



CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP170671

Project Title:
Targeting a Novel Nuclease PAAN in Triple-Negative Breast Cancer

Award Mechanism:
High Impact/High Risk

Principal Investigator:
Wang, Yingfei

Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

MicroRNA is a small non-coding RNA ubiquitously expressed in mammals and controls important physiological and pathological processes. A vast majority of microRNAs are down-regulated in triple-negative breast cancer, leading to tumorigenesis. However, the molecular mechanisms underlying microRNA dysregulation in human triple-negative breast cancer are still elusive. Recently, we identified macrophage migration inhibitory factor as a novel nuclease and named it as PAAN according to its new function. PAAN is highly expressed in primary triple-negative breast tumors. High levels of PAAN in breast tumors are inversely correlated with global down-regulation of microRNAs, but positively correlated with poor survival of patients with breast cancer. Genetic deletion of PAAN blocks triple-negative breast tumorigenesis in xenograft mice. Remarkably, PAAN has the ribonuclease activity and cleaves microRNAs in vitro and in human tumor tissues in vivo, suggesting that PAAN may break down microRNAs to promote triple-negative breast tumor growth. The primary goals of this proposed project are to 1) define the role of PAAN in microRNA degradation and its functional significance in triple-negative breast tumorigenesis; and 2) establish a high throughput screen to discover PAAN inhibitors blocking PAAN ribonuclease activity and triple-negative breast tumor growth. The successful completion of this project will discover a breakthrough new function of PAAN in tumor development, and uncover the fundamental mechanism of microRNA stability in human cancers. More importantly, it may yield the new therapeutic tools for treatment of triple-negative breast cancer. Dr. Weibo Luo, an Assistant Professor in the Department of Pathology at UT Southwestern, who has expertise in the breast cancer research, will serve as a Co-Investigator to ensure the success of the proposed project.