PD-1/SHP-2 Inhibits Tc1/Th1 Phenotypic Responses and the Activation of T Cells in the Tumor Microenvironment
Jing Li, Hyun-Bae Jie, Yu Lei, Neil Gilden-Leapman, Sumita Trivedi, Tony Green, Lawrence P. Kane, and Robert L. Ferris
Précis: This study addresses the mechanisms through which PD-1 antibody therapy restores the ability of the immune system to recognize and attack tumors by skewing intratumoral T cells toward a more potent activation phenotype that is associated with enhanced signaling and a reversal of their immunosuppressed phenotype.

Host miR155 Promotes Tumor Growth through a Myeloid-Derived Suppressor Cell–Dependent Mechanism
Suji Chen, Long Wang, Jie Fan, Cong Ye, Donye Dominguez, Yi Zhang, Tyler J. Curiel, Deyu Fang, Timothy M. Kuzel, and Bin Zhang
Précis: These findings reveal an immunosuppressive function for an miRNA thought to be solely immunostimulatory, establishing a contextual role that prompts caution for suggested strategies to manipulate its expression for cancer therapy.

Lysophosphatidic Acid Receptor LPAR6 Supports the Tumorigenicity of Hepatocellular Carcinoma
Antonio Mazzocca, Francesco Dituri, Flavia De Santis, Addolorata Filannino, Chiara Lopane, Regina C. Betz, Ying-Yi Li, Naofumi Mukaida, Peter Winter, Cosimo Tortorella, Gianluigi Giannelli, and Carlo Sabbà
Précis: These findings link overexpression of a lysophosphatidic acid receptor during liver cancer development to upregulation of the PIM3 oncogene, which is implicated in histone modification and apoptosis, with implications for prognosis and treatment in this disease setting.

Human Pancreatic Cancer Tumors Are Nutrient Poor and Tumor Cells Actively Scavenge Extracellular Protein
Jurje J. Kamphorst, Michel Nofal, Cosimo Commisso, Sean R. Hackett, Wenyun Lu, Elda Grabocka, Matthew G. Vander Heiden, George Miller, Jeffrey A. Drebin, Dafna Bar-Sagi, Craig B. Thompson, and Joshua D. Rabinowitz
Précis: Scavenging of extracellular protein represents a previously unappreciated pathway of nutrient uptake in human pancreatic tumors, providing new insights into how these tumors grow in nutrient-poor conditions.
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**554** Gain of Glucose-Independent Growth upon Metastasis of Breast Cancer Cells to the Brain  
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**Précis:** This study defines a specific metabolic condition required to sustain brain metastasis, with therapeutic implications for how this deadly feature of advanced breast cancer might be eradicated.

**566** Identification of a Functional SNP in the 3'UTR of CXCR2 That Is Associated with Reduced Risk of Lung Cancer  
Bríd M. Ryan, Ana I. Robles, Andrew C. McClary, Majda Haznadar, Elise D. Bowman, Sharon R. Pine, Derek Brown, Mohammed Khan, Kouya Shiraiishi, Takashi Kohno, Hirokazu Okayama, Ramakrishna Modali, Jun Yokota, and Curtis C. Harris  
**Précis:** A genetic polymorphism in a chemokine receptor known to drive myeloid recruitment in the tumor microenvironment confers strong protection against lung cancer, with potential implications in understanding etiology, prognosis, and therapeutic response in this widespread disease.

**576** Perinatal and Familial Risk Factors for Brain Tumors in Childhood through Young Adulthood  
Casey Crump, Jan Sundquist, Weiva Sieh, Marilyn A. Winkleby, and Kristina Sundquist  
**Précis:** In this large national cohort study, high birth weights associated with an increased risk of brain tumors were traced to a role for high growth rates rather than gestational age.

#### THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

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**Précis:** These findings establish a novel functional connection in breast cancer, with implications for ways to combine targeted therapeutics to stratify patients and enhance efficacy.

**594** Bruton Tyrosine Kinase Is a Therapeutic Target in Stem-like Cells from Multiple Myeloma  
Ye Yang, Junmei Shi, Zhimin Gu, Mohamed E. Salama, Satyabrata Das, Erik Wendlandt, Hongwei Xu, Junwei Huang, Yi Tao, Mu Hao, Reinaldo Franqui, Dana Levasseur, Siegfried Janz, Guido Tricot, and Fenghuang Zhan  
**Précis:** These findings provide a preclinical rationale for repositioning a recently approved drug to treat aggressive multiple myelomas, with immediate implications for clinical evaluation of this strategy.

**605** Acute Tissue Injury Activates Satellite Cells and Promotes Sarcoma Formation via the HGF/c-MET Signaling Pathway  
David Van Mater, Leonor Áñó, Jordan M. Blum, Micah T. Webster, Wei-Qiao Huang, Nerissa Williams, Yan Ma, Diana M. Cardona, Chen-Ming Fan, and David G. Kirsch  
**Précis:** Extending early insights from Ewing and other prominent physicians that injury causes sarcoma development, these authors found that tissue injury in a mouse model of soft tissue sarcoma acts as a strong promoter of tumor formation that is mediated by HGF/c-MET signaling.

**615** Retraction: NRH:Quinone Oxidoreductase 2 and NAD(P)H:Quinone Oxidoreductase 1 Protect Tumor Suppressor p53 against 20S Proteasomal Degradation Leading to Stabilization and Activation of p53

**616** Correction: Crosstalk between microRNA30a/b/c/d/e-5p and the Canonical Wnt Pathway: Implications for Multiple Myeloma Therapy

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ABOUT THE COVER

Altered metabolism is a common feature of cancer cells, but little is known as to what metabolic changes benefit breast cancer brain metastases. Fructose-1,6-bisphosphatase 2 (FBP2), a rate limiting enzyme of gluconeogenesis, was found to be significantly upregulated in breast cancer brain metastasis. FBP2 empowers brain metastatic cancer cells with the ability to grow independently of glucose. For details, see article by Chen and colleagues on page 554.