

MIR-146A AN IMPORTANT KEY PLAYER IN BONE METABOLISM

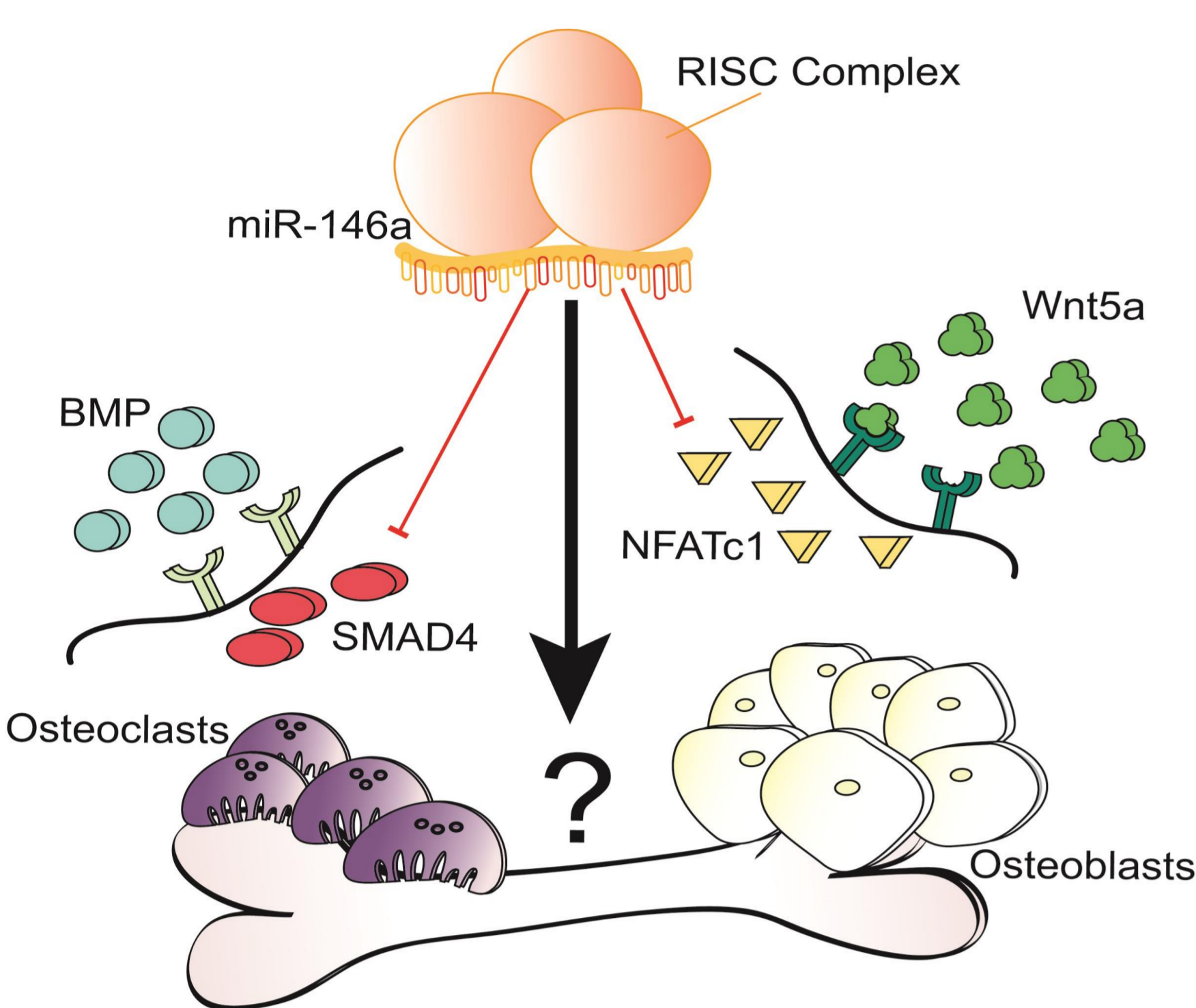
DIVISION OF RHEUMATOLOGY

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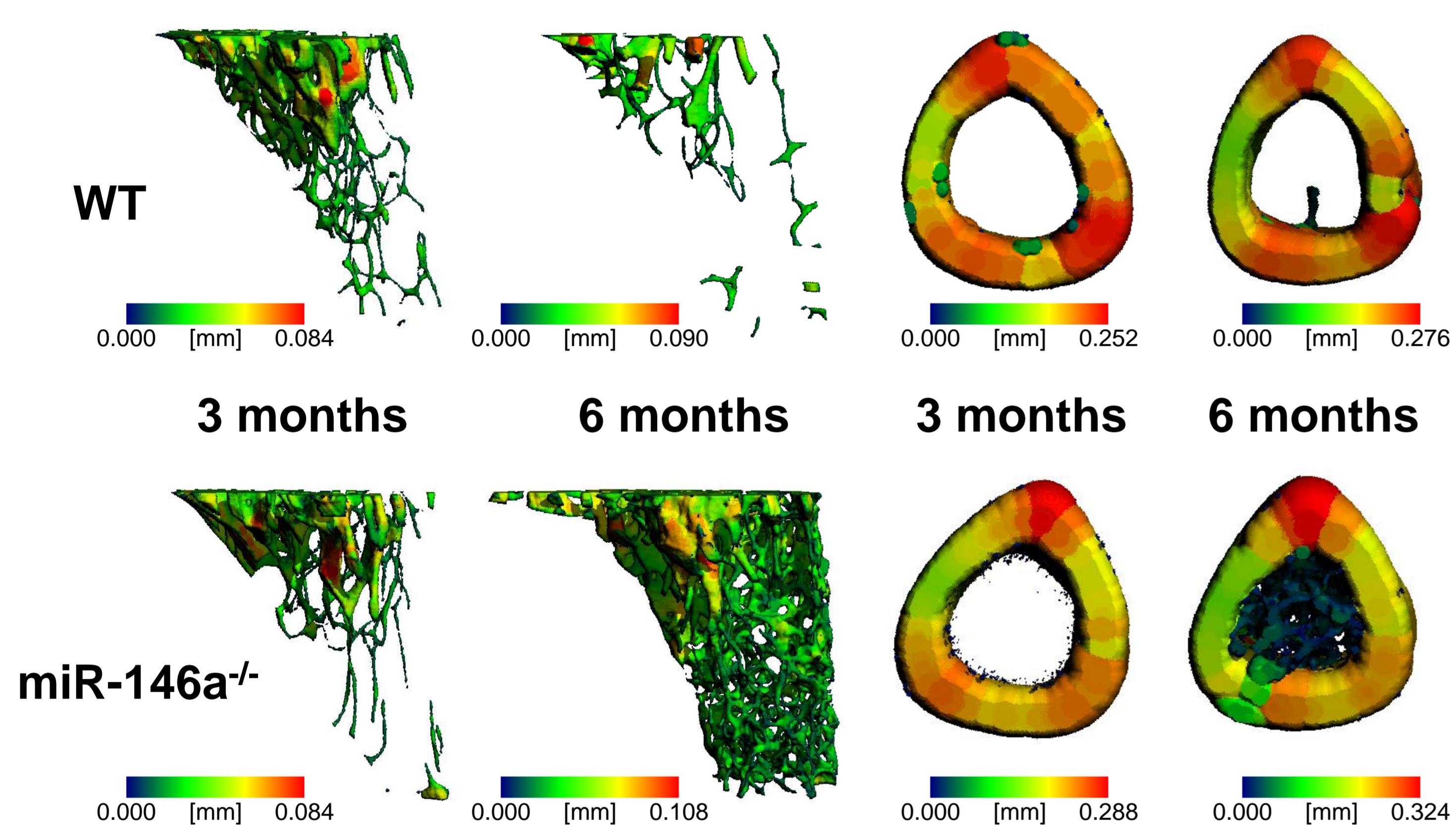
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Background

Micro RNAs (miRNAs) play a crucial role in the regulation of bone metabolism. MiR-146a, an important anti-inflammatory miRNA, was found to negatively impact osteogenesis and bone regeneration in vitro, by controlling the differentiation of mesenchymal stem cells. But to date the role of miR-146a in bone remodelling, its influence on bone stability and development of osteoporosis is not known.

