### Highlights of This Issue 2017

#### SPECIAL FEATURES

**CCR Translations**

- **2019** New Approaches but the Same Flaws in the Search for Prognostic Signatures
  Ramon Salazar and Josep Tabernero
  See related article, p. 2159

- **2023** Emerging Immunologic Biomarkers: Setting the (TNM-Immune) Stage
  Janis M. Taube
  See related article, p. 2147

- **2026** SETting OP449 into the PP2A-Activating Drug Family
  Paolo Neviani and Danilo Perrotti
  See related article, p. 2092

#### CCR Perspectives in Drug Approval

- **2029** U.S. Food and Drug Administration Approval: Crizotinib for Treatment of Advanced or Metastatic Non–Small Cell Lung Cancer That Is Anaplastic Lymphoma Kinase Positive

#### CCR Drug Updates

- **2035** Dabrafenib and Trametinib, Alone and in Combination for BRAF-Mutant Metastatic Melanoma
  Alexander M. Menzies and Georgina V. Long

#### Molecular Pathways

- **2044** Molecular Pathways: Interleukin-15 Signaling in Health and in Cancer
  Anjali Mishra, Laura Sullivan, and Michael A. Caligiuri

- **2051** Molecular Pathways: Molecular Basis for Sensitivity and Resistance to JAK Kinase Inhibitors
  Sara C. Meyer and Ross L. Levine

### Reviews

- **2060** Molecular Biomarkers in Advanced Renal Cell Carcinoma
  Pablo Maroto and Brian Rini

- **2072** Hepatocellular Carcinoma: Reasons for Phase III Failure and Novel Perspectives on Trial Design
  Josep M. Llovet and Virginia Hernandez-Gea

### HUMAN CANCER BIOLOGY

- **2080** High-Throughput Detection of Clinically Relevant Mutations in Archived Tumor Samples by Multiplexed PCR and Next-Generation Sequencing
  Richard Bourgon, Shan Lu, Yibing Yan, Mark R. Lackner, Weiru Wang, Victor Weigman, David Wang, Yinghui Guan, Lisa Ryner, Hartmut Koeppen, Rajesh Patel, Garret M. Hampton, Lukas C. Amler, and Yulei Wang

### CANCER THERAPY: PRECLINICAL

- **2092** Antagonism of SET Using OP449 Enhances the Efficacy of Tyrosine Kinase Inhibitors and Overcomes Drug Resistance in Myeloid Leukemia
  Anupriya Agarwal, Ryan J. MacKenzie, Raffaella Fippa, Christopher A. Eide, Jessica Oddo, Jeffrey W. Tyner, Rosalie Sears, Michael P. Vitek, María D. Odero, Dale J. Christensen, and Brian J. Druker
  See related article, p. 2026

- **2104** Rational Combination Therapy of Vintafolide (EC145) with Commonly Used Chemotherapeutic Drugs
  Joseph A. Reddy, Ryan Dorton, Alicia Bloomfield, Melissa Nelson, Marilynn Vetzel, John Guan, and Christopher P. Leamon

- **2115** Inhibition of RET Increases the Efficacy of Antiestrogen and Is a Novel Treatment Strategy for Luminal Breast Cancer
  Philip M. Spanheimer, Jung-Min Park, Ryan W. Askeland, Mikhail V. Kulak, George W. Woodfield, James P. De Andrade, Anthony R. Cyr, Sonia L. Sugg, Alexandra Thomas, and Ronald J. Weigel
IMAGING, DIAGNOSIS, PROGNOSIS

2126 A Peptide-Based Positron Emission Tomography Probe for In Vivo Detection of Caspase Activity in Apoptotic Cells

2136 A Distinct Metabolic Signature of Human Colorectal Cancer with Prognostic Potential
Yunping Qiu, Guoxiang Cai, Bingsen Zhou, Dan Li, Aihua Zhao, Guoxiang Xie, Houkai Li, Sanjun Cai, Dong Xie, Changzhi Huang, Weiting Ge, Zhanxiang Zhou, Lisa X. Xu, Weiping Jia, Shu Zheng, Yun Yen, and Wei Jia

2147 Occurrence of Tertiary Lymphoid Tissue Is Associated with T-Cell Infiltration and Predicts Better Prognosis in Early-Stage Colorectal Cancers
Giuseppe Di Caro, Francesca Bergomas, Fabio Grizzi, Andrea Doni, Paolo Bianchi, Alberto Malesci, Luigi Laghi, Paola Allavena, Alberto Mantovani, and Federica Marchesi
See related article, p. 2023

