

## Highlights of This Issue 1915

### SPECIAL FEATURES

#### CCR Translations

- 1917 | **Zoom Zoom: Racing CARs for Multiple Myeloma**  
Marcela V. Maus and Carl H. June  
*See article, p. 2048*

#### CCR Drug Updates

- 1920 | **Aflibercept**  
Kristen K. Ciombor, Jordan Berlin, and Emily Chan

#### Molecular Pathways

- 1926 | **Molecular Pathways: Adiponectin and Leptin Signaling in Cancer**  
Michael N. VanSaun
- 1933 | **Molecular Pathways: JAK/STAT Pathway: Mutations, Inhibitors, and Resistance**  
 Alfonso Quintás-Cardama and Srdan Verstovsek

#### Tobacco Statement

- 1941 | **Assessing Tobacco Use by Cancer Patients and Facilitating Cessation: An American Association for Cancer Research Policy Statement**  
Benjamin A. Toll, Thomas H. Brandon, Ellen R. Gritz, Graham W. Warren, and Roy S. Herbst; Writing Committee for the AACR Subcommittee on Tobacco and Cancer

### HUMAN CANCER BIOLOGY

- 1949 | **C-Reactive Protein Downregulates TRAIL Expression in Human Peripheral Monocytes via an Egr-1-Dependent Pathway**  
Paola Secchiero, Erika Rimondi, Maria Grazia di Iasio, Chiara Agnoletto, Elisabetta Melloni, Ilaria Volpi, and Giorgio Zauli

- 1960 | **Copy Number Aberrations of Genes Regulating Normal Thymus Development in Thymic Epithelial Tumors**  
Iacopo Petrini, Yisong Wang, Paolo A. Zucali, Hye Seung Lee, Trung Pham, Donna Voeller, Paul S. Meltzer, and Giuseppe Giaccone
- 1972 | **Notch Pathway Activity Identifies Cells with Cancer Stem Cell-like Properties and Correlates with Worse Survival in Lung Adenocarcinoma**  
Khaled A. Hassan, Luo Wang, Hasan Korkaya, Guoan Chen, Ivan Maillard, David G. Beer, Gregory P. Kalemkerian, and Max S. Wicha
- 1981 | **Aberrant Expression of Mucin Core Proteins and O-Linked Glycans Associated with Progression of Pancreatic Cancer**  
Neeley Remmers, Judy M. Anderson, Erin M. Linde, Dominick J. DiMaio, Audrey J. Lazenby, Hans H. Wandall, Ulla Mandel, Henrik Clausen, Fang Yu, and Michael A. Hollingsworth
- 1994 | **Functional Genetic Screens Identify Genes Essential for Tumor Cell Survival in Head and Neck and Lung Cancer**  
Sanne R. Martens-de Kemp, Remco Nagel, Marijke Stigter-van Walsum, Ida H. van der Meulen, Victor W. van Beusechem, Boudewijn J.M. Braakhuis, and Ruud H. Brakenhoff
- 2004 | **Enhancement of Human Cancer Cell Motility and Invasiveness by Anaphylatoxin C5a via Aberrantly Expressed C5a Receptor (CD88)**  
Hidetoshi Nitta, Yoshihiro Wada, Yoshiaki Kawano, Yoji Murakami, Atsushi Irie, Keisuke Taniguchi, Ken Kikuchi, Gen Yamada, Kentaro Suzuki, Jiro Honda, Masayo Wilson-Morifuji, Norie Araki, Masatoshi Eto, Hideo Baba, and Takahisa Imamura
- 2014 | **The Prognostic Significance and Therapeutic Potential of Hedgehog Signaling in Intrahepatic Cholangiocellular Carcinoma**  
Liang Tang, Ye-Xiong Tan, Bei-Ge Jiang, Yu-Fei Pan, Shuang-Xi Li, Guang-Zhen Yang, Min Wang, Qing Wang, Jian Zhang, Wei-Ping Zhou, Li-Wei Dong, and Hong-Yang Wang

