Bone & Joint

Participating Labs

- **Gantenbein-Lab**
  Tissue Engineering for Orthopedics & Mechanobiology (TOM)
- **Saulacic-Lab**
  Cranio-Maxillofacial Surgery (CMF)

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Link to research program

Selected Collaborators

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The skeletal system is subject to traumatic conditions (fractures and large bone defects) and pathologies due to degeneration (osteoporosis, osteoarthritis, and intervertebral disc [IVD] degeneration). The demand for improved and efficient treatments is increasing as the population of older adults grows and wants to stay physically active. However, surgical procedures for repairing large bone defects or degenerated spinal discs still require significant improvement. The regeneration of skeletal tissues is the focus of the Bone & Joint Research Program. To this aim, strategies based on cells, materials, and growth factors are currently employed, ex vivo (2D/3D cell cultures and bioreactors) and in vivo. Translational orthopaedic research, which has been a long tradition in Bern, requires interactions between surgeons and scientists. The Bone & Joint Research Program will continue to extend this tradition and provide clinicians with tools to improve patient treatment.

Research Highlights 2023 / Outlook 2024

The tissue engineering for orthopedics (TOM) lab has successfully acquired competitive funding for translational and cellular therapies in two main areas. The first focus area is joint research in the field of intervertebral disc regeneration of the spine. The ongoing Marie Skłodowska Curie International Training Network (ITN) "disc4all" (↗ disc4all.upf.edu) with two early-stage researchers (ESRS) and three visiting ESRs continued to train young researchers in the field of wet ab techniques in 2D and 3D cell culturing models in combination with computational simulations and predictions of mechanical loading and mimicking inflammation and cell signaling. A second milestone was the successful completion of the "Silkodisk" project, a tissue engineering project that utilizes silk to repair IVDs. This is an active collaboration with Dr. Michael Wöltje of the Dresden University of Technology (TUD). In this framework, the TOM lab was honored with the best Master's thesis award of Janine Fuhrer, MSc, for her valuable lab work at the Biomedical Sciences and the successful PhD defense of Dr. Andreas Croft, which is nominated for the best PhD thesis at the GCB.

Furthermore, the TOM lab has received a bridge discovery research project (budget 1.3 M CHF for four years) on label-free cell sorting based on electrical impedance to "fish" for rare type of progenitor cells of the IVD. This project is a collaboration with Prof. Patric Eberle and Prof. Fabian Ile, both from the Lucerne University of Applied Sciences. This project is based on cell sorting of a rare stem cell population from the IVD.

Further progress can be made in the second focus field of improved spinal fusion. In this study, an in vivo rat model was established using bone morphogenic protein (BMP) 2 and specific mixtures of a BMP2 analog (L51P) to accelerate spinal fusion to maximum speed, while maintaining concentrations at a low dose close to physiological levels. Future research is foreseen to investigate the role of rheumatoid

arthritis using an identical approach of fixator extern as well as investigate the role of disease-modifying antirheumatic drugs (DMARDs) in patients undergoing treatment for rheumatoid arthritis (RA). In the near future, these drugs will be tested for their effects on healing of impaired spinal fusion.

In collaboration with the Clinic for Radiology at the Inselspital (PD Dr. Rainer Egli), the possible effects of gadolinium-containing contrast agents on bone cell lineages were investigated in vitro. The data demonstrated that both the differentiation and activity of osteoblast and osteoclast lineage cells were inhibited upon exposure to gadolinium, suggesting that long-term exposure to gadolinium-containing contrast agents may affect bone metabolism, which requires further study. Franziska Strunz, the first author of this study, successfully completed her PhD thesis during this reporting period.

The Saulacic lab (CMF) assessed the sequence of osseointegration in 3D-printed titanium implants with a trabecular structure without (R1) or with (R2) an acid-pickled surface in comparison to commercially available titanium implants, in collaboration with the Department of Periodontology, School of Dental Medicine, University of Bern. The 3D-printed implants have been shown to maintain crestal bone height and successfully osseointegrate with adequate fractions of newly mineralized bone formation.

