**Breaking Advances**

473 Highlights from Recent Cancer Literature

**Reviews**

475 Th9 Cells: A Novel CD4 T-cell Subset in the Immune War against Cancer
Frédérique Végran, Lionel Apetoh, and François Ghiringhelli

480 Novel Insights into Head and Neck Cancer using Next-Generation "Omic" Technologies
Lusia Sepiashvili, Jeff P. Bruce, Shao Hui Huang, Brian O’Sullivan, Fei-Fei Liu, and Thomas Kistler

**Microenvironment and Immunology**

487 Role of Chitinase 3–like-1 and Semaphorin 7a in Pulmonary Melanoma Metastasis
Bing Ma, Erica L. Herzog, Chun Geun Lee, Xueyan Peng, Chang-Min Lee, Xiaosong Chen, Sara Rockwell, Ja Seok Koo, Harriet Kluger, Roy S. Herbst, Mario Sznol, and Jack A. Elias

Précis: A member of an ancient gene family that binds the chitin in fungi and other pathogens is found to be needed to program lung microenvironments that are permissive for metastasis, with potential implications for learning how to block dissemination of many types of cancer to this common site.

497 Strict Requirement for Vector-Induced Type I Interferon in Efficacious Antitumor Responses to Virally Encoded IL12
Ignacio Melero, Jose I. Quetglas, Mercedes Reboredo, Juan Dubrot, Juan R. Rodriguez-Madoz, Ulua Manchero, Erkuden Casales, Jose I. Riezu-Boj, Marta Ruiz-Guillen, Maria C. Ochoa, Miguel F. Sannamed, Nathalie Thiebemont, Cristian Smerdou, and Sandra Hervas-Stubbs

Précis: These findings support the argument that efficacy of a cancer gene therapy employing a viral vector for administration may be highly dependent upon a vector-induced type I interferon response, with possible implications for a broad array of translational projects currently being evaluated in the clinic.

**Molecular and Cellular Pathobiology**

532 Lyosphosphatidic 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.

544 Human Pancreatic Cancer Tumors Are Nutrient Poor and Tumor Cells Actively Scavenge Extracellular Protein
Jurje J. Kamphorst, Michel Nofal, Cosimo Commissio, 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..

508 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 Gildener-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.

519 Host miR155 Promotes Tumor Growth through a Myeloid-Derived Suppressor Cell–Dependent Mechanism
Xu Chen, Long Wang, Jie Fan, Cong Ye, Donye Dominguez, Yi Zhang, Tyler J. Curiel, Deyu Fang, Timothy M. Kuxel, 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.
Gain of Glucose-Independent Growth upon Metastasis of Breast Cancer Cells to the Brain
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.

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.

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.

PDGFα and β Play Critical Roles in Mediating Foxq1-Driven Breast Cancer Stemness and Chemoresistance
Fanyan Meng, Cecilia L. Speyer, Bin Zhang, Yongzhou Zhao, Wei Chen, David H. Gorski, Fred R. Miller, and Guojun Wu
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.

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.

Acute Tissue Injury Activates Satellite Cells and Promotes Sarcoma Formation via the HGF/c-MET Signaling Pathway
David Van Mater, Leonor Añó, Jordan M. Blum, Micah T. Webster, WeiQiao 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.

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

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