2159 Hypoxia-Driven Gene Expression Is an Independent Prognostic Factor in Stage II and III Colon Cancer Patients
Jeroen Dekervel, Daphne Hompes, Hannah van Malenstein, Dusan Popovic, Xavier Sagaert, Bart De Moor, Eric Van Cutsem, Xavier Sagaert, Bart De Moor, Eric Van Cutsem, Jeroen Dekervel, Daphne Hompes, Hannah van Malenstein, Dusan Popovic, Xavier Sagaert, Bart De Moor, Eric Van Cutsem, Xavier Sagaert, Bart De Moor, Eric Van Cutsem
See related article, p. 2019

2169 Hypermethylation of the GABRE→miR-452→miR-224 Promoter in Prostate Cancer Predicts Biochemical Recurrence after Radical Prostatectomy
Helle Kristensen, Christa Haldrup, Siri Strand, Kamilla Mundbjerg, Martin M. Mortensen, Kasper Thorsen, Marie Stampe Ostenfeld, Peter J. Wild, Christian Arsov, Wolfgang Goering, Tapios Gavrin, Lars Egervad, Johan Lindberg, Henrik Gronberg, Soren Hoyer, Michael Borre, Torben F. OerttLow, and Karina D. Sorensen

2182 Imaging the Norepinephrine Transporter in Neuroblastoma: A Comparison of [18F]-MBF and 123I-MIBG
Hanwen Zhang, Ruimin Huang, Nai-Kong V. Cheung, Hongfeng Guo, Pat B. Zanzonico, Howard T. Thaler, Jason S. Lewis, and Ronald G. Blasberg

CANCER THERAPY: CLINICAL

2192 A Phase I/II, Multiple-Dose, Dose-Escalation Study of Siltuximab, an Anti-Interleukin-6 Monoclonal Antibody, in Patients with Advanced Solid Tumors
Eric Angevin, Josep Tabernero, Elena Elez, Steven J. Cohen, Rastislav Bahleda, Jean-Luc van Laethem, Christian Ottensmeier, Jose A. Lopez-Martinez, Sally Clive, Florence Joly, Isabelle Ray-Coquard, Luc Drix, Jean-Pascal Machiels, Neil Stevens, Manjula Reddy, Brett Hall, Thomas A. Puchalski, Rajesh Bandekar, Helgi van de Velde, Brenda Tromp, Jessica Vermeulen, and Razelle Kurzrock

2205 First-In-Human Phase I Study of Lurbinectedin (PM01183) in Patients with Advanced Solid Tumors
María Elena Elez, Josep Tabernero, David Geary, Teresa Macarulla, S. Peter Kang, Carmen Kabatt, Arturo Soto-Matos Pita, Carlos Fernandez Teruel, Mariano Sanguino, Martin Cullell-Young, Sergio Szylldergemajn, and Mark J. Ratain

2215 Ultra Low-Dose IL-2 for GVHD Prophylaxis after Allogeneic Hematopoietic Stem Cell Transplantation Mediates Expansion of Regulatory T Cells without Diminishing Antiviral and Antileukemic Activity

2226 Preclinical and Early Clinical Evaluation of the Oral AKT Inhibitor, MK-2206, for the Treatment of Acute Myelogenous Leukemia
LETTERS TO THE EDITOR

Proteomic Markers of DNA Repair and PI3K Pathway Activation Predict Response to the PARP Inhibitor BMN 673 in Small Cell Lung Cancer—Letter
Haifeng Qiu

Proteomic Markers of DNA Repair and PI3K Pathway Activation Predict Response to the PARP Inhibitor BMN 673 in Small Cell Lung Cancer—Response
Robert J.G. Cardnell and Lauren A. Byers

ABOUT THE COVER

The cover shows a class of recurrent hotspot mutations in PIK3R1 and PIK3CA from endometrial cancer patients that are clustered at the interface between the ISH2 domain of PIK3R1 and the C2 domain of PIK3CA. Alteration of some of these crucial amino acids has been shown to be sufficient to disrupt the inhibitory contact by PIK3R1 and may represent a novel mechanism of oncogenic activation of PIK3CA. For details, see the article by Bourgon and colleagues on page 2080 of this issue.