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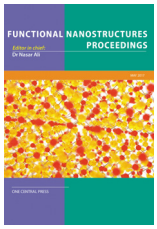

Neurosurgical grade biomaterial, DuraGen™, offers a promising matrix for protected delivery of nanoengineered neural stem cells in combinatorial clinical therapies

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ABSTRACT

Combinatorial regenerative approaches involving transplantation of genetically nano-engineered neural stem cells (NSC) encapsulated within a protective polymer matrix are a promising therapy for neurological injury. NSCs are important self-renewing precursors that can generate the major central nervous system (CNS) cell types-neurons, astrocytes and oligodendrocytes. When genetically engineered to express neuro-regenerative proteins such as brain derived neurotrophic factor, NSCs can simultaneously (a) replace lost cells at the site of injury and (b) release factors to augment the regenerative environment. We have tested, for the first time, the potential of an FDA-approved neurosurgical material -DuraGen™¬ (used widely in neurosurgical procedures as a dural replacement material) as a protective matrix to support the delivery of NSC transplant populations genetically engineered using magnetic nanoparticles (MNPs) in conjunction with advanced minicircle DNA vectors.

METHOD

Rodent NSCs magnetofected with MNPs and f=4 Hz oscillating magnetic fields were seeded into DuraGenTM sheets of optimised thickness. Characterisation of the construct using immuno-histochemical and 3D microscopy methods demonstrated no adverse effects on a range of parameters including: (i) NSC survival; (ii) expression of stem cell specific markers; (iii) NSC proliferative capacity and (iv) stem cell differentiation into daughter phenotypes.

RESULTS

GFP expression was detected in NSCs in the DuraGen™ matrix up to 8 days. High NSC viability was detected in the DuraGen™ matrix, with retention of proliferative capacity and stem cell marker expression. The matrix demonstrated the capacity to support the genesis of all three daughter phenotypes with prolonged astrocytic expression of GFP.

CONCLUSIONS

Our findings support the concept that a 'combinatorial therapy' consisting of NSCs engineered for the production of therapeutic biomolecules and protected within the DuraGen™ construct is a promising regenerative therapy for neurological pathology.