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Stem Cell in Dentistry – Potential Contributions, Challenges and Future

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Abstract:

Stem cells are unspecialised and unclassified cells but their unique property "pluripotency" makes them special because it has opened the new doors of opportunities and possibilities in the field of dentistry and regenerative medicine to regenerate different organs and tissues. Currently, several studies are undergoing on dental stem cells (SCs) to find out their possible uses in oromaxillofacial region and various stem cells have already been identified for their application in orofacial region. Therefore, a new separate branch of dentistry names as "Regenerative Dentistry" is emerging very fast as dental stem cells offer a lot of benefits over outdated procedures andhave the ability to replace the old restorative techniques of repairing oromaxillofacial trauma which involve disadvantages like scarring, loss of function of replaced part, infection and donor site morbidity with early and late complications [1]. Although oromaxillofacial region is difficult to repair because of its complex anatomical structure but undoubtedly,from past few decades, regeneration of this region using stem cell therapy has also fascinated the entire world of stem cell biologists, molecular biologists, geneticists, clinicians and dentists to discover new advancements in the field of craniofacial engineering[2]. Clearly, future of dentistry lies in stem-cell based powerful therapeutic approach which can potentially transform the reparative and regeneration process of defective hard and soft tissues in orofacial region.

Keywords: Dental Stem Cells, Regenerative Dentistry, Dental Pulp Stem Cells (DPSCs), Stem Cells from Human Exfoliated Deciduous Teeth (SHEDS).

I. INTRODUCTION

Stem cells are mainly found in multicellular organisms which are a type of specialised undifferentiated biological cells capable to differentiate into indefinite daughter cells and other kinds of multiple functional cells. Earnst A. McCulloch and James E. Till have been recognised as the Fathers of Stem Cell Science who confirmed the existence of stem cells while they were studying in Ontario Cancer Institute, Toronto (Canada) in 1961. In year 2003, Dr. Songtao Shi, Pedodontist first discovered dental pulp stem cells (DPSCs) using his daughter's primary teeth and named them stem cells from human exfoliated deciduous teeth (SHEDS). Furthermore, in 2005National Institutes of Health, USA announced the discovery ofDPSCs by Dr. Irina Kerkis. Presently, dental research community is broadly studying dental stem cells to deeply understand their exclusive properties for successful clinical application utilising complex in vivo and in vitro techniques[3]. Tooth is nature's storage place as abundant stem cells are found in wisdom teeth, permanent teeth and deciduous teeth.Scientists are continuously working to find out the possible outcomes on how stem cells can be used in dental practices to repair and regenerate dentofacial structures [4]. Moreover, recent study specifies that dental stem cells may have the potential to regenerate bone, periodontal ligament (PDL) and perhaps teeth also [5]. Till date, different types of SCs have already been identified from human tooth and its surrounding tissues. Additionally, special emphasis is now given on preserving the lost tooth in "Tooth Banks" as various experimental studies indicate dental stem cell application in medical field, thereby expanding its horizons beyond limits when compared with past because history reveals that lost tooth was considered as a "waste" before. A revolutionary era in dentistry is now ready to set new benchmarks offering long-term permanent

treatment and patient-comfort at the same time, however, interdisciplinary approach to research is required for achievingfruitful results.

Objectives of Research

1. To study dental stem cells, their types and potential practices in dentistry.
2. To study futuristic scope of dental stem cells in treating defective or injured oromaxillofacial region introducing new methods and techniques for repair.

II. RESEARCH METHODOLOGY

This study is based upon Exploratory Research Technique on prevailing data. The secondary data is collected from attributed sources like Internet white paper(s), international journals and published articles. Collected data is evaluated and studied to reach the conclusion.

