**BREAKING INSIGHTS**

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Highlights from Recent Cancer Literature

**REVIEW**

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Aspirin in Hepatocellular Carcinoma  
Emanuela Ricciotti, Kirk J. Wangensteen, and Garret A. FitzGerald

**CANCER RESEARCH HIGHLIGHTS**

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Hypothermia Is a Potential New Therapy for a Subset of Tumors with Mutant p53  
Wenwei Hu and Zhaohui Feng  
See related article, p. 3905

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How Cancer Risk SNPs May Contribute to Prostate Cancer Disparities  
Mnaya Y. Mavura and Franklin W. Huang  
See related article, p. 3766

**GENOME AND EPIGENOME**

3766  
Susceptibility-Associated Genetic Variation in NEDD9 Contributes to Prostate Cancer Initiation and Progression  
Dong Han, Jude N. Owiredu, Bridget M. Healy, Muqing Li, Maryam Labaf, Jocelyn S. Steinfeld, Susan Patalano, Shuai Gao, Mingyu Liu, Jill A. Macoska, Kourosh Zarringhalam, Kellee R. Siegfried, Xin Yuan, Timothy R. Rebbeck, and Changmeng Cai  
A prostate cancer susceptibility genetic variation in NEDD9, which is strongly associated with the increased risk of patients with African ancestry, increases NEDD9 expression and promotes initiation and progression of prostate cancer.  
See related commentary, p. 3764

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Whole-Exome Sequencing of Radiation-Induced Thymic Lymphoma in Mouse Models Identifies Notch1 Activation as a Driver of p53 Wild-Type Lymphoma  
These findings reveal the mutational landscape and key drivers in murine radiation-induced thymic lymphoma, a classic animal model that has been used to study radiation carcinogenesis for over 70 years.

3791  
LSD1 and Aberrant DNA Methylation Mediate Persistence of Enteroendocrine Progenitors That Support BRAF-Mutant Colorectal Cancer  
Samuel A. Miller, Robert A. Policastro, Shruthi Srinankumar, Tim Lai, Thomas D. Huntington, Christopher A. Ladaika, Daeho Kim, Chunhai Hao, Gabriel E. Zentner, and Heather M. O’Hagan  
This study establishes enteroendocrine progenitors as a targetable population that promotes BRAF-mutant colorectal cancer and can be blocked by LSD1 inhibition to suppress tumor growth.

**METABOLISM AND CHEMICAL BIOLOGY**

3806  
Dual Covalent Inhibition of PKM and IMPDH Targets Metabolism in Cutaneous Metastatic Melanoma  
Marwa Zerhouni, Anthony R. Martin, Nathan Furstoss, Vincent S. Gutierrez, Emilie Jaune, Nedra Tekaya, Guillaume E. Beranger, Patricia Abbe, Claire Regazzetti, Hella Amdouni, Mohsine Driouwy, Patrice Dubreuil, Frédéric Luciano, Arnaud Jacquel, Meri K. Tulic, Thomas Cluzeau, Brendan P. O’Hara, Issam Ben-Sahra, Thierry Passeron, Rachid Benhida, Guillaume Robert, Patrick Auburger, and Stéphane Rocchi  
Glycolytic and purine synthesis pathways are often deregulated in therapy-resistant tumors and can be targeted by the covalent inhibitor described in this study, suggesting its broad application for overcoming resistance in cancer.
USP48 Is Upregulated by Mettl14 to Attenuate Hepatocellular Carcinoma via Regulating SIRT6 Stabilization
Lutao Du, Yang Li, Min Kang, Maoxiao Feng, Yidan Ren, Hongliang Dai, Yumin Wang, Yunshan Wang, and Bo Tang
These findings demonstrate that USP48 is regulated by Mettl14-induced m6A modification and stabilizes SIRT6 to attenuate HCC glycolysis and malignancy.

MOLECULAR CELL BIOLOGY

Epigenetic Induction of Mitochondrial Fission Is Required for Maintenance of Liver Cancer-Initiating Cells
Miaoling Tang, Meisongzhu Yang, Geyan Wu, Shuang Mo, Xingui Wu, Shuxia Zhang, Ruyuan Yu, Yameng Hu, Yingru Xu, Ziwen Li, Xinyi Liao, Jun Li, and Libing Song
These findings show that TBX19/PRMT1 complex-mediated upregulation of MFF promotes mitochondrial fission and tumor-initiating capacity in liver cancer cells, identifying PRMT1 as a viable therapeutic target in liver cancer.

The Transcription Factor SLUG Uncouples Pancreatic Cancer Progression from the RAF-MEK1/2-ERK1/2 Pathway
Faiz Bilal, Enrique J. Arenas, Kim Pedersen, Alex Martínez-Sabadell, Behnam Nabet, Elizabeth Guruceaga, Silvestre Vicent, Josep Tabernero, Teresa Macarulla, and Joaquín Arribas
This study demonstrates that SLUG confers resistance to MEK1/2 inhibitors in pancreatic cancer by uncoupling tumor progression from KRAS-RAF-MEK1/2-ERK1/2 signaling, providing new therapeutic opportunities.

TUMOR BIOLOGY AND IMMUNOLOGY

Host-Dependent Phenotypic Resistance to EGFR Tyrosine Kinase Inhibitors
Yuya Haga, Ilaria Marrocco, Ashish Noronha, Mary Luz Uribe, Nishanth Belugal Nataraj, Arunachalam Sekar, Diana Drago-Garcia, Simone Borgoni, Mosht Lindzen, Suvendu Giri, Stefan Wiemann, and Yosef Yarden
This study reports that stepwise acquisition of kinase inhibitor resistance in lung cancers driven by mutant EGFR comprises a nonmutational, reversible resistant state.

The MNK1/2-eIF4E Axis Supports Immune Suppression and Metastasis in Postpartum Breast Cancer
This study investigates the MNK1/2-eIF4E signaling axis in tumor and stromal cells in metastatic breast cancer and reveals that MNK1/2 inhibition suppresses metastasis and sensitizes tumors to anti–PD1 immunotherapy.

Diet Alters Entero-Mammary Signaling to Regulate the Breast Microbiome and Tumorigenesis
David R. Soto-Pantoja, Mohamed Gaber, Alana A. Arnone, Steven M. Bronson, Nildris Cruz-Diaz, Adam S. Wilson, Kenysha Y.J. Clear, Manuel U. Ramirez, Gregory L. Kucera, Edward A. Levine, Sophie A. Lelièvre, Lesley Chaboub, Akiko Chiba, Hariom Yadav, Pierre-Alexandre Vidi, and Katherine L. Cook
This study demonstrates that diet shifts the microbiome in the gut and the breast tumor microenvironment to affect tumorigenesis, and oral dietary interventions can modulate the tumor microbiota in patients with breast cancer.

TRANSLATIONAL SCIENCE

Hypothermia Effectively Treats Tumors with Temperature-Sensitive p53 Mutations
Junhao Lu, Lihong Chen, Zheng Song, Mousumi Das, and Jiandong Chen

See related commentary, p. 3762
Upregulation of FGF9 in Lung Adenocarcinoma Transdifferentiation to Small Cell Lung Cancer

This study demonstrates that FGF9 plays a role in the transdifferentiation of lung adenocarcinoma to small cell lung cancer.

Quantitative Analysis of Tyrosine Phosphorylation from FFPE Tissues Reveals Patient-Specific Signaling Networks

This study reports a highly sensitive method utilizing FFPE tissues to identify dysregulated signaling networks in patient tumors, opening the door for direct translational insights from FFPE tumor tissue banks in hospitals.