Biomaterial delivery vehicles improve acute retention of cells in the infarcted heart

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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 a panel of biomaterial candidates including two injectable gels and two epicardial patches.

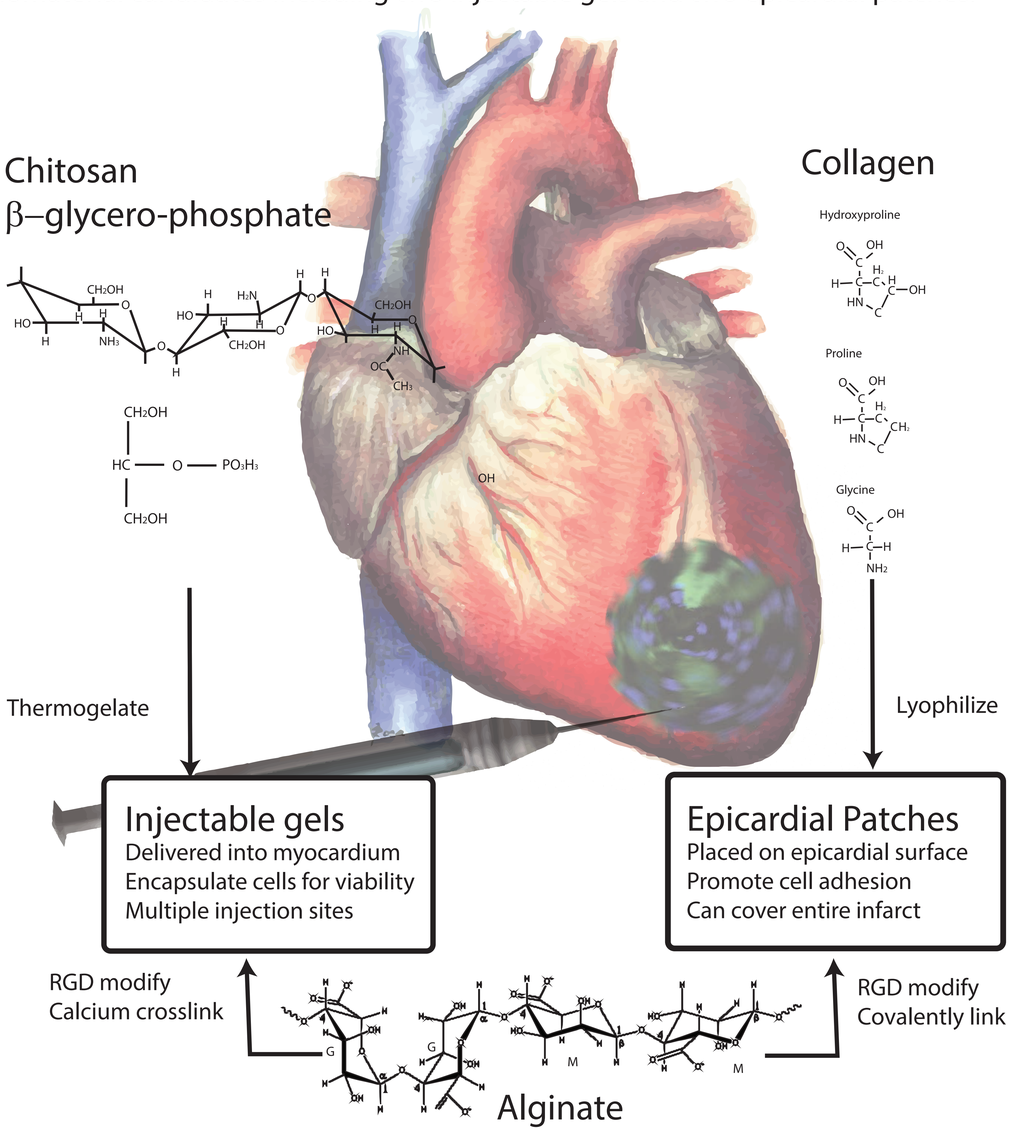

Figure 1: Overview of study : Two injectable gels (an ionically linked alginate hydrogel and a themrogelated chitosan β-gp hydrogel) were compared to two epicardial patches (a covalently linked alginate and a lyophilized collagen) in terms of acute retentionof cells in a myocardial infarct rat model.

Methods

Encapsulated cell survival in hypoxic ischemic conditions was quantified for each biomaterial. Cells were quantified 24 hours post-implantation in a rat myocardial infarct model in five groups (n=8); saline injection (clinical standard) two injectable gels (alginate ,chitosan β-gp) and two epicardial patches (alginate,collagen).

