Tooth Stem Cell Banking-A Review

ABSTRACT

Stem Cells obtained traditionally were either embryonic in origin or from adult tissue which included both ethical concerns as well as invasive methods. Stem cells derived from teeth are simple to obtain and less invasive. In recent times tooth banks have emerged which will be an easy way to store one’s own stem cells. Stem cells can be easily obtained from deciduous teeth and third molars as a result of exfoliation or extraction of impacted teeth. These teeth can be stored for treatment of future diseases by using regenerative procedures. In addition, these cells have minimum risk of rejection. Stem cells from younger teeth have better potential for regeneration.

This review will outline the recent trends in stem cells from human teeth and their banking.

Key words: Stem cells, tooth banking, regeneration.

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1. INTRODUCTION
Stem cell therapy has been used around the world to treat many medical conditions, and the vast extent of its clinical applications has only been glimpsed so far. The pulp of exfoliated deciduous teeth have been researched extensively and have found to contain chondrocytes, osteoblasts, adipocytes, and mesenchymal stem cells. All of these cell types hold enormous potential for the therapeutic treatment. The application of stem cell therapy using SHED (Stem cells from exfoliated human dentition) to treat these diseases is currently being pursued by many researchers at the institutions around the world. At present there has been clear evidence that primary teeth are a better source for therapeutic stem cells than wisdom teeth, and orthodontically extracted teeth. Keeping these aspects in mind, the concept of tooth banking has popularized and various companies have set up tooth banks to tap the potential of this new and innovative approach for preserving stem cells from dental sources. Until recently, stem cells harvested from umbilical cord blood was the only storage option to guard against future illness or disease. Unfortunately, the cord cell harvesting and storage process is beyond the reach of many people. Hence newer techniques like cryopreservation and the use of magnetic field are employed.

2. TYPES OF STEM CELLS IN PULP OF HUMAN TEETH- ADIPOCYTES, CHONDROCYTES, OSTEOBLASTS AND MESENCHYMAL CELLS
Adipocytes have successfully been used to repair damage to the heart muscle caused by severe heart attack. There is also preliminary data to indicate they can be used to treat cardiovascular disease, spine and orthopedic conditions, congestive heart failure, Crohn's disease, and to be used in plastic surgery.

Chondrocytes and Osteoblasts have successfully been used to grow bone and cartilage suitable for transplant. They have also been used to grow intact teeth in animals.

Mesenchymal stem cells have successfully been used to repair spinal cord injury and to restore and movement in paralyzed human patients. Since they can form neuronal clusters, they also have the potential to treat neuronal degenerative disorders such as Alzheimer's and Parkinson's diseases.

3. TOOTH ELIGIBILITY CRITERIA FOR BANKING
Not all teeth hold the same regenerative potential. The teeth especially primary incisors and canines with no pathology and at least one third of root left contain these unique types of cells in sufficient number. Primary teeth distal to the canine are generally not recommended for sampling. Primary molars have a broader root base, and therefore, are retained in the mouth for a longer period of time than anterior teeth. In some instances, early removal of deciduous molars for orthodontic considerations (e.g. early intervention for space maintenance) will present an opportunity to recover these teeth for stem cell banking.
4. STEM CELL BANKING - TOOTH COLLECTION, STEM CELL ISOLATION AND STORAGE

4.1 Tooth Collection - The tooth exfoliated should have pulp red in color, which is indicative of cell viability. Teeth that become very mobile, either through trauma or disease (e.g. Class III or IV mobility), often have a severed blood supply, and are not candidates for stem cell recovery. The tooth is then transferred into the vial containing a hypotonic phosphate buffered saline solution, which provides nutrients and prevent the tissue from drying during transport (up to four teeth in the one vial). Placing a tooth into this vial at room temperature induces hypothermia. The vial is then carefully sealed and placed into the thermette a temperature phase change carrier, after which the carrier is then placed into an insulated metal transport vessel. Store-A-Tooth, a company involved in tooth banking uses the Save-A-Tooth device for transporting stem cells from the dental office to the laboratory. The time from harvesting to arrival at the processing storage facility should not exceed 40 hours.[15]

4.2 Stem Cell Isolation - When the tooth bank receives the vial, the following protocol is followed.[15]

Tooth surface is cleaned by washing three times with Dulbecco’s Phosphate Buffered Saline without Ca++ and Mg++ (PBSA) after which disinfection is done with disinfection reagent such as povidone iodine and again washed with PBSA. The pulp tissue is isolated from the pulp chamber with a sterile small forceps or dental excavator. Stem cell rich pulp can also be flushed out with salt water from the center of the tooth. Contaminated Pulp tissue is placed in a sterile petri dish which was washed at least thrice with PBSA. The tissue is then digested with collagenase Type I and Dispase for 1 hour at 37°C. After this isolated cells are passed through a 70 um filter to obtain single cell suspensions. Then the cells are cultured in a Mesenchymal Stem Cell Medium (MSC) medium which consists of alpha modified minimal essential medium with 2mM glutamine and supplemented with 15% fetal bovine serum (FBS), 0.1Mm L- ascorbic acid phosphate, 100U/ml penicillin and 100ug/ml streptomycin at 37°C and 5% CO2 in air. Usually isolated colonies are visible after 24 hrs. Different cell lines can be obtained such as odontogenic, adipogenic and neural by making changes in the MSC medium.

