# Contents

**Highlights of This Issue** 1345

## SPECIAL FEATURES

**Editors’ Note**

1347  
*Introducing New Strategies in…*  
James L. Abbruzzese, Alexander M.M. Eggermont, and Eric H. Rubin

## CCR New Strategies

1348  
*New Strategies in Kidney Cancer: Therapeutic Advances through Understanding the Molecular Basis of Response and Resistance*  
Brian I. Rini

## CCR Translations

1355  
*Does Lapatinib Work against HER2-negative Breast Cancers?*  
Ingrid A. Mayer and Carlos L. Arteaga  
See article p. 1486

## Statistics in Clinical Cancer Research

1358  
*Testing Clonal Relatedness of Tumors Using Array Comparative Genomic Hybridization: A Statistical Challenge*  
Irina Ostrovnaya and Colin B. Begg

## CCR Drug Updates

1368  
*Everolimus*  
Peter J. Houghton

## Molecular Pathways

1373  
*HER3 Comes of Age: New Insights into Its Functions and Role in Signaling, Tumor Biology, and Cancer Therapy*  
Marcia R. Campbell, Dhara Amin, and Mark M. Moasser

1384  
*Cyclooxygenase-2 and Cancer Treatment: Understanding the Risk Should Be Worth the Reward*  
David G. Menter, Richard L. Schilsky, and Raymond N. DuBois

# HUMAN CANCER BIOLOGY

## High-Resolution Array Comparative Genomic Hybridization in Sporadic and Celiac Disease–Related Small Bowel Adenocarcinomas

Begoña Diosdado, Tineke E. Buffart, Russell Watkins, Beatriz Carvalho, Bauke Ylstra, Marianne Tijssen, Anne S. Boliijn, Fraser Lewis, Karen Maude, Caroline Verbeke, Iris D. Nagtegaal, Heike Grabsch, Chris J.J. Mulder, Phil Quirke, Peter Howdle, and Gerrit A. Meijer

## Critical Role of Ge13,1 and Ge13,13 for Human Small Cell Lung Cancer Cell Proliferation In vitro and Tumor Growth In vivo

Marius Grzelinski, Olaf Pinkenburg, Thomas Büch, Maike Gold, Stefanie Stohr, Hermann Kalwa, Thomas Gudermann, and Achim Aigner

## Association of TGF-β1 Genetic Variants with HPV16-positive Oropharyngeal Cancer

Xiaoxiang Guan, Erich M. Sturgis, Dapeng Lei, Zhensheng Liu, Kristina R. Dahlstrom, Qingyi Wei, and Guojun Li

## ZIP4 Regulates Pancreatic Cancer Cell Growth by Activating IL-6/STAT3 Pathway through Zinc Finger Transcription Factor CREB

Yuqing Zhang, Uddalak Bharadwaj, Craig D. Logsdon, Changyi Chen, Qizhi Yao, and Min Li

## Neuroblastoma Progression Correlates with Downregulation of the Lymphangiogenesis Inhibitor sVEGFR-2

Jürgen Becker, Helena Pavlakovic, Fabian Ludewig, Fabiola Wilting, Herbert A. Weich, Romulo Albuquerque, Jayakrishna Ambati, and Jörg Wilting
CANCER THERAPY: PRECLINICAL

Patient-Derived First Generation Xenografts of Non–Small Cell Lung Cancers: Promising Tools for Predicting Drug Responses for Personalized Chemotherapy
Xin Dong, Jun Guan, John C. English, Julia Flint, John Yee, Kenneth Evans, Nevin Murray, Calum MacAulay, Raymond T. Ng, Peter W. Gout, Wán L. Lam, Janessa Laskin, Victor Ling, Stephen Lam, and Yuzhuo Wang

Comparative Profiling of the Novel Epothilone, Sagopilone, in Xenografts Derived from Primary Non–Small Cell Lung Cancer
Stefanie Hammer, Anette Sommer, Iduna Fichtner, Michael Becker, Jana Rolff, Johannes Merk, Ulrich Klar, and Jens Hoffmann

