

Dental Stem Cells: Potential in Regenerative Endodontics and Periodontics

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ABSTRACT

One of the most exciting technologies that are gaining popularity in regenerative dentistry is dental stem cells because of their unique ability to self-renew, differentiate into multiple lines, and repair tissue. Dental stem cells that come from different sources like dental and oral tissues have the potential to regenerate dentin, pulp, periodontal ligament, cementum, and alveolar bone. Regenerative endodontics and periodontics are increasingly becoming more popular today as minimally invasive biological solutions focused on reconstructing and restoring the structure and function of affected oral tissues instead of replacing them.

Regeneration therapy using dental stem cells can be effectively used in regenerative endodontics in revitalization therapy, pulp-dentin complex regeneration, apexogenesis, and immature necrotic teeth treatment. Likewise, regeneration therapy can be utilized in periodontics in regenerating lost periodontal ligament, alveolar bone, and cementum resulting from periodontal disease.

In spite of all the positive results obtained from experimental and clinical researches, there is still room for improvement in regard to the problems of cell isolation, immunological compatibility, ethics issues, cell stability, and clinical standardization. The current review article gives an extensive description of different types of dental stem cells, biological properties, functioning, and possible areas of application of these cells in dentistry.

KEYWORDS: DENTAL STEM CELLS; REGENERATIVE ENDODONTICS; PERIODONTAL REGENERATION; TISSUE ENGINEERING; PULP REGENERATION; MESENCHYMAL STEM CELLS.

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INTRODUCTION

Traditional methods for treating dental problems mainly involve replacing damaged tissues using synthetic materials. Although these traditional treatments can restore normal tissue functions, they cannot

replace the biological and physiological functions of natural tissues. This is where regenerative dentistry comes into play, as it involves restoring lost natural oral tissues by using various biological approaches involving stem cells, biomaterials, and bioactive substances.¹

Stem cells are undifferentiated cells that have the ability to regenerate themselves and transform into differentiated cell types. Several types of stem cells have been identified, but dental stem cells have been gaining considerable attention due to their easy availability and minimal invasiveness.² These cells belong to the category of mesenchymal stem cells and can form different cell types including odontogenic, osteogenic, chondrogenic, adipogenic, and neurogenic cells.³

The finding of DPSCs in 2000 is one of the landmarks in the development of regenerative dentistry. Later on, several other sources of dental stem cells have been

discovered, including SHED, PDLSCs, SCAP, and DFPCs. Nowadays, researchers actively study the potential use of these stem cells in regenerative endodontics and periodontics.⁴

Regenerative endodontics involves restoration of the pulp-dentin complex in necrotic immature teeth to achieve root maturation and pulp regeneration. Periodontics utilizes stem cell-based therapies for reconstruction of the periodontal tissues damaged due to inflammatory diseases. A combination of dental stem cells, appropriate scaffolds, and growth factors represents the essence of tissue engineering in modern dentistry

