ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 10, Issue, 03, pp.67469-67472, March, 2018

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

STEM CELLS IN DENTISTRY- THE FUTURE IS NOW

Dr. Duggal Nidhi, * Dr. Kaur Amardeep, Dr. Kaur Sarabjeet and Dr. Pratibha

Department of Prosthodontics, Crown and Bridge, Govt. Dental College and Hospital, Patiala, Punjab, India

ARTICLE INFO

Article History:
Received 20th December, 2017
Received in revised form
07th January, 2018
Accepted 19th February, 2018
Published online 30th March, 2018

Key words:
Stem cells, Regeneration, Bone Regeneration, Oromaxillofacial Tissues.

ABSTRACT

Stem cell technology is one of the most recent technologies, receiving considerable attention in fields of dentistry because of growing requirement of esthetic and functional reconstruction of oral tissues. Potential advantages of stem cells in regenerative treatment have been demonstrated in many studies. Stem cells can renew themselves, thus providing new strategies to regenerate missing tissues and treat disorders. Aim of this article is to provide knowledge about stem cells and its applications in prosthetic dentistry.

Citation: Dr. Duggal Nidhi, Dr. Kaur Amardeep, Dr. Kaur Sarabjeet and Dr. Pratibha, 2018. "Stem cells in dentistry- the future is now", *International Journal of Current Research*, 10, (03), 67469-67472.

INTRODUCTION

Oromaxillofacial structure is a complex anatomical structure formed from hard and soft tissues. Their replacement or restoration of oral and maxillofacial tissues is difficult because they are delicate and are responsible for the functions like facial expression, articulation, chewing, swallowing etc. loss of these tissues due to trauma, oral pathology or neoplastic tumors may lead to loss of one or more functions. Tissue engineering and stem cell therapy are considered to be a new frontier in the regeneration of oral tissues and organs and are considered to provide a novel capability to regenerate large defects in oromaxillofacial structure. Stem cell is the important key for regeneration of tissues as all tissues originate from stem cells. In addition to reconstruction of oromaxillofacial tissues, emerging concept of stem cell technology has also been applied to fields of dentistry like prosthodontics and implant dentistry. Loss of alveolar bone due to periodontal disease is a commonly encountered issue that limits the ability of implant or a prosthesis to restore the missing anatomy and function. In this article, we will first review the conventional materials based regenerative dentistry and then current status of stem cell based therapies in dentistry.

Stem cells

What are stem cells?: Stem cells are the unique type of immature and specialized cells that can differentiate into different cell lineages. They continually remove themselves through cell division. Stem cells are the raw materials from which all body's mature differentiated cells are made. Stem cells are dynamic as they can change to one or several cell types under proper condition.

Corresponding author:* **Kaur Amardeep,
Department of Prosthodontics, Crown and Bridge, Govt. Dental College and Hospital, Patiala, Punjab, India.

Stem cells are dynamic as they have these following properties

- They can change to one or several cell types under proper conditions
- They continually reverse themselves through cell division
- Types of stem cells
- There are three sources of stem cells
- Embryonic stem cells
- Adult stem cells
- Induced pluripotent cells (IPS)

Embryonic stem cells

They are also called pluripotent stem cells and are capable of developing into all cell types of body. Derived from the inner cell mass of the blastocyst from which many tissues of embryo arise. They are obtained from 5-7 days old embryos which also results in its destruction. They have an ability to differentiate in each of more 200 cell types of adult body and are involved in correction of genetic alterations.

Advantages

- They have potential to make any type of cell
- They are immortal and provides an endless supply of cells

Disadvantages

- Causes destruction of developing human life
- Capable of forming tumors

Adult stem cells

These are multipotent undifferentiated cells that are derived from differentiated cells in a tissue or organ. They are found within some marrow, liner, epidermis, retina, skeletal muscle, intestine, brain, dental pulp etc. the specific sites in which adult stem cells resides are called Niches which provide cellular environment needed for self regeneration.

Advantages

- Relative ease of procurement (some adult cells are easy to harvest)
- Non tumourogenic
- Donor is not harmed
- Non immunogenic
- Immune rejection is not experienced by the recipients who receive the products of their own stem cells

Disadvantages

- Only limited quantity can be obtained
- May not live as long as embryonic stem cells in culture

Induced pluripotent stem cells

Out of many experiments that were carried out to find whether somatic cells can be transformed to form pluripotent stem cells ,Takahashi found that transformation is possible by the forcing expression of certain transcription factors. Properties of these stem cells will similar to embryonic stem cells. The the capacity of iPS cells to develop into all tissues/organs have drawn considerable attention and is expected to revolutionalize medicine. It also support the emerging field of ''personalized medicine'', in which a patient's own cells are used to provide biologically compatible therapies and individually tailored treatments.

