Endothelial ALK1 Is a Therapeutic Target to Block Metastatic Dissemination of Breast Cancer
Sara I. Cunha, Matteo Bocci, John Lövrot, Nikolas Eleftheriou, Pernilla Roswall, Eugenia Cordero, Linda Lindström, Michael Bartoschek, B. Kristian Haller, R. Scott Pearsall, Aaron W. Mulivor, Ravindra Kumar, Christer Larsson, Jonas Bergh, and Kristian Pietras

Précis: These findings offer preclinical proof of concept for the utility of ALK1 inhibitors to treat metastatic breast cancer, with immediate implications for evaluation of this strategy in the clinic.

Prevention and Epidemiology

Novel Associations between Common Breast Cancer Susceptibility Variants and Risk-Predicting Mammographic Density Measures

Précis: These findings deepen the evidence of shared genetic determinants between breast cancer risk and mammographic density measures, strengthening the likelihood of common etiologic pathways.


Précis: These epidemiologic results indicate that the incidence of HPV-positive oropharyngeal cancer is higher and rising more sharply among men than women in the United States because of gender-associated sexual behaviors.
Effects of Sorafenib Dose on Acquired Reversible Resistance and Toxicity in Hepatocellular Carcinoma
Elizabeth A. Kuczyński, Christina R. Lee, Shan Man, Eric Chen, and Robert S. Kerbel
Précis: Reductions in the plasma levels of the tyrosine kinase inhibitor sorafenib that occur naturally in some patients represent a potential contributing cause of drug resistance, with broader implications for optimal dosing of other tyrosine kinase inhibitors.

TARGETED DELIVERY OF THERAPEUTICS

Grapefruit-Derived Nanovectors Use an Activated Leukocyte Trafficking Pathway to Deliver Therapeutic Agents to Inflammatory Tumor Sites
Qilong Wang, Yi Ren, Jingyao Mu, Nejat K. Egilmez, Xiaoyin Zhuang, Zhongbin Deng, Lifeng Zhang, Jun Yan, Donald Miller, and Huang-Ge Zhang
Précis: This interesting report defines and characterizes the tumor-targeting features of a readily available, generalizable, and nontoxic vehicle to improve the targeted delivery of therapeutic drugs to cancerous or precancerous sites, possibly offering a low-cost clinical formulation strategy to widen the therapeutic window for many drugs.

Drug Redeployment to Kill Leukemia and Lymphoma Cells by Disrupting SCD1-Mediated Synthesis of Monounsaturated Fatty Acids
Andrew D. Southam, Farhat L. Khanim, Rachel E. Hayden, Julia K. Constantinou, Katarzyna M. Koczula, Robert H. Mitchell, Mark R. Viant, Mark T. Drayson, and Chris M. Bunce
Précis: The combination of two drugs found to have anticancer activity in patients is mechanistically linked in this study to decreased levels of a candidate therapeutic target involved in fatty-acid synthesis.

Targeted Models
Précis: These results offer early insight into how acquired resistance arises to a new mutation-selective inhibitor of EGFR that is in fast-track clinical development, illustrating the inescapable cat-and-mouse chase in the evolution of cancer cell–targeting drugs in the management of cancer patients.

Preclinical Models
Précis: These results offer early insight into how acquired resistance arises to a new mutation-selective inhibitor of EGFR that is in fast-track clinical development, illustrating the inescapable cat-and-mouse chase in the evolution of cancer cell–targeting drugs in the management of cancer patients.

Targeted Delivery of Therapeutic Drugs to Cancerous or Precancerous Sites
Précis: This work uncovers new aspects of grade-dependent metabolic reprogramming in renal cancers that could lead to novel personalized treatments, including the use of inhibitors of glucose, glutamine, and tryptophan metabolism that are being developed in other clinical settings.

Proteomics and Metabolomics Analysis in Kidney Cancer Revealed by Combined Proteomics and Metabolomics Analysis
Précis: This work uncovers new aspects of grade-dependent metabolic reprogramming in renal cancers that could lead to novel personalized treatments, including the use of inhibitors of glucose, glutamine, and tryptophan metabolism that are being developed in other clinical settings.

Fatty Acids
Andrew D. Southam, Farhat L. Khanim, Rachel E. Hayden, Julia K. Constantinou, Katarzyna M. Koczula, Robert H. Mitchell, Mark R. Viant, Mark T. Drayson, and Chris M. Bunce
Précis: The combination of two drugs found to have anticancer activity in patients is mechanistically linked in this study to decreased levels of a candidate therapeutic target involved in fatty-acid synthesis.
G-CSF Promotes Neuroblastoma Tumorigenicity and Metastasis via STAT3-Dependent Cancer Stem Cell Activation
Saurabh Agarwal, Anna Lakoma, Zaowen Chen, John Hicks, Leonid S. Metelitsa, Eugene S. Kim, and Jason M. Shohet
Précis: This seminal study challenges the clinical use of G-CSF as a treatment to support white blood cell counts in children with neuroblastoma, based on the ability of this factor to promote the growth of the cancer stem-like cell population in this setting.

ABOUT THE COVER
Ultrasound is a complementary imaging modality for detection of mammographically occult breast cancers, especially in patients with dense breast tissue. Diagnostic accuracy of ultrasound in these patients can be significantly improved using contrast agents targeted at molecular signatures on the tumor neovasculature. In a large scale immunohistochemical staining analysis of human tissues, it was found that B7-H3 is differentially expressed in breast cancer-associated vascular endothelial cells compared with normal, benign, and precursor lesions. Also, B7-H3-targeted ultrasound molecular imaging allowed detection of breast cancer in a transgenic mouse model of breast cancer development. For details, see article by Bachawal and colleagues on page 2501.

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