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1630  
**Undermining Glutaminolysis Bolsters Chemotherapy While NRF2 Promotes Chemoresistance in KRAS-Driven Pancreatic Cancers**  
Suman Mukhopadhyay, Debanjan Goswami, Pavan P. Adiseshaiah, William Burgan, Ming Yi, Theresa M. Guerin, Serguei V. Kozlov, Dwight V. Nissley, and Frank McCormick

These findings illuminate the mechanistic features of KRAS-mediated chemoresistance and provide a rationale for exploiting metabolic reprogramming in pancreatic cancer cells to confer therapeutic opportunities that could be translated into clinical trials.

### MOLECULAR CELL BIOLOGY

1644  
**A Sox2:mIR-486-5p Axis Regulates Survival of GBM Cells by Inhibiting Tumor Suppressor Networks**  
Hernando Lopez-Bertoni, Ivan S. Kotchetkov, Nicole Mihelson, Bachchu Lal, Yuan Rui, Heather Ames, Maria Lugo-Fagundo, Hugo Guerrero-Cazares, Alfredo Quiñones-Hinojosa, Jordan J. Green, and John Laterra

This study identifies a novel axis that links core transcriptional drivers of cancer cell stemness to mIR-486-5p-dependent modulation of tumor suppressor genes that feeds back to regulate glioma stem cell survival.

1656  
**The Tumor Suppressor BAP1 Regulates the Hippo Pathway in Pancreatic Ductal Adenocarcinoma**  
Ho-June Lee, Trang Pham, Matthew T. Chang, Dwight Barnes, Allen G. Cai, Rajkumar Noubade, Klara Totpal, Xu Chen, Christopher Tran, Thijs Hagenbeek, Xiumin Wu, Jeff Eastham-Anderson, Janet Tao, Wyne Lee, Boris C. Bastian, Michele Carbone, Joshua D. Webster, and Anwesha Dey

BAP1 is mutated in a broad spectrum of tumors. Pancreatic Bap1 deficiency causes acinar atrophy but combines with oncogenic Ras to produce pancreatic tumors. BAP1-deficient tumors exhibit deregulation of the Hippo pathway.

See related commentary, p. 1624

1669  
**ATM Paradoxically Promotes Oncogenic Transformation via Transcriptional Reprogramming**  
Xinjian Liu, Mengjie Hu, Pei Liu, Meng Jiao, Min Zhou, Andrew K. Lee, Fang Li, and Chuan-Yuan Li

These findings uncover a novel pro-oncogenic role for ATM and show that contrary to established theory, ATM does not always function as a tumor suppressor, its function is however dependent on cell type.

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**iNOS Regulates the Therapeutic Response of Pancreatic Cancer Cells to Radiotherapy**  

A radiolabeled pH-targeted peptide can be used as a PET imaging tool to assess therapy response within PDAC and blocking iNOS/NO signaling may improve radiotherapy outcomes.
LIN9 and NEK2 Are Core Regulators of Mitotic Fidelity That Can Be Therapeutically Targeted to Overcome Taxane Resistance


Resistance to chemotherapy is a major hurdle for treating patients with cancer. Combining NEK2 inhibitors with taxanes may be a viable approach for improving patient outcomes by enhancing mitotic defects induced by taxanes alone.

TUMOR BIOLOGY AND IMMUNOLOGY

Blockade of DC-SIGN+ Tumor-Associated Macrophages Reactivates Antitumor Immunity and Improves Immunotherapy in Muscle-Invasive Bladder Cancer

Baoying Hu, Zewei Wang, Han Zeng, Yangyang Qi, Yifan Chen, Tao Wang, Jajun Wang, Yuan Chang, Qi Bai, Yu Xia, Yiwei Wang, Li Liu, Yu Zhu, Bo Dai, Jianming Guo, Le Xu, Weijuan Zhang, and Jiejie Xu

DC-SIGN+ TAMs have an immunosuppressive and tumor-promoting function and may serve as a prognostic indicator and therapeutic target in MIBC.

