GLOWBRAIN – AN IN VITRO AND IN VIVO PLATFORM FOR STUDYING THE REGENERATIVE POTENTIAL OF THE MURINE NEURAL STEM CELL APPLICATIONS IN REPAIR OF ISCHEMIC BRAIN INJURY

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Since the central nervous system shows very little capability for self-repair following ischemic injury, regenerative medicine approaches are increasingly interested in the use of neural stem cells (NSCs) for cell replacement strategies. Labelling NSCs with maghemite (γ-Fe2O3) nanoparticles allows direct in vivo tracking and imaging of NSCs during brain repair using medical imaging techniques such as magnetic resonance imaging. In addition, application of biomaterials, such as alginate, represents an interesting tool to carry out cell replacement therapies.

We reported in vitro NSCs viability and initial differentiation in alginate hydrogels. Furthermore, we investigated in vivo the potential of alginate hydrogels as support system for NSCs injection in the brain. Our preliminary in vivo results demonstrate the possibility to obtain injectable alginate hydrogels that crosslink once injected in the brain tissue. Inflammation profiles, obtained using TLR2-luc mouse reporter line after alginate injection, suggest that alginate presence is not harmful for the brain tissue. Taken together these findings show that alginate could be used as an efficient support for NSCs transplantation in the nervous system, able to increase cell survival and integration in an injury-affected brain.

Moreover, using GlowBrain platform we reported that coating γ-Fe2O3 nanoparticles with either poly(L-lysine) or D-mannose improves their biocompatibi-

lity with NSCs and their cell labeling efficiency in vitro when compared to both their uncoated γ-Fe2O3 counterparts and commercially available dextran-coated nanomag®-D-spio nanoparticles. Finally, we used poly(L-lysine)-γ-Fe2O3 and (D-mannose)-γ-Fe2O3 nanoparticles to label NSCs which were transplanted into mouse post-ischemic brain and tracked during brain repair using magnetic resonance. Both poly(L-lysine)-γ-Fe2O3 and (D-mannose)-γ-Fe2O3 could easily be visualized in ex vivo mouse post-ischemic brain, making them an attractive agent for future NSC in vivo tracking studies.

GlowBrain here presents a platform which allows in vitro and in vivo investigation of biocompatibility of biomaterials that can serve as support for NSCs, ultimately allowing their survival and differentiation in post-ischemic brain. Moreover, our platform can be used to assay in vitro the effects of labeling NSCs with differently coated γ-Fe2O3 nanoparticles, namely cell viability and proliferation, cellular uptake efficiency and labeling mechanism as well as potential to be visualized in vivo in mouse ischemic brain.

OPTIMIZATION OF CONDITIONS FOR IN VITRO THREE-DIMENSIONAL CARTILAGE GROWTH

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Articular cartilage is a poorly vascularized and innervated tissue that shows no capacity for effective spontaneous regeneration in cases of damage and injury, which represents a major health problem and unmet medical need. Common methods of the treatment and therapy have proved to be ineffective. Tissue engineering, as a new important field of regenerative medicine, emerges as potential effective alternative. Chondrogenesis, the process by which cartilage is formed, actually represents the consequence of several steps directed by signaling molecules, receptors, transcription factors, cells' interaction with ECM and other environmental factors. In this respect, the aim of our study was to optimize conditions for 3D in vitro chondrogenesis in order to produce functional cartilage implants that could be used in clinical practice to cure some specific cartilage defects.