

Exploring the Role of ERK5 in Triple Negative Breast Cancer

Abigail G. Huddleston, Katherine Hebert, Jack Elliott, Dr.Elizabeth Martin, Dr.Matthew Burow

Tulane University, The United States

Abstract

Breast cancer is the most commonly diagnosed cancer among women and is classified by the presence of hormone receptors and human epidermal receptor 2 (HER2). Receptor positive breast cancers have available targeted therapies for treatment; however, the triple- negative breast cancer (TNBC) subtype lacks these receptors and to date has no targeted therapy. TNBC is a particularly aggressive, challenging to treat breast cancer, and is most prevalent in younger Black and Hispanic women, making this an underserved cancer. Due to the nature of the disease and its prevalence in minority populations, it is imperative to find effective novel targeted therapies.

One avenue researchers are interrogating for novel drug targets is through the exploration of protein kinases. Here, we focused on the extracellular signal-regulated kinase 5 (ERK5) a member of the MEK5/ERK5 pathway which regulates cellular proliferation, survival, differentiation, and apoptosis. The ERK5 pathway is known to have effects on TNBC, however the impact of this kinase on the tumor microenvironment (TME) is not currently evaluated.

ERK5 kinase evaluation was performed through the knockout (KO) of ERK5 in TNBC. Following validation of stable repression, conditioned media(CM) experiments were performed to understand the effects of ERK5 on the TNBC TME. Results demonstrated that MDA- MB-231-ERK5KO CM altered adipose derived stromal/stem cell (ASC) cytokine gene expression and cell death. Results from this study will be used to better understand the role of ERK5 in TNBC microenvironment and better inform novel drug targets.

Keywords: breast cancer, triple negative breast cancer, kinases, MAPK