CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP120394

Project Title:
Molecular Oncogenesis of NANOG in Castration-Resistant Prostate Cancer

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
The University of Texas M.D. Anderson Cancer Center

Lay Summary:

Prostate cancer is generally initially susceptible to therapeutic intervention via androgen ablation (i.e., chemical castration), often in combination with radical prostatectomy. However, the emergence of castration-resistant prostate cancer (CRPC) heralds lethal disease. It is largely due to the devastating consequences of advanced hormone-refractory prostate cancer that even early-stage, relatively benign, prostate cancer is often over-treated to minimize risk. Thus, patients with both early stage and advanced prostate cancer would benefit from further understanding of the cellular and molecular mechanisms driving the emergence of CRPC. My research has focused on the tumor-promoting biological activities of NANOG, a stem cell transcription factor and implicated as a mediator of numerous stem cell properties exhibited by subsets of specialized tumor cells. Although we have previously identified NANOG as a protein functionally expressed in prostate cancer and driving biological processes essential to clinical manifestations, including proliferation, drug-resistance and resistance to androgen-deprivation, little is known about how NANOG imposes these characteristics during prostate cancer development. Here, we aim to establish the clinical relevancy of NANOG to CRPC and determine the molecular mechanisms by which NANOG promotes prostate tumor development and prostate cancer progression. In order to accomplish our objectives, we shall 1) evaluate expression of NANOG in recurrent (i.e., patient relapse) advanced prostate tumor specimens and 2) functionally assay NANOG in human cell lines using molecular tools to genetically alter NANOG's expression levels in combination with gene expression profiling to determine downstream gene targets of NANOG in conditions of androgen stimulation and withdrawal (castration). Our hope is that these findings will lead to the development of novel therapeutics for the treatment of prostate cancer, particularly CRPC.