## 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  
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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, Yinhui Guan, Lisa Ryner, Hartmut Koeppen, Rajesh Patel, Garret M. Hampton, Lukas C. Amier, 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, Raffaela 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

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**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

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**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
A Peptide-Based Positron Emission Tomography Probe for In Vivo Detection of Caspase Activity in Apoptotic Cells
Matthew R. Hight, Yiu-Yin Cheung, Michael L. Nickels, Eric S. Dawson, Ping Zhao, Samir Saleh, Jason R. Buck, Dewei Tang, M. Kay Washington, Robert J. Coffey, and H. Charles Manning

A Distinct Metabolic Signature of Human Colorectal Cancer with Prognostic Potential
Yunping Qiu, Guoxiang Cai, Bingxen 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 Yan, and Wei Jia

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, Paolo Allavena, Alberto Mantovani, and Federica Marchesi
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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, André D’Hoore, Chris Verslype, and Jos van Pelt
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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, Tapio Visakorpi, Lars Egevad, Johan Lindberg, Henrik Gronberg, Soren Hayer, Michael Borre, Torben F. Omtoft, and Karina D. Sorensen

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

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-Martin, Sally Clive, Florence Joly, Isabelle Ray-Coquard, Luc Driks, Jean-Pascal Machiels, Neil Steven, Manula Reddy, Brett Hall, Thomas A. Puchalski, Rajesh Bandekar, Helgi van de Velde, Brenda Tromp, Jessica Vermeulen, and Razelle Kurzrock

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 Kahatt, Arturo Soto-Matos Pita, Carlos Fernandez Teruel, Mariano Siguero, Martin Cullell-Young, Sergio Zyldergemajn, and Mark J. Ratain

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

Preclinical and Early Clinical Evaluation of the Oral AKT Inhibitor, MK-2206, for the Treatment of Acute Myelogenous Leukemia
Marina Y. Konopleva, Roland B. Walter, Stefan H. Faderl, Elias J. Jabbour, Zhihong Zeng, Gautam Borthakur, Xueli Huang, Tapan M. Kadia, Peter P. Ruvolet, Jennie B. Feliu, Hongbo Lu, LaKiesha Debose, Jan A. Burger, Michael Andreoff, Wenbin Liu, Keith A. Baggerly, Steven M. Kornblau, L. Austin Doyle, Elhu H. Estey, and Hagop M. Kantarjian
LETTERS TO THE EDITOR

2236  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

2237  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.