Reveiw Article

Stem Cells: Potential Implications for tooth regeneration and tissue engineering in Dental Science

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Abstract:

Stem Cell has become a booming field for research and therapeutic applications with vast areas yet to be discovered. The pluripotent nature of the stem cells has been studied and used in various scientific fields for curing the disease and regeneration of a body part. Periodontitis, dental caries, craniofacial bone and teeth regeneration are the different areas in dental science which are yet to be studied. Various studies all over the world are going on using stem cells to cure or minimize the pain which a patient goes through diagnosis. This article provides an overview of the different types of stem cells and the different applications of stem cell in dental science.

Key Words: Tissue regeneration, stem cells, pluripotency, regenerative medicine.

Introduction:

Stem cells are unspecialized cells that have a remarkable ability to develop to many different cell types when needed. Theoretically, they can divide without limit to replenish any other cell type and function as a part of a repair system. Stem cells are known to proliferate over very long periods of time. An important area of research is to understand the signals in an organism that cause a stem cell to proliferate and remain unspecialized until differentiated cells are needed for growth or repair of a specific tissue.

Research on stem cells is advancing and needs substantial knowledge about an organism, how it develops from a single cell and how a healthy cell replaces a damaged cell in the adult organism. This is a promising field of science as various studies are still going on and various possibility of cell based therapies to treat diseases which is often referred as “Regenerative Medicine”, are still in progress.

Though stem cells are one of the most fascinating areas of biology today, but like many expanding fields, research on stem cells raises scientific questions as rapidly as it generates new discoveries. Stem cells have two important characteristics which make them different from other cells.

1. They are unspecialized cells that renew themselves for long time through cell division.

2. Under certain physiological conditions they can be induced to become cells with special function such as neurons.

Scientists have identified primarily two types of stem cells: Embryonic stem cells (ESCs) and Adult stem cells (ASCs).

Embryonic Stem Cells:

Embryonic stem cells are derived from embryos that develop from eggs fertilized in-vitro in fertilization clinics donated for research purpose with informed consent of the donors. The embryos from which human embryonic stem cells are derived are four to five days old and in “blastocyst stage”. This blastocyst includes three structures: the trophoblast which is the layer of cells that surrounds the blastocyst; the blastocele, a hollow cavity inside the blastocyst; and the inner cell mass, which is a group of approximately 30 cells at one end of the blastocele. Human embryonic stem cells are isolated by transferring the inner cell mass (ICM) into culture dish containing appropriate culture medium. The original and the best general culture condition for the maintenance of these cells is by co-culture with a mitotically inactivated “feeder layer” of fibroblasts. Several types of cells can provide this feeder functions; the most widely used and tested are the established primary embryo fibroblasts. These ESCs are identified by using various techniques e.g. specific techniques to determine the presence of surface markers that are found only on un-differentiated cells. Another important test is for the presence of a protein called Oct-4, which is
generally produced by undifferentiated cells. Oct-4 is a transcription factor, which helps to turn the genes on and off at the right time, which is an important part of the processes of cell differentiation and embryonic development. The chromosomes are also examined by Karyotyping. This method is used to assess whether the chromosomes are damaged or if the number of chromosomes has changed. Immuno-histochemistry is used for the detection of cells; it utilizes antibodies to identify antigens in tissue sections or cell preparations on a slide. The purified primary antibody reacts with a biotinylated secondary antibody and, thus increases the sensitivity.

As long as the embryonic stem cells in culture are grown under certain special conditions, they can remain undifferentiated. But if cells are allowed to clump together to form embryoid bodies (i.e. round collections of cells that arise when embryonic stem cells are cultured in suspension), they begin to differentiate spontaneously. They can form approximately 200 different cell types; either muscle cells, nerve cells or any other specific cell types. Much has been learnt about how human ESCs become any of the specialized human cells, still there is more to be understood. The major obstacle for using this technique is that human embryonic stem cells (hESCs) are isolated from embryos which ultimately lead to destruction of embryos. Various studies all over the world has led to certain basic protocols for the directed differentiation of embryonic stem cells into specific cell types e.g. cardiomyocytes cells, neurons, osteogenetic cells etc.

