CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP160319

Project Title:
Role of PARP-1 in Estrogen Receptor Enhancer Function and Gene Regulation Outcomes in Breast Cancers

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

Breast cancer is the second leading cause of cancer-related mortality in women, with a 1 in 8 lifetime of risk for women in the United States. A key hurdle in developing better treatments for breast cancers is a lack of understanding of the mechanisms that promote the growth of breast cancer cells, and why some breast cancers grow in response to estrogens, while others do not. Drugs that target PARP-1, a protein involved in many important cellular functions, have shown promise and may be useful for treating estrogen receptor alpha (ERa)-positive breast cancers. In this regard, we have been studying the interplay between ERa and PARP-1 in breast cancers. Specifically, we are focusing on the molecular mechanisms by which PARP-1 controls the gene-regulating activities of ERa. PARP-1 is an enzyme that chemically modifies target proteins through a process called poly(ADP-ribosyl)ation (PARylation). We think that PARP-1 PARylates key target proteins required for ERa function, ultimately controlling the estrogen-dependent growth of breast cancer cells.In the current application, we propose to study the biology of these processes in breast cancer cells to identify (1) the ways in which PARP-1 controls ERa activity, (2) the proteins PARylated by PARP-1, and (3) how interplay between ERa and PARP-1 affects the cancer-related properties of breast cancer cells. Our experiments will answer these questions using an integrated set of state-of-the experimental approaches, including a new method that we have developed for detecting PARylation in cells.Collectively, our studies will explore a facet of breast cancer biology that remains largely unexplored and has great potential to change the way we diagnose and treat breast cancers. In addition, our studies will help reveal the specific molecular endpoints modulated by clinically relevant PARP inhibitors (e.g., Olaparib). Finally, our studies will provide new tools and approaches for studying PARylation in cancer.