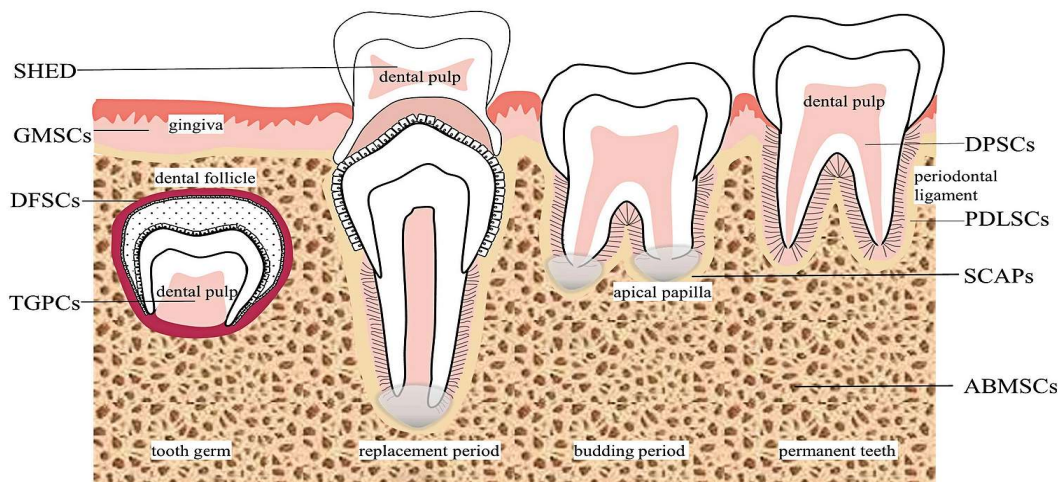


Fig 1: Sources and localization of dental-derived stem cells in regenerative dentistry

TYPES OF DENTAL STEM CELLS

1. Dental Pulp Stem Cells (DPSCs)

These stem cells are derived from the dental pulp tissue of permanent teeth. DPSCs are highly proliferative and have the ability to differentiate into odontoblast-like cells that form dentin. Furthermore, these stem cells show angiogenesis and neurogenesis, thus

making them suitable for endodontic procedures involving regeneration.⁶

Features of DPSCs:

- Self-renewal
- Odontogenic differentiation
- Angiogenesis
- Neuro regeneration
- Readily accessible from tooth extraction⁷

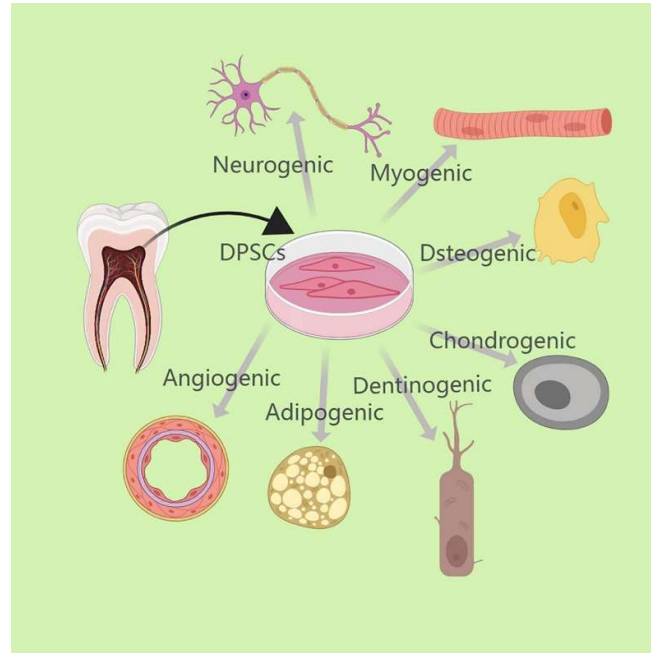


Fig 2: Multilineage differentiation potential of dental pulp stem cells (DPSCs)

2. Stem Cells from Human Exfoliated Deciduous Teeth (SHED)

SHED is derived from the pulp tissues of deciduous teeth and show higher proliferation rates than DPSCs. SHED can differentiate into neural cells, odontoblasts, adipocytes, and osteoblasts.

Significance:

- Faster proliferation
- Osteogenesis
- Application in craniofacial tissue regeneration
- Pediatric applications^{8,9}

