

# Dental Stem Cells: A Perspective Area in Dentistry

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**Abstract** In recent years, stem cell research has grown exponentially due to the recognition that stem cell-based therapies have the potential to improve the life of patients with wide range of conditions, they provides promising methods in vitro as well as in vivo in animal models which make speculation about a future application in human dentistry reasonable. Based on their ability to repair and/or rescue injured tissue and restore organ function even partially, multiple types of stem/progenitor cells have been speculated. Some dental tissues are rich source of mesenchymal stem cells which are suitable for tissue engineering applications. Because they have the potential to differentiate into several cell types, including odontoblasts, neural progenitors, osteoblasts, chondrocytes, and adipocytes. Based on that, an innovatation for generation of clinical material and/or tissue regeneration carried out. Mesenchymal stem cells were founded in dental tissues, including dental pulp, dental papilla, and dental follicle, exfoliated deciduous teeth and periodontal ligament. They can be isolated and grown under defined tissue culture conditions, and used in tissue engineering, including, dental tissue, nerves and bone regeneration.

**Keywords:** regeneration, stem cells, periodontal tissues, cloning, mesenchymal cells

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## 1. Introduction

Stem cells are primitive cells different from all other cells in the body. When a stem cell divides, each new cell has the potential either to remain a stem cell or become another type of cell with a more specialized function, such as a muscle cell, a red blood cell, etc

It is becoming ever more clear that this conceptual come up to therapy, named regenerative medicine, will have its place in clinical practice in the future. Stem cells will play an important role in future medical treatment because they can be readily grown and induced to differentiate in multi lineage cell type in culture.

Recently, mesenchymal stem cells were demonstrated in dental tissues, such cells are therefore a key part of achieving the promise of tissue regeneration.

### 1.1. Unique Properties of Stem Cells

- Regeneration

Stem cells can replicate themselves over longer periods of time than other body cells.

- Differentiation

Stem cells are unspecialized cells that can produce specialized body cells.

The microenvironment regulates the balance between self-renewal and differentiation Figure 1.

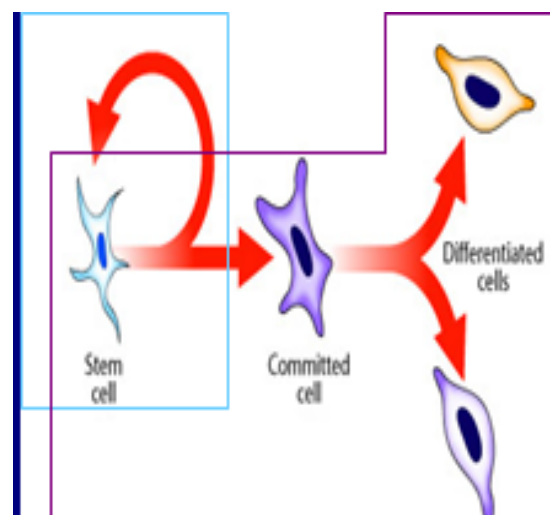


Figure 1. Unique Properties of Stem Cells

### 1.2. Stem Cell Potential

**Totipotent:** Each cell can develop into a new individual. Cells from 1-4 day old embryos.

**Pluripotent EGC:** Cells can form any cell type. Some cells of blastocyst (5-14 days old) Figure 2.

**Multipotent:** Cells differentiated, but can form a number of other tissues. Fetal tissue, cord blood, and adult stem cells.

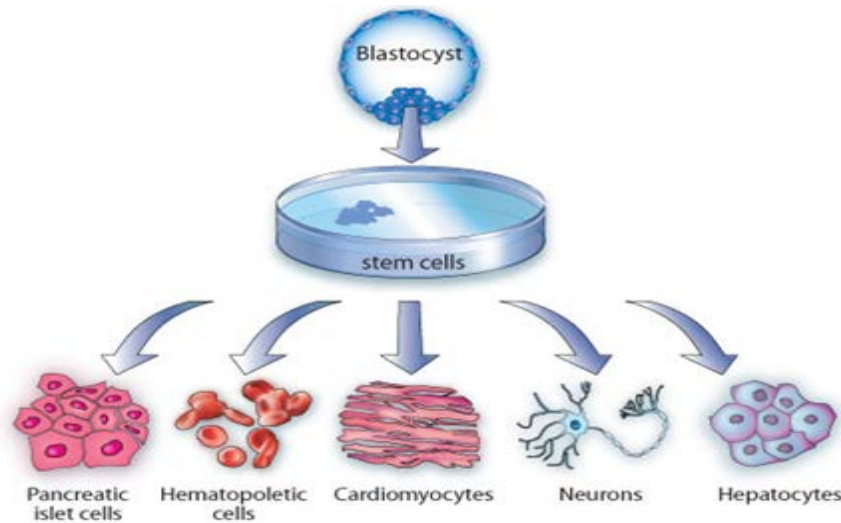


Figure 2. Pluripotent Differentiation

### 1.3. Types of Stem Cells

#### A. Embryonic Figure 3

- Obtained from in vitro fertilization, or aborted embryos 3 or 4 day old embryo, consist of 50-150 cells; blastocyst stage develop into a human being, taking these cells will require destruction of an embryo.
- Grown relatively easily in culture.
- Technically these cells are difficult to control and grow and they might as well form tumors after their injection.
- Ongoing debate regarding use of embryos Embryonic stem cells have both moral and technical problems,
- **Embryonic germ (EG)** cells are collected from fetal tissue at a later stage of development, used in tissue engineering

important distinction, as large numbers of cells are needed for stem cell replacement therapies.

