

## SPECIAL FEATURES

## Highlights of This Issue 1

## CCR Translations

- 3** Genotyping Natural Killer Immune Checkpoints to Discover Biomarkers of Response  
 Nai-Kong Cheung and Katharine C. Hsu  
*See related article, p. 189*


## Reviews

- 6** Head and Neck Carcinoma Immunotherapy: Facts and Hopes  
 Theresa L. Whiteside
- 14** Inhibiting 4EBP1 in Glioblastoma  
 Qi Wen Fan, Theodore P. Nicolaides, and William A. Weiss


## CANCER THERAPY: CLINICAL

- 22** A Multicenter Phase I Study Evaluating Dual PI3K and BRAF Inhibition with PX-866 and Vemurafenib in Patients with Advanced BRAF V600-Mutant Solid Tumors  
 Clinton Yam, Xiaowei Xu, Michael A. Davies, Phyllis A. Gimotty, Jennifer J.D. Morrisette, Michael T. Tetzlaff, Khalida M. Wani, Shujing Liu, Wanleng Deng, Meghan Buckley, Jianhua Zhao, Ravi K. Amaravadi, Naomi B. Haas, Ragini R. Kudchadkar, Anna C. Pavlick, Jeffrey A. Sosman, Hussein Tawbi, Luke Walker, Lynn M. Schuchter, Giorgos C. Karakousis, and Tara C. Gangadhar
- 33** Molecular Subtypes of Pulmonary Large-cell Neuroendocrine Carcinoma Predict Chemotherapy Treatment Outcome  
 Jules L. Derks, Noémie Leblay, Erik Thunnissen, Robert Jan van Suylen, Michael den Bakker, Harry J.M. Groen, Egbert F. Smit, Ronald Damhuis, Esther C. van den Broek, Amélie Charbrier, Matthieu Foll, James D. McKay, PALGA-GroupLynnette Fernandez-Cuesta, Ernst-Jan M. Speel, and Anne-Marie C. Dingemans

- 43** Phase Ib/II Trial of NC-6004 (Nanoparticle Cisplatin) Plus Gemcitabine in Patients with Advanced Solid Tumors

 Vivek Subbiah, Juneko E. Grilley-Olson, Austin J. Combest, Neelesh Sharma, Richard H. Tran, Iulian Bobe, Atsushi Osada, Kazuhiro Takahashi, Jaikrishna Balkissoon, Aaron Camp, Atsuhiko Masada, Dirk J. Reitsma, and Lyudmila A. Bazhenova


- 52** Fluorescein-Guided Surgery for Resection of High-Grade Gliomas: A Multicentric Prospective Phase II Study (FLUOGLIO)

 Francesco Acerbi, Morgan Broggi, Karl-Michael Schebesch, Julius Höhne, Claudio Cavallo, Camilla De Laurentis, Marica Eoli, Elena Anghileri, Maura Servida, Carlo Boffano, Bianca Pollo, Marco Schiariti, Sergio Visintini, Cristina Montomoli, Lorenzo Bosio, Emanuele La Corte, Giovanni Broggi, Alexander Brawanski, and Paolo Ferroli

- 62** Phase Ib Study of Immune Biomarker Modulation with Neoadjuvant Cetuximab and TLR8 Stimulation in Head and Neck Cancer to Overcome Suppressive Myeloid Signals

Gulidanna Shayan, Benjamin A. Kansy, Sandra P. Gibson, Raghvendra M. Srivastava, James Kyle Bryan, Julie E. Bauman, James Ohr, Seungwon Kim, Umamaheswar Duvvuri, David A. Clump, Dwight E. Heron, Jonas T. Johnson, Robert M. Hershberg, and Robert L. Ferris

- 73** Phase III HEAT Study Adding Lyso-Thermosensitive Liposomal Doxorubicin to Radiofrequency Ablation in Patients with Unresectable Hepatocellular Carcinoma Lesions

