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

ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

Role of Stem Cells in Prosthodontics Rehabilitation

Ashika Rachael Samuel, Dr. Revathy Gounder
Saveetha Dental College ,Chennai

Abstract

Aim-

The aim of this review is to understand the role of stem cells in regenerative prosthodontics for various dental procedures.

Objective-

The review will provide knowledge about the stem cells used in prosthetic dentistry and the effectiveness of each type.

Background –

Stem cells are undifferentiated biological cells that can differentiate into specialized cells and can divide to produce extra stem cells. They are originated in multicellular organism. They may be embryonic or adult stem cells . The stem cells of the dental pulp are the mesenchymal stem cells (MSC). They are the most commonly used stem cells . However bone marrow-derived mesenchymal stem cells are a commonly used cell type for utilization in cell-based regenerative approaches in prosthodontics . They help to build the bone structures of the craniofacial region, particularly the maxilla and mandible .

Reason –

Stem cell therapy is one the most recent advances in the dental field . It's use establishes a 100% success rate. Thus , knowing it's value is of prime importance .

INTRODUCTION

Stem cells are a group of undifferentiated cells of biological nature that have the capacity to differentiate into specialised cells and undergoes the process of mitosis to produce newer cells. They were first discovered in the multicellular organisms[1] . To restore a particular tissue or organ, it is very essential to understand the developmental process of the particular structure and then produce it. The stem cells play a trivial role in the development and repair process [2]. Ernest A. McCulloch and James E. Till (1960s) at the University of Toronto were the first to venture into the field of stem cells research [1]. The tissue repair mechanism in the body takes place with the help of the pluripotent embryonic stem cells . Later these cells have the ability to differentiate into multipotent cells of varying origin like, epithelial , mesenchymal and other tissue specific stem cells .[3,4] When the stem cells interact with each other , they lead to the formation of a new tissue or organ.[5] The embryonic stem cells of pluripotent nature wither away with time however the differentiated multipotent adult stem cells lie deep within the tissues and aid in repair when needed. [6]

Characterstics of Stem Cells: 1. Totipotency: Produce all types of cells as well as germ cells (ESCs). 2. Pluripotency: Produce all types of cells apart from cells of the embryonic membrane. Multipotency: Distinguish into more than one adult cell (MSC). 4. Unipotency: (dedicated progenitors): produce one particular cell type.[7]

TYPES OF STEM CELLS

Embryonic Stem Cells: Embryonic stem cells (ESCs) are imitative from embryos that are 2-11 days old known as blastocysts. They are best developed from supernumerary embryos obtained from in vitro fertilization centers. They are totipotent - cells practically capable of differentiating into any type of cell as well as the germ cell. ESCs are considered eternal as they can be propagated and maintained in an undifferentiated state forever. These stem cells have the maximum potential to regenerate and repair unhealthy organs and tissues in the body. However, the therapeutic advantage of ESCs is bogged by a argument owing to the belief that the procedure of taking out of stem cells from an embryo wipe out the embryo itself and some views this as taking life, thereby, increased ethical and moral concerns. Further, it is hard to control the expansion and differentiation of the embryonic stem cells posing risk of teratoma formation and tumorogenicity. While research is on to overcome some of these deficit as of now, ESCs are not so far used therapeutically and have only remained an excellent platform for research.[8]

Adult Stem Cells: These are undifferentiated cells that occur in a differentiated tissue. Sources of Adult Stem Cells (ASCs) consists of bone marrow, brain, blood, eye, skeletal muscle, lining of the gastrointestinal tract, pancreas, dental pulp, skin, these are multipotent. These Stem cells are sited in positions called Niches. These Niches provide a specific cellular environment needed for self-regeneration. Adult stem cells sited outside the bone marrow are called Tissue stem cells. ASCs divide to replenish dying cells and regenerate damaged tissue. Regulation of differentiation in ASCs is by a protein BMI-1, Notch pathway, sonic hedgehog and the Wnt developmental pathway. ASCs are difficult to identify and purify and when grown in culture are difficult to maintain in an undifferentiated state. Finding ways to culture ASCs outside the body is a high priority of Stem cell research. [9,10]

