# Stem Cells: An Emerging Future in Dentistry

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## Abstract
The breakthrough of stem cells has produced new but weird possibilities in the regeneration of different organs and tissues. Currently, studies and research work to know latent and capabilities of stem cells and their utilization in dentistry are becoming an exciting topics. In few years plenty's of studies and revelations have been conceded which shows that stem cells and tissue engineering are giving rise to a separate branch termed "Regenerative Dentistry" that will have its own position in future dental practice. The tooth is nature's "safe" for these precious stem cells, and there is a loads of these cells in wisdom teeth, permanent teeth and deciduous teeth. The stem cells contained within teeth are capable of reproducing themselves and can be voluntarily recovered at the time of an intended dental procedure. Apart from being the most suitable stem cells to access, dental stem cells have considerable medical benefits in the progress of new medical therapies.

**Keywords:** Dentin, Dental Pulp, Stem Cells, Tooth Regeneration.

## Introduction:

Stem cells are undifferentiated biological cells that can differentiate into specialized cells and can divide (through mitosis) to produce extra stem cells. They are originated in multicellular organisms. Research into stem cells raised out of findings by Ernest A. McCulloch and James E. Till (1960s) at the University of Toronto. In 2005 Dr. Irina Kerkis discovered dental pulp stem cells( DPSCs). Later on researchers have recognized the mesenchymal type of stem cell inside dental pulp. This type of stem cells has the future potential to distinguish into a various type of other cells.[1] The Dentin–pulp complex has a usual regenerative potential for configuration of tertiary dentin. The odontoblasts which form major part of dentin may carry on mild injury, such as early caries or attrition, and exude a reactionary dentin matrix. However, greater intensity of trauma, such as restorative procedures or advanced caries, may guide to the loss of the pre-existing odontoblasts. In reaction to stimuli at the dentin–pulp crossing point, new odontoblasts are recruited and set apart at the site of injury to synthesize an atubular reparative dentin, also occasionally referred to as osteodentin. This reparative dentin offer a 'bridge' of mineralized tissue instantly below the extensively broken tissue, in order to protect pulp vitality.[2] Since last few decades, Scientists have been going ahead to seek out the possible applications of stem cells for restoring and regeneration of dental and dentofacial structures.[3]

## Characterstics of Stem Cells:

1. **Totipotency:** Produce all types of cells as well as germ cells (ESCs).
2. **Pluripotency:** Produce all types of cells apart from cells of the embryonic membrane.

3. **Multipotency:** Distinguish into more than one adult cell (MSC).
4. **Unipotency:** (dedicated progenitors): produce one particular cell type.[4]

## Types of Stem Cells:

1. Embryonic stem cells
2. Adult stem cells

## Embryonic Stem Cells:

Embryonic stem cells (ESCs) are imitative from embryos that are 2-11 days old known as blastocysts. They are best developed from supernumerary embryos obtained from in vitro fertilization centers. They are totipotent - cells practically capable of differentiating into any type of cell as well as the germ cell. ESCs are considered eternal as they can be propagated and maintained in an undifferentiated state forever. These stem cells have the maximum potential to regenerate and repair unhealthy organs and tissues in the body. However, the therapeutic advantage of ESCs is bogged by a argument owing to the belief that the procedure of taking out of stem cells from an embryo wipe out the embryo itself and some views this as taking life, thereby, increased ethical and moral concerns. Further, it is hard to control the expansion and differentiation of the embryonic stem cells posing risk of teratoma formation and tumorogenicity. While research is on to overcome some of these deficit as of now, ESCs are not so far used therapeutically and have only remained an excellent platform for research.[5]

## Adult Stem Cells:

These are undifferentiated cells that occur in a differentiated tissue. Sources of Adult Stem Cells (ASCs) consists of bone marrow, brain, blood, eye, skeletal muscle, lining of the gastrointestinal tract, pancreas, dental pulp, skin, these are multipotent. These Stem cells are sited in positions called Niches. These Niches provide a specific cellular environment needed for self regeneration. Adult stem cells sited outside the bone marrow are called Tissue stem cells. ASCs divide to replenish dying cells and regenerate damaged tissue. Regulation of differentiation in ASCs is by a protein BMI-1, Notch pathway, sonic hedgehog and the Wnt developmental pathway. ASCs are difficult to identify and purify and when grown in culture are difficult to maintain in an undifferentiated state. Finding ways to culture ASCs outside the body is a high priority of Stem cell research.

