

# Mesenchymal Stem Cells in Periodontal Regeneration: A Review

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## Abstract

Periodontitis is most predominantly marked and plays a vital burden in dental health as well as in systemic health. It starts from a phase of swelling on supporting structures of tooth thereafter proceeds, destruction of tissues up till damage to tooth arises. Reconstruction of defective supporting tissues in periodontium inclusive of cementum, pdl and alveolar bone is a challenging objective in periodontal regeneration therapy that can adequately diminish periodontitis caused tooth loss. In the regeneration of tooth and their supporting structures that are gone or damaged due to periodontal disease, stem cells perform an essential character. Here we talk about the primary information based on periodontal tissue regeneration using mesenchymal mother cells.

**Keywords:** Periodontitis, mesenchymal mother cells, periodontal regeneration, guided tissue regeneration (GTR).

## Introduction

Periodontium indicate to tissue which simultaneously supply and reinforce the teeth. Periodontal tissues comprise of soft tissues like gingiva, periodontal ligament along with hard tissues like alveolar bone and cementum. The construction and distribution are damaged due to miscellaneous acquired and genetic disorder, out of them periodontal disorder is most frequently seen. That leads to loss of periodontal tissue which brings about tooth damage whenever left untreated. The determined ambition about periodontal reconstruction or regeneration is to reconstruct numerous periodontal tissues inclusive of alveolar bone, cementum and periodontal ligament in impaired periodontium.<sup>1</sup>

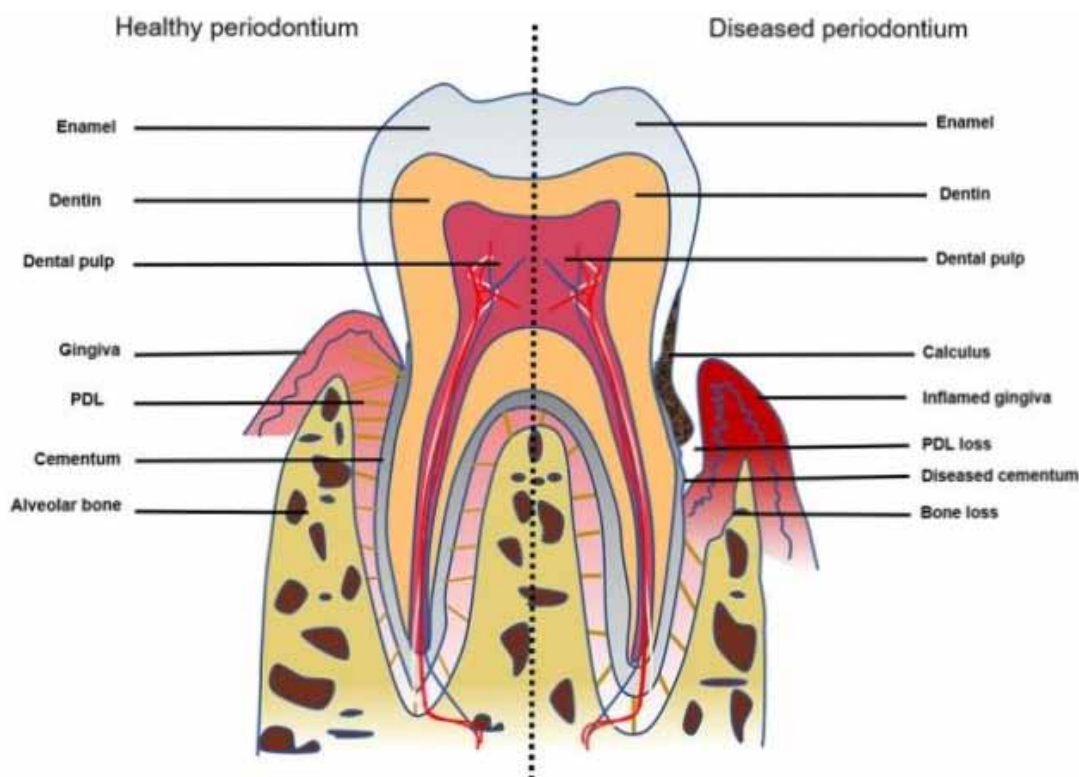
The utilization of applied science like guided tissue regeneration (GTR) towards periodontal surgery may eccentrically rebuild periodontal tissue, but still, complete consequences are not significantly satisfying and present deficiency of clinical predictability.<sup>2</sup> As modern equipment along with growth factors have improved the procedures to govern periodontal injuries, scientific investigations have disclosed that their competence is, however, questionable and the fundamental, as well as occupational reconstruction of destroyed periodontal anatomy, stays demanding. Present-day the need of mother cells is acknowledged as a prevailing approach to periodontal therapy especially for a complete reconstruction of periodontal tissues which include both rehabilitation of alveolar bone and inducing cementogenesis along with root areas including oriented introduction of freshly developed periodontal tissues.<sup>3,4</sup> This manuscript presents the essential concept of periodontitis and mesenchymal stem cells; the role of mesenchymal stem cells (MSCs) in periodontal regeneration therapy; exogenous human mesenchymal stem cell therapy and lastly immunomodulator properties of MSCs with tissue regeneration.

