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Periodontal Stem Cells- The Regeneration Front

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Review Article
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ABSTRACT

The ultimate goal of periodontal regeneration is to restore the damaged alveolar bone proper, root cementum, and periodontal ligament with collagen fibers inserted into the root surface. The search for new regenerative strategies is a challenging field of periodontal research, and tissue engineering, using stem cells, has recently been shown as a promising approach. Periodontal tissue stem cells, which play a crucial role in maintaining the homeostasis of periodontal tissues, are found in the periodontal ligament (PDL). These cells have long been referred to as mesenchymal stem/stromal cells (MSCs), and their clinical applications have been extensively studied. However, tissue stem cells in the PDL have not been thoroughly investigated, and they may be different from MSCs. Recent advances in stem cell biology, such as genetic lineage tracing, identification of label-retaining cells, and single-cell transcriptome analysis, have made it possible to analyze tissue stem cells in the PDL in vivo. In this review, we summarize recent findings on these stem cell populations in PDL and discuss future research directions toward developing periodontal regenerative therapy.

Keywords: Dental Stem Cell, Mesenchymal Stem/Stromal Cell, Periodontal Ligament Stem Cells, Regeneration.

Introduction

Embryonal and adult stem cells represent a very interesting research field particularly mesenchymal Stem cells have gained interest because of its high Differentiation potential and their availability.[1] Melcher was the 1st who proposed the concept that stem cells may reside in periodontal tissue.[2] PDL (periodontal ligament), pulp, Bone marrow & adipose Sources of tissue are tissue described as Potential sources of oral tissue regeneration.[3] When Considering application to periodontal regeneration, Stem cells derived from tissues Surrounding teeth and periodontium should be considered as the first Choice. The periodontal ligament is

complex cellular and highly vascular connective tissue which surrounds the tooth root & connects to the inner wall of the alveolar bone.[4] Early observations indicated that periodontal ligament has regeneration capacity and that a population of multipotent progenitor cells. Complex series associated with periodontal regeneration involves recruitment of locally derived progenitor cells to sites that can differentiate into periodontal ligament Forming cells, mineral Forming cementoblasts, or bone-forming osteoblast/[5] Ernest MC Culloch and James Till discuss the various properties and Future possibilities for use of Stem cells are unspecialized cells that can develop into several different cell types.[6] The two defining characteristics of stem cells are perpetual self-renewal and the ability to differentiate into a specialized adult cell type.

Classification of Stem Cells[2]

Can be classified as totipotent, pluripotent, multipotent, unipotent. Totipotent cells have the capacity to produce all cell types of developing organisms, including both embryonic & extraembryonic (eg. Placenta) tissue. Pluripotent cells can only make cells of the embryo proper, but make all cells of the embryo including germ cells & cells from any of the germ layers. Therefore, they can make any cells of the body. Multipotent Cells can only make cells within a given germ layer eg: Haematopoietic stem cells. Unipotent cells make cells of single cell type. An example is a germ cell stem that makes a stem. The cell matures to become an egg or sperm, but not other cell types.

Classification of Dental Stem Cells[7]

Is based on the differentiation of dental stem cells either into the formation of dentin or periodontium-associated tissues. 1st group is associated with dental pulp consisting of Dental pulp stem cells (DPSC). Stem Cells of Human exfoliated deciduous teeth (SHED). Stem cells from apical papilla (SCAP). 2nd group is associated with periodontium consisting of Periodontal ligament Stem cells (PDISC). Dental Follicle Cells (DFPC) Periodontal ligament stem cells (PDLSC). Periodontal tissue is a complex tissue mainly composed of two hard tissues somatic stem Cells localized in PDL tissue and derived from cranial neural crest cells. These cells have the potential to undergo triploblastic differentiation with the ability to differentiate into not only osteoblast, adipocytes, chondrocytes, cementoblasts & tendon ligament fibroblast but also myocytes, neural cells, retinal cells, endothelial cells, hepatic cells[8] Synthetic cells are formative cells, which are categorized under periodontal ligament cells. cells of periodontal ligaments synthetic cells, resorptive cells & progenitor cells Formative cells are osteoblast Fibroblasts, and cementoblasts while resorptive cells are osteoclast, Fibroclast & cementoblast. the progenitor cells for resorptive originate From hematopoietic stem cells in addition to these Other epithelial & connective tissue cells, Mast cells and macrophages & other types of cells derived from the haemopoietin line are present in the periodontal ligament.[9] Sodek Studied collagen turnover in periodontal tissue by measurement of proline incorporated into newly synthesized and mature collagen in connective tissue, a highly efficient & rapid collagen turnover rate.[10] periodontal tissue was demonstrated in 1980, Gould et al studied the migration and division of progenitor cell populations in PDL after wounding the periodontal ligament of the lower first molar in mice by using radiography & grain counting techniques.[11] McCulloch et al conducted a study to examine Endosteal spaces with the alveolar bone communicate with periodontal ligament & may contribute to its cell populations Here, cell counts, labelling indices, grain counts & progenitor cell ratios were determined.[12] Somerman et al 1988 compared human periodontal ligament cells and gingival fibroblasts, both derived from the same patient, with the same passage in vitro, greater protein & collagen production & higher alkaline phosphatase activity. Both the periodontal & gingival tissue are thought to harbour cells with the ability to stimulate periodontal regeneration, formation of new bone, cementum & connective tissue attachment[13], Seo et al. In 2005 utilized human periodontal ligament to test the hypothesis that cryopreserved human periodontal ligament contains retrievable postnatal Stem cells the study demonstrated that human postnatal Stem cells can be recovered from Cryopreserved human periodontal

