



CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP110132

Project Title:
Posttranscriptional regulation of noncoding RNAs involved in epigenetic regulation of gene expression

Award Mechanism:
Individual Investigator

Principal Investigator:
Conrad, Nicholas K

Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

The defining characteristic of cancer is the growth of cells at times and in places where cell growth does not occur in a healthy individual. Cancer can be caused by "turning on" (activating) genes that promote cell division or by "turning off" (inactivating) genes that inhibit cell division. Considerable attention has been given to a process called epigenetics that maintains gene activation or inactivation. In this process, genes are activated or inactivated in a particular cell and, when that cell divides, the genes in the new cells inherit the state of being "on" or "off". As a result, when tumor cells divide, epigenetic factors ensure that the resulting new cells maintain activated growth-promoting genes and inactivated growth-inhibiting genes. Theoretically, if we could reverse epigenetic regulation in tumor cells, they would lose the ability to maintain their pro-growth state. In this proposal, we investigate factors that control epigenetics. In other words: What regulates epigenetic regulators? Exciting new research has established that an unusual set of molecules called noncoding RNAs (ncRNAs) are essential for epigenetic regulation. A particular ncRNA is directly linked to metastatic breast cancer, but ncRNAs likely contribute to many cancer types. Like other types of RNA, some ncRNAs have a structure at their ends called a polyadenylate tail that helps govern the quantity of that ncRNA. Our preliminary studies show that the polyadenylate tails of ncRNAs are regulated by previously unappreciated mechanisms. In this proposal, we test the hypothesis that cells control ncRNA polyadenylate tails and that this results in the epigenetic regulation. Given the central importance of epigenetic regulation in tumor biology, we believe these studies will significantly advance our knowledge of the molecular basis of cancer. In addition, because ncRNA regulation is a virtually unexplored area of research, these studies may uncover novel therapeutic strategies.