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Précis: An integrative approach combining genomics and proteomics with functional profiling revealed an association between cytoskeletal and actin-binding proteins, a mesenchymal or hybrid EMT phenotype, and invasive properties of lung adenocarcinomas that impact overall survival in patients.

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Lung Tumor Suppressor GPRC5A Binds EGFR and Restrains Its Effector Signaling  
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Précis: These results reveal how common loss of expression of a tumor suppressive G-protein coupled receptor during lung tumorigenesis promotes malignant development.

1815  
Genomic and Functional Analysis of the E3 Ligase PARK2 in Glioma  
De-Chen Lin, Liang Xu, Ye Chen, Haiyan Yan, Masaharu Hazawa, Nga Doan, Jonathan W. Said, Ling-Wen Ding, Li-Zhen Liu, Henry Yang, Shizhu Yu, Michael Kahn, Dong Yin, and H. Phillip Koeffler  
Précis: An E3 ligase that targets both EGFR and β-catenin for destruction may offer a rational new theranostic target in the most deadly form of adult brain cancer.

1828  
Spatially Resolved Metabolic Phenotyping of Breast Cancer by Desorption Electrospray Ionization Mass Spectrometry  
Précis: In evaluating a new mass spectrometry-based tool to analyze breast tumor tissues, this study shows how it can rapidly infer tumor grade and hormone receptor status from the metabolic profile of fresh frozen sections of resected specimens.

1838  
CDK4/6 Inhibitor PD 0332991 Sensitizes Acute Myeloid Leukemia to Cytarabine-Mediated Cytotoxicity  
Chenyi Yang, Cynthia A. Boyson, Maurizio Di Liberto, Xiangao Huang, Jeffrey Hannah, David C. Dorn, Malcolm A.S. Moore, Selina Chen-Kiang, and Pengbo Zhou  
Précis: These findings have immediate clinical implications for the potential treatment of elderly patients with acute myeloid leukemia who are unable to tolerate standard high-dose regimens of Ara-C drug therapy.

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Aberrant Expression of proPTPRN2 in Cancer Cells Confers Resistance to Apoptosis  
Alexey V. Sorokin, Binoj C. Nair, Yongkun Wei, Kathryn E. Aziz, Valentina Evdokimova, Mien-Chie Hung, and Junjie Chen  
Précis: These results define a little studied protein tyrosine phosphatase receptor as a novel candidate biomarker and therapeutic target in cancer.
miR-21 Inhibition Reduces Liver Fibrosis and Prevents Tumor Development by Inducing Apoptosis of CD24⁺ Progenitor Cells

Jing Zhang, Jingjing Jiao, Silvia Cermelli, Kyle Muir, Kwang Hwa Jung, Ruihai Zou, Asif Rashid, Mihai Gagea, Sonya Zabludoff, Raghu Kalluri, and Laura Beretta

Précis: These findings highlight the function of a widely studied oncomiR in the survival of CD24⁺ tumor-initiating cells and reduced liver fibrosis.

Histone Deacetylase Inhibitors Repress Tumoral Expression of the Proinvasive Factor RUNX2

Valentina Sancisi, Greta Gandolfi, Davide Carlo Ambrosetti, and Alessia Ciarrocchi

Précis: These findings offer evidence that the cytotoxic activity of HDAC inhibitors against cancer cells relies not only on reactivating silenced tumor suppressor functions, as widely thought, but also on silencing oncogenes that drive cell survival and malignant progression.

RSPO2 Enhances Canonical Wnt Signaling to Confer Stemness-Associated Traits to Susceptible Pancreatic Cancer Cells

Matthias Ilmer, Alejandro Recio Boiles, Ivonne Regel, Kenji Yokoi, Christoph W. Michalski, Ignacio I. Wistuba, Jaime Rodriguez, Eckhard Alt, and Jody Vykoukal

Précis: These results show how blocking a stemness-promoting pathway in conjunction with established chemotherapy could help disrupt dynamic cancer stem-like cell processes and present novel therapeutic targets and strategies.

CEACAM1-3S Drives Melanoma Cells into NK Cell-Mediated Cytolysis and Enhances Patient Survival

Nico Ullrich, Anja Heinemann, Elena Nilewski, Inka Scheffrahn, Joachim Klode, André Scherag, Dirk Schaden, Bernhard B. Singer, and Iris Helfrich

Précis: These findings define splice isoform-specific immunomodulatory and cell biological functions of cell adhesion protein CEACAM1 in melanoma pathogenesis, shedding light on how different splice isoforms affect the oncogenic versus suppressive actions of this important but complex factor in cancer cells.

TWIST1-Induced miR-424 Reversibly Drives Mesenchymal Programming while Inhibiting Tumor Initiation

David J. Drasin, Anna L. Guarnieri, Deepika Neelakantan, Ji Hyo Kim, Joshua H. Cabrera, Chu-An Wang, Vadym Zaberezhnyy, Pierluigi Gasparini, Luciano Cascione, Kay Huebner, Aik-Choon Tan, and Heide L. Ford

Précis: These findings identify the first microRNA controlling a plastic tumor cell state that must be regulated up or down at different times during metastatic progression, highlighting the dynamism in epigenetic changes needed for metastasis and hence the inherent complexity needed in therapeutic approaches for advanced cancers.

PTEN Loss Contributes to Erlotinib Resistance in EGFR-Mutant Lung Cancer by Activation of Akt and EGFR

Précis: These findings define splice isoform-specific immunomodulatory and cell biological functions of cell adhesion protein CEACAM1 in melanoma pathogenesis, shedding light on how different splice isoforms affect the oncogenic versus suppressive actions of this important but complex factor in cancer cells.
ABOUT THE COVER

GPRC5A was repressed, while EGFR was dysregulated, in inflammatory lung tissues (n = 10) in comparison with those in normal lung tissues (n = 10). The inverse correlation between EGFR and GPRC5A was complete, without one exception. IHC staining for GPRC5A in human inflammatory lung tissue is shown in the representative image. For details, see article by Zhong and colleagues on page 1801.