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ligament, thereby providing a practical clinical approach for utilization of frozen tissues for stem Cell Isolation.[14] Tomokiyo et al aimed to establish the human PDL committed Stem cell line & investigate the effects of basic fibroblast growth factor on osteoblastic.

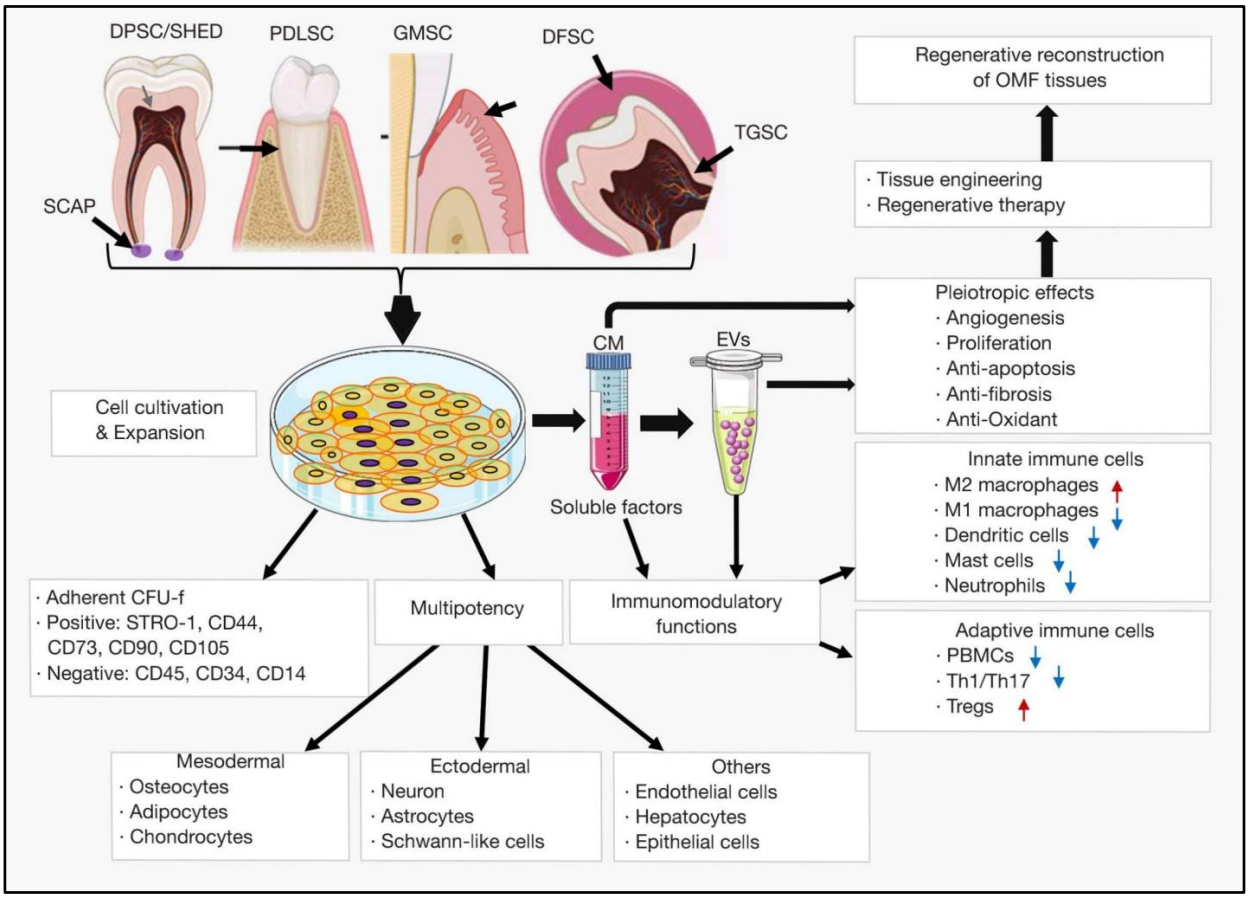

Figure 1: Source, properties and biological functions of dental mesenchymal cells.

