

# Contents

### Highlights of This Issue 947

#### SPECIAL FEATURES

##### CCR Translations

- 949 | **Biology, Models, and the Analysis of Tumor Xenograft Experiments**  
Daniel F. Heitjan  
*See article p. 1057*

##### CCR New Strategies

- 952 | **New Strategies in HER2-Overexpressing Breast Cancer: Many Combinations of Targeted Drugs Available**  
Vandana Abramson and Carlos L. Arteaga

##### Molecular Pathways

- 959 | **Exosomes and Cancer: A Newly Described Pathway of Immune Suppression**  
Huang-Ge Zhang and William E. Grizzle

#### CANCER THERAPY: PRECLINICAL

- 965 | **An Antibody–Drug Conjugate Targeting the Endothelin B Receptor for the Treatment of Melanoma**  
Jyoti Asundi, Chae Reed, Jennifer Arca, Krista McCutcheon, Ronald Ferrando, Suzanna Clark, Elizabeth Luis, Janet Tien, Ron Firestein, and Paul Polakis
- 976 | **Placental Growth Factor Upregulation Is a Host Response to Antiangiogenic Therapy**  
Rebecca G. Bagley, Yi Ren, William Weber, Min Yao, Leslie Kurtzberg, Jason Pinckney, Dinesh Bangari, Cokey Nguyen, William Brondyk, Johanne Kaplan, and Beverly A. Teicher

- 989 | **GSK1120212 (JTP-74057) Is an Inhibitor of MEK Activity and Activation with Favorable Pharmacokinetic Properties for Sustained *In Vivo* Pathway Inhibition**

Aidan G. Gilmartin, Maureen R. Bleam, Arthur Groy, Katherine G. Moss, Elisabeth A. Minthorn, Swarupa G. Kulkarni, Cynthia M. Rominger, Symon Erskine, Kelly E. Fisher, Jingsong Yang, Francesca Zappacosta, Roland Annan, David Sutton, and Sylvie G. Laquerre

- 1001 | **Specifically Targeting Angiopoietin-2 Inhibits Angiogenesis, Tie2-Expressing Monocyte Infiltration, and Tumor Growth**

Hanhua Huang, Jing-Yu Lai, Janet Do, Dingguo Liu, Lingna Li, Joselyn Del Rosario, Venkata R. Doppalapudi, Steven Pirie-Shepherd, Nancy Levin, Curt Bradshaw, Gary Woodnutt, Rodney Lappe, and Abhijit Bhat

- 1012 | **Modulators of Arginine Metabolism Do Not Impact on Peripheral T-Cell Tolerance and Disease Progression in a Model of Spontaneous Prostate Cancer**

Nicolò Rigamonti, Giusy Capuano, Alessia Ricupito, Elena Jachetti, Matteo Gioni, Luca Generoso, Massimo Freschi, and Matteo Bellone

- 1024 | **Human Monoclonal Antibodies to Sialyl-Lewis<sup>a</sup> (CA19.9) with Potent CDC, ADCC, and Antitumor Activity**

Ritsuko Sawada, Shu-Man Sun, Xiaohong Wu, Feng Hong, Govind Ragupathi, Philip O. Livingston, and Wolfgang W. Scholz

- 1033 | **EGFR-Homing dsRNA Activates Cancer-Targeted Immune Response and Eliminates Disseminated**

**EGFR-Overexpressing Tumors in Mice**  
Alexei Shir, Manfred Ogris, Wolfgang Roedl, Ernst Wagner, and Alexander Levitzki

- 1044 | **FKBPL and Peptide Derivatives: Novel Biological Agents that Inhibit Angiogenesis by a CD44-Dependent Mechanism**

Andrea Valentine, Martin O'Rourke, Anita Yakkundi, Jenny Worthington, Michelle Hookham, Roy Bicknell, Helen O. McCarthy, Keeva McClelland, Lynn McCallum, Hayder Dyer, Hayley McKeen, David J. J. Waugh, Jennifer Roberts, Joanne McGregor, Graham Cotton, Iain James, Timothy Harrison, David G. Hirst, and Tracy Robson

1057 **Bayesian Hierarchical Change-point Methods in Modeling the Tumor Growth Profiles in Xenograft Experiments**

Lili Zhao, Meredith A. Morgan, Leslie A. Parsels, Jonathan Maybaum, Theodore S. Lawrence, and Daniel Normolle  
*See commentary p. 949*

1065 **C Terminus of *Clostridium perfringens* Enterotoxin Downregulates CLDN4 and Sensitizes Ovarian Cancer Cells to Taxol and Carboplatin**

Zhijian Gao, Xiaoyin Xu, Bruce McClane, Qing Zeng, Babak Litkouhi, William R. Welch, Ross S. Berkowitz, Samuel C. Mok, and Elizabeth I.O. Garner