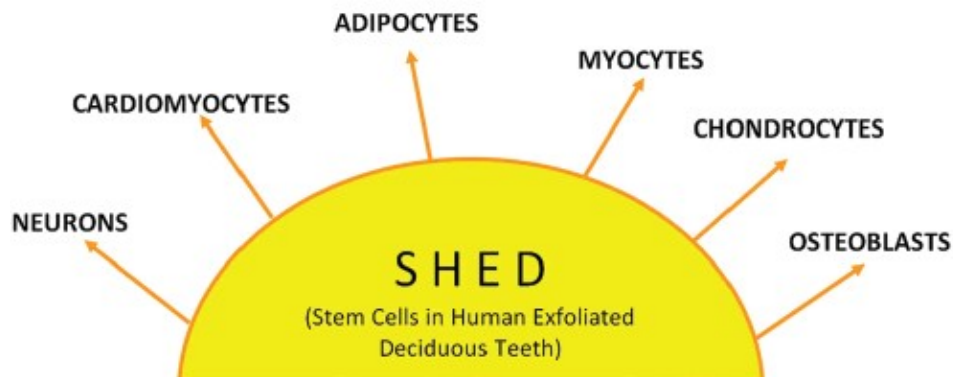


Fig 3: Differentiation potential of stem cells from human exfoliated deciduous teeth (SHED)

3. Periodontal Ligament Stem Cells (PDLSCs)

PDLSCs are isolated from periodontal ligament tissues and are particularly important in periodontal regeneration. These cells can differentiate into cementoblast-like cells, fibroblasts, and osteoblasts.

Applications:

- Periodontal ligament regeneration
- Cementum formation
- Alveolar bone regeneration
- Treatment of periodontal defects^{10,11}

4. Stem Cells from Apical Papilla (SCAP)

SCAP are found at the apex of immature permanent teeth and possess excellent proliferative capacity. These cells are considered crucial in regenerative endodontic procedures because they contribute to root development and dentin formation.¹²

Advantages:

- High survival rate
- Enhanced dentin formation
- Important role in root maturation
- Superior proliferative potential

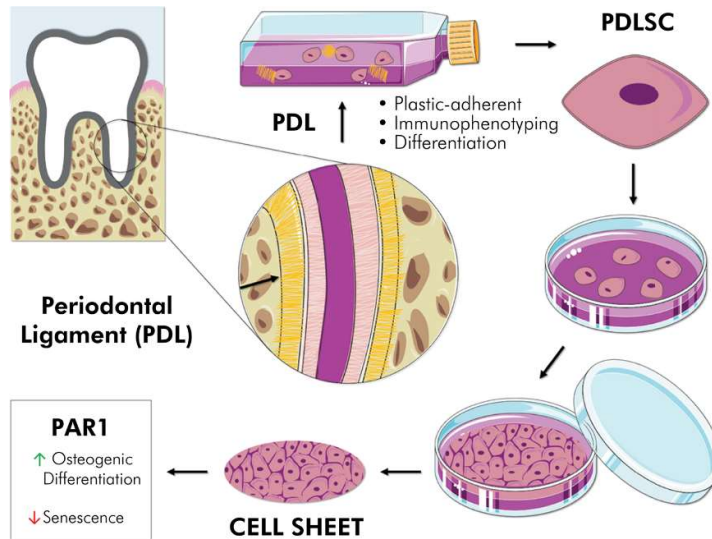


Fig 4: Isolation, characterization, and regenerative application of periodontal ligament stem cells (PDLSCs)

5. Dental Follicle Progenitor Cells (DFPCs)

DFPCs originate from the dental follicle surrounding developing teeth. These stem cells contribute to the formation of periodontal tissues and alveolar bone.¹³

Clinical Uses:

- Periodontal tissue engineering
- Bone regeneration
- Bio-root engineering¹⁴

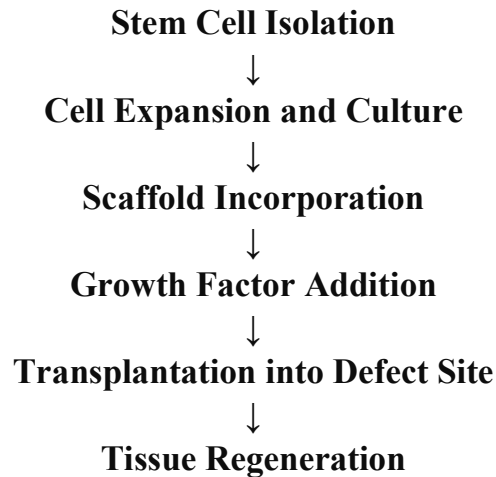
BIOLOGICAL BASIS OF DENTAL TISSUE ENGINEERING

