Mediastinal adipose stem cells improve contractile function of failing hearts
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Background: Mediastinal fat may be excised during mediastinal and cardiac surgeries. It would be valuable if a potent stem cell population could be quickly isolated from the "to-be-discarded" fat tissue for cardiac application. The present study was designed to determine whether the mediastinal fat tissue of human cardiac patients contains potent stem cells and whether the mediastinal adipose-derived stem cells (ASC) improve cardiac function of failing hearts.

Methods: ASC were isolated from the mediastinal fat tissue collected from 24 patients during cardiac surgery. Morphology, surface markers, and differentiation capacity of the ASC were analyzed. To evaluate their cardioprotective capacity, a rat model of congestive heart failure was established by occlusion of the LAD. One week after the LAD occlusion, ASC and cell-culture medium were injected into infarct rim in the group 1 (n = 13) and group 2 (n = 5), respectively. Six weeks after the injections, heart function was assessed with MRI and pressure-volume (P-V) loop technique.

Results: Mediastinal ASC exhibited a fibroblast-like morphology. They expressed some of the mesenchymal stromal cell markers (CD29, 73, and 90) and lacked expression of the hematopoietic markers (CD11b, 34, 45, and 106). Moreover, the ASC expressed a significant level of key pluripotent genes, such as SOX-2 and Nanog. Following adipogenic, osteogenic, and cardiomyogenic inductions, the mediastinal ASC were stained positive for lipid drops, alkaline phosphatase, and myosin light chain 2C, respectively. RT-PCR results confirmed the immunohistochemical findings. The ASC also expressed TGF-β and VEGF. Moreover, MRI showed a significant decline in left ventricular ejection fraction (LVEF) 6 weeks after CCM injection relative to the pre-injection value (41.6 ± 4.7% vs. 48.6 ± 4.1%, P < 0.05). In the ASC-treated rat hearts, in contrast, MRI did not show any decrease in LVEF 6 weeks after the cell transplantation compared to the pre-transplantation (43.1 ± 9.8% vs. 42.9 ± 7.5%, P > 0.05). Furthermore, maximum dp/dt was also significantly greater in the ASC-treated hearts (7340 ± 971 mmHg/s) than in the CCM-treated hearts (5121 ± 2745 mmHg/s). A number of GFP-positive cells were detected on the tissue sections of the ASC-treated hearts. The GFP-positive cells were also stained positive for a human nuclear membrane protein (LAMIN).

Conclusion: The mediastinal stem cells are able to improve cardiac function of infarct hearts. We conclude that the mediastinal fat tissue could be a source of stem cells for treatment of ischemic heart disease.