Symposium

# THE 2nd INTERNATIONAL SCIENTIFIC SYMPOSIUM: *REGENERATIVE PROCEDURES IN DENTAL MEDICINE*

Guest Editor

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# PREFACE

The 2$^{nd}$ Symposium entitled «Regenerative procedures in dental medicine» was organised on 3$^{rd}$ October 2017 by the School of Dental Medicine University of Zagreb and the Croatian Academy of Sciences and Arts, Department of Medical Sciences.

This scientific symposium meeting included six lectures, based on the latest achievements in the field of regenerative dental medicine and medicine. The lectures were related to three different areas. The first one focused on tooth repair and regeneration, understanding stem cell heterogeneity - the key for successful dental regeneration and isolation, characterization and differetiation of potential of oral mucosa stem cells.

These lectures were held by professor Paul Sharpe and dr.med.dent. Maja Sabalić from Kings College in London and professor Ivan Alajbeg from the School of Dental Medicine University of Zagreb. Advancements in regenerative dentistry could soon equip dentists with tools to regenerate dental pulp and other tissues. Developing effective regenerative therapies has proven to be a challenging task due to the complexity of tooth structure, functional and aesthetic requirements, safety and patient factors. However, recent studies looking at behaviour of adult mesenchymal stem cells in murine teeth *in vivo* offer new insights for the development of translational approaches for tissue regeneration. Molecular heterogeneity within the mesenchymal stem cell (MSC) niche has recently been studied *in vivo* using genetic lineage tracing and single-cell RNA sequencing. The role of an established Thy1 (CD90)-marked sub-population is studied in homeostasis and following simulation of increased growth of mouse incisors. Recent results suggest that this sub-population plays a specific role in rapid growth, during development, as well as in stimulated increased growth and can be replenished by activation of dormant stem cells. These findings have implications for development of new, targeted regenerative therapies harnessing the potential of tissue-resident stem cells in a surgical intervention or non-surgical, molecular signal delivery approach.

Human oral mucosal stem cells (hOMSC) originate from the neural crest and possess multipotency, especially differentiation potential towards neuroectodermal lineage. They are easy to collect, as sampling does not result in irreversible destruction of oral tissues. Potential clinical use of hOMSC is also in the other medical fields; hOMSCs have been successfully transplanted to the cornea in patients with limbal defect, and similar cells can be differentiated into cardiomyocytes after myocardial infarction. hOMSC research in animal models of neurological diseases and injuries has shown their potential role in diseases which modern medicine has failed to treat. In this regard, the group from Zagreb started the research of hOMSC and the possibility of their application in the model of ischemic brain stroke. After successfully isolating hOMSC and following their differentiation in the neuroectodermal and mesodermal directions, it was proved that it is possible to produce co-cultures of hOMSC mouse neural stem cells, which we see as an indicator that those cells will be able to coexist and communicate in the mouse model.

The second part referred to the new aspects in the field of regenerative medicine and Osteogrow: a novel drug for bone regeneration  held by academician Slobodan Vukičević and professor Lovorka Grgurević from the School of Medicine University of Zagreb.

Molecular processes required for bone repair are a prerequisite for the development of new biological procedures for stimulation of bone healing. Currently, there is no adequate therapy available that can accelerate long bone fractures healing. Specifically there is a need for the development of a new osteogenic device that will offer safe healing in particular of the trabecular bone. The Osteogrow project has developed a new therapy that promises to be safe and cost-effective and might decrease the need for secondary interventions. The Osteogrow device contains an autologous blood coagulum (ABC) made from the peripheral blood and recombinant bone morphogenetic protein 6 (BMP6). BMP6 has been selected as compared to BMP2 or BMP7/OP1 as it does not bind avidly to the BMP antagonist Noggin. ABC was chosen as a substrate for the delivery since BMP6 binds tightly to the number of plasma proteins resulting in the sustained and linear release over seven to ten days without provoking inflammation and immune responses. With support of the EU FP7 grant we have completed the preclinical development of Osteogrow and started Osteogrow first in humans (FIH) clinical studies. Osteogrow is tested clinically in two indications: the distal radial fracture and high tibial osteotomy to establish the safety and potential efficacy for Osteogrow for regeneration of the metaphyseal bone. Beyond currently tested clinical indications, this therapy would also be employed for posterolateral spinal fusion to treat degenerative spine disorders.

In the third section the area of bioactive composite materials was elaborated by professor Zrinka Tarle from the School of Dental Medicine University of Zagreb.Bioactive dental composite materials offer the potential to prevent secondary caries, which is one of the major causes of failure of contemporary composite restorations. The caries-preventive effect of bioactive composites is attained by two main approaches: antimicrobial activity and remineralization of dental hard tissues. Experimental bioactive composite materials are based on amorphous calcium phosphate and bioactive glasses. Generally, some compromise is always required in balancing the bioactivity and mechanical properties of composite materials. The characteristics of bioactive fillers need to enable sufficient ion release in an aqueous environment, while not negatively affecting basic properties of composite materials. The major benefits of bioactive composite materials include: the capability to regenerate dental hard tissues after an acid attack by supplying calcium, phosphate and other ions, reduction of dentin hypersensitivity and postoperative sensitivity, precipitation of hydroxyapatite in the marginal gap, inhibition of bacterial growth and improvement in the durability of the bonding between the composite material and dentin.

President of the Organising Committee
*Zrinka Tarle*

***Figure 1.*** President of the Croatian Academy of Sciences and Arts Zvonko Kusić, academician Slobodan Vukičević and Rector of the University professor Damir Boras.

***Figure 2.*** President of the Croatian Academy of Sciences and Arts Zvonko Kusić has officially opened the symposium «Regenerative procedures in dental medicine».

***Figure 3***. President of the Organising Committee professor Zrinka Tarle giving her talk at the symposium «Regenerative procedures in dental medicine».