AMELIORATION OF CIGARETTE SMOKE-INDUCED CARDIAC DYSFUNCTION AND INFLAMMATION BY MESENCHYMAL STEM CELLS

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OBJECTIVES: Cigarette smoke (CS) is recognized as a major cause of cardiovascular disease (CVD). Inflammatory responses play important roles in the pathophysiological processes of CS-induced cardiac damage. Mesenchymal stem cells (MSCs) are regarded as a promising candidate for cell-based therapy in CVD. We aimed to compare the effects of bone marrow-derived MSCs (BM-MSCs) and induced pluripotent stem cell-derived MSC (iPSC-MSCs) on cardiac function and inflammation in CS-exposed rat model.

METHODS: Male Sprague-Dawley rats were exposed to 4% CS for one hour daily for 56 days. On day 29 and day 43, human iPSC-MSCs or adult bone marrow-MSCs (BM-MSCs) were administered intravenously to CS-exposed rats. Echocardiography was conducted 24h after the last exposure and animals were sacrificed. Heart tissues were collected for paraffin sectioning and protein extraction to determine levels of pro-/anti-inflammatory cytokines.

RESULTS: iPSC-MSC-treated group had a greater effect in the improvement of CS-induced cardiac dysfunction, myocardial hypertrophy and interstitial fibrosis than BM-MSC-treated group. The CS-induced elevation of cardiac pro-inflammatory cytokines, tumor necrosis factor-alpha (TNF-α), cytokine-induced neutrophil chemoattractant-1 (CINC-1, resemble to human IL-8) and monocyte chemoattractant protein-1 (MCP-1) was attenuated by either iPSC-MSCs or BM-MSCs administration. However, CS-induced reduction of cardiac anti-inflammatory cytokines, interleukin-10 (IL-10) and adiponectin, was restored only by iPSC-MSCs administration. Both treatments reversed CS-induced reduction of cytoplasmic IκBα expression and nuclear translocation of nuclear factor-κB (NF-κB) p65 subunit.

CONCLUSIONS: Our findings demonstrate a higher capacity of iPSC-MSCs than BM-MSCs to ameliorate CS-induced cardiac dysfunction and cardiac remodeling via NF-kB signaling pathway by inhibiting pro-inflammatory cytokines and restoring anti-inflammatory cytokines in CS-exposed rat model. iPSC-MSCs may thus hold promise for the development of cell-based therapy in cardiac protection.