

Lay Abstract

Which overarching challenges does this research address?

This research will address these overarching challenges: 1) to identify why some breast cancers become metastatic; 2) to revolutionize treatment regimens by replacing them with ones that are more effective, less toxic, and which impact survival. Triple-negative breast cancer (TNBC) exhibits frequent metastasis which leads to stage IV breast cancer that is usually very resistant to chemotherapy. The major goal of this proposal is to determine effective therapy targeting cancer metastasis. In addition, this research also focuses on race disparity in breast cancer, which could explain racial disparity in TNBC patient's survival in Black women and identify potential risk alleles related to metastatic TNBC.

What types of patients will it help and how will it help them?

Despite the effort of the research community, breast cancer remains the major cause of cancer death in women. Triple negative breast cancer (TNBC) is the most aggressive subtype with a high mortality and a high recurrent rate. Because TNBC tumors do not express hormone receptors (Estrogen, Progesterone and Her2), there is no approved targeted therapy unless toxic chemotherapy or radiation therapy. As such, there is a great need for further advances in therapy to treat patients with TNBC. Our previous research found that the gene, TRIM37, is overexpressed in TNBC. Levels of TRIM37 also correlate with tumor grade and are the highest in stage IV breast cancer. Knockdown of TRIM37 could efficacy prevent primary tumor progression, as well as indicating potential ability to attenuate metastatic lesions.

In addition, in the section of study of race disparity, my bioinformatical analysis reveals that in normal breast tissue Black women have significantly higher level of TRIM37, which may give early boost to TNBC to metastasize. The study of race disparity could determine which single nucleotide polymorphisms (SNPs) contribute to higher TRIM37 expression in Black women, and thus to offer new approach to find prevention methods and improve diagnostic of TNBC in Black women.

What is the projected time it may take to achieve a patient-related outcome?

This research proposal will have an immediate outcome such as identification of a novel biomarker to predict efficacy of the therapy targeting metastasis with all TNBC patients and a novel diagnostic strategy of TNBC in Black women. It is expected that (pre-)clinical trial could be applied within 3 years.

What is the likely impact of this study on ending breast cancer?

This study opens a new opportunity for treatment in human TNBC patients by identifying and characterizing novel therapeutic target – TRIM37. Silencing of TRIM37 by ASO using innovative delivery approach - nanoparticles coated with anti-FOLR1 antibody - will allow for specific targeting of TNBC cells, leading to tumor growth suppression and metastasis prevention. The second part of this study focuses on very relevant question about TNBC racial disparity in survival and offers new approach to find prevention methods and improve diagnostic of TNBC in Black women.