Human Macrophage Regulation via Pericardial Adipose Tissue-Derived Mesenchymal Stromal Cells

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Background: While mesenchymal stromal cells (MSCs) were found to improve MI repair, their mechanism of action is not fully understood. We aimed to test the hypothesis that MSCs may act via infarct macrophages, and that specifically human pericardial adipose tissue-derived MSCs can polarize human macrophages into reparative, anti-inflammatory (M2)-like phenotype.

Methods: MSCs were isolated and expanded from pericardial adipose tissue of patients undergoing cardiac surgery. Monocytes isolated from human blood using Ficoll and MACS positive selection of $CD14^+$ cells, were cultured 5-7 days, washed, and co-cultured with MSCs 1-14 days directly or through transwell membrane restricting cell contact. M2 macrophage markers (CD206, CD163 and CD16) and phagocytic ability of fluorescent latex beads were examined using FACS. Supernatant was collected on different days, for ELISA of cytokines, while hematoxilin staining demonstrated morphological changes.

Results: Adipose tissue-derived MSCs increased percentage of macrophages expressing alternative macrophage (M2) markers $CD206^+CD163^+$ (1.5 folds) and $CD16^+$ (9 folds). MSCs also increased macrophage secretion of the anti-inflammatory cytokine IL-10 (9 folds, $p<0.001$), VEGF (3 folds, $p<0.01$), IL-13 (2 folds, $p<0.05$) and IL-4 (2 folds, $P<0.05$), while decreasing IL-1 (2 folds, $p<0.01$), TNF-α (1.5 folds, $p<0.001$), IL-12 (1.5 folds, $p<0.001$), IL-17 (3 folds, $p<0.001$), IL-23 (16 folds, $p<0.01$) and IFN-γ (2 folds, $p<0.001$). In addition, co-culturing induced a star-shaped morphology of macrophages and decreased their phagocytic ability (2 folds).

Conclusions: Our findings suggest, for the first time, that human pericardial adipose tissue-derived MSCs can polarize human macrophages towards anti-inflammatory, reparative phenotype. Our findings could be relevant for the mechanism of atherosclerosis and the development of novel immune-modulation therapy for the treatment of MI, atherosclerosis and other inflammatory diseases. <IMAGE01>