### 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.

---

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

S. Ros and A. Schulze
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


Précis: De novo deletion of DEAR1 drives tumor formation and promotes TGF-β-driven EMT and anoikis resistance via upregulation of SMAD3 signaling.

For more News and Research Watch, visit Cancer Discovery online at http://CDnews.aacrjournals.org. Online-only News stories include the following:

• For Adoptive T Cells, Setbacks and Success
• Amgen to Buy Onyx for $10.4 Billion
• Drug Firms Open Up on Trial Data Sharing
• AML Cells Block HSC Differentiation
• Going Public on Cancer Stem Cells
• A Boom in Clinical Genomics Services

ON THE COVER
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.