BREAKING ADVANCES

7149 Highlights from Recent Cancer Literature

INTEGRATED SYSTEMS AND TECHNOLOGIES

7168 The Role of Cell Density and Intratumoral Heterogeneity in Multidrug Resistance
Orit Lavi, James M. Greene, Doron Levy, and Michael M. Gottesman

Point: The new model suggested in this report might improve the design of treatment protocols and the analysis of patient responses to therapy.

A Circadian Clock Transcription Model for the Personalization of Cancer Chronotherapy

Point: A better understanding of a regulatory transcription loop that controls the molecular clock functions of normal cells might critically improve the tolerability of chemotherapy in patients.

MICROENVIRONMENT AND IMMUNOLOGY

7189 OX40 Is a Potent Immune-Stimulating Target in Late-Stage Cancer Patients
Brendan D. Curti, Magdalena Kovacsovics-Bankowski, Nicholas Morris, Edwin Walker, Lana Chisholm, Kevin Floyd, Joshua Walker, Ilana Gonzalez, Tanisha Meeusen, Bernard A. Fox, Tarsem Moudgil, William Miller, Daniel Haley, Todd Coffey, Brenda Fisher, Laurie Delanty-Miller, Nicole Rymarchuk, Tracy Kelly, Todd Crocenzi, Eric Bernstein, Rachel Sanborn, Walter J. Urba, and Andrew D. Weinberg

Point: This study offers clinical validation of a cancer therapy composed of a monoclonal antibody that can agonize signaling by the OX40 coreceptor on T cells, acting to enhance their antitumor properties as a generalized immunotherapy.

7199 Gut Microbiota Protects against Gastrointestinal Tumorigenesis Caused by Epithelial Injury
Yu Zhan, Po-Ju Chen, William D. Sadler, Fuyuan Wang, Sara Poe, Gabriel Núñez, Kathryn A. Eaton, and Grace Y. Chen

Point: This study highlights the beneficial impact of commensal bacteria on limiting colon tumorigenesis and provides a model system that will enable us to identify bacteria that help reduce susceptibility to colon cancer.

POINT–COUNTERPOINT REVIEWS

7151 It Is Not Always Necessary to Do Axillary Dissection for T1 and T2 Breast Cancer—Point
Monica Morrow
See Counterpoint and Reply by Sabel, p. 7156 and 7155

7155 It Is Not Always Necessary to Do Axillary Dissection for T1 and T2 Breast Cancer—Reply to Point
Michael S. Sabel
See Point by Morrow, p. 7151

7156 The Need for Axillary Lymph Node Dissection in T1/T2 Breast Cancer Surgery—Counterpoint
Michael S. Sabel
See Point and Reply by Morrow, p. 7151 and p. 7161

7161 The Need for Axillary Lymph Node Dissection in T1/T2 Breast Cancer Surgery—Reply to Counterpoint
Monica Morrow
See Counterpoint by Sabel, p. 7156

PRIORITY REPORT

7162 TERT Promoter Mutations Occur Early in Urothelial Neoplasia and Are Biomarkers of Early Disease and Disease Recurrence in Urine

Point: TERT promoter somatic mutations occur early in bladder cancer and are detectable in urine, providing an opportunity to develop highly accurate and inexpensive methods for early detection and monitoring of bladder cancer.

