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

PRIORITY REPORT

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

MICROENVIRONMENT AND IMMUNOLOGY

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

It Is Not Always Necessary to Do Axillary Dissection for T1 and T2 Breast Cancer—Point
Monica Morrow
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 seventh paragraph of Morrow's Point  

It Is Not Always Necessary to Do Axillary Dissection for T1 and T2 Breast Cancer—Reply to Point
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The Need for Axillary Lymph Node Dissection in T1/T2 Breast Cancer Surgery—Counterpoint
Michael S. Sabel
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The Role of Cell Density and Intratumoral Heterogeneity in Multidrug Resistance
Orit Lavi, James M. Greene, Doron Levy, and Michael M. Gottesman

A Circadian Clock Transcription Model for the Personalization of Cancer Chronotherapy

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

The Need for Axillary Lymph Node Dissection in T1/T2 Breast Cancer Surgery—Counterpoint
Monica Morrow
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TERT Promoter Mutations Occur Early in Urothelial Neoplasia and Are Biomarkers of Early Disease and Disease Recurrence in Urine

Précis: 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.

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

Précis: 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.
MOLECULAR AND CELLULAR PATHOBIOLOGY

7222 | APOBEC3B Upregulation and Genomic Mutation Patterns in Serous Ovarian Carcinoma
Precis: Mutagenesis by APOBEC3B explains some of the genomic instability seen in ovarian cancer and represents a potential novel drug target for ovarian cancer treatment.

PREVENTION AND EPIDEMIOLOGY

7232 | Functional TLR5 Genetic Variants Affect Human Colorectal Cancer Survival
Precis: Genetic polymorphisms that alter the function of a Toll-like receptor and two of its effector molecules in colorectal cancer cells may exert an important impact on patient survival, with implications for biomarker and therapy development.

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

7243 | Genetic Ancestry and Risk of Mortality among U.S. Latinas with Breast Cancer
Laura Penderman, Donglei Hu, Scott Huntsman, Esther M. John, Mariana C. Stern, Christopher A. Haiman, Eliseo J. Perez-Stable, and Elad Ziv
Precis: 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.

7254 | Lenalidomide Inhibits Lymphangiogenesis in Preclinical Models of Mantle Cell Lymphoma
Kai Song, Brett H. Herzog, Minjia Sheng, Jiaxin Fu, J. Michael McDaniel, Jia Ruan, and Lijun Xia
Precis: 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.

7265 | An Intact Immune System Is Required for the Anticancer Activities of Histone Deacetylase Inhibitors
Alison C. West, Stephen R. Mattarollo, Jake Shortt, Leonie A. Cluse, Ailsa J. Christiansen, Mark J. Smyth, and Ricky W. Johnstone
Precis: These provocative findings suggest that HDAC inhibitors would be most effective if combined with immunotherapy in the clinic.

7277 | Combined Targeting of PDK1 and EGFR Triggers Regression of Glioblastoma by Reversing the Warburg Effect
Kiran Kumar Velpula, Armita Bhasin, Swapna Asuthkar, and Andrew J. Tsung
Precis: 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.
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 Josselein, Josée Adelaide, Tien-Tuan Nguyen, Florence Monville, Jocelyne Jacquier, 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, Miho 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

ABOUT THE COVER
The antitumor effects of histone deacetylase inhibitors (HDACi) are repressed in immunocompromised mice. Rag-2γc−/− mice transplanted with Eμ-myc B-cell lymphomas and treated with HDACi succumb significantly earlier than wild-type tumor-bearing mice and die with high splenic tumor burden as shown in this image (magnification, ×10). HDACi are able to inhibit their target enzymes and mediate tumor cell apoptosis in immunocompromised mice, however, in the absence of a functional immune system, the therapeutic efficacy of HDACi is significantly diminished. These data demonstrate the importance of a host immune system for sustained antitumor responses mediated by HDACi and indicate that these agents could be combined with immunotherapy to enhance efficacy. For details, see article by West and colleagues on page 7265.

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