REVIEW ARTICLE

Periodontal ligament stem cell: An update
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Abstract
The periodontium is a complex of four tissues of which two are hard and rests are soft. The hard tissue being the alveolar bone and the cementum and soft tissue consists of the periodontal ligament and the gingiva. Periodontitis is multifactorial infectious disease of the supporting structures of the teeth, characterized by destruction of the bone and connective tissue. The ability to identify and manipulate stem cells has been the basis of tissue engineering based clinical therapies. This has been successfully applied in the field of regenerative medicine. However, its successful application in the field of dentistry for periodontal regeneration is still in its infancy. Novel techniques such as tissue engineering need to be developed to counter to difficulties associated with achieving predictable periodontal regeneration. However, stem cells can be a promising option in this regard. Thus, this review will explore the immense potential and the contemporary concept of stem cells; also it will highlight the recent developments in identification and clinically implication of these cells.

Introduction
The term stem cell is used to describe a wide variety of cell, which have the properties like ability to self-renew, generate large numbers of progeny and differentiate into multiple mature cell types.[1] Two categories of stem cells are-embryonic and adult, embryonic cells being totipotent and adult stem cells having restricted differentiation potential compared to former. Adult cells are further classified into two main categories depending on their origin and differentiation potential into hematopoietic and mesenchymal stem cell. It is the mesenchymal stem cells that are present in the periodontium and are required for regeneration of cementum, ligament and bone.

History
The concept that a periodontal ligament (PDL) retained a mixed population of cells way back in 1974 and 1976 when different authors like Roberts and Jee and McCulloch suggested that PDL cells can synthesize various tissues.[2] These cells appear localized around and adjacent to blood vessels in the PDL space, and McCulloch identified them as progenitor cells.[3] These cells exhibits the characteristic smaller size than the adjacent cells, high nuclear/cytoplasmic ratio and slow cell division.[4] Seo et al.[5] stated that the progenitor stem cell from the human PDL had the two main properties of mesenchymal stem cell, i.e., multipotency and self-renewal. Also, the mesenchymal stem cells other than those from PDL include dental pulp stem cell, stem cells from the apical papilla, and stem cells from human exfoliated deciduous teeth. Other alternative oral sources recently researched are inflamed adult human dental pulp and periodontitis-affected PDL tissue. Extraoral sites may be bone marrow mesenchymal stem cells and adipose-derived stem cells.[2]

More than any other tissue, the complexity of the periodontium along with the understanding that only certain components are capable of achieving regeneration, makes the identification of stem cells important, not only in the understanding of normal wound healing events but also in designing novel clinical techniques. Seo et al.[5] isolated the multipotent human PDL stem cells by single-colony selection and magnetic-activated cell sorting, and characterized according to their expression of the mesenchymal stem cell markers STRO-1 and CD 146/MUC18. For predictable and desired results after periodontal therapy, one must be able to repopulate the periodontal wound by cells that are capable of regeneration. The current and future researches for obtaining a better regeneration are based on selective repopulation of the wound area by the mesenchymal cells. Karring et al.[6] has demonstrated that PDL s only can result in periodontal regeneration and not...
the gingival connective tissue or bone. Thus, the identification, characterization and manipulation of appropriate cell within the PDL are one of the key factors for the new regenerative procedures in the near future.

Characteristics and Markers Expression

In recent studies, the adult PDL stem cells have been shown to express mesenchymal surface markers such as Stro-1 (best mesenchymal stem cell marker known till date), CD105 (Endoglin, SH2 antigen), CD146 (MUC 18), and CD166 (ALCAM, SB10 antigen), CD106 (3G5), CD-44, VCAM-1, alkaline phosphatase and have a multipotent capacity to differentiate into adipocyte, osteoblast-like, and cementoblast-like cells in vitro, and to form cementum/PDL-like tissues when transplanted into immune-compromised mice. As any single specific antigenic marker for mesenchymal/stromal cells is not available a combination of above stated markers are used to identify these cells. PDL contains about 24% CD105+ cell as concluded by different researchers. Surface markers Stro-1 and Oct-4 (embryonic stem cell marker expression) are the most important among the previously stated markers that governs the phenotypic expression of these PLD mesenchymal cells into different cell lineages. Silvério et al. in their in vitro study demonstrated that upon appropriate signaling mesenchymal progenitor cells can differentiate into adipogenic or osteogenic lineage. Osteogenic lineage induced by ascorbic acid-2-phosphate, dexamethasone, and b-glycerolphosphate produced mineral nodules and adipogenic lineage displayed lipid vacuoles. A strong correlation between the proportion of CD105+/CD166+ cells and osteogenic potential has been suggested by some authors, because the expression of these two surface markers declines during the osteogenic differentiation process in bone marrow derived mesenchymal stem cells. The capacity of PDL stem cells to differentiate into cementoblastic/osteoblastic lineage is regulated by the markers such as, alkaline phosphatase, bone sialoprotein, osteocalcin, transforming growth factor-b receptor Type I, scleraxis and a tendon transcription factor when cultured in vitro.

The percentage of mesenchymal stem cells residing in the PDL space is very minimal. Thus, makes it clinically difficult to obtain sufficient amount or number of these cells for therapeutic use. A clinical trial using this PDL mesenchymal stem cell in infrabony defects in patients has revealed significant better results in terms of regeneration. Thus suggests a safe and promising treatment.

The PDL stem cells from the younger individuals possess a higher ability to differentiate into adipocyte-like cells, rather than osteoblast-like cells, though the biological mechanisms that determine the regulation of lineage-specific differentiation of postnatal mesenchymal stem cells are still unclear. However, in general there is currently no consensus regarding the effect of donor age on postnatal mesenchymal stem cell function. Though some studies have found an age-related decrease in osteoblastic, but not adipogenic, differentiation in human bone marrow-derived mesenchymal stem cells.

Future trends

Despite of numerous clinical techniques for regeneration, including root surface conditioning, bone grafts, barrier membranes and various growth factors, have been utilized over the years. Unfortunately, these current therapeutic measures are unable to achieve predictable regeneration. Thus underscore the importance of restoring or providing the cells and microenvironment capable of initiating and promoting new periodontal tissue formation. From a biological perspective, in order for periodontal regeneration to occur, the availability of appropriate cell types, together with a favorable local environment promoting cell migration, adhesion, proliferation and differentiation, all need to be precisely coordinated both temporally and spatially.

Thus, the knowledge of the presence of PDL stem cell and their inherent potential to regenerate various desired tissues at site of destruction is of great importance. Use of tissue engineering strategies in this respect that explore the regenerative capacity of stem cells residing within the periodontium, grown in a three-dimensional construct and subsequently implanted into the defect may help to overcome many limitations with current regeneration modalities. The plausibility of a stem cell-based tissue engineering approach to achieving periodontal regeneration is supported by animal studies demonstrating that PDL cells cultured in vitro can be successfully reimplanted into periodontal defects in order to promote periodontal regeneration.

Conclusion

In the light of these findings further studies, including the researches on behavior of these cells in vivo, are required to determine their real role and potential to bring about regeneration in clinical conditions. Also in the near future, this novel approach via stem cells will give ways to treat various dental problems.

References

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