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<td>7211</td>
<td>TLR9 Signaling in the Tumor Microenvironment Initiates Cancer Recurrence after Radiotherapy</td>
<td>Chan Gao, Anna Kozlovska, Sergey Nechaev, Haiqing Li, Qifang Zhang, Dewan M.S. Hossain, Claudia M. Kowolik, Peiguo Chu, Piotr Swiderski, Don J. Diamond, Sumanta K. Pal, Andrew Raultsche and Marc Kortylewski</td>
<td>These findings suggest a rationale to improve the efficacy of cancer radiotherapy with inhibitors of the TLR9–STAT3 pathway, the activation of which appears to jump-start the regrowth of irradiated tumors.</td>
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<td>7232</td>
<td>Functional TLR5 Genetic Variants Affect Human Colorectal Cancer Survival</td>
<td>Sascha N. Klimosch, Asta Forstl, Jana Eckert, Jelena Knezevic, Melanie Bevier, Witigo von Schonfels, Nils Heits, Jessica Walter, Sebastian Hinze, Jesus Lascoz, Jochen Hampe, Dominik Hartl, Julia-Stefanie Frick, Kari Hemminki, Clemens Schafmayer, and Alexander N.R. Weber</td>
<td>Genetic factors and/or unmeasured differences in treatment or access to care should be further explored to understand and reduce ethnic disparities in breast cancer outcomes.</td>
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<td>7243</td>
<td>Genetic Ancestry and Risk of Mortality among U.S. Latinas with Breast Cancer</td>
<td>Laura Fejerman, Donglei Hu, Scott Huntsman, Esther M. John, Mariana C. Stern, Christopher A. Haiman, Eliseo J. Perez-Stable, and Elad Ziv</td>
<td>This work suggests that HDAC inhibitors would be most effective if combined with immunotherapy in the clinic.</td>
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<td>7254</td>
<td>Lenalidomide Inhibits Lymphangiogenesis in Preclinical Models of Mantle Cell Lymphoma</td>
<td>Kai Song, Brett H. Herzog, Minjia Sheng, Juanxin Fu, J. Michael McDaniel, Jia Ruan, and Lijun Xia</td>
<td>This is the first report on the novel therapeutic antilymphangiogenic mechanism of the immunomodulatory drug lenalidomide in lymphoma, which highlights the potential pathogenic role of lymphangiogenesis in lymphoma progression and dissemination.</td>
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<td>7265</td>
<td>An Intact Immune System Is Required for the Anticancer Activities of Histone Deacetylase Inhibitors</td>
<td>Alison C. West, Stephen R. Mattarollo, Jake Shortt, Leonie A. Cluse, Ailsa J. Christiansen, Mark J. Smyth, and Ricky W. Johnstone</td>
<td>These provocative findings suggest that HDAC inhibitors would be most effective if combined with immunotherapy in the clinic.</td>
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<td>7277</td>
<td>Combined Targeting of PDK1 and EGFR Triggers Regression of Glioblastoma by Reversing the Warburg Effect</td>
<td>Kiran Kumar Velpula, Arnima Bhasin, Swapna Asutilkar, and Andrew J. Tsung</td>
<td>This work suggests that PDK1 may serve as a novel therapeutic target in treating glioblastoma along with EGFR, and targeting this protein complex may open up further treatment avenues in the metabolic modulation of glioblastoma.</td>
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ALDH1-Positive Cancer Stem Cells Predict Engraftment of Primary Breast Tumors and Are Governed by a Common Stem Cell Program
Emmanuelle Charafe-Jauffret, Christophe Ginestier, François Bertucci, Olivier Cabaud, Julien Wicinski, Pascal Finetti, Emmanuelle Josselin, José Adelaide, Tien-Tuan Nguyen, Florence Monville, Jocelyne Jacquemier, Jeanne Thomassin-Piana, Guillaume Pinna, Aurélie Jalaguier, Eric Lambaudie, Gilles Houvenaeghel, Luc Xerri, Annick Harel-Bellan, Max Chaffanet, Patrice Viens, and Daniel Birnbaum

Précis: This work offers a convincing proof for the functional relevance of CSCs in breast cancer, and it establishes the reliability of patient-derived xenografts for use in developing personalized CSC therapies for breast cancer patients in the clinic.

YEATS4 Is a Novel Oncogene Amplified in Non–Small Cell Lung Cancer That Regulates the p53 Pathway
Larissa A. Pikor, William W. Lockwood, Kelsie L. Thu, Emily A. Vucic, Raj Chari, Adi F. Gazdar, Stephen Lam, and Wan L. Lam

Précis: This study identifies a novel candidate oncogene that may be amplified in up to one fifth of non–small cell lung carcinomas, with implications for understanding etiology and drug resistance.

GLI1 Interferes with the DNA Mismatch Repair System in Pancreatic Cancer through BHLHE41-Mediated Suppression of MLH1
Shingo Inaguma, Mihö Riku, Mitsuyoshi Hashimoto, Hideki Murakami, Shinsuke Saga, Hiroshi Ikeda, and Kenji Kasai

Précis: A pivotal transcription factor in the Hedgehog signaling pathway is found to regulate the DNA mismatch repair system in pancreatic carcinoma cells, with potential implications for understanding how these cancers arise and how they might be controlled by Hedgehog pathway inhibitors.

Acknowledgment to Reviewers