CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP180055

Project Title:
Mechanisms and Treatment of Hippocampal Cognitive Impairment Associated with Androgen Deprivation Therapy for Prostate Cancer

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
The University of Texas Health Science Center at San Antonio

Lay Summary:

Cognitive impairment, including spatial memory impairment, is a serious consequence of androgen deprivation therapy (ADT) that compromises quality of life of prostate cancer survivors treated by ADT. Studies of patients undergoing ADT have shown structural and functional deficits in the hippocampus (Hipp), a brain region that mediates spatial learning and memory, and in one of its major targets, the medial prefrontal cortex (mPFC), which is involved in many cognitive processes. In this project, we will investigate mechanisms in the Hipp that underly spatial memory impairment after ADT. There is currently no satisfactory treatment for cognitive impairment after ADT, so we will also test a potential new treatment, the novel antidepressant drug, vortioxetine. Vortioxetine has actions that are different from other antidepressants, and it has been shown to have positive effects specifically on cognitive impairment in depression. Because prostate cancer occurs in middle-aged to elderly men, we will also investigate the interaction of cognitive impairment associated with ADT with age-related cognitive decline by comparing young adult and middle-aged rats. To measure spatial memory in rats, we will use the Novel Object Location (NOL) test. In a recent pilot study using this test, we showed an impairment in castrated rats that was reversed by vortioxetine. In this project, we will study structural changes in nerve cells in the Hipp, functional changes in its connection to the mPFC, and gene expression changes in the Hipp that might account for the compromised function of this important cognitive circuit after androgen deprivation. And we will test the ability of vortioxetine to reverse these effects. The results of this project will identify mechanisms of cognitive impairment after ADT that may be viable therapeutic targets, inform a potential new use for vortioxetine in treating it, and ultimately improve the quality of life of prostate cancer survivors treated by ADT.