TYPES OF TOOTH STEM CELLS

Dental Pulp Stem Cells: In 2003 Dr. Songtao Shi, a Pedodontist discovered dental pulp stem cells by utilizing the primary teeth of his daughter & he named as stem cells from human exfoliated deciduous teeth. Many researchers have been done work on dental pulp, gazing for stem cells and they established that dental pulp was rich in different types of stem cells, like, adipocytes, chondrocytes, osteoblasts and mesenchymal

stem cells. These mesenchymal stem cells are one of the most prospective stem cells which has wide therapeutic functions. Dental pulp stem cells can be found both in adults and children. Transplantation of Dental pulp stem cells into immune compromised might outcome in the formation of a dentin-like tissue, while bone marrow stem cells generated a tissue approaching that of lamellar bone. Pulpal wound healing and regeneration may be compromised with growing age. Analysis of pulpal cell populations point out those age related declines in pulpal cell numbers take place. Studies have identified a possible progenitor cell population in dental pulp, which comprises less than 1% of the whole cells.8 Severe Injury to a dental pulp from any infection or trauma leads to death of odontoblasts with a limited ability for regeneration. Healing depends on the strength and extent of the injury, presence of bacteria and host factors such as the level of native and systemic immunity.[11]

Stem cells can be separated from the three groups of teeth, they are: (a) Deciduous Teeth: The healthy pulps of deciduous teeth are a rich source of viable stem cells. Scientific data sustains that separated stem cells from healthy pulp of deciduous teeth are extremely proliferative, still when the pulp is recovered in little quantities. (b) Wisdom Teeth: The healthy pulp from wisdom teeth is a further exceptional source for workable stem cells. Entire or sectioned divisions of third molars containing healthy pulp can be recovered at the time of their exclusion. The pulp is often exposed if an impacted third molar needs to be sectioned for removal. (c) Permanent teeth: Healthy pulp from all the permanent teeth are potential resource of stem cells. Bicuspids requiring to be removed for orthodontic suggestions are an example of this. Permanent teeth to not to be included: endodontically-treated or non vital teeth, teeth with lively infections, teeth with rigorous periodontal disease and too much mobility, teeth with large restorations and deep caries, and teeth with calcified or sclerosed pulp chambers.[12]

1. Adipocytes: They have successfully been utilized to repair injure to the heart muscle caused by severe heart attack. There is also initial data to point out that they can be used to treat cardiovascular diseases, orthopaedic problems and spine, Crohn's disease, congestive heart failure, and also used in plastic surgery.
2. Chondrocytes and Osteoblasts: This type of stem cells has effectively been used to grow cartilages and bones suitable for transplant. They have also been utilized to develop intact teeth in animals.
3. Mesenchymal: These stem cells have successfully been used to restore spinal cord damage and to recall feelings and progress of movement in paralyzed patients. Since they can figure neuronal clusters, mesenchymal stem cells also have the possibility to treat neuronal degenerative disorders such as Parkinson's diseases and Alzheimer's, cerebral palsy, as well as a host of other disorders. Any other type of adult stem cells doesn't have more therapeutic potential than mesenchymal stem cells. [13-15]

APPLICATION IN PROSTHODONTICS

1) Tooth regeneration

The regeneration of adult teeth will be possible in future with the help of tissue engineering and newer expansion in stem cell therapy. Regenerative procedures would be improved fitting and substitutes in place of dental implants. Experimental studies with animal models have exposed that the tooth crown formation can be regenerated using tissue engineering techniques that merge stem cells and recyclable scaffolds. Epithelial mesenchymal exchanges are mandatory in tooth development. "These exchanges are considered by the reciprocal exchange of signals between these two native germ layer tissues and outcome in the emergence of inimitable terminal phenotypes with their supporting cells". Three key elements are involve in tooth regeneration which include:

Inductive morphogenes
Stem cells
Scaffold

Following steps are involved in regeneration of tooth:

1. Harvesting and spreading out of adult stem cells.
2. Seeding the stem cells into scaffold which provides optimize environment.
3. Cells are instructed with targeted soluble molecular signals spatially.
4. The gene expression profile is confirming by the cells for next phase in odontogenesis
5. Duailibi et al., in their studies were able to form tooth from single cell suspensions of cultured rat tooth bud cells. They confirmed bioengineered rat teeth grown in 12 weeks with PLGA and PGA scaffold. Honda et al. developed tissue engineered teeth, when implanted into omentum of rat utilizing porcine tooth bud cells and PGA fiber engage scaffold that reminds of the model of odontogenesis. Young et al., using porcine tooth bud cells, PLGA and PGA scaffolds produced a crossbreed tooth bone for the cure of tooth loss beside with alveolar bone resorption.[16-20]

