

# Mystery Inside the Tooth: The Dental Pulp Stem Cells

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## ABSTRACT

Stem cells are distinguished by their ability to differentiate into different types of cells in the body and to self-replicate. During the recent years, stem cells have been used extensively in the field of medicine for the repair and regeneration of defective tissues and organs. However, the knowledge on the stem cell technology is increasing quickly in all medical disciplines and it dictates the need for new protective approaches in all fields, which include reparative

dentistry. Stem cell therapy constitutes a common challenge for dentists as well as for biotechnologists. The aim of this study was to review the knowledge which was related to stem cells and to consider the possibility of use of stem cell populations and their technology in the future clinical applications, to cure diseases like Parkinsonism, Juvenile diabetes, certain forms of cancer, spinal injuries and heart problems.

**Key Words:** Pulp, Stem cells, Regeneration, Disease

## INTRODUCTION

The regeneration of oral tissues that are injured by disease or trauma is now possible due the discovery of dental stem cells and recent advances in the cellular and molecular biology. These have led to the development of novel therapeutic strategies. The knowledge on the stem cell technology is increasing quickly in all the medical disciplines and it dictates the need for new protective approaches in all the fields, which include reparative dentistry. With the help of tissue engineering, the dream of repairing and regenerating defective tissues and organs will be a reality soon [1].

## STEM CELLS

Stem cells are biological cells which are found in all multi cellular organisms, that can divide and differentiate into diverse specialized cell types. They can self renew to produce more cells. They are a promising tool for tissue repair [2]. There are two types of stem cells, embryonic stem cells and adult stem cells. The embryonic stem cells are derived from the inner cell mass of the blastocyst- which is a thin-walled, hollow structure in the early embryonic development, that contains a cluster of cells which is called the inner cell mass, from which the embryo arises. The outer layer of the cells gives rise to the placenta and other supporting tissues which are needed for the foetal development within the uterus, while the inner cell mass cells give rise to the tissues of the body [3]. These cells have the capacity of forming the three germ layers and the ability to develop as many cell types.

Adult stem cells are found in the blood from the umbilical cord, the bone marrow and the blood. The pluripotent stem cells that can be found in the blood from the umbilical cord are only few in numbers. These adult stem cells have been used for many years to treat leukaemia and bone\blood cancers through bone marrow transplantation and some haematopoietic diseases [4].

## THE DENTAL PULP STEM CELLS

A pedodontist, Dr. Songtao Shi, discovered baby tooth stem cells while he used the deciduous teeth of his six year old daughter

in 2003 and he named the cells as stem cells from the human exfoliated deciduous teeth (SHED). Dental Pulp Stem Cells (DPSCs) can be found within the "cell rich zone" of the dental pulp. Their embryonic origin from neural crests, explains their multipotency. These stem cells, under specific stimuli, differentiate into many cell types which include adipocytes, neurons, chondrocytes and mesenchymal stem cells [5-7]. These are the most potential stem cells which have wide therapeutic applications [8]. Dental pulp stem cells can be found both in adults and children [9].

The stem cells of dental origin can certainly generate the dental tissues [10-14]. The SHED and DPSCs are capable of generating a tissue that has morphological and functional characteristics that closely resemble those of the human dental pulp [15-18].

Unlike the umbilical cord blood cells which have to be collected immediately at birth, the dental stem cells are derived from the deciduous and permanent teeth. There are 20 viable deciduous teeth and 32 permanent teeth which can be used for collecting the stem cells. This is non-controversial and the stem cells can be collected without the involvement of any ethical issues. The viable dental stem cells are very simple to collect, without any mortality and morbidity [4].

## THE DENTAL PULP STEM CELL DIFFERENTIATION AND THE SIGNALLING MOLECULES

The growth factors and the morphogenic factors bind to specific membrane receptors and they trigger a series of signalling pathways. During the development, these signalling molecules play a major role in the cellular functions and they have an important role in the signalling reparative processes in the dentin and the pulp [19, 20]. When these are released from the dentin, they are bioactive and are fully capable of inducing the cellular responses, for example, generation of the tertiary dentin and dental pulp repair [20, 21]. The arrangement of the dentin facilitates the movement of the growth factors which are released from the dentin matrix,

that are demineralized by caries, acidic tooth conditioning agents or pulp capping materials. Calcium hydroxide has been shown to solubilize dentin and to allow the release of bioactive molecules that can regenerate dentin [22]. This involves the recruitment of DPSCs, their differentiation into odontoblasts, and the secretion of mineralizable matrices [23,24,25].

