

BREAKING ADVANCES

- 4245** Highlights from Recent Cancer Literature


REVIEWS

- 4247** Mapping the Pathways of Resistance to Targeted Therapies
Kris C. Wood
- 4252** Breast Cancer Tumor Suppressors: A Special Emphasis on Novel Protein Nischarin
Mazvita Maziveyi and Suresh K. Alahari
- 4260** Extracellular DNA: A Bridge to Cancer
Martha C. Hawes, Fushi Wen, and Emad Elquza

PRIORITY REPORT

- 4265** The Neuronal Pentraxin-2 Pathway Is an Unrecognized Target in Human Neuroblastoma, Which Also Offers Prognostic Value in Patients
Alice Bartolini, Daniela Di Paolo, Alessio Noghero, Daniele Murgia, Angela R. Sementa, Michele Cilli, Renata Pasqualini, Wadih Arap, Federico Bussolino, Mirco Ponzoni, Fabio Pastorino, and Serena Marchiò
- Précis:* A ligand-receptor system associated with synapses in the nervous system is shown in this study to have important functional and prognostic roles in deadly pediatric neuroblastomas, where it may offer a tractable new therapeutic target.

INTEGRATED SYSTEMS AND TECHNOLOGIES

- 4272**  A Quantitative System for Studying Metastasis Using Transparent Zebrafish
Silja Heilmann, Kajan Ratnakumar, Erin M. Langdon, Emily R. Kansler, Isabella S. Kim, Nathaniel R. Campbell, Elizabeth B. Perry, Amy J. McMahon, Charles K. Kaufman, Ellen van Rooijen, William Lee, Christine A. Iacobuzio-Donahue, Richard O. Hynes, Leonard I. Zon, Joao B. Xavier, and Richard M. White
- Précis:* In zebrafish, advances in quantitative imaging combined with the ease, tractability, and amenability to genetic analysis produce a powerful tool for studying metastasis and other pathological processes in cancer.

- 4283** Preclinical Validation of the Utility of BLZ-100 in Providing Fluorescence Contrast for Imaging Spontaneous Solid Tumors
Janean Fidel, Katie C. Kennedy, William S. Demell, Stacey Hansen, Valorie Wiss, Mark R. Stroud, Joshua I. Molho, Sue E. Knoblaugh, Jeffrey Meganck, James M. Olson, Brad Rice, and Julia Parrish-Novak

Précis: This preclinical proof-of-concept study for a new fluorescence imaging agent addresses the need in surgical oncology for real-time visualization of solid tumors that can improve their complete and precise resection, a key factor in extending patient remission and survival times.

MICROENVIRONMENT AND IMMUNOLOGY

- 4292** Fas Ligand Deficiency Impairs Tumor Immunity by Promoting an Accumulation of Monocytic Myeloid-Derived Suppressor Cells
Sanam Peyvandi, Stéphanie Buart, Boubekour Samah, Marie Vétizou, Yanyan Zhang, Ludovic Durrieu, Mélanie Polrot, Salem Chouaib, Karim Benihoud, Fawzia Louache, and Saoussen Karray

Précis: These findings establish a new role for a cell death receptor ligand in tumor suppression, which acts by limiting immunosuppressive myeloid cells found in the tumor microenvironment.

- 4302** STAT3 Blockade Inhibits Radiation-Induced Malignant Progression in Glioma
Jasmine Lau, Shirin Ilkhanizadeh, Susan Wang, Yekaterina A. Miroshnikova, Nicolas A. Salvatierra, Robyn A. Wong, Christin Schmidt, Valerie M. Weaver, William A. Weiss, and Anders I. Persson

Précis: These findings implicate therapeutic blockade of JAK2-STAT3 signaling as a supplementary strategy in patients undergoing radiation therapy for high-grade glioma to prevent acquired treatment resistance and invasiveness at recurrence.

- 4312** CCL5-Mediated Th2 Immune Polarization Promotes Metastasis in Luminal Breast Cancer
Qianfei Zhang, Jilong Qin, Lin Zhong, Lei Gong, Bing Zhang, Yan Zhang, and Wei-Qiang Gao

Précis: These findings show that CCL5/CCR3 signaling promotes metastasis by inducing Th2 polarization of CD4⁺ T cells in luminal breast cancers, with implications for prognosis and immunotherapy in this setting.