Stem cells in regenrative therapy

In dentistry, regenerative therapy is especially applied in oro-maxillofacial reconstruction of tissues lost due to trauma or bone loss followed by tooth loss due to periodontal disease.

It is mainly classified as

Material based therapies

First generation: Biomaterial scaffolds

Second generation: Growth factors based approach
Stem cell based therapies

Third generation: MSC's osteo-progenitor cells approach
Fourth generation

Fifth generation: physiologic tissue or organ replacement

First generation

Use of biomaterial scaffolds was the basis of this generation for regenerative therapy such as guided tissue regeneration using biocompatible barrier membranes such as resorbable collagen and polylactic coglycolic acid or non resorbable expanded tetrafluoroethylene. Calcium phosphate based biomaterials including hydroxyapatite, tricalcium phosphate, biphasic calcium phosphate etc were used earlier. These biomaterials are osteoconductive but not osteoinductive and osteoinduction by bone grafting substitutes are very important while placing titanium implants for accelerated bone formation and osseointegration of bone with implant. So osteoinductive calcium phosphate scaffolds were engineered by incorporation of osteogenic bioactive factors. Fibrous silk protein biomaterials from silk worms and spiders are also been used for regeneration but efficacy of these materials have not yet reached towards human application.

Challenges of scaffold based tissue regeneration

To determine appropriate scaffold properties such as porosity, surface geometry and mechanical strength which supports the cell activity necessary for promoting bone re growth by host cells For the controlled release of osteogenic bioactive factors, appropriate carrier properties should be determined

Second generation

Trophic or growth factors are used in second generation to recruit stem cells to tissue defects and stimulate them to achieve regeneration. Various growth factors used are

PRP's: platelet rich plasma consisting autologous platelets concentrated in small volume of plasma. Contains different growth factors and matrix elements for

EMD: Enamel Matrix Derivatives extracted from developing porcine tooth buds and composed of amelogenin, widely used in periodontal regeneration Recombinant factors like BMP(Bone Morphogenetic Proteins), PDGF(Platelet Derived Growth Factor), PGF2(Fibroblast Growth Factor), have also been introduced for periodontal bone regenerative therapy

BMP: Among BMPs BMP2 is characterized by its ability to induce bone and cartilage formation in sinus augmentation and alveolar ridge augmentation

PGDF: In teeth with periodontal defect it promotes the proliferation of gingival and periodontal ligaments fibroblasts and cementum formation around teeth

PGF2: It induces angiogenesis (formation of new blood vessels) and stem cell proliferation

Third generation

It is mesenchymal cells/ osteoprogenitor cell based approach. It includes

- Bone marrow derived cells
- Periosteum derived osteoprogenitor cells
- Adipose derived mesenchymal cells
- Bone marrow derived cells

Derived from adult bone marrow and are multipotent progenitor cells. Can be derived from

Iliac crest: it is an invasive procedure which can be isolated easily from iliac crest by physicians. It can differentiate along osteogenic, chondrogenic, adipogenic, myogenic, or non mesenchymal neurogenic lineages. Till date BMSC's from iliac crest are most common stem cells used for bone regeneration in dental patients.

BMSC's for orofacial bones: BMSC's can also be derived from orofacial(maxilla and mandible) bone marrow aspirates obtained during surgical procedures like dental implants. It can be obtained from older individuals of age 57-62 years but not from young patients (6-53 years of age). Various studies have indicated that bone grafted from craniofacial area provides better results and higher resultant bone volume than bone harvested from iliac crest

Dental tissue derived stem cells: These are

- DPSC's(Dental pulp stem cells)
- SHED(stem cells from exfoliated deciduous teeth)
- PDLSC's(periodontal ligament cells)
- SCAP(stem cells from apical papilla)
- DFPC's(Dental follicle progenitor cells)

Dental pulp stem cells: DPSC's were identified in 2000 by Gronthos *et al*. These stem cells have phenotypic characteristics similar to BMSC's

SHED: Stem cells from human exfoliated deciduous teeth were discovered by Dr Songtao Shi, a Pedodontist by utilizing the primary teeth of his daughter. These immature multipotent clonogenic cells are identified by their high proliferation rate and can specifically induce formation of bone like matrix with a lamellar structure by recruiting host cells.

