Identification of a novel peptide with high affinity towards breast cancer cells

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Triple negative breast cancer (TNBC) is the most aggressive subtype of invasive breast cancer with a poor prognosis compared to other subtypes [1]. It lacks the expression of common cancer receptors remaining as the main barrier for sensitive diagnostic and therapeutic tools. Therefore, peptide ligands that specifically recognize cell surface receptors have been extensively used in cancer research. Phage display emerged as a powerful tool to identify/recognize specific ligands and has been proved useful in biomarker discovery (i.e. membrane protein) [2].

In this study, a random peptide phage library was used to screen for ligands with selective affinity towards specific receptors on the surface of a TNBC mouse mammary carcinoma cell line – mouse breast cancer 4T1 cell line. Five rounds of panning were performed, along with a counter-selection round against a negative control (mouse fibroblast 3T3 cell line), to eliminate non-specific peptides and maximize binding efficiency.

After five rounds of panning, there was a remarkable enrichment in the titer of bound phages. Enriched selected peptides were tested regarding their affinity/selectivity by ELISA using 4T1 cells as target. The ones with higher affinity were characterized by immunohistochemistry using 4T1 tissue samples and by flow cytometry. In this work, we describe a specific ligand with high affinity towards breast cancer cells. Bioinformatic analysis confirmed that the sequence represents a new peptide, as no previous hits were identified, as well as any similarity to target unrelated sequences. Multiple sequence alignment and molecular docking were performed to search for cancer related receptors and interesting targets were identified.

To our knowledge, no ligands that target this specific cell line have been identified so far, therefore the results herein gathered suggest that the identified peptide can be incorporated into a variety of new diagnostic and targeted therapeutic systems for early diagnosis and treatment of breast cancer.

[1] T. F. S. Mendes, L. D. Kluskens, and L. R. Rodrigues, "Triple Negative Breast Cancer: Nanosolutions for a Big Challenge," Advanced Science, 2015, 1-14.
[2] U. B. Rasmussen, V. Schreiber, H. Schultz, F. Mischler, and K. Schughart, "Tumor cell-targeting by phage-displayed peptides.," Cancer Gene Therapy, 9(7), 2002, 606–612.