BREAKING ADVANCES

5681 Highlights from Recent Cancer Literature

REVIEW

5683 DEAR1, a Novel Tumor Suppressor That Regulates Cell Polarity and Epithelial Plasticity
Nanyue Chen, Seetharaman Balasenthil, Jacquelyn Reuther, and Ann McNeill Killary

INTEGRATED SYSTEMS AND TECHNOLOGIES

5690 Novel Drug Candidates for the Treatment of Metastatic Colorectal Cancer through Global Inverse Gene-Expression Profiling
Vera van Noort, Sebastian Schölch, Murat Iskar, Georg Zeller, Kristina Ostertag, Christine Schweitzer, Kristin Werner, Jürgen Weitz, Moritz Koch, and Peer Bork
Précis: These findings provide a rationale to reposition the antidepressant drug citalopram for treatment of late-stage colorectal cancers, with immediate implications for clinical evaluation of this drug.

5700 Development of Novel ADCs: Conjugation of Tubulysin Analogues to Trastuzumab Monitored by Dual Radiolabeling
Ruth Cohen, Danielle J. Vugts, Gerard W.M. Visser, Marijke Stigter-van Walsum, Marije Bolijn, Marco Spiga, Paolo Lazzari, Sreejith Shankar, Monica Sani, Matteo Zanda, and Guus A.M.S. van Dongen
Précis: Radiolabeling both a synthetic tubulysin and the antibody to which it is attached facilitated preclinical validation of a new antibody-drug conjugate (ADC) with excellent tumor-targeting performance and efficacy.

MICROENVIRONMENT AND IMMUNOLOGY

5711 Adiponectin Receptor Signaling on Dendritic Cells Blunts Antitumor Immunity
Peng H. Tan, Helen E.J. Tyrrell, Liquan Gao, Danmei Xu, Jianchao Quan, Dipender Gill, Lena Rai, Yunchuan Ding, Gareth Plant, Yuanhui Yin, Qinyuan Liao, Yang Meng, Yingmei Zhang, Dalong Ma, and Xiaoyan Qiu
Précis: Novel adiponectin signaling pathways revealed in this report are shown to promote immune tolerizing signals in dendritic cells that drive tumoral immune escape in cancer, suggesting broadly applicable new strategies for the immunometabolic control of cancer.

5723 HMGB1 Enhances Immune Suppression by Facilitating the Differentiation and Suppressive Activity of Myeloid-Derived Suppressor Cells
Katherine H. Parker, Pratima Sinha, Lucas A. Horn, Virginia K. Clements, Huan Yang, Jianhua Li, Kevin J. Tracey, and Suzanne Ostrand-Rosenberg
Précis: A secreted alarmin that is ubiquitously present in the tumor microenvironment provides a pivotal proinflammatory contribution to the differentiation and suppressive potency of myeloid-derived suppressor cells, an important driver of immune escape in many solid tumors.

5734 Cytokine-like Molecule CCDC134 Contributes to CD8+ T-cell Effector Functions in Cancer Immunotherapy
Jing Huang, Lin Xiao, Xiaoting Gong, Wenwei Shao, Yanhui Yin, Qinyuan Liao, Yang Meng, Yingmei Zhang, Dalong Ma, and Xiaoyan Qiu
Précis: These findings offer strong evidence for a new member of the yc cytokine family that provides powerful support for CD8+ T-cell-mediated immunity, with potential implications for therapeutic applications.

MOLECULAR AND CELLULAR PATHOBIOLOGY

5746 Metastatic Consequences of Immune Escape from NK Cell Cytotoxicity by Human Breast Cancer Stem Cells
Bin Wang, Qiang Wang, Zhe Wang, Jun Jiang, Shi-Cang Yu, Yi-Fang Ping, Jia Yang, Sen-Lin Xu, Xian-Zong Ye, Chuan Xu, Lang Yang, Cheng Qian, Ji Ming Wang, You-Hong Cui, Xia Zhang, and Xiu-Wu Bian
Précis: These findings reveal how metastasis-initiating breast cancer stem-like cells evade immune surveillance by natural killer cells.

5758 Cellular Disposal of miR23b by RAB27-Dependent Exosome Release Is Linked to Acquisition of Metastatic Properties
Précis: This interesting study suggests that exosome secretion serves as a disposal mechanism for tumor suppressor microRNA during tumor progression, thereby enabling the acquisition of metastatic capabilities.
AEG-1 Promoter–Mediated Imaging of Prostate Cancer

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

Precise: 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

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

Precise: 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

Precise: These results reveal an unexpected role for the distinct 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.

Copper Signaling Axis as a Target for Prostate Cancer Therapeutics


Precise: Clinical trials in oncology of an approved diethyldithiocarbamate 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


Precise: 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.

Therapeutics, Targets, and Chemical Biology

Copper Signaling Axis as a Target for Prostate Cancer Therapeutics


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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, Mazyar Shadman, Darrell R. Fisher, Damian J. Green, Mark D. Hylarides, Oliver W. Press, D. Scott Wilbur, and John M. Pagel

Precis: 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.

TUMOR AND STEM CELL BIOLOGY

β-Catenin Contributes to Lung Tumor Development Induced by EGFR Mutations

Precis: 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.

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. Thorgersson

Precis: 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.
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.