

EDITORIAL – BROTHERS IN ARMS: REGENERATIVE BIOLOGY AND DENTISTRY

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A fundamental biological property of all multicellular organisms is their ability to respond to injuries. Tissue regeneration is one of the most complex and dynamic biological processes and consists of a sequence of cellular and molecular events that are activated immediately upon injury. Successful restoration of tissue integrity and homeostasis relies on the reactivation of a variety of signalling pathways and their coordinated action (Eming *et al.*, 2014). The biological responses to lesions involve the formation of new tissues, their remodelling, neo-vascularisation and re-innervation. Recent progress in genetics, single-cell RNA analyses, proteomics and stem cell biology has expanded the horizons into the principles of health and disease. This knowledge, combined with the latest advances in the fields of biotechnology, tissue engineering and imaging has formed the foundation for translation into innovative therapeutic solutions (Benam *et al.*, 2015; Hendriks *et al.*, 2020; Schutgens and Clevers, 2020).

Teeth exert fundamental physiological functions related to mastication and speech, and are formed by soft (dental pulp, periodontium) and highly mineralised tissues (enamel, dentine, cementum). Teeth are anchored to the alveolar bone *via* the periodontal ligament, which supports their stability and function. The vitality of the soft dental tissues is ensured by a rich network of blood vessels and nerve fibres (Pagella *et al.*, 2020). Dental injuries induce activation of regenerative mechanisms within the dental pulp, periodontal ligament and alveolar bone tissues, involving the reorganisation of their neuronal and vascular networks and the concomitant activation of the various stem cell populations (Pagella *et al.*, 2021a; Pagella *et al.*, 2021b).

Dental treatments employ high-quality imaging techniques and the use of innovative biomaterials that faithfully mimic the properties of dental tissues. However, based on the recent impressive scientific

progress in many biological and technological disciplines, it is tempting to introduce new therapeutic concepts and approaches in dental clinics. An attractive alternative that might complement the actual dental treatments is biological tissue repair, by exploiting the regenerative potential of stem cells (Orsini *et al.*, 2018). The combination of specific stem cell populations, signalling molecules and biocompatible scaffolds has been the subject of intensive investigation in the last decades. Complex microfluidic organ-on-chip devices, supplemented with stem cells, neuronal and endothelial cells, are increasingly used for tissue regeneration purposes since they can successfully emulate the composition, physiology and function of dental pulp or periodontal tissues (Benam *et al.*, 2015; van den Berg *et al.*, 2019). In addition, three-dimensional *in vitro* systems that can contain large numbers of stem cells, such as spheroids and organoids, can be successfully used for dental tissue regeneration. The combination of all these novel biological and technological platforms can provide new concepts and ideas that could revolutionise dentistry and greatly improve dental care practices in the near future.

In the Dental Regenerative Biology Special Issue, renowned researchers provide important information about the biological aspects of dental tissue repair and regeneration and suggest novel approaches for the treatment of pathological or lost teeth. The articles included in the issue highlight important cues involved in the regeneration and repair of dentine, dental pulp, periodontium and alveolar bone, report on the importance of vascularisation, innervation and inflammation during healing, and underline the prerequisite for new technological tools and materials that could still improve the effectiveness of dental treatments. A new era, full of excitement and expectations, has risen in dentistry, allowing the application of innovative and more sophisticated therapies.

Conflict of Interest

The authors confirm that there are no conflicts of interest associated with this work. TAM and OT contributed to the writing, reading, and editing of the present editorial.

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