STUDY OF THE THERAPEUTIC EFFECT OF CYTOKINE-PRECONDITIONED MESENCHYMAL STEM CELLS AND THEIR EXOSOMES IN A MOUSE MODEL OF PSORIASIS

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Psoriasis is a chronic inflammatory skin disease sustained by a cytokine-rich microenvironment that perturbs keratinocyte-immune crosstalk. Mesenchymal stem cells (MSCs) and their exosomes offer a cell-free route to immunomodulation, but basal preparations can be variably potent. We asked whether disease-informed priming of human umbilical cord blood MSCs with psoriasis- relevant cytokines would reprogram paracrine output and generate exosomes with stronger anti- inflammatory activity *in vitro*. Across multiple priming conditions, MSCs adopted a pro-resolving secretory profile characterized by higher levels of canonical mediators (including prostaglandin E2 and TGF-β1) and a coordinated upshift in immunoregulatory genes associated with tolerance, tissue protection, and resolution (such as IDO, iNOS, COX-2, TSG-6, IL-10, HGF, and galectin- 1). These molecular changes translated into function: compared with exosomes from unprimed MSCs, primed MSC exosomes more effectively dampened inflammatory signaling in stimulated target cells, reduced the release of pro-inflammatory cytokines, and preserved markers of barrier- relevant homeostasis in keratinocyte models. The most consistent gains were observed when MSCs were exposed to a combinatorial cytokine milieu that mirrored the psoriatic niche, yielding exosome preparations that coupled robust bioactivity with stable size distribution and expected vesicle markers. Together, the *in vitro* data show that a tractable priming step can tune MSC paracrine biology and produce exosomes with superior immunomodulatory performance without increasing manufacturing complexity. Preliminary *in vivo* observations in an imiquimod-induced mouse model aligned with the *in vitro* potency ranking, providing orthogonal biological support while keeping the emphasis on rigorous cell-based readouts. We demonstrated that disease- relevant priming enhances the anti-inflammatory capacity of MSC-derived exosomes in psoriasis and other cytokine-driven dermatoses.

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Keywords: mesenchymal stem cell, exosome, psoriasis

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