Highlights of This Issue 3717

SPECIAL FEATURES

CCR Translations

3719 Dual PI3K/mTOR Inhibitors: Does p53 Modulate Response?
Olehksandr Ekshyyan, Arunkumar Anandharaj, and Cherie-Ann O. Nathan
See article, p. 3808

CCR Perspectives in Drug Approval

3722 Use of Multiple Endpoints and Approval Paths Depicts a Decade of FDA Oncology Drug Approvals
Michael B. Shea, Samantha A. Roberts, Jessica C. Walrath, Jeff D. Allen, and Ellen V. Sigal

Molecular Pathways

3732 Molecular Pathways: Environmental Estrogens Activate Nongenomic Signaling to Developmentally Reprogram the Epigenome
Rebecca Lee Yean Wong and Cheryl Lyn Walker

3738 Molecular Pathways: PI3K Pathway Targets in Triple-Negative Breast Cancers
Valerie Gordon and Shantanu Banerji

Review

3745 Optical Image-Guided Cancer Surgery: Challenges and Limitations
Stijn Keereweer, Pieter B.A.A. Van Driel, Thomas J.A. Snoeks, Jennifer A. Desimone, Robert J. Baatenburg de Jong, Alexander L. Vahrmeijer, Henricus J.C.M. Sterenborg, and Clemens W.G.M. Löwik

HUMAN CANCER BIOLOGY

3755 TGFβ Cytokines from Malignant Cells Suppress Tα1R1 Responses and Enforce a Global Tα2 Bias in Leukemic Cutaneous T-cell Lymphoma
Emmanuella Guenova, Rei Watanabe, Jessica E. Teague, Jennifer A. Desimone, Ying Jiang, Mitra Dowlatshahi, Christoph Schlapbach, Knut Schuekel, Alain H. Rook, Mariamne Tawa, David C. Fisher, Thomas S. Kupper, and Rachael A. Clark

3764 S100B Promotes Glioma Growth through Chemotraction of Myeloid-Derived Macrophages
Huaqing Wang, Leying Zhang, Ian Y. Zhang, Xuebo Chen, Anna Da Fonseca, Shihhua Wu, Hui Ren, Sam Badie, Sam Sadeghi, Mao Ouyang, Charles D. Warden, and Behnam Badie

3776 Glioma Grade Is Associated with the Accumulation and Activity of Cells Bearing M2 Monocyte Markers

3787 Genotype-Specific Abnormalities in Mitochondrial Function Associate with Distinct Profiles of Energy Metabolism and Catecholamine Content in Pheochromocytoma and Paraganglioma

CANCER THERAPY: PRECLINICAL

3796 Functional Profiling of Receptor Tyrosine Kinases and Downstream Signaling in Human Chondrosarcomas Identifies Pathways for Rational Targeted Therapy
Yi-Xiang Zhang, Jolieke G. van Oosterwijk, Ewa Sicinska, Samuel Moss, Stephen P. Remillard, Tom van Wezel, Claudia Bühennemann, Andrew B. Hassan, George D. Demetri, Judith V.M.G. Boven, and Andrew J. Wagner
PI3K/mTOR Inhibitor PF-04691502 Antitumor Activity Is Enhanced with Induction of Wild-Type TP53 in Human Xenograft and Murine Knockout Models of Head and Neck Cancer
See commentary, p. 3719

Inhibition of GSK3B Bypass Drug Resistance of p53-Null Colon Carcinomas by Enabling Necroptosis in Response to Chemotherapy
Emanuela Grassilli, Robert Narloch, Elena Federzoni, Leonarda Ianzano, Fabio Pisano, Roberto Giovannoni, Gabriele Romano, Laura Masiero, Biagio Eugenio Leone, Serena Bonin, Marisa Donada, Giorgio Stanta, Kristian Helin, and Marialuisa Lavitrano

Leukemia Cell-Rhabdovirus Vaccine: Personalized Immunotherapy for Acute Lymphoblastic Leukemia
David P. Conrad, Jovian Tsang, Meaghan Maclean, Jean-Simon Diallo, Fabrice Le Boeuf, Chantal G. Lemay, Theresa J. Falls, Kelley A. Parato, John C. Bell, and Harold L. Atkins

Targeting Natural Killer Cells to Acute Myeloid Leukemia In Vitro with a CD16×33 Bispecific Killer Cell Engager and ADAM17 Inhibition
Andres Wiernik, Bree Foley, Bin Zhang, Michael R. Verneris, Erica Warlick, Michelle K. Gleason, Julie A. Ross, Xianguhua Lue, Daniel J. Weisdorf, Bruce Walcheck, Daniel A. Vallera, and Jeffrey S. Miller

Therapeutic Potential of HSP90 Inhibition for Neurofibromatosis Type 2

Nanoparticles Engineered with Rituximab and Loaded with Nutlin-3 Show Promising Therapeutic Activity in B-Leukemic Xenografts
Rebecca Voltan, Paola Secchiero, Barbara Ruosi, Flavio Forni, Chiara Agostinis, Lorenzo Caruso, Maria Angela Vandelli, and Giorgio Zauli

