CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP100107

Project Title:
Understanding the Connection Between Alternative mRNA 3' End Formation and microRNA Function During Tumorigenesis

Award Mechanism:
High Impact/High Risk

Principal Investigator:
Wagner, Eric J

Entity:
The University of Texas Health Science Center at Houston

Lay Summary:

The hallmarks of all cancers include uncontrolled growth, overproduction of many cellular proteins, and spreading to distant areas of the body. These observed changes are caused by genetic changes such as the activation of oncogenes or the loss of expression of tumor suppressor genes. Remarkably, recent studies have found that in all cancer cells analyzed thus far, there are significant changes in the length of messenger RNA (mRNA) molecules to a shorter form. mRNAs serve as templates for protein synthesis in the cytoplasm. These shorter forms of mRNA are resistant to the natural repression by cellular microRNAs (miRNAs). miRNAs are 20- to 22-nucleotide long noncoding RNAs that dampen the levels of protein expression by base-pairing to target mRNAs. The mechanism of this change in cancer cells is not known nor is the identity and significance of the gene targets. These are central questions to this proposed study. To identify the genes that are important for the unusual mRNA shortening process, we will carry out experiments using a dual fluorescence-based reporter system to perform a genome-wide screen. We will be using cutting edge technology that involves knocking down each gene in the human genome in breast cancer cells, looking for changes in the length of mRNA molecules. In addition, we will use an emerging technique called “deep-sequencing” to identify potentially important genes of which mRNAs undergo unusual shortening in cancer cells. By understanding how mRNA length is regulated in both normal and cancer cells, we may begin to develop therapies aimed at interfering with the process that causes unusual mRNA shortening during the formation of tumors.