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The Role of Exosomes in Oral Lichen Planus

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Abstract

Background: Oral lichen planus (OLP) is a chronic immune-mediated inflammatory disease of the oral mucosa characterized by persistent T-cell-mediated injury, keratinocyte apoptosis, and recurrent inflammatory activity. Although topical and systemic corticosteroids remain the mainstay of treatment, their prolonged use may be associated with relapse, mucosal atrophy, candidiasis, and systemic adverse effects, highlighting the need for safer and more targeted therapeutic approaches. Exosomes, also referred to as small extracellular vesicles, are nanosized lipid bilayer-bound particles, approximately 30–150 nm in diameter, that originate from the endosomal pathway and mediate intercellular communication through the transfer of proteins, lipids, messenger RNA, microRNA, and other biologically active molecules. Emerging evidence suggests that exosomes participate in the immunopathogenesis of OLP by regulating communication between epithelial and immune cells, promoting inflammatory-cell recruitment, antigen presentation, cytokine signaling, and keratinocyte apoptosis. Conversely, mesenchymal stem cell-derived exosomes may exert therapeutic effects by suppressing pro-inflammatory cytokines, modulating macrophage polarization, restoring immune homeostasis, reducing epithelial injury, and enhancing angiogenesis and tissue regeneration. Exosomal microRNAs detected in saliva, plasma, and oral tissues may also serve as non-invasive biomarkers for diagnosis and assessment of disease severity. This review discusses the biological role, pathogenic mechanisms, diagnostic potential, therapeutic applications, safety advantages, current limitations, and future perspectives of exosomes in OLP.

Keywords: Oral lichen planus; Exosomes; Small extracellular vesicles; Mesenchymal stem cells; MicroRNA; Biomarkers; Immunomodulation; Regenerative therapy.

Introduction:

Exosomes (small extracellular vesicles, sEVs) are the smallest and most extensively studied EV subtype (30–150 nm). They originate from the endosomal pathway through the formation of intraluminal vesicles within multivesicular bodies (MVBs), which subsequently fuse with the plasma membrane to release exosomes. Their biogenesis is mediated mainly by ESCRT-dependent and ESCRT-independent mechanisms **(1,2).**

Extracellular vesicles (EVs) are heterogeneous lipid bilayer-bound particles secreted by virtually all cell types into the extracellular environment. They range from approximately 40–5000 nm in diameter and carry a diverse cargo of bioactive molecules, including DNA, RNA (mRNA and miRNA), proteins, lipids, and metabolites. Although incapable of replication due to the absence of a functional nucleus, EVs play a pivotal role in intercellular communication and regulation of both physiological and pathological processes **(3).**

1 Exosomes (Small Extracellular Vesicles) 2-Microvesicles (Ectosomes)

Microvesicles (100–1000 nm) are generated by outward budding of the plasma membrane following cytoskeletal rearrangement **(1,2).**

1- Apoptotic Bodies

Apoptotic bodies (500–5000 nm) are released during programmed cell death and may contain nuclear fragments and intact organelles **(2).**

Oral lichen planus (OLP) is a chronic immune-mediated inflammatory disorder in which exosomes have recently emerged as important mediators of disease pathogenesis and promising therapeutic agents.

1. Rationale for Exosome Therapy in OLP

Current OLP management mainly depends on topical and systemic corticosteroids, which provide symptomatic relief but are associated with relapse and adverse effects following prolonged use. **(4)**

2. Immunological Mechanisms Relevant to OLP

Exosomes actively participate in the immunopathogenesis of OLP as showed in (**Figure 1)** by mediating communication between immune and epithelial cells. exosomes promote keratinocyte apoptosis, recruitment of inflammatory cells, and participate in antigen presentation, thereby sustaining chronic mucosal inflammation. **(3,5)**

Cytokine	*Lesion*	*Saliva*	*Serum*	*PBMC*	*T-exos*
IL-1	?	●	?	?	IL-1β was ●; IL-1α was ns
IL-2	ns	?	●▼	ns	ns
IL-4	●▼	●▼	●▼	?	ns
IL-5	●	?	ns	●▼	▼
IL-6	●	●		●▼	ns
IL-7	?	?	?	?	●
IL-8	Not detected	●	●	?	ns
IL-10	●	●	●▼	▼	●
IL-12	●	?	?	●▼	●
IL-17	●	●	●▼	?	●
IL-18	ns	●	●	?	?
TGF-β	▼	?	●▼	●▼	?
IFN-γ	●	●▼	●▼	▼	●
TNF-α	●	●	●▼	▼	ns

●: increased; ▼:decreased; ●▼: the expression was inconsistent in different studies; ?: unclear; ns: no significant difference.

FIGURE 1 Summary of expression patterns of cytokines in oral lichen planus **(5)**

3. Therapeutic Effects of Exosomes in OLP :showed in **(Figure 2)**

MSC-derived exosomes exhibit potent therapeutic effects in OLP through suppression of inflammatory cytokines, modulation of macrophage polarization, restoration of immune homeostasis, promotion of angiogenesis, stimulation of fibroblast proliferation, enhancement of collagen deposition, and acceleration of mucosal healing. **(4,6)**

4. Experimental and Clinical Evidence

Several experimental studies have demonstrated altered exosomal profiles in patients with OLP. Salivary and plasma exosomal miRNAs, particularly miR-4484 and miR-34a-5p, have shown potential as diagnostic biomarkers and indicators of disease severity. Furthermore, tissue-derived exosomes exhibit distinct immunological signatures, while in vitro studies suggest that healthy-derived exosomes exert immunosuppressive effects that are diminished in OLP-derived exosomes. **(3,5)**