- Have two properties: First the ability to replicate. Second they divide to create a more differentiated cell than itself.

- They can be found in both children and adult. In umbilical cord.

Hematopoietic Stem Cells.

Mesenchymal Stem Cells Figure 4.

+ Less likely to initiate rejection after transplantation, not need process of immunosuppressant

- General consensus among scientist:

- Adult stem cells DO NOT have as much potential a embryonic stem cells(the number and type of differentiated cell types they can become) 1.

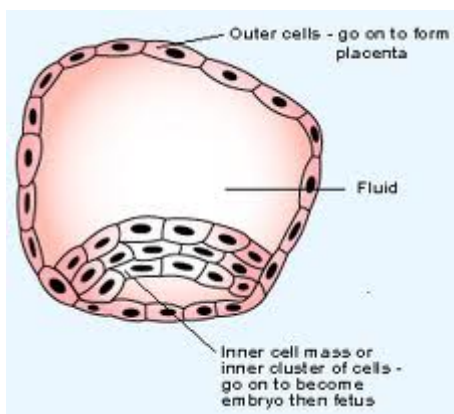


Figure 3. Embryonic stem cell

#### B. Adult-somatic

- Found among some differentiated cells in a specific tissue or organ; placental cord; primary teeth.
- Are rare in mature tissues, so isolating these cells from an adult tissue is challenging, cloning in cell culture have not yet been worked out. This is an

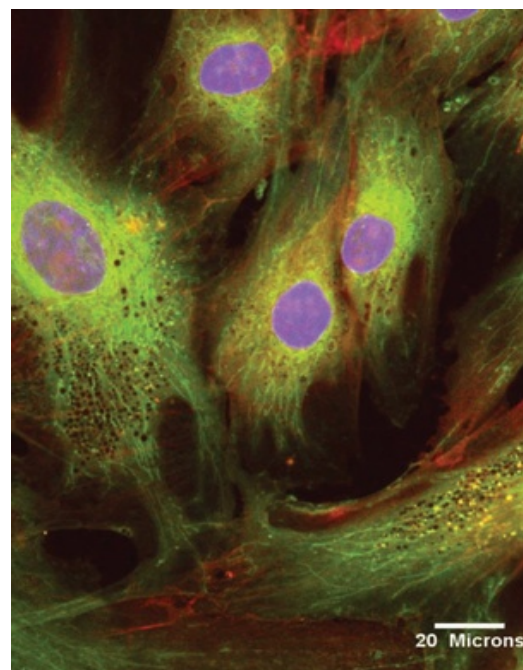


Figure 4. Mesenchymal stem cells

## 2. Cloning: IN GENERAL OF THREE TYPES

1-Reproductive Cloning: in which there will be production of new organisms genetically identical to donor.

2- Therapeutic Cloning

- Make a therapeutic product (vaccine, human protein etc).
- Deliver organs that will not be rejected.
- Act as animal models for human disease.

3-DNA Cloning: Breeding animals or plants with genetically favorable traits (genetic engineering) 2.

## 3. Possible Uses of Stem Cell Technology

- Replaceable tissues/organs.
- Repair of defective cell types.
- Delivery of genetic therapies.

- Delivery chemotherapeutic agents.

## 4. Challenges to Stem Cell/Cloning Research

- Stem cells need to be differentiated to the appropriate cell type(s) *before* they can be used clinically.
- Recently, abnormalities in chromosome number and structure were found.
- Stem cell development or proliferation must be controlled once placed into patients.
- Possibility of rejection of stem cell transplants as foreign tissues is very high.
- Contamination by viruses, bacteria, fungi, and Mycoplasma possible 3-8.

"Genetic services for the prevention, diagnosis, and treatment of disease should be available to all, regardless of the cost factor, and should be provided first to those whose needs are the greatest" WHO".

