

The potential role of ERalpha36 in Inflammatory Breast Cancer

Abstract

Triple negative breast cancer (TNBC) represents approximately 10–15% of all breast cancer cases diagnosed annually worldwide, and patients have a poor outcome compared to other subtypes of breast cancer. Here we are interested in studying the Inflammatory Breast Cancer (IBC); a singular type of breast cancer in which ~40% of the cases are TNBC, reporting a rapid progression and a poor prognosis. To date, little is known about the molecular mechanism responsible for the unique IBC phenotype. Recent studies have identified novel cytoplasmic and membrane localized estrogen receptors (ERs) such as GPR30 and ERs isoforms (ERalpha36) that can be activated by estrogen (E2) and enhance the migration and invasion of IBC cell lines; by a mechanism known as the estrogen “non-genomic” signaling. Curiously, "cross-talk" interactions between these receptors have not been studied extensively in Inflammatory Breast Cancer. We hypothesize that upon activation with estrogen, there is a "cross-talk" reaction between ERalpha36 and GPR30, promoting the activation of EGFR signaling cascades to increase cell growth, invasion and migration. We also hypothesize that upon activation with E2, the ER variant (ERalpha36) can translocate into the nucleus and alters with the transcriptome profile of the SUM149PT IBC cell lines. This finding can lead us to a new signaling pathway mechanism that can be significant for potential therapeutic targets of IBC cases.