 Won Young Tak, Shi-Ming Lin, Yijun Wang, Jiasheng Zheng, Aldo Vecchione, Soo Young Park, Min Hua Chen, Stephen Wong, Ruocai Xu, Cheng-Yuan Peng, Yi-You Chiou, Guan-Tarn Huang, Jianqiang Cai, Basri Johan Jeet Abdullah, June Sung Lee, Jae Young Lee, Jong-Young Choi, Julieta Gopez-Cervantes, Morris Sherman, Richard S. Finn, Masao Omata, Michael O'Neal, Lukas Makris, Nicholas Borys, Ronnie Poon, and Riccardo Lencioni




## PERSONALIZED MEDICINE AND IMAGING

- 84** Comprehensive Pharmacogenomic Profiling of Malignant Pleural Mesothelioma Identifies a Subgroup Sensitive to FGFR Inhibition

Josine M. Quispel-Janssen, Jitendra Badhai, Laurel Schunselaar, Stacey Price, Jonathan Brammeld, Francesco Iorio, Krishna Kolluri, Matthew Garnett, Anton Berns, Paul Baas, Ultan McDermott, Jacques Neefjes, and Constantine Alifrangis



# Table of Contents

## CANCER THERAPY: PRECLINICAL

- 95** Regional Delivery of Chimeric Antigen Receptor–Engineered T Cells Effectively Targets **HER2<sup>+</sup> Breast Cancer Metastasis to the Brain**  
 Saul J. Priceman, Dileshni Tilakawardane, Brook Jeang, Brenda Aguilar, John P. Murad, Anthony K. Park, Wen-Chung Chang, Julie R. Ostberg, Josh Neman, Rahul Jandial, Jana Portnow, Stephen J. Forman, and Christine E. Brown
- 106** Lenalidomide Enhances the Function of CS1 Chimeric Antigen Receptor–Redirected T Cells **Against Multiple Myeloma**  
 Xiuli Wang, Miriam Walter, Ryan Urak, Lihong Weng, Christian Huynh, Laura Lim, ChingLam W. Wong, Wen-Chung Chang, Sandra H. Thomas, James F. Sanchez, Lu Yang, Christine E. Brown, Flavia Pichiorri, Myo Htut, Amrita Y. Krishnan, and Stephen J. Forman
- 120** PQR309 Is a Novel Dual PI3K/mTOR Inhibitor with Preclinical Antitumor Activity in Lymphomas as a Single Agent and in Combination Therapy  
Chiara Tarantelli, Eugenio Gaudio, Alberto J. Arribas, Ivo Kwee, Petra Hillmann, Andrea Rinaldi, Luciano Cascione, Filippo Spriano, Elena Bernasconi, Francesca Guidetti, Laura Carrassa, Roberta Bordone Pittau, Florent Beauflis, Reto Ritschard, Denise Rageot, Alexander Sele, Barbara Dossena, Francesca Maria Rossi, Antonella Zucchetto, Monica Tadorelli, Valter Gattei, Davide Rossi, Anastasios Stathis, Georg Stussi, Massimo Broggin, Matthias P. Wymann, Andreas Wicki, Emanuele Zucca, Vladimir Cmijlanovic, Dorian Fabbro, and Francesco Bertoni
- 130** Degalactotigonin, a Natural Compound from *Solanum nigrum L.*, Inhibits Growth and Metastasis of Osteosarcoma through GSK3 $\beta$  Inactivation–Mediated Repression of the **Hedgehog/Gli1 Pathway**  
 Zhiqiang Zhao, Qiang Jia, Man-Si Wu, Xianbiao Xie, Yongqian Wang, Guohui Song, Chang-Ye Zou, Qinglian Tang, Jinchang Lu, Gang Huang, Jin Wang, De-Chen Lin, H. Phillip Koeffler, Jun-Qiang Yin, and Jingnan Shen
- 145** PTEN Is Fundamental for Elimination of Leukemia Stem Cells Mediated by GSK126 Targeting EZH2 in Chronic Myelogenous Leukemia  
Jingfeng Zhou, Danian Nie, Juan Li, Xin Du, Yuhong Lu, Yangqiu Li, Chang Liu, Wei Dai, Yun Wang, Yanli Jin, and Jingxuan Pan

