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These findings indicate that the osteosarcoma microenvironment composition is a major feature to identify hard-to-treat patient tumors at diagnosis and define the biological pathways and potential actionable targets associated with these tumors.
Targeting LRRC15 Inhibits Metastatic Dissemination of Ovarian Cancer

This study identifies that LRRC15 activates β1-integrin/FAK signaling to promote ovarian cancer metastasis and shows that the LRRC15-targeted antibody–drug conjugate ABBV-085 suppresses ovarian cancer metastasis in preclinical models.

CircRPN2 Inhibits Aerobic Glycolysis and Metastasis in Hepatocellular Carcinoma

The circRNA circRPN2 is a potential prognostic biomarker and therapeutic target in hepatocellular carcinoma that suppresses aerobic glycolysis and metastasis.

EBV Infection in Epithelial Malignancies Induces Resistance to Antitumor Natural Killer Cells via F3-Mediated Platelet Aggregation
Xiaobing Duan, Haiwen Chen, Xiang Zhou, Pingjuan Liu, Xiao Zhang, Qian Zhu, Xinli Zhang, Yanhong Chen, Yan Zhou, Chaopin Yang, Qisheng Feng, Xi-Xin Zeng, Miao Xu, and Tong Xiang

This study reveals a mechanism by which EBV-associated epithelial malignancies escape NK-cell-mediated immune surveillance, providing a new target for improving NK-cell immunotherapy.

Differential Kinase Activity Across Prostate Tumor Compartments Defines Sensitivity to Target Inhibition

Single-cell mass cytometry analyses provide insights into the differences in kinase activity across tumor compartments and cell states, which contributes to heterogeneous responses to targeted therapies.

ATR Inhibitor AZD6738 (Ceralasertib) Exerts Antitumor Activity as a Monotherapy and in Combination with Chemotherapy and the PARP Inhibitor Olaparib
Zena Wilson, Rajesh Odedra, Yann Wallez, Paul W.G. Wijnhoven, Adina M. Hughes, Joe Gerrard, Gemma N. Jones, Hannah Bargh-Dawson, Elaine Brown, Lucy A. Young, Mark J. O’Connor, and Alan Lau

This detailed preclinical investigation, including pharmacokinetics/pharmacodynamics and dose–schedule optimizations, of AZD6738/ceralasertib alone and in combination with chemotherapy or PARP inhibitors can inform ongoing clinical efforts to treat cancer with ATR inhibitors.

Translational Science

Transient Inhibition of the JAK/STAT Pathway Prevents B-ALL Development in Genetically Predisposed Mice

JAK/STAT inhibition suppresses tumorigenesis in a B-ALL–susceptible mouse model, presenting a novel approach to prevent B-ALL onset.

CIC-Mediated Modulation of MAPK Signaling Opposes Receptor Tyrosine Kinase Inhibitor Response in Kinase-Addicted Sarcoma
Igor Odintsov, Michael V. Ortiz, Inna Khodos, Marissa S. Mattar, Allan J.W. Lui, Shini Kohsaka, Elisa de Stanchina, Julia L. Glade Bender, Marc Ladanyi, and Romel Somwar

Novel models of kinase-rearranged sarcomas show that MAPK pathway feedback activation dampens responses to tyrosine kinase inhibitors, revealing the potential of combinatorial therapies to combat these tumors.

Development of Novel Aptamer-Based Targeted Chemotherapy for Bladder Cancer
Yao Wang, Yang Zhang, Peng-Chao Li, Jiajie Guo, Fan Huo, Jintao Yang, Ru Jia, Juan Wang, Qiju Huang, Dan Theodorescu, Hanyang Yu, and Chao Yan

These findings identify a bladder cancer–specific aptamer that can be used for targeted delivery of chemotherapy, potentially reducing toxicity and enhancing therapeutic efficacy.
CORRECTIONS

1153 Correction: PHGDH Expression Is Required for Mitochondrial Redox Homeostasis, Breast Cancer Stem Cell Maintenance, and Lung Metastasis
Debangshu Samanta, Youngrok Park, Shaida A. Andrabi, Laura M. Shelton, Daniele M. Gilkes, and Gregg L. Semenza

1154 Correction: Cytoplasmic Irradiation Results in Mitochondrial Dysfunction and DRP1-Dependent Mitochondrial Fission
Bo Zhang, Mercy M. Davidson, Hongning Zhou, Chunxin Wang, Winsome F. Walker, and Tom K. Hei

ABOUT THE COVER

The image depicts the Battle of Chibi (meaning ‘Red Cliff’ in Chinese), one of the most famous battles in Chinese history. In the Battle of Chibi (208 AD), two groups joined forces to halt the advance of strong enemies. Similarly, Sun and colleagues target MYC-driven cancer with the combined inactivation of CTPS1 and ATR in this issue. The image depicts the two forces (in the shape of arrowheads) joining the battle (depicted by the fire). For details, see the article by Sun and colleagues on page 1013. (Concept, Ji-Long Liu; Illustration, Jia Du.)
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