P-194 - IN SILICO SELECTION OF AN SSDNA APTAMER AGAINST HER2-POSITIVE BREAST CANCER CELLS USING COMPUTATIONAL DOCKING SIMULATION

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Background

Human epidermal growth factor receptor type 2 (HER2/ErbB2) is a breast cancer associated protein overexpressed in 20% of breast cancers, being involved in cell growth regulation, survival and differentiation.[1,2] The location of HER2 on the cell surface has contributed to its appeal as a tumour-targeted therapy.[3] Aptamers, generated from Systematic Evolution of Ligands by EXponential Enrichment (SELEX), emerged as potential tool for application in target cancer therapy due to their three-dimensional structures that recognize cell surface receptors.[4]

Method

In this study, HER2-aptamers were screened and identified using SELEX technology. After cloning and sequencing, aptamers were modelled through m-fold software and posteriorly, the docking simulation was predicted using ZDOCK server.[5,6] These *in silico* predictions measured the aptamer-HER2 interactions through a combination of shape complementarity and statistical potential terms for scoring.

Results & Conclusions

Based on *the interaction score*, a candidate ssDNA-aptamer (HER2-31; 5´-CACGTGCAGGGTGGATAGCAATCTATCCGGTCCCACTGTTCGGTGGTCGC -3') was selected. Targeted-specificity of the selected HER2-31 was validated through cytometry and fluorescence microscopy assays in HER2-positve breast cancer cells. Our results indicate that SELEX technology is an efficient method to screen specific protein-bound ssDNA, and HER2-31 could be used as an agent in HER2-based diagnosis and targeted therapy. Also, the results provide valuable guidelines for the application of docking simulations for the prediction of aptamer-ligand structures, as well as for the design of novel features of ligand-aptamer complexes.

References & Acknowledgments

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Keywords: aptamers, SELEX, breast cancer, HER 2