Adult Stem Cells

An adult stem cell is an undifferentiated cell found among differentiated cells in a tissue or organ; it can renew itself, and can differentiate to yield the major specialized cell types of the tissue or organ. The primary role of the adult stem cell is to maintain and repair the tissues in which they are primarily found. They are also known as “Somatic stem cell”. The regenerative property of the adult stem cell has been reported 40 years ago. As hematopoietic stem cells forms all types of blood cells in the body, similarly the regenerative property of the bone marrow stroma help in repairing fractured bone and is thus likely to be responsible for repairing microfractures that occur on a daily basis.

Adult stem cells were originally thought to have a rather restricted potential for generating new tissues; that is, hematopoietic stem cells could only make new blood cells. But recent studies have changed this perception. New observations suggest that in addition to generating the derivatives of the blood system, stem cells within the bone marrow of an adult organism can also give rise to muscle (Ferrari et al, 1998) and neuron-like cells in the brain (Jackson et al, 1999).

Adult Stem Cells have been identified in many organs and tissues; they specifically reside in specific areas of tissue where they remain quiescent (non-dividing) for many years until they are activated by disease or tissue injury. It has been reported that in central nervous system of mouse, stem cells can differentiate into cells of other tissues such as muscle, blood and heart, in addition to several types of nervous system cells (Bjornson et al, 1999; Clarke et al, 2000; Egliits & Mezey, 1997). Bone marrow stromal cells (Mesenchymal stem cells) give rise to a variety of cell types: bone cells (osteocytes), cartilage cells (chondrocytes), fat cells (adipocytes) and other kind of connective tissue cells such as those in tendons etc. A subpopulation of adult bone marrow known as mesenchymal stem cells (MSCs) have been found to have the capacity to give rise to bone and cartilage, and have been widely studied for use in the repair of skeletal defect (Sottile et al, 2003).

Potential Clinical Applications of Stem Cells in Dentistry:

As stem cells are found to have a great potential in forming various cell types, the major question which arises in our mind is what are the implications of stem cell in dentistry? The focus of stem cell research as it applies to dentistry is on facial reconstruction. Of the estimated 1.6 million bone grafts performed annually to regenerate bone lost to trauma or disease, about 96,000 relate to the face and mouth. Stem cells are used in combination with other basic and translational research that takes advantage of advances in biology, chemistry and material science, nanotechnology, computer science and engineering to develop tissue constructs that mimic structure and function of the tissues.

“Tissue engineering” is another area which has been in boost recently. It refers to the number of ways in which the tissue lost due to trauma or disease is restored. In 2003, Dr. Songtao Shi at the National Institutes of Health in Maryland discovered dental stem cells in his daughter’s baby teeth (Shostak, 2006). Since then, many scientists around the world have
shown that dental stem cells can be coaxed into cells typically found in teeth, bones, nerves, fat, joints, and muscles. Dental stem cells have become a feasible tool for dental tissue engineering. Recently, dental tissues such as periodontal ligament (PDL), dental papilla or dental follicle have been identified as easily accessible sources of undifferentiated cells. Tissue engineering using scaffold and cell aggregate methods has also been used to produce bioengineered teeth from dissociated cells for therapeutic applications (i.e. whole tooth replacement). Dental tissue stem/progenitor cells are particularly useful in dentistry for the development of cell transplantation therapies, for the repair of damaged dentin and for periodontal disorders, and the stem cells are, therefore, currently the subjects of extensive research.

