Title: Bioactive glass as chondro-instructive scaffold for cartilage repair?

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Articular cartilage defects do not heal and require proper reconstruction to prevent the onset of osteoarthritis. Implantable and degradable chondro-instructive scaffolds are needed as appropriate microenvironment to facilitate chondrogenesis at the injury site. Since its discovery 50 years ago, bioactive glasses (BG) have attracted increasing interest as cytocompatible and instructive scaffold materials to support bone repair. Hence, currently studied BG types are known to lead to the deposition of a hydroxyapatite layer which is closely associated with bone formation and might interfere with other applications. However, BG could also present a future strategy for cartilage reconstruction, but so far, a chondro-instructive BG is not available.

Hence, based on previous results of our research group concerning chondrogenesis of hyaline nasoseptal cartilage derived chondrocytes in Poly-L-Lactic acid composite scaffolds supplemented with 1% or 2% BG1393 (Conosenti et al., 2019) we wanted to define the detailed requirements of a BG tailored to support cartilage formation and to develop a novel chondro-instructive BG type.

Highly porous scaffolds (3x3x2 mm, porosity: 80%, strut thickness 60-80 µm, pore size: 150 µm) consisting solely of the novel BG were prepared by melting, homogenization, milling, coating of a polyurethan foam (PU) with the glass powder, sintering and thereby, evaporating of the PU foam followed by acid-mediated leaching of the precursor glass variants of defined ion composition (62.7% SiO_2, 7.0% P_2O_5, 2.0% B_2O_3, 28% Na_2O + K_2O and others [0.3%]). The procedure creates a gel layer which becomes hydrated during culturing in growth media and facilitates continuous ion release. The scaffold possesses a tunable degradation profile. Scaffolds were dynamically seeded with porcine articular chondrocytes (27,777.8 chondrocytes per mm^3) and cultured on a rotatory device for 1-35 days. Cell survival within the scaffolds was monitored by live death assay. Proliferative activity of chondrocytes was determined based on DNA content by Cyquant assay. Chondrocyte distribution, morphology and interaction with the scaffolds were observed by scanning electron microscopical analysis and histology. Expression of cartilage-specific type II collagen and non-specific dedifferentiation-associated type I collagen was visualized by immunofluorescence labelings and confocal laser scanning microscopy.

During the entire observation period articular chondrocytes spread and survived on the novel BG. The pores of the scaffold were more and more filled by cells and extracellular matrix during the observation time. Chondrocytes revealed an intimate cell-scaffold interaction. Chondrocyte proliferation could be shown during the observation time period. Deposition of a fibrous ECM containing cartilage-specific type II collagen and sulfated glycosaminoglycans could be demonstrated confirming the differentiated chondrocytic phenotype in the scaffold.

The novel BG (patent DE102018114946) provides a promising approach for cartilage tissue engineering and could be integrated as a bioactive component in composite scaffolds in future.

Conoscenti G, Carfì Pavia F, Ongaro A, Brucato V, Goegele C, Schwarz S, Boccaccini AR, Stoelzel K, La Carrubba V, Schulze-Tanzil G. Human nasoseptal chondrocytes maintain their differentiated phenotype on PLLA scaffolds produced by thermally induced phase separation and supplemented with bioactive glass 1393. Connect Tissue Res. 2019 Jul;60(4):344-357.

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Gundula Schulze-Tanzil is a veterinarian and submitted her doctoral thesis with a scholarship at the Freie Universität Berlin in 1999 in veterinary microbiology. 1999 she started her postdoc time in human anatomy (habilitation in Anatomy and Cell Biology in 2009 at Charité-Universitätsmedizin in Berlin with a scholarship) and experimental trauma research (2005-2015 at the Dep. of Trauma and Reconstructive Surgery, Charité, CBF). She has more than 20 years of experience in the field of musculoskeletal research and human anatomy. In 2015 she obtained a professorship at Paracelsus Medical University in Nuremberg, Germany and leads the Anatomical department.

Fields of Interest: She and her team investigates tendon/ligament and cartilage reconstruction strategies and pathologies combining in vitro and surgical small/large animal models.