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Stem Cells - The Beginning of New Era

Abstract
Recent advances in materials science and tissue engineering have created for the development of methods to bioengineer tissue and organ replacements, including highly mineralized craniofacial and dental tissues. The identification of post-natal dental stem cell (DSC) populations suggests that Bioengineering approaches can be used to regenerate a variety of dental tissues and whole tooth. The recent demonstration of bioengineered whole tooth crowns from pig and rat tooth bud cells provided the first evidence that post-natal DSCs could be used for whole-tooth tissue engineering applications.
Key Words
Stem cell; tissue engineering; whole tooth regeneration

Dr Shubha Joshi[1], Dr Chandrashekar Sajjan[2], Dr Devarathnamma. MV[3], Dr Indresh Rajawat[4], Dr Nikhat Fatima[5], Dr RM Joshi[6]

[1]Assistant Professor, Department of Prosthodontics, AME Dental College & Hospital, Raichur, Karnataka, India
[2]Reader, Department of Prosthodontics, AME Dental College & Hospital, Raichur, Karnataka, India
[3]Senior Lecturer, Department of Periodontology, Navodaya Dental College, Raichur, Karnataka, India
[4]Senior Lecturer, Department of Prosthodontics, IDEAS Dental College, Gwalior, Madhya Pradesh, India
[5]Assistant Professor, Department of Periodontics, Alfarabi College of Dentistry, Kingdom of Saudi Arabia, Riyadh
[6]Assistant Professor, Department of General Pathology, AME Dental College, Raichur, Karnataka, India

INTRODUCTION

Dental and Medical treatment for loss of tissue or end-stage organ failure is required for millions each year. Current strategies used for treatment of lost tissues include the utilization of autogenous grafts, allografts, and synthetic materials (alloplasts). Although all of these treatment approaches have had successes and have been major advances in medicine and dentistry, each of them has limitations. Tooth loss or absence is a common and frequent situation that can result from numerous pathologies such as periodontal and carious diseases, fractures, injuries or even genetic alterations. In most cases this loss is not critical, but for aesthetical, psychological and medical reasons (e.g. genetic aberrations) replacement of the missing teeth is important. Recent efforts made in the field of biomaterials have led to the development of dental implants composed of biocompatible materials such as titanium that can be inserted in the maxillary and/or mandibular bone to replace the missing teeth. However, implants are still not completely satisfactory and their successful use greatly depends on their osteointegration. To overcome these difficulties, new ideas and approaches have emerged recently from the quickly developing fields of stem cell technology and tissue engineering. Recently, reports have begun to emerge demonstrating that populations of adult stem cells reside in the periodontal ligament of humans and other animals. This opens the way for new cell-based therapies for periodontal regeneration. For this to become a reality a thorough understanding of adult human stem cells is needed. A Google/Medline search was conducted and relevant literature concerning the application of stem cells obtained from various dental tissues and their role in periodontal regeneration was reviewed. The available literature was analyzed and compiled. This review provides an overview of adult human stem cells and their potential role in periodontal regeneration. A stem cell is defined as a cell that can continuously produce unaltered daughters and, furthermore, has the ability to generate cells with different and more restricted properties. Stem cells can divide either symmetrically allowing the increase of stem cell number) o asymmetrically. Asymmetric divisions keep the number of stem cells unaltered and are responsible for the generation of cells with different properties. Stem cells can be classified into three broad categories, based on their ability to differentiate. Totipotent stem cells are found only in early embryos. Each cell can form a complete organism. Pluripotent stem cells exist in the undifferentiated inner cell mass of the blastocyst and can form any of the over 200 different cell types found in the body. Multipotent stem cells are derived from fetal tissue, cord blood and adult stem cells.

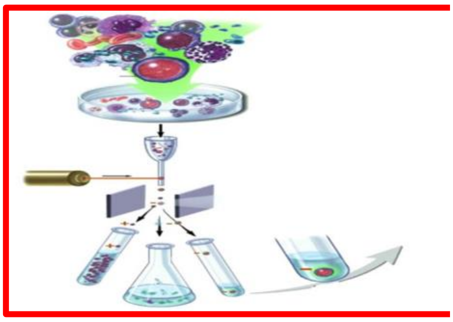

Fig.1: Seperation of Stem Cells

Stem cells can be achieved from

a) Bone Marrow - Of all adult tissues, the bone marrow is an extremely rich source of somatic stem cells.

b) Umbilical Cord - The other rich source of stem cells is the blood left over in the umbilical cord and placenta of a newborn child.

c) Embryonic Germ Cells (EGCS) These pluripotent stem cells are derived from primordial germ cells, which give rise to the gametes.

d) Menstrual Blood-Menstrual fluid contains self-renewing stem cells.

e) Peripheral Blood-Stem cells, in limited quantities, can also be found in the peripheral blood circulation.