Regenerative dentistry relies on the triad of:

1. Stem Cells

2. Scaffolds
3. Growth Factors¹⁵

Flowchart Representation:



The interaction among these three components determines the success of regenerative therapy.¹⁶

ROLE OF SCAFFOLDS IN REGENERATIVE DENTISTRY

Scaffolds provide a three-dimensional framework that supports cell adhesion, proliferation, and differentiation. An ideal scaffold should be biocompatible, biodegradable, porous, and capable of promoting vascularization.^{17,18}

Types of Scaffolds

Natural Scaffolds:

- Collagen
- Fibrin
- Hyaluronic acid
- Chitosan

Synthetic Scaffolds:

- Polylactic acid (PLA)
- Polyglycolic acid (PGA)
- Hydroxyapatite composites
- Bioactive ceramics^{19,20}

GROWTH FACTORS IN DENTAL REGENERATION

Growth factors regulate proliferation and differentiation of cells in tissue regeneration.

Most Common Growth Factors Used in Regenerative Endodontics and Periodontics

Growth factors are biological molecules that have the ability to regulate cellular activities such as proliferation, migration, differentiation, and formation of blood vessels and extra-cellular matrix.^{21,22} These factors have great significance in regenerative endodontics and periodontics since their activities help in initiating tissue regeneration and repair through activation of stem cells and other surrounding cells. The process of regeneration of pulp, dentin, periodontal ligament, cementum and alveolar bone is highly dependent on the activity of these growth factors.²³

Bone Morphogenetic Proteins (BMPs)

Bone morphogenetic proteins are members of the transforming growth factor-beta family and among the most potent osteogenic molecules known in regenerative dentistry.

Important Types

- BMP-2
- BMP-4
- BMP-7

Mechanism of Action

BMPs bind to specific receptors on stem cells and activate intracellular signaling pathways that regulate osteogenesis and dentinogenesis. They enhance the expression of genes responsible for mineralized tissue formation.²⁴

Applications in Dentistry

Regenerative Endodontics:

- Induction of reparative dentin formation
- Pulp-dentin complex regeneration
- Root development in immature teeth

Periodontics:

- Alveolar bone regeneration
- Periodontal defect repair
- Implant site development

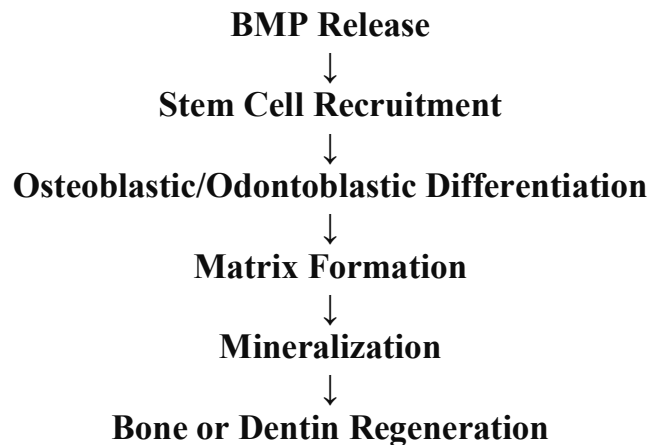
Clinical Advantages:

- Strong osteogenic potential
- Enhanced bone maturation
- Improved periodontal regeneration
- Promotion of angiogenesis indirectly²⁵

Limitations:

- High cost
- Risk of excessive calcification
- Dose-dependent complications
- Short biological half-life

Flowchart Representation:



