Award ID:
RP120474

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

Award Mechanism:
Individual Investigator

Principal Investigator:
Jiang, Qiu-Xing

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.