## Highlights of This Issue 4293

### SPECIAL FEATURES

#### CCR Translations

- **4295** "License to Kill" Reflects Joint Action of CD4 and CD8 T Cells
  - Cornelis J.M. Melief
  - See related article, p. 4508

#### CCR Perspectives in Drug Approval

- **4297** Developing Standards for Breakthrough Therapy Designation in Oncology
  - Sandra J. Horning, Daniel A. Haber, Wendy K.D. Selig, S. Percy Ivy, Samantha A. Roberts, Jeff D. Allen, Ellen V. Sigal, and Charles L. Sawyers
  - See related article, p. 4305

- **4305** Accelerated Approval and Breakthrough Therapy Designation: Oncology Drug Development on Speed?
  - James C. Yao, Funda Meric-Bernstam, J. Jack Lee, and S. Gail Eckhardt
  - See related article, p. 4297

#### Molecular Pathways

- **4309** Molecular Pathways: Reactive Oxygen Species Homeostasis in Cancer Cells and Implications for Cancer Therapy
  - Veronique Nogueira and Nissim Hay

#### Reviews

- **4315** Impact of Bioinformatic Procedures in the Development and Translation of High-Throughput Molecular Classifiers in Oncology
  - Charles Ferté, Andrew D. Trister, Erich Huang, Brian M. Bot, Justin Guinney, Frederic Commio, Solveig Sieberts, Fabrice André, Benjamin Besse, Jean-Charles Soria, and Stephen H. Friend

- **4326** BRAF in Melanoma: Current Strategies and Future Directions
  - April K.S. Salama and Keith T. Flaherty

### HUMAN CANCER BIOLOGY

- **4335** Regulation of Cell Proliferation and Migration by Keratin19-Induced Nuclear Import of Early Growth Response-1 in Breast Cancer Cells
  - Ji-hyun Ju, Wonseok Yang, Kyung-min Lee, Sunhwa Oht, KeeSoo Nam, Sarah Shim, Soon Young Shin, Myung Chan Gye, In-Sun Chu, and Incheol Shin

### CANCER THERAPY: PRECLINICAL

- **4347** Effective Activity of Cytokine-Induced Killer Cells against Autologous Metastatic Melanoma Including Cells with Stemness Features
  - Loretta Gammaitoni, Lidia Giraudo, Valeria Leuci, Maja Todorovic, Giulia Mesiano, Franco Picciotto, Alberto Pisacane, Alessandro Zaccagna, Maria Giuseppa Volpe, Susanna Malo, Daniela Caravelli, Elena Giaccone, Tiziana Venerio, Antonella Balsamo, Ymera Pignochino, Giovanni Grignani, Fabrizio Carnevale-Schianca, Massimo Aglietta, and Dario Sangiolo

- **4359** Contribution of Abcc4-Mediated Gastric Transport to the Absorption and Efficacy of Dasatinib
  - Brian D. Furmanski, Shuiying Hu, Ken-ichi Fujita, Lie Li, Alice A. Gibson, Laura J. Janke, Richard T. Williams, John D. Schuetz, Alex Sparreboom, and Sharyn D. Baker

- **4371** Novel Targeting of Phospho-cMET Overcomes Drug Resistance and Induces Antitumor Activity in Multiple Myeloma
  - Michele Moschetta, Antonio Basile, Arianna Ferrucci, Maria Antonia Frassanito, Luigia Rao, Roberto Ria, Antonio Giovanni Solimando, Nicola Giuliani, Angelina Boccarelli, Fabio Fumarola, Mauro Coluccia, Bernardo Rossini, Simona Ruggieri, Beatrice Nico, Eugenio Maiorano, Domenico Ribatti, Aldo M. Roccaro, and Angelo Vacca
Vemurafenib Synergizes with Nutlin-3 to Deplete Survivin and Suppresses Melanoma Viability and Tumor Growth
Zhenyu Ji, Raj Kumar, Michael Taylor, Anpuchchelvi Rajadurai, Alexander Marzuka-Alcalá, Y. Erin Chen, Ching-Ni Jenny Njuaw, Keith Flaherty, Goran Jonsson, and Hensin Tsao

Acquired Resistance to Anti-VEGF Therapy in Glioblastoma Is Associated with a Mesenchymal Transition
Yuji Piao, Ji Liang, Lindsay Holmes, Verlene Heny, Erik Sulman, and John F. de Groot

β-Mannosylceramide Activates Type 1 Natural Killer T Cells to Induce Tumor Immunity without Inducing Long-Term Functional Anergy
Jessica J. O’Konek, Shingo Kato, Satomi Takao, Liat Izhak, Zheng Xia, Peter Illarionov, Gurdfyal S. Besra, Masaki Terabe, and Jay A. Berzofsky

Sensitization of Pancreatic Cancer to Chemoradiation by the Chk1 Inhibitor MK8776
Carl G. Engelke, Leslie A. Parsels, Yushen Qian, Qiang Zhang, David Karnak, Jordan R. Robertson, Daria M. Tamska, Dongping Wei, Mary A. Davis, Joshua D. Parsels, Lili Zhao, Joel K. Greenson, Theodore S. Lawrence, Jonathan Maybaum, and Meredith A. Morgan

