Highlights of This Issue 4477

SPECIAL FEATURES

CCR Translations

4479

Variants on a Theme: A Biomarker of Crizotinib Response in ALK-Positive Non–Small Cell Lung Cancer?
Adam S. Crystal and Alice T. Shaw
See article p. 4682

4482

MicroRNA Dissects Out Dangerous Pancreatic Cysts from All the Rest
Ryan M. Thomas and Jason B. Fleming
See article p. 4713

CCR New Strategies

4485

New Strategies in Pleural Mesothelioma: BAP1 and NF2 as Novel Targets for Therapeutic Development and Risk Assessment
Marc Ladanyi, Marjorie G. Zauberer, Lee M. Krug, Tatsuo Ito, Robert McMillan, Matthew Bott, and Filippo Giancotti

CCR Perspectives in Drug Approval

4491

The European Medicines Agency Review of Eribulin for the Treatment of Patients with Locally Advanced or Metastatic Breast Cancer: Summary of the Scientific Assessment of the Committee for Medicinal Products for Human Use
Elias Pean, Sigrid Klaar, Eva Gil Berglund, Tomas Salmonson, Jeanett Borregaard, Kenneth F. Mackay, Eitan Amir, and Geoffrey Liu

HUMAN CANCER BIOLOGY

4498

Survival Signals and Targets for Therapy in Breast Implant–Associated ALK− Anaplastic Large Cell Lymphoma
Melissa G. Lechner, Carolina Megiel, Connor H. Church, Trevor E. Angell, Sarah M. Russell, Rikki B. Sevell, Julie K. Jang, Garry S. Brody, and Alan L. Epstein

4508

Molecular Pathways: Targeting Hsp90—Who Benefits and Who Does Not
Maurizio Scatritti, Shaheenah Dawood, and Javier Cortes

4514

Molecular Pathways: Targeting the TGF-β Pathway for Cancer Therapy
Anna L. Smith, Tyler P. Robin, and Heide L. Ford

4522

Perspective

Optimizing Cancer Treatments to Induce an Acute Immune Response: Radiation Abscopal Effects, PAMPs, and DAMPs
Charles M. Ludgate

4526

Reviews

Vascular Endothelial Growth Factor Pathway Polymorphisms as Prognostic and Pharmacogenetic Factors in Cancer: A Systematic Review and Meta-analysis
Lawson Eng, Abul Kalam Azad, Steven Habbous, Vincent Pang, Wei Xu, Anke H. Maitland-van der Zee, Sevtap Savas, Helen J. Mackay, Eitan Amir, and Geoffrey Liu

4538

Promising Personalized Therapeutic Options for Diffuse Large B-cell Lymphoma Subtypes with Oncogene Addictions
James J. Steinhardt and Ronald B. Gartenhaus

4549

Statistics in Clinical Cancer Research

Worth Adapting? Revisiting the Usefulness of Outcome-Adaptive Randomization
J. Jack Lee, Nan Chen, and Guosheng Yin

4560

Molecular Pathways

Chromosome 5q Loss in Colorectal Flat Adenomas
Identifying and Targeting ROS1 Gene Fusions in Non–Small Cell Lung Cancer
Kurtis D. Davies, Anh T. Le, Mariana F. Theodoro, Margaret C. Skokan, Dara L. Aisner, Eamon M. Berge, Luigi M. Terracciano, Federico Cappuzzo, Matteo Incarbone, Massimo Roncalli, Marco Alloisio, Armando Santoro, D. Ross Camidge, Marileila Varella-Garcia, and Robert C. Doebele

Systematic Kinome shRNA Screening Identifies CDK11 (PITSLRE) Kinase Expression Is Critical for Osteosarcoma Cell Growth and Proliferation
Zhenfeng Duan, Jianming Zhang, Edwin Choy, David Harmon, Xianzhe Liu, Petur Nielsen, Henry Mankin, Nathanael S. Gray, and Francis J. Hornicek

