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Editorial

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Mesenchymal Stem Cell Therapy for Oral Lichen Planus: A Paradigm Shift from Palliation to Regeneration

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ABSTRACT

Oral lichen planus (OLP) is a chronic, T-cell-mediated inflammatory disease of the oral mucosa, notable for its symptomatic burden and potential for malignant transformation. While corticosteroids and immunosuppressants remain the standard of care, their transient efficacy and adverse effect profile underscore a significant unmet clinical need. Mesenchymal stem cells (MSCs), with their multifaceted immunomodulatory and regenerative capabilities, are emerging as a compelling therapeutic alternative. This editorial synthesizes current evidence, positing that MSCs can fundamentally disrupt the immunopathogenic cycle of OLP. We explore the mechanisms by which MSCs re-establish immune tolerance and promote tissue repair, and we critically assess the translational pathway from preclinical models to clinical application. Despite promising results, the journey to clinical adoption necessitates overcoming hurdles in standardization, delivery, and safety profiling. We argue that MSC-based therapy represents not merely an incremental improvement, but a potential paradigm shift towards a curative strategy for this recalcitrant disease.

Keywords: Oral lichen planus; Mesenchymal stem cells; Immunomodulation; Regenerative medicine; Cell therapy; Autoimmune disease

INTRODUCTION

Oral lichen planus (OLP) presents a persistent clinical conundrum. Affecting roughly 1% of the population, this chronic inflammatory condition is driven by a complex, dysregulated immune response that targets the oral epithelium[1,2]. The clinical spectrum ranges from innocuous white striae to painful, erosive lesions that significantly impair quality of life[3-5]. Compounding this burden is the well-documented, albeit low, risk of malignant transformation to oral squamous cell carcinoma, mandating vigilant, long-term management [6].

Current first-line therapies, predominantly topical corticosteroids, are fundamentally palliative. They suppress inflammation without resolving the underlying immune dysfunction, leading to a familiar

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cycle of relapse and remission upon withdrawal[7,8]. This landscape of inadequate treatments creates an imperative for novel approaches that move beyond symptom control towards durable disease modification. Here, we examine the compelling case for mesenchymal stem cell (MSC) therapy, a strategy rooted in the principles of regenerative medicine and immunology that promises to do just that.

The Immunopathogenic Cycle of OLP: A Rationale for Intervention

OLP pathogenesis is a self-perpetuating cycle of immune activation. The initiating event is thought to be an unknown antigenic trigger that leads to the activation of autoreactive CD8+ T lymphocytes[9]. These cytotoxic T cells infiltrate the lamina propria, assuming a characteristic band-like distribution, and directly mediate apoptosis of basal keratinocytes via perforin and granzyme B[9, 10]. This process is amplified by mast cell degranulation and matrix metalloproteinase (MMP)-mediated degradation of the basement membrane[10,11]. A sustained pro-inflammatory cytokine milieu, featuring elevated levels of TNF-α, IFN-γ, and IL-17, fuels T-cell recruitment and activation, locking the tissue in a state of chronic inflammation[5, 12].

It is this very cycle that MSCs are exquisitely equipped to break. Their capacity to sense and respond to inflammatory signals, thereby modulating rather than broadly suppressing the immune response, positions them as an ideal, targeted therapeutic agent.

The Limitations of Current Management

The mainstay of OLP management remains entrenched in immunomodulatory drugs with significant limitations. Topical corticosteroids, while effective for many, can cause local side effects including mucosal atrophy and candidiasis, and they often fail in severe or widespread disease[7,13]. Second-line agents like systemic corticosteroids or calcineurin inhibitors introduce risks of systemic immunosuppression, organ toxicity, and opportunistic infections, making them unsuitable for long-term use [14, 15].

Ultimately, these approaches are akin to pressing a pause button on the disease. They do not address the fundamental immune dysregulation, explaining the high frequency of relapse. There is a clear and urgent need for a treatment that can induce long-term remission by resetting the local immune environment.

MSCs: Multipotent Mediators of Repair and Tolerance

MSCs are not simply progenitor cells; they are sophisticated signaling hubs with profound immunomodulatory influence. Their therapeutic effect derives less from direct differentiation and more from their potent paracrine activity. In response to inflammatory cues, MSCs secrete a repertoire of bioactive molecules, including prostaglandin E2 (PGE2), indoleamine 2,3-dioxygenase (IDO), transforming growth factor-beta (TGF-β), and interleukin-10 (IL-10), that collectively suppress effector T-cell and NK-cell function while promoting the expansion of regulatory T cells (Tregs) [10, 16, 17].

