Session 4

Selection of Novel Peptides Homing Alternative Targets in Triple Negative Breast Cancer

Débora Ferreira, Vera Silva, Franklin Nobrega, Ivone Martins, Leon Kluskens and Lígia Rodrigues (CEB-Uminho)

Breast cancer is the most frequent cancer amongst women, representing 25% of all cancer cases, with an estimated 1.67 million new cases in 2012 1. Phenotypically characterized by the lack of known receptors, the triple negative breast cancer (TNBC) subtype is responsible for 10 to 20% of all diagnosed breast cancers 2. Due to its unique profile, aggressive behavior and different patterns of metastasis, the search for effective diagnosis and treatment tools has intensified 3. However, the lack of specific cell targeting remains the main barrier for sensitive diagnostic tools. Therefore, peptide ligands that specifically recognize cell-surface receptors have been extensively used in cancer research. Evolutionary screening techniques as phage display 4 emerged as a powerful tool to recognize specific peptides and has been proved useful for the discovery of new biomarkers 5. To accomplish this purpose, we report the selection of two novel peptides by phage display, using two different libraries, homing the mammary adenocarcinoma murine 4T1 cell line (4T1pep1 –CPTASNTSC and 4T1pep2—EVQSSKFPAHVS) 6. This cell line has been shown to be an accurate model system as it closely resembles human TNBC. The high-affinity identified peptides were screened on the MimoDB database 7 and scanned with SAROTUP webserver 8 to detect homology with previously described cancer-specific peptides and to eliminate the existence of target unrelated peptides and false-positives. Therefore, the peptide sequences were further analyzed by the BLAST algorithm for homology to proteins with known or putative breast cancer correlations against the Homo sapiens and Mus musculus non-redundant protein databases. Bioinformatics analysis suggested that both peptides target human Mucin-16, a well characterized biomarker

and its deregulation has been previously implicated in different types of cancer, showing overexpression in breast, prostate, lung and pancreas cancer 9. Docking experiments using CABS-dock webserver 10 were also performed to prove the role of Mucin-16 as a targeting receptor using these novel peptides. Our results strongly support the need of alternative targeting systems for TNBC and the peptides herein selected by phage display are very promising towards breast cancer therapy.

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