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4322 Androgen-Regulated SPARCL1 in the Tumor Microenvironment Inhibits Metastatic Progression

Paula J. Hurley, Robert M. Hughes, Brian W. Simons, Jessie Huang, Rebecca M. Miller, Brian Shinder, Michael C. Haffner, David Esopi, Yasunori Kimura, Javaneh Jabbari, Ashley E. Ross, Nicholas Erho, Ismael A. Vergara, Sheila F. Faraj, Elai Davicioni, George J. Netto, Srinivasan Yegnasubramanian, Steven S. An, and Edward M. Schaeffer

Précis: Androgen receptor-regulated changes in the prostate are restricted by SPARCL1, a matrix protein in the tumor microenvironment that limits malignant progression by attenuating physical forces needed for local and metastatic invasion of prostate cancer cells.

MOLECULAR AND CELLULAR PATHOBIOLOGY

4335 TIF1 γ Suppresses Tumor Progression by Regulating Mitotic Checkpoints and Chromosomal Stability

Roxane M. Pommier, Johann Gout, David F. Vincent, Lindsay B. Alcaraz, Nicolas Chuvin, Vanessa Arfi, Sylvie Martel, Bastien Kaniewski, Guillaume Devailly, Geneviève Fourel, Pascal Bernard, Caroline Moyret-Lalle, Stéphane Ansieau, Alain Puisieux, Ulrich Valcourt, Stéphanie Sentis, and Laurent Bartholin

Précis: These findings provide insight into how a tumor suppressor inactivated in a variety of human cancers limits malignant development by supporting mitotic cell cycle checkpoints that help ensure chromosomal integrity.

4351 The Estrogen Receptor Cofactor SPEN Functions as a Tumor Suppressor and Candidate Biomarker of Drug Responsiveness in Hormone-Dependent Breast Cancers

Stéphanie Légaré, Luca Cavallone, Aline Mamo, Catherine Chabot, Isabelle Sirois, Anthony Magliocco, Alexander Klimowicz, Patricia N. Tonin, Marguerite Buchanan, Dana Keilty, Saima Hassan, David Laperrière, Sylvie Mader, Olga Aleynikova, and Mark Basik

Précis: This study identifies a novel tumor suppressor gene that in estrogen receptor- α -expressing breast cancers predicts the chemoresponse to tamoxifen, addressing needs for a predictive biomarker in hormone-responsive tumors.

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

4364 ADAPT, a Novel Scaffold Protein-Based Probe for Radionuclide Imaging of Molecular Targets That Are Expressed in Disseminated Cancers



Javad Garousi, Sarah Lindbo, Johan Nilvebrant, Mikael Åstrand, Jos Buijs, Mattias Sandström, Hadis Honarvar, Anna Orlova, Vladimir Tolmachev, and Sophia Hober

Précis: This study offers preclinical proof of concept for a flexible and robust class of in vivo imaging probes that permit high-contrast, noninvasive imaging of molecular targets in tumors, with immediate potential to enable patient stratification for personalized anticancer therapy.

4372 Intratumoral Heterogeneity in EGFR-Mutant NSCLC Results in Divergent Resistance Mechanisms in Response to EGFR Tyrosine Kinase Inhibition

Margaret Soucheray, Marzia Capelletti, Inés Pulido, Yanan Kuang, Cloud P. Paweletz, Jeffrey H. Becker, Eiki Kikuchi, Chunxiao Xu, Tarun B. Patel, Fatima Al-shahrour, Julián Carretero, Kwok-Kin Wong, Pasi A. Jänne, Geoffrey I. Shapiro, and Takeshi Shimamura

Précis: Drug resistance mechanisms for EGFR tyrosine kinase inhibitors in non-small lung cancers converge on epithelial-to-mesenchymal transition (EMT), such that countering EMT-associated resistance may inadvertently select for rare cell subpopulations capable of triggering alternative resistance pathways.

