In Focus
Connecting Genomic Alterations to Cancer Biology with Proteomics: The NCI Clinical Proteomic Tumor Analysis Consortium

ceRNA Cross-Talk in Cancer: When ce-bling Rivalries Go Awry
F.A. Karreth and P.P. Pandolfi

SF3B1 Mutations Are Associated with Alternative Splicing in Uveal Melanoma

Précis: Mutations in splicing factor 3b, subunit 1 (SF3B1) occur in approximately 15% of uveal melanomas and are associated with specific alternative splicing events.

Prostate Cancer Cell Telomere Length Variability and Stromal Cell Telomere Length as Prognostic Markers for Metastasis and Death

Précis: The combination of more variable telomere length among prostate cancer cells and shorter telomeres in cancer-associated stromal cells is associated with increased risk of tumor progression and death.

In The Spotlight
Are Short Telomeres Predictive of Advanced Cancer?
J.W. Shay

New Connections between Old Pathways: PDK1 Signaling Promotes Cellular Transformation through PLK1-Dependent MYC Stabilization
J.T. Cunningham and D. Ruggero

Hypoxia Signaling—License to Metastasize
S. Vanharanta and J. Massagué

Glycolysis Back in the Limelight: Systemic Targeting of HK2 Blocks Tumor Growth
S. Ros and A. Schulze

MINI REVIEW
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RESEARCH BRIEF
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RESEARCH ARTICLES
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A High-Throughput Functional Complementation Assay for Classification of BRCA1 Missense Variants 1142

Bouwman and colleagues developed high-throughput functional complementation assays to predict the pathogenicity of BRCA1 variants of unknown significance (VUS). BRCA1 VUSs were evaluated for their ability to rescue proliferation defects, cisplatin sensitivity, and olaparib sensitivity in murine embryonic stem cells lacking endogenous Brca1. The ability of BRCA1 VUSs to rescue growth defects and drug sensitivity correlated with their homologous recombination activity, indicating that these assays can predict BRCA1 functionality. Interestingly, all unambiguously predicted pathogenic BRCA1 variants were located in the RING and BRCT domains. This approach has the potential to rapidly characterize BRCA1 sequence variants identified during screening for germline mutations associated with increased risk of breast and ovarian cancer. For details, please see the article by Bouwman and colleagues on page 1142.

DEAR1 Is a Chromosome 1p35 Tumor Suppressor and Master Regulator of TGF-β-Driven Epithelial-Mesenchymal Transition 1172


Précis: Loss of DEAR1 drives tumor formation and enhances TGFβ-induced EMT and anoikis resistance via upregulation of SMAD3 signaling.

PDK1 Signaling Toward PLK1–MYC Activation Confers Oncogenic Transformation, Tumor-Initiating Cell Activation, and Resistance to mTOR-Targeted Therapy 1156


Précis: A PDK1–PLK1–MYC signaling cascade promotes cancer cell growth and a cancer stem cell-like phenotype, and inhibition of PDK1/PLK1 is effective in MYC-dependent tumors.

See commentary, p. 1099

DEAR1 Is a Chromosome 1p35 Tumor Suppressor and Master Regulator of TGF-β-Driven Epithelial-Mesenchymal Transition 1172


Précis: Loss of DEAR1 drives tumor formation and enhances TGFβ-induced EMT and anoikis resistance via upregulation of SMAD3 signaling.

Hypoxia-Dependent Modification of Collagen Networks Promotes Sarcoma Metastasis 1190


Précis: Induction of the procollagen lysyl hydroxylase PLOD2 by HIF-1α alters extracellular collagen organization to facilitate migration and metastasis of sarcoma cells.

See commentary, p. 1103

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- Going Public on Cancer Stem Cells