The Pivotal Role of Integrin β1 in Metastasis of Head and Neck Squamous Cell Carcinoma
Dongsheng Wang, Susan M€uller, A.R.M. Ruhul Amin, Donghai Huang, Ling Su, Zhongliang Hu, Mohammad Aminur Rahman, Sreenivas Nannapaneni, Lydia Koenig, Zhengjia Chen, Mourad Tighiouart, Dong M. Shin, and Zhuo G. Chen

Dual Targeting of the Cyclin/Rb/E2F and Mitochondrial Pathways in Mantle Cell Lymphoma with the Translation Inhibitor Silvestrol
Lapo Alinari, Courtney J. Prince, Ryan B. Edwards, William H. Towns, Rajeswaran Mani, Amy Lehman, Xiaoli Zhang, David Jarjoura, Li Pan, Robert A. Baiocchi, and David M. Lucas

Attenuation of the Retinoblastoma Pathway in Pancreatic Neuroendocrine Tumors Due to Increased Cdk4/Cdk6
Laura H. Tang, Tanupriya Contractor, Richard Clausen, David S. Klimstra, Yi-Chieh Nancy Du, Peter J. Allen, Murray F. Brennan, Arnold J. Levine, and Chris R. Harris

Targeting Aurora Kinases with Danusertib (PHA-739358) Inhibits Growth of Liver Metastases from Gastroenteropancreatic Neuroendocrine Tumors in an Orthotopic Xenograft Model
Katharina Fraedrich, Jörg Schrader, Harald Ittrich, Gunhild Keller, Artur Gontarewicz, Verena Matzat, Arno Kromminga, Andrea Pace, Jürgen Moll, Michael Bläker, Ansgar W. Lohse, Dieter Horsch, Tim H. Brummendorf, and Daniel Benten
Epstein-Barr Virus Infection and Expression of B-cell Oncogenic Markers in HIV-Related Diffuse Large B-cell Lymphoma
Chun Chao, Michael J. Silverberg, Otoniel Martinez-Maza, Margaret Chi, Donald I. Abrams, Reina Haque, Hongbin D. Zha, Michelle McGuire, Lanfang Xu, and Jonathan Said

miRNA Biomarkers in Cyst Fluid Augment the Diagnosis and Management of Pancreatic Cysts
Hanno Matthaei, Dennis Wylie, Maura B. Lloyd, Marco Dal Molin, Jon Kemppainen, Skye C. Mayo, Christopher L. Wolfgang, Richard D. Schulick, Laura Langfield, Bernard F. Andruess, Alex T. Adai, Ralph H. Hruban, Anna E. Szafranska-Schwarzbach, and Anirban Maitra See commentary p. 4482

The Use of Quantitative Real-Time Reverse Transcriptase PCR for 5' and 3' Portions of ALK Transcripts to Detect ALK Rearrangements in Lung Cancers
Rui Wang, Yunjian Pan, Chenguang Li, Haichuan Hu, Yang Zhang, Hang Li, Xiaoyang Luo, Jie Zhang, Zhaoyuan Fang, Yuan Li, Lei Shen, Hongbin Ji, David Garfield, Yihua Sun, and Haifuan Chen

A New Approach to Simultaneously Quantify Both TCR α- and β-Chain Diversity after Adoptive Immunotherapy
Minying Zhang, Sourindra Maiti, Chantale Bernatchez, Helen Huls, Brian Rabinovich, Richard E. Champlin, Luis M. Vence, Patrick Hwu, Laszlo Radvanyi, and Laurence J.N. Cooper

CpG Island Methylator Phenotype–Positive Tumors in the Absence of MLH1 Methylation Constitute a Distinct Subset of Duodenal Adenocarcinomas and Are Associated with Poor Prognosis
Tao Fu, Emmonsioul P. Pappou, Angela A. Guzzetta, Jana Jeschke, Ruby Kwak, Pujan Dave, Craig M. Hooker, Richard Morgan, Stephen B. Baylin, Christine A. Iacobuzio-Donahue, Christopher L. Wolfgang, and Nita Ahuja

Specific Mutations in KRAS Codons 12 and 13, and Patient Prognosis in 1075 BRAF Wild-Type Colorectal Cancers
Yu Imamura, Teppei Morikawa, Xiaoyun Liao, Paul Lochhead, Aya Kuchiba, Mai Yamauchi, Zhi Rong Qian, Reiko Nishihiara, Jeffrey A. Meyerhardt, Kevin M. Hainig, Charles S. Fuchs, and Shuji Ogino