1111 **KPNA2 Expression Is an Independent Adverse Predictor of Biochemical Recurrence after Radical Prostatectomy**

Ashkan Mortezaei, Thomas Hermanns, Hans-Helge Seifert, Martin K. Baumgartner, Maurizio Provenzano, Tullio Sulser, Maximilian Burger, Matteo Montani, Kristian Ikenberg, Ferdinand Hofstädter, Arndt Hartmann, Rolf Jaggi, Holger Moch, Glen Kristiansen, and Peter J. Wild

1122 **KRAS Mutation Is Associated with Lung Metastasis in Patients with Curatively Resected Colorectal Cancer**

Jeanne Tie, Lara Lipton, Jayesh Desai, Peter Gibbs, Robert N. Jorissen, Michael Christie, Katharine J. Drummond, Benjamin N.J. Thomson, Valery Usatoff, Peter M. Evans, Adrian W. Pick, Simon Knight, Peter W.G. Carne, Roger Berry, Adrian Polglase, Paul McMurrick, Qi Zhao, Dana Busam, Robert L. Strausberg, Enric Domingo, Ian P.M. Tomlinson, Rachel Midgley, David Kerr, and Oliver M. Sieber

## IMAGING, DIAGNOSIS, PROGNOSIS

1075 **Prostate Cancer Predisposition Loci and Risk of Metastatic Disease and Prostate Cancer Recurrence**

Jiyoung Ahn, Adam S. Kibel, Jong Y. Park, Timothy R. Rebbeck, Hanna Rennert, Janet L. Stanford, Elaine A. Ostrander, Stephen Chanock, Ming-Hsi Wang, Rama D. Mittal, William B. Isaacs, Elizabeth A. Platz, and Richard B. Hayes

1082 **Incidence and Outcome of *BRCA* Mutations in Unselected Patients with Triple Receptor-Negative Breast Cancer**

Ana M. Gonzalez-Angulo, Kirsten M. Timms, Shuying Liu, Huiqin Chen, Jennifer K. Litton, Jennifer Potter, Jerry S. Lanchbury, Katherine Stemke-Hale, Bryan T. Hennessy, Banu K. Arun, Gabriel N. Hortobagyi, Kim-Anh Do, Gordon B. Mills, and Funda Meric-Bernstam

1090 **Engrailed-2 (EN2): A Tumor Specific Urinary Biomarker for the Early Diagnosis of Prostate Cancer**

Richard Morgan, Angela Boxall, Aagna Bhatt, Michael Bailey, Richard Hindley, Stephen Langley, Hayley C. Whitaker, David E. Neal, Mohammed Ismail, Hamish Whitaker, Nicola Annels, Agnieszka Michael, and Hardev Pandha

1099 **Imaging Colon Cancer Response Following Treatment with AZD1152: A Preclinical Analysis of [<sup>18</sup>F]Fluoro-2-deoxyglucose and 3'-deoxy-3'-[<sup>18</sup>F]Fluorothymidine Imaging**

Maxim A. Moroz, Tatiana Kochetkov, Shangde Cai, Jiyuan Wu, Mikhail Shamis, Jayasree Nair, Elisa de Stanchina, Inna Serganova, Gary K. Schwartz, Debabrata Banerjee, Joseph R. Bertino, and Ronald G. Blasberg

## CANCER THERAPY: CLINICAL

1131 **Phase I Dose-Escalation Study of the Pan-HER Inhibitor, PF299804, in Patients with Advanced Malignant Solid Tumors**

Pasi A. Jänne, David S. Boss, D. Ross Camidge, Carolyn D. Britten, Jeffrey A. Engelman, Edward B. Garon, Feng Guo, Steven Wong, Jane Liang, Stephen Letrent, Robert Millham, Ian Taylor, S. Gail Eckhardt, and Jan H.M. Schellens

1140 **A Phase I Clinical-Pharmacodynamic Study of the Farnesyltransferase Inhibitor Tipifarnib in Combination with the Proteasome Inhibitor Bortezomib in Advanced Acute Leukemias**

Jeffrey E. Lancet, Vu H. Duong, Elliott F. Winton, Robert K. Stuart, Michelle Burton, Shumin Zhang, Christopher Cubitt, Michelle A. Blaskovich, John J. Wright, Said Sebti, and Daniel M. Sullivan

1147 **Gefitinib or Placebo in Combination with Tamoxifen in Patients with Hormone Receptor-Positive Metastatic Breast Cancer: A Randomized Phase II Study**

C. Kent Osborne, Patrick Neven, Luc Y. Dirix, John R. Mackey, Jean Robert, Craig Underhill, Rachel Schiff, Carolina Gutierrez, Ilenia Migliaccio, Valsamo K. Anagnostou, David L. Rimm, Patrick Magill, and Mark Sellers

