Immunomodulatory Effects of Human Dental Pulp Stem Cells on Monocyte Polarization via Efferocytosis

Authors: Vitor Rodrigues da Costa, Olívia Fonseca Souza, Irina Kerkis and Rodrigo Pinheiro Araldi

Background: The use of medicinal signaling cells (MSCs) has gained significant attention as a promising therapeutic approach for managing inflammatory disorders, owing to their regenerative and immunomodulatory properties. Among these, human dental pulp stem cells (hDPSCs), which exhibit MSC-like characteristics, have demonstrated substantial potential in modulating immune responses. However, a notable challenge in MSC-based therapies is understanding how their limited lifespan in the host organism after administration can lead to long-lasting therapeutic effects. Monocytes are among the first immune cells to interact with intravenously administered hDPSCs, making this interaction a critical area of study. This raises the hypothesis that the efferocytosis of hDPSCs by monocytes may promote their reprogramming toward an anti-inflammatory phenotype. Investigating this process could provide valuable insights into the mechanisms underlying the immunomodulatory properties of MSCs and inform strategies to enhance their clinical efficacy.

Objective: This study aimed to investigate the immunomodulatory effects of human dental pulp stem cells (hDPSCs) on monocytes derived from peripheral blood and U-937 monocytic cell line.

Methodology: Monocytes derived from peripheral blood mononuclear cells (PBMCs) or the U937 monocytic cell line were cocultured with hDPSCs. Analyses included cytokine secretion and immune cell immunophenotyping via flow cytometry, as well as gene expression profiling using RT-qPCR. This study was approved by the Ethics Committee of UNIFESP (CAAE: 70149923.2.0000.5505).

Results: hDPSCs underwent apoptosis when cultured with human peripheral blood, and circulating monocytes demonstrated preferential efferocytosis of apoptotic hDPSCs. Flow cytometry revealed that monocyte reprogramming following hDPSC efferocytosis led to polarization toward a pro-resolutive phenotype by the upregulation of the markers CD163 and CD206. Co-culture of purified peripheral blood monocytes with hDPSCs significantly increased IL-10 secretion compared to monoculture controls. Similarly, co-culture with U937 monocytes showed a dose-dependent increase in IL-10 secretion induced by hDPSCs, without affecting cell viability. These findings indicate that hDPSCs can polarize monocytes toward an anti-inflammatory phenotype.

Conclusion: This study highlights the immunomodulatory properties of hDPSCs on monocytes, suggesting that efferocytosis may underlie their transient lifespan following intravenous administration.