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# Stem Cells in Endodontics: A Review

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## ABSTRACT

This review discusses the potential applications of stem cells in endodontics, focusing on their role in dental pulp regeneration and repair. Stem cells, including dental pulp stem cells (DPSCs), stem cells from apical papilla (SCAP), and other mesenchymal stem cells (MSCs), offer significant promise for developing regenerative endodontic procedures. The literature highlights their capacity for self-renewal, multipotency, and the influence of various growth factors on their differentiation. This review aims to synthesize current research findings, evaluate clinical implications, and identify future directions in the integration of stem cell therapies in endodontic practice.

## INTRODUCTION

Regenerative dentistry represents an emerging frontier in dental science, focusing on the restoration or replacement of damaged oral tissues through stem cell therapy, tissue engineering, and biomimetic materials.[1] while traditional dental procedures like root canals, bone grafting, and prosthetic replacements have significantly improved patient care, they often fall short in fully regenerating the functionality and architecture of lost tissues. In contrast, regenerative strategies harness the potential of stem cells, particularly mesenchymal stem cells (MSCs), to recreate the structure and function of vital tissues, including dentin, pulp, periodontal ligament, and alveolar bone. Dental stem cells (DSCs), such as dental pulp stem cells (DPSCs), stem cells from human exfoliated deciduous teeth (SHEDs), and stem cells from the apical papilla (SCAPs), possess immunomodulatory and anti-inflammatory properties, as well as the ability to differentiate into multiple cell types. Consequently, these cells have become integral to regenerative strategies across various disciplines, including endodontics, periodontology, oral surgery, and beyond.[2,3] This review aims to synthesize current research findings, evaluate clinical implications, and identify future directions in the integration of stem cell therapies in endodontic practice.

**Types of Stem Cells: Origins and Classification**

Stem cells are remarkable due to their unique ability to self-renew and differentiate into specialized cell types. These properties make them an invaluable tool in regenerative medicine, including in the field of endodontics, where they are being explored for their potential to regenerate dental tissues, particularly the dental pulp. Understanding the different types of stem cells, their origins, and how they are classified is essential to fully comprehend their role in regenerative endodontics.[3,4]

Stem cells are generally classified based on their **potency**, which refers to their ability to differentiate into various cell types. The main categories are:

**Totipotent Stem Cells**: These are the most versatile type of stem cells. They have the potential to differentiate into any cell type in the body, including extra-embryonic tissues such as the placenta. Totipotent stem cells are formed early in embryonic development from the zygote (the fertilized egg).

**Pluripotent Stem Cells**: Pluripotent stem cells can differentiate into any of the three primary germ layers (ectoderm, mesoderm, and endoderm) and therefore have the ability to generate virtually all cell types in the body, but they cannot form extra-embryonic tissues. Embryonic stem cells (ESCs) are classic examples of pluripotent cells.

**Multipotent Stem Cells**: These stem cells are more specialized than pluripotent stem cells but can still differentiate into a range of related cell types. An example of multipotent stem cells are **mesenchymal stem cells (MSCs)**, which can differentiate into a variety of cells such as osteoblasts, chondrocytes, adipocytes, and odontoblasts (the cells responsible for dentin formation in the teeth). Dental stem cells, such as dental pulp stem cells (DPSCs), are also considered multipotent.

**Unipotent Stem Cells**: These stem cells can only differentiate into one cell type, although they still possess the ability to self-renew. While these are the most limited in differentiation potential, they still play an essential role in tissue regeneration and repair.

In the context of endodontics, multipotent stem cells, particularly those derived from dental tissues, are the most relevant due to their potential to regenerate dental tissues such as pulp, dentin, and periodontal ligament.

