

Gingival mesenchymal stem cells

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Abstract

The human gingiva, characterized by its outstanding scarless wound healing properties, is a unique tissue and a pivotal component of the periodontal apparatus, investing and surrounding the teeth in their sockets in the alveolar bone. In the last year's gingival mesenchymal stem/progenitor cells (GMSCs), with promising regenerative and immunomodulatory properties, have been isolated and characterized from the gingival lamina propria. These cells, in contrast to other mesenchymal stem/progenitor cell (MSC) sources, are abundant, readily accessible and easily obtainable through minimally invasive cell isolation techniques. This short communication summarizes the current scientific evidence on GMSCs.

Keywords: Dental follicle progenitor cells, dental pulp stem cells, gingival mesenchymal stem cells, periodontal ligament stem cells, stem cell, stem cells from apical papilla, stem cells from exfoliated deciduous teeth

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INTRODUCTION

Tissue regeneration and regenerative medicine have emerged as a reality in regular day practice of medicine. Source for harvesting progenitor/regenerative/stem cells (SCs) has gained lot of attention in recent past. The oral cavity is also explored by researchers for the reserve cells with the potential to give rise to various differentiated tissue.

Human dental SCs have been isolated from various sources which include dental follicle progenitor cells (PCs), dental pulp SCs (DPSCs), SCs from human exfoliated deciduous teeth, periodontal ligament SCs (PDLSCs), SCs from apical papilla (SCAPs) and of late, from gingival connective tissue as gingival mesenchymal stem/progenitor cells (GMSCs).^[1]

The mesenchymal stem/progenitor cells (MSC) isolated from the gingival lamina propria have been termed variously researchers including GMSCs,^[2] gingival-tissue-derived SCs,^[3] gingival multipotent PCs and gingival margin-derived stem/PCs human oral mucosa SCs and oral mucosa lamina propria PCs.^[4,5]

Gingival connective tissue is embryonically contributed by neural crest ectomesenchyme, perifollicular mesenchyme, and partly the dental follicle proper. It has also been demonstrated that the periodontal ligament (PDL) and the dental follicle proper have a significant contribution to the cells of the lamina propria of the gingiva.^[5] Its embryonic origin and close to the teeth and PDL a known reservoir of MSCs makes the gingival lamina propria cells to stand apart from rest of oral mucosa and as the source of the MSCs. Harvested

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gingival tissue is de-epithelized, and the lamina propria is separated and collected. This lamina propria is minced and used to isolate the MSCs.^[5]

DIFFERENTIATION POTENTIAL

GMSCs have a higher rate of successive culture and proliferation compared with PDLSCs. GMSCs retain a potent capacity for multi-lineage differentiation, its related gene expression, and *in vivo* bone formation.^[6] GMSCs have demonstrated osteoblastic, adipocytic, chondrocytic, endothelial and neural directions when incubated in *in vitro* inductive culture conditions.^[5,6]

CHARACTERISTICS

GMSCs have been studied and have shown to fulfill the minimal standards accepted by the International Society for Cellular Therapy to define human MSCs phenotypically and functionally.^[5] GMSCs, exhibit several unique SC-like properties as MSCs derived from bone marrow (BM), and other postnatal tissues, these characteristics include *in vitro* proliferation as plastic adherent cells with fibroblast-like morphology, colony-forming ability, multipotent differentiation into different cell lineages, including mesodermal (adipocytes, osteocytes), endodermal and neuroectodermal progenies and expression of mesenchymal cell surface markers and SC-specific genes. It was also demonstrated that single colony-derived GMSCs possess *in vivo* self-renewal and differentiation capacities. In addition, compared with MSCs derived from several other adult dental tissues such as DPSCs and PDLSCs, GMSCs express a similar profile of cell surface molecules, a high proliferative rate and an increased population doubling. This makes GMSCs good source for several cell-based clinical applications.^[2]

CLINICAL APPLICATION

Considering its similarities in cultural and genetic characteristics with other MSCs, these cells can gain numerous applications in cell and regenerative therapies. Possible areas being aimed to include skin wound repair, tendon regeneration, bone defect regeneration, periodontal regeneration, peri-implantitis, antitumor effect, oral mucositis, collagen-induced arthritis and contact hypersensitivity.^[5]

UNIQUENESS OF GINGIVAL MSCS

Among the adult dental tissue, DPSCs, SCAP have minimal access. PDLSCs have been studied for decades. It is accepted fact that PDL is a reservoir of pluripotent cells

and they possess the capacity to form mineralized nodules, expression of bone/cementum-associated markers, and response to bone-inductive factors *in vitro*. It is also experimentally demonstrated that the PDLSCs have been promising in regenerating damaged bone, cementum, and functional periodontium. However, still the available tissue for autologous use in a clinical scenario is absolute minimal. Whereas gingiva being accessible and abundant can be envisaged to be an easily accessible and excellent source for the MSCs. Owing to their differentiation, potential and cultural characteristics similar or superior to that of PDLSCs, GMSCs are emerging to be a major source of MSCs in the field of regenerative medicine.

The transplantation of GMSCs could form connective tissue like structures, whereas transplantation of DPSCs and PDLSCs could generate dentin-like and cementum/PDL-like structures. This property of GMSCs makes it a superior or preferred type of MSCs over the other MSCs from the oral cavity when being used for extraoral cell-based clinical application and also intraoral bone regenerative procedures.^[2]

BM-MSCs have been considered as main source of MSC for cell therapy. Compared to BM-MSCs,^[3] have successfully demonstrated and concluded that GMSCs are easy to isolate, uniformly homogeneous, proliferate faster without any growth factor. They also state, these cells display stable phenotype, and maintain normal karyotype and telomerase activity in long-term cultures, and are not tumorigenic and large number of functionally competent clinical grade MSCs can be generated in short duration from a small biopsy of human gingiva for cell therapy.^[4,7-9]

CONCLUSION

Gingiva has fascinated researchers since long due to its unscarred healing capacity and regenerative potential. This can be owed to the hidden treasure gingiva reserves. The GMSCs, its unique origin, easy access to harvest and abundance make the GMSCs a unique source for MSCs for cell therapy. These cells have been proven superior in many ways not only in abundance and easy access compared to the oral SCs, but they have also shown superior characteristics compared to the preferred BM-MSCs. Envisaging the possible areas of application, GMSCs are a promising field for research as future of medicine is looking toward regenerative therapy.

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Conflicts of interest

There are no conflicts of interest.

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