Their low immunogenicity and availability from multiple tissues, including readily accessible oral sources like gingiva and dental pulp, make them highly tractable for clinical use [17, 18]. The choice of source can influence potency and practicality, as summarized in Table 1.

Mechanisms of MSC Action in OLP: A Multi-Pronged Assault

As dedicated in Table 2, the therapeutic promise of MSCs in OLP lies in their ability to intervene at multiple pathological nodes simultaneously:

- Re-establishing Immune Tolerance: MSCs shift the local cytokine profile from a pro-inflammatory (Th1/Th17) to an anti-inflammatory (Th2/Treg) state. They directly inhibit the production of IFN-γ and IL-17 while promoting the secretion of IL-10 and TGF-β, thereby quelling the autoimmune attack [5, 12, 21].
- Halting Apoptosis: By secreting anti-apoptotic factors and stanniocalcin-1, MSCs protect basal keratinocytes from T-cell-mediated cytotoxicity, helping to preserve epithelial integrity [10, 22].

- Driving Functional Regeneration: Through the release of vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), and fibronectin, MSCs stimulate angiogenesis and promote the proliferation and migration of keratinocytes, essential processes for healing erosive and ulcerative lesions [19, 20].

Table 1: Comparative Characteristics of MSCs from Different Sources

Source of MSCs	Ease of Access	Immunomodulation	Regenerative Potential	Clinical Relevance for OLP
Bone Marrow (BM-MSCs)	Invasive	High	High	Gold standard, widely studied [16, 19]
Adipose Tissue (AD-MSCs)	Moderately invasive	High	Moderate to High	Promising alternative [20]
Gingiva (G-MSCs)	Easy (minimally invasive)	High	High	Site-specific, highly relevant [18]
Dental Pulp (DP-MSCs)	Easy (from extracted teeth)	Moderate to High	High	Autologous potential [17]
Umbilical Cord (UC-MSCs)	Postnatal tissue	High	High	Allogeneic "off-the-shelf" option

Table 2: MSC-Mediated Therapeutic Mechanisms in OLP

Mechanism	Pathogenic Target in OLP	MSC-Mediated Action
Immunomodulation	Pro-inflammatory cytokines (IFN-γ, IL-17, TNF-α)	Secretion of IL-10, TGF-β, PGE2; induction of Tregs
Cytotoxic Inhibition	CD8+ T-cell activity & keratinocyte apoptosis	Secretion of anti-apoptotic factors (e.g., stanniocalcin-1)
Antioxidant Effects	Oxidative stress in epithelium	Release of SOD, catalase, glutathione
Angiogenesis & Remodeling	Impaired healing & tissue breakdown	Secretion of VEGF, FGF; balanced MMP regulation
Re-epithelialization	Epithelial atrophy & ulceration	Secretion of EGF; stimulation of keratinocyte migration

Translational Evidence and Clinical Correlates

Robust preclinical data supports the efficacy of MSCs in oral mucosal repair. Studies in models of oral ulceration and mucositis demonstrate that local administration of MSCs, particularly from gingival or bone marrow sources, accelerates wound closure, reduces inflammatory infiltrates, and restores tissue architecture [18-20, 23].

While direct, large-scale clinical trials for OLP are still forthcoming, the mechanistic rationale is powerfully supported by positive outcomes in other inflammatory conditions. For instance, a recent prospective study demonstrated that intra-arterial delivery of MSCs via genicular artery embolization significantly improved pain and function in patients with knee osteoarthritis, showcasing the potential of targeted MSC delivery for managing localized chronic inflammation[24]. Furthermore, a one-year follow-up study of patients with severe COVID-19 treated with Wharton's jelly-derived MSCs reported no long-term safety signals, a critical finding that bolsters confidence in the long-term profile of allogeneic MSC therapies for immune-mediated conditions[25]. The choice of delivery method, be it local injection, scaffold-based systems, or hydrogel encapsulation, will be paramount to ensuring sufficient cell retention and survival within the inflammatory OLP microenvironment to exert a durable effect [26-28].