Table 1. Thematic overview of the literature-in vivo & in vitro 9

Stem cells	Target tissue/target cells	Literature
DPSCs	Odontoblasts	BATOULI et al. 2003, BRAUT et al. 2003, IOHARA et al. 2004, MINA & BRAUT 2004, NAKASHIMA et al. 2004, ZHANG et al. 2005, HUANG et al. 2006, KUMABE et al. 2006, Yu J. et al. 2006, YANG X. et al. 2007, TAKEDA et al. 2008, YANG X. et al. 2008b, Yu J. et al. 2008, ZHANG et al. 2008a, ZHANG et al. 2008b, HE F. et al. 2009, YANG X. et al. 2009, Yu V. et al. 2009, NAKASHIMA et al. 2002, SUMITA et al. 2009
	Dentin & pulp tissue	GRONTHOS et al. 2002, Yu J. et al. 2006, EL-BACKLY et al. 2008, HE H. et al. 2008
	Osteoblasts	GRONTHOS et al. 2000, GRONTHOS et al. 2002, BRAUT et al. 2003, MINA & BRAUT 2004, LAINO et al. 2005, PIERDOMENICO et al. 2005, KERKIS et al. 2006, LAINO et al. 2006, PAPACCIO et al. 2006, Yu J. et al. 2006, d'AQUINO et al. 2007, Jo et al. 2007, Liu H. S. et al. 2007, OTAKI et al. 2007, Yu J. et al. 2007, CHENG et al. 2008, DE MENDONCA COSTA et al. 2008, GRAZIANO et al. 2008, Lu et al. 2008, TAKEDA et al. 2008, Yu J. et al. 2008, KOYAMA et al. 2009
	Chondrocytes	KERKIS et al. 2006, CHENG et al. 2008, KOYAMA et al. 2009
	Adipocytes	PIERDOMENICO et al. 2005, Jo et al. 2007, Liu H. S. et al. 2007, CHENG et al. 2008, HE H. et al. 2008, ZHANG et al. 2008a, KOYAMA et al. 2009
	Endothelocytes	d'AQUINO et al. 2007
	Neurons	GRONTHOS et al. 2002, KERKIS et al. 2006, d'AQUINO et al. 2007, Liu H. S. et al. 2007, ARTHUR et al. 2008, HE H. et al. 2008
	Musculature	KERKIS et al. 2006, Zhang et al. 2008a
SHEDs	Odontoblasts	MIURA et al. 2003, CORDEIRO et al. 2008
	Osteoblasts	Seo et al. 2008, SINGHATANADGIT et al. 2009, Xu N. et al. 2009, ZHENG et al. 2009, KOYAMA et al. 2009
	Neurons	MIURA et al. 2003, MORSZCEK et al. 2009b
	Adipocytes	MIURA et al. 2003, Xu N. et al. 2009, KOYAMA et al. 2009
	Endothelocytes	CORDEIRO et al. 2008
PDLSCs	Odontoblasts	TRUBIANI et al. 2007
	Periodontal tissue	Seo et al. 2004, SONOYAMA et al. 2006, Liu Y. et al. 2008, YANG Z. et al. 2009
	Osteoblasts	GAY et al. 2007, FUJII et al. 2008, CHANG et al. 2009, SINGHATANADGIT et al. 2009
	Cementoblasts	Seo et al. 2004, MA et al. 2008, CHANG et al. 2009, YANG Z. et al. 2009
	Chondrocytes	GAY et al. 2007
	Adipocytes	Seo et al. 2004, GAY et al. 2007, FUJII et al. 2008
DFSCs	PDL progenitor cells	YOKOI et al. 2007
	Osteoblasts	MORSZCEK et al. 2005, MORSZCEK 2006, MORSZCEK et al. 2009a
	Cementoblasts	MORSZCEK et al. 2005, MORSZCEK 2006, KEMOUN et al. 2007, Wu J. et al. 2008b
	Neuroblasts	VÖLLNER et al. 2009, MORSZCEK et al. 2009b
SCAPs	Odontoblasts	KIKUCHI et al. 2004, SONOYAMA et al. 2006
	Osteoblasts	IKEDA et al. 2006, TETE et al. 2008, PARK et al. 2009

## 5. Dental Stem Cells

In dentistry, interest in tissue engineering (which combine up biology, chemistry engineering and clinical sciences) researches on different types of dental stem cells done in vivo and in vitro, increased rapidly among researchers and institutes Table 1. Stem cell research is one of the most fascinating areas of contemporary biology, but, as with many expanding fields of scientific inquiry,

research on stem cells raises scientific questions as rapidly as it generates new discoveries.

### 5.1. Potential Applications for Dental Stem Cells

Dental stem cells display multi differentiation potential, with the capacity to give rise to distinct cell lineages, osteo/osteogenic, adipogenic, and neurogenic. Therefore, these cells have been used for tissue-engineering studies to assess their potential in preclinical applications Table 2.

Table 2. applications for dental stem cells

Dental Applications
Pulpal regeneration
Craniofacial reconstruction
Engineering of new teeth
Medical Applications
Corneal repair
Lamellar bone generation
Treatment of liver disease
Cardiac repair following myocardial infarction
Treatment of muscular dystrophy
Treatment following a stroke
Spinal cord regeneration
Treatment of diabetes

### 5.2. Source of Adult Stem Cells

Dental tissues are specialized tissues that do not undergo continuous remodeling as shown in bony tissues Figure 5.

Dental Tissue MSC's

Human Pulp Tissue (DPSC's, post-natal dental pulp stem cells)/Gronthos et al, 2000.

Exfoliated Deciduous Teeth (SHED)/Miura et al, 2003.

Periodontal Ligament (PDLSC)/Seo et al, 2004.

Apical Papilla (SCAP)/Sonoyama et al, 2006, 2008.

Dental Follicle Precursors (DFPC)/Morsczeck et al, 2005.

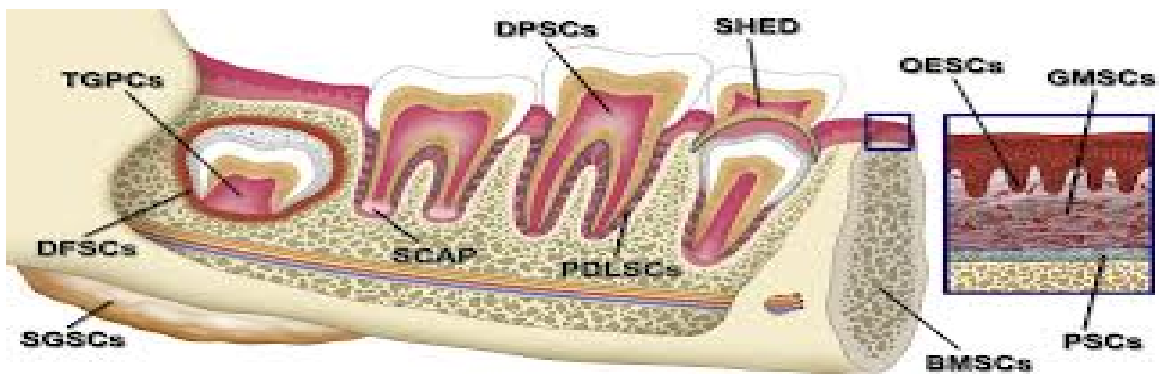


Figure 5. dental stem cells

Selected medical waste from clinical dentistry that may be used for stem cell isolation, such as teeth extracted for impaction, orthodontic or irreversible periodontitis reasons, exfoliated deciduous teeth (15).