TRANSLATIONAL SCIENCE

MIR-30e-3p Influences Tumor Phenotype through MDM2/TP53 Axis and Predicts Sorafenib Resistance in Hepatocellular Carcinoma

Laura Gramantieri, Daniela Pollutri, Martina Gagliardi, Catia Giovannini, Santina Quarta, Manuela Ferracin, Andrea Casadei-Gardini, Elisa Callegari, Sabrina De Carolis, Sara Marinelli, Francesca Benevento, Francesco Vassuri, Matteo Ravailioti, Matteo Cescon, Fabio Piscaglia, Massimo Negri, Luigi Bolondi, and Francesca Fornari

The dual role of miR-30e-3p in HCC clarifies how the molecular context dictates the tumor suppressor or oncogenic function played by miRNAs.

CHK1 Inhibition Is Synthetically Lethal with Loss of B-Family DNA Polymerase Function in Human Lung and Colorectal Cancer Cells

Rebecca F. Rogers, Michael I. Walton, Daniel L. Cherry, Ian Collins, Paul A. Clarke, Michelle D. Garrett, and Paul Workman

These findings demonstrate how the therapeutic benefit of CHK1 inhibitors may potentially be enhanced and could have implications for patient selection and future development of new combination therapies.

Adipocyte-Induced FABP4 Expression in Ovarian Cancer Cells Promotes Metastasis and Mediates Carboplatin Resistance

Abir Mukherjee, Chun-Yi Chiang, Helen A. Daifotis, Kristin M. Nieman, Johannes F. Fahrmann, Ricardo R. Lastra, Iris L. Romero, Oliver Fiehn, and Ernst Lengyel

Ovarian cancer metastatic progression can be restricted by targeting a critical regulator of lipid responses, FABP4.

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Raman Spectroscopy Reveals That Biochemical Composition of Breast Microcalcifications Correlates with Histopathologic Features

Renzo Vanna, Carlo Morasso, Beatrice Marcinnò, Francesca Piccotti, Emanuele Torti, Davide Altamura, Sara Albasini, Manuela Agozzino, Laura Villani, Luca Sorrentino, Oliver Bunk, Francesco Leporati, Cinzia Giannini, and Fabio Corsi

Raman spectroscopy could be a quick and accurate diagnostic tool to precisely characterize and distinguish benign from malignant breast microcalcifications detected on mammography.

CONVERGENCE AND TECHNOLOGIES

Diagnostic Accuracy of Quantitative Micro-Elastography for Margin Assessment in Breast-Conserving Surgery

Kelsey M. Kennedy, Renate Zilkens, Wes M. Allen, Ken Y. Foo, Qi Fang, Lixin Chin, Rowan W. Sanderson, James Ansie, Philip Wisjesinghe, Andrea Curatolo, Hsien Ern I. Tan, Narelle Morin, Bindu Kunjuraman, Chris Yeomans, Synn Lynn Chin, Helen Dejong, Katharine Giles, Benjamin F. Dessauvage, Bruce Latham, Christobel M. Saunders, and Brendan F. Kennedy

An optical imaging technology probes breast tissue elasticity to provide accurate assessment of tumor margin involvement in breast-conserving surgery.
ABOUT THE COVER

Metabolic reprogramming in cancer cells is linked to upregulated glutaminolysis, which contributes to pancreatic cancer survival. Oncogenic KRAS–induced NRF2 mediates chemoresistance, whereas it also causes metabolic rewiring and elevates pathways involved in glutamine metabolism. Blocking glutamine metabolism prevents cancer cells from resisting chemotherapy, which indicates that targeting glutaminolysis is a potential therapeutic strategy for pancreatic cancer patients. In combination with gemcitabine, this treatment appears to be a promising therapeutic strategy. Cover artwork by Ella Marushchenko. For details, see article by Mukhopadhyay and colleagues on page 1630.