SuperParamagnetic Iron Oxide Nanoparticles: a multifunctional tool in biomedical applications

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INTRODUCTION: We have previously developed SuperParamagnetic Iron Oxide Nanoparticles (SPIONs) with a core size of 9-10 nm diameter and a coating made of polyvinyl alcohols (PVA) [1]. Our objectives are to evaluate their biocompatibility, their potential for uptake by cells and their cellular localization in various types of cells in culture and in organs in animal models.

METHODS: To evaluate cell uptake we used either 2-dimensional and 3-dimensional cell culture models, tumor cell spheroids and brain cell aggregates. In animal models, SPIONs were injected i.v. in normal mice, and organs were examined for their SPIONs content. In order to evaluate the cell and tissue uptake of these SPIONs we combined detection of their fluorescent coating, of the iron oxide core using confocal microscopy, prussian blue detection of iron and transmission electron microscopy. In order to determine their biocompatibility we evaluated cell survival by evaluating mitochondrial activity and DNA synthesis.

RESULTS & DISCUSSION: We showed that in 2-dimensional cell cultures the presence of amino groups on the SPIONs coating was mandatory for cell uptake, and this uptake did not modify cell proliferation. SPIONs uptake by cells was increased in the presence of an external magnetic field. The results demonstrated that the polymer coating and the iron oxide core of SPIONs can be internalized by cells *in vitro* (Fig. 1). In various tridimensional cell culture models SPIONs were found associated with cells, being able to invade tumor spheroids but not differentiated brain aggregates [2]. *In vivo* SPIONs were found associated with cells in the spleen and the liver but not the brain and kidneys.

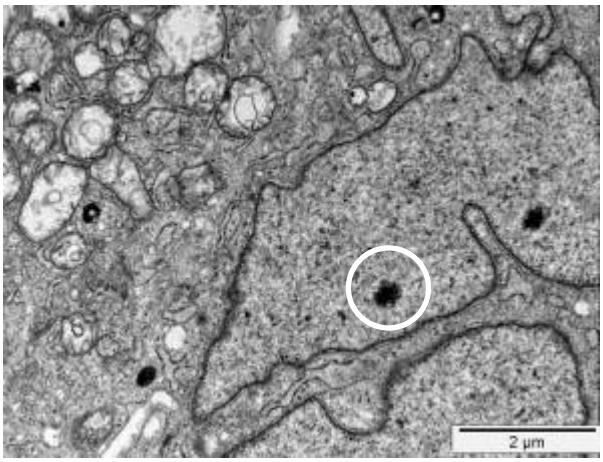

Fig. 1: Transmission electron microscopy showing aminoPVA-coated-SPIONs uptake in the nucleus of human melanoma cells, after 4h of exposure.

CONCLUSIONS: These approaches gave a proof of concept of the feasibility of using such SPIONs in biological systems, and their potential to be selectively taken up by living cells.

REFERENCES: [1] A. Petri-Fink, M. Chastellain, L. Juillerat-Jeanneret, et al (2005) *Biomaterials* **26**:2685-2694. [2] F. Cengelli, D. Maysinger, F. Tschudi-Monnet, et al (2006) *JPET* **318**:108-116.

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