Characterization of ERα36 as a mediator of oncogenic phenotypes via non-genomic signaling pathways in inflammatory breast cancer

Inflammatory Breast Cancer (IBC) is the most aggressive form of breast cancer with a low overall 5-year survival rate of ~30-60%. To this date the molecular signature associated with IBC is not completely characterized, which lead to a lack of effective targeted therapeutics, especially for those patients that account for the 20-40% of triple-negative (TNBC) IBC cases. Thus, the poor prognosis for patients with IBC emphasizes the need to better understand the molecular signature of this disease with the long-term goal of developing effective targeted therapeutics. Recently, several studies have shown that estrogen can exert non-genomic effects in triple-negative IBC and other TNBCs, mediated by the expression of alternate estrogen receptors, including ERα36. Estrogen non-genomic signaling refers to the rapid action of these alternate estrogen receptors that upon estrogen binding activates protein-kinase cascades in the cytoplasm. Our goal is to investigate the role of estrogen non-genomic signaling as part of the molecular signature responsible for IBC aggressive phenotype. We hypothesize that estrogen, via ERα36, can elicit a specific non-genomic signaling cascade that promotes the acquisition of aggressive oncogenic phenotypes in IBC. This study will provide the foundation for further characterization of the role of ERα36 in the progression of IBC and the identification of novel candidates to be tested as therapeutics targets in vitro and in vivo IBC studies.