The transcription Factor Islet-1: A novel Gene Target for Future Cardiac Repair?

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The LIM-homeobox transcription factor isl1 plays a crucial role during heart embryogenesis. Embryonic isl1+ precursors give rise to over two-thirds of the heart and to its subsequent lineages: cardiac muscle, smooth muscle and endothelium. Interestingly, a subset of Isl1+ progenitors remains embedded in the postnatal heart.

We have previously showed that isl1 retroviral transduction to endothelial cells improves their angiogenic properties. In this study, we investigated whether isl1 is expressed in adult mesenchymal stem cells (MSCs) physiologically, and after acute myocardial infarction (MI). Additionally, we examined whether isl1 gene transfer to MSCs could promote the cells' vasculogenic properties, and the therapeutic potential of isl1 gene delivery to the infarcted heart.

We used the transgenic mice *isl1-cre/Z/EG*, in order to detect isl1 expression in MSCs of adult mice, complemented by RT-PCR and immunostaining for isl1 detection in rats' MSCs. Four weeks after MI was induced in rats, isl1 expression was assessed in bone marrow and peripheral blood by RT-PCR and immunostaining. Isl1 was retrovirally transduced to MSCs. endothelial markers were examined by FACS and tube formation capacity was assessed on matrigel. Furthermore, intramyocardial injection of plasmid encoding isl1 to mice after ligation of the LAD has been performed.

We report for the first time, the identification of isl1+ progenitors in *adult* bone marrow. The number of isl1+ progenitors increased after *in vitro* cell culture, and also in the splenocytes after acute experimental myocardial infarction. Isl1 overexpression in MSCs promoted their differentiation towards endothelium.

These data point at the broad potential that isl1 gene therapy has in engendering cardiac repair.