Alginate Hydrogels to encapsulate hiPSC-derived neurons for Parkinson's Disease

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Background: Over the past decade cell therapy for CNS injury and disease has looked extremely promising. However, both pre-clinical and clinical evidence shows high rates of cell death after implantation and one cause of this is the host cellular response. The overall aim of this programme of work is to develop an advanced therapeutic for PD which overcomes the challenges of cell survival, focusing on protecting the cells from detrimental host glial cell and immune responses.

Methods: GMP-ready human induced pluripotent stem cells (hiPSCs; UK Cell and Gene Therapy Catapult) were expanded and maintained in Essential 8 media, then differentiated into midbrain neurons characterised by immunocytochemistry (Kirkeby, Nelander, & Parmar, 2013). SH-SY5Y cells (Sigma) were maintained in 1:1 Hams F12:EMEM. 2% Alginate solution was made using 2g Alginate sodium salt in media specific to cell type. Hydrogels were created using 2% alginate solution with 50,000 cells/100µl loaded into 24 well Thincerts with a 102mM calcium chloride solution in the well, incubated for 15 minutes the hydrogels were then removed and placed in respective media to cells. Viability was assessed using fluorescence microscopy to detect SYTO-21 and Propidium Iodide. Host cell responses to encapsulated and unencapsulated donor cells were modelled in vitro using 3D reactive gliosis culture models, expression of MHC-I and II in hiPSCs was quantified at different stages of differentiation, and the ability of encapsulation to protect cells against inflammatory and hypoxic insults was tested.

Results: hiPSCs were successfully expanded and differentiated to a neural phenotype. A new protocol for encapsulating cells in an alginate hydrogel was developed and optimised using SH-SY5Y cells. Alginate gels were then used to encapsulate hiPSC-derived neurons and the ability of encapsulation protect cells post transplantation was tested in vitro.

Conclusion: A new alginate encapsulation technique using 24-well Thincerts was developed. Encapsulation of hiPSC-derived neurons using alginate has the potential to protect therapeutic cells from detrimental host cell responses. Future work will further investigate the ability of biomaterial encapsulation to improve the long-term survival of these cells.