An Adenoviral Vaccine Encoding Full-Length Inactivated Human Her2 Exhibits Potent Immunogenicity and Enhanced Therapeutic Efficacy without Oncogenicity
Zachary Hartman, Junping Wei, Takuya Osada, Oliver Glass, Gangjun Lei, Xiao-Yi Yang, Sharon Peplinski, Dong-Wan Kim, Wenle Xia, Neil Spector, Jeffrey Marks, William Barry, Amy Hobeika, Gayathri Devi, Andrea Amalfitano, Michael A. Morse, H. Kim Lyerly, and Timothy M. Clay

Lestaurtinib Enhances the Antitumor Efficacy of Chemotherapy in Murine Xenograft Models of Neuroblastoma
Radhika Iyer, Audrey E. Evans, Xiaoxue Qi, Ruth Ho, Jane E. Minturn, Huaqing Zhao, Naomi Balamuth, John M. Maris, and Garrett M. Brodeur

Lapatinib Restores Hormone Sensitivity with Differential Effects on Estrogen Receptor Signaling in Cell Models of Human Epidermal Growth Factor Receptor 2–Negative Breast Cancer with Acquired Endocrine Resistance

Lapatinib, a Dual EGFR and HER2 Kinase Inhibitor, Selectively Inhibits HER2-Amplified Human Gastric Cancer Cells and is Synergistic with Trastuzumab In vitro and In vivo
Zev A. Wainberg, Adrian Anghel, Amrita J. Desai, Raul Ayala, Tong Luo, Brent Safran, Marlena S. Fejzo, J. Randolph Hecht, Dennis J. Slamon, and Richard S. Finn

Defucosylated Humanized Anti-CCR4 Monoclonal Antibody KW-0761 as a Novel Immunotherapeutic Agent for Adult T-cell Leukemia/Lymphoma
Toshihiko Ishii, Takashi Ishida, Atae Utsunomiya, Atsushi Inagaki, Hiroki Yano, Hirokazu Komatsu, Shinsuke Iida, Kazunori Imada, Takashi Uchiyama, Shiro Akinaga, Kenya Shitara, and Ryuzo Ueda

IMAGING, DIAGNOSIS, PROGNOSIS

Accurate Outcome Prediction in Neuroblastoma across Independent Data Sets Using a Multigene Signature
Katleen De Preter, Joëlle Vermeulen, Benedikt Brors, Olivier Delattre, Angelika Egger, Matthias Fischer, Isabelle Janoueix-Lerosey, Cinzia Lavarrino, John M. Maris, Jaune Mora, Akira Nakagawara, André Obertuer, Miki Ohira, Gudrun Schleiermacher, Alexander Schramm, Johannes H. Schulte, Qun Wang, Frank Westermann, Frank Speleman, and Jo Vandesompele

Evaluation of Treatment-Associated Inflammatory Response on Diffusion-Weighted Magnetic Resonance Imaging and 2-[18F]-Fluoro-2-Deoxy-D-Glucose-Positron Emission Tomography Imaging Biomarkers

