

## Chapter 13

# Dental Tissue Engineering Research and Translational Approaches towards Clinical Application

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### ABSTRACT

*Stem cell-based dental tissue regeneration is a new and exciting field that has the potential to transform the way that we practice dentistry. It is, however, imperative its clinical application is supported by solid basic and translational research. In this way, the full extent of the potential risks involved in the use of these technologies will be understood, and the means to prevent them will be discovered. Therefore, the aim of this chapter is to analyze the state-of-the-science with regard to dental pulp stem cell research in dental tissue engineering, the new developments in biomimetic scaffold materials customized for dental tissue applications, and to give a prospectus with respect to translational approaches of these research findings towards clinical application.*

### INTRODUCTION

Dental diseases, such as caries, periodontitis, tooth loss, and orofacial/dental trauma are major public health problems worldwide, with a profound effect on an individual's quality of life (Petersen, et al., 2005). The experience of pain, problems with eating, chewing, smiling, and communication due

to missing, discoloured, or damaged teeth have a major impact on people's daily lives and well-being. It is estimated that teeth congenital abnormalities account for 20% of all inherited disorders (Line, et al., 2003; Koussoulakou, et al., 2009), whereas, dental pathology occupies a leading position in the list of human diseases. In addition, dental infectious diseases, such as periodontitis,

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have an associated risk of systemic complications (e.g. diabetes, cardiovascular diseases, etc.) and therefore an impact on general health. All these factors have led to increased demand for effective management of dental diseases and replacement of missing tooth structures/teeth. Current strategies of replacement are based on non-biological artificial substitutes, such as dental fillings, fixed and removable partial dentures supported by teeth and/or implants, complete dentures, etc. All these substitutes have several disadvantages, including uncomfortable sensation, insufficient biocompatibility, damage to the surrounding tissues and unpredictable long-term therapeutic efficacy (Dodson, 2006; Jung, et al., 2008). The need for alternative therapies is evident in reports by the United States Department of Health and Human Services (USDHHS, 2000) and WHO Global Oral Health Data Bank, which reveal startling statistics about the high incidence of tooth loss and edentulism.

Recent progress in dental tissue engineering methodologies have provided the opportunity for novel and innovative alternative therapies based on regeneration strategies of the lost dental, periodontal and bone tissues in the craniofacial area (Sartaj & Sharp, 2006). These regenerative approaches are mainly based on the use of stem cells in combination with biomimetic scaffolds and relevant growth and differentiation factors, which make the classical tissue engineering triad (Vats, et al., 2005). It is envisioned that these novel regenerative therapies will be based on the use of bioengineering methods to regenerate the lost dental or surrounding bone tissues from easily harvested, donor-derived autologous tissues (Zivkovik, et al., 2010). It is also expected that these strategies will significantly reduce the cost of dental care. According to the 2006 National Health Expenditure Accounts, the annual US expenditures on dental services totaled 91.5 billion dollars (NHEA, 2006). It is estimated that 90% of adults have caries lesions and that 40% of the Western population is missing one or more teeth

(Hacking, et al., 2009; Garcia-Godoy & Murray, 2006). Tissue engineering strategies for tooth replacement could potentially account for 90 million instances of caries, 45 million fractured or avulsed teeth, and 21 million procedures for endodontic surgery each year only in the USA (Garcia-Godoy & Murray, 2006).

However, before moving from reparative treatment to regenerative therapy in dentistry several scientific challenges must be addressed. First, a profound understanding of the developmental and functional characteristics of the dental organ must be acquired, including the complex cell interactions leading to dental tissue development, but also the regenerative processes that take place as a response to external stimuli. But even if this knowledge is acquired, the major challenge will then be the translational pathway from the basic scientific data through the *in vitro* studies, animal studies and clinical studies to commercialization and finally availability to the patient, who will be the final recipient of this knowledge and technology. Several questions will have then to be answered. For example, how several risks will be outweighed, including the possibility of transformation of the stem cells after implantation, the risk of unwanted contamination with pathogens during these procedures or the possible immunogenicity of these cells on the recipient (Casagrande, et al., 2011). Another critical issue is how to deliver the right signals at the right place and time, which prerequisites a profound understanding of the molecular signals orchestrating cell function during odontogenesis. Moreover, what is the role of the cells going to be: replacement of the endogenous cell population or a biological “factory” by secreting matrix, growth factors, etc.?

One of the most important and decisive evolutions towards the development of novel therapeutic strategies for the regeneration of lost or damaged oral tissues was the discovery and characterization of stem cells of dental origin. Molecular biology studies focused on these cells have certainly significantly improved our understanding of tooth

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