DEVELOPMENTS OF IMPLANTS FOR THE TRAPPING OF GLIOBLASTOMA CELLS

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INTRODUCTION AND AIM

Glioblastoma (GBM) is the most common form of brain cancer. The diffusive nature of GBM tumours makes them impossible to be removed completely by surgery. As a result, the residual GBM cells contribute to ≥90% rate of tumour recurrence. This project aims to develop implants that gradually release chemoattractant molecules and support cell infiltration to induce chemotaxis and trapping of the residual GBM cells, which will subsequently enable their selective killing[1].

MATERIALS AND METHODS

Stromal cell-derived factor-1α (SDF-1α) chemoattractant was initially encapsulated into biodegradable nanoparticles with protein stabilizing excipients such as poloxamer 188 (Kolliphor®) using a phase separation process. The SDF-1α-loaded nanoparticles were then embedded within a chitosan scaffold by electrospinning to obtain nano-structured implants that mimic the brain extracellular matrix (ECM) structure to encourage GBM cell infiltration.

RESULTS AND DISCUSSION

Spherical SDF-1α-loaded nanoparticles of 253 ± 5 nm in size with a narrow size distribution and high encapsulation efficiency (76%) were successfully synthesized. With the inclusion of protein stabilizing excipients, there was no significant difference between the bioactivity of encapsulated SDF-1α and its native counterpart[2]. The nanoparticles were also conveniently co-electrospun with chitosan to produce nanoparticle-nanofibre composite scaffolds.

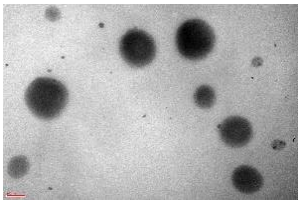

Fig. 1. Transmission electron microscopy of SDF-1α-loaded nanoparticles. Scale bar: 100 nm.

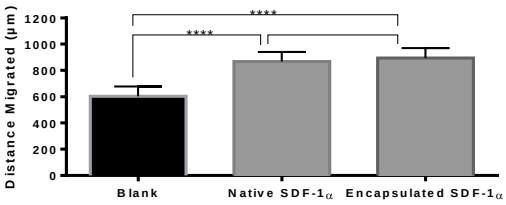

Fig. 2. GBM cell migration assay showing similar bioactivity of native and encapsulated SDF-1α.

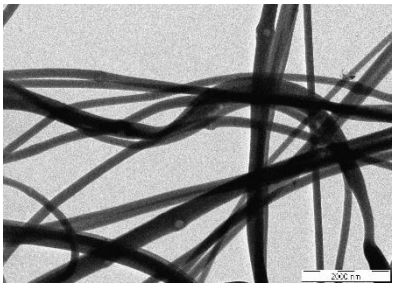

Fig. 3. Transmission electron microscopy of chitosan nanofibres containing SDF-1α-loaded nanoparticles.

CONCLUSIONS

A non-denaturing nanoparticle formulation process was developed to encapsulate SDF-1α. The SDF-1α-loaded nanoparticles were incorporated into chitosan scaffolds to achieve sustained delivery of SDF-1α into the brain that may induce chemotaxis of GBM cells for their trapping. In future work, focus will shift towards coating the nanoparticle-containing nanofibres with ECM molecules (such as hyaluronic acid) to maximize cell-scaffold interactions and subsequently promote GBM cell infiltration into the scaffolds.

REFERENCES

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2. Haji Mansor et al. *Eur. J. Pharm. Biopharm.* **2018**, 125, 38-50

KEYWORDS

Drug delivery, SDF-1α, Poloxamer 188, Sustained release, Nanoparticle formulation, Chemotaxis, Glioblastoma