**CANCER THERAPY: PRECLINICAL**

- 2025 **Targeting the NF- $\kappa$ B and mTOR Pathways with a Quinoxaline Urea Analog That Inhibits IKK $\beta$  for Pancreas Cancer Therapy**  
Prakash Radhakrishnan, Vashti C. Bryant, Elizabeth C. Blowers, Rajkumar N. Rajule, Nagsen Gautam, Muhammad M. Anwar, Ashley M. Mohr, Paul M. Grandgenett, Stephanie K. Bunt, Jamie L. Arnst, Subodh M. Lele, Yazen Alnouti, Michael A. Hollingsworth, and Amarnath Natarajan
- 2036 **hTERT Inhibition Triggers Epstein-Barr Virus Lytic Cycle and Apoptosis in Immortalized and Transformed B Cells: A Basis for New Therapies**  
Silvia Giunco, Riccardo Dolcetti, Sonia Keppel, Andrea Celeghin, Stefano Indraccolo, Jessica Dal Col, Katy Mastorci, and Anita De Rossi
- 2048 **B-cell Maturation Antigen Is a Promising Target for Adoptive T-cell Therapy of Multiple Myeloma**  
Robert O. Carpenter, Moses O. Ebuomwan, Stefania Pittaluga, Jeremy J. Rose, Mark Raffeld, Shicheng Yang, Ronald E. Gress, Frances T. Hakim, and James N. Kochenderfer  
*See commentary, p. 1917*
- 2061 **A Targeted RNAi Screen of the Breast Cancer Genome Identifies *KIF14* and *TLN1* as Genes That Modulate Docetaxel Chemosensitivity in Triple-Negative Breast Cancer**  
Stina Mui Singel, Crystal Cornelius, Kimberly Batten, Gail Fasciani, Woodring E. Wright, Lawrence Lum, and Jerry W. Shay
- 2071 **Extracellular Signal-Regulated Kinase 5: A Potential Therapeutic Target for Malignant Mesotheliomas**  
Arti Shukla, Jill M. Miller, Christopher Cason, Mutlay Sayan, Maximilian B. MacPherson, Stacie L. Beuschel, Jedd Hillegass, Pamela M. Vacek, Harvey I. Pass, and Brooke T. Mossman
- 2084 **Abcc4 Together with Abcb1 and Abcg2 Form a Robust Cooperative Drug Efflux System That Restricts the Brain Entry of Camptothecin Analogues**  
Fan Lin, Serena Marchetti, Dick Pluim, Dilek Iusuf, Roberto Mazzanti, Jan H.M. Schellens, Jos H. Beijnen, and Olaf van Tellingen

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**Targeting miR-21 Inhibits *In Vitro* and *In Vivo* Multiple Myeloma Cell Growth**

Emanuela Leone, Eugenio Morelli, Maria T. Di Martino, Nicola Amodio, Umberto Foresta, Annamaria Gullà, Marco Rossi, Antonino Neri, Antonio Giordano, Nikhil C. Munshi, Kenneth C. Anderson, Pierosandro Tagliaferri, and Pierfrancesco Tassone

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**Inhibition of Established Micrometastases by Targeted Drug Delivery via Cell Surface-Associated GRP78**

Yu Rebecca Miao, Bedrich L. Eckhardt, Yuan Cao, Renata Pasqualini, Pedram Argani, Wadih Arap, Robert G. Ramsay, and Robin L. Anderson

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**The Combination of Sorafenib and Everolimus Abrogates mTORC1 and mTORC2 Upregulation in Osteosarcoma Preclinical Models**

Ymera Pignochino, Carmine Dell'Aglio, Marco Basiricò, Federica Capozzi, Marco Soster, Serena Marchiò, Stefania Bruno, Loretta Gammaitoni, Dario Sangiolo, Erica Torchiaro, Lorenzo D'Ambrosio, Franca Fagioli, Stefano Ferrari, Marco Alberghini, Piero Picci, Massimo Aglietta, and Giovanni Grignani

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**Growth and Activation of Natural Killer Cells *Ex Vivo* from Children with Neuroblastoma for Adoptive Cell Therapy**

Yin Liu, Hong-Wei Wu, Michael A. Sheard, Richard Sposto, Srinivas S. Somanchi, Laurence J.N. Cooper, Dean A. Lee, and Robert C. Seeger

