뇌신경재활

발표일시 및 장소 : 10 월 19 일(토) 14:50-15:00 Room B(5F)

OP2-4-6

Toxicity and neuroprotection by magnetic-guided targeted delivery of erythropoietin and nanoparticle

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Objective

To overcome limitations of very short therapeutic time window and phylogenetic hematopoietic/non-hematopoietic receptor heterogeneity of erythropoietin (EPO), authors demonstrated the targeted delivery of biodegradable polymers-encapsulated EPO and magnetic nanoparticles (MNPs) under magnetic guidance.

Material and methods

MNPs consisting of ferric-ferrous mixture ($FeCl_3 6H_2O$ and $FeCl_2 4H_2O$) were prepared using a co-precipitation method, followed by sonification. The drug delivery system (DDS) was manufactured via the spray-drying technique using a nanospray-dryer. The DDS comprised 7.5 mg/ml sodium alginate, 150 mg/ml MNPs, and 1000 IU EPO.

Results

Scanning electron microscopy (SEM) revealed DDS particles as small as no more than 500 nm. Tiny micro-particles on the rough surfaces of the DDS particles composed of MNPs and EPO, unlike the smooth surfaces of the only alginate particles (Figure 1). Fourier-transform infrared (FTIR) spectroscopy revealed DDS peaks characteristic of MNPs as well as of alginate. Meanwhile, the concentration of EPO (0.000084 mg/mL) was lower than the MNPs (1.5 mg/mL) so that FTIR spectroscopy was not expected to reveal peaks specific to EPO on the surface. Standard soft lithography was applied to DDS particles prepared with fluorescent beads using a microchannel fabricated to have one inlet and two outlets in a Y-shape. The fluorescent DDS particles reached only one outlet reservoir in the presence of a neodymium magnet (Figure 2). The neuronal and systemic toxicities were evaluated, by treating SH-SY5Y and NIH-3T3 cells, respectively, in 48-well plates (1 X 105 cells/well) with alginate, MNPs, and/or EPO. A cell viability colorimetry was used to identify a 94% viability in SH-SY5Y cells and a 88% viability in NIH-3T3 cells, compared with the control ($p < 0.01$). For neuro-protection by DDS, SH-SY5Y cell viability, in 48-well plates (1 X 105 cells/well), was assessed after chemical injury using Thapsigargin (non-competitive inhibitor of the sarco-/endo-plasmic reticulum Ca^{2}+ ATPase). A cell viability colorimetry showed more flourishing (125%) than just survival, compared with the control (100 %).

Conclusions

The DDS-EPO construct developed here is very evenly encapsulated by alginate and is small enough to be administered into systemic circulation through the lung capillary after intravenous injection. It can be guided using external magnetic control. In point of in-vitro view, it can display neuro-regeneration as well as neuro-protection, showing no significant neuronal/non-neuronal cell toxicity.

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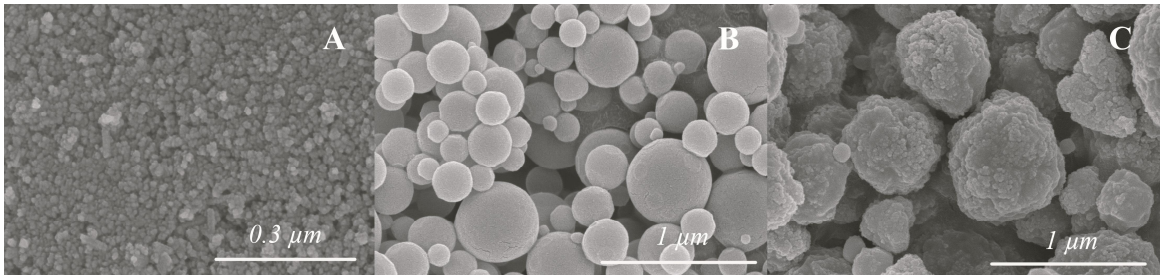

Figure 1. Scanning electron microscopy; SEM images showing (A) the synthesized MNPs, (B) the spray-dried alginate, and (C) the DDS composed of MNPs, alginate, and EPO. The MNPs and EPO were well mixed with alginate, and both components formed a rough surface on the DDS particles.

