

Regenerative Dentistry and Rehabilitating the Oral Cavity

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Abstract

Stem cells, harvested bone, dentin derivatives, and scaffolds have become key in regenerative dentistry. They each are used in different ways to renew and repair damaged tissue in the oral cavity. Stem cells or mesenchymal cell's ability to differentiate into diverse lineages help in the wound healing process and with bone reconstruction. Not only stem cells are used for bone remodeling, but harvested bone and dentin derivatives are being used to diminish alveolar bone resorption and aid as a new source of grafting material. Moreover, different types of scaffolds, such as platelet rich plasma scaffolds, platelet fibrin scaffolds, silk scaffolds, and polymer scaffolds are being tested in order to reach newly formed and fully functional tissues. A study performed by Ulusoy et al., (2019) using the previously mentioned scaffolds resulted in successful regeneration of root surfaces in the primary teeth involved in this experiment. In spite of all the research that has been completed, there are still some doubts about these types of techniques used to regenerate the oral health tissue. Thereby, it would be great if the dental field would continue to research all these new mechanisms that can be very helpful for future dentists as well as the patients in need.

Keywords: scaffold, stem cells, regenerative dentistry, alveolar bone, platelet

Regenerative dentistry is a newly studied field of regenerative medicine that utilizes tissue engineering techniques with the primary goal of rehabilitating the dental tissues of the oral cavity (Tran et al., 2019). Some of the many different types of regenerative dentistry that are being researched include the application of stems cells, scaffolds, and the use of harvested bone. The purpose of this review is to broaden the knowledge of the public and dental professionals on this subject and possibly to encourage its implementation into future procedures. Research and experiments conducted using these regenerative dentistry methods have shown great potential and bring new and alternative treatment options to the dental field.

Stem cells and their role in dentistry

Stem cells have become a major player regarding regenerative dentistry. Stem cells or mesenchymal stem cells (MSCs) exist in almost all human tissues, involving dental tissues, periodontal ligament, apical papilla, and other soft and hard tissues of the oral cavity (Tatullo, 2018). They have the ability to distinguish into different lineages that can stimulate the renewal of injured tissues (Tatullo, 2018). These mesenchymal stem cells are able to differentiate due to the consistency of the extracellular matrix surroundings which provides mechanical signal to regrow (Tatullo et al., 2020). Corresponding to Jinhee et al., (2021) the primary focus of this differentiation is based on the various microenvironments that the stem cells are being cultured, which is referred to as a stem cell niche. According to Tatullo et al., (2020) for the last decade, mesenchymal stem cells have been used to repair dental and bone tissue diseases. Furthermore, stem cells niches are thought to be able to play an important role in the stimulation of those mesenchymal stem cells that are responsible for wound healing and repair, and the circulating stem cells in charge of targeting specific sites in guidance of tissue and organ regeneration (Tatullo, 2018). Other experiments being conducted regarding stem cell niches focus on the

subject of organoids which are complex heterogeneous cell bases composed to resemble an organ (Tatullo, 2018). These organoids play a role in the creation of in-vitro functional salivary glands and can promote the migration of circulating stem cells to the target tissue and sustain the growth of a functional complex tissue (Tatullo, 2018). Moreover, migration and engraftment of mesenchymal stem cells are crucial in bone reconstruction, where these MSCs are obtained from the bone marrow (Tatullo et al., 2020). Not only have mesenchymal stem cells studies been conducted, but adipose stem cells findings have taken place in respect to the treatment of jaw defects after a certain period of time apart from the graft implantation (Tatullo et al., 2020).

Use of harvested bone and dentin derivatives in regenerative dentistry

The human jawbone is a distinctive bone tissue due to its histological, anatomical, and physiological properties (Bernardi et al., 2020). Because of its unique composition, harvested bone and dentin derivatives are being used in regenerative dentistry to minimize alveolar resorption, vertical ridge augmentation, and sinus lifts interventions (Bernardi et al., 2020). A bone tissue harvested from the same human being is called autologous bone (Bernardi et al., 2020). This type of bone has all the properties needed for facial bone regeneration and/or reconstruction (Bernardi et al., 2020). The sites that autologous bone can be extracted includes the iliac crest, ramus of the mandible, tibial bone, chin symphysis, and maxillary tuberosity (Bernardi et al., 2020). Autologous bone provides support for osteoconduction, a certain amount of vital osteoblast, and vascular supply required for osteoinduction (Bernardi et al., 2020). With all these essential characteristics, autologous bone is able to play a crucial role when considering a material for bone regenerative procedures pertaining to the dental field (Bernardi et al., 2020). Besides autologous bone, dentin derivatives are crucial for regenerative dentistry as well (Bernardi et al., 2020). Seventy percent minerals, 20% of organic matrix, and 10% of water is the

biological make up of dentin which makes it a valid grafting material (Bernardi et al., 2020). Additionally, dentists are more prone to use dentin derivatives than the other regenerative materials because it is more readily accessible (Bernardi et al., 2020).

