HIGHLIGHTS

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CANCER GENES AND NETWORKS

1441 ATE1 Inhibits Liver Cancer Progression through RG55-Mediated Suppression of Wnt/β-Catenin Signaling
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1454 Demethylation of the SFRP4 Promoter Drives Gastric Cancer Progression via the Wnt Pathway
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1465 LINC00239 Interacts with C-Myc Promoter-Binding Protein-1 (MBP-1) to Promote Expression of C-Myc in Esophageal Squamous Cell Carcinoma
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1476 Mastermind Like Transcriptional Coactivator 3 (MAML3) Drives Neuroendocrine Tumor Progression
   Nathaniel Alzofon, Katrina Koc, Kristin Panwell, Nikita Pozdeyev, Carrie B. Marshall, Maria Albuja-Cruz, Christopher D. Raeburn, Katherine L. Nathanson, Debbie L. Cohen, Margaret E. Wierman, Katja Kiseljak-Vassiliades, and Lauren Fishbein

1486 RAD51AP1 Loss Attenuates Colorectal Cancer Stem Cell Renewal and Sensitizes to Chemotherapy

1498 SOHLH2 Suppresses Angiogenesis by Downregulating HIF1α Expression in Breast Cancer
   Weiwei Cui, Yunling Xiao, Ruilong Zhang, Na Zhao, Xianghong Zhang, Fuwu Wang, Yang Liu, Xiaoli Zhang, and Jing Hao

CANCER “-OMICS”

1510 High Response Rate and Durability Driven by HLA Genetic Diversity in Patients with Kidney Cancer Treated with Lenvatinib and Pembrolizumab
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CELL FATE DECISIONS

1522 p53 Frameshift Mutations Couple Loss-of-Function with Unique Neomorphic Activities
   David R. Tong, Wen Zhou, Chen Katz, Kausik Regunath, Divya Venkatesh, Chinyere Ihuugbe, James J. Manfredi, Oleg Laptenko, and Carol Prives

METABOLISM

1534 Adipokine Apelin/APJ Pathway Promotes Peritoneal Dissemination of Ovarian Cancer Cells by Regulating Lipid Metabolism
   Samrita Dogra, Deepika Neelakantan, Maulin M. Patel, Beth Griesel, Ann Olson, and Sukyung Woo

1546 EMT-Derived Alterations in Glutamine Metabolism Sensitize Mesenchymal Breast Cells to mTOR Inhibition
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SIGNAL TRANSDUCTION AND FUNCTIONAL IMAGING

1559  Defining the Energetic Basis for a Conformational Switch Mediating Ligand-Independent Activation of Mutant Estrogen Receptors in Breast Cancer
       Christopher G. Mayne, Wei Yi Toy, Kathryn E. Carlson, Trusha Bhatt, Sean W. Fanning, Geoffrey L. Greene, Benita S. Katzenellenbogen, Sarat Chandarlapaty, John A. Katzenellenbogen, and Emad Tajkhorshid

TUMOR MICROENVIRONMENT AND IMMUNOBIOLOGY

1571  Cytidine Deaminase APOBEC3A Regulates PD-L1 Expression in Cancer Cells in a JNK/c-JUN-Dependent Manner
       Kailiang Zhao, Qiang Zhang, Sheryl A. Flanagan, Xueting Lang, Long Jiang, Leslie A. Parsels, Joshua D. Parsels, Weiping Zou, Theodore S. Lawrence, Rémi Buisson, Michael D. Green, and Meredith A. Morgan

CORRECTION

1609  Correction: Dephosphorylation of the Proneural Transcription Factor ASCL1 Re-Engages a Latent Post-Mitotic Differentiation Program in Neuroblastoma

ABOUT THE COVER

Estrogen receptor alpha (ERα) is a ligand-activated transcription factor that is therapeutically targetable with endocrine therapies in approximately 70% of breast cancers. Ligand binding initiates an extended hydrogen bonding network (pink arrows) terminating in an ionic lock that allows helix 12 (H12; yellow) to fold into the active conformation capable of binding coactivating proteins that initiate transcriptional cascades. In their study on page 1559, Mayne and colleagues perform free energy calculations of clinically relevant mutations in the helix 11-12 loop of ERα to determine their effect on H12 conformation and receptor activation. The colored balls and associated histograms characterize the dynamics of the loop preceding H12. Each of the point mutations changes the energy landscape of ERα in a manner that no longer requires ligand binding to form the ionic lock and adopt the active conformation, thereby driving therapy resistance and metastatic disease.

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