Low Level Her2 Overexpression Is Associated with Rapid Tumor Cell Proliferation and Poor Prognosis in Prostate Cancer
<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1587</td>
<td>Development of Immunohistochemistry Assays to Assess GALNT14 and FUT3/6 in Clinical Trials of Dulanermin and Drozitumab</td>
<td>Howard M. Stern, Mary Padilla, Klaus Wagner, Lukas Amler, and Avi Ashkenazi</td>
</tr>
<tr>
<td>1597</td>
<td>IDH1 and IDH2 Mutations Are Prognostic but not Predictive for Outcome in Anaplastic Oligodendrogial Tumors: A Report for the European Organization for Research and Treatment of Cancer Brain Tumor Group</td>
<td>Martin J. van den Bent, Hendrikus J. Dubbink, Yannick Marie, Alba A. Brandes, Martin J.B. Taphoorn, Pieter Wesseling, Marc Frenay, Coes C. Tijsse, Denis Lacombe, Ahmed Idsbaal, Ronald van Marion, Johan M. Kroos, Winand N.M. Dinjens, Thierry Gorlia, and Marc Sanson</td>
</tr>
<tr>
<td>1605</td>
<td>Cyclooxygenase-2 Inhibition Does Not Improve the Reduction in Ductal Carcinoma In situ Proliferation with Aromatase Inhibitor Therapy: Results of the ERISAC Randomized Placebo-Controlled Trial</td>
<td>Nigel J. Budded, Angela Cramer, Julie Morris, Lorna Renshaw, Kwok-Leung Cheung, Pamela Flint, Rachael Johnson, Oliver Young, Göran Landberg, Sue Grassby, Lorraine Turner, Andrew Baildam, Lester Barr, and J. Michael Dixon</td>
</tr>
<tr>
<td>1624</td>
<td>Estrogen Receptor-α Phosphorylation at Serine 305, Nuclear p21-Activated Kinase 1 Expression, and Response to Tamoxifen in Postmenopausal Breast Cancer</td>
<td>Josefine Becker, Lambert Skoog, Tommy Fomander, Bo Nordenskjöld, and Olle Stål</td>
</tr>
<tr>
<td>1634</td>
<td>A Phase II Clinical Trial of Ixabepilone (Ixempra; BMS-247550; NSC 710428), an Epothilone B Analog, in Patients with Metastatic Renal Cell Carcinoma</td>
<td>Hui Huang, Michael Menefee, Maureen Edgerly, Sen Zhuang, Herb Kotz, Marianne Poruchynsky, Lyn Mickley Huff, Susan Bates, and Tito Fojo</td>
</tr>
<tr>
<td>1642</td>
<td>Diverse Patterns of T-Cell Response against Multiple Newly Identified Human Y Chromosome–Encoded Minor Histocompatibility Epitopes</td>
<td>Yishai Ofran, Haesook T. Kim, Vladimir Brusic, Lorna Blake, Michael Mandrell, Catherine J. Wu, Stefanie Sarantopoulos, Roberto Bellucci, Derin B. Keskin, Robert J. Soiffer, Joseph H. Antin, and Jerome Ritz</td>
</tr>
</tbody>
</table>
### Pharmacokinetic and Pharmacodynamic Modeling of an Anti–Interleukin-6 Chimeric Monoclonal Antibody (Siltuximab) in Patients with Metastatic Renal Cell Carcinoma

| Thomas Puchalski, Uma Prabhakar, Qun Jiao, Birge Berns, and Hugh M. Davis |

### Modulation of Lymphocyte Regulation for Cancer Therapy: A Phase II Trial of Tremelimumab in Advanced Gastric and Esophageal Adenocarcinoma

| Christy Ralph, Eyad Elkord, Deborah J. Burt, Jackie F. O’Dwyer, Eric B. Austin, Peter L. Stern, Robert E. Hawkins, and Fiona C. Thistlewaite |

### Pharmacokinetic and Pharmacodynamic Modeling of an Anti–Interleukin-6 Chimeric Monoclonal Antibody (Siltuximab) in Patients with Metastatic Renal Cell Carcinoma

| Thomas Puchalski, Uma Prabhakar, Qun Jiao, Birge Berns, and Hugh M. Davis |

### Implications of LINE1 Methylation for Bladder Cancer Risk in Women


### Is High-Grade Prostate Cancer Easier to Find in Smaller Prostates Because There Is More High-Grade Disease to Find? - Letter

| Patrick Walsh |

### Correction: PIK3CA Mutations Predict Local Recurrences in Rectal Cancer Patients

| 1692 |

### Correction: MicroRNA Expression in Squamous Cell Carcinoma and Adenocarcinoma of the Esophagus: Associations with Survival

| 1692 |

### ABOUT THE COVER

The featured image is a lung adenocarcinoma stained with a novel, highly sensitive and specific antibody recognizing the ALK oncoprotein (brown staining) and counterstained with hematoxylin (blue staining). The tumor was shown to harbor a rearrangement of the ALK locus by genetic analysis. This assay will facilitate the routine identification of ALK-rearranged lung adenocarcinomas in clinical practice and detect lung cancers that may be responsive to ALK inhibitors. For details, see the article by Mino-Kenudson and colleagues on page 1561 of this issue.