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<td>Highlights from Recent Cancer Literature</td>
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<td>DEAR1, a Novel Tumor Suppressor That Regulates Cell Polarity and Epithelial Plasticity</td>
<td>Nanyue Chen, Seetharaman Balasenthil, Jacquelyn Reuther, and Ann McNeill Killary</td>
<td>Precisé: 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.</td>
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<td>Novel Drug Candidates for the Treatment of Metastatic Colorectal Cancer through Global Inverse Gene-Expression Profiling</td>
<td>Vera van Noort, Sebastian Schlöch, Murat Iskar, Georg Zeller, Kristina Ostertag, Christine Schweitzer, Kristin Werner, Jürgen Weitz, Moritz Koch, and Peer Bork</td>
<td>Precisé: 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.</td>
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<td>Development of Novel ADCs: Conjugation of Tubulysin Analogues to Trastuzumab Monitored by Dual Radiolabeling</td>
<td>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</td>
<td>Precisé: 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.</td>
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<td>Adiponectin Receptor Signaling on Dendritic Cells Blunts Antitumor Immunity</td>
<td>Peng H. Tan, Helen E.J. Tyrrell, Liquan 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</td>
<td>Precisé: Novel adiponectin signaling pathways revealed in this report are shown to promote immune tolerance, counteracting proinflammatory signals in dendritic cells that drive tumoral immune escape in cancer, suggesting broadly applicable new strategies for the immunometabolic control of cancer.</td>
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<td>Katherine H. Parker, Pratima Sinha, Lucas A. Horn, Virginia K. Clements, Huan Yang, Jianhua Li, Kevin J. Tracey, and Suzanne Ostrand-Rosenberg</td>
<td>Precisé: 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.</td>
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<td>Precisé: 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.</td>
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<td>Metastatic Consequences of Immune Escape from NK Cell Cytotoxicity by Human Breast Cancer Stem Cells</td>
<td>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</td>
<td>Precisé: 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.</td>
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<td>Precisé: 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.</td>
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PREVENTION AND EPIDEMIOLOGY

AEG-1 Promoter–Mediated Imaging of Prostate Cancer 5772
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Metabolic Vulnerabilities in Endometrial Cancer 5832
In Vivo Localization of $^{90}\text{Y}$ and $^{177}\text{Lu}$ 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

**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, Otette 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, Ilikjana Bajjami, Clare Verrill, Asha Kigozi, Djamaï 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 Thalman, Shazad Q. Ashraf, Jennifer L. Wilding, Walter F. Bodner, 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.

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. 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 Sirt2-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.