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

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

MICROENVIRONMENT AND IMMUNOLOGY

5711  Adiponectin Receptor Signaling on Dendritic Cells Blunts Antitumor Immunity
Peng H. Tan, Helen E.J. Tyrrell, Liping Gao, Danmei Xu, Jianchao Quan, Dipender Gill, Lena Rai, Yunchuan Ding, Gareth Plant, Yuan Chen, John Z. Xue, Ashok I. Handa, Michael J. Greenall, Kenneth Walsh, and Shao-An Xue

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

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

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

MOLECULAR AND CELLULAR PATHOBIOLOGY

5758  Cellular Disposal of miR23b by RAB27-Dependent Exosome Release Is Linked to Acquisition of Metastatic Properties

 précis: These findings reveal how metastasis-initiating breast cancer stem-like cells evade immune surveillance by natural killer cells.

 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: 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

Preciso: 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.

5808 The 19q12 Bladder Cancer GWAS Signal: Association with Cyclin E Function and Aggressive Disease
Yi-Fing Fu, Indu Kobaar, Lee E. Moore, Petra Lenz, Jonine D. Figueroa, Wei Tang, Patricia Porter-Gill, Wanyuan Chen, Xiangleigr, and Chengchao Shou

Preciso: 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.

582 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, Meihua Ye, Wanyuan Chen, Xianglei He, and Chengchao Shou

Preciso: 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.

5832 Metabolic Vulnerabilities in Endometrial Cancer
Frances L. Byrne, Ivan K.H. Poon, Susan C. Modesitt, Jose L. Tomsig, Jenny D.Y. Chow, Marin E. Healy, William D. Baker, Kristen A. Atkins, Johnathan M. Lancaster, Susan C. Modesitt, Jose L. Tomsig, and Donald P. McDonnell

Preciso: 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.

5819 Copper Signaling Axis as a Target for Prostate Cancer Therapeutics
Rachid Safi, Erik R. Nelson, Satish K. Chitnani, Katherine J. Franz, Daniel J. George, Michael R. Zalutsky, and Donald P. McDonnell

Preciso: 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.

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY
In Vivo Localization of \(^90\)Y and \(^{177}\)Lu 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, Damien 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 Lii, Cassandra Gianna Hoffman-Luca, Jianfeng Lu, Sanjeev Shangary, Shanghai Yu, Denzil Bernard, Angelo Aguilar, Odette Dos-Santos, Laurent Besret, Stéphane Guéris, 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, Liríjana Bajzami, Clare Verrill, Asha Kigozi, Djamilha Ouare, 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 Laurent Debussche

**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.
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.