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

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Aims

Transplantation of neural stem cells (NSCs) into sites of neurological injury is being investigated in clinical trials around the world. These important self-renewing and multipotent precursors can generate the major central nervous system cell types – neurons, astrocytes and oligodendrocytes, and have a major role in 'restorative cell therapeutics'. However, high stem cell death in host tissue (>~90%) following surgical delivery procedures is a critical barrier to clinical translation. Polymer-based encapsulating biomaterials offer protective matrices to improve stem cell survival but the majority of studies use laboratory based formulations unsuitable for human use. We have tested the potential of an FDA-approved, commercially manufactured neurosurgical material (DuraGen™), used widely in neurosurgical procedures as a dural replacement material, as a matrix to support the delivery of NSC transplant populations.

Methods

NSCs derived from the subventricular zone of postnatal mice were directly seeded into DuraGen™ sheets of optimised thickness. A range of key parameters underpinning the regenerative capacity of the stem cells were assessed up to 16 days using immuno-histochemical and 3D microscopy methods. These include NSC survival, expression of stem cell specific markers, NSC self-renewal / proliferative capacity and stem cell differentiation into the three daughter phenotypes.

Results

High NSC viability (>~94%) was detected in the DuraGen™ matrix at all time points, with retention of stem cell marker expression. The matrix demonstrated the capacity to support growth of all three daughter phenotypes with cells generated in the expected proportions, indicating that stem cell fate is not altered by the material. Notably, there was clear evidence of ongoing cellular, maturation of neurons, astrocytes and oligodendrocytes (Fig 1) with evidence of simple neural network formation within the matrix.

Conclusion

Our findings support the concept that DuraGen™ is a highly promising biomaterial to support the protected delivery of NSC populations to sites of neurological pathology, with no adverse effects on the fate of the stem cell population. We consider our findings have important implications for the use of this material for delivery of a range of clinical transplant populations for human neural cell therapy. Our findings also raise the possibility that surgical delivery of pre-formed neural circuits may be feasible to replace multiple cell populations in injury foci. ■

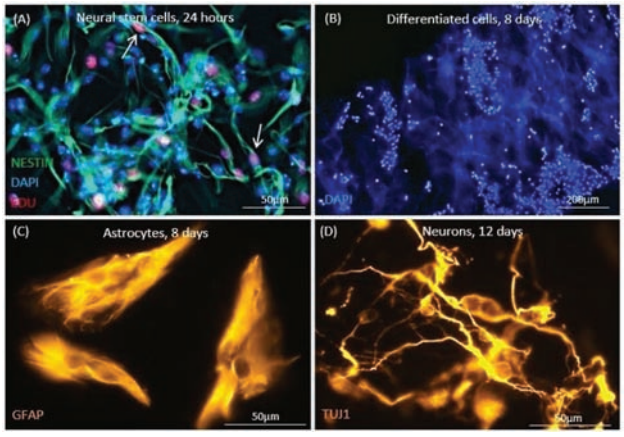

Fig 1. DuraGen™ promotes growth, proliferation and differentiation in neural stem cells and maturation of daughter cell types. A. Proliferating neural stem cells (arrows) reveal the proliferation-permissive profile of the DuraGen™ matrix. B. Clusters of cells derived from neural stem cells in the visible fibrous DuraGen™ matrix. C. Supportive astrocytes growing in the porous DuraGen™ matrix. D. Complex neuronal processes growing in the 3D DuraGen™ matrix.

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Conflict of interest statement

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