

Within the <u>SNSF Sinergia project SLIHI4BONE</u> (collaboration partners: M. Bohner, RMS Foundation, Bettlach; R. Müller, ETH Zurich; E. Wehrle, ARI Davos), the <u>Laboratory for Bone Biomechanics</u> (<u>LBB</u>) at the Institute for Biomechanics at ETH Zurich is offering an

SNSF-funded PhD Position in Advanced *In Vivo* Imaging of Heterotopic Ossification

The PhD position is embedded within the SNSF Sinergia project SLIHI4BONE (Nr. 213520, project start 01.04.2023) focusing on a newly-proposed mechanism explaining the formation of bone in soft tissue, also called heterotopic ossification (doi:10.1016/j.mattod.2018.10.036). According to this mechanism, tissue mineralization may provoke a sustained local ionic homeostatic imbalance (SLIHI), and this local decrease in extracellular calcium may modulate inflammation to trigger bone formation. The general project aim is to assess the validity of this mechanism and to use it for healing large bone defects.

Heterotopic ossification (HO) is a very common and sometimes highly debilitating pathology characterized by the formation of mature bone in soft tissues. The underlying mechanisms are still poorly-understood and therapies to prevent and heal HO have a low efficiency. It is not uncommon that bone has to be removed surgically. This formation of bone in soft tissue is the result of an osteoinductive process during which stem cells are differentiated into bone cells. This property is essential to treat large bone defects. Currently, osteoinduction can be achieved by the implantation of bone morphogenetic proteins (BMPs), but the safety of BMP has been questioned. Another approach is to implant osteoinductive bone graft substitutes, but their potency is low, and the underlying mechanisms are still debated. Demonstrating that a low extracellular calcium concentration is key in triggering bone formation and having a better understanding of this process could open up new opportunities in the design of potent osteoinductive bone graft substitutes and the treatment of impaired bone healing.

Project team and setup: Within the project, we will follow a multidisciplinary collaborative approach for which we are recruiting 3 PhD students focusing on material science (PhD position at RMS Foundation), advanced *in vivo* imaging and computation (PhD position at LBB, ETH Zurich) and *in vivo* molecular biology (PhD position at ARI Davos). An additional Postdoc position (LBB, ETH Zurich) will be focusing on the development of multiphoton intravital imaging technology. This multidisciplinary team setup will allow to design calcium phosphate materials with controlled architecture, composition, and to assess their rate of mineralization *in vitro* and *in vivo*. The level of extracellular calcium and the tissue response around the materials will be followed by multimodal approaches including (among others) time-lapsed *in vivo* imaging, multiphoton intravital microscopy, spatial transcriptomics and proteomics.

For the advanced *in vivo* imaging work packages within SLIHI4BONE, we are looking for a motivated PhD candidate to join the Institute for Biomechanics at ETH Zurich. The successful candidate will closely interact with the Sinergia collaboration partners at RMS Foundation and ARI Davos. The PhD candidate will be enrolled in the PhD program of ETH Zurich. Tasks and activities will include:

- Development of advanced *in vivo* imaging protocols for HO and impaired bone healing using time-lapsed micro-computed tomography and multiphoton imaging
- Extension of internal Python-based computational framework for 4D image analysis and morphometric quantification
- Imaging and computational support for in vivo experiments

Your profile

MSc degree in engineering science or related discipline

- Previous programming experience in Python is required
- Previous experience with imaging and/or image analysis is advantageous
- Experience with computed tomography and/or multiphoton microscopy is advantageous
- Excellent communication skills in English (oral and written) are a must
- High motivation, strong interest in skeletal research, durability to cope with challenges
- Ability to solve complex tasks in a highly independent manner
- Familiarity with a cross-cultural/interdisciplinary environment is an advantage

We offer

- An interesting and varied job in exciting and innovative organizations
- Working in a highly committed multidisciplinary team
- Regular meetings and close collaboration with the Sinergia project partners
- Enrolment in the PhD program of ETH Zurich
- ETH Zurich is a family-friendly employer with excellent working conditions with an exciting working environment, cultural diversity and attractive offers and benefits

We value diversity

In line with our values, ETH Zurich encourages an inclusive culture. We promote equality of opportunity, value diversity and nurture a working and learning environment in which the rights and dignity of all our staff and students are respected. Visit our Equal Opportunities and Diversity website to find out how we ensure a fair and open environment that allows everyone to grow and flourish.

Curious? So are we

We look forward to receiving your online application with the following documents:

- Motivation letter
- Curriculum Vitae
- University transcripts
- Names and contact details of two references

Please note that we exclusively accept applications submitted through our <u>online application portal</u>. Applications via email or postal services will not be considered.

Further information about the Laboratory for Bone Biomechanics can be found on our website www.bone.ethz.ch. Questions regarding the position should be directed to Prof. Dr. Ralph Müller at ram@ethz.ch (no applications).