Different dental stem cells has different properties as shown in Table 3.

Selected cell surface markers of dental stem cells (DPSCs) that are commonly used for dental stem cell characterisation. PDLSCs, periodontal ligament stem cells; DFCs, dental follicle cells; SCAP, stem cells from the root apical papilla; OCT-4, octamer-binding transcription factor-4; SSEA-1, stage-specific embryonic antigen-1; SSEA-4, stage-specific embryonic antigen-4.

Recent research has also clarified that dental follicles, if extracted in a very early stage, when dental roots did not start to be formed, contain a lineage of DFCs, characterised by high levels of embryonic stem cell (ESC) markers such as CD90, tumour rejection antigen (TRA)-1-60, TRA-1-81, OCT-4, CD133 and SSEA-4 (15).

In 2003 Dr. Songtao Shi who is a pediatric dentist discovered baby tooth stem cells by using the deciduous teeth of his six year old daughter, he was luckily able to isolate, grow and preserve these stem cells' regenerative ability, he named them as SHED (Stem cells from Human Exfoliated Deciduous teeth).

Table 3. properties of different dental stem cells

Properties	DPSC	SCAP	SHED	PDLSC	DFPC
Location	Permanent tooth pulp	Apical papilla of developing root	Exfoliated deciduous tooth pulp	Periodontal ligament	Dental follicle of developing tooth
Proliferation rate	Moderate	High	High	High	High
Heterogeneity	Yes	Yes	Yes	Yes	Yes
Multipotentiality	Odontoblast, osteoblast, chondrocyte, myocyte, neurocyte, adipocyte, corneal epithelial cell, melanoma cell, iPS	Odontoblast, osteoblast, neurocyte, adipocyte, iPS	Odontoblast, osteoblast, chondrocyte, myocyte, neurocyte, adipocyte, iPS	Odontoblast, osteoblast, chondrocyte, cementoblast, neurocyte	Odontoblast, osteoblast, neurocyte
Tissue repair	Bone regeneration, neuroregeneration, myogenic regeneration, dentin-pulp regeneration	Bone regeneration, neuroregeneration, dentin-pulp regeneration, root formation	Bone regeneration, neuroregeneration, tubular dentin	Bone regeneration, root formation, periodontal regeneration	Bone regeneration, periodontal regeneration

DPSC = dental pulp stem cells; SCAPs = stem cells from the apical papilla; SHED = stem cells from the pulp of human exfoliated deciduous teeth; PDLSC = periodontal ligament stem cells; DFPC = dental follicle precursor cells.

(16)-Carlos ESTRELA, Ana Helena Gonçalves de ALENCAR, Gregory Thomas KITTEN, Eneida Franco VENCIO, Elisandra GAVA. Mesenchymal Stem Cells in the Dental Tissues: Perspectives for Tissue Regeneration. *Braz Dent J* (2011) 22 (2): 91-98.

### 5.3. Types of Dental Stem Cells

#### 5.3.1. SHED (Exfoliated Deciduous Teeth SC's)

- Fast proliferation.
- Greater population doubling.
- Sphere like cluster formation (cultured neurogenic medium).

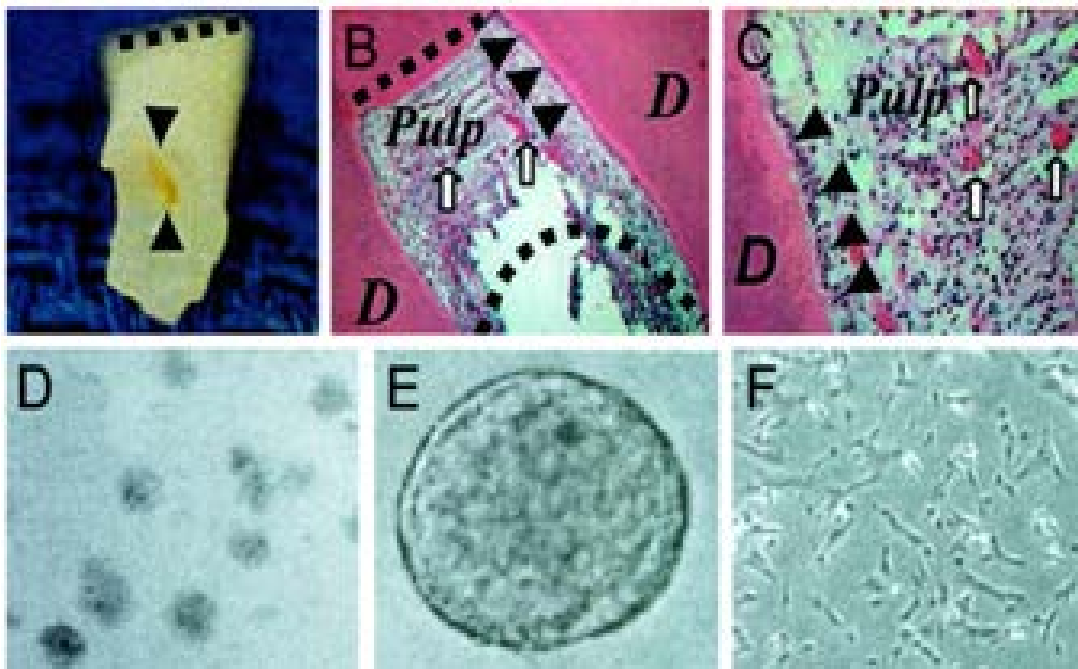


Figure 6. Exfoliated Deciduous Teeth SC's Masako Miura, et al 2003 (17)

- Also termed “immature stem cells”.
- Unable to regenerate a complete dentin-pulp complex in vivo.
- Unlike DPSC's can differentiate into bone forming cells.

