

BIO_10 - Development of a new theragnostic based on DNA aptamers against heparinase1 for the treatment of breast cancer

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Introduction: Aptamers (APt) against heparanase-1 (HPSE1) were produced by our group and had their antimetastatic property proven. HPSE1 is overexpressed in several types of breast cancer favoring tumor progression. The efficacy of these aptamers in cancer control could be improved by its combination with other treatments capable of controlling tumor growth. Once acting on tumors that overexpress the HPSE1 protein, these combinations could also be used as diagnostic strategies for these types of tumors.

Objective: To develop a new theragnostic molecule targeting the HPSE1 protein, we propose an innovative molecule combining the antimetastatic property of APt with the cytostatic action of a chemotherapeutic agent, coupled in a nanoparticle to improve the pharmacokinetics of the complex.

Methodology: Pemetrexed (PMX) molecules were conjugated to APt by peptide bond and then bound to liposomes (LPs) by electrostatic reaction or in AuNPs by S-S (covalent) bond. The new molecules were characterized by their hydrodynamic size and ζ -Potential in solution. The rapid test was employed to qualitatively measure the affinity of the constructs for the HPSE1 protein and to provide a proof of concept for diagnostic tests.

Results: DLS analysis showed an increase in the hydrodynamic size of the APt+LPs conjugate (144.7 nm) compared to the LPs (112.3 nm). The APt+LPs+PMX conjugate showed an increase in its diameter (250 nm) when compared to the LPs or APt+LPs. Furthermore, LPs has a positive ζ -potential (+60.38 mV), which is altered by the addition of APt (-32.73 mV). When conjugating the APt to the LPs and to PMX, the zeta potential remained negative (-28.04 mV). The APt+AuNPs conjugate showed an increase in hydrodynamic diameter (65.95 nm) when compared to AuNPs (29.38 nm) in addition to being more negative (-38.38 mV) when compared to AuNPs (- 17.51 mV). The APt+AuNPs and APt+AuNPs+PMX conjugates maintained their ability to recognize HPSE1.

Conclusion: We demonstrated that all the conjugations were effective and the APt+AuNPs with or without PMX maintained their affinity for the HPSE1 enzyme. We thus demonstrate that the new aptamer-based theragnostic was successfully developed in different configurations to be tested in functional assays.

Keywords: Aptamer; Breast cancer; Therapy and diagnosis