Abstract

Mesenchymal stem cells (MSCs) possess significant immunomodulatory potential. This *in silico* study investigated the effects of double-stranded DNA (dsDNA) on MSC immunomodulation via Toll-like receptor 9 (TLR-9) signaling, hypothesizing that dsDNA downregulates pro-inflammatory effectors and adhesion molecules while upregulating anti-inflammatory mediators. A list of differentially expressed genes from adipose tissue-derived MSCs (AD-MSCs) treated with dsDNA was obtained from submitted gene expression data in the Gene Expression Omnibus (GEO) database (GSE122556). The gene expression analysis includes gene expression profile visualization using Uniform Manifold Approximation and Projection (UMAP), Gene Ontology (GO) enrichment, canonical pathway analysis, Ingenuity Pathway Analysis (IPA) networks, and heatmaps. Results revealed that dsDNA induced a transcriptional shift in MSCs, marked by concurrent activation of inflammatory pathways and upregulation of the negative regulatory mechanisms of immune response. IL-10 signaling was prominently upregulated, alongside increased expression of immunosuppressive genes. These findings suggest that dsDNA primes MSCs toward an immunomodulatory phenotype by balancing pro-inflammatory and anti-inflammatory responses. These findings serves as preliminary evidence for further experimental validation to confirm these computational findings and assess the therapeutic potential of dsDNA-primed MSCs in immune-related conditions.

Keywords: *double-stranded DNA (dsDNA), Immunomodulation, Interleukin-10 (IL-10), Mesenchymal stem cells (MSCs), TLR-9 signaling*