CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP160884

Project Title:
RNA processing stress: a new therapeutic entry point in triple-negative breast cancer

Award Mechanism:
High Impact/High Risk

Principal Investigator:
Westbrook, Thomas

Entity:
Baylor College of Medicine

Lay Summary:

More than 400,000 women will succumb to breast cancer this year, underlining the urgent need for new strategies to prevent and treat breast cancer. While new therapies and early detection have reduced the incidence of advanced disease, many patients are not helped by our current standard of care. It is clear that new medicines are necessary. However, a major obstacle to helping cancer patients is the current paradigm used to discover new therapies.

Significant advances in targeted therapies have been made for patients with two subtypes of breast cancer (ER-positive and HER2-amplified). These so-called “targeted therapies” strike at the heart of tumors by focusing on the genetic abnormalities driving the cancer to grow uncontrollably. However, a third major subtype of breast cancer, called TNBC, do not harbor a specific genetic problem to which a therapy can be targeted. Consequently, TNBC patients have a poor prognosis and are exposed to chemotherapies with extensive systemic side effects. Herein, we propose a new direction for developing anti-cancer therapies.

In addition to promoting tumorigenesis, the genetic abnormalities of cancer also produce unique stresses in cancer cells, collectively termed tumor-specific stresses (TSS). Consequently, cancer cells become dependent on pathways enabling them to tolerate such TSS. These stress-support pathways are ideal therapeutic targets, because cancer cells (but not normal cells) become dependent on them for their growth and survival. However, the genes underlying TSS and their corresponding support pathways are largely unexplored. In this application, we explore a new class of TSS in which tumors can be fooled into executing an anti-virus response and tumor cell suicide in the absence of a viral infection. Using new technologies we developed for rapidly delineating the weaknesses of living tumors, we will discover new signaling pathways that serve as entry points for anti-cancer therapies.