Inhibition of Protein Phosphatase 2A Radiosensitizes Pancreatic Cancers by Modulating CDC25C/CDK1 and Homologous Recombination Repair
Dongping Wei, Leslie A. Parsels, David Karnak, Mary A. Davis, Joshua D. Parsels, Amanda C. Marsh, Lili Zhao, Jonathan Maybaum, Theodore S. Lawrence, Yi Sun, and Meredith A. Morgan

Development and Preclinical Characterization of a Humanized Antibody Targeting CXCL12

Memantine Protects Rats Treated with Intrathecal Methotrexate from Developing Spatial Memory Deficits

A Novel Aldehyde Dehydrogenase-3 Activator (Alda-99) Protects Submandibular Gland Function from Irradiation without Accelerating Tumor Growth
Nan Xiao, Hongbin Cao, Che-Hong Chen, Christina S. Kong, Rehan Ali, Cato Chan, Davud Sirjani, Edward Graves, Albert Koong, Amato Giaccia, Daria Mochly-Rosen, and Quynh-Thu Le

Nimboline, a Limonoid Triterpene, Inhibits Growth of Human Colorectal Cancer Xenografts by Suppressing the Proinflammatory Microenvironment
Subash C. Gupta, Sahdeo Prasad, Dhanya R. Sethumadhavan, Mangalam S. Nair, Yin-Yuan Mo, and Bharat R. Aggarwal

BROAD ENCAPSULATING PERSPECTIVES ON CANCER

Identification of Circulating MicroRNA Signatures for Breast Cancer Detection
Maurice Chan, Chiew Suan Liaw, Shen Mo Ji, Hwee Huang Tan, Chow Yin Wong, Aye Aye Thike, Puay Hoon Tan, Gay Hui Ho, and Ann Siew-Gek Lee

CANCER THERAPY: CLINICAL

Phase II Randomized Trial Comparing High-Dose IFN-α2b with Temozolomide Plus Cisplatin as Systemic Adjuvant Therapy for Resected Mucosal Melanoma
Bin Lian, Lu Si, Chuanliang Cui, Zhihong Chi, Xinan Sheng, Lili Mao, Siming Li, Yan Kong, Bixia Tang, and Jun Guo

Phase I Trial of a New Schedule of Romidepsin in Patients with Advanced Cancers
Laleh Amiri-Kordestani, Victoria Luchenko, Cody J. Peer, Kambiz Ghaforian, James Reynolds, Deb Draper, Robin Frye, Sue Woo, David Venzon, John Wright, Monica Skarulis, William D. Figg, Tito Fojo, Susan E. Bates, and Richard L. Piekarz

IMAGING, DIAGNOSIS, PROGNOSIS

Identification of Circulating MicroRNA Signatures for Breast Cancer Detection
Maurice Chan, Chiew Suan Liaw, Shen Mo Ji, Hwee Huang Tan, Chow Yin Wong, Aye Aye Thike, Puay Hoon Tan, Gay Hui Ho, and Ann Siew-Gek Lee
Identification of Promiscuous KIF20A Long Peptides Bearing Both CD4⁺ and CD8⁺ T-cell Epitopes: KIF20A-Specific CD4⁺ T-cell Immunity in Patients with Malignant Tumor

Yusuke Tomita, Akira Yuno, Hirotake Tsukamoto, Satoru Senju, Yasuhiro Kuroda, Masatoshi Hirayama, Atsushi Irie, Kenta Kawahara, Junji Yatsuda, Akinobu Hamada, Hirofumi Jono, Koji Yoshida, Takuya Tsunoda, Hirotsgu Kohrogi, Yoshihiro Yoshitake, Yusuke Nakamura, Masanori Shinohara, and Yasuharu Nishimura

See commentary, p. 4295

Clinical, Pathologic, and Biologic Features Associated with BRAF Mutations in Non–Small Cell Lung Cancer

Stephanie Cardarella, Atsuko Ogino, Mizuki Nishino, Mohit Butaney, Jeanne Shen, Christine Lydon, Beow Y. Yeap, Lynette M. Sholl, Bruce E. Johnson, and Pasi A. Jänne

LETTER TO THE EDITOR

Oncolytic Virotherapy Trials—Letter

Akseli Hemminki, Minna Oksanen, and Maiju Merisalo-Soikkeli

PREDICTIVE BIOMARKERS AND PERSONALIZED MEDICINE

Ki67 Measured after Neoadjuvant Chemotherapy for Primary Breast Cancer


Ki67 Measured after Neoadjuvant Chemotherapy for Primary Breast Cancer


Correction: MSH6 Mutations Arise in Glioblastomas during Temozolomide Therapy and Mediate Temozolomide Resistance

AC icon indicates Author Choice

CME icon indicates that this article is available for continuing medical education credit at http://cme.aacrjournals.org

For more information please visit www.aacrjournals.org

ABOUT THE COVER

The cover shows Rad51 foci (red) in pancreatic cancer cells treated with gemcitabine and radiation. Nuclei are stained with DAPI (blue). For details, see the article by Engelke and colleagues on page 4412 of this issue.