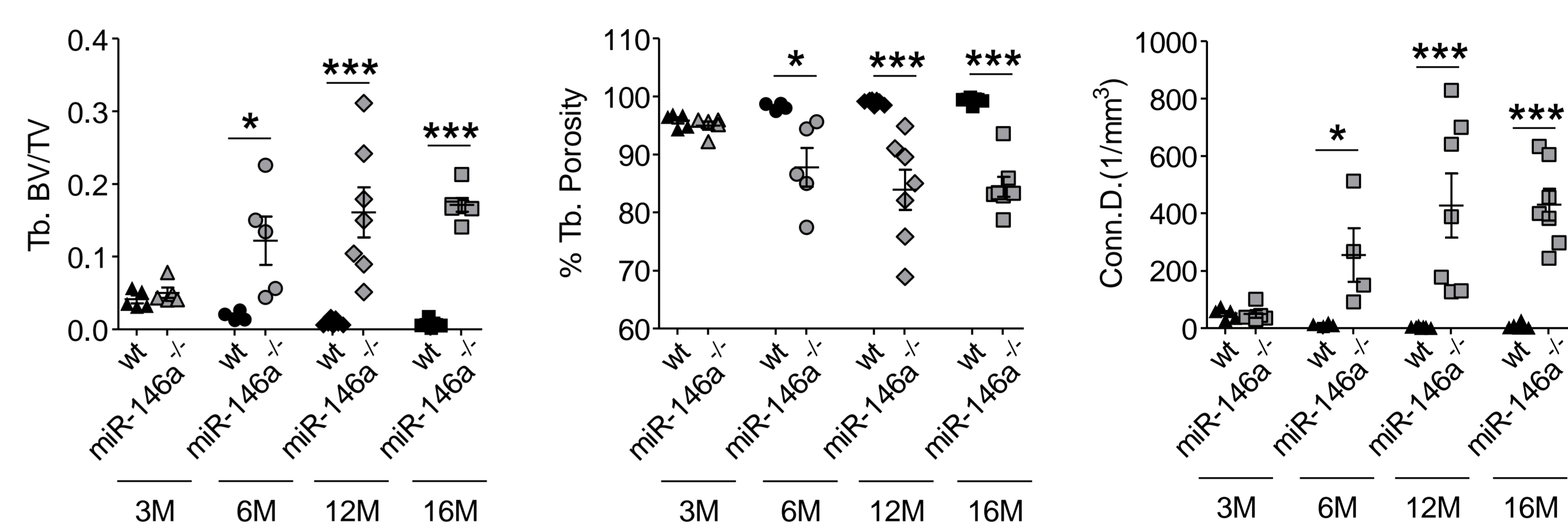


A Trabecular and cortical bone volume of miR-146a^{-/-} animals increases with age



