CO-TRANSPLANTATION OF INDUCED PLURIPOTENT STEM CELL-DERIVED CARDIOMYOCYTES WITH MESENCHYMAL STEM CELLS REDUCES THE INFARCT SCAR SIZE AND IMPROVES THE RECOVERY OF LEFT VENTRICULAR FUNCTION

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Objectives: The effects of co-transplanting mesenchymal stem cells (MSC) with cardiomyocytes derived from induced pluripotent stem cells (iPS-CM) were examined in a murine model of myocardial infarction.

Methods: Immediately after myocardial cryo-infarction, mice were subjected to intramyocardial injections into the peri-infarction area of either: a) enhanced green fluorescent protein (EGFP) and luciferase-expressing iPS CM, b) para-magnetically-labelled MSC, c) a combination of both or d) saline. Bioluminescent imaging (iPS CM) or magnetic resonance imaging (MSC) was used to track transplanted cells. Left ventricular ejection fraction (LVEF) was assessed by magnetic resonance imaging. Size of infarction scar and structural integration of transplanted cells were analysed histologically.

Results: Relative bioluminescence intensity of transplanted iPS CM was decreased to 43±7% on day 1 and further to 18±2% on day 28 for iPS-CM and to 49±11% on day 1 and 19±2% on day 28 for iPS-CM + MSC. Transplanted MSC were detectable in the peri-infarct region of the left ventricular wall up to four weeks. LVEF increased significantly in a) iPS-CM, 51.8±3.3% and c) iPS CM/MSC, 55.7±2.3%, compared to b) MSC, 47.6±1.9%, both P<0.001, and d) saline, 44.2±2.6%, both P<0.001 after four weeks. Infarct scar size was significantly decreased in a) iPS-CM, 2.77±1.35 mm² and c) iPS-CM/MSC, 2.73±1.18 mm² compared to b) MSC, 4.9±1.79 mm², both P<0.05, and d) saline, 5.73±2.68 mm², both P<0.05. Structurally organized expression of cardiac α-actinin-2 and connexin-43 was detected in transplanted iPS CM indicating cardiogenic maturation.

Conclusions: Intramyocardial co-transplantation of iPS CM and MSC improved recovery of heart function and reduced infarct scar size, confirming the significant potential of this approach for regenerative therapies.