

Selective inactivation of Stat3 in osteoclasts affect bone mass differently in female and male mice

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Signal Transducer and Activator of Transcription 3 (Stat3) is activated by the binding of various cytokines to their receptors, such as IL-6. Previous studies have revealed that conditional knockouts of Stat3 in osteoblasts and osteocytes cause a decrease in bone mineral density and strength. To study the role of Stat3 in osteoclasts, osteoclast-specific knockout mice were created using cre-lox recombination. Bone mineral density (BMD) and bone mineral content (BMC) were calculated for femurs and the fourth lumbar vertebra (L4) of 8 weeks old mice. Analysis revealed a decrease in BMD of femurs of osteoclast-selective Stat3 knockout (KO^{Oc}-Stat3) mice compared to their littermate control ($p < 0.05$). There was also a decrease in BMC of the femurs of KO^{Oc}-Stat3 mice compared to the littermate controls ($p < 0.05$).

Analysis of μ CT data from trabecular bone in the distal femur showed significant decreases in trabecular number and bone volume/tissue volume in both male and female KO^{Oc}-Stat3 mice. Trabecular separation was increased in male and female KO^{Oc}-Stat3 mice.

Bone histomorphometry at the distal femur revealed a significant decrease in bone formation rate in males and females KO^{Oc}-Stat3 mice compared to the littermate controls. Osteoclast number identified by tartrate resistant acid phosphatase (TRAP) stain in female KO^{Oc}-Stat3 mice was significantly deficient from their control.

These data suggest that inactivation of Stat3 in osteoclasts influences bone metabolism through both osteoblasts and osteoclasts. Knockout of Stat3 in either cell type leads to decreases in bone strength, making Stat3 a good drug target for treatment of diseases such as osteoporosis.

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