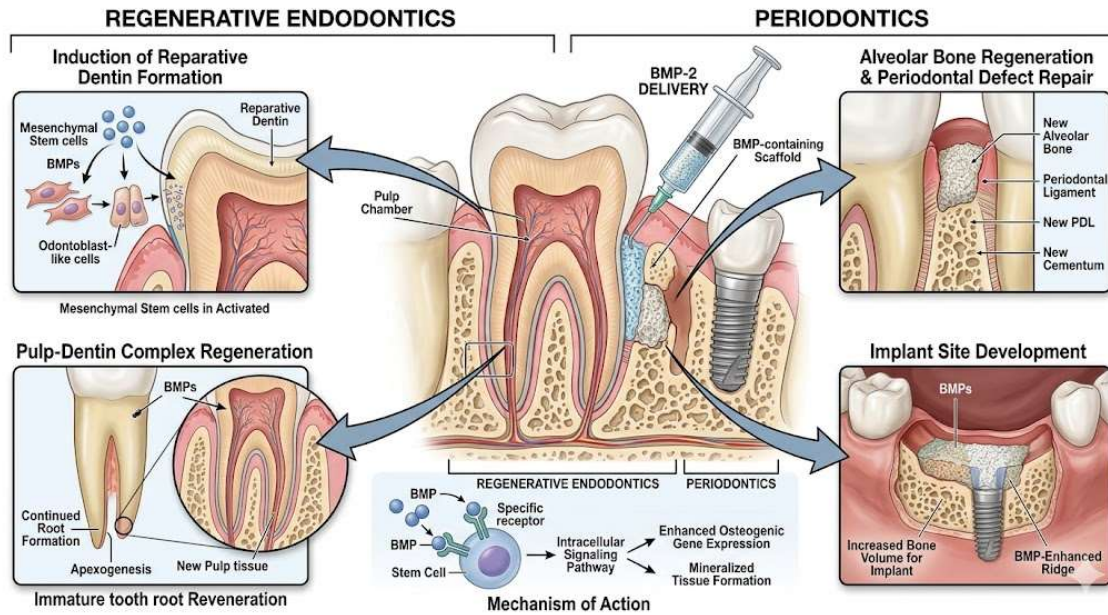


Fig 5: Role of BMP in Periodontics and Endodontics

Transforming Growth Factor-Beta (TGF-β)

Transforming growth factor-beta is a multifunctional cytokine involved in tissue healing, extracellular matrix production, and regulation of inflammation. TGF-β is naturally stored in dentin matrix and released during dentin demineralization or injury.²⁶

Important Isoforms

- TGF-β1
- TGF-β2
- TGF-β3

Biological Functions:

- Regulation of stem cell proliferation
- Collagen synthesis stimulation
- Modulation of inflammatory responses
- Promotion of odontoblast differentiation

Role in Regenerative Endodontics

TGF-β stimulates dental pulp stem cells to differentiate into odontoblast-like cells capable of producing tertiary dentin. It also contributes to pulp healing following restorative procedures.

Role in Periodontal Regeneration

- Promotes fibroblast proliferation
- Enhances extracellular matrix deposition
- Supports periodontal ligament healing
- Encourages connective tissue attachment

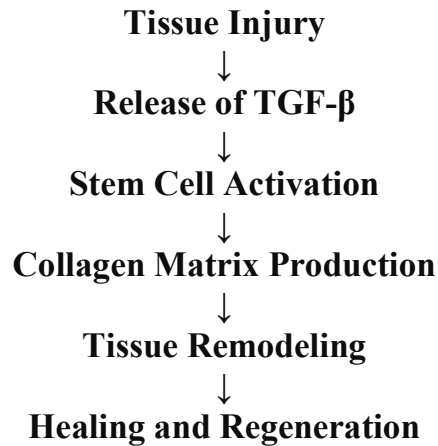
Clinical Significance

TGF-β is particularly important in wound healing and soft tissue regeneration because it regulates both inflammatory and reparative phases of healing.

Limitations

- Excessive fibrosis in high concentrations
- Complex signaling pathways
- Variable clinical outcomes

Flowchart Representation:



Platelet-Derived Growth Factor (PDGF)

PDGF is a powerful mitogenic and chemotactic factor released primarily from platelets during tissue injury. It plays a major role in wound healing and periodontal regeneration.²⁷

Biological Functions

- Cellular migration
- Angiogenesis stimulation
- Fibroblast proliferation
- Collagen synthesis
- Bone regeneration

Applications in Periodontics

PDGF is widely used in periodontal regenerative procedures because it enhances periodontal ligament cell proliferation and accelerates healing.

