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Review Article

The regenerative revolution in dentistry: stem cells as the future of oral health

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ABSTRACT

Stem cell-based therapies represent a transformative frontier in regenerative dentistry, offering biologically driven solutions for the restoration of dental and craniofacial tissues. Unlike conventional approaches that rely on synthetic materials, regenerative dentistry utilizes the self-renewing and multipotent nature of stem cells to regenerate pulp, dentin, periodontal ligaments, and even alveolar bone. Various stem cell sources- such as dental pulp stem cells (DPSCs), stem cells from human exfoliated deciduous teeth (SHED), periodontal ligament stem cells (PDLSCs), bone marrow mesenchymal stem cells (BMMSCs), and adipose-derived stem cells (ADSCs)- demonstrate diverse regenerative potentials suited for specific dental applications. Clinical advances include pulp-dentin complex regeneration, periodontal tissue repair, and jawbone reconstruction using stem cells combined with bioactive scaffolds and growth factors like BMPs, VEGF, and PDGF. Innovations in 3D bioprinting, scaffold engineering, and cell-free therapies using exosomes continue to enhance therapeutic outcomes. Despite promising results, challenges remain in standardization, immune compatibility, and cost-effectiveness, alongside ethical constraints particularly regarding embryonic stem cells. Ongoing clinical trials and emerging technologies like CRISPR gene editing and artificial intelligence offer new avenues for precision regenerative therapies. As personalized dental medicine evolves, interdisciplinary collaboration will be key to translating laboratory success into accessible, scalable clinical solutions. Stem cells not only offer hope for functional tissue regeneration but also mark a paradigm shift in patient-specific dental care.

Keywords: Stem cells, Regenerative dentistry, Dental pulp stem cells, Periodontal regeneration, Tissue engineering, Biomimetic scaffolds

INTRODUCTION

Dentistry has evolved through regenerative approaches which use stem cell regenerative capabilities to achieve dental restoration. Regenerative dentistry represents a transformative shift in dental care, focusing on biologically based therapies to restore or replace damaged tissues. Stem cells play a pivotal role in this field due to their unique ability to self-renew and differentiate into various cell types. Their application in dentistry includes the regeneration of pulp tissue, periodontal structures, and even entire teeth. Advances in stem cell biology, scaffold design, and signaling molecules have significantly expanded the potential of regenerative treatments. This article explores the promise and current status of stem cell-based therapies in dentistry, highlighting their role in revolutionizing future clinical practices. The regeneration of damaged dental tissues including pulp and dentin and the periodontal ligament as well as whole teeth becomes possible through stem cells because of their unique ability to both renew themselves and develop into different cell types. The methodology differs from conventional restorative methods since it avoids using synthetic materials by using stem cell approaches to activate natural body regeneration. Regenerative dentistry now leads translational research fields because scientists isolated dental-derived stem cells from dental pulp stem cells (DPSCs) and stem cells from human exfoliated deciduous teeth (SHED). Medical practices apply genomic insights to develop personalized medical solutions which match patients' individual healthcare requirements.[1]

TYPES OF STEM CELLS

Regenerative dentistry employs different types of stem cells which demonstrate specialised properties for their particular applications. Permanent teeth provide dental pulp stem cells (DPSCs) which demonstrate extensive growth potential as well as the ability to become odontoblasts, osteoblasts and neural cells. The cells play a critical role in dental pulp restoration while helping repair dentin tissue.[2] The stem cells derived from human exfoliated deciduous teeth (SHED) outperform DPSCs in terms of proliferation rate and potential to become various cell types which makes them perfect for paediatric treatment applications.[3] Periodontal ligament stem cells (PDLSCs) serve as fundamental elements for periodontal tissue regeneration because they help fix cementum and ligaments during periodontitis development.[4] Medical practitioners use bone marrow mesenchymal stem cells (BMMSCs) to regenerate alveolar bone and integrate implants, but these cells lack dental cell specificity.[5] Scientists investigate using adipose-derived stem cells (ADSCs) since they are easily obtainable and plentiful for soft tissue restoration and graft procedures.[6] The different stem cell sources create a flexible set of tools that medical professionals need to treat multiple dental and craniofacial abnormalities.