2) Periodontal regeneration

Due to the difficult structure of the periodontium (having hard and soft tissues), its entire regeneration has always stay a challenge. All the present regenerative techniques such as allografts, autologous bone grafts, or alloplastic materials have restrictions and cannot be utilized in all clinical condition. Therefore, a cell-mediated bone regeneration technique will be a possible therapeutic alternative. Kawaguchi et al. verified that the transplantation of ex vivo prolonged autologous MSCs can regenerate fresh cementum, periodontal ligament and alveolar bone in class III periodontal deficit in dogs. Going a step ahead Hasegawa et al, confirmed that periodontal ligament cells cultured in vitro were effectively reimplanted into periodontal defects in order to endorse periodontal regeneration. A

consequent study by the same group stated a parallel approach in humans. This study reported certain evidence that stem cells can be utilized to regenerate a tissue as complex as the periodontium.[8]

3) Craniofacial regeneration

Regenerative medicine aims to use tissue engineering to restore damaged and lost tissue [21]. In this report, we describe the first randomized, controlled, human trial employing stem cell therapy for the regeneration of craniofacial bone. TRCs were grafted into osseous defects of the jaw and biopsies harvested for analyses at 6 and 12 weeks. Reconstruction of these sites was completed with oral implant therapy and treatment sites were followed for 12 months postoperatively. Clinical and laboratory analyses of treatment sites demonstrated that the cell therapy accelerated the regenerative response as determined clinically, radiographically, and histologically. Further, there was a significantly reduced need for secondary bone grafting procedures in the group that originally received the cell therapy.[22]

4) Alveolar bone regeneration

Bone development involves the aggregation of MSCs into mesenchymal condensations, which is partly similar to tooth development but without the epithelial invagination. There are two types of bone formation: intramembranous and endochondral. In endochondral bone formation, the mesenchymal condensations first undergo chondrogenesis and then ossification to form cartilage and bone.[23] During adulthood, bone possesses the intrinsic capacity for regeneration throughout life. In most bone injuries (fractures), the damaged bone tissue can be functionally regenerated by the local cells (including chondroblasts, osteoblasts, endotheliocytes, and fibroblasts). However, when the fractures are serious (such as large bone defects created by trauma, infection, tumor resection, and skeletal abnormalities) enough that self-healing cannot repair, an adequate supply of stem cells (such as bone marrow stem cells) is required for efficient bone regeneration.[24] Oral MSCs seem to be ideal candidates for bone regeneration. Both dental and nondental MSCs are able to differentiate into chondroblasts and osteoblasts under inductive conditions in vitro.[25-29]

5) Muscle regeneration

Some research groups have focused on the muscle- and tendon-forming properties of oral stem cells. Armiñán et al [30] first reported that DPSCs could differentiate into cardiomyocyte-like cells when cocultivated with neonatal rat cardiomyocytes for about 4 weeks in vitro. Yang et al [31] demonstrated that DPSCs were able to differentiate into dystrophin-producing muscle cells in cardiotoxin-paralyzed muscles in a mouse model, which has implications for the study and treatment of muscular dystrophy.

SUCESS RATE OF STEM CELLS IN DENTISTRY

Case report - The extraction socket created following tooth removal serves as a reasonable model of bone repair being that the resulting defect is reproducible and has a limited capacity to heal completely without intervention. Pelegrine and colleagues used this model recently to investigate the potential of a bone marrow graft in preserving alveolar bone following tooth removal [22]. Upon evaluation of the grafted sites at 6 months, the graft provided better results in maintaining the alveolar bone relative to when no graft was used. Though the results suggested that bone marrow constituents provided benefit, the cellular component of the graft was not characterized, and thus, homogeneity of the graft from patient to patient could not be ascertained. Other promising preliminary reports of successful craniofacial regenerative procedures using bone marrow-derived grafts are similarly confounded by the lack of characterization of the grafted biological cell type or construct [32-34] Meijer and colleagues spoke to this limitation in a study evaluating the use of bone marrow grafts for craniofacial reconstructions [35] These treatments resulted in clinical bone formation in only three of the six patients treated and because the constituents of the grafts were not characterized, the authors indicated that the cause for the 50% failure rate could not be definitively determined.

