IMPROVEMENT OF CARDIAC FUNCTION AND MODULATION OF PERIPHERAL BLOOD INFLAMMATORY CYTOKINES AND IMMUNE CELLS BY TRANSPLANTATION OF HTERT-IMMORTALIZED MOUSE CARDIAC STEM CELL LINES

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Background: Recent studies have reported the existence of resident cardiac stem cells (CSCs) that have potential differentiating into cardiomyogenic and endothelial cell lineage, and therefore promising candidates for cell therapy in cardiovascular field. Mouse CSC lines were transplanted into myocardial infarction (MI) rats to investigate their effects on cardiac regeneration and immune response.

Methods: Mouse CSCs were infected with retroviruses harboring the hTERT-IRES eGFP genes, and selected on the basis of their morphology, GFP intensity and phenotypic characterization. Fifteen MI rats were divided into 3 groups (group 1, medium; group 2, CD31- CSC; group 3, CD31+ CSC), and 5 X 10^5 cells per rat were transplanted. Cardiac function and peripheral blood inflammatory cytokines and immune cells were analyzed at 1 day, 1 week, 2 weeks and 4 weeks after cell transplantation.

Results: Significant improvements in ejection fraction value were observed in the CD31- CSC and CD31+ CSC transplanted group compared with the control group at 4 week. Peripheral blood MCP-1 at both transcript and protein levels was significantly decreased in the CD31- CSC and CD31+ CSC transplanted group at day 1 and 4 weeks compared to medium transplanted group. Peripheral blood IL-6 mRNA and protein were also significantly decreased at 1 week, 2 and 4 weeks in the CD31- CSC and CD31+ CSC transplanted group compared to medium transplanted group. Peripheral blood NK cells were significantly decreased at 1 day in the CD31- CSC transplanted group, and at 4 weeks in the both CD31- CSC and CD31+ CSC transplanted group. In contrast, peripheral blood NKT cells were significantly increased in the CD31+ CSC transplanted group at 1 week, and 4 weeks in the both CD31- CSC and CD31+ CSC transplanted group. However, peripheral blood CD4T, CD8T and B cells were not affected by transplantation of mouse CSC lines.

Conclusions: Transplantation of mouse CSCs into infarcted myocardium improved cardiac function in rat MI model, and modulated expressions of peripheral blood inflammatory cytokines and immune cells in a cell line-specific manner.