PDLCS's : Seo BM *et al* isolated PDLSC's from periodontal ligament of 25 human third molars. When PDLSC's were transplanted in experimental animals, regeneration of periodontal tissues (cementum, alveolar bone and pdl) was seen

SCAP: As the name suggests these mesenchymal stem cells were isolated from apical papilla by Soyonama *et al*. when transplanted in immuno-compromised mice, SCAP demonstrated better regeneration of dentine matrix compared to DPSC's

DFPC's: These cells were obtained from dental follicle by Molczeck *et al*. Dental follicle is a loose ectomesenchymal derived connective tissue surrounding the enamel organ. They can form cementoblasts, pdl cells and osteoblasts

Fourth generation has been recently introduced that includes cell construction technologies Fifth generation includes physiologically analogous tissue or organ replacement approach. These are future approaches which are expected to use oral tissue derived induced pluripotent stem cells and genetically modified stem cells which will create more physiologically analogous replacement tissue or organs such as bio engineered periodontal tissues and teeth.

Applications of stem cells

Alveolar defects

A need for robust bone augmentation in atrophic ridge and maxillary sinus is due to a recent increase in demand for dental implants. Bone has an intrinsic capacity to regenerate throughout life and its development involves aggregation of mesenchymal stem cells into mesenchymal condensations . In most of the cases, damaged bone functionally repairs regenerate by local cells ie chondroblasts, osteoblasts, endotheliocytes and fibroblasts. In large defects created by trauma, infection, tumor resction or skeletal abnormality , self healing cannot repair the defect itself. Oral mesenchymal cells are considered to be ideal candidates for bone regeneration. Under inductive conditions both dental and non dental MSCs can differentiate into chondroblasts and osteoblasts. Stem cells theray has also been useful in patients with compromised supply and impaired wound healing because it may improve vascularity to facilitate hard tissue augmentation at local sites in oral cavity.

Tooth regeneration

Tooth regeneration has been a desired ultimate dental treatment which will be better fitting and alternative tool in place of dental implants. Dental implants donot function identically same as natural tooth because they integrate directly to bone without an intervening PDL through osseointegration. In the development of tooth epithelial mesenchymal exchanges are mandatory. The key elements involved in tooth regeneration are inductive morphogenes, stem cells and scaffold.in a study by Duailibi etal, a tooth was formed from single cell suspensions of cultured rat tooth bud cells. Honda etal also developed tissue engineered teeth , when implanted into omentum of rat using porcine tooth bud cells and PGA(pologlycolic acid) fibre mesh scaffold, similar to model of odontogenesis. Young *et al* generated a hybrid tooth bone for treatment of tooth loss along with the alveolar bone resorption using porcine tooth cells, PGA and PLGA scaffolds.

Craniofacial defects

The closure of the craniofacial bone defect is mostly carried out by transfer of the tissue from a donor site, which has disadvantages like donor morbidity, unique function of lost part is not restored, scarring and infection. Stem cells can be useful in restoration of damaged and lost tissue in craniofacial defects. Adipose cells can be used in reconstruction of soft tissues when used with appropriate shaped scaffold. In a study by Alhaldlaq *et al*, it was found that human MSCs can turn into adipose cell when they are exposed to adipogenic medium. Stem cells derived from dental pulp are a good source for bone formation as it has a potential to develop into osteoblasts. In a study collagen sponge scaffolds and dental pulp were used in maxillofacial repair and had successful results.

Periodontal regeneration

Complete regeneration of periodontium always stay a challenge as it implies simultaneous reproduction of 2 hard

(alveolar bone and cementum) and 2 soft tissues (pulp and dentin). Present regenerative techniques such as allografts, autogenous bone grafts or alloplastic materials cannot be used in all clinical conditions. So, only a cell mediated bone regeneration technique will be a possible therapeutic technique. Some authors suggest the use of allogenic MSCs in periodontal regeneration .Kawaguchi *et al* used BMSCs and observed that they have ability to regenerate fresh cementum, periodontal ligament and alveolar bone. Nagatamo *et al* in their study observed that PDL derived cells when transplanted into animal models were able to regenerate periodontal tissue. Liu etal used scaffolds seeded with periodontal ligament derived stem cells and periodontal tissue was regenerated by a miniature swine.

Conclusion

We have entered a new era in which tremendous research in stem cell therapy is in path of making it a realistic alternative in or omaxillofacial regeneration. It can be used to improve and expendite clinical outcomes. Excellent regenerative ability of oral and mesenchymal stem cells can be applied not only in dentistry but also in various fields of regenerative medicine. Moreover, they are easily obtained as discarded biological materials. Despite of some studies demonstrating regenerative potential of stem cells, there is a lack of strict quantitative analysis for testing the ability of these cells to self renew, proliferate and differentiate in vivo. So more intensive, basic and transitional research is necessary that can ultimately offer long term benefits to the patients.

