ORT_05 - Identification of novel breast cancer cell-surface targets by gene expression profiling and tissue microarray

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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 breast cancer include systemic toxicity, drug resistance, and debilitating side effects. Thus, new targets for alternative therapeutic strategies are urgently required, as well as the improvement of tumor tracking.

Objective: In this context, this study 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 TCGA (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 transcripts that encode membrane proteins with increased expression in tumor tissue as compared to healthy tissue.

Results: Here, we identified four targets, which present increased transcripts levels (patent pending) from this inference using data from 111 breast tumor patients paired with their own healthy tissue (discovery set). This strategy was further validated by an amplified TCGA breast cancer cohort (n=991) and by a genetic chip-based database including 7569 breast tumors, 242 normal and 82 metastasis samples. The overexpression of these four transcripts was validated remaining high in all molecular subtypes and we also observed high expression in metastatic samples. Beyond that, immunofluorescence analysis also confirmed this data in breast tumor cell lines from the different molecular subtypes, such as MDA-MB-231, T47D, HCC1954 in comparison with a non-tumor breast line MCF10A. In addition, these selected transcripts demonstrate high accuracy, specificity and sensitivity according to data from the area under the curve (AUC) of the ROC curve. Then, we performed an immunohistochemistry assay in a tissue microarray (TMA) including clinical and pathological data, and observed increased protein expression of the four targets in tumor tissue compared to non-tumor breast tissue.

Conclusion: Consequently, we expect that these proteins could be considered as suitable targets for individual therapies with a lower rate of undesirable side effects.

Keywords: Breast Cancer; Diagnosis; Target Therapy