Applications in Endodontics

- Enhancement of pulp healing
- Support of angiogenesis
- Recruitment of progenitor cells

Sources

PDGF is commonly delivered through:

- Platelet-rich plasma (PRP)
- Platelet-rich fibrin (PRF)
- Recombinant growth factor preparations

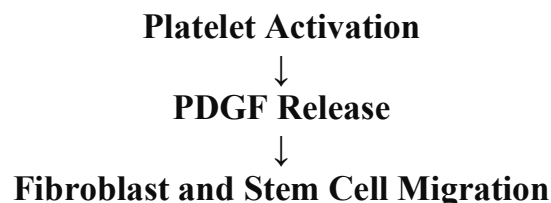
Clinical Benefits

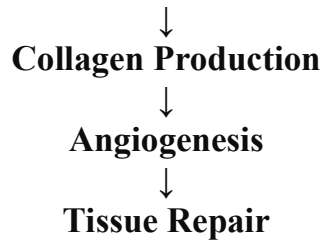
- Faster wound healing
- Improved bone fill
- Enhanced soft tissue regeneration
- Better attachment gain

Limitations

- Short duration of activity
- Need for controlled delivery systems
- Variable concentration in autologous preparations

Flowchart Representation:





Vascular Endothelial Growth Factor (VEGF)

VEGF is one of the most important growth factors responsible for angiogenesis, which is essential for successful tissue regeneration. Newly formed blood vessels provide nutrients, oxygen, and immune defense to regenerating tissues.

Biological Functions

- Formation of new blood vessels
- Increased vascular permeability
- Endothelial cell proliferation
- Enhanced tissue survival

Role in Regenerative Endodontics

In pulp regeneration, angiogenesis is critical because regenerated pulp tissue requires a vascular supply for long-term survival. VEGF enhances revascularization inside the root canal system.

Role in Periodontics

- Improved blood supply to healing tissues
- Enhanced bone regeneration
- Better integration of graft materials

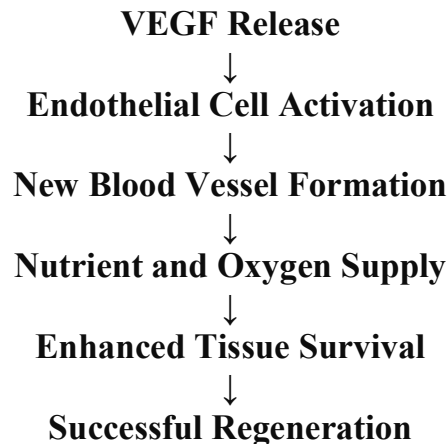
Clinical Importance

VEGF significantly improves survival of transplanted stem cells and accelerates tissue maturation.

Limitations

- Excessive vascularization may occur
- Instability in delivery systems
- Rapid degradation in vivo

Flowchart Representation:



Fibroblast Growth Factor (FGF)

Fibroblast growth factors constitute a large family of signaling proteins involved in tissue development, angiogenesis, and wound healing. FGF-2 is particularly important in regenerative dentistry.²²

Biological Functions

- Cell proliferation

- Angiogenesis
- Collagen synthesis
- Tissue remodeling
- Stem cell maintenance

Applications in Regenerative Endodontics

FGF promotes proliferation of dental pulp stem cells and enhances formation of vascularized pulp-like tissue.