**Stem Cells in Dental Pulp: Sources and Characteristics:** The dental pulp is a soft tissue located at the center of the tooth, and it contains a rich supply of cells, including fibroblasts, endothelial cells, immune cells, and odontoblasts. Among the various types of cells found in the pulp, **dental pulp stem cells (DPSCs)** have garnered significant attention for their regenerative potential. DPSCs are unique because they have the ability to differentiate into various cell types and play a key role in tooth repair and regeneration.[5,6]

**Sources of Stem Cells in Dental Pulp:** Dental pulp stem cells are primarily found in the soft tissue of the pulp. However, other tissues in and around the tooth also serve as sources of stem cells for regenerative endodontics. These include:[7-9]

**Dental Pulp**: DPSCs are found in the pulp tissue of both developing and mature teeth. In the developing tooth, these stem cells are involved in the formation of the pulp and dentin. In adult teeth, DPSCs reside in the pulp and can be recruited to sites of injury or damage to promote healing.

**Periodontal Ligament (PDL)**: The periodontal ligament, which anchors the tooth to the alveolar bone, also contains mesenchymal stem cells capable of differentiating into various tissue types, including cementum, bone, and periodontal ligament itself. These cells are often used in regenerative endodontics to enhance healing and promote tissue regeneration.

**Apical Papilla**: Located at the apex of the tooth, the apical papilla contains stem cells that are essential for the development and maturation of the root during tooth formation. These stem cells, known as **stem cells from the apical papilla (SCAP)**, are also considered a promising source for tooth regeneration.

**Tooth Germ and Exfoliated Deciduous Teeth**: The developing tooth germ and shed baby teeth are another source of stem cells. These cells are often collected from exfoliated deciduous teeth, which are naturally shed during childhood. These cells can then be cultured and used for regenerative therapies.

**Characteristics of Dental Pulp Stem Cells:** Dental pulp stem cells (DPSCs) are multipotent stem cells that possess several unique characteristics, which make them ideal candidates for use in regenerative endodontics:

**Multipotency**: DPSCs can differentiate into a variety of cell types, including odontoblasts (which form dentin), osteoblasts (which form bone), and chondrocytes (which form cartilage). This ability makes them invaluable for the regeneration of not only the pulp tissue but also the surrounding periodontal tissues.

**Proliferation and Self-Renewal**: DPSCs have an exceptional ability to proliferate and self-renew, ensuring that a sufficient number of cells are available for regeneration. This proliferation capacity is critical in enabling large-scale tissue repair.

**Secretion of Growth Factors**: DPSCs secrete a range of growth factors, including **vascular endothelial growth factor (VEGF)** and **platelet-derived growth factor (PDGF)**, which play crucial roles in angiogenesis (the formation of new blood vessels) and tissue repair. This makes DPSCs particularly useful for regenerating tissues that require a robust blood supply, such as dental pulp.

**Immunomodulatory Properties**: DPSCs exhibit immunomodulatory properties, meaning they can regulate the immune response. This is particularly important in preventing inflammation and promoting tissue healing after injury or infection. Their ability to modulate the immune response also helps to avoid complications during transplantation or stem cell therapy.

**Low Immunogenicity**: DPSCs are considered to have low immunogenicity, which reduces the risk of immune rejection when they are transplanted into the body. This property makes them particularly attractive for autologous therapies, where stem cells are sourced from the same individual.

**Dental Pulp Stem Cells (DPSCs) and Their Potential:** DPSCs hold immense potential for regenerative endodontics due to their unique characteristics and regenerative abilities. Their use in regenerative endodontics aims to restore tooth vitality, heal pulp injuries, and regenerate dentin. Below are the key areas in which DPSCs have demonstrated significant promise:[9,10]

**Regeneration of Dental Pulp:** DPSCs are capable of regenerating the dental pulp, which is crucial in cases of pulp necrosis or severe injury. Studies have shown that when DPSCs are introduced into the root canal or pulp cavity, they can differentiate into odontoblast-like cells that produce dentin and restore the pulp's vital functions. This regeneration can help prevent tooth loss and the need for more invasive treatments such as extractions or root canal procedures.

