CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP120194

Project Title:
Defining and Subverting Allele-Specific Regulatory Networks in Cancer

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
The University of Texas at Austin

Lay Summary:

Cancer is a genetic disease, but it is a big challenge to understand how the hundreds of different genetic changes that have been associated with different cancers can drive so many forms of the disease. Many of these changes occur in parts of the DNA that do not code for a protein, so their effects are harder to interpret. One way in which "non-coding" DNA can work is by altering the regulation of genes, by affecting the binding of protein gene regulators called transcription factors, or by affecting the binding of RNA regulators, called microRNAs (miRNAs). We propose that many of the non-coding genetic changes in cancers differentially affect the binding of transcription factors and miRNA regulators. We term this "allele-specific" regulation, where the term "allele" refers to the different variants of the binding site of regulators. Tumors from different patients would have different sets of non-coding changes and therefore different effects on the binding of transcription factors and miRNAs, leading to differences in gene regulation. We will use methods based on next-generation sequencing technologies to identify allele-specific binding and regulation by transcription factors and miRNAs in glioblastoma. Glioblastoma is the most common primary adult brain cancer, and has a very poor prognosis. We have access to tumor samples from patients along with their normal DNA, which will enable us to distinguish inherited changes from somatic mutations that arose in the cancer. We foresee that the impact of our work will be that we will be able to better classify glioblastoma cases based on the set of non-coding DNA changes they contain, and how these changes affect networks of gene regulation by transcription factors and miRNAs. Such a classification of tumor sub-types can guide more personalized therapies that are targeted to the different molecular pathways that are affected in different patients based on their genetic make up.