MASTER OF SCIENCES - BIOMEDICAL ENGINEERING
MASTER THESIS PROPOSAL

UNIVERSITÄT BERN

Berner Fachhochschule BFH

IRON AS A CO-FACTOR MODULATING BONE FORMATION

Introduction. Iron is an essential element in many physiological processes. Iron is crucial for oxygen transport in blood, for mitochondrial ATP synthesis and it acts as a co-factor in many essential enzymes. The many roles of the metal require a tight regulation of iron levels in blood and tissues, and a small number of binding proteins and molecular transporters take care of this task. Transferrin receptor and *Divalent Metal Transporter* (DMT) 1 mediate cellular uptake of iron. Again DMT1 and ferritin ensure intracellular transport and finally, iron is released from the cells through Ferroportin. In the past, we investigated the expression of the components of iron homeostasis in bone cells and we found them to be regulated during the process of osteoclast development *in vitro*. Subsequently, we found iron to support the proliferation of osteoclast precursors and the expression of a macrophage phenotype, while suppressing the development of osteoclasts. While our studies focused on iron and osteoclasts, within the present project, the role of iron on the development and the function of osteoblast lineage cells, the cells forming bone, will be elucidated.
Research Work. To approach the questions of iron effects on osteoblast lineage cells, we will culture primary murine osteoblasts from calvarial bones in differentiation media. Differentiation of osteoblasts will be characterized by the expression of specific marker genes and by the cells' ability to lay down a mineralized matrix. Levels of transcripts encoding the components of iron homeostasis will be determined by quantitative PCR. Osteoblast function, i.e. gene expression and i*n vitro* deposition of a mineralized matrix will be assessed in dependence of exogenously added iron, of removal of iron by adding a chelator, and of selective inhibitors of DMT1. Intracellular translocation of iron transporters in response to exogenous iron will be elucidated by immunocytochemistry and confocal microscopy.
Relevance. Excess and deficiency in iron not surprisingly affect a variety of organs. In this context, it is important to differentiate between a direct impact of impaired iron homeostasis and indirect secondary effects. Anemia, which leads to a deficiency in oxygen may finally result in a decrease in bone mass due to reduced bone turnover. On the other hand, hemochromatosis, an excess of iron, will cause precipitation of iron in tissues, inducing an inflammatory response, which will contribute to osteoporosis by stimulating bone resorption. It is therefore relevant to understand the direct effects of iron on the skeletal system to actively protect bone from the deleterious effects of impaired iron homeostasis.
This project is part of the NCCR Platform "TransCure" which has been set up to "To apply excellence in membrane transporter research to the treatment of human diseases".

September 2015
Bone Biology & Orthopaedic Research, Department Clincal Research

Nature of the Thesis
Experimental: 85%
Documentation: 15%

Specific Requirements
Interest in Cell Biology, Molecular Biology and experimental work. Knowledge and interest in skeletal physiology (bone and cartilage) required. The candidate should enjoy work in an interdisciplinary group.

Supervisor
Prof. Willy Hofstetter
University of Bern, Department Clinical Research, Bone Biology & Orthopaedic Research
(http://www.bonebiology.dkf.unibe.ch/)

First Examiner
Prof. Willy Hofstetter
University of Bern, Department Clinical Research, Bone Biology & Orthopaedic Research
(http://www.bonebiology.dkf.unibe.ch/)

Contact
Prof. Willy Hofstetter: hofstetter@dkf.unibe.ch / +41 31 632 8786