**IMAGING, DIAGNOSIS, PROGNOSIS**

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**Mammographic Breast Density Response to Aromatase Inhibition**

Celine M. Vachon, Vera J. Suman, Kathleen R. Brandt, Matthew L. Kosel, Aman U. Buzdar, Janet E. Olson, Fang-Fang Wu, Lynn M. Flickinger, Giske Ursin, Catherine R. Elliott, Lois Shepherd, Richard M. Weinshilboum, Paul E. Goss, and James N. Ingle

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**Potentially Prognostic miRNAs in HPV-Associated Oropharyngeal Carcinoma**

Angela B.Y. Hui, Alice Lin, Wei Xu, Levi Waldron, Bayardo Perez-Ordóñez, Ilan Weinreb, Wei Shi, Jeff Bruce, Shao Hui Huang, Brian O'Sullivan, John Waldron, Patrick Gullane, Jonathan C. Irish, Kelvin Chan, and Fei-Fei Liu

2163 **Quantitative Ultrasound Evaluation of Tumor Cell Death Response in Locally Advanced Breast Cancer Patients Receiving Chemotherapy**  
Ali Sadeghi-Naini, Naum Papanicolau, Omar Falou, Judit Zubovits, Rebecca Dent, Sunil Verma, Maureen Trudeau, Jean Francois Boileau, Jacqueline Spayne, Sara Iradji, Ervis Sofroni, Justin Lee, Sharon Lemon-Wong, Martin Yaffe, Michael C. Kolios, and Gregory J. Czarnota

2175 **Epstein-Barr Virus DNA Load in Nasopharyngeal Brushings and Whole Blood in Nasopharyngeal Carcinoma Patients before and after Treatment**  
Marlinda Adham, Astrid E. Greijer, Sandra A.W.M. Verkuijlen, Hedy Juwana, Sabine Fleig, Lisnawati Rachmadi, Octavia Malik, A.N. Kurniawan, Averi Roezin, Soehartati Gondhowiardjo, Djumhana Atmakusumah, Servi J.C. Stevens, Bambang Hermani, I. Bing Tan, and Jaap M. Middeldorp

2187 **MicroRNA Profiling Can Classify Acute Leukemias of Ambiguous Lineage as Either Acute Myeloid Leukemia or Acute Lymphoid Leukemia**  
David C. de Leeuw, Willemijn van den Ancker, Fedor Denkers, Renée X. de Menezes, Theresia M. Westers, Gert J. Ossenkoppele, Arjan A. van de Loosdrecht, and Linda Smit

2197 **CD44 and OTP Are Strong Prognostic Markers for Pulmonary Carcinoids**  
Dorian R.A. Swarts, Mieke E.R. Henfling, Leander Van Neste, Robert-Jan van Suylen, Anne-Marie C. Dingemans, Winand N.M. Dinjens, Annick Haesevoets, Martina Rudelius, Erik Thunnissen, Marco Volante, Wim Van Criekinge, Manon van Engeland, Frans C.S. Ramaekers, and Ernst-Jan M. Speel

2208 **An International Collaboration to Harmonize the Quantitative Plasma Epstein-Barr Virus DNA Assay for Future Biomarker-Guided Trials in Nasopharyngeal Carcinoma**  
Quynh-Thu Le, Qiang Zhang, Hongbin Cao, Ann-Joy Cheng, Benjamin A. Pinsky, Ruey-Long Hong, Joseph T. Chang, Chun-Wei Wang, Kuo-Chien Tsao, YM Dennis Lo, Nancy Lee, K. Kian Ang, Anthony T.C. Chan, and K.C. Allen Chan

2216 **Methylation of the *hTERT* Promoter: A Novel Cancer Biomarker for Leptomeningeal Metastasis Detection in Cerebrospinal Fluids**  
Stéphanie Bougel, Benoit Lhermitte, Gabrielle Gallagher, Jeanne-Chantal de Flaugergues, Robert C. Janzer, and Jean Benhattar

