Bioimplants for the trapping of glioblastoma cells

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Abstract

Glioblastoma (GB) is the most common and lethal form of brain cancer. The diffusive nature of GB tumours makes them impossible to be removed completely by surgery. As a result, the residual GB cells contribute to ≥90% rate of tumour recurrence. An implant that gradually releases chemoattractant molecules called stromal cell-derived factor-1α (SDF-1α), which binds selectively to the CXCR4 receptors of GB cells, is useful for inducing chemotaxis and trapping of the residual GB cells (Figure 1A) that will subsequently enable their selective killing and reduce recurrence rate. In this work, SDF-1α was initially encapsulated into biodegradable poly-lactic-co-glycolic acid (PLGA)-based particles. 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 GB cell infiltration. Latest results showed that SDF-1α molecules can be loaded into spherical PLGA-based nanoparticles (Figure 1B) with high encapsulation efficiency (76%). The SDF-1α-loaded nanoparticles were also conveniently co-electrospun with chitosan to produce nanoparticle-nanofiber composite scaffolds (Figure 1C). Release studies revealed that the composite scaffolds permitted a gradual release of SDF-1α up to day 35, in contrast to the short-term burst release achieved with nanoparticles alone. The sustained SDF-1α release will be useful for establishing local SDF-1α concentration gradient, which is critical for inducing chemotaxis of GB cells and their trapping. The scaffolds also exhibited excellent cytocompatibility. More importantly, we observed extensive adhesion of human GB cells to the scaffold surface. This, coupled with their slow degradation rates, suggests that the composite scaffolds possess good cancer cell trapping ability. In future work, focus will shift towards validating the *in vitro* efficacy of the implants in trapping CXCR4-expressing GB cells and developing a GB tumour resection cavity model for *in vivo* analysis.

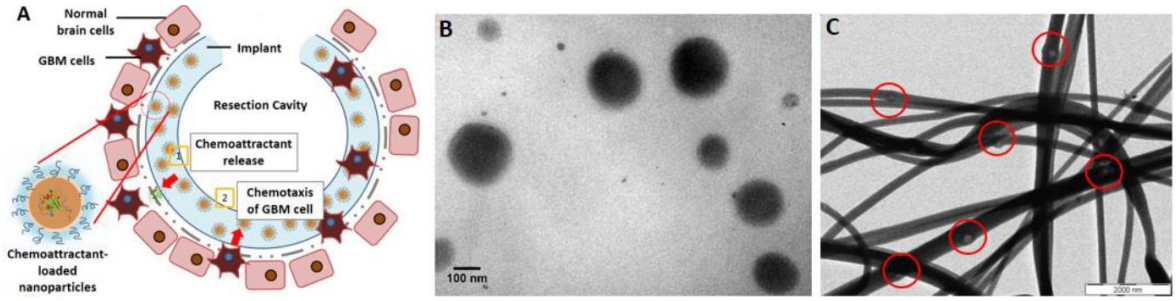

Figure 1. (A) Design of an implant for trapping of GB cells. (B) TEM image of SDF-1α-loaded nanoparticles. (C) SEM image of SDF-1α-loaded nanoparticles (in red circles) within chitosan nanofibres.

Related references :

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