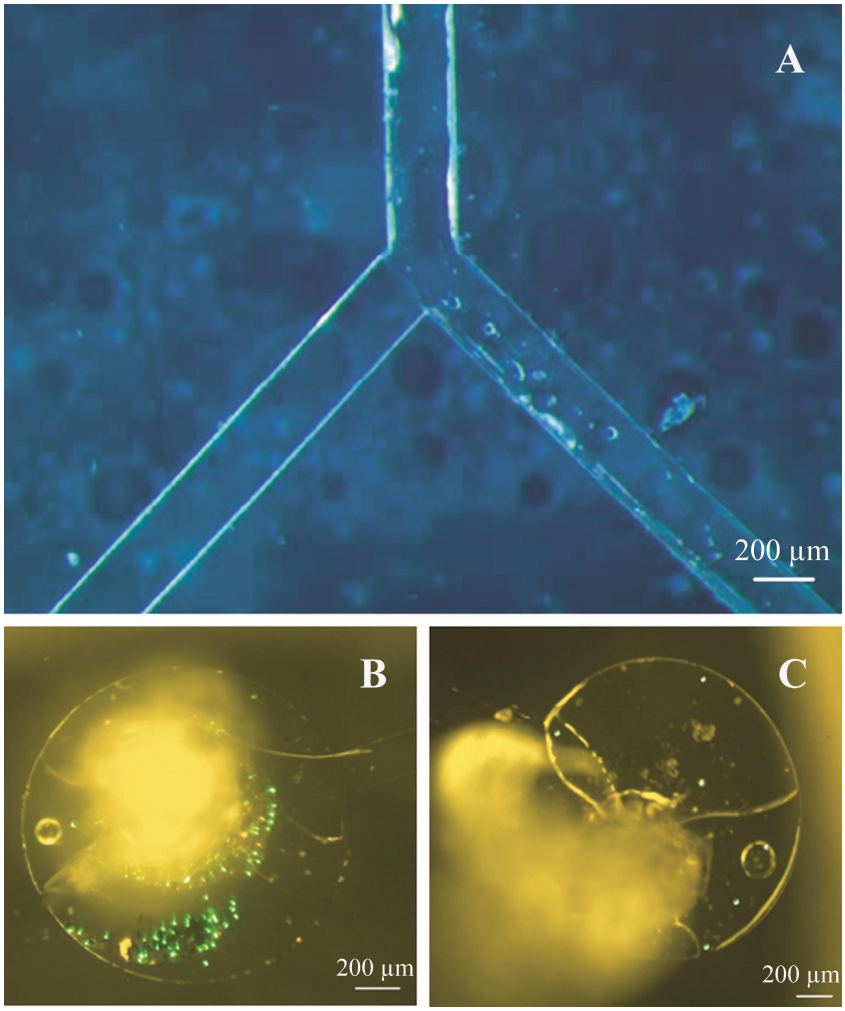

Figure 2. Magnetic guidance of the drug delivery system; DDS guidance experiment results. (A) Bifurcated polydimethylsiloxane microchannel. The magnet was positioned in the left area of the microchannel but is

not shown. (B) Magnetically guided fluorescent DDS particles. (C) No DDS was harvested in the absence of guidance.

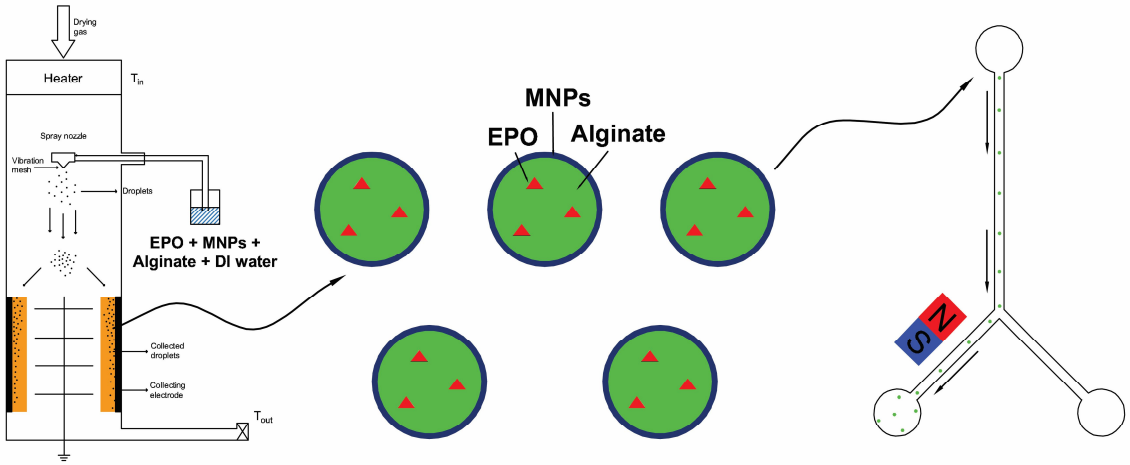

Figure 3. Schematic diagram of the magnetically guided targeted delivery of alginate-encapsulated erythropoietin and nanoparticles following dry-spraying.