CONCLUSION

Oral epithelial and mesenchymal stem cells are easily obtained as discarded biological materials. Their excellent regenerative ability can be applied not only in dentistry but also in various fields of regenerative medicine. The oral stem cells show their capability to repair cornea, dental pulp, periodontal, neural, bone, muscle, tendon, cartilage, and endothelial tissues without neoplasm formation. However, despite these experimental studies demonstrating the regenerative potential of oral stem cells, most of the studies lack strict quantitative analysis for testing the ability of these cells to self-renew, proliferate, and differentiate, especially in vivo. Moreover, before their clinical application, the experimental studies need to resolve the following issues: 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[36] therefore, viability and functional differentiation of oral stem cells in vivo need to be improved); particularly for neuronal regeneration, 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 is required for understanding their fate and behavior; 4) since oral stem cells, especially oral epithelial stem cells, are often involved in neoplasia, the cellular and molecular mechanisms that allow oral stem cells to choose self-renewal, canceration, and differentiation should be well studied.

REFERENCES

1. Stem cell - Wikipedia, the free encyclopedia. en.wikipedia. org/wiki/ Stem_cell.
2. Behjati S, Huch M, van Boxtel R, et al. Genome sequencing of normal cells reveals developmental lineages and mutational processes. Nature. 2014;513:422–425.
3. Doetschman TC, Eistetter H, Katz M, Schmidt W, Kemler R. The in vitro development of blastocyst-derived embryonic stem cell lines: formation of visceral yolk sac, blood islands and myocardium. J Embryol Exp Morphol. 1985;87:27–45.
4. Odorico JS, Kaufman DS, Thomson JA. Multilineage differentiation from human embryonic stem cell lines. Stem Cells. 2001;19(3):193–204.
5. Vainio S, Karavanova I, Jowett A, Thesleff I. Identification of BMP-4 as a signal mediating secondary induction between epithelial and mesenchymal tissues during early tooth development. Cell. 1993;75(1):45–58.
6. Kørbling M, Estrov Z. Adult stem cells for tissue repair–a new therapeutic concept? N Engl J Med. 2003;349(6):570–582.
7. Desai VD, Varma b, Maheshwari S, Bumb D. Tooth Regeneration By Stem Cells -An Innovative Approach. Asian J. Pharm. Hea. Sci. 2012; 2(3):433-7.
8. Saraswathi K Gopal Lankupalli AR, Stem Cell Therapy. J Clin Diagn Res. 2012 6(1): 142-4.
9. Kompalli PV, Stem Cells - A Review. Webmedcentral Biomedical Engineering 2013;4(2):Wmc004046.
10. Buch A & Choksi D. Clinical Applications Of Stem Cells In Dentistry. Dharmsinh Desai University, Faculty od Dental Science, Journal od Dental Sciences. 2010; 1(1): 26-31
11. Friedlander LT, Cullinan MP & Love RM. Dental Stem Cells And Their Potential Role In Apexogenesis And Apexification. Int Endod J. 2009;42:955–62.
12. Cherian E, Kurien J, Kurien A, Jayasekharan VP. Stem Cells In Dental Tissue. Ijoonline. 2013; 1(1): 26-32
13. Petrovic V, Stefanovic V. Dental Tissue--New Source For Stemcells. Scientificworldjournal. 2009; 14(9):1167-77.
14, Gronthos S, Brahim J, Li W, Fisher Lw, Cherman N, Boyde A, Denbesten P, Robey Pg, Shi S. Stem Cell Properties Of Human Dental Pulp Stem Cells. J Dent Res. 2002; 81(8): 531-5.
15. Stem Cell Information. The National Institutes Of Health Resource For Stem Cell Researchhttp://Stemcells.Nih.Gov/Info/Media/Pr omise.Htm.
16. Chandra Mouli PE, Kumar S Manoj, Senthil B, Parthiban S, Priya R, Subha R. Stem Cells In Dentistry- A Review. J. Pharm. Sci. & Res. 2012; 4(7); 1872 – 6.
