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Dental Stem Cells: A Boon in Regenerative Medicine

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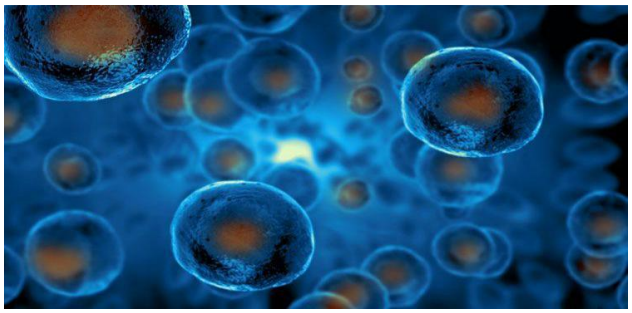
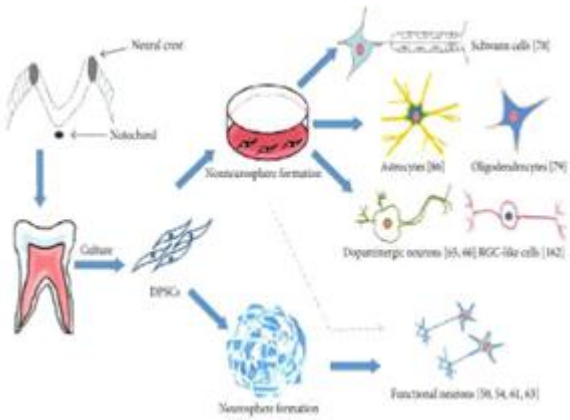
Abstract: ***Human dental pulp-derived stem cells have varied applications in regenerative medicine. Dental pulp stem cells (DPSCs) are considered to be neural crest cells. They are known to have higher regenerative potential than the bone marrow-derived mesenchymal stem cells. DPSCs have multipotency, immunomodulatory function, and self-renewal capacity. They are highly proliferative, clonogenic and are capable of differentiating into adipocytes, neural cells, odontoblasts, and various other cells. DPSCs are effective for various diseases, such as spinal cord injuries, Parkinson's disease, Alzheimer's disease, cerebral ischemia, myocardial infarction, muscular dystrophy, diabetes, liver diseases, eye diseases, immune diseases, and oral diseases.***

Keywords: dental stem cells, regenerative medicine, applications in medicine

1. Introduction

The dental pulp cells {DPSCs} develops from both cranial neural crest-derived mesenchymal stem cells (MSCs) and oral-derived epithelial stem cells in the early stages of embryogenesis. The first dental pulp-related stem cells were isolated from the third molar dental pulp by Gronthos et al. in 2000, it is also said that DPSCs could also be isolated from other dental pulps including human exfoliated deciduous teeth and supernumerary teeth. Human DPSCs have a higher reprogramming efficiency than human dermal fibroblasts because they have a rapid proliferation rate and endogenously express high levels of the reprogramming factors c-MYC and Klf4. DPSCs are potentially an important patient-specific cell source of iPSCs for clinical applications in regenerative medicine.

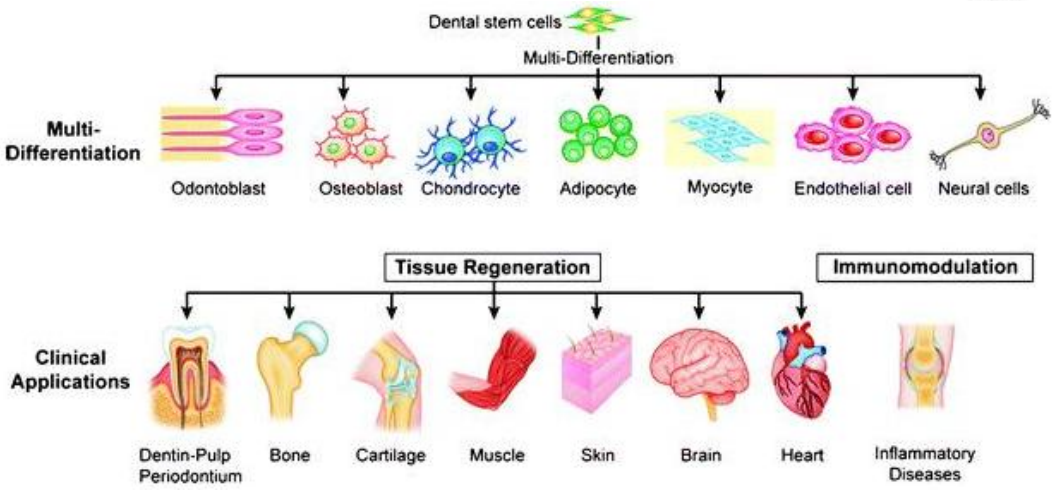




Properties of DPSCS

- Multipotency
- *High proliferation activity*
- *Self renewal capacity*
- *Colony-forming unit-fibroblasts forming ability*
- *Immunomodulation*

