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Review

Recent advancements in regenerative dentistry: A review

Pouya Amrollahi [a], Brinda Shah [b], Amir Seifi [b], Lobat Tayebi [b,c,*]

[a] Helmerich Advanced Technology Research Center, School of Material Science and Engineering, Oklahoma State University, Tulsa, OK 74106, USA
[b] Marquette University School of Dentistry, Milwaukee, WI 53201, USA
[c] Department of Engineering Science, University of Oxford, Oxford OX1 3PJ, UK

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ABSTRACT

Although human mouth benefits from remarkable mechanical properties, it is very susceptible to traumatic damages, exposure to microbial attacks, and congenital maladies. Since the human dentition plays a crucial role in mastication, phonation and esthetics, finding promising and more efficient strategies to reestablish its functionality in the event of disruption has been important. Dating back to antiquity, conventional dentistry has been offering evacuation, restoration, and replacement of the diseased dental tissue. However, due to the limited ability and short lifespan of traditional restorative solutions, scientists have taken advantage of current advancements in medicine to create better solutions for the oral health field and have coined it "regenerative dentistry." This new field takes advantage of the recent innovations in stem cell research, cellular and molecular biology, tissue engineering, and materials science *etc.* In this review, the recently known resources and approaches used for regeneration of dental and oral tissues were evaluated using the databases of Scopus and Web of Science. Scientists have used a wide range of biomaterials and scaffolds (artificial and natural), genes (with viral and non-viral vectors), stem cells (isolated from deciduous teeth, dental pulp, periodontal ligament, adipose tissue, salivary glands, and dental follicle) and growth factors (used for stimulating cell differentiation) in order to apply tissue engineering approaches to dentistry. Although they have been successful in preclinical and clinical partial regeneration of dental tissues, whole-tooth engineering still seems to be far-fetched, unless certain shortcomings are addressed.

Contents

1. Introduction

After the first successful kidney transplant between two non-genetically identical patients was performed by Murray, the Nobel prize winner and scientist in the early 1960s [1], transplantation has been the treatment for most of organ injuries and failures. However, transplantation has major drawbacks such as severe shortage in organ donors, gradual crescendo in the number of organ failure cases, indeterminate immune responses, and unreliable organ acceptability [1]. Therefore, scientists with backgrounds in cellular and molecular biology, materials science, and stem cell engineering came together and

* Corresponding author.
E-mail address: lobat.tayebi@marquette.edu (L. Tayebi).

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developed a new field called Tissue Engineering and Regenerative Medicine (TERM). As a rapidly growing field of research, TERM offers novel treatments for patients suffering from slight injuries to end-stage organ failure for nearly every type of human body tissue and organ. The clinically available treatments include but are not limited to strategies for urethral tissue [2], bladder wall tissue [3], genital tissues and organs [4], female reproductive tissue [5], blood vessel [6], heart valves [7], liver [8] and tracheal tissue [9]. In all of these cases, there are still substantial problems which need to be resolved; however, the recent advancements and their potential benefits seem to be revolutionary. In dentistry, scientists have always placed significant emphasis on the study of novel strategies that apply TERM to the dental practice [10].

Human teeth and orofacial tissues are responsible for phonation, mastication, esthetics, respiration, and emotional and facial expressions. Although teeth have high abrasion resistance and lifelong architectural durability, oral tissue, as one of the excessively used parts of the body, is prone to several common diseases from congenital maladies to chemical, physical, and microbial attacks [11]. While the oral cavity plays an essential role in daily life, it is severely exposed to microbial infections—therefore, any defect, induced by infections, decay or trauma and all other oral diseases including autoimmune and malignancies in the dental tissue should be addressed quickly [12]. More specifically, any large size defect that is close to pulp exposure, including moderate to advance decay, needs to be treated urgently. Often, trauma induced by mastication, accidents or even pathogens can disrupt the oral epithelium protective barrier.

