



CANCER PREVENTION & RESEARCH
INSTITUTE OF TEXAS

Award ID:
RP120474

Project Title:
Enabling the structure determination of functional human telomerase holoenzyme

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

Cancer cells need to divide continuously, and the replication of their genome requires the proper maintenance of the telomeres at the ends of their linear chromosomes. The majority of human cancer cells utilize elevated telomerase activity to satisfy this requirement and avoid replicative senescence and growth arrest. Suppression of the telomerase activity selectively in cancer cells therefore becomes a viable strategy in cancer treatment, and structure determination of fully functional human telomerase is critical for the success of such a strategy. Due to its very low expression level in cancer cells, the telomerase complex has been a challenging target for structural studies, and no three-dimensional structure of the whole enzyme is available. The proposed study is aimed at filling this knowledge gap and will apply newly-developed technology in my laboratory to the selective enrichment of the human telomerase holoenzyme for electron cryo-microscopic imaging and three-dimensional reconstruction. Our study will lead to the structures of fully functional telomerase in different conformational states, and will pave a new avenue in the structural investigation of the telomerase activity in human cancer research and prevention.