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Significance: This study defines a tumor suppressor function for the protein tyrosine phosphatase PTP1B in myeloid lineage cells, with evidence that its genetic inactivation in mice is sufficient to drive acute myeloid leukemia.

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Significance: These findings expand knowledge of how MYC drives cancer cell proliferation by identifying an oncogenic long noncoding RNA that is widely overexpressed in human cancers.

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Significance: RUNX3 inactivation in cancer removes an antioxidant barrier against DNA double strand breaks induced by TGF\(\beta\) expressed in the tumor microenvironment.

Metabolism and Chemical Biology

36 Adaptive Evolution of the GDH2 Allosteric Domain Promotes Gliomagenesis by Resolving IDH1\(^{R132H}\)-Induced Metabolic Liabilities
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Significance: These findings show that the hominid-specific brain enzyme GDH2 may be essential to mitigate metabolic liabilities created by IDH1 mutations in glioma, with possible implications to leverage its therapeutic management by IDH1 inhibitors.

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51 CBX8 Exhibits Oncogenic Activity via AKT/\(\beta\)-Catenin Activation in Hepatocellular Carcinoma
Chris Zhiyi Zhang, Shi-Lu Chen, Chun-Hua Wang, Yang-Fan He, Xia Yang, Dan Xie, and Jing-Ping Yun

Significance: Elucidation of a key new element of the \(\beta\)-catenin signaling pathway in liver cancer may suggest new therapeutic targets.

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Significance: RUNX3 inactivation in cancer removes an antioxidant barrier against DNA double strand breaks induced by TGF\(\beta\) expressed in the tumor microenvironment.
103 An Akt3 Splice Variant Lacking the Serine 472 Phosphorylation Site Promotes Apoptosis and Suppresses Mammary Tumorigenesis
Kimita Suyama, Jiahong Yao, Huizhi Liang, Ouithiriaardjou Berard, Olivier D. Loudig, Dulguun Angyalan, Wendy M. McKinson, Greg R. Phillips, Jeffrey Segall, Yihong Wang, Susan Fineberg, Larry Norton, Richard N. Kitis, and Rachel B. Hazan

Significance: These results illuminate an unexpected function for an endogenously expressed Akt isoform in promoting apoptosis, underscoring the likelihood that different Akt isoforms exert distinct functions in human cancer.

115 CD39 Expression Defines Cell Exhaustion in Tumor-Infiltrating CD8+ T Cells
Fernando P. Canale, Matia C. Ramello, Niccolò Nuñez, Cintia L. Araujo Furlan, Sabrina N. Bossio, Melissa Gorosito Serrán, Imena Tosello Boari, Andrés del Castillo, Marta Ledesma, Christinne Sedlik, Eliane Piaggio, Adriana Gruppi, Eva V. Acosta Rodríguez, and Carolina L. Montes

Significance: The tumor microenvironment elicits a subset of functionally exhausted CD8+ T cells by creating conditions that induce cell surface expression of CD39, an immunosuppressive molecule that can be therapeutically targeted to restore effector T-cell function.

129 A Subpopulation of Stromal Cells Controls Cancer Cell Homing to the Bone Marrow
Stephanie Rossnagl, Hiba Ghura, Christopher Groth, Eva Altrock, Franz Jakob, Sarah Schott, Pauline Wimberger, Theresa Link, Jan Dominik Kuhlmann, Arnulf Stenzl, Pauline Wimberger, Theresa Link, Jan Dominik Kuhlmann, Arnulf Stenzl, Jorg Hemenlotter, Tilmann Todenhöfer, Markus Rojewski, Karen Bieback, and Ronald M. Nakshbandi

Significance: These findings establish an inverse relationship between a subpopulation of mesenchymal stromal cells and cancer cells in the bone marrow.

157 CCR5+ Myeloid-Derived Suppressor Cells Are Enriched and Activated in Melanoma Lesions

Significance: These findings validate the importance of the CCR5/CCR5 ligand axis not only for MDSC recruitment but also for further activation of their immunosuppressive functions in the tumor microenvironment, with potentially broad therapeutic implications, given existing clinically available inhibitors of this axis.

182 Interleukin-27 Exerts Its Antitumor Effects by Promoting Differentiation of Hematopoietic Stem Cells to M1 Macrophages
Yukino Chiba, Izuru Mizoguchi, Junichi Furusawa, Hideaki Hasegawa, Mio Ohashi, Mingli Xu, Toshiya Okui, Takayuki Yoshimoto, Hideaki Hasegawa, Mio Ohashi, Mingli Xu, Toshiya Okui, Takayuki Yoshimoto

Significance: These findings show how the interleukin 27 exerts potent antitumor activity by enhancing the generation of myeloid progenitor cells that can differentiate into antitumorigenic M1 macrophages.

