Human mesenchymal stromal cells modulate T-cell immune response via transcriptomic regulation

ABSTRACT

Background aims: Mesenchymal stromal cells (MSCs) have been identified as pan-immunosuppressant in various in vitro and in vivo inflammatory models. Although the immunosuppressive activity of MSCs has been explored in various contexts, the precise molecular signaling pathways that govern inhibitory functions remain poorly elucidated. Methods: By using a microarray-based global gene expression profiling system, this study aimed to decipher the underlying molecular pathways that may mediate the immunosuppressive activity of umbilical cord–derived MSCs (UC-MSCs) on activated T cells. Results: In the presence of UC-MSCs, the proliferation of activated T cells was suppressed in a dose-depended manner by cell-to-cell contact mode via an active cell-cycle arrest at the G_0/G_1 phase of the cell cycle. The microarray analysis revealed that particularly, IFNG, CXCL9, IL2, IL2RA and CCND3 genes were down-regulated, whereas IL11, VSIG4, GFA1, TIMP3 and BBC3 genes were up-regulated by UC-MSCs. The dysregulated gene clusters associated with immune-response-related ontologies, namely, lymphocyte proliferation or activation, apoptosis and cell cycle, were further analyzed. Conclusions: Among the nine canonical pathways identified, three pathways (namely T-helper cell differentiation, cyclins and cell cycle regulation, and gap/tight junction signalling pathways) were highly enriched with these dysregulated genes. The pathways represent putative molecular pathways through which UC-MSCs elicit immunosuppressive activity toward activated T cells. This study provides a global snapshot of gene networks and pathways that contribute to the ability of UC-MSCs to suppress activated T cells.

Keyword: Cell-cycle arrest; Gene expression; Immunomodulation; Mesenchymal stromal cells; T cells