Poster

CHARACTERIZATION OF DEXTRAN COATED NANOPARTICLES UPTAKE BY GLIOBLASTOMA CELLS

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Dextran coated iron oxide nanoparticles have been used as an experimental magnetic label for magnetic resonance imaging (Moore et al, 2000).

Dextran-coated iron oxide nanoparticles provide enhanced detection of intracranial tumours by magnetic resonance (MR), for more than 24 hours and can be imaged histologically by iron staining (Neuwelt et al, 2004). When linked with tumor targeting ligands such as monoclonal antibodies, peptides or small molecules, these nanoparticles can be used to target tumor antigens with high specificity (Petri-Fink et al., 2005).

The aim of this study was to determine the magnitude of dextran coated nanoparticles uptake by glioblastoma cells (*in vitro*), in order to use them as contrast agents in posterior studies, with the purpose to be applied in tumoral diagnosis and treatments *in vivo*.

We report here the development and validation of an efficient protocol to label human glioblastoma cells with two different sizes dextran coated magnetic nanoparticles. We optimized both the nanoparticle concentration and the incubation time of the cells, achieving effective labeling of the glioblastoma cells *in vitro*, without impairment of their biological properties, proliferation or cell survival. We measured apoptotic activity in nanoparticles treated cells and studied the persistence of the labeling over time. These data have allowed us to define labeling protocols based on optimized doses and incubation times that do not affect short-term cell survival and proliferation. Uptake into tumor cells was confirmed by immunocytochemistry and confocal microscopy.

To test the detectability in MRI, increasing concentrations of nanoparticles were injected intracerebrally by stereotactic injection into the striatum of control rats. The results show that MRI can efficiently detect low nanoparticles concentration, and that the intensity of the signal is proportional to the number of injected nanoparticles. These studies demonstrate the efficacy of iron-based MRI contrast agents in the brain and provide imaging parameters and time course data for future studies in brain tumors and neurological lesions.

Future research will lead to the development of bioconjugate nanoparticles probes for molecular and cellular imaging, targeting biofunctionalized nanoparticles to tumors, for early cancer detection and cancer therapy.

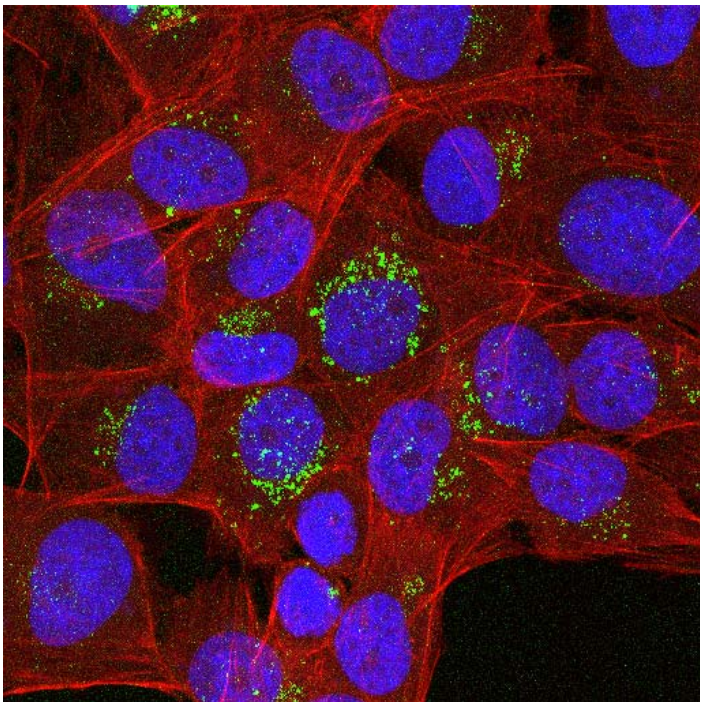
REFERENCES:

-Moore A, Marecos E, Bogdanov A Jr, Weissleder R.
Tumoral distribution of long-circulating dextran-coated iron oxide nanoparticles in a rodent model.
Radiology. 2000 Feb;214(2):568-74.

-Neuwelt EA, Várallyay P, Bagó AG, Muldoon LL, Nesbit G, Nixon R.
Imaging of iron oxide nanoparticles by MR and light microscopy in patients with malignant brain tumours.
Neuropathol Appl Neurobiol. 2004 Oct;30(5):456-71.

-Petri-Fink A, Chastellain M, Juillerat-Jeanneret L, Ferrari A, Hofmann H.
Development of functionalized superparamagnetic iron oxide nanoparticles for interaction with human cancer cells.
Biomaterials. 2005 May; 26 (15):2685-94.

Figures:



Dextran coated magnetic nanoparticles (green) in human glioblastoma cells (red with nucleus in blue).

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