ORIGINAL RESEARCH PAPER

Prosthodontics

APPLICATIONS OF STEM CELLS IN PROSTHODONTICS – A REVIEW

KEY WORDS:

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ABSTRACT

Stem cells can self-revitalize and form specific cell types, thus providing new strategies to regenerate missing tissues and treat diseases. oral mucosal cells are thought to provide potential source for genetically reprogrammed cells such as induced pluripotent stem (iPS) cells as adult mesenchymal stem cell are found mostly in oral mucosal cells and form a therapeutic target for stem cells. As stem cell and tissue engineering therapies in dentistry continue to attract increasing clinical interest, this review outlines various types of intra- and extra-oral tissue-derived stem cells with regard to clinical availability and applications in dentistry.

INTRODUCTION:

Stem cells have inherent capability of forming in to many specialized cells by mitosis in the body during early life and growth[1]. Appreciation of developmental process of specific structure is very important to reinstate a specific tissue[2]. Ernest A. McCullough and James E. Till (1960s) were the first to set forth into the field of stem cells research at the University of Toronto[1]. Development of new tissue or organ begin by the tissue rebuilding with the help of pluripotent stem cells and these evolve in to multipotent cells of different origin like, epithelial, mesenchymal and other tissue specific stemcells[3,4,5]. Totipotency, pluripotency, multipotency and unipotency are various characteristics of stem cells[6].

Over recent years, studies have shown that oral tissues are a source of stem cells[7]. So auther's used tissue engineering and utilization of stem cells in dentistry to overcome the clinical complications such as gingival recession, gingival inflammation, crestal bone loss and inflammation of the surrounding periodontal tissues in substitution of missing teeth with dental implants in partially edentulous and completely edentulous patients as bone resorption continues throughout the life significantly in mandible as they incapable of mimicking the chemical, physical and biological properties of natural tooth materials (i.e. enamel, dentin, cementum, pulp and periodontal ligament) and their physiological functioning[8,9,10].

One of the foremost inventive by professor paul sharpe and his team from kings college of london in 2004 was the development of "lab tooth " from cellular components. They used embryonic oral epithelium from 10 day old developing murine embryoes with bone marrow cells from 6-9 week old mice. these formed to explants when transplanted to renal capsule.The resultant teeth simulated late cap/earlybell stage morphology and composed of ameloblasts, odontoblasts, enamel, dentin, dental pulp and surrounding bone tissues. A well developed teeth with dentin, predentin and periodontal ligament was formed by implanting the above mentioned explants in to the tooth-less region of adult mice. As a sequence additional studies were done to traverse the use of human cells in cellular combination and transplantation experiments. For this, human gingival epithelial cells were collected, cultured and combined with embryonic mesenchymal cells from 14-day-old mice embryos.Then the resultant explants were transplanted into murine renal capsules and after six weeks of in vivo development, the resultant teeth shows dentin, dental pulp, and cementum and some hard tissues[11].

In 2003 Dr. Songtao shi, a pedodontist found dental pulp stem cells in exfoliated deciduous teeth of his daughter. Numerous scientists have been accomplished work on dental pulp, looking for stem cells and they confirmed that dental pulp was rich in various forms of stem cells as, adipocytes, chondrocytes, osteoblasts and mesenchymal stem cells. These are seen in both children and adults and has wide therapeutic actions. Aging and death of odontoblasts due to severe injury to dental pulp from trauma or infection limited the regenarative ability of dental pulp stem cells[12].

Undifferentiated cells can be isolated from the three types of teeth, they are[13]:

- Deciduous Teeth: These are rich source of viable stem cells and have extreme proliferative capability even in small quantities.
- Wisdom teeth: This is exceptional source for dental pulp stem cells.
- Permanent teeth: These are potential resource of stem cells.

Prosthodontic applications:

1) **Regeneration of tooth:** Tooth development requires epithelial mesenchymal exchanges. It includes reciprocal exchange of signals between the two germ layers. Which results in the formation of inimitable terminal phenotypes with their suppoerting cells. In ductive morphogens, stem cells and scaffolds are the key elements in tooth regeneration.

Regeneration of teeth involves the following steps:

1. Adult stem cells are harvested and spread out.
2. Optimized environment is facilitated by seeding the stem cells as scaffolds.
3. Targeted soluble molecular signals are given to cells.
4. For odontogenesis gene expression profile is confirmed by the cells[14,15,16,17,18].

2) **Regeneration of periodontium:** Regeneration of periodontal tissue allways shows certai challenges because it includes both soft and hard tissues. Allografts, autologous bone grafts or alloplastic materials of recent techniques have restrictions and can not be used in all clinical conditions. Therefore, the therapeutic alternative is a cellmediated bone regeneration technique. Kawaguchi et al. and Hasegawa et al, stated that periodontal ligament cells cultured invitro were effectively reimplanted into periodontal defects in order to countersign periodontal regeneration. Resultant studies by the same group stated a parallel approach in humans. This studies presented certain evidence that stem cells are to regenerate a tissue as complex as the periodontium[19].
3) **Regeneration of craniofacial structures:** osseous defects of the jaw were grafted with TRCS and biopsies harvested for 6 and 12 days for analysis and followed for 12 months after oral implant therapy. Clinical, radiographical and histological findings demostrated that cell therapy accelerated the regenerative response[20].
4) **Regeneration of Alveolar bone:** Mesenchymal condensation by aggregation of mesenchymal stem cells seen in the development of bone. It includes intramembranous and endochondral bone formation mechanisms[21]. Bone have the intrinsic capability of regeneration during adulthood. Incase of minor injuries regeneration takes place by the local cells like chondroblasts, osteoblasts, endothelioblasts and fibroblasts. In severe injuries self healing alone can't repair the defect. So adequate supply of stem cells is requird for the regeneration of efficient bone[22]. Oral mesenchymal stem cells have more potential of bone regeneration[23].
5) **Regeneration of muscle tissue:** Arminan et al said that cardiomyocytes-like cells can be separated from dentin pulpal stem cells when cultivated with neonatal rat cardiomyocytes for about 4 weeks in vitro[24].Yang et al said that dystrophin producing muscle cells can be separated from dental pulp stem cells in cardiotoxin- paralyzed muscles in a mouse model and can be used as a treatment of choice for muscular dystrophy[25].

CONCLUSION:

Excellent regenerative ability of oral epithelial and mesenchymal stem cells can be applied not only in dentistry but also in various fields of medicine like repair of cornea, neural, bone, muscle, tendon, cartilage, and endothelial tissues without neoplasm formation. But most of the studies lack strict quantitative analysis for testing the ability of these cells to self-renew, proliferate, and differentiate, especially in vivo. experimental studies need to resolve the following issues before clinical application: 1) massive cell death in the transplanted site (it has been reported that in the damaged spinal cord only a few percent of the transplanted oral stem cells could survive, and they have difficulty to integrate into the local tissue therefore, viability and functional differentiation of oral stem cells in vivo need to be improved); particularly for neuronal regeneration[26], 2) the interaction between transplanted oral stem cells and local cells or microenvironment needs to be analyzed; 3) in vivo cell lineage tracing of transplanted oral stem cells isrequired for understanding their fate and behavior; 4) since oral stem cells, especially oral epithelial stemcells, are often involved in neoplasia, the cellular and molecular mechanisms that allow oral stem cells tochoose self-renewal, canceration, and differentiation should be well studied.

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