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**INTRODUCTION** The ability to direct stem cells to the heart is critical in producing an effective cell therapy for myocardial infarction. Mesenchymal stem cells (MSCs) have been shown to be beneficial in myocardial infarction (MI). We have developed a transient cell painting method which enables the incorporation of peptides onto the surface of cells. Using a panel of peptides developed using phage display we investigated their effect on the homing of MSCs to infarcted hearts in a mouse model.

**METHODS** Mesenchymal stem cells were cultured in FGF (5 ng/ml) containing DMEM supplemented with FBS (10 %). At 70-90 % confluence cells were trypsinized, labelled with Vybrant Green, washed with DMEM and coated with palmitated peptides (CRPPR, CRKDKC, KSTRKS, SK(bio)NSCARSKNKDC(CARBio)) at 37 °C. The coated cells were then washed with cold DMEM and stored on ice until injection. Assessment of coating (CARBio) was made using streptavidin-PE and flow cytometry. C57BL6 mice were anaesthetized, intubated and the left anterior descending artery ligated. After 30 minutes the ligation was released and the mouse allowed to recover overnight before cells were administered via injection through the left ventricle ( $1 \times 10^6$  cells/200 ul). Cells were allowed to circulate for 1 h before blood was collected for assay of Troponin I levels. Upon excision, hearts were immersed immediately in phosphate buffered saline (10 mL), cross-sectioned sagittally through the infarct site at the level of the suture, and the pairs of rostral atrial and caudal apical sections were embedded in OCT cryomounting medium for immediate freezing. Hearts were cryosectioned 8 microns thick, mounted in sequence onto slides and viewed for the fluorescent label of the cells. Areas were calculated from representative cross-sections and numbers of cells were counted on a series of sections taken through the heart.

**RESULTS** Peptides were stable on the surface of cells at 4 °C for over 3h, at 37 °C the peptide is lost over time with a half life of approximately 1h. In the in vivo MI studies, there was considerable variation in the extent of ischemic damage assessed using cardiac troponin (Fig. 1). CARBio appears to exhibit a damage response with increased homing correlating with increased damage. All peptides showed greater numbers than cells only.

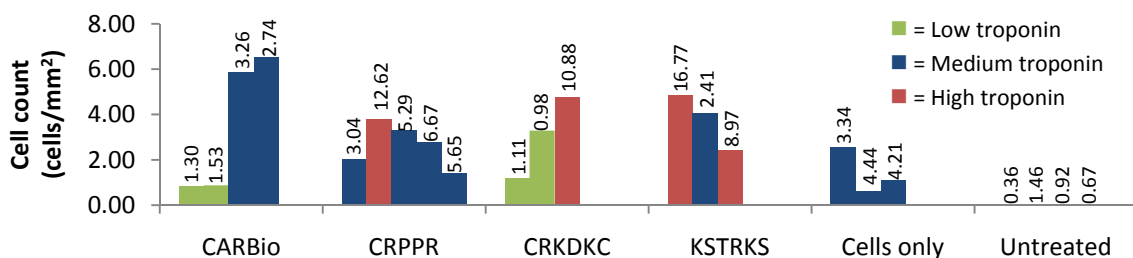


Figure 1. Assessment of cell homing and heart damage in the mouse MI reperfusion model

Each bar represents the average cell count of an animal (30 sections); three to five mice were tested for each treatment cohort. The number above the bar is the ELISA assessment of plasma concentration of cardiac troponin I.

#### Conclusions

All peptide-targeted MSCs show increased homing to infarcted hearts over non-coated MSCs. These preliminary data support future studies on the efficacy of targeted-MSCs in MI.