SOURCES OF STEM CELLS

The field of dentistry extracts stem cells from different tissues, including adult teeth, baby teeth, periodontal ligament tissue, bone marrow, and fat tissue. The dental pulp, along with exfoliated deciduous teeth, stands out as an optimal source since researchers can access them easily, and they demonstrate excellent potential for regeneration.

Periapical cyst-derived mesenchymal stem cells (hPCy-MSCs) are being investigated as a new cellular source for medical regenerative techniques.[7] Multiple different sources exist for stem cell harvesting that allow providers to obtain stem cells with low-impact procedures, which make them suitable for medical use.

ISOLATION AND CULTURE TECHNIQUES

Isolation and culture of dental stem cells are fundamental to their application in regenerative dentistry. DPSCs stem cells from human exfoliated deciduous teeth (SHED), and PDLSCs are typically isolated through enzymatic digestion and cultured under sterile in vitro conditions. For example, DPSCs are obtained by extracting the pulp tissue from the crown and root canals of teeth, followed by collagenase type I and dispase enzyme digestion to break down the extracellular matrix. The resulting cell suspension is then filtered and cultured in α-MEM (minimum essential medium alpha) supplemented with fetal bovine serum (FBS), antibiotics, and L-glutamine. SHED are isolated similarly from exfoliated deciduous teeth, demonstrating higher proliferative potential. PDLSCs are retrieved from the middle third of the periodontal ligament attached to extracted teeth and undergo the same enzymatic digestion protocol.[1]

These stem cells are characterised using flow cytometry to express mesenchymal markers such as CD73, CD90, and CD105, and lack of hematopoietic markers such as CD34 and CD45. Maintaining proper culture conditions, including low passage numbers and appropriate humidity and CO_2 levels (37°C, 5% CO_2), is critical to preserve their multipotency and therapeutic efficacy.

MECHANISMS OF REGENERATION

Stem cell regeneration depends on their two essential properties: specialisation into new cells along with the secretion of tissue-healing bioactive molecules. Laboratory evidence shows that DPSCs seeded on biocompatible scaffolds produced functional pulp tissue when tested on animal subjects.[8] Recovery of periodontal ligaments and treatment of chronic periodontitis through PDLSC cell therapy with BMP-2 or PDGF growth factor supplements demonstrates successful results in clinical trials.[9] Stem cell-derived exosomes serve as cell-free regenerative solutions whose research aims to avoid transplantation obstacles.[10] The various mechanisms demonstrate how stem cells can treat multiple dental and craniofacial medical conditions.

The classic tissue engineering triad consists of three key components: (a) cells: typically, stem cell or progenitor cells capable of differentiating into the desired tissue type; (b) scaffolds: biocompatible structures that provide a 3D environment for cell growth and tissue formation; and (c) signalling molecules: growth factors and other bioactive molecules that guide cell behaviour and tissue development.

APPLICATIONS IN DENTISTRY

The implementation of stem cells has extended into multiple fields of regenerative dentistry. The application of DPSCs leads to effective vital pulp therapy and in pulp regeneration.[11]

According to their findings, the clinical trial by Nakashima et al demonstrated that pulp tissue regeneration succeeded after seeding DPSCs on collagen scaffolds for patients with irreversible pulpitis.[12] Combining PDLSCs with growth factors leads to decreased pocket depths in patients with chronic periodontitis, which promotes better tissue regeneration, according to research.[13] Liu et al conducted a trial showing that PDLSCs successfully enhanced the healing of periodontal ligaments in people with severe periodontitis, thus demonstrating their therapeutic effectiveness.[14]

Academic research combines 3D-printed scaffolds, BMMSCs, and DPSCs to reconstruct alveolar bone defects after traumatic incidents or tumour removal procedures.[15] Scientists continue to investigate the possibility of constructing entire teeth from stem cells combined with biomimetic matrices. However, they still need to solve problems related to tissue vascularisation and complex tooth structure.[16]

STEM CELL-BASED REGENERATIVE THERAPIES IN DENTISTRY

Pulp regeneration

Pulp regeneration aims to restore the vitality of the dental pulp, especially in cases of pulp necrosis and irreversible pulpitis. Unlike traditional root canals, which remove the pulp, this approach regenerates the pulp-dentin complex, including nerves and blood vessels.