4384 Targeting the miR-221–222/PUMA/BAK/BAX Pathway Abrogates Dexamethasone Resistance in Multiple Myeloma

Jian-Jun Zhao, Zhang-Bo Chu, Yu Hu, Jianhong Lin, Zhongqiu Wang, Meng Jiang, Ming Chen, Xujun Wang, Yue Kang, Yangsheng Zhou, Triona Ni Chonghaile, Melanie E. Johncilla, Yu-Tzu Tai, Jin Q. Cheng, Antony Letai, Nikhil C. Munshi, Kenneth C. Anderson, and Ruben D. Carrasco

Précis: The miRNAs on which this study focuses may offer useful diagnostic or prognostic markers for drug resistance as well as possible targets to improve therapeutic outcomes.

4398 Kinome RNAi Screens Reveal Synergistic Targeting of MTOR and FGFR1 Pathways for Treatment of Lung Cancer and HNSCC

Katherine R. Singleton, Trista K. Hinz, Emily K. Kleczko, Lindsay A. Marek, Jeff Kwak, Taylor Harp, Jihye Kim, Aik Choon Tan, and Lynn E. Heasley

Précis: These results suggest that synergistic growth inhibition of lung cancers and head and neck cancers can be achieved by combined treatment with FGFR and MTOR inhibitors, offering a simple strategy to improve clinical management of FGFR1-driven cancers.

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- 4407** Combining miR-10b–Targeted Nanotherapy with Low-Dose Doxorubicin Elicits Durable Regressions of Metastatic Breast Cancer
Byunghee Yoo, Amol Kavishwar, Alana Ross, Ping Wang, Doris P. Tabassum, Kornelia Polyak, Natalia Barteneva, Victoria Petkova, Pamela Pantazopoulos, Aseda Tena, Anna Moore, and Zdravka Medarova

Précis: These striking results suggest the existence of pathways that regulate the viability and proliferation of tumor cells only after they have acquired the ability to grow at distant metastatic sites, with important implications for selective targeting of advanced cancers.

TUMOR AND STEM CELL BIOLOGY

- 4416** Selective Inhibition of Parallel DNA Damage Response Pathways Optimizes Radiosensitization of Glioblastoma Stem-like Cells

Shafiq U. Ahmed, Ross Carruthers, Lesley Gilmour, Salih Yildirim, Colin Watts, and Anthony J. Chalmers

Précis: Radioresistance acquired by glioblastoma stem-like cells appears to be driven by both enhanced cell cycle checkpoint activation and DNA repair, implying that optimal radiosensitization might only be achieved by dual inhibition of both pathways.

- 4429** Mitochondrial Genetics Regulate Breast Cancer Tumorigenicity and Metastatic Potential

Kyle P. Feeley, Alexander W. Bray, David G. Westbrook, Larry W. Johnson, Robert A. Kesterson, Scott W. Ballinger, and Danny R. Welch

Précis: These striking findings suggest that mitochondrial DNA polymorphisms may have a far greater impact on breast cancer development and metastasis than suspected currently.

CORRECTION

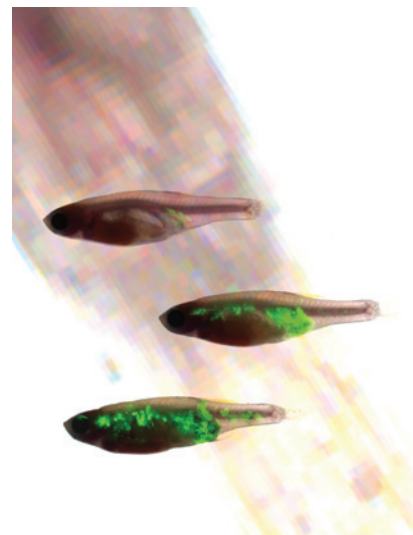
- 4437** Correction: ADAM28 Is Overexpressed in Human Breast Carcinomas: Implications for Carcinoma Cell Proliferation through Cleavage of Insulin-like Growth Factor Binding Protein-3

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ABOUT THE COVER

A stable, fluorescently labeled zebrafish melanoma cell line derived from transgenic *mitfa*-*BRAF*^{V600E}; *p53*^{-/-}; *mitfa*-GFP fish was transplanted into casper, a transparent adult zebrafish. Green fluorescent melanoma cells metastasize to various regions of the transparent host fish over time. Shown here are sequential images of a tumor transplant that enable the quantitative assessment of metastatic spread *in vivo*. For details, see article by Heilmann and colleagues on page 4272.



Cancer Research

The Journal of Cancer Research (1916–1930) | The American Journal of Cancer (1931–1940)

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