CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP150451

Project Title:
SRC-2 driven “Metabolic Switch” in metastatic prostate cancer- Prognostic and Therapeutic implications

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
Baylor College of Medicine

Lay Summary:

Prostate cancer is the second most common epithelial cancer and one of the leading causes of cancer related death for men. In order to better understand the reasons for cancer development, researchers during the last decade decoded the entire genetic makeup of prostate cancer patients to identify ‘cancer-specific’ genes. One of the genes to be identified was ‘Steroid Receptor Coactivator-2’ (SRC-2). SRC-2 gene was found to be increased in 8% of primary tumors (cancer-confined to the prostate) and 37% of metastatic tumors (cancer-spread to other organs). Strikingly, patients with primary tumor who had increased SRC-2 expression developed early disease recurrence, suggesting SRC-2 expression may predict aggressive and metastatic prostate cancer. Implanting human prostate cancer cells in mouse, we observed increased expression of SRC-2 allows the tumor cells to spread to other organs rapidly, a common phenotype observed in aggressive castration-resistant prostate cancer (CRPC). We also found that SRC-2 provides added advantage to the tumor cells to utilize various nutrients like amino acids (glutamine), and convert them to fat. All these biochemical products are required for tumor cell multiplication and rapid growth. These findings suggest SRC-2 expression confers a unique metabolic advantage to the rapidly growing tumor cells promoting aggressive behavior (metastasis). Here we propose to characterize SRC-2 driven metabolic program in CRPC to develop novel metabolic markers for early detection of aggressive prostate cancer. Further, we will also develop and characterize Bufalin as a key inhibitor of SRC-2 for metastatic prostate cancer for which currently there are limited treatment options.