Molecular Cancer Research

Highlights

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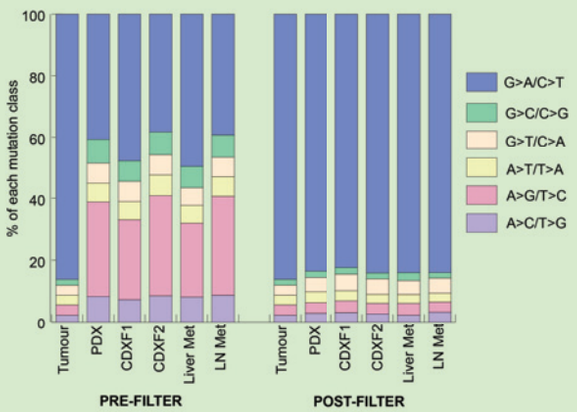
Selected Articles from This Issue



Improved PDX and CDX Data Processing

Khandelwal *et al.* Page 1012

Patient-derived xenograft (PDX) and CTC-derived explant (CDX) models are powerful tools for studying tumors, particularly when used in combination with next-generation sequencing (NGS) approaches. This depends on data analysis pipelines that accurately distinguish between sequencing reads arising from the host, and those that come from the xenograft itself. Here, Khandelwal and colleagues reveal that failure to do this effectively leads to incorrect mutation calls and inaccurate measures of differential expression. Importantly, an open source software tool is described for removing contaminating host sequences and its utility as a highly sensitive and selective tool for correcting PDX/CDX-derived NGS data is demonstrated.

IGH/MYC-Positive Cells are Sensitive to PARP1 Inhibitors

Maifrede *et al.* Page 967

Cancer-specific defects in DNA repair pathways create the opportunity to employ synthetic lethality, already applied against breast and ovarian cancer cells harboring deleterious mutations in *BRCA1* and *BRCA2*, by using PARP1 inhibitors. The current Rapid Impact, demonstrates that Burkitt lymphoma/leukemia (BL) cells carrying the IGH/MYC translocation display low levels of BRCA2 tumor suppressor protein accompanied by inhibition of homologous recombination (HR) repair of potentially lethal DNA double-strand breaks. BRCA2-deficient BL cells are hypersensitive to PARP1 inhibitors used either alone or in combination with cytarabine. Therefore, patients with BL may benefit therapeutically from PARP1 inhibitors, such as the recently FDA-approved olaparib.

Regulation of SLC1A4 and SLC1A5 in Prostate Cancer

White *et al.* Page 1017

Much of our understanding of metabolism in cancer involves the study of glucose. However, cancer cells often take up and metabolize increased levels of glutamine, relative to benign cells, to help satisfy the demands of a rapidly growing tumor. By mining clinical cohorts and functional testing in cell models, White and colleagues demonstrate that three well-established oncogenic drivers of prostate cancer (AR, MYC and mTOR) converge to increase the expression of the glutamine transporters SLC1A4 and SLC1A5, thereby promoting glutamine uptake and subsequent prostate cancer cell growth. Thus, SLC1A4 and SLC1A5 may offer promise as new therapeutic targets and/or biomarkers.

Basal p53 Activates Multiple Tumor Suppressor Genes

Pappas *et al.* Page 1051

The tumor suppressor p53 is mutated in about half of all cancers and its mutation drives tumorigenesis. In this study, Pappas and colleagues found that p53 maintains baseline expression of thirteen tumor suppressor genes through consensus DNA binding sites in enhancer and promoter elements. These tumor suppressor targets of basally expressed p53, together with stress-responsive targets of p53, mediate the ability of p53 to act as a tumor suppressor. Importantly, these results indicate that mutation of p53 results in reduced expression of multiple tumor suppressor genes in parallel, and helps to explain the high frequency of p53 mutations in cancer.

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