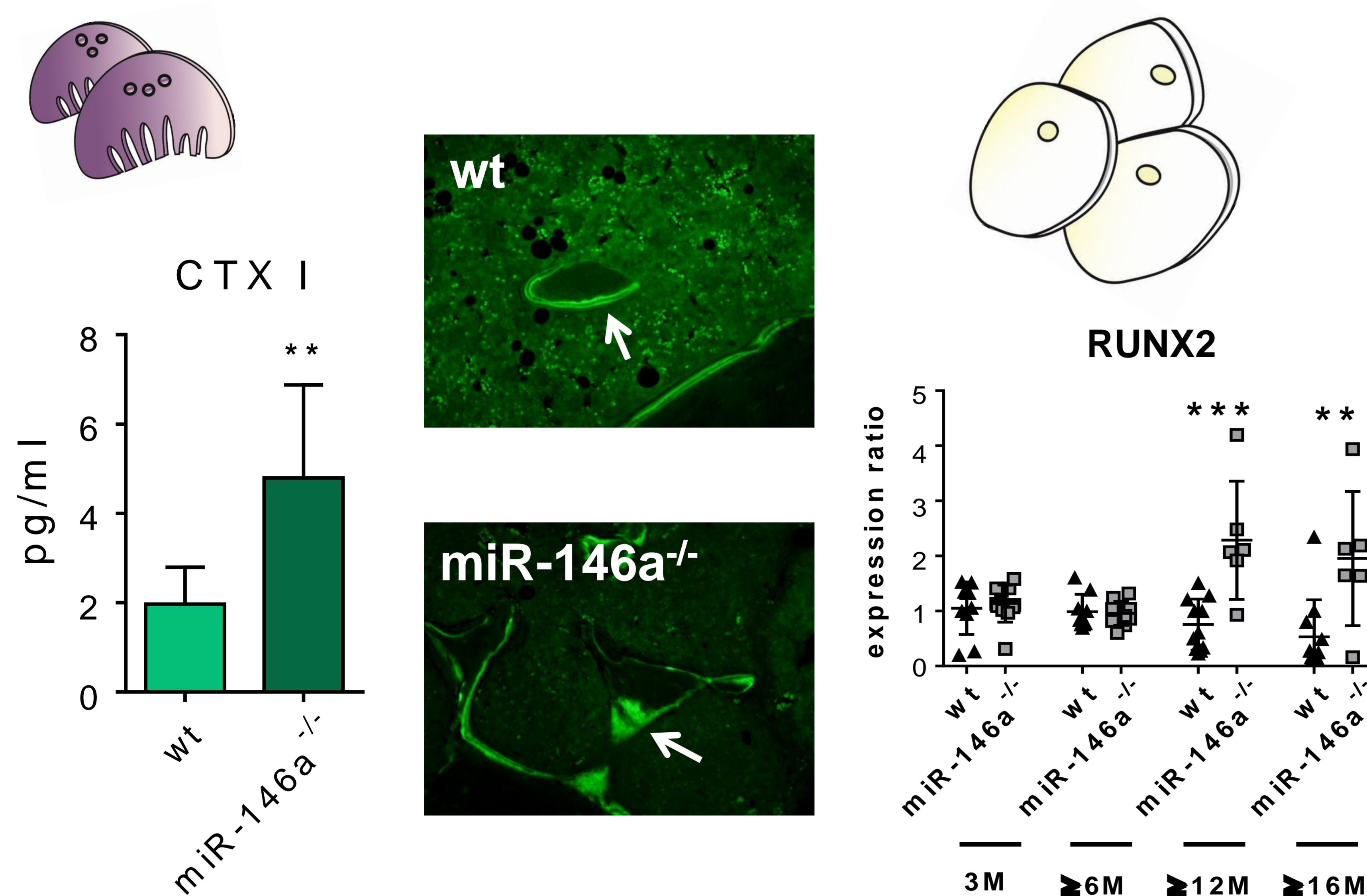
A, μ CT pictures of trabecular and cortical bone from wild type (wt) and miRNA-146a deficient tibial bone, over an age of 3 to 6 months.

B Trabecular bone of miR-146a^{-/-} animals show different porosity and interconnectivity