2. Applications



1) Dentin/Pulp Regeneration
Autologous transplantation of DPSCs is clinically tried to regenerate the dentin-pulp complex. Tubular dentin formation was observed when human pulp stem cells with scaffold (HA/tricalcium phosphate) were implanted in immunocompromised mice. Reparative dentin formation on amputated pulp was found when stem cells were combined with recombinant human bone morphogenetic protein 2 in experimental studies on animal models.

2) PDL Regeneration
Marei et al. in their experiment on goat was able to regenerate periodontal tissues around titanium implant using autologous bone marrow stem cells with the scaffold. Transplantation of PDL derived cells into animal models was shown to regenerate periodontal tissue.

3) Bone Regeneration
Positioning of a biocomplex of collagen sponge filled with DPSCs in the extracted site of mandibular third molar resulted in a higher rate of mineralization and cortical levels leading to complete regeneration. The samples also showed a well-organized and vascularized bone with a lamellar architecture surrounding the Haversian canal was observed. They also prove to be a useful tool for the treatment of degenerative diseases involving the maxilla and mandible.

4) Root Regeneration
SCAP has remarkable cell migration activity; which is considered to involve root growth in tooth development. when a root formed carrier containing SCAPs covered with PDLSC- immersed absorbable gelatin sponge is implanted into a socket of the mandibular bone of a swine, the root-form carrier is reconstructed with newly formed dentin/pulp-complex and is surrounded by regenerated PDL on de novo cementum.

5) CNS
DPSCs will lead to both regeneration of new neural precursor cells and their enhanced neuronal and glial differentiation. They will also lead to survival and maintenance of existing neural cells through secretion of trophic factors.

6) Stroke
Some in vivo studies have shown that transplantation of DPSCs into the ischemic areas of middle cerebral artery occlusion in Sprague-Dawley rats promoted locomotor functional recovery and decreased infarct areas by their differentiation into dopaminergic (DA) neurons and secretion of neurotrophic factors.

7) Parkinson

Intrathecal transplantation of DPSCs into the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) induced old-aged mouse model of PD, promoted recovery of behavioral deficits, restored DA functions, and attenuated MPTP-induced damage by reducing the secretion of proinflammatory factors such as IL-1α, IL-1β, IL6, IL8, and tumor necrosis factor (TNF)-α and by upregulating the expression levels of anti- inflammatory factors such as IL2, IL4, and TNF-β.

8) Peripheral Nerve Injury
Studies suggest that DPSC-embedded biomaterial nerve conduits such as polylactic glycolic acid tubes have the ability to promote regeneration of injured facial nerve and to improve functional recovery comparable to that of autografts. Collagen conduits loaded with Schwann-like cells induced from DPSCs in vitro have facilitated repair and regeneration of 15 mm sciatic nerve defect.