## CANCER THERAPY: CLINICAL

2224 **Long-term Vaccination with Multiple Peptides Derived from Cancer-Testis Antigens Can Maintain a Specific T-cell Response and Achieve Disease Stability in Advanced Biliary Tract Cancer**  
Atsushi Aruga, Nobuhiro Takeshita, Yoshihito Kotera, Ryuji Okuyama, Norimasa Matsushita, Takehiro Ohta, Kazuyoshi Takeda, and Masakazu Yamamoto

2232 **Efficacy and Safety of Retreatment with Ipilimumab in Patients with Pretreated Advanced Melanoma Who Progressed after Initially Achieving Disease Control**  
Caroline Robert, Dirk Schadendorf, Marianne Messina, F. Stephen Hodi, and Steven O'Day, for the MDX010-20 investigators

2240 **Analysis of Tumor Specimens at the Time of Acquired Resistance to EGFR-TKI Therapy in 155 Patients with *EGFR*-Mutant Lung Cancers**  
Helena A. Yu, Maria E. Arcila, Natasha Rekhtman, Camelia S. Sima, Maureen F. Zakowski, William Pao, Mark G. Kris, Vincent A. Miller, Marc Ladanyi, and Gregory J. Riely

2248 **Phase Ib Dose-Escalation Study (PX-171-006) of Carfilzomib, Lenalidomide, and Low-Dose Dexamethasone in Relapsed or Progressive Multiple Myeloma**  
Ruben Niesvizky, Thomas G. Martin III, William I. Bensinger, Melissa Alsina, David S. Siegel, Lori A. Kunkel, Alvin F. Wong, Susan Lee, Robert Z. Orlowski, and Michael Wang

## PREDICTIVE BIOMARKERS AND PERSONALIZED MEDICINE

2257 **Phase II Trial of MEK Inhibitor Selumetinib (AZD6244, ARRY-142886) in Patients with *BRAF*<sup>V600E/K</sup>-Mutated Melanoma**  
Federica Catalanotti, David B. Solit, Melissa P. Pulitzer, Michael F. Berger, Sasinya N. Scott, Tunc Iyriboz, Mario E. Lacouture, Katherine S. Panageas, Jedd D. Wolchok, Richard D. Carvajal, Gary K. Schwartz, Neal Rosen, and Paul B. Chapman

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**Promoter CpG Island  
Hypermethylation of the DNA Repair  
Enzyme MGMT Predicts Clinical  
Response to Dacarbazine in a Phase  
II Study for Metastatic Colorectal  
Cancer**

Alessio Amatu, Andrea Sartore-Bianchi,  
Catia Moutinho, Alessandro Belotti,  
Katia Bencardino, Giuseppe Chirico,  
Andrea Cassingena, Francesca Rusconi,  
Anna Esposito, Michele Nichelatti,  
Manel Esteller, and Salvatore Siena

**CORRECTION**

2273

**Correction: Polyphenon E Enhances  
the Antitumor Immune Response in  
Neuroblastoma by Inactivating  
Myeloid Suppressor Cells**

AC icon indicates Author Choice

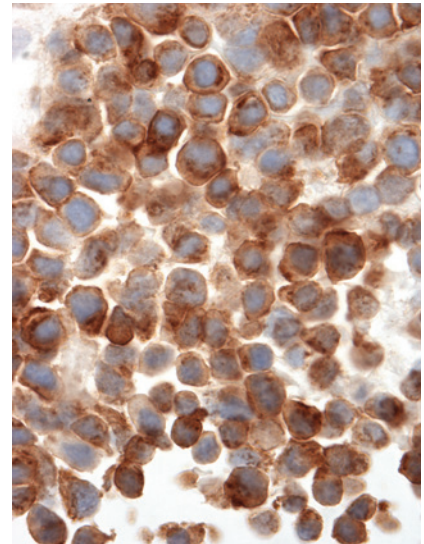
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**ABOUT THE COVER**

The cover shows a section from a plasmacytoma that was resected from a patient with advanced multiple myeloma. Immunohistochemistry staining revealed that the malignant plasma cells expressed B-cell maturation antigen. For details, see the article by Carpenter and colleagues on page 2048 of this issue.



# Clinical Cancer Research

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