CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP100320

Project Title:
A Novel Approach to Selectively Inhibit Androgen Receptor Action to Treat Prostate Cancer

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
Baylor College of Medicine

Lay Summary:

Prostate cancer is an androgen dependent disease. The actions of androgen are mediated by the androgen receptor, a hormone activated transcription factor. Some form of androgen blockade is the primary therapy for metastatic prostate cancer. Tumors become resistant to this treatment, but remain dependent upon androgen receptor activated by local hormone synthesis, altered cell signaling, and/or through expression of newly discovered AR variants that lack the hormone binding domain and do not require hormone for activity. Thus, new means of inhibiting androgen receptor activity that target other regions of the receptor are needed. Our data suggest that targeting a coactivator binding site in the androgen receptor amino terminus will provide a universal inhibitor of androgen receptor action in hormone dependent and castration resistant prostate cancer. Accomplishing our aims will: 1. Identify the common and unique actions of androgen receptor and its variants. 2. Test the hypothesis that an SRC-1 coactivator derived peptide (SRCdp) will inhibit AR activities leading to reduced cell/tumor growth and metastasis in three independent prostate cancer mouse models. We also will determine whether targeting this region can prevent/delay recurrence after androgen blockade. 3. Establish a novel targeted high throughput microscopy based screen to identify small molecules that will mimic the actions of SRCdp as potential therapeutic agents. Although our own screens may not identify an ideal drug, a demonstration of peptide efficacy in vivo coupled with an established screen will place us in an excellent position to partner with others to identify optimal compounds.