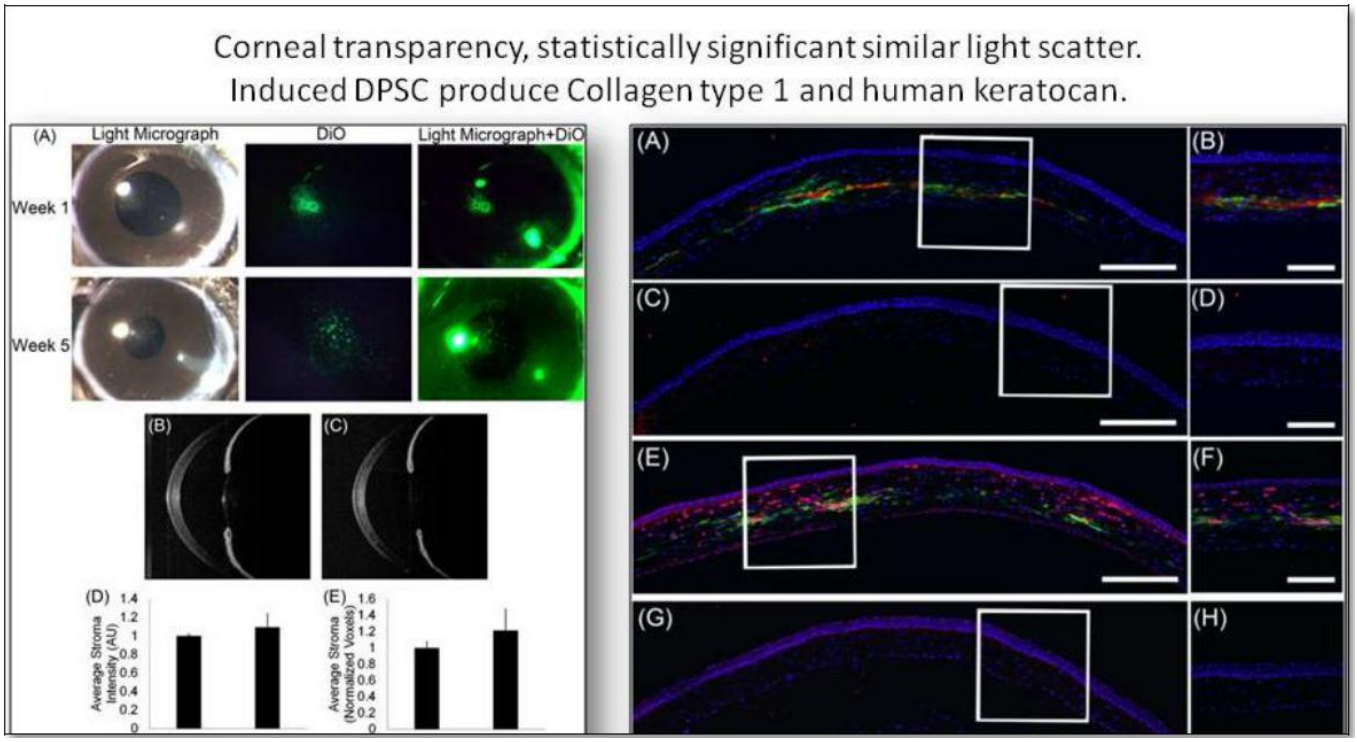
9) Bone Diseases
Systemic transplantation of mesenchymal stem cells could ameliorate bone loss and autoimmune disorders in a MRL/lpr mouse SLE mode by suppression of Interleukin-17 and maintaining a regular positive bone metabolism.

10) Liver Diseases
DPSCs prevented the progression of liver fibrosis in the liver of CCl4-treated rats and contributed to the restoration of liver function. Engraftment of DPSCs and SHED morphologically and functionally ameliorate acute and chronic injury of livers in CCl4-treated rats.

11) Muscular
DPSCs can differentiate into dystrophin-producing multinucleated muscle cells and can be utilized in disorders such as muscular dystrophy, wherein, the body is unable to produce dystrophin. Utilization of myogenic progenitor cells derived from dental pulp produced more dystrophin as compared to the heterogeneously present stem cells proving to be a potential alternative for stem cell therapy in muscular dystrophy patients.

12) Diabetes
Diabetes is a chronic degenerative disease. One of the treatments for diabetes includes transplantation of pancreatic islet cells. Chen et al. demonstrated that insulin-producing cells can be derived from monoclonal and polyclonal DPSCs. Govindasamy et al. demonstrated that DPSCs have the capacity to differentiate into islet-like aggregates.

13) Corneal Stoma Transplantation
DPSCs are a potential alternative to cadaveric tissue grafts. Autologous stem cells that are capable of remodeling the corneal tissue into the proper structure (without scarring) could bypass the limitation of current treatments Study findings demonstrated that DPSCs have the capacity to create engineered corneal stromal-like constructs with an organized matrix similar to that of native corneal tissue. Also, data showed that human DPSCs have the ability to maintain their keratocyte phenotype after in vivo implantation into mouse corneas, indicating that the DPSCs secreted the appropriate matrix in the in vivo corneal stromal microenvironment without triggering rejection. All of these properties indicate that human DPSCs have potential use in regenerative corneal therapies.



3. Conclusion

DPSCs are indeed a major asset in regenerative medicine. They can be obtained safely and easily without significant morbidity or ethical concerns; however there are some flaws in understanding the mechanisms underlying the therapeutic effects of DPSCs which requires more studies. The future treatment modality will be regenerative based; however, further studies are needed to test the various other applications of DPSCs with long-term follow-up.

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