Significance of estrogen receptor alpha isoforms in breast cancer

Anna Nagel, Laboratory of Cell Biology, Department of Medical Biotechnology, Intercollegiate Faculty of Biotechnology UG and MUG

Supervisor: dr. hab. Anna Żaczek, dr Aleksandra Markiewicz

Breast cancer is still one of the most common invasive cancers among European women[1], one in eight women has a chance of developing breast cancer over an eighty-year lifespan.

Breast cancer is classified by stage, histological type and molecular subtype. The most common molecular subtypes are Luminal A and B, which carry steroid hormone receptor for estrogen (ER) and/or progesterone (PR). Estrogen Receptor alpha is a 66kDa (ERα66) ligand activated transcription factor involved in cell proliferation. It is also one of the most valuable prognostic and predictive markers in breast cancer. The relationship between ER and cellular responsiveness to estrogens and antiestrogens has been extensively studied and makes ER an efficient target for treatment of hormone-dependent breast cancers. Receptor alpha is encoded by *ESR1* gene. Previously our team investigated its amplification in order to assess the prognostic value of *ESR1* gene dosage. Results indicated that *ESR1* amplification may occur also in ER-negative patients and may confer a poor prognosis[2]. Because of this phenomenon we hypothesize, that high *ESR1* gene dosage may affect presence of other ER isoforms. Wang et. al. described new alternatively spliced variant of ERα – ERα36, which lacks both transcriptional activation domains of ERα66 but retains its DNA-binding domain[3].

The project is focused on assessing the importance of ERα36 presence in breast cancer patients. Furthermore, *in vitro* studies are planned in order to investigate the ERα36 influence on malignancy of cancer cells.

To assess the clinical significance of ERα36 expression in breast cancer patients, I have isolated RNA from 190 patients and analyzed the expression levels for both ER isoforms (ERα36 and ERα66) using qPCR. Additionally, ER gene expression was correlated with protein level assessed by immunohistochemistry. The data was correlated with patients clinic-pathological data, disease free survival (DFS) and overall survival (OS).

1. Stewart BW, Wild CP, editors (2014). World Cancer Report 2014. Lyon, France: International Agency for Research on Cancer.
2. Markiewicz A, Wełnicka-Jaśkiewicz M, et al. (2013) Prognostic Significance of ESR1 Amplification and ESR1 PvuII, CYP2C19*2, UGT2B15*2 Polymorphisms in Breast Cancer Patients. PLoS ONE 8(8): e72219.
3. Wang ZY, Zhang XT, et. al. (2006) A variant of estrogen receptor-α, hER-α36:Transduction of estrogen- and antiestrogen dependent membrane-initiated mitogenic signaling. PNAS 103 (24) 9063–9068