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The 19q12 Bladder Cancer GWAS Signal: AEG-1 Promoter–Mediated Imaging of Prostate Cancer

Akrita Bhatnagar, Yuchuan Wang, Ronnie C. Mease, Matthew Gabrielson, Polina Sysa, II Minn, Gilbert Green, Brian Simmons, Kathleen Gabrielson, Siddik Sarkar, Paul B. Fisher, and Martin G. Pomper

Precis: This study offers a sensitive, specific, and noninvasive method to image prostate cancer, including in bone metastases that lack a reliable clinical imaging agent, offering a preclinical proof of concept that rationalizes immediate clinical translation and evaluation in patients with advanced prostate cancer.

Mycoplasma Hyorhinis Infection Promotes NF-κB–Dependent Migration of Gastric Cancer Cells

Hongying Duan, Ling Chen, Like Qu, Hua Yang, Sonya Wei Song, Yong Han, Meihua Ye, Wanyuan Chen, Xianglei He, and Chengchao Shou

Precis: These findings unveil the effect of a mycoplasmic infection that has been linked to stomach cancer and other types of cancer but not understood in terms of its possible functional contributions, as revealed for the first time in this study.

PCTAIRE1 Phosphorylates p27 and Regulates Mitosis in Cancer Cells

Teruki Yanagi, Maryla Krajewska, Shu-ichi Matsuzawa, and John C. Reed

Precis: These results reveal an unexpected role for the distant CDK relative PCTAIRE1 in cancer cell division and offer a preclinical proof of concept for its candidacy as a new disease-selective target for cancer treatment.

Metabolic Vulnerabilities in Endometrial Cancer


Precis: This study reports key progress in identifying a marker of aggressive behavior in bladder cancer, a disease in which there has been a paucity of knowledge about key genetic drivers.

Copper Signaling Axis as a Target for Prostate Cancer Therapeutics

Rachid Safi, Erik R. Nelson, Satish K. Chitmeni, Katherine J. Franz, Daniel J. George, Michael R. Zalutsky, and Donald P. McDonnell

Precis: Clinical trials in oncology of an approved dithiol compound have failed to produce efficacy, but the findings of this study suggest that this compound should be reexplored with the addition of copper to the regimen, particularly with regard to treatment of prostate cancers resistant to androgen ablation.

Metabolic Vulnerabilities in Endometrial Cancer


Precis: This study reveals that the survival of endometrial cancer cells relies critically on GLUT6-mediated glucose transport, along with glycolytic and lipogenic metabolic pathways, with implications for therapeutic strategies in this setting.
**In Vivo Localization of 90Y and 177Lu Radioimmunoconjugates Using Cerenkov Luminescence Imaging in a Disseminated Murine Leukemia Model**
Ethan R. Balkin, Aimee Kenoyer, Johnnie J. Orozco, Alexandra Hernandez, Maziyar Shadman, Darrell R. Fisher, Damian J. Green, Mark D. Hylarides, Oliver W. Press, D. Scott Wilbur, and John M. Pagel

_Précis:_ Results demonstrate the feasibility of using a novel noninvasive imaging technique called Cerenkov Light Imaging (CLI) to optimize the use of radioimmunoconjugates used to treat aggressive leukemias.

**SAR405838: An Optimized Inhibitor of MDM2–p53 Interaction That Induces Complete and Durable Tumor Regression**
Shaomeng Wang, Wei Sun, Yujun Zhao, Donna McEachern, Isabelle Meaux, Cédric Barrière, Jeanne A. Stuckey, Jennifer L. Meagher, Longchuan Bai, Liu Liu, Cassandra Gianna Hoffman-Luca, Jianfeng Lu, Sanjeev Shangary, Shanghai Yu, Denzil Bernard, Angelo Aguilar, Odette Dos-Santos, Laurent Besret, Stéphane Guerif, Pascal Pannier, Dimitri Gorge-Bernat, and Laurent Debussche

_Précis:_ Despite the risk of applying a selection for p53 mutations that escape MDM2 control, blocking MDM2-p53 protein–protein interaction has long been considered by many to offer an attractive cancer therapeutic strategy, a position strongly supported by the findings of this preclinical study.

**Dsh Homolog DVL3 Mediates Resistance to IGFIR Inhibition by Regulating IGF-RAS Signaling**
Shan Gao, Ilirjana Bajrami, Clare Verrill, Asha Kigozi, Djamila Ouaret, Tamara Aleksic, Ruth Asher, Cheng Han, Paul Allen, Deborah Bailey, Stephan Keller, Takeshi Kashima, Nicholas Athanasou, Jean-Yves Blay, Sandra Schmitz, Jean-Pascal Machiels, Nav Upile, Terry M. Jones, George Thalmann, Shazad Q. Ashraf, Jennifer L. Wilding, Walter F. Bodmer, Mark R. Middleton, Alan Ashworth, Christopher J. Lord, and Valentine M. Macaulay

_Précis:_ This mechanistic study is important because it addresses the lack of predictive biomarkers for stratifying and recruiting cancer patients who might benefit from IGF-1 inhibitors, a key gap in their clinical development as cancer drugs.

**AXL Inhibition Sensitizes Mesenchymal Cancer Cells to Antimitotic Drugs**
Catherine Wilson, Xiaofen Ye, Thinh Pham, Eva Lin, Sara Chan, Erin McNamara, Richard M. Neve, Lisa Belmont, Hartmut Koeppen, Robert L. Yauch, Avi Ashkenazi, and Jeff Settleman

_Précis:_ These findings challenge a purported role for AXL in drug resistance while offering a novel rationale to combine AXL-targeting drugs with antimitotic agents to eradicate invasive cancers.

**β-Catenin Contributes to Lung Tumor Development Induced by EGFR Mutations**
Solvei Nakayama, Natasha Sng, Julian Carretero, Robert Werner, Yuichiyo Hayashi, Mihoko Yamamoto, Alistair J. Tan, Norihiro Yamaguchi, Hiroyuki Yasuda, Danan Li, Kenzo Soejima, Ross A. Soo, Daniel B. Costa, Kwok-Kin Wong, and Susumu S. Kobayashi

_Précis:_ Drug resistance to EGF receptor antagonists in lung cancer may be mediated in part by activation of the β-catenin pathway, reinforcing its importance as an oncogenic driver in this setting.

**MYC Activates Stem-like Cell Potential in Hepatocarcinoma by a p53-Dependent Mechanism**
Hirofumi Akita, Jens U. Marquardt, Marian E. Durkin, Mitsuteru Kitade, Daekwan Seo, Elizabeth A. Conner, Jesper B. Andersen, Valentina M. Factor, and Snorri S. Thorgeirsson

_Précis:_ Cancer stem-like cell populations in liver cancer appear to be expanded under conditions in which MYC is activated and p53 is downregulated, with potential implications for understanding etiology, progression, and treatment in this disease.

**Zfx Facilitates Tumorigenesis Caused by Activation of the Hedgehog Pathway**
Colin J. Palmer, Jose M. Galan-Caridad, Stuart P. Weisberg, Liang Lei, Jose M. Esquillín, Gust F. Croft, Brandon Wainwright, Peter Canoll, David M. Owens, and Boris Reizis

_Précis:_ This preclinical genetic study identifies new candidate targets for the control of tumors driven by the Hedgehog pathway, the aberrant activation of which has been implicated widely in many types of human solid tumors.
SIRT6 Promotes COX-2 Expression and Acts as an Oncogene in Skin Cancer

Mei Ming, Weinong Han, Baozhong Zhao, Nagalingam R. Sundaresan, Chu-Xia Deng, Mahesh P. Gupta, and Yu-Ying He

Précis: This study challenges an existing view of the Sir2-related protein SIRT6 as a tumor suppressor, finding instead in a genetically deficient mouse that it functions as an oncogene in the skin epidermis.

ABOUT THE COVER

The AXL receptor tyrosine kinase has been implicated as a cellular signaling protein that is specifically upregulated in the context of the epithelial-to-mesenchymal transformation seen in some epithelial cancers and the emergence of acquired drug resistance. Among the tumor types in which a mesenchymal, largely drug-refractory phenotype appears to be prevalent is triple-negative breast cancer (TNBC). This immunohistological image illustrates the expression of AXL in a TNBC tumor specimen, revealing punctate cytoplasmic staining of AXL in tumor cells as well as focal vascular staining. For details, see article by Wilson and colleagues on page 5878.