**Bioactive glasses releasing multiple biologically active ions for regenerative medicine**

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**Abstract**
Bioactive materials, specially surface reactive materials such as bioactive glasses (BGs), are being increasingly considered in the tissue engineering (TE) field, for both hard (bone) TE and soft tissue repair and wound healing. Such applications rely on the biochemical reactions occurring at the interface between the material surface and the biological environment, which involve the (controlled) release of biologically active ions as dissolution products to stimulate specific cellular responses involved in new tissue growth [1]. In addition, immunomodulatory effects of BGs in the framework of bone regeneration and wound healing are being increasingly investigated [2].
Selected metal ions released from BGs have been shown to induce an angiogenic effect, e.g. in specific concentrations they enhance the secretion of vascular endothelial growth factor from stem cells, a very important property for tissue regeneration. Such angiogenic effects of BGs will be discussed showing results on different scaffold types and BG compositions. Moreover, the result of cell culture studies characterizing the variation of ion concentration (BG dissolution) in the medium and resultant time dependent effects on stem cells will be presented. In addition, strategies employed to affect immune cell response for enhancing tissue repair and regeneration based on BGs will be discussed, including surface functionalization, morphological optimization and controlled release of immunomodulatory ions.
In this context, applications of ion releasing BGs (e.g. as mesoporous nanoparticles) in the field of 3D bioprinting (biofabrication) have emerged in the last few years expanding the application potential of BGs in TE. In the second part of the presentation, the progress in the development and characterization of TE scaffolds made purely from BGs or by combining BGs and biopolymers, including their application in the field of 3D bioprinting, will be discussed. Examples of such applications will be presented highlighting the latest developments of multimaterial bioinks based on hydrogel-bioactive glass composites for cell encapsulation and for biofabrication of cell laden scaffolds of increasing complexity [3]. The author's views on the challenges and opportunities for further research in the field will be presented.

**References**

[1] A. Hoppe, et al., A review of the biological response to ionic dissolution products from bioactive glasses and glass-ceramics, *Biomaterials* 32 (2011) 2757-2774.

[2] K. Zheng, et al., Immunomodulatory bioactive glasses for tissue regeneration, *Acta Biomater.*133 (2021) 168-186.

[3] H. Zhu, et al., 3D Bioprinting of Multifunctional Dynamic Nanocomposite Bioinks Incorporating Cu-Doped Mesoporous Bioactive Glass Nanoparticles for Bone Tissue Engineering, *Small* (2022) 2104996.