Novel Progenitors Derived from Epicardial and Pericardial Fat have Unique Reparative Properties

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Background and Objective: Human cardiac progenitor cells are rare and difficult to isolate. Thus, there is a need for alternative viable cell sources for cardiovascular repair. Since it has been shown that adipose tissue (AT) contains a population of adult mesenchymal stromal cells (MSCs) with regenerative properties, we aimed to test the hypothesis that AT surrounding the heart is a better cell source for myocardial regeneration and repair.

Methods and Results: Tissue samples were collected from patients undergoing open-heart surgery or liposuction. Cells were isolated from atrial tissue and four different ATs: epicardial, pericardial, thymus, and abdominal liposuction fat. All cultured cells demonstrated a fibroblast-like shape and displayed self-renewal capacity. Flow cytometry analysis showed that cells from all tissues expressed high levels of common human MSC markers, including: CD105, CD73, CD90, but lacked the hematopoietic lineage markers CD45 and CD34. Cells successfully differentiated into osteogenic and adipogenic lineages. Furthermore, after incubation with the de-methylating agent 5-azacytidine, cells derived from both epi- and pericardial ATs exhibited myogenic markers such as cardiac Troponin I and α-actinin, detected by immunostaining. We also evaluated the cells' paracrinic profiles by measuring the level of secreted angiogenic factors, and found high levels of VEGF in all AT-derived, but not in atrial-derived cells. Interestingly, epicardial AT-derived cells secreted the highest levels of most angiogenic factors ($p<0.05$). Finally, MSCs derived from epicardial AT were injected into mice ischemic hind limb and improved perfusion in the ischemic limb 10 days after injection ($p<0.0001$).

Conclusions: Our findings show, for the first time, that epicardial and pericardial fat retain unique cell populations with progenitor cell properties. Compared with peripheral fat, these progenitor cells seem to have better reparative properties.