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**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

**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

**Molecular and Cellular Pathobiology**

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, Yunchuan Ding, Zhe Wang, Yang Meng, Yingmei Zhang, Dalong Ma, and Xiaoyan Qiu

**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.

5746  **Development of Novel ADCs: Conjugation of Tubulysin Analogues to Trastuzumab Monitored by Dual Radiolabeling**

Bin Wang, Qiang Wang, Zhe Wang, Jun Jiang, Shi-Cang Yu, Yi-Fang Ping, Ling Yang, Jun Lin, Shen-Chao Xu, 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.
The 19q12 Bladder Cancer GWAS Signal: PCTAIRE1 Phosphorylates p27 and Regulates Mycoplasma Hyorhinis Infection Promotes NF-κB–Dependent Migration of Gastric Cancer Cells

PCTAIRE1 Phosphorylates p27 and Regulates Mitosis in Cancer Cells

Copper Signaling Axis as a Target for Prostate Cancer Therapeutics

Metabolic Vulnerabilities in Endometrial Cancer
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5846 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, Maziar 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.

5855 SAR405838: An Optimized Inhibitor of MDM2–p53 Interaction That Induces Complete and Durable Tumor Regression
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 therapeutical strategy, a position strongly supported by the findings of this preclinical study.

5866 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 Feller, 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.

5878 AXI 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 AXI in drug resistance while offering a novel rationale to combine AXI-targeting drugs with antimitotic agents to eradicate invasive cancers.

TUMOR AND STEM CELL BIOLOGY

5891 β-Catenin Contributes to Lung Tumor Development Induced by EGFR Mutations
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.

5903 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. Thorgerisson
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.

5914 Zfx Facilitates Tumorigenesis Caused by Activation of the Hedgehog Pathway
Colin J. Palmer, Jose M. Galan-Caridad, Stuart P. Weisberg, Liang Lei, Jose M. Esquilin, Gist 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. 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.