IN VIVO STUDY OF IRON OXIDE NANOPARTICLES DESIGNED FOR THERANOSTIC IN TRIPLE-NEGATIVE BREAST CANCER CONTEXT

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Breast cancer is the 1st common and lethal cancer worldwide for women, with more than 2.3 million new patients and approximately 700 000 deaths in 2020[1]. Breast cancer is a family of diseases, among them, triple-negative breast cancer (TNBC) presents the worst prognosis: aggressive subtype and hard to target (no hormone receptor)[2]. Our objective is to develop targeted multifunctional dendronized iron oxide nanoparticles (DNPs) designed for theranostic: MRI contrast agent to visualize tumors and magnetic hyperthermia to treat them. To target tumor cells, peptide 22 (P22) has been chosen for its specificity to EGFR, a receptor known to be overexpressed in many cancer cells, such as MDA-MB-231, a human TNBC cell line model[3]. This peptide is conjugated to dendrons surrounding the iron oxide core of nanoparticles

In previous work, we have proved the absence of toxicity of DNPs to cells with complementary cytotoxicity tests (LDH release assay and Alamar blue). In order to show the potential of P22, we have measured the amount of nanoparticles internalized by cells after 24h of incubation in presence and absence of P22 at the DNPs surface[4]. Presence of P22 increases the amount of iron measured in cells from 0.82 to 2.15 pg_{iron}/cell, allowing us to consider P22 as a good candidate to target MDA-MB-231 cell line.

After this *in vitro* chapter, we injected DNPs to normal mouse strain in order to evaluate the *in vivo* toxicity and also the uptake of nanoparticles in this healthy model. It appears that DNPs accumulate in reticuloendothelial system tissues (ie liver and bone marrow), leading to a negative contrast in T_2 weighted MRI. DNPs effect on MR signal can be seen in these organs one month after the injection, no sign of toxicity or side effects being observed. At last, we grafted MDA-MB-231 cells on SCID mice in order to evaluate the targeting abilities of our platform. DNPs with or without P22 were intravenously injected to tumor-bearing mice. DNPs accumulation in tumoral region was evaluated using T_2^*-weighted MRI technique. Those experiments did not allow us to find a difference between DNPs and DNPs+P22 in terms in of tumor uptake.

References

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