As adult stem cells are not totipotent, they can be advance classified depending on their beginning and their differential possible into:

1. Haematopoietic Stem Cells.
2. Non-haematopoietic Stem Cells or Mesenchymal Stem Cells.[6,7]

## Dental Pulp Stem Cells:

In 2003 Dr. Songtao Shi, a Pedodontist discovered dental pulp stem cells by utilizing the primary teeth of his daughter & he named as stem cells from human exfoliated deciduous teeth. Many researchers have been done work on dental pulp, gazing for stem cells and they established that dental pulp was rich in different types of stem cells, like, adipocytes, chondrocytes, osteoblasts and mesenchymal stem cells. These mesenchymal stem cells are one of the most prospective stem cells which has wide therapeutic functions. Dental pulp stem cells can be found both in adults and children. Transplantation of Dental pulp stem cells into immune compromised might outcome in the formation of a dentin-like tissue, while bone marrow stem cells generated a tissue approaching that of lamellar bone. Pulpal wound healing and regeneration may be compromised with growing age. Analysis of pulpal cell populations point out those age related declines in pulpal cell numbers take place. Studies have identified a possible progenitor cell population in dental pulp, which comprises less than 1% of the whole cells.[8] Severe Injury to a dental pulp from any infection or trauma leads to death of odontoblasts with a limited ability for regeneration. Healing depends on the strength and extent of the injury, presence of bacteria and host factors such as the level of native and systemic immunity.[9]

Stem cells can be separated from the three groups of teeth, they are:

(a) **Deciduous Teeth:** The healthy pulps of deciduous teeth are a rich source of viable stem cells. Scientific data sustains that separated stem cells from healthy pulp of deciduous teeth are extremely proliferative, still when the pulp is recovered in little quantities.

(b) **Wisdom Teeth:** The healthy pulp from wisdom teeth is a further exceptional source for workable stem cells. Entire or sectioned divisions of third molars containing healthy pulp can be recovered at the time of their exclusion. The pulp is often exposed if an impacted third molar needs to be sectioned for removal.

(c) **Permanent teeth:** Healthy pulp from all the permanent teeth are potential resource of stem cells.

- Bicuspids requiring to be removed for orthodontic suggestions are an example of this.

Permanent teeth to not to be included: endodontically-treated or non vital teeth, teeth with lively infections, teeth with rigorous periodontal disease and too much mobility, teeth with large restorations and deep caries, and teeth with calcified or sclerosed pulp chambers.[10]

## Stem Cell Handling and Cryopreservation:

Stem cells are discharge from minute amounts of tissues, in the case of stem cells from dental pulp. The tissue is positioned in an enzyme solution so as to release the stem cells, which are then cultured to increase. This can be completed using serum-free medium, eliminating the need for use of animal serum. Differentiation then arises and the cells are transplanted – either single or with a scaffold or other biomaterials, depending on the purpose.

Extracted permanent and primary (including exfoliating) teeth can be conserved for future use with cryopreservation. The cells are quickly cooled to sub-zero temperature as low as -196° C, impeding any cellular or biochemical action. Rapid freezing is essential to prevent ice from forming around or within the cells and to avoid dehydration, as these would origin cell harm and demise. Research has confirmed that stem cells obtained from the dental pulp of extracted third molars hold on to the ability to differentiate into numerous cell types following defrosting after cryopreservation using liquid nitrogen. Stem cells removed from the periodontal ligament are workable following cryopreservation. After two years of cryopreservation, stem cells have been capable to distinguish and to multiply, and it has been concluded that dental stem cells can go through long-term cryopreservation.[11]

## Different Types of Tooth Stem Cells:

1. **Adipocytes:** They have successfully been utilized to repair injure to the heart muscle caused by severe heart attack. There is also initial data to point out that they can be used to treat cardiovascular diseases, orthopaedic problems and spine, Crohn's disease, congestive heart failure, and also used in plastic surgery.
2. **Chondrocytes and Osteoblasts:** This type of stem cells has effectively been used to grow cartilages and bones suitable for transplant. They have also been utilized to develop intact teeth in animals.
3. **Mesenchymal:** These stem cells have successfully been used to restore spinal cord damage and to recall feelings and progress of movement in paralyzed patients. Since they can figure neuronal clusters, mesenchymal stem cells also have the possibility to treat neuronal degenerative disorders such as Parkinson's diseases and Alzheimer's, cerebral palsy, as well as a host of other disorders. Any other type of adult stem cells doesn't have more therapeutic potential than mesenchymal stem cells.[12-14](Table No. 1)[4]

## Periodontal Regeneration:

Regenerating the periodontium has all the time been a higher priority in craniofacial regenerative biology. Due to the difficult structure of the periodontium (having hard and soft tissues), its entire

**Table No. 1: Types of dental stem cells[4]**

| Properties | DPSCs | SCAPs | SHEDs |
|---|---|---|---|
| **Location** | Permanent tooth pulp | Apical papilla of developing root | Tooth pulp of exfoliated deciduous tooth |
| **Proliferation rate** | Moderate | High | High |
| **Multi-potentiality** | Odontoblast, osteoblast, condrocyte, myocyte, neurocyte, adipocyte, comeal epithelial cell, melanoma cell | Odontoblast, osteoblast, neurocyte, adipocyte | Odontoblast, osteoblast, condrocyte, myocyte, neurocyte, adipocyte, |
| **Potential contributions to systemic diseases** | Bone regeneration, central nervous degeneration, liver fibrosis, myocardial infarction, comeal reconstruction | Bone regeneration | Bone regeneration |
| **Potential contributions to bio-tooth** | Dentin, pulp | Dentin, root, pulp | Dentin, pulp |

