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Review

Tissue engineering: From research to dental clinics

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ABSTRACT

Tissue engineering is an interdisciplinary field that combines the principles of engineering, material and biological sciences toward the development of therapeutic strategies and biological substitutes that restore, maintain, replace or improve biological functions. The association of biomaterials, stem cells, growth and differentiation factors has yielded the development of new treatment opportunities in most of the biomedical areas, including Dentistry. The objective of this paper is to present the principles underlying tissue engineering and the current scenario, the challenges and the perspectives of this area in Dentistry.

Significance. The growth of tissue engineering as a research field has provided a novel set of therapeutic strategies for biomedical applications. Indeed, tissue engineering may lead to new strategies for the clinical management of patients with dental and craniofacial needs in the future.

Contents

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1. Introduction

The use of synthetic restorative materials as substitutes for dental structures is a practice nearly as old as Dentistry itself [1]. To date, most of the procedures performed in Dentistry are limited to the replacement of damaged tissues for biocompatible synthetic materials that may not present chemical, biological, or physical characteristics and behaviors similar to the host tissues. These discrepancies, together with the hostile environment of the oral cavity, result in relatively short-lived successful outcomes and frequent need for re-treatment. Tissue engineering is a multi-disciplinary field focused on the development of materials and strategies to replace damaged or lost tissues for biological materials by merging principles, methods and knowledge of chemistry, physics, engineering and biology [2]. The achievements obtained by tissue engineering in the past few years have resulted in new therapies such as the production of skin to treat burns [3], bone grafts to replace large bone defects [4], small-caliber arteries to treat atherosclerotic vascular disease [5] and cartilage for plastic and reconstructive surgeries [6]. Important advances have been reported in Dentistry aiming the regeneration of temporo-mandibular joint [7], periodontal ligament [8,9], dentin [10], enamel [11,12], pulp [10,13] and integrated tooth tissues [14,15].

The concept underlying tissue engineering was first proposed in the United States in the mid-1980s in order to reduce the donor scarcity to organ transplantation [16]. The classical cell-based tissue engineering approach involves the seeding of biodegradable scaffolds with cells and/or growth factors, then, implanting it in order to induce and conduct the tissue growth [17]. Obtaining good responses from this model demands the fine orchestration of the three tissue engineering fundamental elements: cells, scaffold and cell signaling. The objective of this review is to present the fundaments of the tissue engineering components and their application in Dentistry.

2. Tissue engineering

2.1. *Cells*

Stem cells are clonogenic cells capable of self-renewal and capable of generating differentiated progenies. These cells are responsible for normal tissue renewal as well as for healing and regeneration after injuries [18]. Some stem cells are said to be pluripotent, *i.e.* have the ability to differentiate into many different cell types while the range of others are more restricted. The most pluripotent cells are found in the inner cell mass of blastocyst during the early stages of embryo development [19]. They can differentiate into each of the more than 200 cell types of the adult body [20] when exposed to appropriate stimuli. Along with the potential applications of totipotent cells lies a strong ethical discussion regarding the use of human embryos. This issue has strengthened the rational for the use of adult stem cells, which have been identified in every tissue formed after embryonic development and can be used to the same purpose of embryonic stem cells.

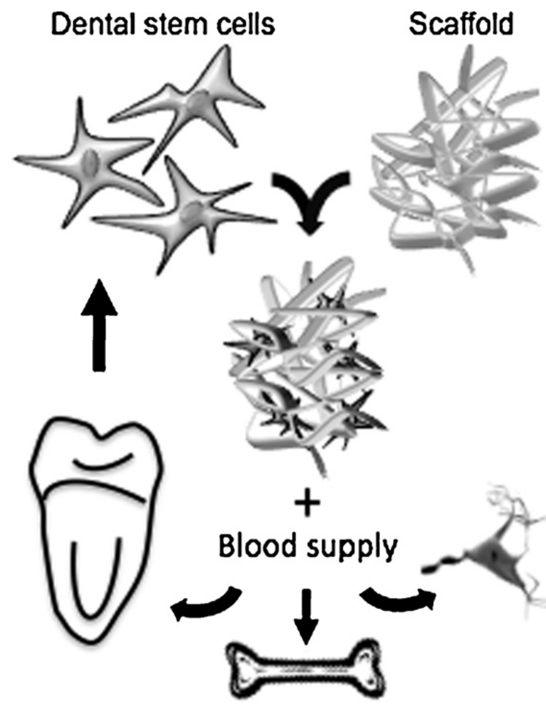

Fig. 1 – The principles of tissue engineering using dental stem cells may allow the regeneration of osseous, neural and tooth-related tissues.

Studies have showed that it is possible to isolate clonogenic and highly proliferative cells from dental pulp using similar research protocol to isolate and characterize bone marrow stem cells [21]. Dental pulp stem cells (DPSC) can differentiate into multiple cell lineages, such as adipocytes, chrondocytes, neurons and odontoblasts [22–24]. Stem cells from human exfoliated deciduous teeth (SHED) were also identified and isolated [24]. SHED has the advantage of being retrievable from naturally exfoliated teeth, which are one of the only disposable post-natal human tissues. As primary teeth are clearly a feasible source of post-natal stem cells, the interest toward the differentiation power of SHED cells has increased. Indeed, today we know that SHED can undergo adipogenic, chondrogenic, osteogenic, endothelial and odontoblastic differentiation [10,25,26]. The ability that these cells have to cross lineage boundaries expands the potential use of SHED for therapies involving a large number of tissues (Fig. 1).

Although both DPSC and SHED cells are originated from the dental pulp, they present differences regarding the odontogenic differentiation and osteogenic induction. For example, the levels of alkaline phosphatase activity and osteocalcin production during osteogenic differentiation are higher for SHED than for DPSC [23]. However, the ability to regenerate a dentin-pulp-like complex found in DPSC [21,24] is also observed in SHED cells [25]. Furthermore, SHED may present an osteoinductive potential once they were able to induce differentiation from recipient murine cells into bone-forming cells [24].

The periodontal ligament was found to be a source of que a novel population of dental stem cell (PDLSC – periodontal ligament stem cell). This cell express high levels of telomerase [27], a key molecule in mediating cell