5. Safety and Therapeutic Advantages

Compared with conventional corticosteroid therapy, exosomes offer several advantages including low immunogenicity, high biocompatibility, targeted delivery, and reduced risk of systemic adverse effects. Unlike stem cell therapy, exosomes are cell-free vesicles lacking replicative capacity, thereby minimizing the risks of

tumorigenicity and unwanted differentiation while maintaining therapeutic efficacy. **(4)**

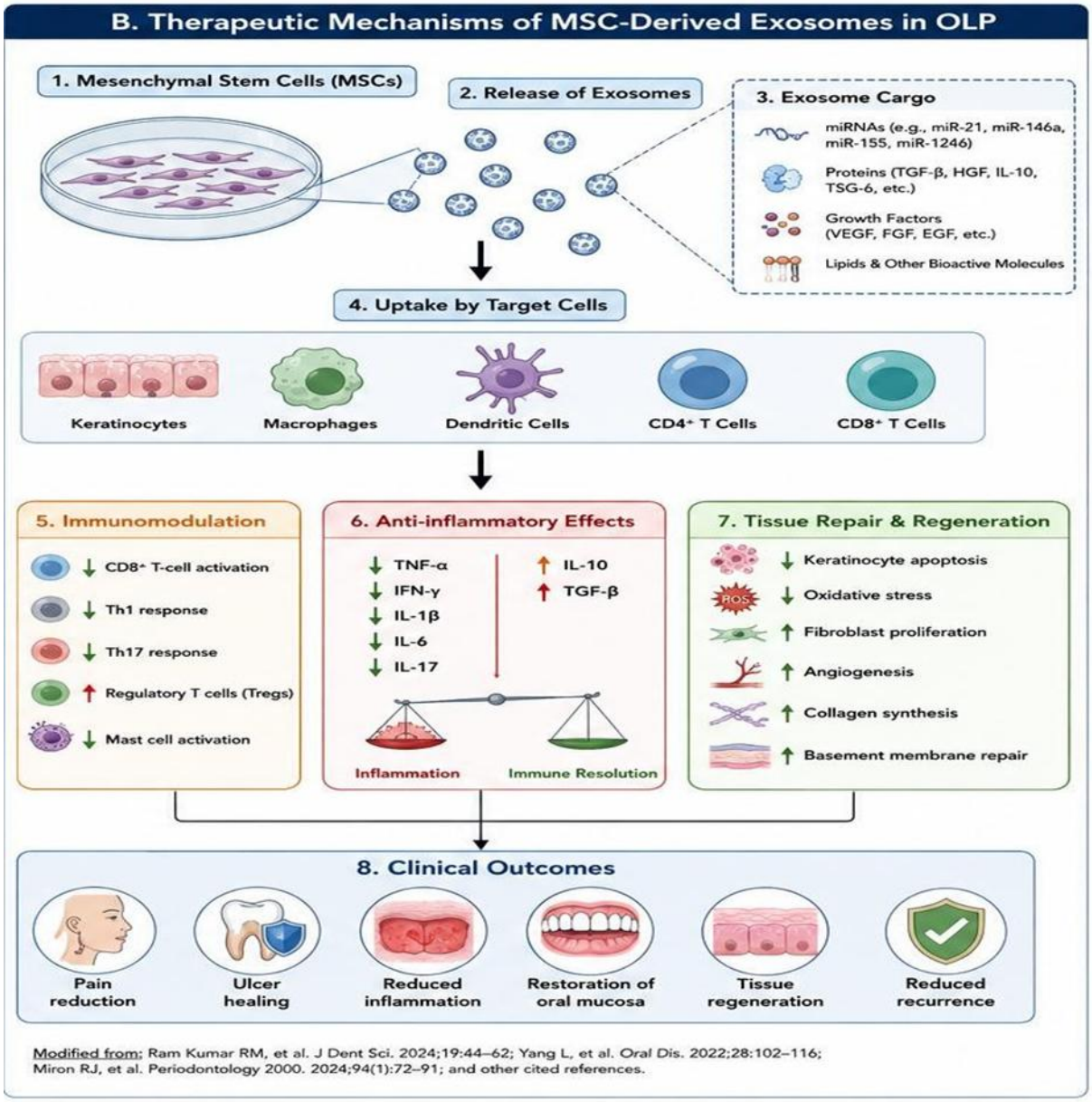

Figure 2. Proposed therapeutic mechanisms of mesenchymal stem cell-derived exosomes in Oral LichenPlanus.

The figure summarizes the proposed therapeutic actions of MSC-derived exosomes in OLP. Following cellular uptake, exosomes modulate both innate and adaptive immune responses, suppress pro-inflammatory cytokines, enhance anti-inflammatory mediators, reduce keratinocyte apoptosis, and promote tissue regeneration, ultimately resulting in pain relief, lesion healing, and restoration of oral mucosal integrity. Modified from **(4,5)**

6. Current Challenges and Future Perspectives

Despite their promising therapeutic potential, several challenges continue to limit the clinical translation of exosome therapy in OLP. These include the lack of standardized isolation and characterization protocols, low production yield, manufacturing difficulties, biological heterogeneity, and the scarcity of large randomized clinical trials. Future research is expected to focus on engineered exosomes for targeted drug delivery, salivary liquid biopsy, personalized therapy, and artificial intelligence-assisted therapeutic prediction. **(4,5)**

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