Classification of Stem Cells

Stem cells make up the tissues and organs of plants and animals. Currently, their promising uses are directing the replacement therapies towards a revolutionary era for repairing defective and traumatised tissues. Depending upon the sources, stem cells can be mainly classified into:

- **Embryonic Stem Cells:**
  *Source:*2-11 days old embryo known as blastocyst
  Characteristic: Pluripotent
- **Adult Stem Cells:**
  Source: Brain, blood, eye, bone marrow, skeletal muscle, gastro-intestinal tract lining
  Characteristic: Multipotent
- **Induced Pluripotent Stem Cells**
  Source: Genes found in stem cells
  Characteristic: Pluripotent

Stem Cells in Dentistry

With the advancement of technology, like every field is unfolding new concepts of improvement in scientific approaches, the same has not left the dentistry untouched. Today, dentistry is not only limited to teeth as it is contributing to other medical fields by continuously expanding horizons with the help of newly invented upgraded research techniques and improved infrastructure leading towards safe and permanent treatment. Stem cells being an interesting topic of research from few decades has entirely given a new direction in treating dental related diseases and oromaxillofacial defects. Dental stem cells are derived from adult stem cells. Basically, adult stem cells are of two types:

- Haematopoietic Stem Cells
- Non-Haematopoietic/ Mesenchymal Stem Cells (MSCs)

Out of the above mentioned, dental stem cells are formed from mesenchymal stem cells, which are capable of self-renewal and can differentiate into other multiple cell lineages. Remarkable progress in ongoing researches is guiding the future path of dental treatment combined with stem cell biology and tissue engineering both. Presently, studies based upon human teeth and animals, mainly five forms of dental stem cells are isolated which show future possibilities in treating life-threatening diseases. Dental stem cells along with their types and properties are categorised in the following table 1.1[4][5][6]:

Table 1.1 Representing Type and Properties of Dental Stem Cells

Types / **Properties**	**Dental Pulp Stem Cells**	**Stem Cells from Exfoliated Deciduous Teeth**	**Periodontal Ligament Stem Cells**	**Stem Cells from Apical Papilla**	**Dental Follicle Progenitor Cells**
Isolated from	Impacted 3rd molar	Coronal Pulp Tissue	Periodontal Ligament of Impacted 3rd	Apical Papilla of Human	Dental Follicle of Human Impacted 3rd

			Molar Roots	Immature Teeth	Molar
Type of Tooth	Permanent	Primary	Permanent	Permanent	Permanent
Appearance	Fibroblast-like	*Isolated Cells*- Clustered into numerous colonies. *After Separation* Fibroblast-like	Clonogenic Fibroblast-like	Clonogenic Fibroblast-like	Fibroblast-like
Proliferation Rate	Moderate	High	High	High	High
Multilineage Differentiation Potential	Adipogenic, Chondrogenic, Myogenic, Neurogenic, Odontogenic, Osteogenic	Same as Dental Pulp Stem Cells	Same as Dental Pulp Stem Cells except Myogenic is Uncertain	Same as Dental Pulp Stem Cells except Chondrogenic and Myogenic is Uncertain	Same as Dental Pulp Stem Cells
Markers	CD146, Nestin, OCT4, STRO-1	CD146, Nanog, Nestin (when induced), OCT4, STRO-1	CD146, STRO-1	CD146, Nestin, STRO-1	CD146, Nestin, Notch-1, STRO-1
Possible Roles- To Bio-Tooth	Pulp, Ectopic and Reparative Dentine or Dentine-Pulp Complex	Dentine and Pulp	Periodontal Repair	Dentine and Pulp with Odontoblast-like cells	Periodontium Regeneration
Possible Roles- In Systemic Diseases	Bone Regeneration, CNS degeneration, Heart Attack, Hepatic Fibrosis	Bone Regeneration	Bone Regeneration	Bone Regeneration	Neuronal Regeneration

Apart from these dental tissues-derived stem cells, it is significant to know about the following stem cells which are now considered for clinical applications in dentistry and they are [1]:

- Bone marrow derived mesenchymal stem cells (BMSCs) from orofacial bones
- Oral mucosa derived Stem Cells
- Periosteum derived Stem Cells
- Salivary gland derived Stem Cells
- Adipose tissue derived Stem Cells
- Pluripotent Stem Cells

