Cancer Research

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David Y. Oh, Jason Cham, Li Zhang, Grant Fong, Serena S. Kwek, Mark Klinger, Malek Faham, and Lawrence Fong

MICROENVIRONMENT AND IMMUNOLOGY

1250 Précis: These findings present a mechanistic rationale to relieve the severe bone pain experienced by multiple myeloma patients, with immediate clinical implications for treatment.

1296 Précis: Combination therapy using an agonistic antibody can significantly enhance CAR T-cell response, concomitant with reduced numbers of immunosuppressive cell types, suggesting a potentially powerful approach to treat solid cancers with adoptive immunotherapy.

1310 Précis: Immumomodulatory aptamers can be targeted directly to tumors by binding to radiation-induced tumor stress products, increasing therapeutic index.

1322 Précis: Autoimmune side effects often seen with immune checkpoint inhibitors are associated with rapid increases in the diversity of the circulating T-cell pool.
MOLECULAR AND CELLULAR PATHOBIOLOGY

1331 Bone Metastasis of Prostate Cancer Can Be Therapeutically Targeted at the TBX2–WNT Signaling Axis

1345 RelB Expression Determines the Differential Effects of Ascorbic Acid in Normal and Cancer Cells
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1357 A Transposon-based Analysis Reveals RASA1 Is Involved in Triple-Negative Breast Cancer
Cristian Suárez-Cabrera, Rita M. Quintana, Ana Bravo, M. Llanos Casanova, Angustias Page, Josefa P. Alameda, Jesus M. Paramio, Alicia Maroto, Javier Salamanca, Adam J. Dupuy, Angel Ramirez, and Manuel Navarro

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1383 Aberrant Phosphorylation of SMAD4 Thr277-Mediated USP9x–SMAD4 Interaction by Free Fatty Acids Promotes Breast Cancer Metastasis
Yong Wu, Xiaoting Yu, Xianghua Yi, Ke Wu, Sami Dwabe, Mohammad Atefi, Yahya Eshimali, Kevin T. Kemp II, Kruttika Bhat, Jose Haro, Mariana Sarkissian, and Jaydutt V. Vadgama

1395 Tumor-Associated Neutrophils and Macrophages Promote Gender Disparity in Hepatocellular Carcinoma in Zebrafish
Chuan Yan, Qiqi Yang, and Zhiyuan Gong

Précis: These findings provide a mechanism-based targeting rationale to inhibit bone metastasis in advanced prostate cancer, a common feature of late stage disease.

Précis: Changing ROS levels affects levels of the NF-κB transcription factor RelB, thereby affecting the capability of i.v. ascorbic acid to differentially and usefully influence the radiosensitivity of normal and cancer tissues.

Therapeutically Targeted at the TBX2

Précis: Alleric loss of Rasa1, a gene controlling the Ras pathway, is a frequent occurrence in triple-negative breast cancer.

Précis: This study uncovers a positive feedback loop in the metabolism of cancer-associated fibroblasts and epithelial ovarian cancer cells critical for their metastatic progression.

Therapeutically Targeted at the TBX2–WNT Signaling Axis

Précis: These findings reveal a role for endolysosomal two-pore channels in leading edge formation in cancer cells, suggesting their novelty as targets for treatment of invasive tumors.

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

1408 Biomarker Dynamics in B-cell Lymphoma: A Longitudinal Prospective Study of Plasma Samples Up to 25 Years before Diagnosis
Florentin Spath, Carl Wilbom, Esmeralda J.M. Kroop, Ann-Sofie Johansson, Ingear A. Bergdahl, Roel Vermeulen, and Beatrice Melin

Précis: Sustained B-cell activation is a dynamic process during lymphomagenesis that may be indicative of occult disease or disease progression in monitoring patients with indolent lymphomas.

1416 Reprogramming Medulloblastoma-Propagating Cells by a Combined Antagonism of Sonic Hedgehog and CXCR4
Stacey A. Ward, Nicole M. Warrington, Sara Taylor, Najla Kfoury, Jingqin Luo, and Joshua B. Rubin

Précis: These findings suggest a mechanism-based approach to eradicate the most recalcitrant cells in one common type of pediatric brain cancer.