Navigating the Path to Clinical Adoption

The translational pathway for MSCs in OLP is paved with both promise and pragmatic challenges:

- Standardization: Donor- and source-dependent heterogeneity in MSC function demands rigorous standardization of isolation, expansion, and potency assays [17, 29.]
- Protocol Definition: The critical parameters—optimal dose, timing, and frequency of administration—remain to be defined through well-designed dose-finding studies.
- Safety and Regulation: Although near-term safety is well-documented, long-term risks in the context of a potentially malignant disorder require meticulous post-marketing surveillance (30). Navigating the complex regulatory pathway for Advanced Therapy Medicinal Products (ATMPs) is a significant hurdle [31].
- Accessibility: The high cost and logistical complexity of cell therapy currently limit its widespread adoption, highlighting the need for scalable, cost-effective manufacturing platforms [32].

Future progress hinges on several key developments:

1. Definitive Clinical Trials: Conducting rigorous, randomized, placebo-controlled trials with clearly defined clinical and immunological endpoints.
2. Next-Generation Products: Advancing cell-free therapies utilizing MSC-derived exosomes and secretomes, which offer an "off-the-shelf" product with a potentially superior safety profile [33, 34].
3. Precision Medicine: Leveraging biomarker signatures to identify patient subgroups most likely to respond and potentially using genetic engineering to enhance MSC homing or potency [35, 36.]

CONFLICT OF INTEREST

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Ethical Approval

Not applicable. This article is a narrative review based exclusively on previously published literature. No studies involving human participants or animals were conducted by the authors.

Informed Consent

Not applicable. This manuscript does not include any individual patient data, images, or case details requiring informed consent.

REFERENCES

1. González-Moles M, Warnakulasuriya S, González-Ruiz I, et al. Worldwide prevalence of oral lichen planus: A systematic review and meta-analysis. Oral Dis. 2021;27(4):813–28.
2. Nukaly HY, Halawani IR, Alghamdi SMS, et al. Oral Lichen Planus: A Narrative Review Navigating Etiologies, Clinical Manifestations, Diagnostics, and Therapeutic Approaches. J Clin Med. 2024;13(17):5280.
3. El-Howati A, Thornhill MH, Colley HE, et al. Immune mechanisms in oral lichen planus. Oral Dis. 2023;29(4):1400–15.
4. Hassan AAA, Elgendi M, Shaker O, et al. Salivary level of interleukin-17 in patients having atrophic and erosive oral lichen planus before and after treatment with topical steroids (A Controlled clinical trial). Egypt Dent J. 2021;67(1):379–85.
5. Dvorak G, Monshi B, Hof M, et al. Gender aspects in oral health-related quality of life of oral lichen planus patients. Int J Stomatol Occlusion Med. 2015;8(2):33-40.
6. Monteiro BV, Pereira Jdos S, Nonaka CF, et al. Immunoexpression of Th17-related cytokines in oral lichen planus. Appl Immunohistochem Mol Morphol. 2015;23(6):409–15.
7. Parashar P. Oral lichen planus. Otolaryngol Clin North Am. 2011;44(1):89–107, vi.
8. Sugerman PB, Savage NW, Walsh LJ, et al. The pathogenesis of oral lichen planus. Crit Rev Oral Biol Med. 2002;13(4):350–65.
9. Scully C, Carrozzo M. Oral mucosal disease: Lichen planus. Br J Oral Maxillofac Surg. 2008;46(1):15–21.
10. Srinivas K, Aravinda K, Ratnakar P, et al. Oral lichen planus - Review on etiopathogenesis. Natl J Maxillofac Surg. 2011;2(1):15–6.
11. El-Refai I, Maged A, El-Saady D. Assessment of IL-17 in Oral Lichen Planus and in Pemphigus Vulgaris. Egypt Dent J. 2019;65(1):343–50.
12. Lodi G, Scully C, Carrozzo M, et al. Current controversies in oral lichen planus: report of an international consensus meeting. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2005;100(2):164-78.
13. Farhi D, Dupin N. Pathophysiology, etiologic factors, and clinical management of oral lichen planus, part I: facts and controversies. Clin Dermatol. 2010;28(1):100–8.
14. Chen E, Sami N. Systemic tacrolimus in the treatment of recalcitrant mucosal lichen planus. JAAD Case Rep. 2017;3(3):253–5.
15. Ficarra G, Flaitz CM, Gaglioti D, et al. White lichenoid lesions of the buccal mucosa in patients with HIV infection. Oral Surg Oral Med Oral Pathol. 1993;76(4):460-6.
16. Kim RH, Mehrazarin S, Kang MK. Therapeutic potential of mesenchymal stem cells for oral and systemic diseases. Dent Clin North Am. 2012;56(3):651–75.
17. Zhang Q, Nguyen AL, Shi S, et al. Three-dimensional spheroid culture of human gingiva-derived mesenchymal stem cells enhances mitigation of chemotherapy-induced oral mucositis. Stem Cells Dev. 2012;21(6):937–47.
18. Wu Y, Chen L, Scott PG, et al. Mesenchymal stem cells enhance wound healing through differentiation and angiogenesis. Stem Cells. 2007;25(10):2648–59.
19. El-Menoufy H, Aly LA, Aziz MT, et al. The role of bone marrow-derived mesenchymal stem cells in treating formocresol induced oral ulcers in dogs. J Oral Pathol Med. 2010;39(4):281–9.
20. Aziz Aly LA, Menoufy HE, Ragae A, et al. Adipose stem cells as alternatives for bone marrow mesenchymal stem cells in oral ulcer healing. Int J Stem Cells. 2012;5(2):104–14.
21. Shaker O, Hassan AS. Possible role of interleukin-17 in the pathogenesis of lichen planus. Br J Dermatol. 2012;166(6):1367–8.
22. Ding G, Wang W, Liu Y, et al. Mesenchymal stem cell transplantation: a potential therapy for oral lichen planus. Med Hypotheses. 2011;76(3):322–4.
23. Ryu HS, Abueva C, Padalhin A, et al. Oral ulcer treatment using human tonsil-derived mesenchymal stem cells encapsulated in trimethyl chitosan hydrogel: an animal model study. Stem Cell Res Ther. 2024;15(1):103.
24. Ghanaati H, Rouzbahani M, Golzarian J, et al. Genicular Artery Embolization Using Mesenchymal Stem Cells for the Treatment of Knee Osteoarthritis: A Prospective Study. J Vasc Interv Radiol. 2025;36(10):1523-1531.e1.
25. Saleh M, Vaezi AA, Sohrabpour AA, et al. Wharton's jelly-mesenchymal stem cells treatment for severe COVID 19 patients: 1-year follow-up. Gene Rep. 2022;29:101691.
26. Shi S, Gronthos S. Perivascular niche of postnatal mesenchymal stem cells in human bone marrow and dental pulp. J Bone Miner Res. 2003;18(4):696–704.
27. Huang M, Huang Y, Liu H, et al. Hydrogels for the treatment of oral and maxillofacial diseases: current research, challenges, and future directions. Biomater Sci. 2022;10(22):6413–46.
28. Zhou Ll, Liu W, Wu Ym, et al. Oral Mesenchymal Stem/Progenitor Cells: The Immunomodulatory Masters. Stem Cells Int. 2020;2020:1327405.

