Michele Milella, Soldano Ferrone, Carmelo Carlo-Stella, Alessandro M. Gianni, Roberta Mortarini, and Andrea Anichini

3328 **Bevacizumab-Induced Alterations in Vascular Permeability and Drug Delivery: A Novel Approach to Augment Regional Chemotherapy for In-Transit Melanoma**

Ryan S. Turley, Andrew N. Fontanella, James C. Padussis, Hiroaki Toshimitsu, Yoshihiro Tokuhisa, Eugenia H. Cho, Gabi Hanna, Georgia M. Beasley, Christina K. Augustine, Mark W. Dewhirst, and Douglas S. Tyler

3340 **Coadministration of Epithelial Junction Opener JO-1 Improves the Efficacy and Safety of Chemotherapeutic Drugs**

Ines Beyer, Hua Cao, Jonas Persson, Hui Song, Maximilian Richter, Qinghua Feng, Roma Yumul, Ruan van Rensburg, Zongyi Li, Ronald Berenson, Darrick Carter, Steve Roffler, Charles Drescher, and André Lieber

3352 **A Small-Molecule Inhibitor Targeting the Mitotic Spindle Checkpoint Impairs the Growth of Uterine Leiomyosarcoma**

Weiwei Shan, Patricia Y. Akinfenwa, Kari B. Savannah, Nonna Kolomeyevskaya, Rudolfo Laucirica, Dafydd G. Thomas, Kunle Odunsi, Chad J. Creighton, Dina C. Lev, and Matthew L. Anderson

3366 **Darinaparsin: Solid Tumor Hypoxic Cytotoxin and Radiosensitizer**

Junqiang Tian, Hongjuan Zhao, Rosalie Nolley, Stephen W. Reese, Sarah R. Young, Xuejun Li, Donna M. Peehl, and Susan J. Knox

IMAGING, DIAGNOSIS, PROGNOSIS

3377 **A Molecular Taxonomy for Urothelial Carcinoma**

Gottfrid Sjö Dahl, Martin Lauss, Kristina Lövgren, Gunilla Chebil, Sigurdur Gudjonsson, Srinivas Veerla, Oliver Patschan, Mattias Aine, Mårten Fernö, Markus Ringné, Wiking Månsson, Fredrik Liedberg, David Lindgren, and Mattias Höglund

3387 **Defining a Gene Promoter Methylation Signature in Sputum for Lung Cancer Risk Assessment**

Shuguang Leng, Kieu Do, Christin M. Yingling, Maria A. Picchi, Holly J. Wolf, Timothy C. Kennedy, William J. Feser, Anna E. Baron, Wilbur A. Franklin, Malcolm V. Brock, James G. Herman, Stephen B. Baylin, Tim Byers, Christine A. Stidley, and Steven A. Belinsky

CANCER THERAPY: CLINICAL

3396 **A Phase I First-in-Human Trial of Bardoxolone Methyl in Patients with Advanced Solid Tumors and Lymphomas**

David S. Hong, Razelle Kurzrock, Jeffrey G. Supko, Xiaoying He, Aung Naing, Jennifer Wheler, Donald Lawrence, Joseph Paul Eder, Colin J. Meyer, Deborah A. Ferguson, James Mier, Marina Konopleva, Sergej Konoplev, Michael Andreeff, Donald Kufe, Hillard Lazarus, Geoffrey I. Shapiro, and Bruce J. Dezube

3407 **A Phase II Pharmacodynamic Study of Preoperative Figitumumab in Patients with Localized Prostate Cancer**

Kim N. Chi, Martin E. Gleave, Ladan Fazli, S. Larry Goldenberg, Alan So, Christian Kollmannsberger, Nevin Murray, Anna Tinker, and Michael Pollak