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**Figure 1. Healthy periodontium versus diseased periodontium**

**Periodontitis the condition:** Periodontitis is a continuing incendiary disorder of periodontium. This disorder is induced due to various microbes that produce pharmaceutical disintegration of collagen fibers of the cementum; continuous damage to PDL as well as alveolar process including raised intensity of exploration establishment; receding gums; apical shifting of junctional epithelium<sup>5</sup>. It was a condition that damages the supportive tissues of the tooth that further leads to a lack of tooth from the socket and brings about numerous periodontal problems<sup>6,7</sup>. Disproportion between favorable and harmful microbes is the most crucial factor to cause periodontitis. Dysbacteriosis in primary period which mostly caused by low oral hygiene that provokes aggregation of various microbes like *Aggregatibacter actinomycetemcomitans* (*A. actinomycetemcomitans*), *Porphyromonas gingivalis* (*P. gingivalis*), *Tannerella forsythia* (*T. forsythia*), and *Treponema denticola*.

Periodontitis may occur at different age groups. In late adolescence gingivitis is seen which includes redness and inflammation of the gingiva. In adult age group aggressive periodontitis is most commonly seen which affects mostly incisors and first molars. Chronic periodontitis is mostly seen in the elder age group where

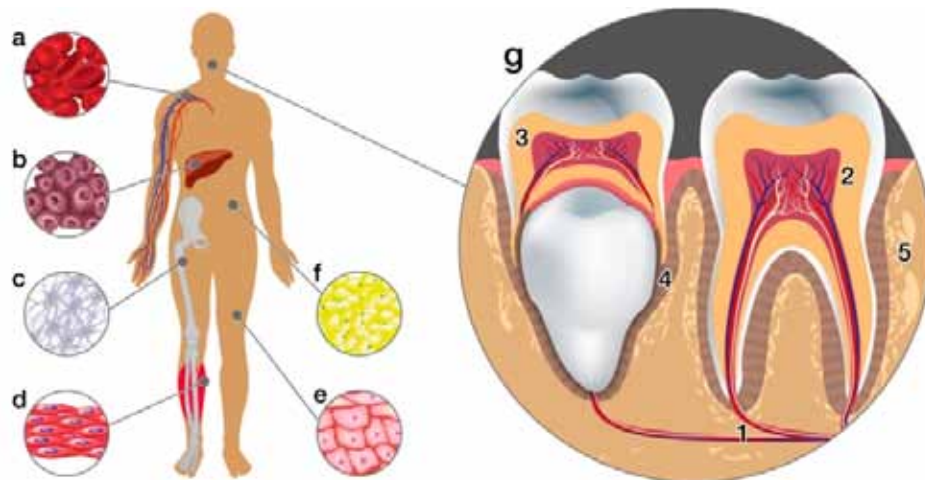
attachment loss and destruction of periodontal tissue seen.

