Investigating Stem Cell-Based Regenerative Therapies for Treatment of Periodontitis

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Introduction

Periodontitis is the eleventh most prevalent medical condition worldwide affecting 20-50% of the global population. New clinical treatments are desired to generate new periodontal tissue attachment rather than the formation of long junctional epithelium. Stem cell- based regenerative therapies have been investigated as an attractive treatment approach for periodontitis. Stem/progenitor cells from various sources have been applied for periodontal regeneration via cell transplantation or tissue engineering to replace severely damaged or degenerative periodontal tissues.

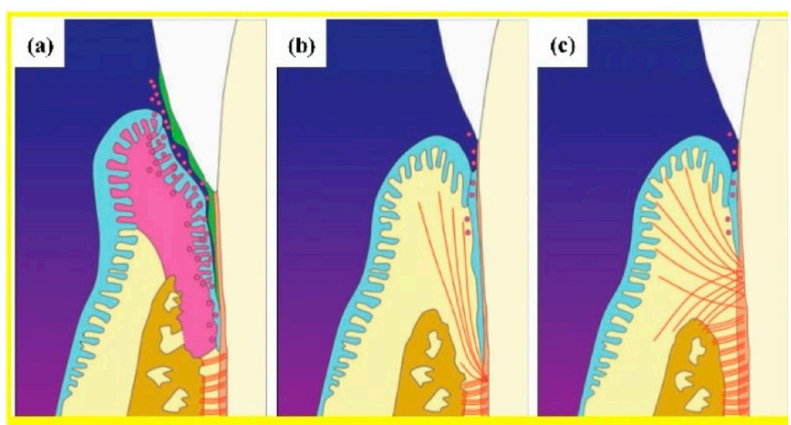
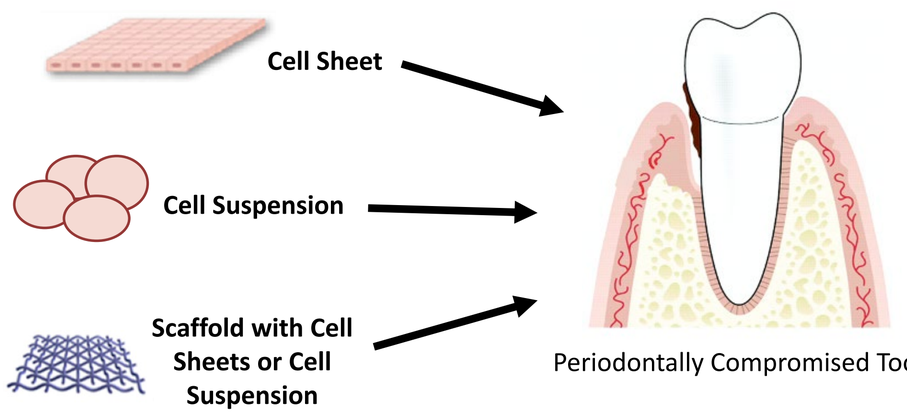


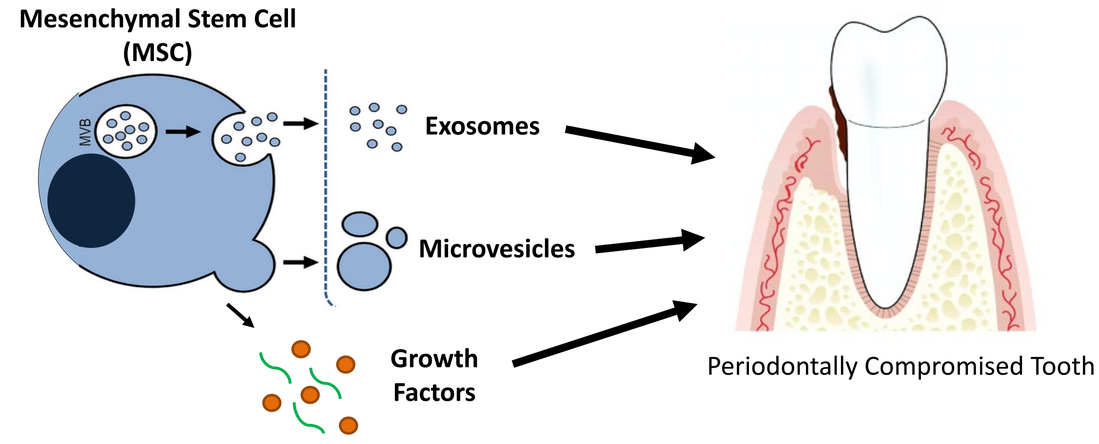
Figure from Liu, Jin et al (2019)

(a) Illustration of soft tissue inflammation and bone destruction exhibited in periodontitis
(b) Current therapeutics including guided tissue regeneration merely facilitates the formation of long junctional epithelium to reduce periodontal pocket depths
(c) Ideal periodontal ligament regenerative therapies would generate well organized fiber attachments to cementum and bone.

Stem Cell Transplantation



Stem-Cell Derived Tissue Engineering



Direct Delivery of PDLSCs

Periodontal Ligament Stem Cells (PDLSCs) are a stem cell population which reside in the perivascular space of the periodontium. They are commonly used in periodontal tissue regeneration due to their multilineage differentiation potential, anti-inflammatory properties, and ability to grow clonally. Pre-clinical studies, carried out using different animal in vivo models, show promising results regarding the effectiveness of PDLSCs in regeneration of the periodontal complex.