Clinical Applications of Stem Cells in Dentistry

To date, various studies on animal models indicate enormous benefits and marvellous opportunities to medical field as stem cells due to their dynamic properties are capable of regenerating complex anatomical structures. Experimental studies reveal that unlike dental tissue derived stem cells, other type of mesenchymal stem cells do not have therapeutic potential. Regeneration of periodontium was always challenging because of its difficult formation. Furthermore, existing restoratives procedures are restricted to bone grafts or alloplastic materials. Hence, stem cell mediated bone regeneration will serve as a potential healing method. Many trials (in-vivo and ex-vitro) on dogs and some other researches demonstrate a possible method to restore periodontal

defects in humans. Similarly, pulp tissue regeneration technique will offer remarkable benefits by duplicating the physical and mechanical properties of tooth because until now, other restorative materials are not able to do the same especially in newly erupted permanent teeth requiring apexification or apexogenesis[4].

Additionally, orofacial bone marrow derived stem cells(BMSCs) have quite distinct phenotype and functional properties when compared with BMSCs from iliac crest which may deliver an advantage for regeneration of orofacial bones. Also, other experiments suggesting the effect of source of transplanted cells on the properties of redeveloped bone has significantly encouraged the dentists to look for the use of periosteum for orofacial bone regeneration.

Lombaert et al., 2008 reported a culture method (in-vitro stem cell floating sphere culture), which may perhaps be used for isolating a specific type of cells showing stem cell markers from parted mouse submandibular glands and can differentiate into salivary gland ducts with acinar cells producing mucin and amylase[1]. Thus, this report proposes a room for astonishing future therapies offering relieve to patients who receive radiation therapies. In that way, some of the irreversible losses and hypofunction of salivary glands such as xerostomia due to radiotherapy can be prevented[7]. Moreover, adipose tissue derived stem cells may play an incredible role in vertical bone augmentation for implant treatment and in periodontal regeneration.

Presently, scientific work and researches are still in process exploring the innovative technologies to regenerate periodontal ligament (PDL) tissues, missing maxillary or mandibular bones, salivary glands and lost teeth. All of the above, temporomandibular joint (TMJ) is considered a difficult tissue to treat because of limited blood supply. But try-outs on adipose tissues derived stem cells have given a ray of hope for TMJ reconstruction. Subsequently, large craniofacial defects as a result of cyst enucleation, trauma and tumour resection can also be treated using stem cells to close bone defects.

Regenerative Dentistry and Tooth Regeneration

With continuous progress in stem cell research and tissue engineering, 'Regenerative Dentistry' has become a field on its own which is undoubtedly a boon to periodontologyendodontics, orthodontics and oral pathology.Besides, tooth regeneration is a stem cell based process of regenerative medicine which will be possible in future, utilising stem cell therapy and tissue engineering. Experimental studies on animal models reveal three basic fundamentals involved in regeneration of tooth:

- Inductive morphogenes
- Stem Cells
- Scaffolds

Tooth regeneration completes through the following steps:

1. Harvesting and proliferation of adult stem cells.
2. Seeding the stem cells into scaffolds to provide optimal atmosphere.
3. Cells are instructed with targeted soluble molecular indicators for three-dimensional organisation.
4. Confirmation of gene expression profile of cells for subsequent stage in odontogenesis.

Challenges Encountered

Stem cell has always remained an interesting but controversial topic for medical community as it is accompanied with some ethical issues. Till,researches for embryonic stem cells are limited to certain ethical boundaries. Contrarily, adult stem cells are already used to treat various systemic diseases, yet their usage in several conditions is not validated or is under clinical experiments, despite some claim to the conflicting [8].