1427 Two-Pore Channel Function Is Crucial for the Migration of Invasive Cancer Cells
Ong Nam Phuong Nguyen, Christian Grimm, Lina S. Schneider, Yu-Kai Chao, Carina Atzberger, Karin Bartel, Anna Watermann, Melanie Ulrich, Doris Mayr, Christian Wahl-Schott, Martin Biel, and Angelika M. Vollmar

Précis: These findings reveal a role for endolysosomal two-pore channels in leading edge formation in cancer cells, suggesting their novelty as targets for treatment of invasive tumors.

1439 Constitutive NOTCH3 Signaling Promotes the Growth of Basal Breast Cancers
Lisa Choy, Thiis J. Hagenbeek, Margaret Solon, Dorothy French, David Finkle, Amy Shelton, Rayna Venoook, Matthew J. Brauer, and Christian W. Siebel

Précis: An antibody that can directly assess receptor signaling distinguishes constitutive and ligand-independent activity of the oncogenic Notch pathway in enabling the malignant growth of basal breast cancers.
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### 1453 Bone Marrow Adipocytes Facilitate Fatty Acid Oxidation Activating AMPK and a Transcriptional Network Supporting Survival of Acute Monocytic Leukemia Cells


**Précis:** These findings suggest that targeting metabolic abnormalities in leukemia cells located in the bone marrow is potentially promising and innovative therapeutic approach.

### 1465 Fibrinolytic Enzyme Cotherapy Improves Tumor Perfusion and Therapeutic Efficacy of Anticancer Nanomedicine

Ameya R. Kirtane, Tanmoy Sadhukha, Hyunjoon Kim, Vidhi Khanna, Brenda Koniar, and Jayanth Panyam

**Précis:** These findings suggest that cotherapy with a fibrinolytic enzyme could be used to improve diffusion, intratumoral distribution, and overall effectiveness of anticancer nanomedicine.

### 1476 \( ^{[18F]}(2S,4R)4\)-Fluoroglutamine PET Detects Glutamine Pool Size Changes in Triple-Negative Breast Cancer in Response to Glutaminase Inhibition

Rong Zhou, Austin R. Pantel, Shihong Li, Brian P. Lieberman, Karl Ploesel, Hoon Choi, Eric Blankemeyer, Hsiaoju Lee, Hank F. Kung, Robert H. Mach, and David A. Mankoff

**Précis:** These findings reveal the utility of a noninvasive PET imaging method to monitor pharmacodynamic responses to cancer drugs that target glutamine breakdown.

### 1485 Prostate Cancer Patients with Late Radiation Toxicity Exhibit Reduced Expression of Genes Involved in DNA Double-Strand Break Repair and Homologous Recombination

Bregje van Ooischot, Lon Uitterhoeve, Ilja Oomen, Rosemarie ten Cate, Ian Paul Medema, Harry Vrieling, Lukas J.A. Stalpers, Perry D. Moerland, and Nicolaas A.P. Franken

**Précis:** Patients who are inherently less efficient at DNA double-strand break repair may be at risk for severe late radiation toxicity.

### 1492 Aberrant SYK Kinase Signaling Is Essential for Tumorigenesis Induced by TSC2 Inactivation

Ye Cui, Wendy K. Steagall, Anthony M. Lamattina, Gustavo Pacheco-Rodriguez, Mario Stylianou, Pranav Kidambi, Benjamin Stump, Fernanda Golzarri, Ivan O. Rosas, Carmen Priolo, Elizabeth P. Henske, Joel Moss, and Souheil El-Chemaly

**Précis:** These results illuminate how mutations in the tumor suppressor gene TSC2 lead to formation of a variety of organ lesions.

### CORRECTIONS

1503 Correction: Long Noncoding RNA GCASPC, a Target of miR-17-3p, Negatively Regulates Pyruvate Carboxylase-Dependent Cell Proliferation in Gallbladder Cancer

1504 Correction: Cdk5 Directly Targets Nuclear p21\(^{CDKI}\) and Promotes Cancer Cell Growth

1505 Correction: Differential Regulation of the Melanoma Proteome by eIF4A1 and eIF4E

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ABOUT THE COVER

Many human tumors are characterized by extensive fibrin deposition in their extracellular matrix. Shown here is a representative image of a human colon tumor section stained for fibrin. For details, see article by Kirtane and colleagues on page 1465.