Targeting Treatment-Resistant Breast Cancer Stem Cells with FKBPL and Its Peptide Derivative, AD-01, via the CD44 Pathway
Lana McClements, Anita Yakkundi, Angelos Papaspyropoulos, Hannah Harrison, Matthew P. Ablett, Puthen V. Jithesh, Hayley D. McKeen, Rachel Bennett, Christopher Donley, Adrien Kissel, Stuart McIntosh, Helen O. McCarthy, Eric O’Neill, Robert B. Clarke, and Tracy Robson

USP8 Is a Novel Target for Overcoming Gefitinib Resistance in Lung Cancer

Ketogenic Diets Enhance Oxidative Stress and Radio-Chemo-Therapy Responses in Lung Cancer Xenografts

Temporal and Spatial Evolution of Therapy-Induced Tumor Apoptosis Detected by Caspase-3–Selective Molecular Imaging
Quang-Dé Nguyen, Ioannis Lavdas, James Gubbins, Graham Smith, Robin Fortt, Laurence S. Carroll, Martin A. Graham, and Eric O. Aboagye

Spinophilin Loss Correlates with Poor Patient Prognosis in Advanced Stages of Colon Carcinoma

Developing a Common Language for Tumor Response to Immunotherapy: Immune-Related Response Criteria Using Unidimensional Measurements
Mizuki Nishino, Anita Giobbie-Hurder, Maria Gargano, Margaret Suda, Nikhil H. Ramaiya, and F. Stephen Hodi
### Evaluation of Midkine as a Diagnostic Serum Biomarker in Hepatocellular Carcinoma

Wen-Wei Zhu, Jia-Jian Guo, Lei Guo, Hu-Liang Jia, Ming Zhu, Ju-Bo Zhang, Christopher A. Loffredo, Marshonna Forgues, Hua Huang, Xu-Jian Xing, Ning Ren, Qiong-Zhu Dong, Hai-Jun Zhou, Zheng-Gang Ren, Nai-Qing Zhao, Xin Wei Wang, Zhao-You Tang, Lun-Xiu Qin, and Qing-Hai Ye

### The Prognostic Value of MicroRNAs Varies with Patient Race/Ethnicity and Stage of Colorectal Cancer

Liselle C. Bovell, Chandrakumar Shanmugam, Balananda-Dhurjati K. Putcha, Venkat R. Katkoori, Bin Zhang, Sejong Bae, Karan P. Singh, William E. Grizzle, and Upender Manne

### Antibiotic Treatment Decreases Microbial Burden Associated with Pseudomyxoma Peritonei and Affects β-Catenin Distribution

Cristina Semino-Mora, Traci L. Testerman, Hui Liu, Jeannette M. Whitmire, Kimberly Studeman, Yali Jia, Thomas J. McAvoy, Jennifer Francis, Carol Nieroda, Armando Sardi, D. Scott Merrell, and Andre Dubois

### Exposure–Response Relationships of the Efficacy and Safety of Ipilimumab in Patients with Advanced Melanoma

Yan Feng, Amit Roy, Eric Masson, Tai-Tsang Chen, Rachel Humphrey, and Jeffrey S. Weber

### Phase II Study of Everolimus in Patients with Metastatic Colorectal Adenocarcinoma Previously Treated with Bevacizumab-, Fluoropyrimidine-, Oxaliplatin-, and Irinotecan-Based Regimens

Kimmie Ng, Josep Taberner, Jimmy Hwang, Emilio Bajetta, Sunil Sharma, Salvatore A. Del Prete, Edward R. Arrowsmith, David P. Ryan, Michaela Sedova, Jin Jin, Kamel Malek, and Charles S. Fuchs

### PD-L1 Expression in B-cell Lymphomas and Virus-Associated Malignancies—Letter

Mads Hald Andersen

### Correction: Concomitant BRAF and PI3K/mTOR Blockade Is Required for Effective Treatment of BRAFV600E Colorectal Cancer

**LETTER TO THE EDITOR**

**CORRECTION**

AC icon indicates Author Choice

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

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

β-catenin is a transmembrane protein that associates with junctional proteins and assists with the maintenance of cell attachment. As revealed through immunofluorescent staining, β-catenin (shown in green) localizes to the cell membranes and within the lateral junctional complex in normal appendix tissue. In contrast, tissue samples from patients with pseudomyxoma peritonei display primarily cytoplasmic staining of β-catenin and virtually no staining at the intercellular boundaries. However, antibiotic treatment of patients with pseudomyxoma peritonei results in a significant increase in β-catenin within the cell membranes, appearing to aid in the renormalization of β-catenin distribution. For details, see the article by Semino-Mora and colleagues on page 3966 of this issue.