Comparative characterization of from SHED and dental pulp stem cells by Xi Wang et al, archive oral biology 2012.

SHED showed a higher proliferation rate and differentiation capability in comparison with DPSCs in vitro,

- In vivo transplantation suggested that SHED have a higher capability of mineralization than the DPSCs. SHED may represent a suitable, accessible and potential alternative source for regenerative medicine and therapeutic applications Figure 7 (18).

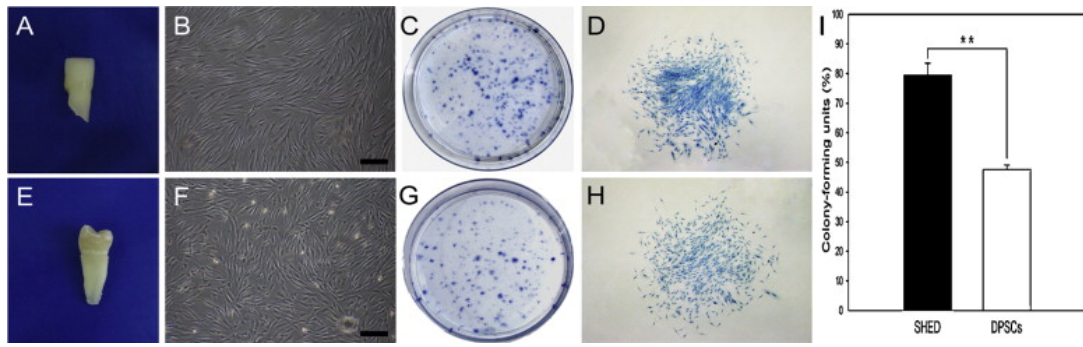


Figure 7. Xi Wing, et al 2012 (18)



Figure 8. Primary teeth banking necessary step

- The first stem cells isolated from adult human 3ed molar.
- Dental pulp stem cells (DPSCs) represent a kind of adult cell colony which has the potent capacity of self-renewing and multilineage differentiation
- Some studies have proved that DPSCs are capable of producing dental tissues *in vivo* including dentin, pulp, and crown-like structures. Whereas other investigations have shown that these stem cells can bring about the formation of bone-like tissues. Theoretically, a bio-tooth made from autogenous DPSCs should be the best choice for clinical tooth reconstruction.

**5.3.2. Isolation of Dental Pulp Stem Cells**

- Enzymatically isolated and seeded onto dentin to promote “Odontoblast-like” cells.
- Multilineage differentiation of DPSC subpopulations:
  - Adipogenic
  - Neurogenic
  - Osteogenic
  - Chondrogenic
  - Myogenic

**Ectopic Formation of Dentin-Pulp-like Complex**

Transplanted DPSC’s mixed with hydroxyapatite/tricalcium phosphate (HA/TCP) forms ectopic pulp-dentin like tissue complexes in immunocompromised mice. (Gronthos et al., 2000; Batouli et al., 2003). Odontoblast-like cells express sialophosphoprotein (DSPP), producing dentinal tubules similar to natural dentin. These studies provide a novel advance for future pulp tissue preservation and a new alternative for the biological treatment for endodontic diseases. The differentiation of DPSC to a specific cell lineage is mainly determined by the components of local microenvironment, such as, growth factors, receptor molecules, signaling molecules, transcription factors and extracellular matrix protein.

**5.3.3. SCAP ( Apical Papilla SC’s)**

- Hidden Treasure in Apical Papilla: The Potential Role in Pulp/Dentin Regeneration and BioRoot Engineering
- Odontogenic differentiation; They are capable of forming odontoblast-like cells and produce dentin *in vivo* and are likely to be the cell source of primary odontoblasts for the root dentin formation 20. Figure 9

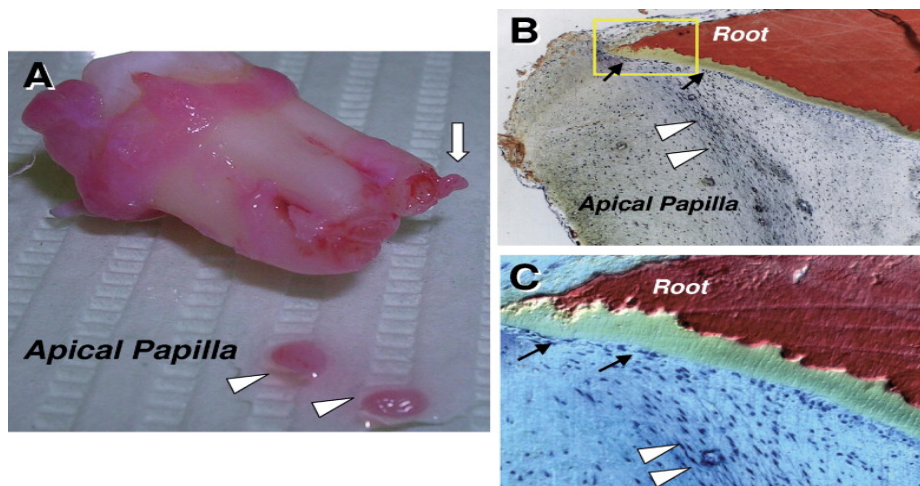


Figure 9. Apical Papilla SC’s

When distal buccal root apical papilla of the lower first molar was surgically removed from a 9-month-old minipig, the distal buccal root stopped developing at the

3-month follow-up (*black arrows*), but other roots show a normal growth and development (*red arrows*) 20. Figure 10.