## THE ISOLATION OF THE DENTAL PULP STEM CELLS

The stem cells are identified by various techniques like flow cytometry, fluorescence-activated cell sorting and magnetic-activated cell sorting and by using biomarkers (surface markers and side populations) [26]. Magnetic-Activated Cell Sorting (MACS) is a method which is used for the separation of various cell populations, depending on their surface antigens. This method allows the cells to be separated, by allowing their incubation with magnetic nanoparticles which are layered with antibodies against a particular surface antigen. This causes the cells which express this antigen, to join the magnetic nanoparticles. Afterwards, they are placed in a strong magnetic field. During this process, the cells attached to the nanoparticles which stay on the column, while the other cells flow through. With this method, the cells can be separated with respect to the particular antigen. Fluorescence-Activated Cell Sorting (FACS) is a specific type of flow cytometry. It provides a way for sorting a heterogeneous mixture of cells into two or more containers, one cell at a time, based upon the specific light scattering and the fluorescent characteristics of each cell. It provides a fast, objective and a quantitative recording of the fluorescent signals from individual cells, as well as the physical separation of the cells which are of particular interest. The cell surface markers are useful for classifying and isolating stem cells and for monitoring their states of differentiation, because they can be visualized directly with the intact cells [27].

## CRYOPRESERVATION

The haematopoietic stem cells have been cryopreserved and successfully utilized for transplantation. The dental pulp can be easily cryostored for long periods [28] and it can be used to form a cryobank for adult tissue regeneration [29]. The dental pulp stem cells retain their potential after cryopreservation [30]. In a study which was performed on the cryopreserved tissue samples of periodontal ligaments [31]. The cryopreservation of the whole dental pulp leads to a safe recovery. Different cryopreservation techniques are required for the whole pulp. These features make these cells for a therapeutic three-dimensional tissue reconstruction, with the potential of storage and recovery as per the needs of the patient. Dental pulp stem cells can also be obtained from the patient's vital pulp, since we have 20 deciduous and 32 permanent teeth. This can be done with the help of stem cell markers, which help in the identification of stem cells.

## REGENERATION OF THE TOOTH TISSUE AND BLOOD VESSELS

It has been observed that SHED have the potential to differentiate into functional vascular endothelial cells by a process that resembles that of vasculogenesis [32,33]. These findings raise the hope that the stem cells of dental pulp origin may be useful in treating severe ischaemic conditions of the heart, brain, or the limbs. Specifically, one of the challenges of dental pulp tissue engineering is the production of a functional vascular network, considering the fact that all vascularizations must access the root canal through the

apical foramen. Hence, more research is needed for the induction of vasculogenesis accompanying efforts for dental pulp tissue engineering.

## WHOLE TOOTH REGENERATION

By placing the stem cells on biodegradable scaffolds, tooth-like tissues have been generated. Ikeda *et al* reported a fully functioning tooth replacement in an adult mouse, which was achieved by the transplantation of a bioengineered tooth germ into the alveolar bone in the lost tooth region [34]. Xu *et al.*, seeded a tooth bud from the rat on scaffolds which were fabricated from silk fibroin, with 2 pore sizes that were either used as fabricated or treated, with the Arg-Gly-Asp attachment site binding peptide [35]. Although dental tissues are regenerated, the success rate for the correct arrangement of a natural tooth is only 15-20%. So, further studies are required to achieve structurally sound teeth.

## BONE TISSUE REGENERATION

DPSCs, when they undergo differentiation into pre-osteoblasts, form an extracellular matrix that becomes a calcified woven bone tissue [36]. Other than this, it has been demonstrated that such tissues undergo remodelling, when they were transplanted in immunocompromised rats, and that they form a lamellar bone with entrapped osteocytes [37].

## IN TREATING VARIOUS DISEASES

Stem cells play a vital role in treating various lives threatening diseases. Other than forming the bone, the blood vessels, the whole tooth and the dental tissues, the dental pulp stem cells can also be used to treat myocardial infarction, Parkinson's disease, Diabetes mellitus and certain forms of cancer.

## CONCLUSION

The identification of several types of epithelial and mesenchymal stem cells in the tooth is a significant achievement. But still, the control of morphogenesis and cytodifferentiation is a challenge that necessitates a thorough understanding of the cellular and the molecular events which are involved in the development, repair and the regeneration of teeth. The current research which is being carried out on stem cells also helps us in understanding the cancer stem cells and in turn, in developing novel therapies to eliminate cancer [38]. But still, the need persists to find out new and easily accessible sources of both epithelial and mesenchymal stem cells that can be reprogrammed for an odontogenic potential and which can be then associated to form a fully functional tooth. Until the stem cells in the dental pulp are completely explored, they still remain a mystery inside the tooth.

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**FINANCIAL OR OTHER COMPETING INTERESTS:**

None.

Date of Submission: **Dec 05, 2012**

Date of Peer Review: **Jan 30, 2013**

Date of Acceptance: **Mar 12, 2013**

Date of Publishing: **May 01, 2013**