Applications of Dental tissue-derived Stem cells in systemic conditions

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Abstract

Ever since their discovery, the aim of stem cell research has been to develop therapeutic solutions to various disease conditions. Earlier challenged, it is now established that adult stem cells in the human body are capable of differentiating into cell/tissue types other than their source of origin and lineage; therefore, show promise in regenerative medicine research and cell-based therapy. These cells can be isolated from deciduous teeth, apical papilla of the tooth, dental pulp, as well as periodontal ligament. Stem cells isolated from various oral/dental tissues show similar or higher proliferation and differentiation potentials when compared to other systemically derived stem cells. This communication highlights the potential application of dental stem cells in systemic conditions.

Key Words: Dental stem cell, Mesenchymal stem cell, Systemic disease.

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Alexander Maksimov, a Russian histologist, proposed the term 'stem cell' in 1868.[1] However, it was the seminal works of Friedenstein et al. between the 1960s and 70s that laid the groundwork for mesenchymal stem and stromal cells.[2] These cells were considered 'building blocks' of the body and were responsible for homeostasis. By definition, stem cell is one that has the ability to continuously divide to either replicate itself (self-renewing), or produce specialized cells than can differentiate into various other types of cells or tissues (multilineage differentiation).[3]

Research is currently booming in the field of regenerative medicine and cell-based therapy. Adult stem cells that were earlier thought to be present only in specific sites such as bone marrow, adipose tissue etc., are now being isolated from various other tissues such as skin, hair, muscles, as well as oral and dental structures among others. Dental stem cells can be isolated from different parts of teeth and include those derived from exfoliated deciduous teeth, apical papilla, tooth germs, and periodontal ligament.

Adult stem cells (ASC) can be further divided into hematopoietic and mesenchymal stem cells (MSC) depending on the tissue of origin. ASCs were assumed to have restricted proliferative ability, considering that these were cells that are already differentiated for tissue/organ-specific functions. Contradicting the earlier reports, recent studies have suggested that, in addition to generating the derivatives of their specific system, hematopoietic and mesenchymal stem cells can also give rise to muscle and neuron-like cells in the brain among others.[4,5]

Self-renewal, multipotency, and immunosuppressive functions of MSCs have been extensively investigated for therapeutic applications. It is known that MSCs isolated from dental and orofacial tissues possess the ability to differentiate into odontoblasts, cementoblasts, and periodontal ligament cells. However, recent studies have also shown that dental stem cells have the capacity to generate adipocytes, osteoblasts, cartilage, smooth and skeletal muscle cells.[6,7] Moreover, dental stem cells are also capable of switching lineage to form ectodermal tissues (such as neurons or epithelial-like stem cells) and endodermal lineage (such as endothelial cells, hepatocytes, and insulin-producing cells).[8] Dental pulp stem cells (DPSC) are presumed to be derived from migrating neural crest cells; therefore, express neuronal markers such as nestin and βIII tubulin.[9]

An interesting aspect is the fact that stem cells from human exfoliated deciduous teeth (SHED) represent a population of multipotent stem cells that are perhaps more immature than previously examined postnatal stromal stem-cell populations. Miura et al. reported that SHED were able to induce bone formation, generate dentin, and survive in

mouse brain along with expression of neural markers.[7] SHEDs are considered to have higher proliferation rate and increased cell-population doublings. As deciduous teeth exfoliate naturally, there is potential for these stem cells to be preserved for later use in neurological conditions such as stroke, Parkinson's disease, multiple sclerosis etc.

Similarly, stem cells isolated from the dental pulp are known to produce neurotrophic factors and rescue motor neurons after spinal cord injury.[10] In the aforementioned study, by Nosrat et al., it was observed that co-culturing DPSCs with trigeminal neurons promoted survival and a specific and elaborate neurite outgrowth pattern, whereas skin fibroblasts did not provide a similar support.[10] Dental pulp stem cells have shown positivity for mesenchymal lineage markers (CD13, CD29, CD44, CD73, and CD105) but are negative for a monocytic marker (CD14), and hematopoietic lineage markers (CD34, and CD45). This makes them attractive target-specific candidates in cases of cerebral ischemia, muscular dystrophy, liver disease, cardiovascular conditions, diabetes, among others.[11,12]

Studies have also shown that dental pulp tissue becomes innervated when transplanted into the anterior chamber of the eye, and upregulates the nerve fiber density of the irises.[13] Recent studies have explored the potential of DPSC-mediated repair of ocular diseases, such as corneal blindness and glaucoma. It has been reported that DPSCs share similar characteristics with limbal stem cells and have the capability to differentiate into keratocytes.[14]

DPSCs and SHEDs have also been found to possess immunomodulatory functions, comparable to or even higher than those of bone marrow derived MSCs.[15] Therefore, these cells may be beneficial in cell-based therapies for a variety of immune and inflammation-related diseases. DPSCs have been shown to more strongly inhibit T-cell responses than bone marrow MSCs. DPSCs also inhibit allogeneic immune responses by release of TGF-β through stimulation of T lymphocytes. Similarly, SHEDs also significantly inhibit Th 17 cells compared to bone marrow MSCs. In animal experiments, SHEDs have been demonstrated to effectively reverse systemic lupus erythematosus.[15,16]

Plasticity of stem cells is currently being investigated widely. The capability of cells from dental tissues to induce regeneration of neural, muscle, and other tissues widens horizons in cell-based therapy.[17] DPSCs and SHED display an MSC-like character, including the capacity for self-renewal and multilineage differentiation. Owing to their accessibility, ease of isolation, minimally invasive procedure, and limited ethical concerns, dental stem cells can be considered an alternative to other systemic sources of stem cells.

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Conflict of Interest

Nil

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