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### Priority Report

4265 The Neuronal Pentraxin-2 Pathway Is an Unrecognized Target in Human Neuroblastoma, Which Also Offers Prognostic Value in Patients
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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.

### Microenvironment and Immunology

4292 Fas Ligand Deficiency Impairs Tumor Immunity by Promoting an Accumulation of Monocytic Myeloid-Derived Suppressor Cells
Sanam Peyvandi, Stephanie Buart, Boubekeur Samah, Marie Vetizou, Yanyan Zhang, Ludovic Durrieu, Melanie 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.

### Integrated Systems and Technologies

4272 A Quantitative System for Studying Metastasis Using Transparent Zebrafish

**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.

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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Cancer Research

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, 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.

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

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Androgen-Regulated SPARC1 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, Srivivasan Vegnasubramanian, Steven S. An, and Edward M. Schaeffer

Precis: Androgen receptor-regulated changes in the prostate are restricted by SPARC1, 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

TIF1γ 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, Genevieve Fourel, Pascal Bernard, Caroline Moyret-Lalle, Stéphane Anseau, Alain Puisieux, Ulrich Valcourt, Stéphanie Sentis, and Laurent Bartholin

Precis: 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. Tomin, Marguerite Buchanan, Dana Keilty, Saima Hassan, David Lapertrière, Sylvie Mader, Olga Aleynikova, and Mark Basik

Precis: 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 Tolvachev, and Sophia Hober

Precis: 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

Precis: 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

Precis: 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. Klecza, Lindsay A. Marek, Jeff Kwak, Taylor Harp, Jihye Kim, Aik Choon Tan, and Lynn E. Heasley

Precis: 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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<td>Byunghee Yoo, Amol Kavishwar, Alana Ross, Ping Wang, Doris F. Tabassum, Kornelia Polyak, Natalia Barrenece, Victoria Petkova, Pamela Pantazopoulos, Aseda Tena, Anna Moore, and Zdravka Medarova</td>
<td>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.</td>
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<td>4416</td>
<td>Selective Inhibition of Parallel DNA Damage Response Pathways Optimizes Radiosensitization of Glioblastoma Stem-like Cells</td>
<td>Shafiq U. Ahmed, Ross Carruthers, Lesley Gilmour, Salih Yildirim, Colin Watts, and Anthony J. Chalmers</td>
<td>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.</td>
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<td>Mitochondrial Genetics Regulate Breast Cancer Tumorigenicity and Metastatic Potential</td>
<td>Kyle P. Feeley, Alexander W. Bray, David G. Westbrook, Larry W. Johnson, Robert A. Kesterson, Scott W. Ballinger, and Danny R. Welch</td>
<td>These striking findings suggest that mitochondrial DNA polymorphisms may have a far greater impact on breast cancer development and metastasis than suspected currently.</td>
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**ABOUT THE COVER**

A stable, fluorescently labeled zebrafish melanoma cell line derived from transgenic mitfa-BRAG100; 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.
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