**Dentin Formation:** The most important contribution of DPSCs in endodontics is their ability to form **dentin**. Dentin is the hard tissue that surrounds the pulp and forms a significant part of the tooth structure. DPSCs can differentiate into **odontoblasts**, the cells responsible for producing dentin, and can be guided to form dentin-like tissue in vitro or in vivo. This ability is particularly useful in regenerating dentin in response to trauma, infection, or disease (Moraes et al., 2019).

**Periodontal Tissue Regeneration:** Beyond pulp regeneration, DPSCs have also been shown to contribute to the regeneration of **periodontal tissues**, including the periodontal ligament, cementum, and alveolar bone. This makes DPSCs a valuable source for regenerating the entire tooth-supporting apparatus, which is crucial in cases where the tooth's surrounding structures are damaged or compromised.

**Potential in Tooth Repair and Reattachment:** DPSCs have shown potential in repairing or reattaching avulsed or fractured teeth, particularly in pediatric patients. Using stem cells and scaffolds, it may be possible to regenerate the dental pulp and reattach the tooth to its socket, providing a more biologically viable solution than traditional methods (Gupta et al., 2017). Table 2 summarizes the extensive potential of DPSCs in tooth repair and reattachment, focusing on their various applications, benefits, and ongoing research challenges.

Table 1: Potential of Dental Pulp Stem Cells in tooth repair and reattachment[10-14]

| Feature | Description | Applications | Potential Benefits |
|---|---|---|---|
| **Source** | DPSCs are harvested from the dental pulp of extracted teeth, often third molars. | Tooth regeneration and repair after injury or extraction. | Easily accessible and non-invasive source of stem |

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| | | | cells for dental regeneration. |
| **Regenerative Capacity** | DPSCs are capable of differentiating into odontoblasts, the cells responsible for dentin formation. | Repair of dentin and enamel, regeneration of pulp tissue in case of damage. | Enables regeneration of tooth structures, improving overall tooth health. |
| **Dentin Formation** | DPSCs can form dentin-like structures by differentiating into odontoblasts. | Regeneration of dentin following trauma or decay. | Replaces lost dentin, potentially saving teeth from extraction. |
| **Pulp Regeneration** | DPSCs can regenerate the dental pulp after injury, restoring tooth vitality. | Dental pulp regeneration following trauma or disease. | Ensures tooth survival and function by regenerating the soft tissue inside the tooth. |
| **Tooth Reattachment** | DPSCs can promote the reattachment of tooth fragments after trauma. | Reattachment of avulsed or fractured teeth using DPSCs and scaffolds. | Enhances the chances of successful reattachment and recovery of damaged teeth. |
| **Scaffold Integration** | DPSCs can be combined with biocompatible scaffolds to enhance tooth repair. | Tissue-engineering scaffolds used in dental repairs, enhancing regeneration and reattachment. | Supports structural integration and ensures continuous cell growth. |
| **Mechanism of Action** | DPSCs release growth factors such as TGF-β, BMP, and VEGF to stimulate healing. | Facilitate healing in tooth fractures, pulp damage, and tissue regeneration. | Promotes faster healing and tissue regeneration by stimulating local growth factors. |
| **Pulp Capping** | DPSCs can be used for pulp capping to protect the pulp after cavity preparation. | Used in restorative dentistry for the treatment of deep cavities. | Protects the vital pulp tissue, preventing pulp exposure and improving treatment success. |
| **Regenerative Endodontics** | DPSCs are a potential source for regenerative endodontic procedures. | Used in root canal therapy to promote healing of the pulp tissue. | Encourages natural healing of pulp tissue, reducing the need for root canal fillings. |
| **Biocompatibility** | DPSCs are highly compatible with existing dental tissues, reducing immune response. | Dental implant integration, tissue regeneration in dental injuries. | Minimizes rejection risks, leading to more predictable and safer procedures. |
| **Dental Implant Support** | DPSCs can support osseointegration of dental implants, improving stability. | Enhance the integration of dental implants into the jawbone. | Boosts the success rate of dental implants by promoting natural bone formation. |
| **Bone Regeneration** | DPSCs can differentiate into osteoblasts and support bone healing. | Repair of jawbone or alveolar bone following extraction or injury. | Promotes bone healing around teeth or implants, improving long-term dental health. |
| **Periodontal Regeneration** | DPSCs can aid in regenerating periodontal ligaments after injury or disease. | Periodontal ligament regeneration in cases of tooth mobility or disease. | Helps maintain tooth support structures and prevents tooth loss due to gum disease. |
| **Tooth Sensitivity Treatment** | DPSCs may help in treating tooth sensitivity by repairing dentin and pulp. | Relief from dentin hypersensitivity after dental procedures or due to tooth wear. | Reduces discomfort and restores normal tooth sensitivity levels post-treatment. |
| **Dental Tissue Engineering** | DPSCs can be used in 3D tissue engineering for creating full tooth structures. | Used in experimental approaches for creating teeth from stem cells for future applications. | Potential to regenerate entire teeth, providing solutions for tooth loss. |
| **Vascularization in Tooth Repair** | DPSCs secrete angiogenic factors to support blood vessel formation in tooth tissue. | Enhancement of vascularization in tooth regeneration for better healing and nutrient supply. | Ensures adequate blood supply to regenerate tissues effectively. |
| **Infection Control** | DPSCs exhibit immunomodulatory properties that may help control infection. | Treatment of infected dental pulp or surrounding tissues in regenerative procedures. | Decreases the risk of infection and promotes a more sterile healing process. |
| **Bioactive Molecules Secretion** | DPSCs secrete bioactive molecules like collagen and elastin to promote tissue healing. | Used for repairing soft tissues like the dental pulp and periodontal ligaments. | Promotes optimal tissue regeneration through the secretion of healing proteins. |
| **Clinical Applications** | Clinical trials and studies are ongoing to determine the effectiveness of DPSCs in tooth repair. | Clinical trials for pulp regeneration, tooth reattachment, and bone repair are underway. | Future clinical success could revolutionize tooth repair and regenerative therapies. |
| **Challenges in Clinical Use** | Limited data on long-term success and integration in human applications. | Clinical application still requires refinement and validation. | Further research and clinical studies are necessary to validate safety and efficacy. |