Conflict of interest statement

All authors state that they have no conflicts of interest

REFERENCES

Abdul, R. and Shaikh, R. 2013.Therapeutic Potential Of Stem Cells In Regenerative Dentistry; A Review Of Literature. *International Dental Journal Of Student's Research*, 1(4): 22-30.

Ashika Rachael Samuel *et al*., 2017. *J. Pharm. Sci. and Res*, Vol. 9(4), 497-500

Chandra Mouli, PE., Kumar, S., Manoj, Senthil, B., Parthiban, S., Priya, R. and Subha, R. 2012. Stem Cells In Dentistry- A *Review. J. Pharm. Sci. and Res*, 2012; 4(7); 1872 – 6.

Duailib, Mt., Duailibi, Se., Young, Cs., Bartlett, Jd., Vacanti, Jp. and Yelick, Pc. 2004. *Bioengineered,* Teeth From Cultured Rat Tooth Bud Cells. *J Dent Res,* 83:523-8.

Egusa, H., Sonoyama, W., Nishimura, M., Atsuta, I. and Akiyama, K. 2012. *Journal of Prosthodontic Research,* 56 151–165

Egusa, H., Sonoyama, W., Nishimura, M., Atsuta, I. and Akiyama, K. 2012. Stem cells in dentistry--Part II: Clinical applications. *J Prosthodont Res,* 56(4):229-248.

Gardner, RL. 2002. Stem cells: Potency, plasticity and public perception. *J Anat*, 200:277-82.

Gronthos, S., Mankani, M., Brahim, J., Robey, PG. and Shi, S. 2000. Postnatal human dental pulp stem cells(DPSCs) in vitro and in vivo. *Proc Natl Acad Sci,* USA. 97(25):13625 - 13630

Honda, Mj., Sumita, Y., Kagami, H. and Ueda, M. 2005. Histological And Immunohistochemical Studies Of Tissue Engineered Odontogenesis. *Arch Histol Cytol*, 68:89-101

Liu, Y., Zheng, Y., Ding, G., Fang, D., Zhang, C., Bartold, PM., *et al*., 2008. Periodontal ligament stem cell- mediated treatment for periodontitis in miniature swine. Stem Cells 26(4):1065-1073.

Morsczeck, C., Götz, W., Schierholz, J., Zeilhofer, F., Kühn, U., Möhl, C., *et al*., 2005. Isolation of precursor cells (PCs) from human dental follicle of wisdom teeth. *Matrix Biol,* 24:155-65.

Seo, B., Miura, M., Gronthos, S., Bartold, Pm., Batouli, S., Brahim, J., *et al*., 2004. Investigation Of Multipotent Postnatal Stem Cells From Human Periodontal Ligament. *Lancet,* 36(4):149-55.

Singh, H., Bhaskar, DJ., Rehman, R., Jain, CD. and Khan, M. 2014. Stem Cells: An Emerging Future in Dentistry. *Int J Adv Health Sci,* 1(2): 17-23

Sonoyama, W., Liu, Y., Yamaza, T., Tuan, Rs., Wang, S., Shi, S., *et, al*., 2008. Characterization Of The Apical Papilla And Its Residing Stem Cells From Human Immature Permanent Teeth: Pilot Study. *J Endod,* 34:166-71.

Stem cell - Wikipedia, the free encyclopedia. en.wikipedia. org/wiki/ Stem_cell.

Takahashi, K., Tanabe, K., Ohnuki, M., Narita, M., Ichisaka, T., Tomoda, K., *et al*., 2007. Induction of pluripotent stem cells from adult human fibroblasts by defined factors. Cell 131:861–72.

Thomas, GV., Thomas, NG., John, S. and Ittycheria, PG. 2015. The Scope of Stem Cells in Periodontal Regeneration. *J Dent Oral Disord Ther,* 3(2): 1-9.

Yamada, Y., Ito, K., Nakamura, S., Ueda, M. and Nagasaka, T. 2011. Promising cell-based therapy for bone regeneration using stem cells from deciduous teeth, dental pulp, and bone marrow. *Cell Transplant*, 20(7): 1003–1013.

Young, C., Abukawa, H., Asrican, R., Ravens, M., Troulis, Mj., Kaban, Lb., *et al*., 2005. Tissue-Engineered Hybrid Tooth And Bone. *Tissue Eng,* 11:1599-610.

****