**Mesenchymal Stem Cells:** They are grown up connective tissue cells which originating at mesoderm. MSCs are undifferentiated cells capable of self-renewal and differentiating into specialized cells. Stem cells may be confined either in the beginning periods of embryogenesis (embryonic mother cells) or within numerous Postnatal tissues (non-embryonic mother cells). As embryonic mother cells get great lifetime as well as the capability for huge differentiation, the virtuous features included in their construction put concentration on nonembryonic mother cells that are multipotent and present within almost all tissues, having the capacity for reconstruction of impaired tissues or else re-establish cell populations which are regularly getting interchangeable.<sup>8,9</sup>

MSCs are concerned with development, trauma healing, re-establishment of cells that are destroyed everyday either due to desquamation or in pharmaceutical circumstances. According to various research, it has been proven that they generate reconstruction of neural, liver as well as skeletal muscle

following infusion in pre-clinical together with objective modes.<sup>10-13</sup> Those characteristic features of MSCs lead to feasible equipment during tissue engineering along with tissue reconstruction. MSCs may be acquired from different sources of developed tissues like bone marrow,

skin, adipose tissues, and tissues of the orofacial zone. The initial cells obtained from the dental pulp of the third molar of the orofacial region<sup>14,15</sup>. They have been obtained from the periodontal ligament, deciduous teeth, apical papilla.<sup>16,17</sup>



**Figure 2: Sources of adult stem cells in human organisms; (a) Peripheral blood, (b) Liver, (c) Bone marrow, (d) Muscles, (e) Skin, (f) Adipose tissue, (g) Dental tissues: (1. Apical dental papilla, 2. Adult pulp, 3. The pulp of deciduous teeth, 4. Periodontal ligament, 5. Alveolar bone)**

**Human mesenchymal stem cells and periodontal regeneration therapy:** Currently, according to methodical analysis about the potentiality of MSCs in periodontal regeneration therapy some authors confirmed that using MSCs, periodontal reconstruction might utilize the valuable responses somewhat in the pre-clinical aspect based on modern information. While other authors fail to determine the excellent combo about MSCs, bio-materials and biomolecules of different clinical conditions by the help of animal models which are an excellent representative of the etiopathogenesis of human periodontal disease. As there is no confirmation about the source that might be better products as well as scientifically achievable in human clinical conditions, depending entirely on xenotransplantation, we should recognize the beneficial effect of MSCs in the case of sick persons. The tissue engineering procedure needs MSCs, that are obtained from bone marrow, dental pulp of the patient along with developed in vitro. For generating an osteogenic constitute, MSCs are additionally cultivated with osteogenic factors as well as a scaffold (beta-tricalcium phosphate, hydroxyapatite/tricalcium phosphate, etc.)<sup>18</sup>

Some scientific experiments have noted that the usage of human MSCs generates reconstruction of periodontal tissue. There are some experiments certified to periodontal reconstruction with the help of MSCs. Additionally, an inspection of the usage of MSCs to generate periodontal reconstruction, few investigations of gingival fibroblast-like cells, periosteum osteoblast-like cells, and periosteal cells are involved<sup>19,20</sup> even though they possibly don't perform the necessities of Universal Community of biological remedial treatment for human MSCs. There are investigations in individuals who have used homologous mesenchymal stem cells from bone marrow (BMSCs) along with established this is desirable for periodontal reconstruction.

On the other hand, even though they exhibit the potentiality of the cells to individualize former to the process of transplantation, nobody has considered the MSC immunophenotype. Based on these, Kaigler along with co-workers and Behnia along with co-workers used BMSCs to generate jaw bone restoration as well as rehabilitation of periodontal tissues, correspondingly, inducing excellent outcomes. On the other hand as both of them used BMSCs, they noted various

immunophenotypes also considered the individualization potentiality former the transplant with various specifications for the consideration. Based on clinical research d'aquino concluded that dental pulp stem cells (DPSCs) may generate a complete reconstruction of bone even though they are phonologically different from those proposed for periodontal tissue. Those cells show raised potentiality of self-expansion as well as differentiation in pre-osteoblasts. They also have a property of self-maintenance with renewal for a lengthy period. Other sources like infected pulp/adipose tissue, have been utilized in periodontal reconstruction along with appropriate outcomes.<sup>21,22</sup> Mesimaki and his co-workers utilize adipose stem cells to generate maxillary bone regeneration in elderly patients.