Future Tissues and Tooth Banking

Considering the remarkable benefits of stem cells, cranial structures, tissues engineered bone grafts and TMJ are possible to develop in upcoming stem cell era using stem cell therapy. Therefore, extracted tooth are not considered as an unwanted material now. Instead, they are now preserved using various methods. The term tooth banking was first raised in 1966 [5], later on, in year 2004 [5], the first tooth bank was established in Japan (National Hiroshima University). Teeth are preserved using a unique and systematic method named as "cryopreservation" or specifically "tooth cryopreservation". Worldwide, different techniques are followed to preserve the tooth and tooth derived stem cells. Various countries across the globe such as United States,

Denmark, Japan, Taiwan and Korea[5] are extensively participating in tooth banking via using various cryopreservation method(s). In this process, based upon the appropriate method to be adopted, teeth are stored in different solutions like saline, antibiotic, glycerol, human serum, BAMBANKER2, dimethyl sulfoxide, Dulbecco's Modified Eagle Medium at optimum temperature range.

III. CONCLUSION

Dental tissue regeneration is a phenomenal alternative to more conventional restorative practices because it offers replacement of infected or diseased tissue with natural tissue thereby restoring the functional ability. However, stem cells must be differentiated to appropriate cell lineages before clinical-use in order to avoid deleterious effects. Restoration of edentulous mouth, regeneration of defective/injured structures and treatment of systemic diseases should be considered on priority basis offering impressive and effective permanent treatment together with patient comfort and ease. Moreover, tooth banking procedure should be incorporated in dentistry for dental stem cell preservation as a preventive measure in treatment. Stem cell therapy and tissue engineering practices are becoming less fictional and progressing towards reality. Although biological tooth regeneration is not yet achievable but emerging possibilities in stem cell therapy may shift the paradigm in future. This could possibly help in treating suggesting permanent cure of some common irreversible conditions such as caries and periodontal diseases through establishing new approaches. Altogether, regenerative dentistry and regenerative medicine are ready to set milestones for future therapeutic practices and has got a paramount role in dentistry.

REFERENCES

[1] ***"****Stem Cells in Dentistry: A Boon to Oral & Maxillofacial Surgery",* Author: Saba Majid, Dr. Ramesh Ram Fry, Dr. Samta Goyal, Dr. Jatinder Pal Singh Chawla, Publication: IOSR Journal of Dental and Medicine Sciences, Volume 15, Issue 1 Ver. III (Jan. 2016), PP 62-68

[2] "*Stem Cells in Dentistry-A Review",* Author: Dr. P.E. Chandra Mouli, Dr. S.Manoj Kumar, Dr. B.Senthil, Dr. S.Parthiban, Dr. R.Priya, Dr. R.Subha, Publication: Journal Of Pharmaceutical Sciences and Research, Vol 4(7), 2012, 1872-1876

[3] *"Stem Cells of Dental Origin: Current Research Trends and Key Milestones towards Clinical Application",* Author: Athina Bakopoulou, Imad About, Publication (Online): Stem Cells International, Volume 2016 (2016), Article ID 4209891, Online Reference Source: http://dx.doi.org/10.1155/2016/4209891

[4] *"Stem Cells: An Emerging Future in Dentistry",* Author: Harender Singh, D.J. Bhaskar, Rahila Rehman, Chatainya Dev Jain, Mohsin Khan, Article Publication (Online Reference Source): http://www.ijahs.net/uploads/2/6/7/7/26772457/ijahs_vol_1_issue_2_3.pdf

[5] *"Dental Stem Cells and Tooth Banking for Regenerative Medicine",* Author: Yen-Hua Huang, Jen-Chang Yang, Chin-Wei Wang, Sheng Yang Lee, Publication: Journal of Experimental and Clinical Medicine (Taiwan), 2010;2(3):111-117

[6] *"Dental Stem Cells and Their Potential Role in Regenerative Medicine",* Author: Mohamed Jamal, Sami Chogle, Harold Goodis, Sherif M. Karam, Publication: Journal of Medical Sciences (2011): 4(2), Pages-53-61, 2011

[7] *"Regenerative Perspective in Modern Dentistry",* Author: Mihnea Ioan Nicolescu, Publication: MDPI-Dentistry Journal, Volume 4, Issue 2, April 2016

[8] *"Ethical Issues in Stem Cell Research",* Author: Bernard Lo and Lindsay Partham, Online Reference Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2726839/,Publication:April 14, 2009

