CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP100726

Project Title:
14-3-3zeta-induced microRNA deregulation in early stage breast cancer progression

Award Mechanism:
Individual Investigator

Principal Investigator:

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

Lay Summary:

Studying the transition from non-invasive ductal carcinoma in situ (DCIS) to life-threatening invasive breast cancers (IBC) is listed in the top quartile of the 100 priorities of comparative effectiveness research by the Institute of Medicine of the National Academies. Development of effective detection and intervention strategies for early stage breast cancer is in high demand also due to advances in diagnostic tools allowing earlier detection of breast diseases/cancers. This study is aiming at understanding how early stage DCIS progress to life-threatening IBC. Recently, we discovered that 14-3-3z, a protein that participates in many important cellular functions, is expressed at a very high level in >50% of non-invasive DCIS and promotes DCIS transition to IBC. We also found that 14-3-3? high expression in mammary epithelial cells (MECs) inhibited the miR-200 family and miR-203 miRNAs. These 14-3-3?- inhibited miRNAs have been reported to suppress early malignancy of MECs. Therefore, we hypothesize that 14-3-3? high expression in MECs and early stage breast cancers leads to DCIS transition to IBC by inhibiting miR-200 and miR-203 family miRNAs. Here, we propose to explore the unknown roles and novel mechanisms of 14-3-3?-mediated miRNA deregulation in early breast cancer and examine their clinical relevance in patients' DCIS samples. The studies may identify novel "miRNA signatures" for early detection and intervention of the deadly transition from DCIS to IBC. This study will open a new venue for development of effective early detection and intervention strategies for breast cancer, which impacts on one out of eight women in this country. Additionally, little is known about how miRNA expression is regulated. Our studies create a new paradigm investigating the deregulation of microRNA-biogenesis by 14-3-3?.