CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP160852

Project Title:
Chemo-preventive Approach to Cancer Exploiting a Presumptive Link between Genomic Instability and Structural Stability of non-B DNA Sequences

Award Mechanism:
High Impact/High Risk

Principal Investigator:
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Entity:
Texas State University

Lay Summary:

Genetic instability contributes to the development of a variety of human diseases, most significantly cancer. The mechanisms underlying genetic instabilities that lead to the genetic changes associated with the development of cancer have yet to be fully clarified, but it has recently been shown that certain DNA sequences that are found near these sites of genetic changes have the capacity to adopt alternative structures to the commonly found double-helical “B-form” of DNA. We propose a new model of genetic instability in which these non-B DNA-forming sequences serve as hotspots for DNA damage by environmental factors, such as chemicals found in combustion products and exposure sunlight. Furthermore, we propose that the DNA damage that occurs at these hotspots is refractory to repair, thus stimulating mutations that can lead to cancer. Based on this model, we will determine if non-B DNA-forming sequences are more readily modified by one specific carcinogen, BPDE, or ultra-violet (UV) light. We will determine if DNA damage at these sites is less readily repaired than damage in B-DNA regions, and if these non-B DNA sequences lead to mutations, especially in the presence of BPDE or UV light. We will also find compounds that can make these non-B DNA structures more or less stable, and determine the effects of these “molecular probes” on the susceptibility of non-B DNA to damage and mutations. Ultimately, this work may lead to drugs that can prevent cancer by modulating the structural stability of these non-B DNA structures.