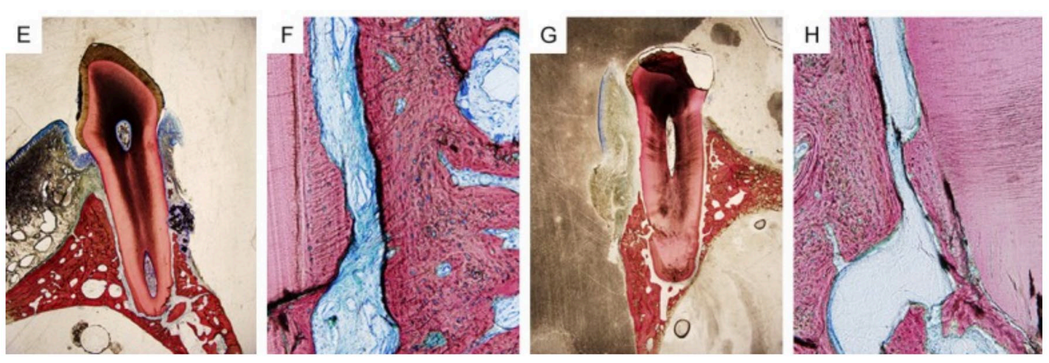


Figure from Shi, H et al (2018)

In a study conducted by Shi, H et al, PDLSCs were cultured, osteogenically induced and then seeded on a biphasic calcium phosphate scaffold. Then the PDLSC-seeded scaffolds were transplanted into six dogs with periodontitis. The results shown in the figures above demonstrate that the transplantation of PDLSC-seeded BCP (Figures E and F) promoted effective periodontal regeneration. Figures E and F are H&E stains of the experimental group which demonstrate new bone formation and PDL with reorganized and reborn collage fibers inserting into adjacent cementum and bone at the right angle, along with abundant blood vessels at 12 weeks as compared to the control group which received no therapy (Figures G and H).

Use of BMSC-derived Extracellular Vesicles

Although direct cell delivery has shown regenerative potential in the treatment of periodontal defects, the clinical translation of cell therapies has been hampered by challenges in cell expansion and viability, storage, delivery to patients, and safety. A new approach utilizes the paracrine factors derived from Mesenchymal Stem Cells (MSCs), such as extracellular vesicles and growth factors, to stimulate tissue repair by host cells, rather than through cell replacement.

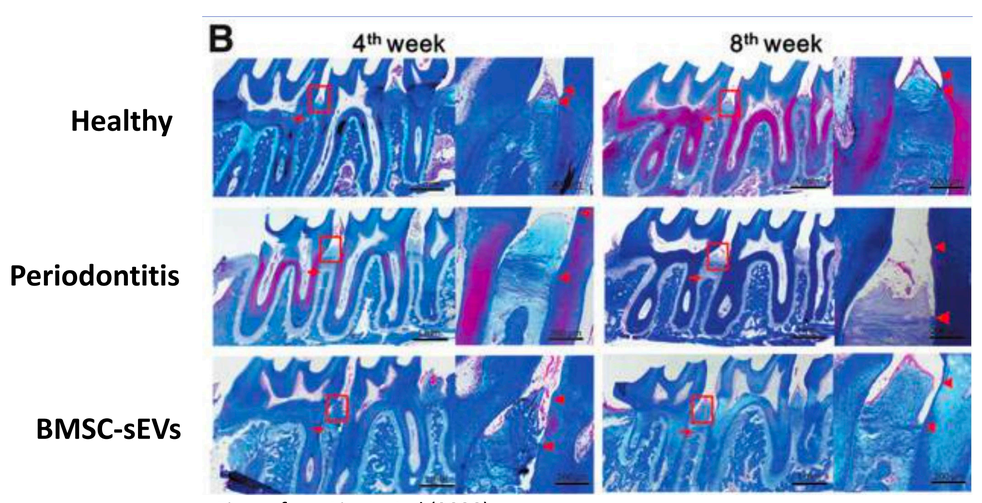


Figure from Liu, L et al (2020)

Liu, L et al used Bone Marrow Mesenchymal Stem Cell (BMSC)-derived small extra-cellular vesicles (BMSC-sEVs) to stimulate periodontal repair in an experimental periodontitis rat model. The BMSC-sEV loaded by hydrogel was injected into experimental periodontitis rats to verify the therapeutic effect. Masson Trichrome staining in Figure B illustrate that the BMSC-sEV hydrogel conditions decreased fiber destruction and the epithelial downgrowth along the root surfaces compared to the periodontitis group.

Conclusion

Stem cell-based periodontal tissue engineering applications for periodontal regeneration have made promising progress. However, the application of direct stem cell delivery still faces numerous challenges, including the safety of cell expansion in vitro, inherent immunogenicity, precision of scaffold materials, cytocompatibility, and material degradation. Cell-free therapies such as the use of growth factors and extracellular vesicles to promote endogenous regeneration in organisms has partially addressed the limitations of cell therapy. However, defining proper treatment doses and potency of exosome activity require additional studies. Stem cell-based regenerative therapies pose an exciting new treatment approach to greatly enhance the periodontal bone-ligament-cementum regeneration efficacy.

References

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