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### BREAKING ADVANCES

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### REVIEWS

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<td>The Neuronal Pentraxin-2 Pathway Is an Unrecognized Target in Human Neuroblastoma, Which Also Offers Prognostic Value in Patients</td>
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**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

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**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.

### MICROENVIRONMENT AND IMMUNOLOGY

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**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.

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**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.

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

October 15, 2015 • Volume 75 • Number 20

Preclinical Validation of the Utility of BLZ-100 in Providing Fluorescence Contrast for Imaging Spontaneous Solid Tumors
Janean Fidel, Katie C. Kennedy, William S. Dernell, Stacey Hansen, Valerie 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.

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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.
Androgen-Regulated SPARCL1 in the Tumor Microenvironment Inhibits Metastatic Progression
Paula J. Hurley, Robert M. Hughes, Brian W. Simons, Jesse 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.

TIFF1 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 Devalilly, Geneviève Fourdel, Pascal Bernard, Caroline Moyret-Lalley, Stéphane Anseaux, 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.

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 Sinois, Anthony Magliocco, Alexander Klimowicz, Patricia N. Tonin, Marguerite Buchanan, Dana Keilty, Saima Hassan, David Lapertière, 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.

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

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.

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, Chunxia Xu, Tanun B. Patel, Fatima Al-shahrour, Julián Carretero, Kwook-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.

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

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.

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.
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 Barreneche, Victoria Pekova, Pamela Pantazopoulou, Aseeda 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.

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.

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

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