A TOOTH FOR A TOOTH: DENTAL STEM CELL BANKING IN INDIA

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ABSTRACT: Regenerative medicine is based on stem cells. The dental pulp contains the progenitor/stem cells which have the self renewal capability, multi-lineage differentiation capacity and clonogenic efficiency. Dental stem cells can generate many types of tissues including bone, nerve, cartilage, teeth and fat. However teeth can actually be a rich source of stem cells. Deciduous teeth or the so-called milk teeth and wisdom teeth have an abundance of stem cells. Stem cells have become the rage across the world after the health potential emerged some years ago. For years scientists all over the world have been working on possibilities of using these stem cells to regenerate human cells which are damaged due to illness, developmental defects and accidents. Recently stem cell banks are present, and even some of these banks do not only freeze cord stem cells but also dental stem cells of baby teeth. Hence this paper reviews the history, current concepts, evolution of stem cells in dentistry, dental stem cell banking in India, characterization of the stem cells in dentin regeneration and stem cell therapy in dentistry.

Key words: Progenitor cells; Stem cells; Stem cell banking; Tooth germs; Dental pulp; Dentin regeneration.

INTRODUCTION

Dental exfoliation in humans is a genetically regulated event during childhood. If the permanent teeth are damaged or lost, they do not regenerate. At present, teeth can only be replaced with conventional prostheses, i.e., removable prostheses, fixed dental prostheses, or implants, with prior bone augmentation if necessary. However progress in stem cell biology and tissue engineering may present new options for replacing heavily damaged or lost teeth, or even individual tooth structures. The promise of such treatment possibilities puts stem cells in the focus of dental research. The inability of most tissues and organs in adult humans to regenerate after damage has been a profound frustration throughout history to physicians, dentists, and, of course, patients. As we all know tooth development is a complex process. A tooth germ starts as an aggregation of cells that forms a hard tissue called the crown. Tooth development then proceeds through the following stages: crown completed, root-formative, and finally root-completed. Recently, the researchers have identified a population of putative post-natal stem cells in human dental pulp, dental pulp stem cells (DPSCs). Dental stem cells enjoy a host of benefits such as ease of harvesting and high regeneration capacity. It can now be stored in private stem cell bank of the rich and affluent through the country for a fee. This is one of the major evolutions that has taken place in the field of stem cells in dentistry facilitating new aura’s in stem cell therapy.

Stem cells are generally defined as clonogenic cells capable of both self renewal and multi-lineage differentiation. Post-natal stem cells have been isolated from various tissues, including bone marrow, neural tissue, skin, retina, and dental epithelium. The most striking feature of DPSCs is their ability to regenerate a dentin-pulp-like complex that is composed of mineralized matrix with tubules lined with odontoblasts, and fibrous tissue containing blood vessels in an arrangement similar to the dentin-pulp complex found in normal human teeth. Human dental pulp stem cells (hDPSCs) isolated from adult tooth pulps are characterized in terms of their self-renewal capability. hDPSCs are multipotent cells known to form ectopic dentin and associated pulp tissue in vivo. Dental pulp is the soft living tissue inside a tooth. Stem cells are found inside the soft living tissue. Here, the human DPSCs represent a novel adult stem cell population that possesses the properties of high proliferative potential and the capacity of self-renewal. Scaffold surface features are thought to be important regulators of stem cell performance and endurance in tissue engineering applications, but details about these fundamental aspects of stem cell biology remain largely unclear. Hence the aim of this paper is to review the complete characterization and current concepts of stem cells in dentistry.