regeneration has always stay a challenge. All the present regenerative techniques such as allografts, autologous bone grafts, or alloplastic materials have restrictions and cannot be utilized in all clinical condition. Therefore, a cell-mediated bone regeneration technique will be a possible therapeutic alternative. Kawaguchi et al. verified that the transplantation of ex vivo prolonged autologous MSCs can regenerate fresh cementum, periodontal ligament and alveolar bone in class III periodontal deficit in dogs. Going a step ahead Hasegawa et al, confirmed that periodontal ligament cells cultured in vitro were effectively reimplanted into periodontal defects in order to endorse periodontal regeneration. A consequent study by the same group stated a parallel approach in humans. This study reported certain evidence that stem cells can be utilized to regenerate a tissue as complex as the periodontium.[5]

## Regeneration of Pulp and Damaged Coronal Dentin:

No restorative material has been able to imitate all physical and mechanical properties of tooth tissue. Moreover, we have not been successful in providing an ideal solution to certain situations, such as an immature tooth with broad coronal devastation and reversible pulpitis. If the regeneration of tooth tissue is achievable in these situations, it makes easy physiologic dentin deposition that forms an important part of the tooth in that way restoring structural integrity, reducing interfacial failure, microleakage, and other consequent complications. Equally, newly permanent teeth that need apexification or apexogenesis are the ideal candidates for the regeneration of pulp as they let to completion of together vertical and lateral root development, improving the long-term prognosis. On the other hand, pulp regeneration in fully shaped teeth may not be of huge advantage, although there is enough evidence to say that a restored vital tooth serves more than a root-canal-treated tooth. Pulp tissue regeneration engages either delivery of autologous/allogenic stem cells into the root canals or implantation of the pulp that is developed in the laboratory with the use of stem cells. Both these techniques will have benefits and certain restrictions that need more research. Gronthoset al. demonstrated both in vivo and in vitro in animals that dental pulp stem cells (DPSCs) were able of forming ectopic dentin and related pulp tissue.[5,15,16]

## Tooth Regeneration:

The regeneration of adult teeth will be possible in future with the help of tissue engineering and newer expansion in stem cell therapy. Regenerative procedures would be improved fitting and substitutes in place of dental implants. Experimental studies with animal models have exposed that the tooth crown formation can be regenerated using tissue engineering techniques that merge stem cells and recyclable scaffolds. Epithelial mesenchymal exchanges are mandatory in tooth development. "These exchanges are considered by the reciprocal exchange of signals between these two native germ layer tissues and outcome in the emergence of inimitable terminal phenotypes with their supporting cells".

Three key elements are involve in tooth regeneration which include:

- Inductive morphogenes
- Stem cells
- Scaffold

Following steps are involved in regeneration of tooth:

1. Harvesting and spreading out of adult stem cells.
2. Seeding the stem cells into scaffold which provides optimize environment.
3. Cells are instructed with targeted soluble molecular signals spatially.
4. The gene expression profile is confirming by the cells for next phase in odontogenesis.

Duailibi *et al*., in their studies were able to form tooth from single cell suspensions of cultured rat tooth bud cells. They confirmed bioengineered rat teeth grown in 12 weeks with PLGA and PGA scaffold. Honda *et al*. developed tissue engineered teeth, when implanted into omentum of rat utilizing porcine tooth bud cells and PGA fiber engage scaffold that reminds of the model of odontogenesis. Young *et al*., using porcine tooth bud cells, PLGA and PGA scaffolds produced a crossbreed tooth bone for the cure of tooth loss beside with alveolar bone resorption.[17-21]

## Conclusion:

Regeneration of the dental tissues offers an eye-catching alternative to more conventional restorative approaches because the infected tissue is replaced by natural tissue, which forms an essential part of the tooth. Fresh methods based on progenitor cell enrolment and consequent stimulation offer considerable potential to extensively impact on dental disease treatment and the promotion of vital pulp therapy. The progress of such approaches, still, requires specific regulation of the regenerative measures to be effective. If uncontrolled, abolition of the pulp chamber will arise with unavoidable loss of tooth vitality. An understanding of this concern is crucial to our future development of any dental regenerative therapies based on utilization of the progenitor cells in the dental pulp. It is appealing to consider that such new clinical treatments will come to execution, but we are some way from taking this information from laboratory to clinic. We evidently have a chance to move restorative dentistry into a new age, attaching the biological activity of the dental tissues to make easy wound healing and tissue regeneration. Certainly, current moves towards isolation, gathering, and cryopreservation of dental pulp progenitor cells for banking and clinical are now viable and commercially possible. Though, we have to approach the face up with careful consideration. We are still some distance from fully accepting the potential and behaviour of dental pulp progenitor cells, and successive clinical treatment modalities. However, the opportunities for their utilization in dental tissue regeneration are becoming clearer and will escort to considerable benefits in the management of the effects of dental disease.

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