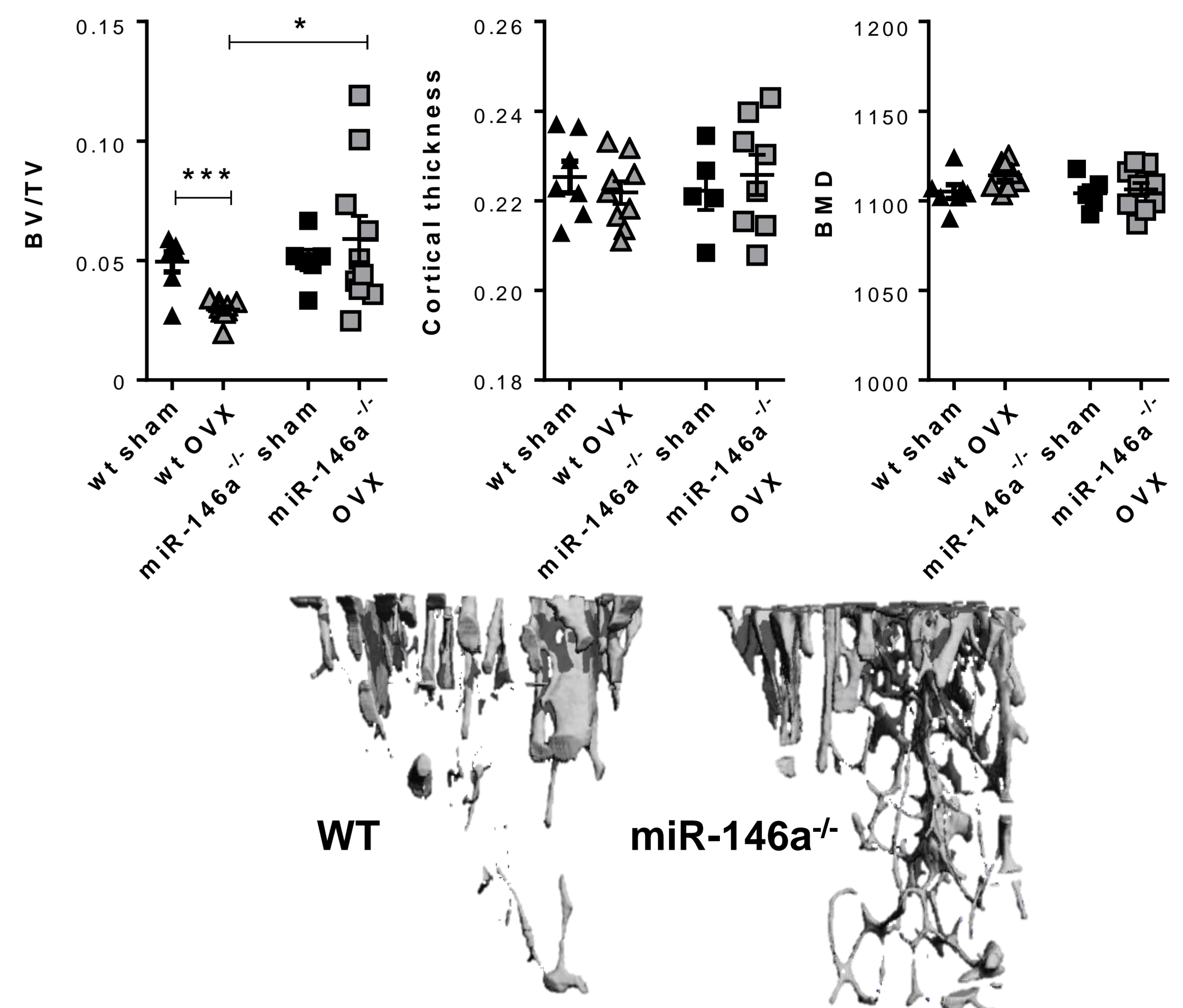
B, μ CT analysis of trabecular bone from wt and miR-146a^{-/-} tibiae (Tb) was done over an age of 3 to 16 month. Shown are Bone volume per Tissue volume (BV/TV), trabecular Porosity (Tb.Porosity) and Connectivity Density (Conn.D.).

C Aged miR-146a deficient animals show activated Osteoclasts as well as Osteoblasts



C, Protein expression level of β -CrossLaps (CTXI) in sera of wt and miR-146a deficient animals was analysed by Elisa. Histological pictures of Calcein labelled trabecular bone of wt and miR-146a^{-/-} animals. Expression level of RUNX2 was assessed in femoral bones of wt and miR-146a^{-/-} animals over an age of 3 to 16 months.

D MiR-146a^{-/-} animals are protected from OVX induced bone loss



D, WT and miR-146a^{-/-} animals were ovariectomized, sham operated animals were used as controls. After four weeks μ CT analysis of bone volume per tissue volume (BV/TV), Cortical thickness and Bone mineral density (BMD) was done.

Conclusion

MiR-146a seems to control bone turnover and miR-146a deficient mice accrue bone over time. Moreover this miRNA has a negative influence on bone loss occurring during oestrogen loss induced osteoporosis. Therefore miR-146a could be possibly used as therapeutic target in the treatment of osteoporosis.