CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP160255

Project Title:
Structural and Functional Analyses of the Spindle Checkpoint

Award Mechanism:
Individual Investigator

Principal Investigator:
Luo, Xuelian

Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

The spindle checkpoint ensures the fidelity of chromosome segregation during mitosis and meiosis. Studies in mouse models have firmly established that malfunction of the spindle checkpoint leads to chromosome missegregation and aneuploidy, which can result in tumorigenesis, premature aging, and other defects. Several spindle checkpoint genes, including Bub1, are mutated in human cancers, albeit with low frequency. Their expression is regulated by tumor suppressors and oncogenes and is frequently altered in cancer cells. This proposal investigates the basic molecular mechanisms of chromosome segregation in human cells, with a focus on the enigmatic roles and regulation of the checkpoint kinase Bub1. We also aim to elucidate the structural basis for the defined functions and regulation of Bub1 and its downstream targets. Our proposed research will significantly advance our fundamental understanding of the spindle checkpoint and chromosome segregation, identify the underlying reasons of aneuploidy in human cancers and other aneuploidy diseases, and may also uncover new ways of exploiting defects in the spindle checkpoint to treat these diseases.