

Offre de thèse : Rôle des ostéocytes dans la réparation osseuse

Osteocyte role in bone repair

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Résumé / abstract:

Bone regeneration is one of nature's perfectly adapted processes to allow for a scar-free healing of a fractured bone. Yet, when this mechanism is pathologically impaired e.g. with a critical defect, or due to underlying diseases, research solutions are required. Scaffolds bridging the defect and aiding the healing process are a promising avenue, and while new biomaterials will be useful for clinical applications in the future, it is of paramount importance to firstly understand the detailed mechanistic cellular interplay with bone regeneration. Already, the biochemical communication of osteoprogenitor cells, endothelial and immune cells during bone regeneration are subject to ongoing studies. We hypothesize that osteocytes, as inhabitants of the mineralized bone matrix, contribute to healing and possess a functional significance in bone regeneration. Osteocytes represent the vast majority of bone cells (90-95%) and form a connective, mechanosensory cellular network with their long cytoplasmic processes called dendrites. Historically the functional analysis of osteocytes was challenging because they are encased in the mineralized bone matrix, and only recently osteocytes were described as secretory cells of endocrine importance. With their potential high expression of second messengers, osteocytes are orchestrating the local bone remodeling, controlling new bone formation by osteoblasts and the resorption of matrix by osteoclasts. On the other hand, the death of osteocytes and the impaired dendritic network are seen with several bone pathologies i.e. osteoporosis, a disease in which the fracture risk is increased due to lower bone density and a lack of a physiological balance of bone remodeling. With the disruption of the osteocyte network due to a fractured bone, and bone regeneration involving an intricate regulation of matrix turnover, a regulatory role of osteocytes seems likely. However, their role in the complex process of bone repair is not well known. Our project aims to investigate the role of osteocytes in the healing process of bone, utilizing a murine calvarial defect model. Our three objectives are: i) to characterize the role of a viable osteocyte-network in the healing of calvarial bone defects in female and male WT mice, ii) to determine the role of osteocyte network-vessel communication during calvarial bone healing using a transgenic mouse model, and iii) to dissect the effect of impaired osteocyte networks on the healing of calvarial bone defects, using an aged mouse model and a transgenic mice model with deficient mechanosensation. This project will be realized in collaboration with a German team from Hamburg, who possesses a joint expertise on osteocyte biology, defect healing and imaging that will result in novel discoveries in the field that are also of importance for general bone biology.

Key words for this project: osteocytes, mice model, calvaria defect, cell culture, imaging, laser micro dissection, qPCR, microCT analysis

Qualities of the future PhD student: curious, smart, independent, enthusiast about research, good English and communication skills, good abilities to work with other people, background in biology or physiology