- 158** Multilayered Omics-Based Analysis of a Head and Neck Cancer Model of Cisplatin Resistance Reveals Intratumoral Heterogeneity and Treatment-Induced Clonal Selection  
Franziska Niehr, Theresa Eder, Tanja Pilz, Robert Kunschak, Denise Treue, Frederick Klauschen, Michael Bockmayr, Seval Türkmen, Korinna Jöhrens, Volker Budach, and Ingeborg Tinhofer
- 169** Hypoxia-Inducible PIM Kinase Expression Promotes Resistance to Antiangiogenic Agents  
Andrea L. Casillas, Rachel K. Toth, Alva G. Sainz, Neha Singh, Ankit A. Desai, Andrew S. Kraft, and Noel A. Warfel

## BIOLOGY OF HUMAN TUMORS

- 181** Liquid Biopsies Using Plasma Exosomal Nucleic Acids and Plasma Cell-Free DNA Compared with Clinical Outcomes of Patients with Advanced Cancers  
Lino Möhrmann, Helen J. Huang, David S. Hong, Apostolia M. Tsimberidou, Siqing Fu, Sarina A. Piha-Paul, Vivek Subbiah, Daniel D. Karp, Aung Naing, Anne Krug, Daniel Enderle, Tina Priewasser, Mikkel Noerholm, Erez Eitan, Christine Coticchia, Georg Stoll, Lisa-Marie Jordan, Cathy Eng, E. Scott Kopetz, Johan Skog, Funda Meric-Bernstam, and Filip Janku
- 189** Neuroblastoma Patients' KIR and KIR-Ligand Genotypes Influence Clinical Outcome for Dinutuximab-based Immunotherapy: A Report from the Children's Oncology Group  
 Amy K. Erbe, Wei Wang, Lakeesha Carmichael, KyungMann Kim, Eneida A. Mendonça, Yiqiang Song, Dustin Hess, Patrick K. Reville, Wendy B. London, Arlene Naranjo, Jacquelyn A. Hank, Mitchell B. Diccianni, Ralph A. Reisfeld, Stephen D. Gillies, Katherine K. Matthay, Susan L. Cohn, Michael D. Hogarty, John M. Maris, Julie R. Park, M. Fevzi Ozkaynak, Andrew L. Gilman, Alice L. Yu, and Paul M. Sondel  
*See related commentary, p. 3*
- 197** Epithelial-to-Mesenchymal Transition Antagonizes Response to Targeted Therapies in Lung Cancer by Suppressing BIM  
 Kyung-A Song, Matthew J. Niederst, Timothy L. Lochmann, Aaron N. Hata, Hidenori Kitai, Jungoh Ham, Konstantinos V. Floros, Mark A. Hicks, Haichuan Hu, Hillary E. Mulvey, Yotam Drier, Daniel A.R. Heisey, Mark T. Hughes, Neha U. Patel, Elizabeth L. Lockerman, Angel Garcia, Shawn Gillespie, Hannah L. Archibald, Maria Gomez-Caraballo, Tara J. Nulton, Brad E. Windle, Zofia Piotrowska, Sinem E. Sahingur, Shirley M. Taylor, Mikhail Dozmorov, Lecia V. Sequist, Bradley Bernstein, Hiromichi Ebi, Jeffrey A. Engelman, and Anthony C. Faber

# Table of Contents

**209** Cell-Cycle and DNA-Damage Response Pathway Is Involved in Leptomeningeal Metastasis of Non–Small Cell Lung Cancer



