A211 PPARß REGULATES BONE-METABOLISM BY FACILITATING WNT-SIGNALLING

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Background Peroxisome proliferator-activated receptors (PPARs) act as key factors during the regulation of fat and glucose metabolism. In addition, the PPARγ isoform has been implicated as major catabolic regulator of bone homeostasis in mice and humans.

Materials and methods By using PPARß-specific agonists and PPARß-deficient mice, the authors analysed the role of PPARß in osteoblasts and bone homeostasis in vitro and in vivo.

Results Here the authors describe a novel role of its family member PPARß as anabolic regulator of bone. In contrast to PPARγ, PPARß acted in a permissive manner on Wnt-signalling in osteoblasts. Activation of PPARß induced expression of the Wnt-co-receptor LRP5, promoted nuclear accumulation of ß-catenin and consequently enhanced TCF-driven transcriptional activity. Thereby, PPARß augmented expression of different Wnt-dependent genes, such as *osterix* and *osteoprotegerin* (*opg*), in osteoblasts. Consequently, activation of PPARß in osteoblasts blocked the differentiation of bone-resorbing osteoclasts. Mice deficient in PPARß, displayed reduced Wnt-signalling activity and low serum levels of OPG associated with increased differentiation of osteoclasts and osteopenia. Conversely, pharmacological treatment with PPARß-specific agonist blocked the formation of osteoclasts in vivo and protected mice from ovariectomy-induced bone loss.

Conclusion These data reveal a so far unrecognised role of PPARß in the crosstalk between energy metabolism and bone homeostasis and highlights its potential to serve as a target for the treatment of osteoporosis.

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