Key methods

Stem cell-based

Using DPSCs and SHED.

Cell-free approaches

Revascularization techniques utilising the body's stem cells. (a) growth factors- VEGF (blood vessels), bFGF (cell growth), TGF-β (odontoblast differentiation), and BMPs (dentin formation); and (b) advanced techniques- injectable scaffolds, 3D-printed scaffolds, cell sheet technology.

Clinical studies

Successful trials with DPSCs showing new nerve and blood vessel formation. 80% success in revitalising necrotic immature teeth. Long-term studies are needed for stability and predictability.

Periodontal regeneration

This focuses on restoring structures around teeth like alveolar bone, cementum, and periodontal ligament.

Key approaches

PDLSCs- (a) Differentiate into cementoblasts, osteoblasts, and fibroblasts; (b) BMMSCs: Multipotent cells modulating immune responses; and (c) cell sheet technology: Preserves extracellular matrix, enhancing cell survival.

Growth factor

PDGF (cell growth), EMD (cementum formation), BMPs (bone and cementum regeneration), FGF-2 (periodontal ligament repair).

Innovations

Scaffolds delivering cells and growth factors. 3D-printed scaffolds and gene therapy for enhanced regeneration.

Jaw and facial bone regeneration

Regenerative strategies for oral and maxillofacial applications aim to address significant bone defects, alveolar ridge augmentation, and sinus lift procedures. Various stem cell sources have shown promise in these areas. Bone marrow mesenchymal stem cells (BMMSCs), typically harvested from the hip or jaw, are widely used for their strong osteogenic potential. Dental pulp stem cells (DPSCs) and stem cells from human exfoliated deciduous teeth (SHED) can differentiate into bone-forming cells, thereby contributing to the regeneration of complex tissues. Additionally, adipose-derived stem cells (ADSCs), which can be obtained through minimally invasive procedures, offer therapeutic benefits by enhancing bone healing and regeneration through their stromal vascular fraction.

Scaffolds play a crucial role in bone tissue engineering by providing a 3D framework that supports cell attachment and tissue growth. These structures can be fabricated from synthetic polymers, natural polymers, bioceramics, or composite materials.

Recent innovations include 3D-printed, patient-specific scaffolds and scaffolds enhanced with growth factors or gene therapy for improved regenerative outcomes. Growth factors, such as Bone Morphogenetic Proteins (BMPs), promote bone formation. Platelet-Rich Plasma (PRP) and Platelet-Rich Fibrin (PRF) deliver a concentrated mix of healing factors, while Vascular Endothelial Growth Factor (VEGF) stimulates blood vessel formation.

Emerging trends, such as gene therapy, are being explored to enhance bone regeneration further, although they remain in the experimental phase.

Stem cell sources

BMMSCS- From the hip or jaw; (b) DPSCS & SHED: Differentiating into bone-forming cells; and (c) ADSCs: obtained minimally invasively, with stromal vascular fractions enhancing therapy.

Scaffolds

3D structures from synthetic polymers, natural polymers, bioceramics, and composites.

Innovations

D-printed, customised scaffolds, and growth factor- and gene-enhanced scaffolds.

Growth factors

BMPs (bone formation), PRP/PRF (growth factors), and VEGF (blood vessels).

Emerging trends

Gene therapy for enhanced bone regeneration is still in the experimental stages.

