PPARβ REGULATES BONE-METABOLISM BY FACILITATING WNT-SIGNALLING

Carina Scholtysek,1 He Fu,2 Julia Katzenbeisser,1 Stefan Uderhardt,1 Christina Böhm,1 Jean-Pierre David,1 Béatrice Desvergne,2 Georg Schett,1 Gerhard Krönke1 1Department of Internal Medicine 3, University of Erlangen-Nuremberg, Germany; 2Center for Integrative Genomics, National Research Center Frontiers in Genetics, University of Lausanne, Lausanne, Switzerland

10.1136/ard.2010.149021.21

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 PPARβ-specific agonists and PPARβ-deficient mice, the authors analysed the role of PPARβ in osteoblasts and bone homeostasis in vitro and in vivo.

Results Here the authors describe a novel role of its family member PPARβ as anabolic regulator of bone. In contrast to PPARγ, PPARβ acted in a permissive manner on Wnt-signalling in osteoblasts. Activation of PPARβ induced expression of the Wnt-co-receptor LRP5, promoted nuclear accumulation of β-catenin and consequently enhanced TCF-driven transcriptional activity. Thereby, PPARβ augmented expression of different Wnt-dependent genes, such as osterix and osteoprotegerin (opg), in osteoblasts. Consequently, activation of PPARβ in osteoblasts blocked the differentiation of bone-resorbing osteoclasts. Mice deficient in PPARβ, displayed reduced Wnt-signalling activity and low serum levels of OPG associated with increased differentiation of osteoclasts and osteopenia. Conversely, pharmacological treatment with PPARβ-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 PPARβ in the crosstalk between energy metabolism and bone homeostasis and highlights its potential to serve as a target for the treatment of osteoporosis.