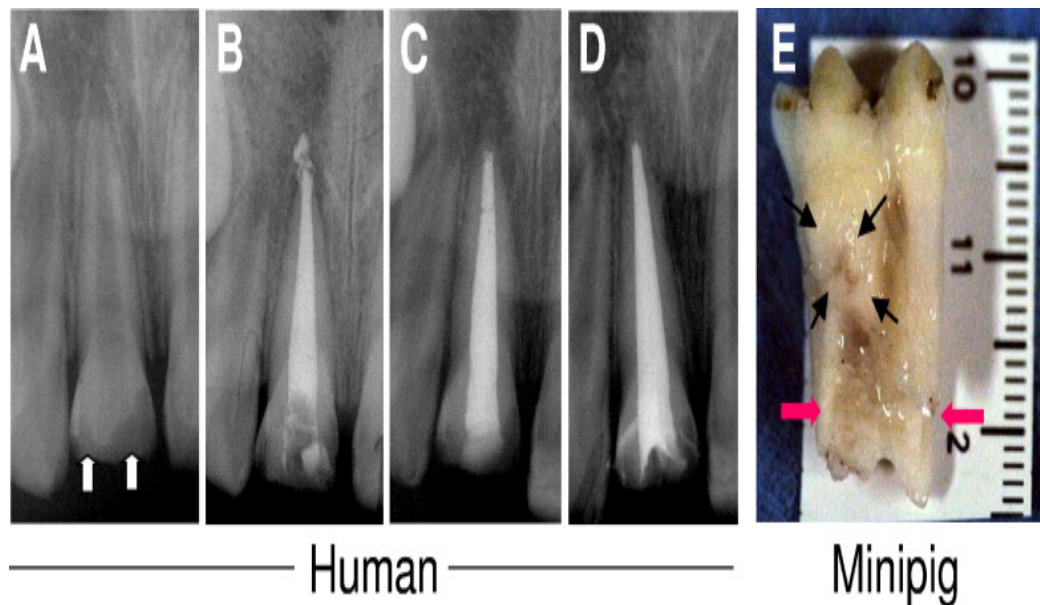


Figure 10. Apical Papilla SC's experiment

#### 5.3.4. PDLSC's (periodontal ligament sc's)

- The concept that stem cells may reside in the periodontal tissues was first proposed almost 30 years ago by Melcher.
- Form cementoblasts and osteoblasts
- Homeostasis and regeneration of perio tissues
- Mesenchymal stem cells serve as a source of renewable progenitor cells generating cementoblasts, osteoblasts, and fibroblasts 21.

#### -Regeneration of Perio Defects with PDLSC's

- PDGF (platelet derived growth factor)
- IGF (insulin derived growth factor)
- PRP (platelet rich plasma)
- Cell based regenerative therapy:
  - Ex vivo expanded autologous BMMSC's facilitated repair of perio defects (Yamada et al., 2006)
  - PDL regeneration is as important as bone regeneration otherwise ankylosis ensues
- PDLSC's may be an ideal source to regenerate PDL (Liu et al., 2008)
- Human PDLSC expanded *ex vivo* and seeded in three dimensional scaffolds (fibrin sponge, bovine-derived substitutes) were shown to generate bone.

These cells have also been shown to retain stem cell properties and tissue regeneration capacity. These findings suggest cells might be used to create a biological root that could be used in a similar way as a metal implant, by capping with an artificial dental crown.

#### -DPSC's vs. SCAP

- Apical papilla is a precursor to radicular pulp
- Earlier line of stem/progenitor cells (SCAP)
- SCAP's superior source of stem cells

#### 5.3.5. DFPC's (Dental Follicle Precursor Cells)

- DFSCs are the origin of the periodontium, including the cementum, PDL, and alveolar bone

- The dental follicle is a loose connective tissue that surrounds the developing tooth. DFPC's could therefore be a cell source for mesenchymal stem cells
- Cells can be isolated and grown under defined tissue culture conditions, and recent characterization of these stem cells has increased their potential for use in tissue engineering applications, Periodontium, cementum, PDL, alveolar bone precursors

Source: impacted third molars

#### -Applications in dentistry

- MSCs are a valuable cell source for cell-based tissue engineering therapy.
- Regenerative Dentistry & Tooth Stem Cells idea is that instead of figuring out how to ameliorate symptoms with devices and drugs, will regenerate lost function of the body by regenerating the function of organs and damaged tissue.
- The ultimate goal of tooth regeneration is to replace the lost teeth. Stem cell-based tooth engineering is deemed as a promising approach to the making of a biological tooth (bio-tooth). Dental pulp stem cells (DPSCs) represent a kind of adult cell colony which has the potent capacity of self-renewing and multilineage differentiation. A bio-tooth made from autogenous DPSCs should be the best choice for clinical tooth reconstruction.
- Stem cells therapeutic potential in Periodontics it could help in regeneration of vital structures like bone, cementum, periodontal ligament fibers, and dental pulp.
- Several craniofacial structures-such as the mandibular condyle, calvarial bone, cranial suture, Salivary gland and subcutaneous adipose tissue-have been engineered from mesenchymal stem cells, growth factor, and/or gene therapy approaches.
- A promising option to replace bone tissue and solve problems associated with morbidity of autogenous grafting. tissue-engineering techniques an alternative

to repair bone maxillary atresia and discuss the concepts and potentials of bone regeneration through cell culture techniques as an option for restorative maxillofacial surgery.