Periodontal Ligament Stem Cells

The PDL that anchors the tooth root to the alveolar bone influences the lifespan of the tooth & PDL lost through periodontitis is difficult to regenerate[15] Iwata et al aim were to know whether the periodontal ligament is a reliable source of periodontal regeneration & So they followed an optimal protocol for the extraction, expansion & characterization of human PDL cells was examined for Clinical trials[16] Park et al had an Objective to study mesenchymal stem cells that could be isolated from healthy periodontal ligaments. They aimed to isolate & characterize human PDL stem cells From inflamed PDL tissue, & evaluate their regenerative potential.[17] Periodontal ligament is a connective tissue that connects the cementum to alveolar bone & its main function is to maintain the root of the tooth in the alveolar socket PPI Contains progenitor cells that can migrate & differentiate into either cementoblasts or osteoblasts in response to lesions[23] Gronthos et al demonstrated that CD1ob+ Ovine PDLSCS demonstrated the capacity to form adherent clonogenic clusters of Fibroblast-like cells when plated at low densities in vitro.[24] Techhawatlenawisal et al 2007 showed that isolated multipotent stem cells from rat periodontal ligament using neurosphere forming culture system & enzymatically dissociated PDL Cells were cultured in Serum-free basal medium containing EGF, BFGF & Free Floating spheres expressing nestin, GFAP and vementin were formed by 7 days of the

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Culture & data gathered indicated that PDL spheres Contain multipotent adult Stem cells capable of differentiating into both neural and mesodermal progeny. This was the first report of isolation of PDL-derived stem with primitive neural crest cell features. The neural crest cells t contain pluripotent cells that give rise to neurons and glial cells of the peripheral nervous system, endocrine cells, Connective tissue cells, and pigment cells during embryonic development. Stem cell-derived from neural crest may still reside in neural crest derivatives including the PDL. However, the pluripotency of PPL-derived Stem cells has not been investigated. Gray et al isolated & characterized PDLSC to assess their capability to differentiate into bone, cartilage & adipose tissue & Found human PDL tissue Recent studies have shown that mesenchymal Stem Cells obtained from PDL MSCs are multipotent cells that have similar features to bone marrow and dental pulp MSCs are capable of proliferation and producing different types of tissues such as bone & tooth associated tissues Human PDL MSCs expanded ex vivo Osteogesis, seeded in three-dimensional biocompatible Scaffolds (Fibrin sponge, bovine-derived substitutes) and examined using light, Scanning & transmission electron microscopy Morphology observations showed extensive growth of cellular biomass partially covering the scaffolds after 4 weeks of incubation in mineralization medium.[25]

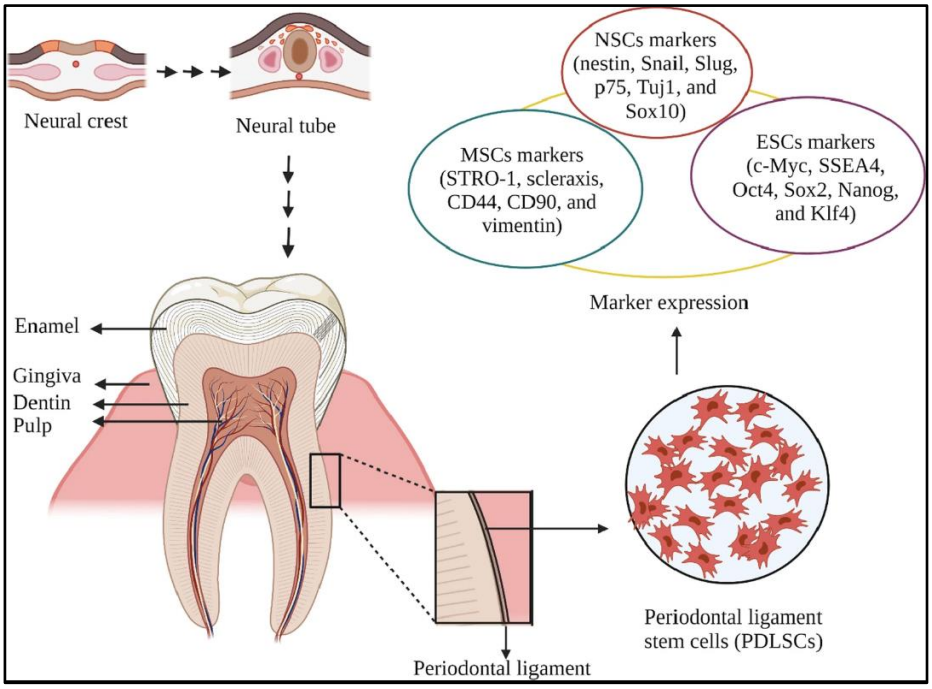

Figure 2: Schematic illustration of periodontal ligament stem cells characteristics.

