CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP160451

Project Title:
Protein Truncation Mutations in WIP1: Effects on Cancer and Hematopoiesis

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
Baylor College of Medicine

Lay Summary:

The single most frequent deleterious event that occurs in human cancer may be disruption of function in a protein called p53. A major function of p53 is to protect the normal cell from various types of damage and stress and assist in repairing the cell damage. One protective function of p53 is to protect the normal cell from evolving into a cancer cell. Most human cancers evolve through altering p53 in a way that it no longer functions in its usual protective way. Some cancer-targeted therapies are being developed that attempt to restore or enhance p53 function in a cancer cell that has lost it. In so doing, the therapy-induced p53 will actually induce death of the cancer cell. Our laboratory has been studying p53 functions for 25 years and has identified another protein that interacts with p53 called WIP1. We found that a primary role of WIP1 is to suppress p53 functions. Interestingly, a subset of human cancers that appear to have normal p53 display altered WIP1 that is much more active. In addition, older individuals sometimes display WIP1 activation in their blood cells, and this is associated with higher risk of leukemia. We believe that those cancers and normal cells with activated WIP1 are dangerous in part because p53 protective functions are lost due to WIP1 activities. Because WIP1 alterations seem to drive cancer progression, we have been collaborating with the pharmaceutical company GlaxoSmithKline to develop anti-WIP1 therapeutic drugs. The goals of this application are (1) to perform a series of experiments to better understand how WIP1 alterations affect cancer development and blood cell functions, and (2) to test whether our anti-WIP1 therapeutic drugs can effectively target cells with altered WIP1. Successful inhibition of cancer cell growth by anti-WIP1 targeted drugs in our pre-clinical tests would provide a potential weapon in the oncologist's armamentarium and could encourage further clinical trials for certain cancers.