## 6. Stem Cell-delivery Therapeutics for Periodontal Tissue Regeneration

- Use of guided tissue/bone regeneration technology.
- A variety of growth factors and various bone grafts/substitutes toward the design and practice of endogenous regenerative technology by recruitment of host cells (cell homing) or stem cell-based therapeutics by transplantation of outside cells to enhance periodontal tissue regeneration and its biomechanical integration.
- Pre-clinical and clinical studies delivering autologous or allogenic stem cells of either dental or non-dental origin to the periodontium via biomaterials-free or biomaterials-based approaches. Most of stem cell delivery-based therapy was and continues to be autologous.
- Therapy typified by the harvest of tissue biopsies from the donor, isolation and expansion of the cells and, finally, the delivery of cell therapeutics back to the donor.
- The use of allogeneic cells deposited in a cell bank is much cheaper and more practical than the use of autologous stem cells.
- The decision to incorporate stem cells into clinical periodontal therapy, especially those from an allogeneic source, requires careful analysis of the risks and benefits associated with the procedure.
- Particularly in cases where the disease has caused large tissue defects in the periodontium.
- Delivery of periodontal ligament stem cells (PDLSCs) to periodontal intra-bony defects via either cell sheets (A) or cell pellets (B). A clinical trial that involves the use of autologous PDLSCs derived from the patient's third molar(s) for periodontal therapy 15.
- Periodontal ligament cell sheet transplantation. Human periodontal ligament cells are isolated from an extracted tooth and cultured on temperature-responsive culture dishes at 37°C. Transplantable cell sheets are harvested by reducing temperature to 20°C, and grafted onto an athymic rat periodontitis model 24. Figure 11 A & B

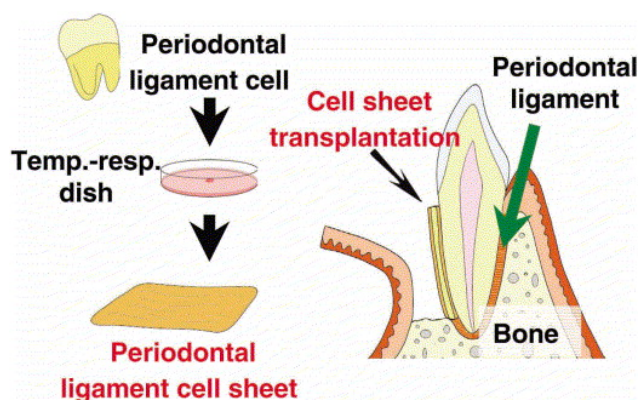


Figure 11 A. Cell sheet engineering

Periodontal ligament regeneration 4 weeks after transplantation, periodontal ligament tissues have regenerated (left). No regeneration was observed in the control without cell sheet transplantation (right) 24.

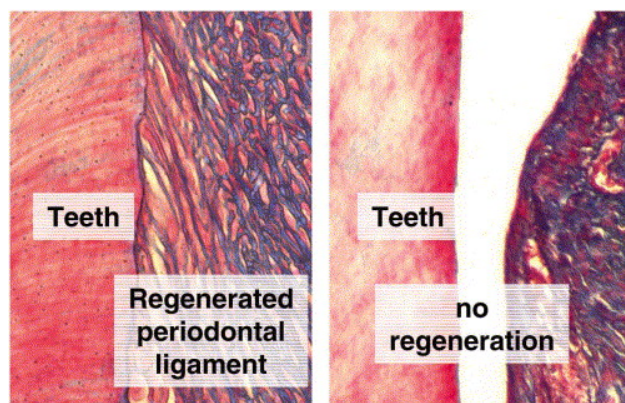


Figure 11 B

- Most scientists are optimistic that tissue engineering, with its sophisticated mix of biology and chemistry, will be more predictable in the years ahead.”
- Guided tissue regeneration has become the gold-standard surgery for periodontal tissue regeneration. This procedure involves draping a biocompatible membrane over the periodontal defect from the root surface to the adjacent alveolar bone, often in combination with a bone graft 25.

## 7. Bio Tooth

Organ formation during embryogenesis is a complex process that involves various local cell-cell interactions at the molecular and mechanical levels to form highly complex specialized arrangements of differentiated cells, create a matrix (scaffold) in the shape of a tooth, throw in some cells and hope for the best. It's considered one of the most successful techniques for tissue engineering of simple tissues is the use of biodegradable scaffolds into which cells are seeded and adopt the shape of the scaffold 26. (Figure 12).

