

The Use of Dental Stem Cell Therapy in the Treatment of Gum Deterioration

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Abstract

The study of dental mesenchymal stem cells, also known as DMSC, has been very beneficial in gum repair and preventing gum deterioration. Dental mesenchymal stem cells contribute to tooth growth and repair. Due to their accessibility, mesenchymal stem cells provide a favorable model system for studying stem cell function and properties. When monitoring oral health, the study of dental mesenchymal stem cell research is beneficial. Due to tooth accessibility, researchers are given a valuable opportunity to test stem-cell-based treatments for dental disorders. Within the oral cavity, there are many different types of fibroblasts that assist with the formation of the connective tissue that provides support within the mouth. When there is decay of those fibroblast cells, unique dental mesenchymal stem cells are isolated and used to reverse any deterioration or decay. A major stem cell that allows for a healthy oral cavity are human gingival mesenchymal stem cells, also known as GMSCs. GMSCs are essential due to their high proliferation and differentiation rate. By differentiating into cell lineages, GMSCs can be used for regenerative therapy within the oral cavity, specifically the gums.

Keywords

Dental mesenchymal stem cells; Gum deterioration; Periodontitis; Gingiva mesenchymal stem cells; Regeneration

Introduction

The human oral cavity contains several different habitats, including teeth, gingival sulcus, tongue, hard and soft palates, and tonsils; it acts as a tube that connects the outside and the digestive tract and respiratory tract of the human body, providing the appropriate space for the colonization of microorganisms [1]. Proper knowledge of oral diseases is crucial in medical practice for many reasons. Some include the fact that periodontal disease is associated with multiple systemic conditions of medical interest, and many systemic diseases have oral manifestations, which means that the anatomy of the oral cavity needs to be studied and understood [2]. In addition, there are many drugs that are associated with oral adverse drug reactions. While the oral cavity is a major component of the human body, the lack of detection by physicians can allow health issues to go unnoticed and worsen [3].

A major component within the oral cavity is the gingiva. The gingiva, also known as gums, is the tissue that surrounds and protects the teeth and underlying bone [4]. It functions as a protective barrier by forming a seal around the underlying bone preventing infection. The soft, pink tissue is rich in nerves and blood vessels, acting as a cushion [5]. Good oral hygiene keeps this seal around the bone intact, while poor oral hygiene can result in damage to the gingiva, leading to gingivitis. Poor oral hygiene leads to the buildup of bacterial plaque, which cause inflammation and the onset of gingivitis [6]. Gum disease, resulting from poor oral hygiene, is a progressive disorder that starts off as mild gingivitis. Mild gingivitis occurs when the bacterial plaque, also known as biofilm, builds up along and under the gumline [7]. If the plaque is left untreated, it will begin to produce toxins that irritate the gums and cause the seal between the gingiva and the tooth to become loose, which may lead to infection, and tooth breakdown, also known as periodontitis [8]. The bacteria that is found within the plaque under the gumline can pose a health threat to the whole body by entering the bloodstream; it can cause inflammation in arteries, which would increase the risk of stroke and heart attack. At the same time, the arteries are inflamed, the proliferation of bacteria in the body can suppress the immune system, and the immune system can weaken [8]. The formation of plaque affects the structure of the gingiva once it reaches a severe point, which is why it is essential to have good dental hygiene (Figure 1).



Figure 1: Inflamed gingiva with plaque build-up along the gum line.

As seen below in (Figure 2), the structure of the gingiva is quite complex; it is composed of an outer epithelium and an inner network of connective tissue [9]. The gingival tissue runs from the mucogingival line, which marks the boundary with the non-keratinized buccal mucosa and covers the coronal aspect of the alveolar process [9]. On the palatal aspect, the mucogingival line is absent, and the gingiva is

continuous with the keratinized, non-mobile palatal mucosa [9]. In simpler terms, the outer epithelial layer is keratinized, which allows for the formation of a protective layer around the tooth. The gingiva ends at the cervix of each tooth, surrounds it, and is attached to it by a ring of specialized epithelial tissue, known as the junctional epithelium [9]. The junctional epithelium functions to attach the connective tissue to the tooth surface by forming a 2-3 mm wide band around the tooth [10]. The junctional epithelium complex is continuously renewed throughout life and serves an essential role in preventing gingivitis. Even when the gingiva does not appear inflamed, the junctional epithelium has many polymorphonuclear leukocytes that move toward the sulcus and form an important part of the defense mechanism [10].

