A Retrospective Comparison of *In Silico* Pharmaceutical Recommendations with Tumor Board Recommendations in Pediatric Oncology

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Background and Hypothesis:

The objective of this study was to analyze available whole genome sequencing from an adolescent male patient diagnosed with osteosarcoma (OS) in 2014. OS is a primary bone malignancy that most commonly affects the pediatric population. Precision medicine techniques provide new opportunities to improve treatment of OS patients. Pharmaceutical annotation tools such as PharmacoDB and DGIdb can help indicate chemotherapy agents that may benefit patients based on their molecular profiles. We hypothesize that these tools can indicate genome-specific chemotherapy agents for OS after genomic data has been aligned and analyzed.

Project Methods:

A PDX pipeline and retrospective study were performed that identified and compared pharmaceutical treatment options from software tools with the chemotherapy provided. Gene alignment and variant calling were used to process and analyze DNA sequencing data; germline and somatic mutations were also identified. Ensembl VEP was used for variant annotation. PharmacoDB and DGIdb were then applied to identify potentially beneficial medications.

Results:

Gene variant annotation indicated 54 potentially high impact mutations. Of these, DGIdb identified 15 drug-gene interactions. PharmacoDB identified no drugs that target any of the genes containing the 54 high impact mutations. For the entire mutated gene list, DGIdb identified 398 drug-gene interactions. After gene set enrichment, DGIdb identified medications targeting genes of pathways such as “O-glycan processing” and “Diseases of glycosylation”. Potentially harmful variants in the NPRL3 gene were identified. Because NPRL3 is a component of the Gator1 complex that serves as a negative regulator of mammalian target of rapamycin complex 1 (mTORC1), the identified variants in NPRL3 could have played a role in the patient’s OS.

Potential Impact:

This study will foster future collaborations to evaluate the pharmaceutical tool recommendations for this patient’s derived cell lines. These efforts will determine the efficacy of and identify improvements for computational treatment recommendation systems.