**Exogenous human mesenchymal stem cell therapy:** Exogenous MSCs may have the ability to manage the action of endogenous MSCs via paracrine components. Paracrine components have a great character during cell to cell communication or interplay which promote reconstruction of periodontal tissues. Based on research it is concluded that about 50 percent of cases showed analytical advancement and about 4.3 percent showed short-term reactions after MSCs infusion. But no one had harsh or dull reactions due to this therapy<sup>23</sup>. Exogenous MSCs therapy does not induce any type of crucial reactions and also there is no necessity of donor to recipient matching. In this therapy superficial or slight side effects may be seen for a short period. Utilizing human exogenous wharton's extract MSCs, survival as well as an assurance of myocardial reconstruction is an exclusive curative factor where no objective significant evidence is associated with it. It also found that epicardial or myocardial deterioration along with arrhythmias were not associated till 48 weeks which is a reason to treat with wharton's extract MSCs. As exogenous MSCs brought about noticeable advancement it is concluded that usage of exogenous MSCs therapy is desirable for reconstruction treatment of periodontal tissue.

**Immunomodulatory properties of mesenchymal stem cells and tissue regeneration:** According to various information, human MSCs may suppress in a close-dependent aspect, propagation together with cytokine reproduction of enough extrinsic immune cells like natural killer cells, T cells, B cells including dendritic cells. They discharge certain dissolved immunosuppressive components like interleukin-6, HLA-G5 together indoleamine 2,3-dioxygenase which

are included in MSC interposed immunoregulation<sup>24</sup>. Depending upon potentiality that one may construct massive description about dissolved peptides as well as proteins. MSCs may trigger adjoining parenchymal cells to diminish apoptosis, decrease tissue loss, promote progenitor cell self-renewal, trigger angiogenesis as well as promote repair. Numerous bioactive particles like enamel matrix derived growth factor; platelet-derived growth factor, plant extract (osthole, reveratol, quercetin) along with medicaments (aspirin, melatonin) are analyzed to improve results about tissue reconstruction of periodontium.<sup>25</sup>

Fu with his co-workers explained two techniques that negotiate the advantageous impacts of MSCs in periodontal tissue reconstruction. They are construction of extracellular vesicles together with the establishment of tunneling nanotubes (TNTs) which associate with various cells as well as deliver a variety of trophic components. Aliotta and his co-workers recommended that cells in the impaired tissue deliver information as mRNA to stem cells via extracellular vesicles that generate epigenetic revolution in stem cells. Sanchez together with his co-workers used MSCs of extract of Wharton along with exhibited tunneling nanotubes, that are elongate, narrow, F-actin positioned membranous mediums which associate cells along with having the potential to transfer their factors to associated cells. The utilization of those cells, even under hypothetically adverse situations will restore alveolar tissue and influence analytical advancement in patients with periodontitis.

## Conclusion

As restoration of a destructed or injured Tooth is necessary, re-establishment towards operative or active and vital teeth is the biggest auspicious beneficial approach in the field of dentistry. Re-establishment towards operative or active and vital teeth is the biggest auspicious beneficial approach as the restoration of an injured or destructed tooth is much needed<sup>26</sup>. Depending upon the tissue engineering, value towards the microorganisms, biomaterials as well as growth factors recommended for advanced perception, considering treatment of periodontal disease.

According to various experiments, it is concluded that the capability of MSCs to induce periodontal tissue regeneration may give rise to the auspicious outcome even in unfavorable situations like in the

older age group. Periodontal tissue reconstruction is a complicated process that takes place from the interaction between stem cells and biomaterials. Utilizing MSCs for treatment of damaged periodontal tissue is one of the relevant alternatives, due to the interrelation of these cells with target tissue with miraculous convenience. This manuscript emphasized on application of stem cells that repair the tissue of periodontium and increase periodontal tissue restoration as well as reconstruction.

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**Conflict of Interests:** None

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