17. Nakahara T, Ide Y. Tooth Regeneration: Implications For The Use Of Bioengineered Organs In Irst-Wave Organ Replacement. Hum Cell 2007; 20:63-70.
18. Duailibi Mt, Duailibi Se, Young Cs, Bartlett Jd, Vacanti Jp, Yelick Pc. Bioengineered Teeth From Cultured Rat Tooth Bud Cells. J Dent Res 2004; 83:523-8.
19. Honda Mj, Sumita Y, Kagami H, Ueda M. Histological And Immunohistochemical Studies
20. Young C, Abukawa H, Asrican R, Ravens M, Troulis Mj, Kaban Lb, Et Al. Tissue-Engineered Hybrid Tooth And Bone. Tissue Eng 2005;11:1599-610.
21. Langer R, Vacanti JP. Tissue engineering. Science. 1993; 260(5110):920–926. [PubMed: 8493529]
22. Pelegrine AA, da Costa CE, Correa ME, Marques JF Jr. Clinical and histomorphometric evaluation of extraction sockets treated with an autologous bone marrow graft. Clin Oral Implants Res. 2010; 21(5):535–542. [PubMed: 20337664]
23. Khurana JS. Bone pathology. 2nd ed. Philadephia, PA: Springer; 2009.
24. Dimitriou R, Jones E, McGonagle D, Giannoudis PV. Bone regeneration: current concepts and future directions. BMC Med. 2011;9:66.
25. Yamada Y, Ito K, Nakamura S, Ueda M, Nagasaka T. Promising cell-based therapy for bone regeneration using stem cells from deciduous teeth, dental pulp, and bone marrow. Cell Transplant. 2011;20(7): 1003–1013.
26. Graziano A, d'Aquino R, Laino G, Papaccio G. Dental pulp stem cells: a promising tool for bone regeneration. Stem Cell Rev. 2008;4(1): 21–26.
27. Mori G, Brunetti G, Oranger A, et al. Dental pulp stem cells: osteogenic differentiation and gene expression. Ann N Y Acad Sci. 2011;1237: 47–52.
28. Chadipiralla K, Yochim JM, Bahuleyan B, et al. Osteogenic differentiation of stem cells derived from human periodontal ligaments and pulp of human exfoliated deciduous teeth. Cell Tissue Res. 2010;340(2):323–333.
29. d'Aquino R, Graziano A, Sampaolesi M, et al. Human postnatal dental pulp cells co-differentiate into osteoblasts and endotheliocytes: a pivotal synergy leading to adult bone tissue formation. Cell Death Differ. 2007;14(6):1162–1171.
30. Armiñán A, Gandía C, Bartual M, et al. Cardiac differentiation is driven by NKX2.5 and GATA4 nuclear translocation in tissue-specific mesenchymal stem cells. Stem Cells Dev. 2009;18(6):907–918.
31. Yang R, Chen M, Lee CH, Yoon R, Lal S, Mao JJ. Clones of ectopic stem cells in the regeneration of muscle defects in vivo. PLoS One. 2010;5(10):e13547.
32. Filho Cerruti H, Kerkis I, Kerkis A, Tatsui NH, da Costa Neves A, Bueno DF, da Silva MC. Allogenous bone grafts improved by bone marrow stem cells and platelet growth factors: Clinical case reports. Artif Organs. 2007; 31(4):268–273. [PubMed: 17437494]
33. Marcacci M, Kon E, Moukhachev V, Lavroukov A, Kutepov S, Quarto R, Mastrogiacomo M, Cancedda R. Stem cells associated with macroporous bioceramics for long bone repair: 6- to 7year outcome of a pilot clinical study. Tissue Eng. 2007; 13(5):947–955. [PubMed: 17484701]
34. Soltan M, Smiler D, Soltan C, Prasad HS, Rohrer MD. Bone grafting by means of a tunnel dissection: Predictable results using stem cells and matrix. Implant Dent. 2010; 19(4):280–287. [PubMed: 20683284]
35. Meijer GJ, de Bruijn JD, Koole R, van Blitterswijk CA. Cell based bone tissue engineering in jaw defects. Biomaterials. 2008; 29(21):3053–3061. [PubMed: 18433864]
36. Sakai K, Yamamoto A, Matsubara K, et al. Human dental pulp-derived stem cells promote locomotor recovery after complete transection of the rat spinal cord by multiple neuro-regenerative mechanisms. J Clin Invest. 2012;122(1):80–90.