Yun Fan, Xuehua Zhu, Yan Xu, Xuesong Lu, Yanjun Xu, Mengzhao Wang, Haiyan Xu, Jingyan Ding, Xin Ye, Luo Fang, Zhiyu Huang, Lei Gong, Hongyang Lu, Weimin Mao, and Min Hu

**217** Tumor Microvessel Density as a Prognostic Marker in High-Risk Renal Cell Carcinoma Patients Treated on ECOG-ACRIN E2805

Lucia B. Jilaveanu, Maneka Puligandla, Sarah A. Weiss, Xin Victoria Wang, Christopher Zito, Keith T. Flaherty, Marta Boeke, Veronique Neumeister, Robert L. Camp, Adebowale Adeniran, Michael Pins, Judith Manola, Robert S. DiPaola, Naomi B. Haas, and Harriet M. Kluger

**224** KRAS Mutation and Consensus Molecular Subtypes 2 and 3 Are Independently Associated with Reduced Immune Infiltration and Reactivity in Colorectal Cancer

Neeraj Lal, Brian S. White, Ghaleb Goussous, Oliver Pickles, Mike J. Mason, Andrew D. Beggs, Philippe Taniere, Benjamin E. Willcox, Justin Guinney, and Gary W. Middleton

**234** Concurrent Inhibition of Pim and FLT3 Kinases Enhances Apoptosis of FLT3-ITD Acute Myeloid Leukemia Cells through Increased Mcl-1 Proteasomal Degradation

Shivani Kapoor, Karthika Natarajan, Patrick R. Baldwin, Kshama A. Doshi, Rena G. Lapidus, Trevor J. Mathias, Mario Scarpa, Rossana Trotta, Eduardo Davila, Manfred Kraus, Dennis Huszar, Adriana E. Tron, Danilo Perrotti, and Maria R. Baer

## LETTER TO THE EDITOR

**248** FDG PET and FES PET Predict PFS on Endocrine Therapy—Letter

Lemonitsa H. Mammatas, Erik J. van Helden, Henk M.W. Verheul, and Catharina W. Menke-van der Houven van Oordt

**249** FDG PET and FES PET Predict PFS on Endocrine Therapy—Response

Brenda F. Kurland, Lanell M. Peterson, Hannah M. Linden, and David A. Mankoff

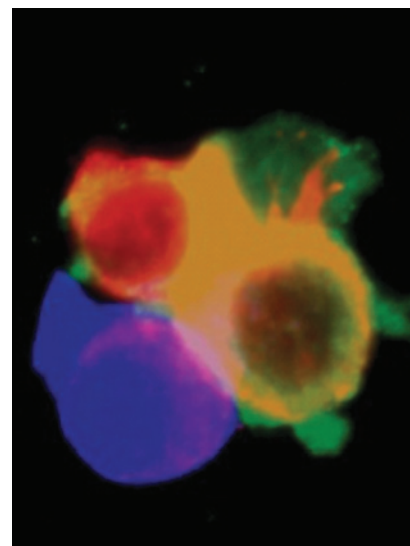


AC icon indicates AuthorChoice

For more information please visit [www.aacrjournals.org](http://www.aacrjournals.org)

## ABOUT THE COVER

The cover shows an image of synapses (yellow) between CS1 CAR T cells (green) and MM.1S tumor cells (blue) in coculture, as detected by immunofluorescent staining (F-actin labeled in red). For details, see the article by Wang and colleagues on page 106 of this issue.



# Clinical Cancer Research

**24 (1)**

*Clin Cancer Res* 2018;24:1-250.

**Updated version** Access the most recent version of this article at:  
<http://clincancerres.aacrjournals.org/content/24/1>

**E-mail alerts** [Sign up to receive free email-alerts](#) related to this article or journal.

**Reprints and Subscriptions** To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at [pubs@aacr.org](mailto:pubs@aacr.org).

**Permissions** To request permission to re-use all or part of this article, use this link <http://clincancerres.aacrjournals.org/content/24/1>. Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.