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COMPARATIVE IMMUNOMODULATORY EFFECTS OF MESENCHYMAL STROMAL CELLS AND THEIR EXTRACELLULAR VESICLES DERIVED FROM DIFFERENT TISSUES

Background/Aim. Mesenchymal stromal cells (MSCs) and MSC-derived extracellular vesicles (EVs) possess immunomodulatory and regenerative properties and are considered promising tools for cell-free therapy. This study aimed to compare the immunomodulatory activity of MSCs and EVs derived from adipose tissue (ADSCs), dental pulp (DPSCs), and umbilical cord (UC-MSCs). **Methods.** MSCs were characterized by morphology, differentiation, and immunophenotype. EVs were isolated by ultracentrifugation and characterized by nanoparticle tracking analysis, BCA assay, and ELISA. The immunomodulatory activity of MSCs and EVs was evaluated using PHA-stimulated PBMNCs. Statistical analysis was performed using Student's t-test ($p \leq 0.05$). **Results.** All MSC cultures met the minimal criteria for multipotent mesenchymal stromal cells. The highest EV yield was obtained from DPSCs and UC-MSCs. EVs from all MSC types expressed CD63 and CD81. Elevated IL-6 levels were detected in MSC and EV samples, whereas IL-10 was not detected. IL-1RA expression was highest in DPSC- and ADSC-derived EVs. All analyzed MSC types demonstrated dose-dependent suppression of PBMNC proliferation, with UC-MSCs showing the greatest inhibitory effect. In contrast, MSC-derived EVs exhibited distinct source- and concentration-dependent effects. UC-MSC-derived EVs inhibited PBMNC proliferation at lower concentrations but enhanced proliferation at higher doses. ADSC-derived EVs promoted PBMNC proliferation at lower concentrations and inhibited it at higher concentrations, whereas DPSC-derived EVs promoted PBMNC proliferation at all tested concentrations. **Conclusions.** MSCs and their EVs exhibited tissue-specific immunomodulatory properties, likely reflecting differences in the composition of bioactive signaling molecules. EV effects on PBMNC proliferation were source- and concentration-dependent, highlighting the importance of MSC source selection for further development of EV-based therapeutics.

Keywords: mesenchymal stromal cells, extracellular vesicles, immunomodulation.

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