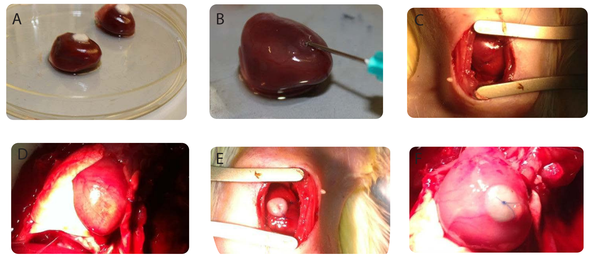

Figure 2: (A,B) In vitro optimization (C-F) Surgical procedure steps

400, 000 DiD labeled GFP human mesenchymal stem cells were injected intramyocardially in the infarct border zone in 60ul of gel/saline or seeded onto patches and implanted epicardially at infarct border zone. At 24 hours retained cells were quantified with a Xenogen imaging system. Hearts were perfused, fixed and sectioned to stain for retained cells.

Results

Cells in biomaterials had superior viability than those in the control (2D TC plate) at 6 days in hypoxia/ischemia.

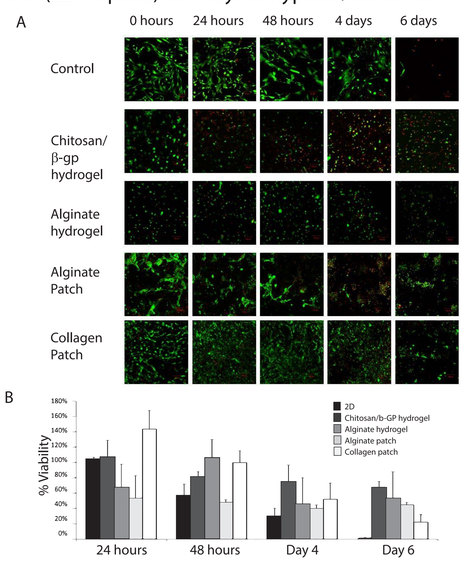

Figure 3: (A)Live/dead staining (green=live, red=dead) for each bbiomaterial at different timepoints (B) Quantification of live/ cells as a % of original cell number

All biomaterials significantly improved retention compared to a saline control with 14 and 8-fold increases for chitosan and alginate injectables and 47 and 59-fold increases achieved with collagen and alginate patches respectively (Fig 4A-C). Immunohistochemical analysis qualitatively confirmed these findings (Fig 4D). Maintenance of cells in 24 hours was significantly better than control for all groups (Fig 4E)

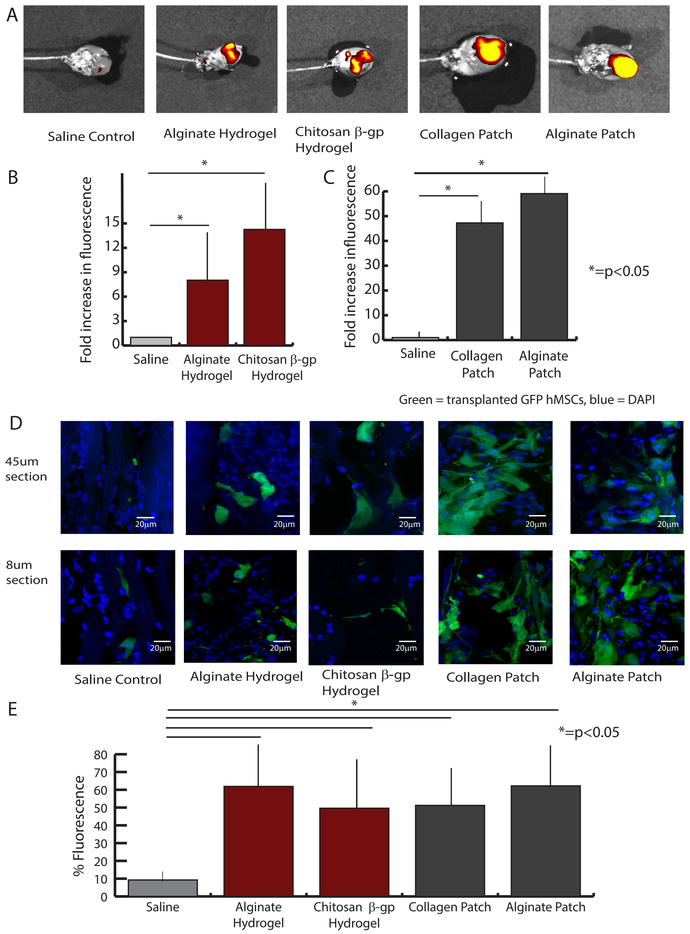

Figure 4: (A) Representative images from the Xenogen system (B,C) Fold increase in fluorescence at 24 hours for hydrogels and patches compared to control (D) Corresponding IHC
(E) Fluorescence of cells in heart for each biomaterial at 24 hours normalized by 0 hours

Conclusion

Injectable gels and epicardial patches were demonstrated to improve acute retention of cells when compared to a saline control. 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 cell therapy applications.