Historical overview

The term stem cell was proposed for scientific use by Russian histologist Alexander Maksimov in 1908. While research on stem cells grew out of findings by Canadian scientists in the 1960s. In general there are two broad types of stem cells which are: Embryonic stem cells, and
Adult stem cells. Embryonic stem cells were harvested from embryos, they are cells derived from the inner cell mass of the blastocyst (early stage embryo, 4-5 days old, consist of 50-150 cells) of earlier morula stage embryo. In other words these are the cells that form the three germ layers, and are capable of developing more than 200 cell types. In 1998 the first human embryonic stem cell line was derived at university of Wisconsin-Madison.\(^6\) In 2003 NIH announced the discovery of DPSCs by Dr. Songtao Shi \(^8\) in 2006 IDPSC Kerkis reported discovery of immature Dental Pulp Stem Cells (IDPSC), \(^11\) a pluripotent sub-population of Dental Pulp Stem Cells (DPSC) using dental pulp organ culture. In 2007 DPSC conducted the 1st animal studies on bone regeneration.\(^12,14\) and dental end uses.\(^11,15,16\) Later in 2008 DPSC conducted the 1st animal studies begin on heart therapies \(^9\), for muscular dystrophy therapies \(^17,18\), for regenerating brain tissue \(^16,19\), for bone grafting and reconstruction of large size cranial bone defects in rats.\(^20\) Currently, clinical application is hindered by unpredictable timepoints of tooth eruption, the morphology and color of the generated tooth, and the as yet impossible regeneration of human dental enamel. No systematic literature review exists yet on the topic of “implementation of stem cell biology in tooth development” and “the current status of dental stem cell banks in India”.\(^20\)

**Evolution of Stem Cells in Dentistry in India**

In the year 2003 Dr. Songtao Shi who is a paediatric dentist discovered baby tooth stem cells by using the deciduous teeth of his six year old daughter, he was lucky able to isolate, grow and preserve these stem cells’ regenerative ability, and he named them as SHED (Stem cells from Human Exfoliated Deciduous teeth).\(^21\)

Dental stem cell banking now gives parents the option to store their child’s stem cells from the milk tooth. Dental stem cell banking is complementary to umbilical cord blood banking. Dental stem cells consist of mesenchymal variety of stem cells. “The advantage dental stem cells give is possibility of a larger collection. Instead of a 15-20 minute window post-delivery in case of umbilical cord blood banking, dental stem cells can be acquired from milk tooth or wisdom tooth. This increases the opportunity of collection. If one tooth is rejected, the next tooth can be considered for banking.”\(^6,24\)

After the scientists studied the dental pulp looking for stem cells they found that the dental pulp was rich in different stem cell types such as:

1. **Chondrocytes**: which are stem cells that have the ability to regenerate cartilage and these cells play an important role in the treatment of arthritis and joint diseases.
2. **Osteoblasts**: They are stem cells that have the ability to regenerate bone.
3. **Adipocytes**: Another type of stem cells that have the ability to repair damaged cardiac tissues following a heart attack.
4. **Mesenchymal Stem Cells**: Those are the most potent among all tissue stem cells and have the ability to differentiate into various types of reparative cells. In general Mesenchymal Stem Cells MSC are non-haematopoietic stromal cells capable of differentiating into a range of cells, those cells were first discovered in bone marrow and they were noticed to have the ability to double into many populations without loss of function, they also have the so called homing property which means that when they are delivered systemically they migrate to the site of injury. So it is to say that MSC are more promising for therapeutic applications than other types of stem cells.\(^22\)

**Stem cell banking in India**

Recently stem cell banks are present, and even some of these banks do not only freeze cord stem cells but also dental stem cells of baby teeth. This can be done easily when a child’s anterior milk tooth is shedding, the tooth is extracted by the dentist and preserved in a special kit provided from the stem cell bank company who then in their turn transfer the tooth to their special labs to harvest the dental stem cells and store them in their bank for each child confidentially until they are needed later for the child himself or a member of his family.

The first-ever dental stem cell bank in India called “Store your Cells” has now been launched. This unique bank is the venture started by dentists at Dhruv Polyclinic, Mumbai. The venture was formed under the guidance of Dr. Kedar Gadgil, who is a successful implant dentist practising at London (UK), Kent (UK), and Mumbai. After having established presence in Mumbai and New Delhi, Stemade Biotech, the country’s first private dental stem cell bank, is expanding its reach to at least 10 more cities such as Pune, Hyderabad, Surat, Chennai in the next 8-10 months buoyed by initial response at the Bangalore launch of operations. The collection of stem cells from bone-marrow presents multiple collection frequency options but the procedure is invasive and quite painful. On the other hand, dental stem cells can be collected between 6-12 years for children and from adults extracting their third molars. According to researchers the right time to recover baby teeth with stem cells is before the teeth become very loose. It is necessary for these stem cell banks to be licensed and patented. The patent gives the technology for extraction, multiplication and banking of the dental stem cells. Deciduous teeth especially the canines are the best sources and 12 deciduous teeth are sufficient and for the adults a minimum of 2 molars during the extraction of the third molars. Once collected, the dental stem cells should arrive at the storage facility within 16 hours, much ahead of the 72-hour deadline. The teeth are preserved in the Special Cryogenic storage facilities. Once stored, the dental stem cells can be pulled from inventory and...
Stem cell therapy in dentistry

