CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP140456

Project Title:
Role of DNA2 Nuclease in Cellular Tolerance of Replication Stress and Telomere Maintenance - Implications for Cancer Biology and Anticancer Therapy

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
Baylor College of Medicine

Lay Summary:

The key to successful targeted cancer therapy is to identify intrinsic features that distinguish cancer cells from normal cells. Cancer specific unlimited proliferation signals, due to the activation of the oncogenes or loss of tumor suppressors, result in immortalization. The consequences of unlimited proliferation include loss of chromosome ends, called telomeres, and largely increased spontaneous DNA damage associated with uncontrolled chromosomes duplication. To counteract these processes, cancer cells increase the usage of a specific DNA repair pathway called Break-Induced Replication, which helps cells to repair frequent chromosome breaks and, in some cancers types such as sarcomas, helps to maintain chromosome ends. In this project we provide evidence that a specific protein called DNA2 is needed for break-induced replication. Cancer cells often have increased amounts of this protein and its depletion results in cancer specific cell death. Thus it is proposed that DNA2 inhibition is a good approach in cancer therapy. There are two basic goals of this proposal. First is to understand the exact function of the DNA2 protein in the repair of chromosomal breaks, and second, to develop and test small molecule inhibitors of this enzyme that will selectively decrease the growth of cancer cells. It is our hope that with the support from a CPRIT grant, we will be able to translate this breakthrough from our laboratory studies to clinical applications and benefit cancer patients.