Potential Regeneration Front

Implantation of periodontal ligament stem cells is emerging as a potential regenerative procedure. This review considers the evidence from animal models investigating the use of periodontal ligament stem cells for successful periodontal regeneration. In tissue engineering, appropriate exogenous cells are another important requirement. Exogenous cells are required when the precursor cell is imbedded or greatly has been diminished by previous surgery or concomitant disease. Therefore the required cells must be identified as the cells that can produce unaltered daughters and also has the ability to produce daughter cells that have different and more restricted properties.[2] Stem cell-based therapies are considered promising treatments for many clinical uses such as tooth regeneration, spinal cord injury, and so on. However, the ideal stem cell for stem cell-based therapy still remains to be elucidated.[19] soft dental tissues have been identified as an easily

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acceptable source of multipotent postnatal stem cells. Dental stem cells are mesenchymal stem cells capable of differentiating in to least three distinct cell lineages Osteo/odontogenic, adipogenic & neurogenic[20] Ding et al granulation tissue from tooth extraction socket[22] but the ideal stem cell is still questionable, including which may be a good stem cell-based therapy in a certain disease.

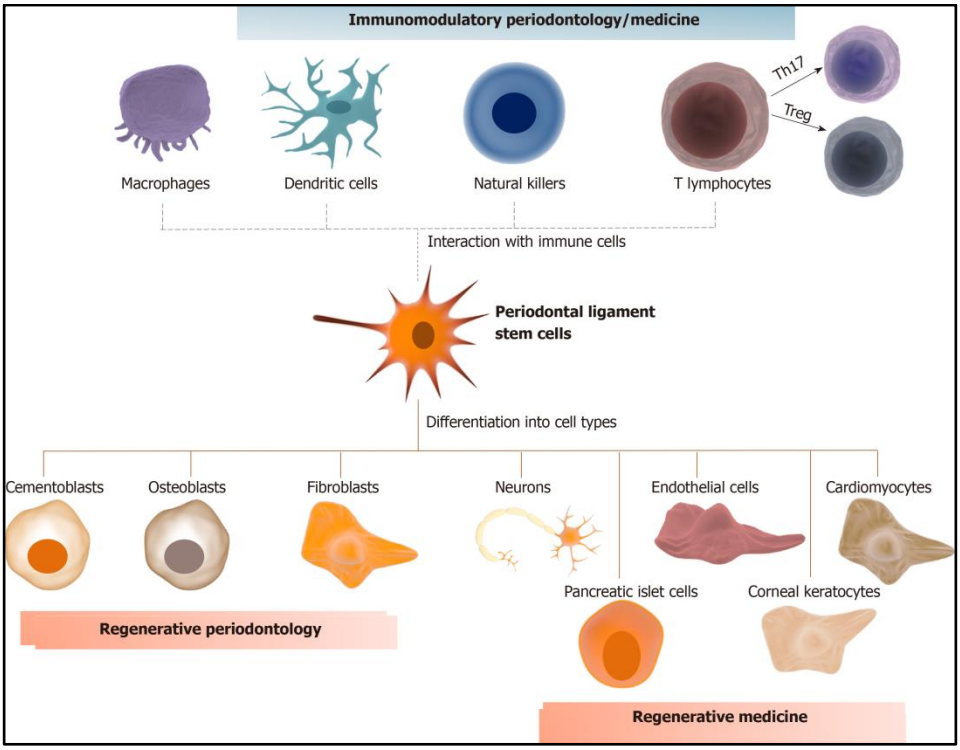

Figure 3: Potential regeneration front of PDL stem cells.

Conclusion

Stem cell-based dental tissue regeneration is a new and exciting field that has the potential to Transform the way that we practice dentistry. future will depend on understanding the biology of cells that will be used to regenerate tissues & its boundaries will be demarcated by in-depth knowledge of potential risks and likely benefits associated with each regenerative procedure. The field of stem cell-based regenerative dentistry is complex & multidisciplinary by nature Progress will depend on the Collaboration between clinicians and researchers from diverse fields (e.g. biomaterial Stem cell biology endodontics) working together towards the goal of developing biological approaches to regenerate dental & craniofacial tissue.

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