BREAKING ADVANCES
1775 Highlights from Recent Cancer Literature

REVIEWS
1777 Nerve–Cancer Cell Cross-talk: A Novel Promoter of Tumor Progression
Phillip Jobling, Jay Pandavera, Sonia M.R. Oliveira, Séverine Roselli, Marjorie M. Walker, and Hubert Hondermarck

1782 Amino Acid Transporters in Cancer and Their Relevance to “Glutamine Addiction”: Novel Targets for the Design of a New Class of Anticancer Drugs
Yangzom D. Bhutia, Ellappan Babu, Sabarish Ramachandran, and Vadivel Ganapathy

INTEGRATED SYSTEMS AND TECHNOLOGIES
1789 Molecular Portraits of Epithelial, Mesenchymal, and Hybrid States in Lung Adenocarcinoma and Their Relevance to Survival
Mark J. Schliekelman, Ayumu Taguchi, Jun Zhu, Xuoding Dai, Jaime Rodriguez, Muge Celiktas, Qing Zhang, Alice Chin, Chee-Hong Wong, Hong Wang, Lisa McFerrin, Suhaida A. Selamat, Chenchen Yang, Evan M. Kroh, Kavita S. Garg, Carmen Behrens, Ada F. Gazdar, István Pál-Földes, Priya M. Parihar, Jennifer M. Brill, Jean P. Thiery, and Samir M. Hanash
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.

MOLECULAR AND CELLULAR PATHOBIOLOGY
1801 Lung Tumor Suppressor GPRC5A Binds EGFR and Restrains Its Effector Signaling
Shuangshuang Zhong, Huiling Yin, Yuanlin Liao, Feng Yao, Qi Li, Jie Zhang, Huike Jiao, Yongxin Zhao, Dongliang Xu, Shuli Liu, Hongyong Song, Yong Gao, Jingyi Liu, Lina Ma, Zhi Pang, Ruiyu Yang, Chengyi Ding, Beibei Sun, Xiaofeng Lin, Xiaofeng Ye, Wenzheng Guo, Baochun Han, Binhuai P. Zhou, Y. Eugene Chin, and Jingjing Dong
Précis: These results reveal how common loss of expression of a tumor suppressive C-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 Kuhn, Dong Yin, and H. Phillip Koehler
Précis: An E3 ligase that targets both EGFR and β-catenin for destruction may offer a rational new theragnostic 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.

1846 Aberrant Expression of proPTPRN2 in Cancer Cells Confers Resistance to Apoptosis
Alexey V. Sorokin, Binoj C. Nair, Yongkun Wei, Kathryn E. Aziz, Valentina Evdokimnova, 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 Filmer, Alejandro Recio Boiles, Iovone 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.

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

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.

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.

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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.