Stem cells of dental origin

Stem cells have also been isolated from orofacial tissues that include adult tooth pulp tissue, deciduous tooth pulp tissue, periodontal ligament, apical papilla (SCAPs), dental follicle precursor cells (DFPCs) and buccal mucosa. Stem cells from human exfoliated deciduous teeth (SHED) are multipotent and are very immature in the cell hierarchy than the adult pulp stem cells. Recently mesenchymal stem cells from apical papilla of incompletely developed teeth have been isolated.

Sources of Embryonic Stem Cells

a) Excess fertilized eggs from IVF (in-vitro fertilization) clinics

Tens of thousands of frozen embryos are routinely destroyed when couples finish their treatment. These surplus embryos can be used to produce stem cells. Regenerative medical research aims to develop these cells into new, healthy tissue to heal severe illnesses.

b) Therapeutic cloning (somatic cell nuclear transfer)

The nucleus of a donated egg is removed and replaced with the nucleus of a mature, "somatic cell" (a skin cell, for example). No sperm is involved in this process, and no embryo is created to be implanted in a woman’s womb.The resulting stem cells can potentially develop into specialized cells that are useful for treating severe illnesses.

Seperation of Stem Cells

Cells in suspension are tagged with fluorescent markers specific for undifferentiated stem cell. Labeled cells are sent under pressure through a small nozzle and pass through an electric field. A cell generates a negative charge if it fluoresces and a positive charge if it does not. Stem cells cannot be identified with certainty in any tissue. Scientists rely on indirect properties such as the expression of a repertoire of surface proteins, slow cell cycle, clonogenicity, or an undifferentiated state. However, none of these criteria are specific. The evaluation of self renewal is the ultimate way to show “stemness”.

Potential Uses of Stem Cells

It is a procedure by which damaged, diseased, or malfunctioning cells anywhere in the body are replaced by introducing healthy stem cells to that area of the body. Stem cell therapy is a promising treatment for all kinds of degenerative diseases because of the stem cells’ regenerative abilities. Presently stem cells are used in the treatment of Baldness, Blindness, Deafness, Amyotrophic lateral sclerosis, Myocardial Infarction, Muscular Dystrophy, Diabetes, Multiple sites of Cancer, Crohn’s disease, Osteoarthritis, Rheumatoid Arthritis, Spinal Cord Injury, Stroke, Traumatic Brain Injury, Alzheimer’s Disease, Parkinson’s Disease, wound healing and missing teeth.

Steps in Regenerating a Whole Tooth

1. Harvest tooth-derived postnatal stem cells;
2. Expand the cells in culture, with cell banking for future organ regeneration needs;
3. Seed the cells into ananotextured, information-rich scaffold that provides an optimized biochemical and biomechanical environment;

4. Instruct the cells with spatially targeted, soluble molecular signals and/or induce with porcine
5. Sources of odontogenic tissue;
6. Create a map of gene expression associated with the progression of native stem cells to their odontogenic fate;
7. Confirm that the gene expression profile of the cells demonstrates readiness for the next stage in the odontogenesis pathway;
8. Repeat these steps until the cells have expressed genes associated with the cap stage of odontogenesis;
9. create a new science for controlling fast new experimental techniques for non-destructive in situ monitoring of cell development;
10. Establish an understanding of the cell and molecular biology required for the regeneration of tooth roots and their adnexa necessary to ensure successful biological integration of the cap stage with the jaw bone following transplantation.

Challenges in Stem Cell Therapy

Stem cells need to be differentiated to the appropriate cell type(s) *before* they can be used clinically. 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.

Conclusion

Stem cell therapies have virtually unlimited applications. All the challenges must be overcome before this novel therapy can be translated from labs to clinics. Collaboration between basic scientists and clinicians is required to achieve this goal. Recent advancements in scaffold designing, better understanding of growth factor biology and interactions between allogenic stem cells and immune system result in new discipline in dentistry, 'regenerative dentistry'. It is clear that current regenerative procedures are less than ideal but the identification of stem cells in human dental tissues in recent years holds promise to the development of novel, more effective approaches to regeneration and reconstructive therapy. However, before this is feasible, many biological, technical and clinical hurdles need to be overcome and a thorough understanding of underlying healing processes in regeneration is required.

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