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PRIORITY REPORT

3327 An Alternatively Spliced Gain-of-Function NT5C2 Isoform Contributes to Chemoresistance in Acute Lymphoblastic Leukemia

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Alternative splicing is a potent mechanism of acquired drug resistance in relapsed/refractory acute lymphoblastic leukemias that has diagnostic and therapeutic implications for patients who lack mutations in known chemoresistance genes.

CANCER BIOLOGY

3337 Natural Killer Cell Regulation of Breast Cancer Stem Cells Mediates Metastatic Dormancy

Grace G. Bushnell, Deeksha Sharma, Henry C. Wilmot, Michelle Zheng, Toluwaleke D. Fashina, Chloe M. Hutchens, Samuel Osipov, Monika Burness, and Max S. Wicha

The immune system controls disseminated breast cancer cells during disease latency, highlighting the need to utilize immunocompetent models to identify strategies for targeting dormant cancer cells and reducing metastatic recurrence.

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3354 Targeting the Sodium-Potassium Pump as a Therapeutic Strategy in Acute Myeloid Leukemia

Constanze Schneider, Hermes Spaink, Gabriela Alexe, Neekesh V. Dharia, Ashleigh Meyer, Lucy A. Merickel, Delan Khalid, Sebastian Scheich, Björn Häupl, Louis M. Staudt, Thomas Oellerich, and Kimberly Stegmaier

ATP1B3 is a lethal selective paralog dependency in acute myeloid leukemia that can be eliminated to destabilize the sodium-potassium pump, inducing cell death.

3371 Cancer-Associated Fibroblasts Expressing Sulfatase 1 Facilitate VEGFA-Dependent Microenvironmental Remodeling to Support Colorectal Cancer

Huijuan Wang, Jiaxin Chen, Xiaoyu Chen, Yingqiang Liu, Jiawei Wang, Qing Meng, Huogang Wang, Ying He, Yujia Song, Jingyun Li, Zhenyu Ju, Peng Xiao, Junbin Qian, and Zhangfa Song SULFI⁺ cancer-associated fibroblasts play a tumor-promoting role in colorectal cancer by stimulating extracellular matrix deposition and angiogenesis and can serve as a biomarker for the therapeutic response to HDAC inhibitors in patients.

CANCER METABOLISM AND MOLECULAR MECHANISMS

3388 Targeting YAP Activity and Glutamine Metabolism Cooperatively Suppresses Tumor Progression by Preventing Extracellular Matrix Accumulation

Mihyang Park, Jonghwa Jin, Da Young An, Dong-Ho Kim, Jaebon Lee, Jae Won Yun, Ilseon Hwang, Jae Seok Park, Mi Kyung Kim, You Mie Lee, Jun-Kyu Byun, Yeon-Kyung Choi, and Keun-Gyu Park

Blocking glutamine utilization activates YAP to promote ECM deposition by fibroblasts, highlighting the potential of YAP inhibitors and antifibrotic strategies as promising approaches for effective combination metabolic therapies in cancer.

3402 m⁶A-Mediated Induction of 7-Dehydrocholesterol Reductase Stimulates Cholesterol Synthesis and cAMP Signaling to Promote Bladder Cancer Metastasis

Youmiao Zeng, Yongbo Luo, Keyuan Zhao, Sheng Liu, Kaiwen Wu, Yudong Wu, Kaixuan Du, Wenbang Pan, Yiheng Dai, Yuanhao Liu, Mengda Ren, Fengyan Tian, Lijie Zhou, and Chaohui Gu

Inhibiting DHCR7 induces cholesterol metabolism reprogramming and lipid raft remodeling to inactivate the cAMP/protein kinase A/FAK axis and suppress bladder cancer metastasis, indicating the therapeutic potential of targeting DHCR7.

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Louise Cadzow, Jehrod Brenneman, Erica Tobin, Pamela Sullivan, Sumeet Nayak, Janid A. Ali, Sol Shenker, Jim Griffith, Michael McGuire, Paula Grasberger, Yuji Mishina, Morgan Murray, Anne E. Dodson, Hugh Gannon, Elsa Krall, Jeff Hixon, Edmond Chipumuro, Kerstin Sinkevicius, Prafulla C. Gokhale, Suthakar Ganapathy, Ursula A. Matulonis, Joyce F. Liu, Andrew Olaharski, Dipen Sangurdekar, Hanlan Liu, Jeremy Wilt, Michael Schlabach, Frank Stegmeier, and Andrew A. Wylie

KSQ-4279 is a potent and selective inhibitor of USP1 that induces regression of PARP inhibitor-resistant tumors when dosed in combination with PARP inhibitors, addressing an unmet clinical need for BRCA-mutant tumors.