Phase I Pharmacokinetic/Pharmacodynamic Study of MLN8237, an Investigational, Oral, Selective Aurora A Kinase Inhibitor, in Patients with Advanced Solid Tumors
Andres Cervantes, Elena Elez, Desamparados Roda, Jeffrey Ecsedy, Teresa Macarulla, Karthik Venkatakrishnan, Susana Roselló, Jordi Andreu, JungAh Jung, Juan Manuel Sanchis-Garcia, Adelaida Piera, Inma Blasco, Laura Maños, José-Alejandro Pérez-Fidalgo, Howard Fingert, Jose Baselga, and Josep Tabernero

Phase I Study of Aurora A Kinase Inhibitor MLN8237 in Advanced Solid Tumors: Safety, Pharmacokinetics, Pharmacodynamics, and Bioavailability of Two Oral Formulations
E. Claire Dees, Roger B. Cohen, Margaret von Mehren, Thomas E. Stinchcombe, Hua Liu, Karthik Venkatakrishnan, Mark Manfredi, Howard Fingert, Howard A. Burris III, and Jeffrey R. Infante

Phase I Studies of Sirolimus Alone or in Combination with Pharmacokinetic Modulators in Advanced Cancer Patients
<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>4830</td>
<td>A Phase I Single-Agent Study of Twice-Weekly Consecutive-Day Dosing of the Proteasome Inhibitor Carfilzomib in Patients with Relapsed or Refractory Multiple Myeloma or Lymphoma</td>
<td>Melissa Alsina, Suzanne Trudel, Richard R. Furman, Peter J. Rosen, Owen A. O’Connor, Raymond L. Comenzo, Alvin Wong, Lori A. Kunkel, Christopher J. Molineaux, and Andre Goy</td>
</tr>
<tr>
<td>4841</td>
<td>Bone-Related Complications and Quality of Life in Advanced Breast Cancer: Results from a Randomized Phase III Trial of Denosumab versus Zoledronic Acid</td>
<td>Miguel Martin, Richard Bell, Hugues Bourgeois, Adam Bruzsky, Ingo Diel, Alexandru Eniu, Lesley Fallowfield, Yasuo Fujiwara, Jack Jassem, Alexander H.G. Paterson, Diana Ritchie, Günther G. Steger, Alison Spoke, Charles Vogel, Michelle Fan, Qi Jiang, Karen Chung, Roger Dansney, and Ada Braun</td>
</tr>
<tr>
<td>4850</td>
<td>Myeloma-Specific Multiple Peptides Able to Generate Cytotoxic T Lymphocytes: A Potential Therapeutic Application in Multiple Myeloma and Other Plasma Cell Disorders</td>
<td>Joo-eun Bae, Robert Smith, John Daley, Naoya Mimura, Yu-Tzu Tai, Kenneth C. Anderson, and Nikhil C. Munshi</td>
</tr>
</tbody>
</table>

**LETTER TO THE EDITOR**

Biomarkers in Hepatocellular Carcinoma—Letter
Nicola Personeni, Lorenzo Rimassa, and Armando Santoro

**ABOUT THE COVER**

Wright–Giemsa-stained cytopin of early passages of TLBR-2 cells in culture. This cell line derived from an aggressive breast implant–associated T-cell CD30⁺ALK⁺ anaplastic large cell lymphoma (ALCL) shows typical morphologic features, including enlarged nuclei with frequent mitotic figures, multiple prominent nucleoli, pale cytoplasm with vesiculation, and occasional multinucleated giant cells (original magnification, ×400). Along with TLBR-1 and -3, it represents a new model for breast implant–associated ALCL and is characterized by a near triploid karyotype, specific chemotherapy drug sensitivities, and high expression of several pathway signals including Notch1, survivin, antiapoptotic genes, IL-6 and IL-2 autocrine cytokines, and STAT3, which seem to be associated with the oncogenesis and growth for these unique cancers. For details, see the article by Lechner and colleagues on page 4549 of this issue.