

# Angiogenic and inflammatory potential of Scleral Ossicles, novel natural biomaterials for bone regeneration

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Recovering and regeneration of significant bone defects is one of the big challenge that researchers would like to win in the field of regenerative medicine. When a fracture happens it is possible to incur in a so called critical-size defects, a sever lesion that affect a skeletal segment by preventing its self-recovery. Current standard treatments include autografting, allografting and other implant techniques which may imply some issues, such as limitations connected to costs and side effects like potential infections and nonunion. The tissue engineering directed its efforts in developing new scaffold to combine with cells and stimuli with the aim to reproduce the interaction between cells and Extracellular Matrix during the osteogenesis process. In particular, many different scaffolds have been developed with different properties, proposing new materials to be used for new 3D printing techniques in order to optimize the cell growth; a variety of different exogenous chemical or physical stimuli were tested, such as soluble growth and differentiation factors as well as mechanical forces; finally many types of cells have been used alone or in co-culture. The most important obstacle emerged so far is the lack of a proper vascularization by which cells inside the scaffold receive a sufficient blood supply. The aim of this work is the analysis of the angiogenic and inflammatory potential of the Scleral Ossicles (SOs), already analysed by the structural viewpoint [1], and the development of a functionalized-SOs-construct. Recently, we have already characterized the SO proposing it as innovative and naturally decellularized material easily available at no cost [2]. Currently, the SOs has been tested for angiogenic potential in ovo utilizing the Chorioallantoic Membrane (CAM) system. The preliminary results have shown the induction by SO of a strong vasculo-proliferative reaction on CAM in which the neo-formed vessels have an extremely tortuous and irregular course. The inflammatory potential will be evaluate in vivo by means of subcutaneous implant of SOs in rat models. Finally, we are developing a 3D-printed scaffold made by Dental SG Resin, which will host the SOs, with the aim to adapt this functionalized-SOs-construct (3D scaffold + SOs) to the dimensions of a critical fracture in diverse species.

## References

- [1] Palumbo et al. (2012) Osteocyte Apoptosis and Absence of Bone Remodeling in Human Auditory Ossicles and Scleral Ossicles of Lower Vertebrates: A Mere Coincidence or Linked Processes? *Calcif. Tissue Int*, 90: 211–218; doi 10.1007/s00223-012-9569-6
- [2] Checchi et al. (2017) Proposal of a novel natural biomaterial, scleral ossicle, for the development of vascularized bone tissue in vitro. *Biomedicines*, 6 (1): 3; doi:10.3390/biomedicines6010003

## Key words

Scleral Ossicle, CAM, inflammation, angiogenesis, 3D printing.