Somatic stem cell which differentiates into odontoblasts have been identified in pulp tissue of human permanent teeth, exfoliated deciduous teeth, and impacted teeth (Gronthos et al, 2000; Miura et al, 2003; Sonoyama et al, 2006). Dental precursor cells are necessary and are an attractive novel approach to treat diseases like periodontitis, dental caries or to improve dental pulp healing and the regeneration of craniofacial bone and teeth. Tooth maladies are widespread in different parts of the world. Many people suffer from periodontitis which is the frequent cause of tooth loss. Therapies based upon cell replacement and tissue engineering, underpinned by stem cell biology, are emerging as potentially powerful strategies in modern regenerative medicine. Dental pulps were basically extirpated from healthy permanent teeth (third molars and premolars). After splitting the teeth, the pulps were removed and cultured in basal media or osteogenic, chondrogenic and adipogenic conditions (Bowen et al, 2006). Constructing complex structures like periodontium, which provides the functional connection between a tooth and an implant, could effectively improve modern dentistry.

Dental regenerative therapy using stem cell transplantation and bio-engineered tooth replacement by scientists from Department of Biological Science and Technology, Japan (Kazuhisa & Takashi, 2007) has shown the treatment of tooth defects and tooth loss. Dental regenerative therapies which restore or replace defective teeth using autologous explants are being investigated using current understanding of developmental biology, stem cell biology and regenerative medicine. Recently, dental tissue stem/progenitor cells, which can differentiate into dental cell lineages, have been identified in both impacted and erupted human teeth, and these cells can be used to regenerate some dental tissues. With the advent of dental stem cells, companies such as Store-A-Tooth™, 99 Hayden Avenue, Suite 200 Lexington, Massachusetts (USA), are providing services to properly preserve a child’s dental stem cells-a sort of biological insurance in anticipation of these cells becoming important as the field advances.

Research on whole tooth regeneration is also advancing using a strategy of transplanting artificial tooth germ and allowing it to develop in the adult oral environment. Tissue engineering builds a tissue such as skin, bone, and cartilage, by seeding cells onto a scaffold (Langer & Vacanti, 1999). Research on the fabrication of teeth from dissociated cells was first performed using tooth germ cells (Iwatsuki et al, 2005). When explants, seeded with porcine third impacted tooth bud cells, made of polyglycolate/poly-l-lactate (PGA/PLLA) or poly-l-lactate-co-glycolate (PLGA), were transplanted for 20–30 weeks into omentum, bioengineered teeth were visible within the explant (Young et al, 2002). The cultured molar bud cells increased in number and were also able to form bioengineered teeth (Duailibi et al, 2004). These raised the possibility that tissue engineering techniques using a scaffold could be used in dental regenerative therapies. However, it seems that improvement is necessary in the success rate of tooth formation and in the morphology of regenerated teeth in tissue engineering methods using scaffolds. Recently, it has been reported that use of a collagen sponge scaffold formed teeth with a higher rate of success than use of biodegradable polymer (Sumita et al, 2006). In addition, arranging epithelial cells and mesenchymal cells within the scaffold by seeding them sequentially, instead of the conventional method of seeding, a mixture of epithelial cells and mesenchymal cells, improved the tissue arrangement in bioengineered teeth (Honda et al, 2007).

Artificial tooth germ has been produced by combining a dental epithelial tissue and a cell pellet of mesenchymal cells isolated from E13.5 mice molar tooth germ, and the resulting artificial tooth germ was then able to generate a correct tooth structure by transplantation into a subrenal capsule (Yamamoto et al, 2003). The bioengineered tooth germ regenerated...
Future Prospects of Stem cells in Dentistry:

Although there is great excitement in scientific community about stem cells and regenerative medicines, it is yet to be known about the clinical applications of stem cells. Therapies based upon cell replacement and tissue engineering, under pinned by stem cell biology is emerging as potentially powerful strategies in modern regenerative medicines. Additional research to coordinate advances in various fields, such as clinical medicine, biology, materials science, nanotechnology, and chemistry will increase the advancement of regenerative therapies. The bioengineering technologies developed for tooth regeneration will make substantial contributions to understanding the developmental process and will encourage future organ replacement by regenerative therapies in a wide variety of organs, such as the liver, kidney, and heart.

Bibliography:

