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 Schönch, Murat Iskar, Georg Zeller, Kristina Ostertag, Christine Schweitzer, Kristin Werner, Jürgen Weitz, Moritz Koch, and Peer Bork

MOLECULAR AND CELLULAR PATHOBIOLOGY

5711 Adiponectin Receptor Signaling on Dendritic Cells Blunts Antitumor Immunity
Peng H. Tan, Helen E.J. Tyrrell, Lijuang 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

5734 Cytokine-like Molecule CCDC134 Contributes to CD8+ T-cell Effector Functions in Cancer Immunotherapy
Jing Hu, Lin Xiao, Xiaoting Gong, Wenwei Shao, Yanhui Yin, Qinyuan Liao, Yang Meng, Yingmei Zhang, Dalong Ma, and Xiaoyan Qiu

MICROENVIRONMENT AND IMMUNOLOGY

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, Jing 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

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.
5772  AEG-1 Promoter–Mediated Imaging of Prostate Cancer
Akriti 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

Précis: 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.

5782  Mycoplasma Hyorhinis Infection Promotes NF-kB–Dependent Migration of Gastric Cancer Cells
Hongying Duan, Ling Chen, Like Qu, Hua Yang, Sonya Wei Song, Yong Han, Meihsia Ye, Wanyuan Chen, Xianglei He, and Chengchao Shou

Précis: These findings unveil the effect of a mycoplasma 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.

5795  PCTAIRE1 Phosphorylates p27 and Regulates Mitosis in Cancer Cells
Teruki Yanagi, Maryla Krajewska, Shu-ichi Matsuzawa, and John C. Reed

Précis: 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.

PREVENTION AND EPIDEMIOLOGY

5808  The 19q12 Bladder Cancer GWAS Signal: Association with Cyclin E Function and Aggressive Disease
Yi-Feng Fu, Indu Kobaar, Lee E. Moore, Petra Lenz, Jonine D. Fiquetero, Wei Tang, Patricia Porter-Gill, Nilanjan Chatterjee, Alexandra Scott-Johnson, Montserrat Garcia-Closas, Brian Muchmore, Dalsu Baris, Ashley Paquin, Kris Ylaya, Molly Schwenn, Andrea B. Apolo, Margaret R. Karagas, McAnthony Tarway, Alison Johnson, Adam Mummy, Alan Schned, Liliana Guevez, Michael A. Jones, Masatoshi Kida, GM Monawar Hosain, Nuria Malats, Manolis Kogevinas, Adonina Tardon, Consol Serra, Alfredo Carrato, Reina Garcia-Closas, Josep Lloreta, Xifeng Wu, Mark Purdue, Gerald L. Andriole Jr, Shu-ichi Matsuzawa, and John C. Reed

Précis: 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

5819  Copper Signaling Axis as a Target for Prostate Cancer Therapeutics

Précis: 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.

5832  Metabolic Vulnerabilities in Endometrial Cancer

Précis: 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.
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

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.

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.
SIRT6 Promotes COX-2 Expression and Acts as an Oncogene in Skin Cancer

Mei Ming, Weinong Han, Baozhong Zhao, Nagalingam R. Sundaesan, 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.