Precision Care for Leukemia: Discovery of Novel Therapeutics for High-Risk ALL via Epigenetic and Computational Transcriptome Profiling

Sayana, Ruhi (School: The Harker School)

Hypodiploid B-cell acute lymphoblastic leukemia (B-ALL) is a high-risk form of acute leukemia with a dismal prognosis. Because standard chemotherapy is largely ineffective for this subtype, there is an urgent and unmet clinical need to develop targeted treatments. My research aims to optimize a precision medicine approach for this cancer by translating findings from large-scale transcriptome profiling that identified epigenetic factors as therapeutic targets into effective, targeted treatments. Using in vitro methods, I discovered that panobinostat, an HDAC inhibitor, preferentially induced apoptosis in cancer cells at clinically optimal concentrations (IC50s<10 nM), surpassing the current gold standard of FDA-approved chemotherapy options. To comprehensively characterize the role of epigenetics in this cancer and identify new specific targets, I developed a computational model to map protein-gene relations between aberrantly expressed epigenetic modulators and tumor suppressors that induce leukemia progression and subsequently validated my findings in vitro via western blots. I also developed and optimized a CRISPRi system in hypodiploid cell lines to further validate my computational findings. To my knowledge, this is the first time biologically-validated computational models have been used to link aberrantly expressed genes to tumor suppressor activation, confirming epigenetic regulation of the aggressive progression of hypodiploid B-ALL. By using a combined wet-lab and computational approach, my study identifies highly-specific therapeutic targets and treatments for this high-risk leukemia to advance a streamlined, precision care approach for disease.

Awards Won:
Third Award of $1,000
Drug, Chemical &amp
Associated Technologies Association (DCAT): $10,000 scholarship will be for a senior high school student planning to major in chemistry, chemical engineering, bioengineering or biochemistry. &#x0D
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Serving Society Through Science: Second Award of $500