Applications in Periodontics

- Periodontal ligament regeneration
- Bone formation
- Gingival tissue healing
- Cementum repair

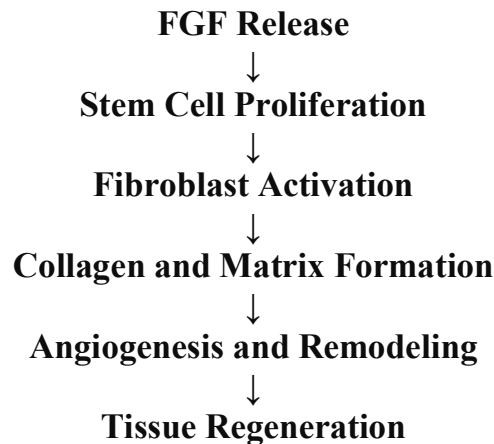
Clinical Advantages

- Accelerated healing
- Enhanced vascularization
- Improved stem cell survival
- Better tissue organization

Limitations

- Short half-life
- Need for sustained-release scaffolds
- Sensitivity to degradation

Flowchart Representation:



Combined Role of Growth Factors in Regenerative Dentistry

Growth factors rarely function independently. Instead, they work synergistically to regulate various stages of tissue healing and regeneration.

Growth Factor	Main Function	Major Dental Application
BMPs	Hard tissue formation	Bone and dentin regeneration
TGF-β	Matrix synthesis and healing	Pulp and periodontal healing
PDGF	Cell migration and proliferation	Periodontal regeneration
VEGF	Angiogenesis	Pulp revascularization
FGF	Cell proliferation and remodeling	Soft tissue and ligament repair

The controlled delivery of these growth factors using scaffolds and biomaterials represents one of the most promising approaches in modern regenerative dentistry.

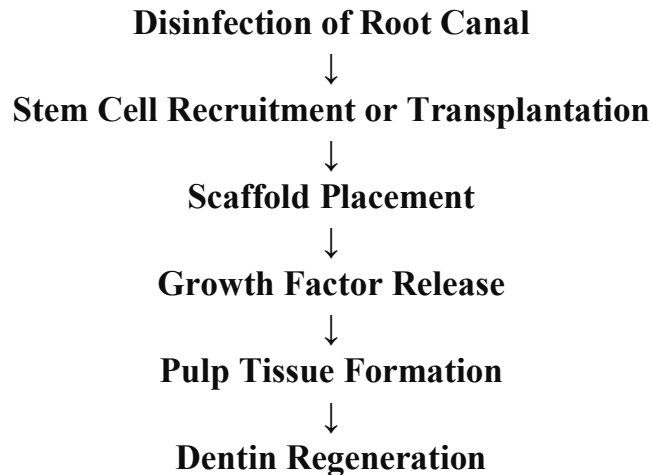
These molecules enhance angiogenesis, matrix formation, and tissue healing.^{23,25}

APPLICATIONS IN REGENERATIVE ENDODONTICS

Pulp-Dentin Complex Regeneration

One of the primary goals of regenerative endodontics is the regeneration of functional pulp tissue capable of producing dentin. Dental stem cells seeded into scaffolds can differentiate into odontoblast-like cells and regenerate dentinal tissue.

Mechanism:



This process restores vitality and immune defense mechanisms within the tooth.

Revitalization Procedures

Regenerative endodontic procedures (REPs) are widely used in immature necrotic teeth. The induction of bleeding into the root canal introduces stem cells from apical papilla, which contribute to continued root development.

Advantages

- Increased root length
- Thickening of dentinal walls
- Apical closure
- Restoration of vitality

Apexogenesis and Apexification

Stem cell-based therapies can improve apexogenesis by preserving pulp vitality and promoting physiological root development. In cases requiring apexification, regenerative methods may provide more biological outcomes compared to traditional calcium hydroxide techniques.

Regeneration of Periapical Tissues

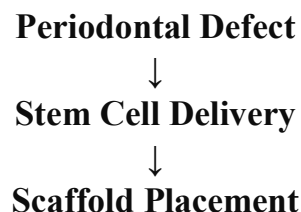
Dental stem cells can contribute to the healing of periapical lesions by reducing inflammation and promoting bone regeneration around the root apex.

