CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP160822

Project Title:
Exploring Geminivirus-encoded suppressor of histone methyltransferases as an anti-cancer drug

Award Mechanism:
High Impact/High Risk

Principal Investigator:
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Entity:
Texas Agrilife Research

Lay Summary:

The primary goal of this research is to engineer our newly discovered small protein that specifically targets histone methyltransfereases (HMTases) to control tumorigenesis in human. In human, DNA is packaged around proteins called histones to form a structure called chromatin. Small chemical tags like "methyl-group" attached to the histones can alter the structure of chromatin to block transcription and lower the activity of a gene. The enzymes that add the methyl-group to histone are known as HMTases. SUV39H and EZH2 are such two HMTases that add repressive marks onto histone tails in chromatin, blocking transcription of numerous tumor suppressors such as P15 and P16. As such, SUVH1 and EZH2 play critical roles in tumorigenesis of acute myeloid leukemia, prostate and breast cancers among many others; and release of SUVH1 and EZH2-controlled tumor suppressors could be an efficient way to conquer tumor initiation, progression and metastasis.

Recently we discovered that a small protein, produced by a devastating virus, specifically targets SUVH1 and EZH2 to release the virus DNA to evade the host's defenses. We would like to investigate whether the protein could inhibit SUVH1 and EZH2 in cancer cells to release the HMTase-controlled tumor suppressors to block tumorigenesis. The proposed study focuses on the cell lines of prostate cancer (PC3) and acute myeloid leukemia (HL-60) to explore this possibility.

As compounds or drugs that alter chromatin methylation might ultimately be the most effective means of combating cancers. The fact that TrAP targets various HMTases presents a unique and unprecedented opportunity to manipulate trans-methylation modifications and to control cancers that result from the epigenetic disorders in human. Thus, the proposed study, given successful, will likely pioneer world-wide effort to develop a new generation of anti-cancer therapeutic strategies based on our newly discovered HTMase-specific inhibitor.