CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP110183

Project Title:
Role of the Histone Demethylase UTX in Breast Cancer Events

Award Mechanism:
Individual Investigator

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

Lay Summary:

Epigenetic changes -- heritable changes in molecular expression or phenotypes of a cell type without alterations in the genetic material (DNA) -- are critical during breast cancer events that cause about 40,000 deaths every year and more than 192,000 new cases in US in 2009. However, the molecular basis of such changes remains to be studied. Histone lysine methylation, which represents the addition of a small molecule group termed methyl group at the amino acid lysine (K) in the DNA partner proteins known as histones, has emerged as a hallmark associated with the epigenetic regulation of gene expression process -- an essential life process by which information in a genetic unit called gene is used to synthesize a functional product (e.g., a protein). In particular, trimethyl H3K27, a key type of lysine methylation, is associated with silencing of numerous genes and commonly altered in breast tumors. In a recent breakthrough study, we identified UTX as a novel trimethyl H3K27 modifier that acts as a molecular eraser of trimethyl H3K27. Our new studies indicated that this enzyme is crucial for the growth of breast cancer cells regardless the status of estrogen receptor (ER), an important protein used to classify breast tumors. We propose to study the role of UTX in epigenetic changes that occur during breast cancer progression and metastasis. Our innovative sets of studies are fundamental to understanding the molecular pathogenesis that are commonly responsible for both ER-positive and ER-negative breast tumors. These studies also promise to provide critical information for treating breast cancer patients with ER-negative tumors and their metastasized forms that have generally a poor prognosis and that are considered a major clinical challenge in breast cancer treatment. Finally, accomplishing our goal is highly relevant to the development of novel therapeutic agents that modulate enzymatic functions of UTX to inhibit breast cancer progression and metastasis.