29. Li J, Wu Z, Zhao L, et al. The heterogeneity of mesenchymal stem cells: an important issue to be addressed in cell therapy. Stem Cell Res Ther. 2023;14(1):381.
30. Lalu MM, McIntyre L, Pugliese C, et al. Safety of cell therapy with mesenchymal stromal cells (SafeCell): a systematic review and meta-analysis of clinical trials. PLoS One. 2012;7(10):e47559.
31. Song SJ, Nam Y, Rim YA, et al. Comparative analysis of regulations and studies on stem cell therapies: focusing on induced pluripotent stem cell (iPSC)-based treatments. Stem Cell Res Ther. 2024;15(1):447.
32. Wei L, Yan W, Shah W, et al. Advancements and challenges in stem cell transplantation for regenerative medicine. Heliyon. 2024;10(16):e35836.
33. Műzes G, Sipos F. Mesenchymal stem cell-derived secretome: a potential therapeutic option for autoimmune and immune-mediated inflammatory diseases. Cells. 2022;11(15):2300.
34. Keshtkar S, Azarpira N, Ghahremani MH. Mesenchymal stem cell-derived extracellular vesicles: novel frontiers in regenerative medicine. Stem Cell Res Ther. 2018;9(1):63.
35. Hazrati A, Malekpour K, Soudi S, et al. CRISPR/Cas9-engineered mesenchymal stromal/stem cells and their extracellular vesicles: A new approach to overcoming cell therapy limitations. Biomed Pharmacother. 2022;156:113943.
36. Carp DM, Liang Y. Universal or Personalized Mesenchymal Stem Cell Therapies: Impact of Age, Sex, and Biological Source. Cells. 2022;11(13):2077.