Evaluation Of Regenerative Potential Of Pulp -derived Stem Cells And Gingival-derived Stem Cells In The Regeneration Of Periodontal Defects

(Experimental study)

Submitted in partial fulfillment of the requirements of Master Degree in Oral Medicine, Periodontolgy, and Oral Diagnosis

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Aim of the study

To compare the regenerative potential of pulp derived stem cells and gingival derived stem cells in periodontal alveolar defects.

- **Clinically:**

  In terms of probing depth (PD), clinical attachment loss (CAL), and defect size (DS).
- **Histologically.**
- **Histomorphometrically:**

  In terms of optical density, number of osteoblasts, and area percentage of the newly formed bone.

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Abbreviations

ALP: Alkaline phosphatase**.**

ASCs: Adipose stem cells**.**

bFGF: Basic fibroblast growth factor.

BMPs: Bone morphogenetic proteins.

BMSSCs: Bone marrow stromal stem cells**.**

CaP: Calcium phosphate.

CD: Cluster of Differentiation.

CFU-Fs: Colony forming units-fibroblastic.

Col: Collagen**.**

DFCs: Dental follicle progenitor cells**.**

DMEM: Dulbecco's Modified Eagle's Medium.

DPSCs: Dental pulp stem cells**.**

DSPP: Dentin sialophospohoprotein**.**

ECM: Extracellular matrix**.**

EDTA: Ethylenediaminetetraacetic acid.

EMD: Enamel matrix derivative**.**

ES: Embryonic stem cell.

FBS: Fetal Bovine Serum.

FGF: Fibroblast growth factor**.**

GF: Gingival fibroblast**.**

GMSC: Gingival mesenchymal stem cells.

GTR: Guided tissue regeneration.

H&E: Hematoxylin and Eosin.

HA/TCP: Hydroxyapatite/tricalcium phosphate**.**

HA: Nanohydroxyapatite.

HBSS: Hank's Balanced Salt Solution.

HEPES: Hydroxyethyl piperazine ethanesulfonic acid.

HLA class II: Human Leukocyte Antigen class II.

IGF-I: Insulin-like growth factor-I.

iPS: induced pluripotent stem**.**

IV: Intravenous.

KLF4: Kruppel-like factor 4.

LAB: Living autologous bone**.**

MEM: Minimum Essential Medium.

MMP: Matrix metalloproteinase.

MSCs: Mesenchymal stem cells.

OCT3/4: Octamer binding transcription factor 3/4.

PBS: Phosphate buffered saline.

PDGF: Platelet-derived growth factor.

PDL: Periodontal ligament.

PDLSCs: Periodontal ligament stem cells.

PGA: Poly glycolic acid.

PLA: Poly lactic acid.

PLGA: Poly lactic-co-glycolic acid.

rpm: Revolutions per minute.

SBP-DPSCs: Stromal Bone Producing Dental Pulp Stem Cells**.**

SCAP: Stem cells from apical papilla**.**

SCF: Stem cell factor**.**

SHED: Stem cells from exfoliated deciduous teeth**.**

SSEA-4: Stage-specific embryonic antigen-4.

SubQ: Subcutaneous.

TGF: Transforming growth factor.

β-TCP: Beta-tricalcium phosphate.

Introduction and Review of Literature

Periodontitis is one of the most wide spread chronic inflammatory diseases, and it progressively destroys the tooth-supporting structure, which consists of the gingiva, periodontal ligament (PDL), alveolar bone, and root cementum. If left untreated, periodontitis may eventually lead to the loosening and subsequent loss of teeth.[1]

The ideal goal of periodontal therapy is to regenerate these lost tissues to their original form, architecture and function, which poses a challenging task, requiring the harmonization of many cellular and molecular events.[2] Periodontal regeneration can be defined as the complete restoration of the lost tissues to their original architecture and function by recapitulating the crucial wound healing events associated with their development.[3]

Healing following conventional periodontal therapy is more complicated than simple soft tissue healing because of the involvement of mineralized tissues (i.e., cementum and bone) in addition to soft tissue components. Most mechanical and surgical periodontal procedures (e.g., scaling, debridement and flap procedures of various types) favor the healing of anatomical defects produced by periodontitis. This largely involves repair of the gingival connective tissues and the coronal portion of the periodontal ligament with virtually no repair of the cementum or alveolar bone. These events, by definition, do not constitute regeneration of the periodontium.[4] Indeed, healing after flap surgery is mediated by a range of reparative responses, none of which can be considered to be tissue regeneration. For regeneration to occur, healing events should progress in an ordered and programmed sequence both temporally and spatially, replicating the key events in periodontal development[2,5] (Table 1).[6] The course of healing is dependent on the availability of appropriate cells, inductive factors and extracellular matrix secreted by these cells.[7] Progenitor and stem cells are of particular interest in periodontal wound healing and regeneration as they are most likely the parental cells of synthetic cells (e.g., osteoblasts, cementoblasts and fibroblasts) responsible for the restoration of lost periodontal tissues (Fig.1).[8-10]

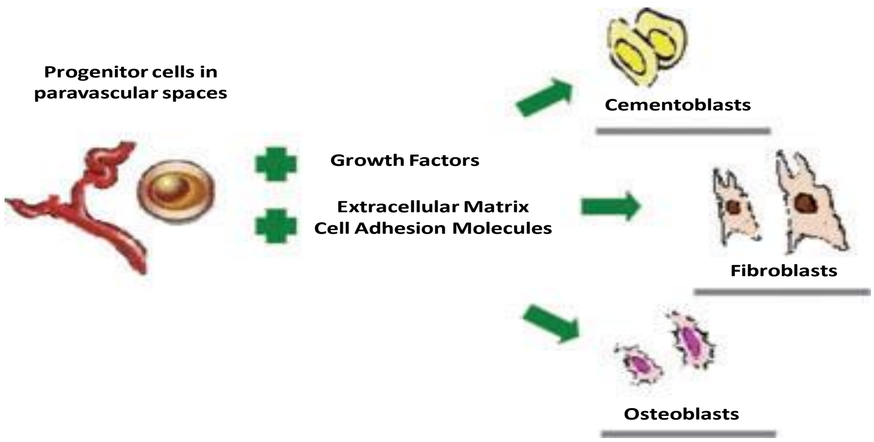

Fig.1. The role of stem cells in periodontal regeneration. Cells in the paravascular areas of mature periodontal ligament have the potential to differentiate into mature osteoblasts, periodontal ligament fibroblasts and cementoblasts.[6]

Table 1. Possible periodontal wound healing responses[6]	
Repair	Control of inflammation. Long junctional epithelium. Connective tissue attachment to the root surface (reattachment or new attachment). New bone separated from the root surface by long functional epithelium. New bone with root resorption or ankylosis or both.
Regeneration	New functional attachment apparatus with formation of cementum, periodontal ligament and alveolar bone.