Postnatal dental stem cells and deciduous teeth stem cells

According to Yelick & Sharpe, (2019) studies conducted about postnatal dental stem cells first appeared in the 2000s. This revolutionary discovery was the first to show cloning and a quick proliferation of cells harvested from an adult human pulp (Yelick & Sharpe, 2019). These cells could form dentin when implanted in vivo with the ability to generate ectopic dentin and reside in the perivascular niche of the dental pulp, however, they could not differentiate into adipocytes (Yelick & Sharpe, 2019). Furthermore, they could be distinguished from bone marrow stroma cells due to their densely calcified nodule (Yelick & Sharpe, 2019). Other studies conducted were the extraction of the dental pulp from human exfoliated deciduous teeth (SHED) (Yelick & Sharpe, 2019). Deciduous teeth became a great tool as a source of bioengineering and tooth replacement therapy (Yelick & Sharpe, 2019). SHED have played an important role in regenerative dentistry since they can differentiate into various cell types including natural cells and odontoblast-like cells (Yelick & Sharp, 2019).

What are scaffolds?

One way that stem cells are being introduced into the body in the regenerative dentistry field is through the application of scaffolds. The primary goal of scaffolds is to act as a supporting structure to help with the repair and formation of new tissues, such as dentin and pulp, when damage and loss of tissue has occurred (Raghavendra & Gathani, 2016). Scaffolds are able to play a part in tissue regeneration because they provide a space for new cells to be

introduced to the tissue and serve as a foundation for the vital cell interactions to take place. They are three dimensional structures that are composed of certain biomaterials that can be either naturally found in the body or synthetically made (Raghavendra & Gathani, 2016). A few examples of materials that are used to engineer scaffolds are platelet rich plasma, platelet rich fibrin, silk, and polymers. According to Raghavendra and Gathani (2016), the extracellular matrix, which is the substance surrounding the cells, of the desired tissue in its most immature form provides the best material to create an engineered tissue because it can act as a natural scaffold. There are many factors and requirements that scaffolds must meet in order for them to be successful in the regeneration of tissues. A scaffold has to have a suitable pore size and be porous enough to promote cell seeding of stem cells and to allow successful diffusion and transportation of nutrients such as oxygen that are necessary for growth (Raghavendra & Gathani, 2016). Another important characteristic is biodegradability. A scaffold has to be able to degrade or absorb into the surrounding tissue and not require any surgical procedures for removal (Raghavendra & Gathani, 2016). Scaffolds also must be strong enough in order to facilitate tissue regeneration and not dissolve before all stages of tissue formation are complete. Lastly, a scaffold needs to be biocompatible with the host and not cause any adverse reactions or toxicity once it is placed in the body. A scaffold that possesses many of these characteristics can be defined as a multiphasic scaffold, which initiates the attachment of bone, cementum, and periodontal tissues which aids in the healing and regeneration of the tissue (Volponi et al., 2018).

Types of scaffolds

There are many different types of scaffolds that are being tested with in order to achieve a newly formed and fully functioning tissue. Some examples of the different types of scaffolds are platelet rich plasma scaffolds, platelet rich fibrin scaffolds, silk scaffolds, and polymer scaffolds

and these are categorized based on the material used to make them (Raghavendra & Gathani, 2016). The platelet rich plasma scaffolds are composed of a concentration of the individuals own platelets that creates a three-dimensional fibrin matrix that is capable of capturing growth factors (Raghavendra & Gathani, 2016). The number of platelets that can be found in a platelet rich plasma is over one million per millimeter, which is five times more than what is found in normal platelet (Raghavendra & Gathani, 2016). With more platelets present, there is an increase in the secretion of growth factors, such as epidermal and epithelial cell growth factor which in turn facilitates the differentiation and maturation of stem cells to influence tissue repair and regeneration (Raghavendra & Gathani, 2016). Another type of scaffold that has been experimented with is the platelet rich fibrin scaffold. This type of scaffold is created when blood has been drawn and is immediately centrifuged without an anticoagulant which creates a three-layered structure with multiple growth factors (Raghavendra & Gathani, 2016). According to Raghavendra & Gathani (2016), the platelet rich fibrin serves as the ideal material to regenerate the pulp-dentin complex, acts a stable barrier against the invasion of unwanted cells, and initiates faster closure of wounds and healing of the mucous membranes. A randomized trial was conducted by Ulusoy et al., (2019) using four types of autologous scaffolds including the platelet rich plasma, platelet rich fibrin, platelet pellet, and blood clot to test how efficient each scaffold was in tissue regeneration. Sixty-seven healthy children between the ages of eight to eleven years old with 88 immature teeth that exhibited tissue necrosis were used for this experimental trial. Each tooth was randomly assigned to one of the 4 types of scaffolds, creating 4 groups with 22 teeth in each one. Results showed that all the teeth except for 2 which were included in the platelet rich fibrin and blood clot groups showed successful healing of the apices, positive response to sensitivity tests, and noticeable root development on radiographs (Ulusoy et

al., 2019). These types of scaffolds show great promise for discovering new ways to save and maintain the natural tooth.

The dental field is constantly evolving and changing due to new discoveries and methods in regenerative dentistry. The many different types of stem cells and the application of scaffolds and harvested bone play a major part in this evolution. Nevertheless, there has been some doubts about the subject. In spite of those doubts, these regenerative dentistry experiments and studies have shown great potential and can pave the way for future dental professionals in this new era of biotechnology. They can be used as a new alternative to regenerate fully functional and healthy tissues of the oral cavity (Tatullo, 2018). It would make a crucial difference if these new studies were included into school programs as another subject to teach to the new generation of dentists (Tatullo, 2018). Only the surface of regenerative dentistry has been scratched and with more time and research, what new discoveries could be made?

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