

The promise of biomaterial delivery vehicles for improving stem cell retention in the infarcted heart

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Introduction and Hypothesis: Cell delivery to the infarcted heart has emerged as a promising therapy, but is limited by very low acute retention and engraftment of cells. The hypothesis was that acute retention can be improved with a biomaterial carrier, and the study compared several biomaterials.

Methods: Cells were quantified 24 hours post-implantation in a rat myocardial infarct model (Fig. 1a) in five groups (n=8 per group); saline injection (current clinical standard), two injectable gels (alginate, chitosan) and two epicardial patches (alginate, collagen). For injectable groups 60 μ l of saline or gel containing 400,000 human mesenchymal stem cells was injected intramyocardially in the infarct border zone. 400,000 cells were seeded on alginate or collagen patches, and implanted on the epicardial surface at infarct border zone. At 24 hours, retained cells were quantified with an *in vivo* imaging system. Hearts were also perfused and sectioned to stain for retained cells.

Results: All biomaterials significantly improved retention compared to a saline control, with 8 and 14-fold increases for alginate and chitosan injectables, and 47 and 59-fold increases achieved with collagen and alginate patches, respectively (Fig. 1b-c). Immunohistochemical analysis qualitatively confirmed these findings (Fig. 1d). Maintenance of cells in the first 24 hours was similar in all biomaterials and superior to control (Fig 1e). Encapsulated/seeded cell survival was assessed in hypoxia/ischemia to further compare biomaterials.

Conclusion: Injectable gels and epicardial patches were demonstrated to improve acute retention of cells when compared to a saline control. Biomaterials can influence localization of cells in myocardium. Biomaterials improve maintenance of cells in myocardium in first 24 hours. Injectable gels enable immediate myocardial delivery while epicardial patches facilitate superior retention and could potentially sustain cell delivery over extended periods. These biomaterial approaches should be considered for future cardiac cell therapy applications.

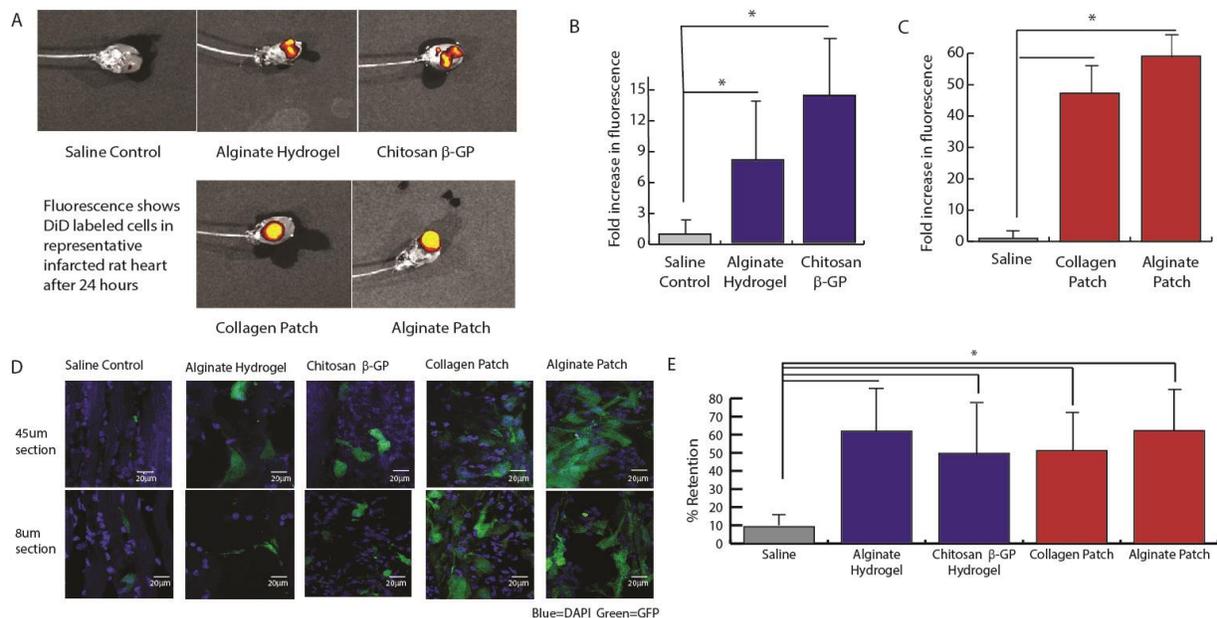


Figure 1: (A) Representative fluorescent images of infarcted rat hearts 24 hours after cell administration (B) Quantification of fluorescent signal of injectables (C) and patches (D) at 24 hours as a fold-change to saline group (*=p<0.05, ANOVA on ranks). (D) Representative cryosections, with GFP-positive cells clearly visible. (E) % retention of signal at 24 hr, as normalized to immediately following transplantation.