

## ORT\_06 - Identification and validation of genes candidates as targets for treatment and diagnosis of breast cancer

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**Introduction:** Breast cancer is one of the most common malignancies among women worldwide. The main limitations of the efficacy of currently used drugs for the treatment of cancer include systemic toxicity, drug resistance and debilitating side effects. Possible effective solutions to overcome these limitations are the use of (i) overexpressed membrane proteins as targets to address the delivery system of drugs encapsulated in second generation nanoparticles, and (ii) monoclonal antibodies or aptamers against specific targets on the membrane of tumor cells.

**Objective:** In this context, this project outlines a strategy for the optimal selection of membrane proteins in tumors focusing on the development of specific therapy and diagnosis for breast cancer.

**Methodology:** Our strategy involves the use of the TCGA data bank (The Cancer Genome Atlas) exploring transcriptome data from both tumor and non-tumor breast human tissues; and other healthy tissues. By this strategy, it was possible to identify membrane proteins with increased expression in tumor tissue as compared to healthy tissue.

**Results:** A list of four target proteins (patent pending) was proposed from this inference for 111 breast tumor patients that included the different molecular subtypes; Luminal A, Luminal B, HER2 + and Triple Negative. The validation process was performed using a cohort of 991 breast cancer patients and 111 non-tumor samples; and patients were separated into clusters according to their molecular subtype classification. The overexpression of these four proteins was validated remaining high in all molecular subtypes. Furthermore, immunofluorescence analysis also confirmed this data in breast tumor cell lines from the different molecular subtypes, such as MDA-MB-231 (Triple Negative), T47D (Luminal A), HCC1954 (HER2 +) in comparison with a non-tumor breast line MCF10A. In addition, the identified proteins demonstrated specificity and sensitivity, around 80%, according to data from the area under the curve (AUC) of the ROC curve. To understand which intracellular pathways could be involved with these proteins, analysis from the human interactome data was performed by automated counting the possible connections between pairs of neighbors' proteins. We observed that the proteins downstream the intracellular signaling pathway present important roles in many processes of tumor progression.

**Conclusion:** Consequently, we expect that these proteins could be considered as suitable targets for therapy with a lower rate of undesirable side effects and greater therapeutic efficacy.

**Keywords:** breast cancer; tumor biomarker; personalized treatment