

Newly appreciated membrane estrogen receptor important therapeutic target for breast cancer

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New research at Rhode Island Hospital has uncovered the biological effects of a novel membrane estrogen receptor, a finding that has potential implications for hormonal therapy for breast cancer. The study is published in the July edition of the journal *Molecular Endocrinology*. This new study by Edward Filardo, MD, and his research team further supports earlier published work by the group that linked the transmembrane receptor, GPR30/GPER-1, to specific estrogen binding, rapid estrogen signaling and breast cancer metastasis.

"What is exciting about this new work," says Filardo, "is that it provides some insight into the influence of GPR30 at the cellular level. It shows that [estrogen](#) action through GPR30 allows for [breast tumor](#) cell survival, and not breast tumor cell proliferation." Prior studies by Filardo's group showed that estrogen acts through GPR30 to promote the rapid release of preformed growth factors that are tethered to the surface of [breast cancer](#) cells. Their latest study was conducted in an effort to better understand the mechanism by which GPR30 triggered the release of epidermal growth factor (EGF) polypeptides from the surface of breast cancer cells.

The investigator's found that the "growth factors" did not promote cellular growth, which by itself is not a novel finding. It has long been appreciated that EGF-related factors are also important in other cellular activities such as cellular survival. Filardo and the research team,

however, found that estrogen action through GPR30 had a more profound effect on tumor cell survival. They found that GPR30 promoted the assembly of what is called a "provisional extracellular matrix" -- a crucial event in cellular survival. More specifically, they found that release of growth factor by GPR30 required the activation of a latent adhesion receptor (known as integrin alpha 5 beta 1).

Filardo says, "Activation of integrin alpha 5 beta 1 by GPR30 is a significant event because it provides a way for invading cells to gain hold once they metastasize to tissues distant to the primary breast cancer. This happens because activated integrin alpha 5 beta 1 can convert soluble plasma protein fibronectin into an insoluble cage. The breast cancer cells can use this to adapt to a new environment."

In general, about two-thirds of all breast cancer cases involve tumors that retain expression of estrogen receptors (ER). They are presumed to proliferate in response to estrogen produced by the patient. Consequently, patients with ER-positive tumors receive hormonal agents (known as ER antagonists) that act by blocking the proliferative effects of estrogen promoted by the ER. As a result, the capacity of breast cancers to grow is reduced. The development of new drugs targeting GPR30 may be an important step in controlling breast cancer because this newly appreciated [estrogen receptor](#) is not promoting estrogen-dependent growth but may be critical in promoting breast tumor cell survival.

Filardo says, "There has been a recent shift toward treating ER-positive breast tumor patients with aromatase inhibitors such as tamoxifen that block estrogen biosynthesis. The thought is that this is yet another way to prevent estrogen from acting as its sole receptor, the ER." He concludes, "The discovery that GPR30 represents yet another estrogen receptor with biological significance for breast cancer furthers the argument that aromatase inhibitors would effectively block estrogen action at both

types of estrogen receptors."

Source: Lifespan ([news](#) : [web](#))

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