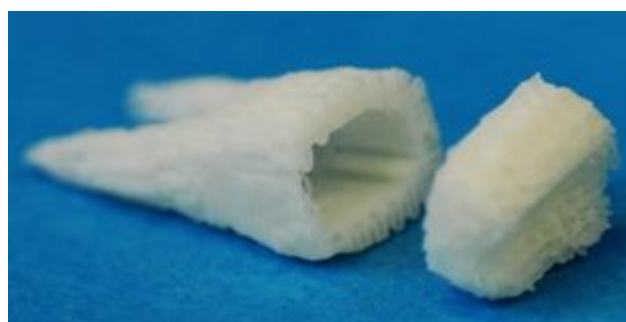


Figure 12. Treated dentin matrix (TDM) as a biological scaffold

### 7.1. Biological Tooth Replacement

(A) Stimulation of third dentition (tertiary tooth) (Otto et al. 1997).

(B) Construction of an adult tooth *de novo* (Robey, 2005).

(C) Seeding of dissociated third molar tooth bud cells into tooth-shaped scaffolds (Young et al. 2002; Duailibi et al. 2004).



(D) Generation of a tooth primordium from cultured stem cells (Ohazama et al. 2004).

Research into using stem cells to re grow new teeth has been around for at least 10 years.

In 2002, Professor Paul Sharpe at the Dental Institute of King's College in London translate tooth re growth with stem cells in mice into regenerative dentistry for humans.

Researchers from Tokyo University in 2009 reportd success with implantation of stem cell tooth germs in mice which grew into fully.

Functional teeth within few months. Scaffold was also successfully used to re grow anatomically correct teeth in nine weeks by researchers at Colombia University Medical Center.

In 2011 Tokyo Medical and Dental University research group has provided a proof of concept for bioengineered mature organs, in this instance a mature tooth developed from a bioengineered tooth germ, being successfully transplanted.

The engrafted bioengineered tooth displayed physiological tooth functions, such as mastication, periodontal ligament function for bone remodeling and responsiveness to noxious stimulations. The study represents a substantial advance and demonstrates the real potential for bioengineered mature organ replacement as a next generation regenerative therapy.

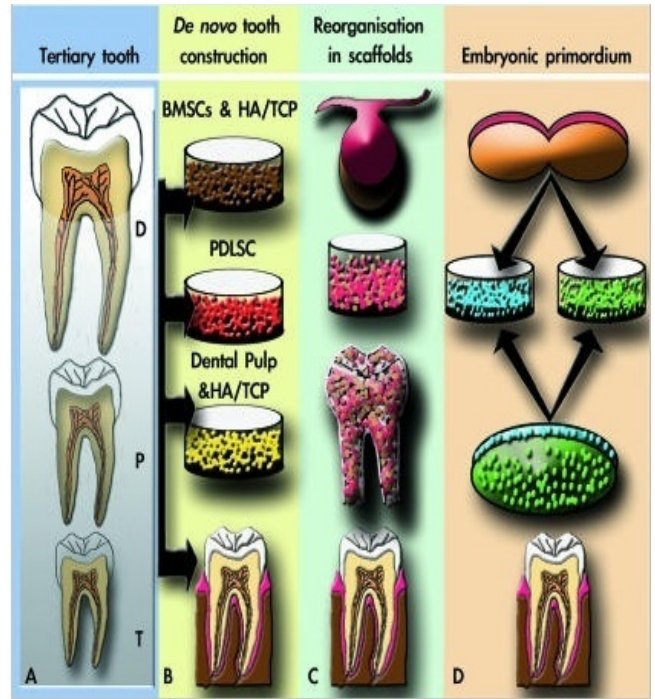


Figure 13. Schematic summary representation of four different possible approaches to tissue engineering teeth. Rachel Sartaj and Paul Sharpe 2006

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## Scientists use stem cells to grow fully functioning teeth in mice

Team at Tokyo University of Science hope breakthrough could lead to technology to replace damaged or lost organs in humans

Haroon Siddique and agencies  
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A green fluorescent protein was used to track the genes in the 'tooth germ'. Photograph: Takashi Tsuji, Tokyo University/PA

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In mice, stem cells grew into a tooth (in green) that had similar properties to natural teeth.

## 7.2. Obstacles to Tooth Regeneration

- Abnormal (small) tooth size.
- Lack of consistent root formation.
- Incomplete eruption into functional occlusion.

## 8. Pulp Tissue Engineering/Regeneration

Early attempts (Myers and Fountain, 1974) allowed a blood clot to form in the canal but only connective tissue formed.

More recently pulp cells grown on polyglycolic acid (PGA) formed pulp-like tissue in vitro and in vivo (Gu et al., 1996; Moony et al., 1996, and Burma et al., 1999).

Since the isolation and characterization of DPSC's SHED and SCAP, more sophisticated regenerative investigation has occurred (Huang et al., 2006, 2008; Murray et al., 2007; Prescott et al., 2008).

### 8.1. Modern Pulp Regeneration

SHED seeded onto synthetic scaffolds seated into pulp chamber space formed odontoblast-like cells that located against the existing dentin surface. (notorthopic) (Cordeiro et al., 2008).

Speculation: undifferentiated MSC's residing in the periapical tissue and BMMSC's in the alveolar bone of the jaws can be introduced into the root canal space and via blood clots to allow for pulp tissue regeneration and formation of odontoblasts (Myers and Fountain, 1974)

More realistically: the known characteristics of PDLSC's, DPSC's, and SCAP suggest that it is unlikely that odontoblasts can be derived from PDL or periapical bone.

Dental stem cells display multifactorial potential Mesenchymal stem cells in the dental tissues such as

- high proliferation rate,
- multi-differentiationability,
- easy accessibility,
- high viability and
- easy to be induced to distinct cell lineages.

Solid research into the basic science and biology behind stem cells must be performed before scientists leap into the clinical trials.

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