**Other Stem Cell Sources for Regenerative Endodontics:** While DPSCs are the most studied stem cells in the context of endodontics, other sources of stem cells are being explored for their regenerative potential in dental tissue repair. These sources include:[15-17]

**Periodontal Ligament Stem Cells (PDLSCs)**: As mentioned earlier, PDLSCs can regenerate periodontal tissues, and their use in regenerative endodontics has been explored for the repair of both the pulp and the surrounding structures (Moraes et al., 2019).

**Stem Cells from the Apical Papilla (SCAP)**: SCAP cells are another promising source for regenerative endodontics. These cells can differentiate into odontoblasts, osteoblasts, and cementoblasts, making them valuable for both pulp and periodontal regeneration.

**Induced Pluripotent Stem Cells (iPSCs)**: iPSCs, derived from reprogrammed adult somatic cells, offer the potential for creating patient-specific stem cells. These cells can be directed to differentiate into various dental tissues, providing an exciting avenue for personalized regenerative therapies.

## CONCLUSION

Stem cells play a central role in the evolving field of regenerative endodontics. The ability to regenerate dental pulp, dentin, and periodontal tissues using stem cells, particularly dental pulp stem cells (DPSCs), has opened up new avenues for the treatment of dental diseases that were previously considered irreversible. The regenerative potential of stem cells from various dental tissues, including the periodontal ligament and apical papilla, further enhances the promise of regenerative therapies in endodontics. As research continues to advance, stem cell-based therapies may offer a biologically favorable, minimally invasive alternative to traditional endodontic treatments, ultimately improving patient outcomes and preserving natural tooth function.

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