TRANSLATIONAL CANCER BIOLOGY

3435 Single-Stranded DNA Gap Accumulation Is a Functional Biomarker for USP1 Inhibitor Sensitivity

Alexandre A. da Costa, Ozge Somuncu, Ramya Ravindranathan, Sirisha Mukkavalli, David B. Martignetti, Huy Nguyen, Yuqing Jiao, Benjamin P. Lamarre, Golbahar Sadatrezaei, Lisa Moreau, Joyce Liu, Divya R. Iyer, Jean-Bernard Lazaro, Geoffrey I. Shapiro, Kalindi Parmar, and Alan D. D'Andrea USP1 inhibitors kill BRCA1-deficient cells and cause ssDNA gap accumulation, supporting the potential of using

ssDNA gap detection as a functional biomarker for clinical trials on USP1 inhibitors.

3447 FANCI Inhibition Induces PARP1 Redistribution to Enhance the Efficacy of PARP Inhibitors in Breast Cancer

Yu-Zhou Huang, Ming-Yi Sang, Pei-Wen Xi,

Ruo-Xi Xu, Meng-Yuan Cai, Zi-Wen Wang, Jian-Yi Zhao, Yi-Han Li, Ji-Fu Wei, and Qiang Ding Targeting FANCI is a promising therapeutic strategy for enhancing PARP inhibitor sensitivity in breast cancer that holds potential for broader therapeutic applications beyond cancers harboring BRCA mutations.

COMPUTATIONAL CANCER BIOLOGY AND TECHNOLOGY

3464 Chromosome 7 Gain Compensates for Chromosome 10 Loss in Glioma

Nishanth Ulhas Nair, Alejandro A. Schäffer, E. Michael Gertz, Kuoyuan Cheng, Johanna Zerbib, Avinash Das Sahu, Gil Leor, Eldad D. Shulman, Kenneth D. Aldape, Uri Ben-David, and Eytan Ruppin Increased expression of multiple rescuer genes on the gained chromosome 7 could compensate for the downregulation of several vulnerable genes on the lost chromosome 10, resolving the long-standing mystery of this frequent cooccurrence in gliomas.

CONVERGENCE SCIENCE

3478 A Genomics-Driven Artificial Intelligence-Based Model Classifies Breast Invasive Lobular Carcinoma and Discovers CDH1 Inactivating Mechanisms

Fresia Pareja, Higinio Dopeso, Yi Kan Wang, Andrea M. Gazzo, David N. Brown, Monami Banerjee, Pier Selenica, Jan H. Bernhard, Fatemeh Derakhshan, Edaise M. da Silva, Lorraine Colon-Cartagena, Thais Basili, Antonio Marra, Jillian Sue, Qiqi Ye, Arnaud Da Cruz Paula, Selma Yeni Yildirim, Xin Pei, Anton Safonov, Hunter Green, Kaitlyn Y. Gill, Yingjie Zhu, Matthew C.H. Lee, Ran A. Godrich, Adam Casson, Britta Weigelt, Nadeem Riaz, Hannah Y. Wen, Edi Brogi, Diana L. Mandelker, Matthew G. Hanna, Jeremy D. Kunz, Brandon Rothrock, Sarat Chandarlapaty, Christopher Kanan, Joe Oakley, David S. Klimstra, Thomas J. Fuchs, and Jorge S. Reis-Filho Genetic alterations linked to strong genotypicphenotypic correlations can be utilized to develop Al systems applied to pathology that facilitate cancer diagnosis and biologic discoveries.

RETRACTIONS

3490 Retraction: Differential Effects of VEGFR-1 and VEGFR-2 Inhibition on Tumor Metastases Based on Host Organ Environment

Yoon-Jin Lee, Daniel L. Karl, Ugwuji N. Maduekwe, Courtney Rothrock, Sandra Ryeom, Patricia A. D'Amore, and Sam S. Yoon

3491 Retraction: Variable Inhibition of Thrombospondin 1 against Liver and Lung Metastases through Differential Activation of Metalloproteinase ADAMTS1

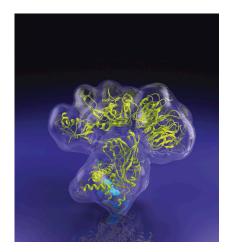
Yoon-Jin Lee, Moritz Koch, Daniel Karl, Antoni X. Torres-Collado, Namali T. Fernando, Courtney Rothrock, Darshini Kuruppu, Sandra Ryeom, M. Luisa Iruela-Arispe, and Sam S. Yoon

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ABOUT THE COVER

Defects in DNA repair pathways play a pivotal role in tumor development and response to therapy. USP1 is a critical dependency in tumors with homologous recombination (HR) repair deficiency. The cover image illustrates a CryoEM structure of the newly developed USP1 inhibitor, KSQ-4279, binding to the USP1/UAF1 deubiquitinase complex. Treatment with KSQ-4279 is an effective strategy for inducing regression of HR-deficient tumors and overcoming PARP inhibitor resistance. For details, see article by Cadzow and colleagues on page 3419.

doi: 10.1158/0008-5472.CAN-84-20-CVR



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