---

## PREDICTIVE BIOMARKERS AND PERSONALIZED MEDICINE

1160 **Pretreatment EGFR T790M Mutation and BRCA1 mRNA Expression in Erlotinib-Treated Advanced NonSmall-Cell Lung Cancer Patients with EGFR Mutations**

Rafael Rosell, Miguel Angel Molina, Carlota Costa, Sara Simonetti, Ana Gimenez-Capitan, Jordi Bertran-Alamillo, Clara Mayo, Teresa Moran, Pedro Mendez, Felipe Cardenal, Dolores Isla, Mariano Provencio, Manuel Cobo, Amelia Insa, Rosario Garcia-Campelo, Noemi Reguart, Margarita Majem, Santiago Viteri, Enric Carcereny, Ruth Porta, Bartomeu Massuti, Cristina Queral, Itziar de Aguirre, Jose Miguel Sanchez, Maria Sanchez-Ronco, Jose Luis Mate, Aurelio Ariza, Susana Benlloch, Jose Javier Sanchez, Trever G. Bivona, Charles L. Sawyers, and Miquel Taron

1169 **Rebiopsy of Lung Cancer Patients with Acquired Resistance to EGFR Inhibitors and Enhanced Detection of the T790M Mutation Using a Locked Nucleic Acid-Based Assay**

Maria E. Arcila, Geoffrey R. Oxnard, Khedoudja Nafa, Gregory J. Riely, Stephen B. Solomon, Maureen F. Zakowski, Mark G. Kris, William Pao, Vincent A. Miller, and Marc Ladanyi

1181 **Serum Soluble Mesothelin Concentrations in Malignant Pleural Mesothelioma: Relationship to Tumor Volume, Clinical Stage and Changes in Tumor Burden**

Jenette Creaney, Roslyn J. Francis, Ian M. Dick, Arthur W. Musk, Bruce W. S. Robinson, Michael J. Byrne, and Anna K. Nowak

1190 **Evaluation of KRAS Mutations, Angiogenic Biomarkers, and DCE-MRI in Patients with Advanced Non-Small-Cell Lung Cancer Receiving Sorafenib**

Ronan J. Kelly, Arun Rajan, Jeremy Force, Ariel Lopez-Chavez, Corrine Keen, Liang Cao, Yunkai Yu, Peter Choyke, Baris Turkbey, Mark Raffeld, Liqiang Xi, Seth M. Steinberg, John J. Wright, Shivaani Kummer, Martin Gutierrez, and Giuseppe Giaccone

1200 **Novel Chemosensitive Single-Nucleotide Polymorphism Markers to Targeted Regimens in Metastatic Colorectal Cancer**

Jin C. Kim, Seon Y. Kim, Dong H. Cho, Ye J. Ha, Eun Y. Choi, Chan W. Kim, Seon A. Roh, Tae W. Kim, Hyoungseok Ju, and Yong S. Kim

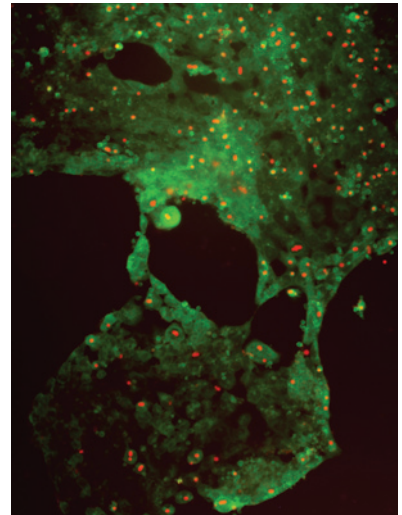
## CORRECTION

1210 **Correction: Modulating Endogenous NQO1 Levels Identifies Key Regulatory Mechanisms of Action of  $\beta$ -Lapachone for Pancreatic Cancer Therapy**

---

## ABOUT THE COVER

EGFR-overexpressing A431 cells were transfected with PolyIC/MPPE at 0.1 mcg/mL, 24 hours later, 500,000 PBMCs per well were added to the cancer cells and cocultured for another 24 hours. Apoptotic cells (red fluorescence) were visualized using an Annexin-V-Biotin kit. To distinguish tumor cells from PBMCs, tumor cells were labeled with FITC-conjugated EGFR antibody (green fluorescence). Cells were visualized with a fluorescent microscope and photographed using a digital camera. For further details, please see Shir and coworkers on page 1033 in this issue.



# Clinical Cancer Research

**17 (5)**

*Clin Cancer Res* 2011;17:947-1211.

**Updated version** Access the most recent version of this article at:  
<http://clincancerres.aacrjournals.org/content/17/5>

**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/17/5>.  
Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.