195 Type I IFN Receptor Signaling Controls IL7-Dependent Accumulation and Activity of Promutational IL17A-Producing γδT Cells in Breast Cancer
Emmanuel C. Patin, Daphnée Soulard, Sébastien Fleury, Maya Hassane, David Dombrowicz, Christelle Faveeuw, François Trottein, and Christophe Paget

Significance: Tumor-derived IL7 can represent a therapeutic target to prevent accumulation of immune cells endowed with potent protumoral activities.
205 MUC1-C Induces PD-L1 and Immune Evasion in Triple-Negative Breast Cancer
Takahiro Maeda, Masayuki Hiraki, Caining Jin, Hasan Rajabi, Ashuji Tagde, Manoof Alam, Audrey Boulillez, Xufeng Hu, Yoao Suzuki, Masaaki Mihyo, Tsuyoshi Hata, Kunihiko Himohara, and Donald Kufe

Significance: These findings show how upregulation of the transmembrane mucin MUC1 contributes to immune escape in an aggressive form of breast cancer, with potential implications for a novel immunotherapeutic approach.

216 miR-519d Promotes Melanoma Progression by Downregulating EphA4
Kuo-Tai Hua, Jin-Bong Hong, Yi-Shuan Sheen, Hsin-Yi Huang, Yi-Ling Huang, Jau-Shiuh Chen, and Yi-Hua Liao

Significance: These results suggest a significant role for miR-519d in determining expression of a pivotal cell adhesion molecule that may impact risks of malignant progression in many cancers.

230 Evidence for Kaposi Sarcoma Originating from Mesenchymal Stem Cell through KSHV-induced Mesenchymal-to-Endothelial Transition
Yuqing Li, Canrong Zhong, Dawei Liu, Wenjing Yu, Weikang Chen, Yan Wang, Songtuo Shi, and Yan Yuan

Significance: These findings indicate that Kaposi sarcomas, which arise frequently in AIDS patients, originate from neural crest-derived mesenchymal stem cells, with possible implications for improving the clinical treatment of this malignancy.

246 Small-Molecule Inhibition of Axl Targets Tumor Immune Suppression and Enhances Chemotherapy in Pancreatic Cancer

Significance: These results establish a preclinical mechanistic rationale for the clinical development of AXL inhibitors to improve the treatment of PDAC patients.

CONVERGENCE AND TECHNOLOGIES

290 ConsensusDriver Improves upon Individual Algorithms for Predicting Driver Alterations in Different Cancer Types and Individual Patients
Denis Bertrand, Sibyl Drissler, Burton K. Chia, Jia Yu Koh, Chenhao Li, Chayaporn Suphavilai, Iain Beehuat Tan, and Niranjan Nagarajan

Significance: These findings assess state-of-the-art cancer driver prediction methods and develop a new and improved consensus-based approach for use in precision oncology.
Results from the European Prospective Investigation into Cancer and Nutrition Link Vitamin B6 Catabolism and Lung Cancer Risk

Hui Zuo, Per M. Ueland, Øivind Midttun, Stein E. Vollset, Geethe S. Tell, Despoina Theofylaktopoulou, Ruth C. Travis, Marie-Christine Boutron-Ruault, Agnès Fournier, Gianluca Severi, Marina Kvaskoff, Heiner Boeing, Manuela M. Bergmann, Renee T. Fortner, Rudolf Kaaks, Antonia Trichopoulou, Anastasia Kotanidou, Pagona Lagiou, Domenico Palli, Sabina Sieri, Salvatore Panico, H. Bas Bueno-de-Mesquita, Petra H. Peeters, Kjell Granlövist, Mikael Johansson, Antonio Agudo, Jose Ramon Quiros Garcia, Nerea Larranaga, Maria-Jose Sanchez, Maria Dolores Chirlaque, Eva Andanaz, Shu-Chun Chuang, Valentina Gallo, Paul Brennan, Mattias Johansson, and Arve Ulvik

Significance: This large cohort study firmly establishes an association between an index of vitamin B6 levels with lung cancer risk.

Correction: Germline BAP1 Mutational Landscape of Asbestos-Exposed Malignant Mesothelioma Patients with Family History of Cancer

Kinases are master regulators of cell signaling networks that are frequently dysregulated in cancer, and members of the kinome family have been successfully targeted for therapeutic benefit. In this figure, the activity, cellular requirement, disease association, availability of protein structures and drugs, and research publications associated with each of the 535 members of the human protein kinome are displayed. It highlights how most research attention has been focused on relatively small subsets of the kinome. In the associated resource-based review, the authors discuss their current understanding of the human protein kinome, highlight emerging and overlooked areas, and describe key aspects of kinase signaling biology and some of the challenges associated with treating perturbed kinase networks in patients. For details, see article by Wilson and colleagues on page 15.