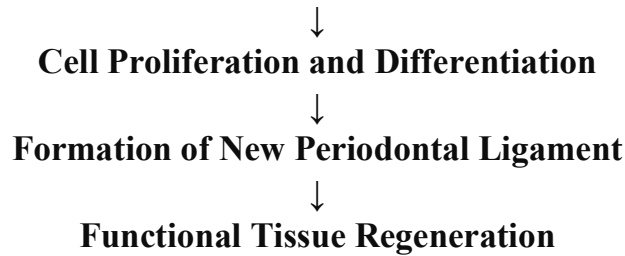
APPLICATIONS IN PERIODONTICS

Periodontal Ligament Regeneration

Periodontal disease leads to destruction of periodontal ligament fibers, cementum, and alveolar bone. PDLSCs have shown promising results in regenerating these tissues.

Flowchart Representation:





Cementum Regeneration

Stem cells can differentiate into cementoblast-like cells and aid in the formation of new cementum, which is essential for periodontal attachment.

Alveolar Bone Regeneration

Osteogenic differentiation of dental stem cells plays a critical role in regenerating alveolar bone lost due to periodontal disease, trauma, or tooth extraction.

Clinical Benefits

- Improved bone density
- Enhanced implant stability
- Better periodontal support
- Reduced pocket depth

Treatment of Intrabony Defects

Stem cell therapy combined with guided tissue regeneration techniques has demonstrated improved clinical attachment levels and bone fill in intrabony defects.

IMMUNOMODULATORY PROPERTIES OF DENTAL STEM CELLS:

Dental stem cells possess anti-inflammatory and immunomodulatory effects. They can regulate immune responses by secreting cytokines and growth factors that suppress inflammation and promote healing.²⁴

Clinical Importance

- Reduction in inflammatory tissue destruction
- Improved wound healing
- Enhanced tissue integration
- Reduced postoperative complications

ADVANTAGES OF DENTAL STEM CELL THERAPY:

Advantage	Clinical Significance
Biocompatibility	Reduced immune rejection
Regenerative Potential	Restoration of natural tissues
Minimally Invasive	Less surgical trauma
Multilineage Differentiation	Formation of multiple tissue types
Easy Accessibility	Stem cells obtainable from extracted teeth
Improved Healing	Faster tissue repair

CHALLENGES AND LIMITATIONS:

Ethical and Legal Constraints

While dental stem cells do not present ethical problems as embryonic stem cells, securing regulatory approval and standardizing clinical applications are still formidable tasks.

Expensive Treatment

The processes of extracting, storing, and manipulating stem cells come at a considerable cost.

Sensitive Procedure

Regenerative techniques require stringent aseptic precautions and accurate clinical procedures.

Short Follow-Up Studies

Most data available today comes from experimental research and short follow-up clinical trials. The long-term effects are unknown.

Contamination Risk

Inadequate stem cell culturing procedures could result in bacterial infection and reduced viability.

POTENTIAL FUTURES:

Potential developments in regenerative dentistry may encompass:

- In-chair stem cell manipulation devices
- Genetically engineered stem cell therapy
- Bioprinting of dental structures
- Scaffolds created using nanotechnology
- Individualized regenerative treatment
- Tissue engineering with artificial intelligence

Advanced bioprinting methods could one day facilitate the biological restoration of teeth through stem cells and biomimetic scaffolds.^{28,29}

CONCLUSION:

The use of dental stem cells is considered a major advance in regenerative dentistry owing to their unique regenerative and immunomodulatory properties. The potential of dental stem cells in regenerative endodontics and periodontics has yielded positive results in repairing damaged dental and periodontal tissues. Combining stem cells with scaffolding and growth factors has greatly increased the range of biological treatments in dentistry.

Despite various problems and difficulties in clinical practice, advances in tissue engineering, biomaterial science, and molecular biology will likely make stem cell-based treatments more predictable and effective. In the future, regenerative dentistry may revolutionize traditional methods of treatment through biological regeneration of tissues instead of artificial replacement.

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