The reports outline that 41% of the children aged 2–11 years (in their primary teeth), 42% of children and adolescents aged 6–19 years, and approximately 90% of human adults (in their permanent teeth) suffer from at least one of the dental diseases, such as caries [13], which makes it important to find approaches that can restore oral tissue to normal function and form. Although the techniques used in conventional dentistry—such as restoration with filling materials, whole tooth replacement with synthetic restorative materials, and teeth removal—date back to antiquity, they have major drawbacks that necessitate exploration of more effective approaches and novel technologies in modern dentistry [14]. The current efforts are focused on the investigation of the possibility of engineering the whole tooth, as well as all of the individual dental structures separately. Both of these routes require utilization and development of stem cells, biomaterials, scaffolds, and growth factors. However, before outlining the details, grasping a better understanding of the human tooth structure and development is necessary.

Despite the presence of different morphologies, all four types of human teeth—incisor, canine, premolar, and molar—go through the same stages of morphogenesis, depicted in Fig. 1A. Tooth development

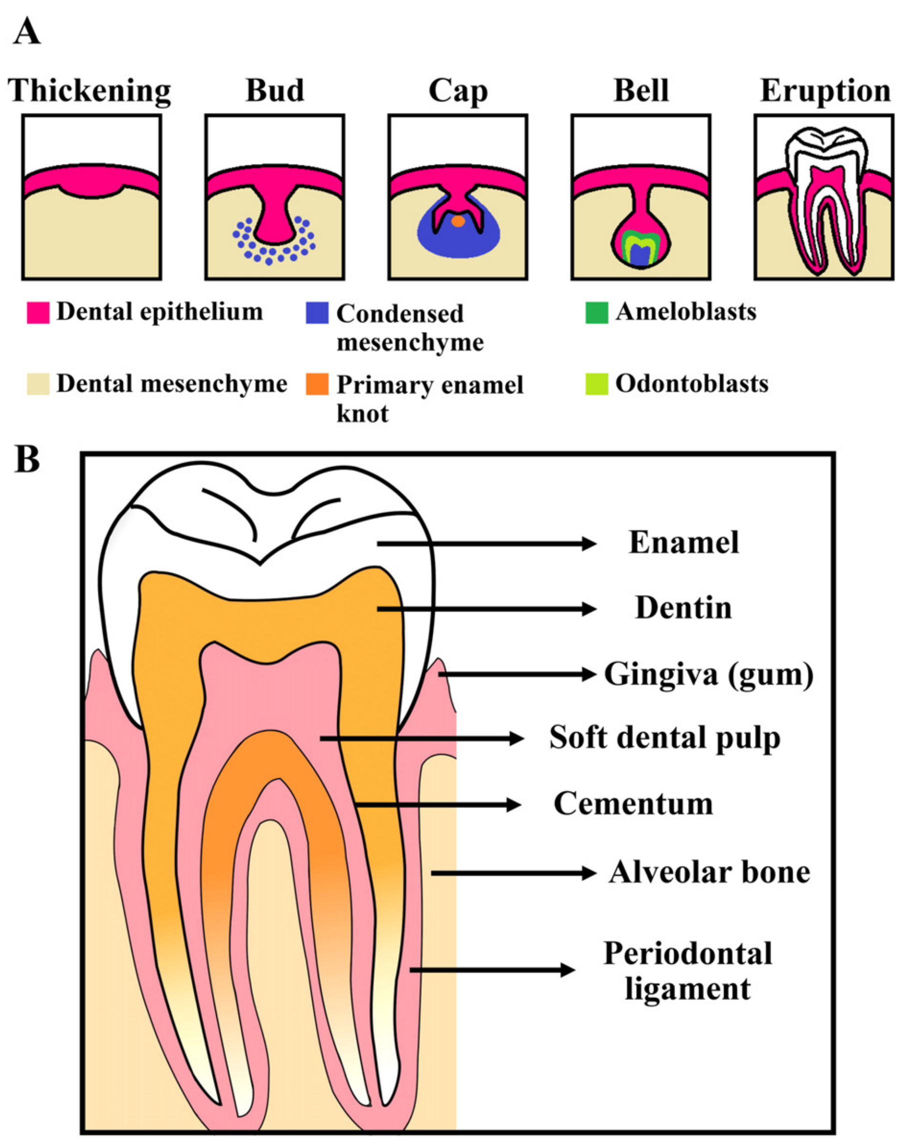

Fig. 1. (A) Tooth development process and (B) human tooth structure.