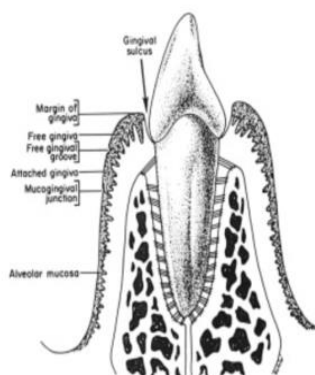


Figure 2: Structure of the gingiva, including the different layers of gum tissue.

Outside of the junctional epithelium layer, the outer keratinized layer plays a major role in tooth health. If the outer layer gets damaged, and the tooth is unprotected, there is a greater risk for other health issues. The inner gingival connective tissue contains gingival fibroblasts, embryonic-like cells with the capacity for self-renewal and clonogenicity [9]. Gingival fibroblasts are extremely significant due to their multipotent potential; they can differentiate into multiple cell types and generate induced pluripotent stem cells. Dental pulp fibroblasts are the most abundant cell type in the dental pulp [11]. When damage arises to the gingiva, using stem cells can be crucial for repair. Stem cells can be defined as clonogenic, self-renewing, progenitor cells that can generate one or more specialized cell types [12]. These cells are the building blocks of all organs, tissues, blood, and the immune system, which means they play a pivotal role in gingiva regeneration [13]. In many tissues, stem cells serve as an internal repair system, constantly regenerating to replace lost or damaged cells over a person's lifespan. In the case of gingiva, stem cells can be used to replace the fibroblast cells to make the gums strong and healthy. Specifically, in the oral cavity, there is a range of stem cells that each have their own role in keeping the mouth in a healthy state [13]. Some stem cells can self-renew and exhibit multilineage differentiation. Oral stem cells can be classified as mesenchymal stem cells, also referred to as MSCs [14]. MSCs can be isolated from a variety of tissues, such as umbilical cord tissue, endometrial polyps, menses blood, bone marrow, adipose tissue, etc [15]. The ability to isolate MSCs from these tissues is based on the ease of harvest and the quantity that can be obtained for experimental and clinical use. The multipotent properties of MSCs make them a good choice for clinical applications, especially in the dental setting. Currently, there are eight known dental mesenchymal stem cells that can be used in the dental clinical setting, which each serve a purpose in oral health [16]. The eight known dental mesenchymal stem cells include:

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1. Dental Pulp Stem Cells (DPSCs) originating from the dental pulp [17].
2. Stem Cells from Human Exfoliated Deciduous teeth (SHEDs) originate from the tooth pulp cavity [18].
3. Periodontal Ligament Stem Cells (PDLSCs) originate from the periodontal tissue [19].
4. Dental Follicle Stem Cells (DFSCs) originating from the tooth germ [20].
5. Stem Cells from the Apical Papilla (SCAPs) originating in the upper dental papilla [21].
6. Alveolar Bone Derived MSCs (ABMSCs) originating in maxilla and mandible bone [22].
7. Tooth Germ Progenitor Cells (TGPCs) originating in 3rd molars [23].
8. Gingival MSCs (GMSCs) originating in the gingiva [24].

Each of these eight stem cells is classified by their location and tissue origin. While discussing the gingiva, the stem cells that are most observed include, the dental pulp stem cells (DPSCs), which originate from the dental pulp, the dental follicle stem cells (DFSCs), which originate from the tooth germ, and finally, the gingival mesenchymal stem cells (GMSCs), which originate in the gingiva [25]. Each of these three dental mesenchymal stem cells can be used to treat diseases that occur within, and around the gingiva due to oxidative stress and chronic inflammation [14]. For example, periodontitis, also known as gum disease, is a serious gum infection that damages the soft tissue around teeth. Without treatment, periodontitis can destroy the bone that supports the teeth; this may lead to gum deterioration and, eventually, tooth loss. Using MSCs, the gingiva can be restored and repaired, which can prevent full deterioration [16].

Although periodontitis is a major factor that causes gum deterioration, there are many factors that may lead to gum and tooth decay that are uncontrollable, regardless of someone's oral hygiene [2]. The main factors that determine immune fitness are the same factors that determine their response to the biofilm [26]. They include genetic and epigenetic factors, lifestyle factors, such as smoking, diet, and psychosocial conditions, comorbidities, such as diabetes, and local and dental factors, as well as randomly determined factors. Classical twin studies have demonstrated the extent of genetic and environmental contributions to the susceptibility to periodontal diseases. The studies have suggested that the heritability of periodontal disease is generally intermediate. Environmental risk factors, including age, gender, weight, smoking, and socio-economic status, are all considered to be important risk factors. The "environmental factors" also have genetic components [2].

