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**MAPK-ACTIVATED PROTEIN KINASE-2 REGULATES
PHYSIOLOGICAL BONE TURNOVER**

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Mitogen-activated protein kinase (MAPK)-activated protein kinase-2 (MK2) is a main target of MAPK p38, a key intracellular signal transduction molecule mediating osteoclastogenesis and inflammation. MK2 deficient mice are healthy and fertile in contrast to p38 deficient mice. Aim of this study is to determine whether MK2 contributes to the regulation of physiological bone turnover and to identify a potential mechanism.

To determine the bone phenotype the authors analysed a Tartrate resistant acid phosphatase (TRAP)-staining and a goldner staining of the tibia by histomorphometrie and did a μ CT scan of the tibia. The mechanical stability of the bone was detected using the four point bending experiment. Serum bone turnover markers (Osteocalcin and RatLaps) and serum level of Receptor activator of nuclear factor κ B ligand (RANKL) and Osteoprotegrin (OPG) were detected by ELISA. To analyse osteoclastogenesis the authors determined the number of osteoclast precursor cells in the bone marrow by Fluoreszenz activated cell sorter (FACS) and generated osteoclasts from bone marrow cells ex vivo. To analyse intracellular signalling pathways, the authors stimulated these osteoclasts with tumour necrosis factor α (TNF α) and detected the phosphorylation of kinases by western blot. Gene expression of osteoclasts was detected by real-time PCR.

Histomorphometrie showed increased trabecular volume and trabecular number and decreased trabecular separation in MK2 deficient mice compared to wildtype. The μ CT analysis confirmed these results and showed an increased bone density in MK2 deficient mice. Thus the four point bending experiment demonstrated a higher mechanical stability of bone of these mice. The number of osteoclasts was reduced while the number of osteoblasts was not altered in MK2 deficient mice. Serum Osteocalcin and RatLaps levels were decreased while OPG was increased and RANKL was not altered. Ex vivo osteoclastogenesis was clearly reduced in MK2 deficient mice compared to wildtype mice while the number of CD11b precursors in the bone marrow was equal. The phosphorylation of p38, serine/threonine protein kinase (AKT) and extracellular signal regulated kinase (ERK) was increased in TNF α stimulated MK2 deficient osteoclasts. Gene expression of TRAP, osteoclast associated receptor (OSCAR), matrix metalloproteinase 9 and receptor activator of nuclear factor κ B (RANK) was decreased in MK2 deficient osteoclasts.

MK2 deficient mice have an increased bone density and a reduced number of osteoclasts. This is due to impaired osteoclastogenesis in consequence of reduced expression of osteoclast specific genes. Thus MK2 plays an important role in physiological bone turnover by regulating osteoclastogenesis.