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. Ruggiero
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.

ON THE COVER

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