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Biological characteristics of Stem Cells from Human Exfoliated Deciduous Teeth (SHEDs) and its therapeutic applications in regenerative medicine

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Abstract

Stem cells isolated from human exfoliated deciduous teeth (SHEDs) are multipotent mesenchymal stem cells that are isolated from dental pulp tissues. These cells have a high proliferative capacity, multipotential ability, immunomodulatory function, and minimal risk of oncogenesis. Recent studies have shown that SHEDs are a feasible cell source for cell therapy and regenerative medicine.

Keywords: mesenchymal stem cells, SHEDs, regenerative medicine, dental pulp

Statement

Mesenchymal stem cells (MSCs) are multipotent stem cells, which can be isolated from different tissues and characterized by self-renewal and multilineage differentiation into a variety of mature cells (1, 2). According to the International Society for Cellular Therapy, three criteria have been proposed to define MSCs, which are: adherence to tissue culture flasks in standard culture conditions, expression of specific surface antigens (such as CD105, CD73, and

CD90), additionally, lack expression of some surface antigens (such as CD45, CD34, and CD14 or CD11b, CD79a or CD19 and HLA class II) that measured by flow cytometry and differentiation potential into osteoblasts, adipocytes, and chondroblasts under standard differentiating conditions (3).

So far, several populations of dental MSCs have been identified from teeth and related supporting tissues, including dental pulp stem cells (DPSCs), periodontal ligament stem cells (PDLSCs), dental follicle precursor cells (DFPCs), stem cells from the apical papilla (SCAP), gingiva-derived mesenchymal stem cells (GMSCs) and SHEDs (4). Among them, DPSCs and SHEDs are interesting for their easy accessibility from teeth, which are considered as disposable during the management of occlusion (4). Although DPSCs and SHEDs have similarities in phenotypic profiles and conventional MSC markers, they also have differences due to the separation of dental pulp tissues from different age groups; For example, SHEDs have higher expression of embryonic markers and better differentiation capability to osteogenesis and adipogenesis than DPSCs (4). SHEDs are multipotent stem cells with fibroblastic features, high proliferation capacity, and clonogenic abilities that capable of differentiating into neural cells, adipocytes, odontoblasts, and several types of cells (5, 6).

Masako Miura et al, for the first time isolated SHEDs from the remnant crown tissue of human exfoliated deciduous incisors of 7- to 8-year-old children and used these cells for dental pulp tissue regeneration (5). They showed that SHEDs were able to survive and proliferate in immunocompromised mice and form dentin-like tissues. They also suggest the neural developmental potential of SHED by injecting them into the dentate gyrus of the hippocampus of mice.

A study by Yamaza et al. Showed that SHEDs can modulate regulatory T cells (Tregs) and have a better inhibitory effect in reducing interleukin-17 levels than bone marrow mesenchymal stem cells (BMMSCs) (7). They found that SHED transplantation can effectively reverse systemic lupus erythematosus (SLE)-associated symptoms in MRL/lpr mice. Therefore, they suggest that SHEDs are feasible MSC sources for treating immune disorders like SLE.

Tomoaki Taguchi et al transplanted SHEDs to the mouse model of liver fibrosis for evaluation of the capabilities of homing, hepatocyte differentiation, and therapeutic efficacy of these cells and their results showed that SHEDs had an anti-fibrotic effect on mouse liver (2).

Because SHEDs are able to differentiate into islet-like cell aggregates (ICAs), they proposed as an alternative towards cell replacement therapy for diabetes (3, 8). Takako Izumoto-Akita et al injected mouse pancreatic β-cell line MIN6 with SHED conditioned medium into mice and found that insulin secretion increased in a glucose concentration-dependent manner (9).

Therefore, due to the high potential of SHEDs in the field of tissue engineering and regenerative medicine, they can be used to treat many diseases, including neural diseases (5), SLE (7), liver diseases (2), diabetes (8, 9), hypoxic-ischemic brain injury (10), and ulcerative colitis (11) in the future.

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