ERβ as a mediator of estrogen signaling in inflammatory breast cancer

July 3 2023

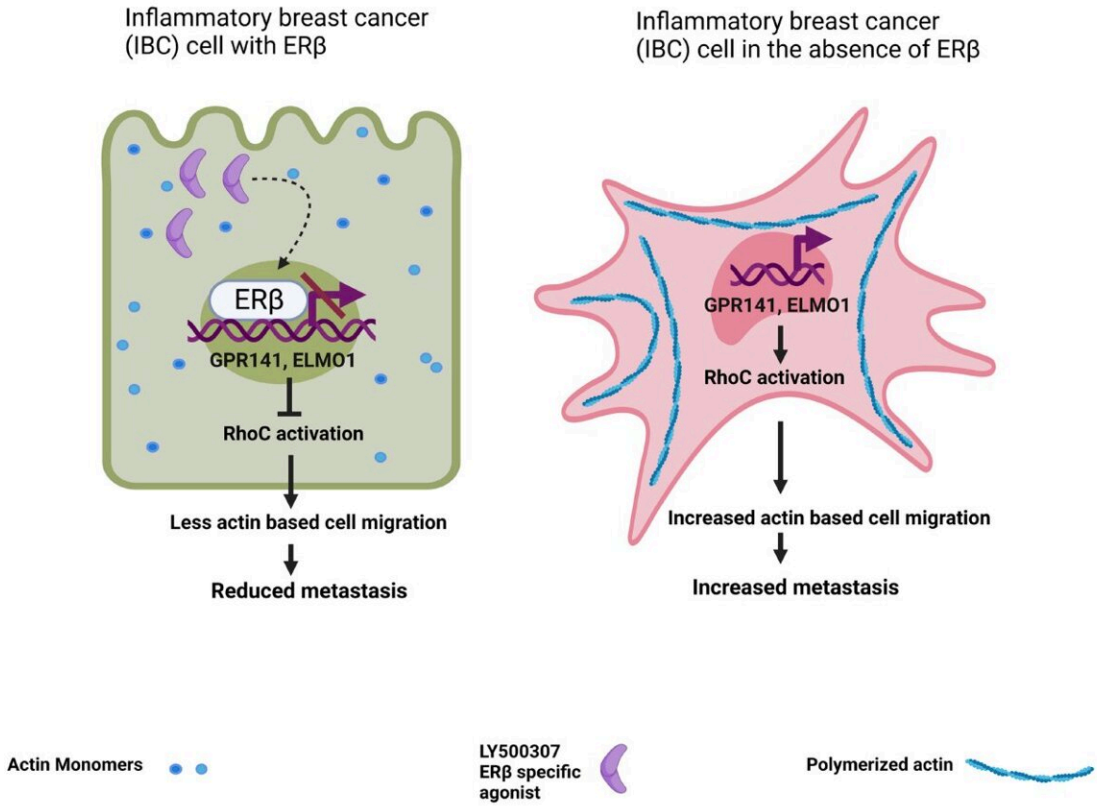

Figure 1: Upon activation by the specific agonist LY500307 ERβ binds to estrogen receptor binding elements (ERE) inregulatory regions of GPR141 and ELMO1 genes and suppresses their transcription, which in turn leads to diminishedRhoC activation, reduced actin-based cell migration and metastasis. Credit: *Oncotarget* (2023). DOI: 10.18632/oncotarget.28425

A new editorial paper titled "ERβ as a mediator of estrogen signaling in inflammatory breast cancer" has been published in *Oncotarget*.

In this new editorial, researchers Harika Nagandla and Christoforos Thomas from Houston Methodist Neal Cancer Center discuss inflammatory breast cancer (IBC)—a rare and aggressive form of breast cancer that accounts for 2–4% of all new breast cancer cases detected in the United States. Even with the application of standard multi-modality treatment approach that incorporates neoadjuvant chemotherapy, radiation and surgery, the 5-year survival rate for IBC is only about 40–50%. Breast cancer can be typically stratified into different types based on the presence of molecular drivers such estrogen receptor (ERα), progesterone receptor (PR) or human epidermal growth factor receptor 2 (HER2), which inform the treatment choice.

For IBC, there is a substantially higher incidence of ERα negativity compared with other forms of breast cancer that can reach up to 60%. A specific targetable driver signaling pathway has not been identified so far. About one in three patients already have distant metastasis at the time of diagnosis, contributing to the aggressiveness and poor outcomes associated with IBC.

Despite the absence of ERα from the majority of IBC tumors, estrogen signaling has been implicated in progression of the disease through ERα-independent pathways. ERβ is a ligand activated transcription factor that mediates effects of estrogen, along with ERα in different tissues during growth and development by regulating transcription of target genes. Tumor suppressive effects of ERβ have been documented in diverse cancer types such as thyroid, kidney, prostate, glioblastoma, ovarian and breast cancer.

The researchers state, "The work from our group establishes ERβ as a tumor suppressor in IBC by demonstrating its strong antimetastatic

activity in preclinical models of the disease and delineating the mechanism of action."

More information: Harika Nagandla et al, ERβ as a mediator of estrogen signaling in inflammatory breast cancer, *Oncotarget* (2023). DOI: 10.18632/oncotarget.28425