

5th World Congress on

BREAST CANCER

June 15-17, 2017 London, UK

A functional cross-talk between GPER and IGF1/IGF1R signaling drives breast tumor angiogenesis via activation of the HIF-1 α /VEGF transduction pathway

De Francesco EM, Maggiolini M, Sotgia F, Lisanti MP and Clarke RB
University of Manchester, UK

Compelling experimental evidence indicate that a member belonging to the G-protein coupled receptor superfamily, named GPER/GPR30, acts as a receptor for estrogens in diverse physio-pathological conditions, including breast cancer. Furthermore, GPER signaling has been shown to mediate stimulatory responses in breast cancer associated fibroblasts (CAFs), which are key components of the tumor microenvironment driving disease progression. In this context, we have recently demonstrated that GPER is involved in breast cancer cells adaptation to hypoxic microenvironment, through the activation of HIF-1 α /VEGF transduction pathway and the angiogenic response. Worthy, a functional cross-talk between GPER- and growth factor (EGF, insulin and IGF1)-signaling has been demonstrated to integrate complex biological events in breast cancer, like cell proliferation and migration. Here, we evaluate the angiogenic-promoting role of GPER through the regulation of VEGF expression and function triggered by IGF1. Using estrogen receptor (ER)-negative and GPER positive SkBr3 breast cancer cells and CAFs derived from mammary ductal carcinomas, we demonstrate that IGF1 activates through IGF1R the ERK1/2 and AKT cascades, leading to the increase of HIF-1 α and its targets GPER and VEGF. RT-PCR, western blotting, immunofluorescence and reporter assays, gene silencing strategies and in vitro angiogenesis studies show that a functional cross-talk between HIF-1 α and GPER regulates VEGF expression and function, toward new blood vessel formation in breast cancer. Taken together, our findings demonstrate that targeting the interactions between GPER and IGF1/IGF1R may represent an innovative strategy for halting the angiogenic response in breast cancer.

Biography

De Francesco EM has completed her PhD in 2013 at the University of Calabria, where she has been involved in the characterization of estrogen signaling through GPER since 2009. She has published more than 25 papers in reputed journals and she has joined the University of Manchester in 2015, where her research is currently supported by an EU and AIRC (Associazione Italiana per la Ricerca sul Cancro) co-funded fellowship.

ernestinamarianna@yahoo.it

Notes: