A Novel Functional Splice Variant of AKT3 Defined by Analysis of Alternative Splice Expression in HPV-Positive Oropharyngeal Cancers
Précis: This study describes the discovery and characterization of a novel splice isoform of the kinase AKT3 that drives oncogenesis in HPV-related oral cancers of increasing incidence.

PRC2-Mediated Transcriptomic Alterations at the Embryonic Stage Govern Tumorigenesis and Clinical Outcome in MYCN-Driven Neuroblastoma
Shoma Tsubota, Satoshi Kishida, Tepppei Shimamura, Miki Ohita, Satoshi Yamashita, Dongliang Cao, Shinichi Kyonari, Toshikazu Ushijima, and Kenji Kadomatsu
Précis: A novel spheroid culture for tumorigenic cells revealed that the transcriptomic alterations associated with PRC2 deregulation found at embryonic stages have a strong impact on tumorigenesis and clinical outcome in neuroblastoma.

Aneuploid Cell Survival Relies upon Sphingolipid Homeostasis
Yun-Chi Tang, Hui Yuwen, Kaiying Wang, Peter M. Bruno, Kevin Bullock, Amy Deik, Stefano Santaguida, Marianna Trakala, Sarah J. Pfau, Na Zhong, Tao Huang, Lan Wang, Clary B. Clish, Michael T. Hemann, and Angelika Amon
Précis: These findings suggest that sphingolipid metabolism may be an Achilles’ heel in aneuploid cells, with immediate implications for development of a small molecule-based approach to broadly prevent or treat cancers.

JCAD Promotes Progression of Nonalcoholic Steatohepatitis to Liver Cancer by Inhibiting LATS2 Kinase Activity
Juan Ye, Tian-Sheng Li, Gang Xu, Yi-Ming Zhao, Ning-Ping Zhang, Jia Fan, and Jian Wu
Précis: These findings identify the Hippo signaling pathway as a candidate for targeted therapeutic intervention in fatty liver-associated development of hepatocarcinoma, which is rising rapidly in Western countries along with increasing rates of obesity.
5301 Nuclear FAK and Runx1 Cooperate to Regulate IGFBP3, Cell-Cycle Progression, and Tumor Growth

Marta Canel, Adam Byron, Andrew H. Sims, Jessy Cartier, Hitesh Patel, Margaret C. Frame, Valerie G. Brunton, Bryan Serrels, and Alan Serrels

Précis: These findings enhance understanding of the basic biology underlying ongoing clinical trials of FAK inhibitors for cancer therapy.

5313 HNF1β Loss Exacerbates the Development of Chromophobe Renal Cell Carcinomas

Mianen Sun, Pan Tong, Wen Kong, Baijun Dong, Yiran Huang, In Young Park, Xian-De Liu, Zhiyong Ding, Xuesong Zhang, Shanshan Bai, Peter German, Reid Powell, Quan Wang, Xuefei Tong, Nizar M. Tannir, Surena F. Matin, W. Kimryn Rathmell, Gregory N. Fuller, Ian E. McCutcheon, Cheryl L. Walker, Jing Wang, and Eric Jonasch

Précis: These findings provide new insights into key epigenetic events, which drive an unusual type of kidney tumor, where additional loss of TP53 function promotes poor prognosis.

5327 MRE11 Promotes Tumorigenesis by Facilitating Resistance to Oncogene-Induced Replication Stress

Elizabeth Spehalski, Kayla M. Capper, Cheryl J. Smith, Mary J. Morgan, Maria Dinkelmann, Jeffrey Buis, JoAnn M. Sekiguchi, and David O. Ferguson

Précis: New insights into how a DNA repair complex can promote tumorigenesis suggest new approaches to selectively improve cancer cell killing.

TUMOR AND STEM CELL BIOLOGY

5339 Chromatin-Associated Protein SIN3B Prevents Prostate Cancer Progression by Inducing Senescence

Anthony J. Bainor, Fang-Ming Deng, Yu Wang, Peng Lee, David J. Cantor, Susan K. Logan, and Gregory David

Précis: These results suggest a tumor suppressor function for SIN3B in prostate cancer, with potential implications for the use of SIN3B and its target genes as candidate diagnostic markers to distinguish indolent from aggressive disease.