3414	<p>Safety and Pharmacokinetics of Ganitumab (AMG 479) Combined with Sorafenib, Panitumumab, Erlotinib, or Gemcitabine in Patients with Advanced Solid Tumors</p> <p>Lee S. Rosen, Igor Puzanov, Gregory Friberg, Emily Chan, Yuying C. Hwang, Hongjie Deng, Jill Gilbert, Devalingam Mahalingam, Ian McCaffery, Shaunita A. Michael, Alain C. Mita, Monica M. Mita, Marilyn Mulay, Poornima Shubhakar, Min Zhu, and John Sarantopoulos</p>	3462	<p>Detection of Tumor <i>PIK3CA</i> Status in Metastatic Breast Cancer Using Peripheral Blood</p> <p>Michaela J. Higgins, Danijela Jelovac, Evan Barnathan, Brian Blair, Shannon Slater, Penny Powers, Jane Zorzi, Stacie C. Jeter, George R. Oliver, John Fetting, Leisha Emens, Carol Riley, Vered Stearns, Frank Diehl, Philipp Angenendt, Peng Huang, Leslie Cope, Pedram Argani, Kathleen M. Murphy, Kurtis E. Bachman, Joel Greshock, Antonio C. Wolff, and Ben H. Park <i>See commentary p. 3209</i></p>
3428	<p>Phase I Trial of Combretastatin A4 Phosphate (CA4P) in Combination with Bevacizumab in Patients with Advanced Cancer</p> <p>Paul Nathan, Martin Zweifel, Anwar R. Padhani, Dow-Mu Koh, Matthew Ng, David J. Collins, Adrian Harris, Craig Carden, Jon Smythe, Nita Fisher, N. Jane Taylor, J. James Stirling, Shiao-Ping Lu, Martin O. Leach, Gordon J.S. Rustin, and Ian Judson</p>	3470	<p>Clinical Outcomes in Non–Small Cell Lung Cancers Harboring Different Exon 19 Deletions in EGFR</p> <p>Kuei-Pin Chung, Shang-Gin Wu, Jenn-Yu Wu, James Chih-Hsin Yang, Chong-Jen Yu, Pin-Fei Wei, Jin-Yuan Shih, and Pan-Chyr Yang</p>
3440	<p>A Phase I Clinical Trial of Ad5.SSTR/TK.RGD, a Novel Infectivity-Enhanced Bicistronic Adenovirus, in Patients with Recurrent Gynecologic Cancer</p> <p>Kenneth H. Kim, Igor Dmitriev, Janis P. O'Malley, Minghui Wang, Souheil Saddekni, Zhiying You, Meredith A. Preuss, Raymond D. Harris, Rosemarie Aurigemma, Gene P. Siegal, Kurt R. Zinn, David T. Curiel, and Ronald D. Alvarez</p>	3478	<p>Analysis of Fcγ Receptor IIIa and IIa Polymorphisms: Lack of Correlation with Outcome in Trastuzumab-Treated Breast Cancer Patients</p> <p>Sara A. Hurvitz, David J. Betting, Howard M. Stern, Emmanuel Quinaux, Jeremy Stinson, Somasekar Seshagiri, Ying Zhao, Marc Buyse, John Mackey, Adrian Driga, Sambasivarao Damaraju, Mark X. Sliwkowski, Nicholas J. Robert, Vicente Valero, John Crown, Carla Falkson, Adam Brufsky, Tadeusz Pienkowski, Wolfgang Eiermann, Miguel Martin, Valerie Bee, Omkar Marathe, Dennis J. Slamon, and John M. Timmerman</p>

PREDICTIVE BIOMARKERS AND PERSONALIZED MEDICINE

3452	<p>Ribonucleotide Reductase Large Subunit (<i>RRM1</i>) Gene Expression May Predict Efficacy of Adjuvant Mitotane in Adrenocortical Cancer</p> <p>Marco Volante, Massimo Terzolo, Martin Fassnacht, Ida Rapa, Antonina Germano, Silviu Sbiera, Fulvia Daffara, Paola Sperone, Giorgio Scagliotti, Bruno Allolio, Mauro Papotti, and Alfredo Berruti</p>
------	--

LETTERS TO THE EDITOR

3487	<p>KRAS-LCS6 Genotype as a Prognostic Marker in Early-Stage CRC—Letter</p> <p>Brid M. Ryan, Ana I. Robles, and Curtis C. Harris</p>
3489	<p>KRAS-LCS6 Genotype as a Prognostic Marker in Early-Stage CRC—Response</p> <p>Kim M. Smits, Trupti Paranjape, Sunitha Nallur, Kim A.D. Wouters, Matty P. Weijenberg, Leo J. Schouten, Piet A. van den Brandt, Fred T. Bosman, Joanne B. Weidhaas, and Manon van Engeland</p>

CORRECTIONS

3491

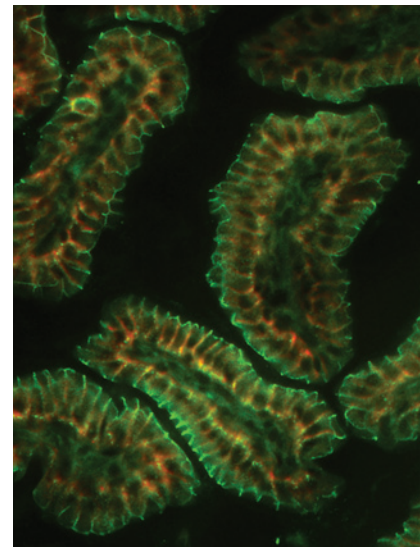
3490

Correction: Decreased Selenium-Binding Protein 1 in Esophageal Adenocarcinoma Results from Posttranscriptional and Epigenetic Regulation and Affects Chemosensitivity

Correction: Evaluation of CYP2D6 and Efficacy of Tamoxifen and Raloxifene in Women Treated for Breast Cancer Chemoprevention: Results from the NSABP P1 and P2 Clinical Trials

ABOUT THE COVER

Epithelial junctions between tumor cells inhibit the penetration of anticancer drugs into tumors and represent one of the mechanisms that cancers use to protect themselves from attacks by the host-immune system as well as elimination by cancer therapeutics. Beyer and colleagues have developed a recombinant protein (JO-1), which triggers transient opening of intercellular junctions in epithelial tumors through binding to desmoglein 2 (DSG2) and thus increases the safety and therapeutic efficacy of monoclonal antibodies and chemotherapy drugs. Whereas DSG2 is readily accessible in tumors, in intestinal epithelial cells it is trapped in intercellular junctions as shown in the figure by overlapping signals for the DSG2 (green) and the junction marker claudin 7 (red). Therefore, JO-1 preferentially acts on epithelial junctions in tumors, thereby creating a "sink" for therapeutics. For details, see the article by Beyer and colleagues on page 3340 of this issue.



Clinical Cancer Research

18 (12)

Clin Cancer Res 2012;18:3207-3491.

Updated version Access the most recent version of this article at:
<http://clincancerres.aacrjournals.org/content/18/12>

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/18/12>.
Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.