Stem cell therapy which was once a science fiction is now becoming more towards reality, and it might make the dream of many people come true. So parents taking the decision to bank their children’s milk teeth might be the best gift they could ever give to their child. Milk teeth which were kept by children under their pillows to be collected by the tooth fairy might have a greater meaning; the tooth fairy might be able one day to save their one Cell therapy utilizing pulp progenitor/stem cells has the potential to improve on conventional pulp-capping with calcium hydroxide or other artificial materials that can induce only a small amount of regeneration beneath the exposed or amputated site of the pulp.23-25

Well, there are three approaches which were investigated by some researchers to implant stem cells from teeth in humans and these are: reparative dentin

1. Placing the stem cell into a mold of tooth crown which is made of Enamel-like substance with a scaffold material, and then they will start to loop blood vessels through this scaffold, after that this will be implanted elsewhere in the body and wait until it is mature, then these teeth will be extracted and implanted in the oral cavity.

2. Harvesting a wisdom tooth of a person and releasing stem cells from their pulp tissue, the stem cells are then implanted in a severely injured tooth, for example in cases of car accidents or falling down, and these implanted stem cells will help to regenerate the pulp of the injured teeth sparing them root canal treatments.

3. If there are no teeth present in the oral cavity from which stem cells can be harvested, we can take stem cell from unerupted wisdom tooth, organize them into three dimensional structures and give proper cues to them before putting them back into the socket; this is like planting a seed and waiting for it to grow.23-25

Current concept of stem cell therapy in dentistry

One of the major advantages one gets from harvesting stem cells from his/her own body and then using them later in his/her tissue regeneration if he has an illness is that there will be no refusal of these cells as they are already body parts, in other words the patient will not need to go through the process of immunosuppressant and that will spare him/her lots of suffering and time.

Specifically talking about the dental field, years from now dental stem cells will hopefully be able to correct cleft palate sparing children from multiple surgeries, stem cells will also have the potential to save injured teeth and jaw bones, correct periodontal defects, and most strikingly regenerating entire teeth structures is the horizon. Dental pulp tissue has the potential to regenerate dentin in response to noxious stimuli, such as caries. The progenitor/stem cells are responsible for this regeneration.

The regenerative potential of adult stem cells obtained from various sources including dental tissues has been of interest for clinicians over the past years and most research is directed toward achieving the following:

- Regeneration of damaged coronal dentin and pulp
- Regeneration of resorbed root, cervical or apical dentin, and repair perforations
- Pericoronal regeneration
- Repair and replacement of bone in craniofacial defects
- Whole tooth regeneration.24

Thus, stem cell therapy has considerable promise in dentin regeneration as well as whole tooth regeneration. Currently a huge amount of active medical research is underway for using these stem cells for therapy applications.

CONCLUSION

Stem cell biology, an emerging field of research, provides promising methods in vitro as well as in vivo in animal models which make speculation about a future application in human dentistry reasonable. For dentistry, stem cell biology and tissue engineering are of great interest. Various in vivo and in vitro studies provide hope of future application in humans. The parents of the child and the adults need to be motivated and educated about the importance of storing their dental stem cells and create awareness regarding the use of stem cell banking and evolution of stem cell therapy in India. Although of recent origin, stem cell banking is gaining popularity in view of its affordability, easy extraction, awareness among parents to safeguard their kid's health for long life and the emphasis in modern medical research towards therapies from regenerative tissues. Stem cell therapy has brought in a lot of optimistic hope amongst researchers, doctors, and not to forget the patients who are the chief beneficiary of this innovation. Stem cells regenerate hope and not all that is happening in research. However, a great deal of research must be done before it is possible to cultivate entire teeth as natural, autologous tooth replacements.

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