According to the Centers for Disease Control and Prevention, 47.2% of adults aged 30 years and older have some form of periodontal disease [27]. In addition, periodontal disease increases with age, 70.1% of adults 65 years and older have periodontal disease, also known as gum disease. Recent studies have suggested that periodontal disease is more common in men than women; there is a 54.6% chance that men will experience gum deterioration, while 38.4% chance women will have gum disease. It was also found that 65.4% of individuals living below the federal poverty line experience gum disease, 66.9% are individuals who have less than a high school education, and 64.2% are current smokers [27]. This data suggests that periodontal disease is highly influenced by the environment and socio-economic status.

Although gum deterioration is prevalent in much of the population, there are ways to remove and limit plaque buildup. An effective way to remove plaque and maintain healthy teeth and gums is to brush and

floss twice per day. Dental professionals can also assist by performing scaling and plaque removal, gum surgery, and stem cell therapy.

Discussion

The human gingiva, characterized by its scarless wound-healing properties, is a unique tissue and a major component of the periodontal apparatus that surrounds the teeth in their sockets in the alveolar bone [24]. Within the gingiva, there are very specific fibroblast cells that help keep the gums strong and healthy [24]. The main task of fibroblast cells is to maintain the health and strength of the gums, which can be diminished due to illness, time, or other factors [25]. Within the gums, there are different types of fibroblast cells that each perform a task to prevent deterioration. Human Gingival Fibroblasts (HGFs) are the most abundant cells in gingival connective tissue, while Human Periodontal Ligament Fibroblasts (HPLFs) are located between the teeth and the alveolar bone [19]. Both HGFs and HPLFs are crucial for maintaining the homeostasis of connective tissue through the secretion and degradation of components of the extracellular matrix [28]. When HGFs begin to lose regulation, there can be inflammation and, eventually, degeneration of the gingiva [25]. When the gingiva begins to go through degeneration, stem cells are crucial.

The purpose of stem cells, which are the basic cells that make up the tissues and organs in the body, is to provide regeneration and repair in damaged tissues or organs by transforming themselves into the respective cell of that tissue or organ [29]. Stem cells are crucial because they can divide indefinitely. Stem cells provide healing and regeneration in the region that they are directed to without causing genetic errors, which is very important [29]. Stem cell therapy in gum deterioration is used to replace fibroblast cells. Gingival fibroblasts are of particular interest due to their ability to differentiate into multiple cell types and generate induced pluripotent stem cells, also known as iPSCs [24]. Gingival mesenchymal stem cells give promising regenerative properties that can be isolated and characterized from the gingival lamina propria [24]. Gingival mesenchymal stem cells, also known as GMSCs, are abundant, readily accessible, and easily obtainable through cell isolation techniques.

In the process of gum treatment, the fibroblast cells that are specific to the gums are taken from a small piece of tissue in gum overgrowth. The process of stem cell treatment with restoration can be very beneficial, but also very time-consuming. The dentist removes 3-4 mm tissue from the gums and sends it to a stem cell laboratory approved by the Ministry of Health. Under laboratory conditions, fibroblast cells that make up the gums are grown for 45 days. The cells are generated and injected back into the gums every 30 days [30]. The cells then continue to multiply in the gingiva. At the same time the cells are multiplying, they are being repaired. This allows for gum deterioration to be slowed down, and even prevented. In the first state of stem cell restoration, the removal of tissue to be sent for stem cell generation takes a maximum of 15 minutes. It then usually takes around 30-45 days for the cells to grow in the stem cell laboratory, which would make the first application of the stem cells 3-45 days after the removal of tissue, and the other 2 applications are about 1 month apart. Each application session takes about 1 hour, and the gums are usually fully recovered about 8-12 months later [30]. Immediately after the application of the mesenchymal stem cells, the process of proliferation and activation of the cells in the gums begins. Although this can be a very long and tedious process, it is very critical to maintain gum

health to support a healthy body.

Stem cell treatment for gum deterioration causes very little risk since the cells are taken from the individual's own body and returned to that same individual without any additives in the treatment [31]. This practice reduces complications related to incompatibility or allergic reactions. Although it can be a long process, it is a very safe and easy application that can benefit an individual and provide a healthy oral cavity.

Conclusion

Mesenchymal stem cells derived from dental tissue have been beneficial in not only reversing the effects of gum deterioration but also in preventing deterioration in other areas of the oral cavity. The health of the oral cavity is significant due to its impact on the health of the entire body; therefore, monitoring gum deterioration and tooth health is of extreme importance. Gingival mesenchymal cells have led to many scientific advancements by making it possible for dentists to use a patient's own gum tissue to repair deterioration and prevent further tooth decay. The field of dentistry is continuing to advance as new technology and procedures become available. Through expanding research and knowledge of the oral cavity, specifically on the use of stem cells, the field of regenerative therapy will continue to excel.

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