Challenges and limitations

The use of stem cell-based therapies encounters multiple obstacles during their implementation. The standardisation process becomes complex due to cell source variability because donor-dependent stem cell potency and viability affect treatment results.[17] Scaffold design presents a difficulty because developers must meet three demanding requirements that guarantee successful tissue regeneration: optimal biocompatibility, appropriate degradation rate and proper mechanical strength.[18] The progress of embryonic stem cells slows down because of ethical regulations and strict clinical trial requirements.[19] The high expenses associated with cellular growth systems and scaffold production barriers restrict worldwide access to these technologies, thus creating inequalities in healthcare access.[20] The immunogenicity challenge during allogeneic stem cell transplants requires customised solutions because patients face risks of immune system rejection.[21]

CURRENT CLINICAL TRIALS

Multiple scientific studies have proven the effectiveness of stem cell treatments as a solution for dental restoration. The research by Kaigler et al. revealed that BMMSCs improve alveolar ridge wound healing and result in higher implant success rates.[22] Researchers studied SHED cells for paediatric pulp therapy and discovered successful outcomes in neural regeneration according to their findings.[23] The experimental studies demonstrate how stem cells create opportunities to treat intricate dental and craniofacial problems.

FUTURE DIRECTIONS

The gene-editing technology known as CRISPR-Cas9 can improve stem cell differentiation and reduce the immune rejection response.[24] Stem cell-derived exosomes show promise as cell-free regenerative solutions because they eliminate the need for transplantation procedures.[25]

One of the most promising directions is the development of bioengineered tooth structures, where stem cells are combined with scaffolds and signalling molecules to create whole or partial tooth constructs. Early animal studies have shown encouraging results, and while human applications are still in preliminary stages, the potential to replace lost or severely damaged teeth biologically rather than prosthetically represents a paradigm shift in dental care.[26,27]

The advent of 3D bioprinting technology is also expected to revolutionise regenerative strategies. By precisely placing cells, growth factors, and biomaterials layer-by-layer, it becomes feasible to fabricate complex dental tissues, including the pulp-dentin complex and periodontal structures.[28] This approach could lead to personalised, patient-specific regenerative treatments with improved functional and aesthetic outcomes.

Another promising area is personalised stem cell therapy. Autologous stem cell banking, particularly from deciduous teeth (SHED) or extracted third molars, could allow for individual-specific regenerative solutions, minimising immunogenic reactions and ethical concerns.[29,30] This concept aligns with the broader movement toward precision medicine.

Moreover, gene editing technologies like CRISPR-Cas9 are being explored to enhance stem cells' regenerative capacity and safety profile. For example, editing specific genes involved in differentiation or immunomodulation could result in more efficient and targeted regeneration of oral tissues.[31] However, translating these innovations into clinical reality requires overcoming several hurdles, including regulatory approvals, cost-effectiveness, scalability, and long-term safety. Interdisciplinary collaboration among dental researchers, molecular biologists, material scientists, and clinicians will be key to unlocking the full potential of stem cell-based regenerative therapies in everyday dental practice.[32]

Research findings show that artificial intelligence stands to improve scaffold design and outcome predictions, which will enhance regenerative therapy precision, and 3D bioprinting demonstrates capabilities to construct highly accurate complex dental tissue structures.[1,2] Medical studies involving large numbers of participants will confirm the safety and effectiveness across different ethnic groups so laboratory research can become practical clinical practice.[3]

CONCLUSION

Stem cells enable future developments in oral healthcare by creating biologically functioning tissue replacements for areas that have suffered loss. Interdisciplinary collaboration between dental professionals, bioengineers, and geneticists will advance this field because standardisation, cost issues, and ethical concerns continue to persist. Improved patient quality of life will become possible through regenerative dental research developing curative solutions that diminish the need for synthetic materials. These therapies become more specific through genomic integration because they now enable medical solutions customised for each patient's individuality. This paradigm shift in oral care practice will deliver more proactive, precise, patient-specific care, which will lead to better health results and improved patient care methods. Dental, along with medical and genomic experts, need to collaborate for building the future direction of oral healthcare.

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