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

See article, p. 1130

New Connections between Old Pathways: PDK1 Signaling Promotes Cellular Transformation through PLK1-Dependent MYC Stabilization

J.T. Cunningham and D. Ruggero

See article, p. 1156

Hypoxia Signaling—License to Metastasize

S. Vanharanta and J. Massagué

See article, p. 1190

Glycolysis Back in the Limelight: Systemic Targeting of HK2 Blocks Tumor Growth

S. Ros and A. Schulze

See commentary, p. 1096
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.

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


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

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**Hyoxia-Dependent Modification of Collagen Networks Promotes Sarcoma Metastasis**


Précis: Induction of the procollagen lysyl hydroxylase PLD2 by HIF-1α alters extracellular collagen organization to facilitate migration and metastasis of sarcoma cells. See commentary, p. 1103.