5349 Oncogenic KRAS and p53 Loss Drive Gastric Tumorigenesis in Mice That Can Be Attenuated by E-Cadherin Expression

Jacob E. Till, Changhwan Yoon, Bang-Jin Kim, Kerry Roby, Prince Addai, Evan Jonokuchi, Laura H. Tang, Sam S. Yoon, and Sandra Ryeom

Précis: These findings describe the first autochthonous mouse model of gastric adenocarcinoma that can recapitulate the metastatic processes that occur widely in patients.

5360 S100A4 Is a Biomarker and Regulator of Glioma Stem Cells That Is Critical for Mesenchymal Transition in Glioblastoma

Kin-Hoe Chow, Hee Jung Park, Joshy George, Keiko Yamamoto, Andrew D. Gallup, Joel H. Graber, Yuanxin Chen, Wen Jiang, Dennis A. Steinleider, Eric G. Neilson, Betty Y.S. Kim, and Kyuson Yun

Précis: These findings demonstrate the role of S100A4 in glioblastoma as a regulator of the stemness and mesenchymal transition.

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

5374 Trastuzumab Increases HER2 Uptake and Cross-Presentation by Dendritic Cells

Victor A. Gall, Anne V. Philips, Na Qiao, Karen Clise-Dwyer, Alexander A. Perakis, Mao Zhang, Guy T. Clifton, Pariya Sukhumalchandra, Qing Ma, Sangeetha M. Reddy, Dihua Yu, Jeffrey J. Molldrem, George E. Peoples, Gheath Alatrash, and Elizabeth A. Mittendorf

Précis: These findings describe a potential mechanism by which patients treated with trastuzumab, followed by vaccination with a CDB T-cell-eliciting vaccine, may experience a robust antitumor immune response.

5384 Combination Therapy with Bispecific Antibodies and PD-1 Blockade Enhances the Antitumor Potency of T Cells

Chien-Hsing Chang, Yang Wang, Rongxiu Li, Diane L. Rossi, Donglin Liu, Edmund A. Rossi, Thomas M. Cardillo, and David M. Goldenberg

Précis: Bispecific antibodies that can bind a T cell along with a tumor cell antigen and redirect the T cell to the tumor can leverage the therapeutic benefits of PD1 blockade, an important present goal in immuno-oncological treatment of solid tumors.

5395 Mitotic Vulnerability in Triple-Negative Breast Cancer Associated with LIN9 Is Targetable with BET Inhibitors


Précis: These findings demonstrate that BET inhibitors can target genes such as LIN9, whose chromatin lacks super-enhancer-associated epigenetic marks.
INTEGRATED SYSTEMS AND TECHNOLOGIES

5409 Integrating Models to Quantify Environment-Mediated Drug Resistance
Noemi Picco, Erik Sahai, Philip K. Maini, and Alexander R.A. Anderson
Précis: Quantification of the environmental contribution to drug resistance reveals that tumor heterogeneity altering treatment dynamics can be exploited for therapeutic gain.

CLINICAL STUDIES

5419 Genomic Alterations in Circulating Tumor DNA from Diverse Cancer Patients Identified by Next-Generation Sequencing
Précis: This milestone study showcases the power of genomic profiling of tumors by next-generation sequencing of circulating tumor DNA, as illustrated in the first large and diverse cohort of cancer patients, including for difficult-to-biopsy tumors.

CORRECTION

5438 Evolution of Cancer Stem-like Cells in Endocrine-Resistant Metastatic Breast Cancers Is Mediated by Stromal Microvesicles
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ABOUT THE COVER

JCAD and LATS2 were stained immunohistochemically with specific primary antibodies and secondary antibodies labeled with Alexa-488 (green for JCAD) or Alexa-594 (red for LATS2). The nucleus was visualized by DAPI staining in blue. JCAD is overlaid with LATS2 in the proximity of the nucleus and appears in yellow. For details, see article by Ye and colleagues on page 5287.
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