An alginate-based encapsulation system for the delivery of therapeutic cells to the CNS

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INTRODUCTION: Cell therapy has emerged as a promising strategy for reducing brain dysfunction and modifying neurodegenerative disease progression. However, both pre-clinical and clinical evidence shows high rates of cell death after implantation, possibly due to the host immune response[1]. One of the most commonly employed immunoisolation technologies is encapsulation of cells in spherical microbeads made of polymers for local delivery[2]. Here we have developed a novel approach aimed at protecting therapeutic cells for long periods after implantation into the CNS.

METHODS: PC12 cells were used as a model cell line and encapsulated in hydrogel matrices. Alginate concentrations of 1.5% w/v and 2% w/v were tested, as well as composite formulations based on alginate and other natural polymers. The most suitable biomaterial was selected to form the core of microbeads for subsequent experiments. Finally, possible alginate microbead modifications were examined that could regulate cell survival, maintain phenotypic characteristics, and reduce adverse host cell responses. Physicochemical characterization was performed via stability testing, dynamic mechanical analysis, diffusion studies, and rheometry. Upon encapsulation, cell viability and metabolic activity were determined via live/dead staining and CellTiter-Glo® 3D assay. In vitro assays were used to replicate host cell responses to encapsulated cells and determine the efficiency of microbeads to act as a barrier.

RESULTS: New microbeads (mean size 2.33–1.29±0.1 mm) with dual functionality as smart delivery systems were developed and optimized. Hydrogel composition was found to influence degradation (stable up to 28 days), elastic modulus E' and nutrient diffusion. In addition, the physical properties of microbeads could be manipulated to comply with those of the native brain tissue, improving their biomechanical integration. Encapsulation of PC12 cells sustained their viability up to 69.2–75.9±2.4%. after 24 hours.

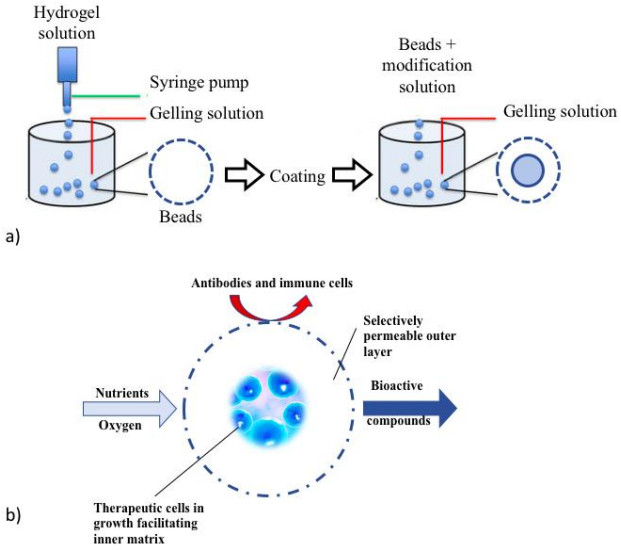

Fig. 1: Schematic representation of a) the methodology to generate capsules and b) the novel complex encapsulating system concept.

DISCUSSION & CONCLUSIONS: Encapsulation in alginate-based formulations designed for implantation into the brain has the potential to facilitate therapeutic cell survival and reduce detrimental host cell responses. Future work will further investigate the ability of selected material to improve the long-term viability of therapeutic cells.

REFERENCES:

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