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Developing superparamagnetic iron oxide nanoparticles (SPIONs) as cancer nanomedicines

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Background

SPIONs, owing to their inducible magnetic properties (superparamagnetism), provide a versatile platform for diagnostic and therapeutic applications. Currently, SPIONs are used as MRI contrast agents but their ability to generate heat when placed in an external magnetic field has potential to provide an exciting hyperthermia treatment for cancer. MRI-contrast SPIONs are rapidly cleared from the circulation by the reticuloendothelial system (RES), a challenge to be addressed before achieving cancer targeting.

Method

Ferucarbotran (Meito Sangyo Co. LTD., Japan) (Resovist®), a clinically approved MRI contrast SPION with excellent heating potential was studied. The uptake of Ferucarbotran was investigated in different cell types; macrophages (RAW 264.7), tumour cell lines and neural stem cells. Ferrozine assay was used to measure intracellular iron uptake. Confocal and transmission electron microscopy were used to assess internalisation. In vivo uptake was tested in BALB/C mice using a readily traceable Nanomag®-D-Spio-NH2 (Micromod Partikeltechnologie GmbH, Germany) labelled with DyLight® 800 NHS-ester (Thermo Scientific, Pierce Biotechnology, Rockford, USA) a near infrared dye. A range of sulfated and unsulfated dextrans were evaluated as blocking agents.

Results

Ferucarbotran was taken up in a dose dependent manner by all the tested cell lines. Internalisation was confirmed using confocal and transmission electron microscopy. A range of sulfated dextrans were shown to block this uptake in vitro. Macrophages pretreated with blockers had up to 16 times less iron uptake compared to unblocked controls ($p=0.00007$). In vivo, the blood concentrations of Nanomag®-D-Spio-NH2-Dylight® 800 significantly improved by 37 times ($p=0.0026$) in mice pre-treated with one of the blockers, indicating the possibility of blocking uptake by liver Kupffer cells.

Conclusion

The results show that it is feasible to significantly reduce unwanted SPIONs uptake in vitro and in vivo. The work forms a platform to develop cancer specific SPIONs by functionalisation with cancer-targeting ligands.

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