5. STEM CELL STORAGE - CRYOPRESERVATION AND MAGNETIC FREEZING.

5.1 Cryopreservation is the process of preserving cells or whole tissues by cooling them to sub-zero temperatures.[9] At these freezing temperatures, biological activity is stopped, as are any cellular processes that lead to cell death.[16,17] Cells harvested near end of log phase growth are best for cryopreservation. The cells are preserved in liquid nitrogen vapor at a temperature of less than -150°C. This preserves the cells and maintains their potency. In a vial, 1-2x 10^6 cells in 1.5 ml of freezing medium is optimum. Ice injury is a major concern for tissue cryopreservation. Kawasaki et al. suggested that the slow and rate-controlling freezing reduced the ice injury of cryopreserved living cells. Papaccio G et al (2006) studied the differentiation and morpho-functional properties of cells derived from stem cells after long-term cryopreservation to evaluate their potential for long-term storage with a view to subsequent use in therapy. They concluded that dental pulp stem cells and their osteoblast-derived cells can be long-term cryopreserved and may prove beneficial for clinical applications.[20]
The most serious problem during freezing is cell damage induced by ice crystal formation inside the cells as well as mechanical stresses by extracellular ice formation. To prevent cell damage vitrification can be utilised, which freezes cells quickly before ice crystals can form, is an efficient approach used to cryopreserve oocytes and embryos.

5.2 Magnetic freezing is the Cell Alive System (CAS). Under the condition of CAS magnetic field energy, water clusters do not accumulate but remain in smaller groups, thus minimizing restraining the expansion of the water. This technology, is called CAS and uses the phenomena that applying even a weak magnetic field to water or cell tissue will lower the freezing point of that body by up to 6-7 degrees Celsius. Once the object is uniformly chilled, the magnetic field is turned off and the object snap freezes. The Hiroshima University company is the first expression of this new technology. Using CAS, Hiroshima University claims that it can increase the cell survival rate in teeth to as high as 83%. This compared to 63% for liquid nitrogen (-196 degrees C), 45% for ultra-cold freezing (-80 degrees C), and just 21.5% for a household freezer (-20 degrees C). Maintaining a CAS system is a lot cheaper than cryogenics and more reliable as well.\textsuperscript{[21]}

6. COMMERCIAL ASPECT OF TOOTH BANKING

These cells can be best utilized for the patients from which they are harvested, and to a certain extent their immediate family and blood relatives. As such, it is inevitable that the key to successful stem cell therapy lies in being able to harvest the cells at the right point of development and to safely store them until accident or disease requires their usage. They can be potentially stored for decades, and the cost and technical difficulty of doing this properly make stem cell therapy using one's own cells a still uncertain bet. Till date, tooth banking is not very popular but the trend is catching up mainly in the developed countries.

In the USA, BioEden(Austin, Texas), has international laboratories in the UK (serving Europe) and Thailand (serving South East Asia) with further expansion plans for Russia, Australia, India and the Middle East. StemSave (USA) and Store -A- Tooth (USA) are also companies involved in banking tooth stem cells and expanding their horizon in other countries.

In Japan, the first tooth bank was established in Hiroshima University and the company was named as "Three Brackets" (Suri Buraketto) in 2005. Nagoya University (Kyodo, Japan) also came up with a tooth bank in 2007. Taipei Medical University (TMU) in collaboration with Hiroshima University opened the nation's first tooth bank in September, 2008 with the goal of storing teeth for natural implants and providing a potential alternative source for harvesting and freezing stem cells including SHED.\textsuperscript{[21]}

The Norwegian Tooth Bank set up in 2008 is collecting exfoliated primary teeth from 100,000 children in Norway. The Tooth Bank is a sub-project in the Norwegian Mother and Child Cohort Study (MoBa).\textsuperscript{[22]}

7. CONCLUSION

Stem cell therapy is emerging as a revolutionary treatment modality to treat diseases and injury, with wide-ranging medical benefits. SHED are stem cells found in the exfoliated deciduous/ primary teeth of children. Recent studies show that they appear to have the ability to develop into more types of body tissue than other types of stem cells. This difference opens the door to more therapeutic applications. The existing research has clearly shown that primary teeth are a better source for stem cells. While the promise of the immense scope and magnitude that stem cell therapies will have upon the
population will only be fully realized in the future, Dental Professionals have realized that the critical time to act is now. The available opportunities to bank their patients’ dental stem cells will have the greatest future impact if seized while patients are young and healthy.

8. REFERENCES

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