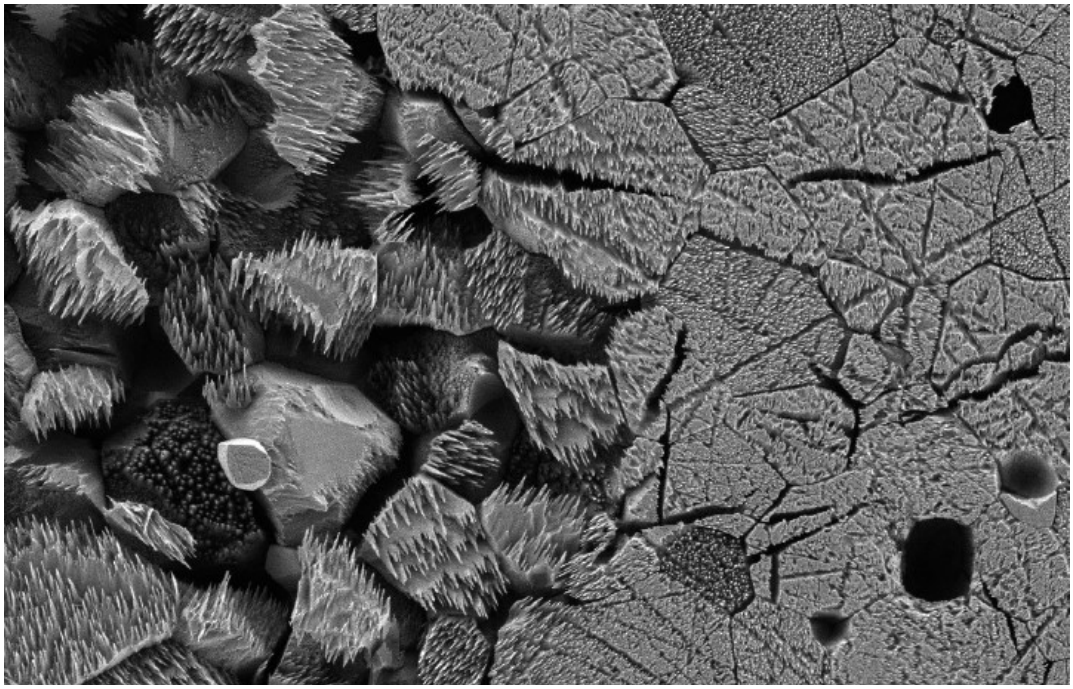
Selected Publications

Croft, AS; Fuhrer, J; Wöltje, M.; Gantenbein, B (2023). ↗ *Creating tissue with intervertebral disc-like characteristics using gdf5 functionalized silk scaffolds and human mesenchymal stromal cells*. European Cells & Materials eCM, 46, pp. 1-23. ↗ 10.22203/eCM.v046a01

Crump KB, Alminnawi A, Bermudez-Lekerika P, Compte R, Gualdi F, McSweeney T, Munoz-Moya E, Nuesch A, Geris L, Dudli S, Karppinen J, Noailly J, Le Maitre C, Gantenbein B (2023). ↗ *Cartilaginous endplates: A comprehensive review on a neglected structure in intervertebral disc research*. JOR Spine, 6(4), e1294. ↗ 10.1002/jsp2.1294

Croft AS, Corluka S, Fuhrer J, Woltje M, Silva-Correia J, Oliveira JM, Erbach GF, Reis RL, Gantenbein B (2023). ↗ *Repairing Annulus Fibrosus Fissures Using Methacrylated Gellan Gum Combined with Novel Silk*. Materials, 16(8), p. 3173. ↗ 10.3390/ma16083173

Lang NP, Imber JC, Lang KN, Schmid B, Munoz F, Bosshardt DD, Saulacic N (2023). ↗ *Sequential osseointegration of a novel implant system based on 3D printing in comparison with conventional titanium implants*. Clinical Oral Implants Research, 34(6), pp. 627-638. ↗ 10.1111/clr.14072



Scanning electron microscope image of the surface of a ß-TCP cylinder after 24 h resorption by *in vitro* generated osteoclasts (from: LeGars Santoni B et al. (2023) Acta Biomaterialia 169:566-578. PMID: 37595772)