

OSTEOSCOOP

News on current events in osteoporosis and rheumatology

Mechanical loading, PPAR γ , and osteoblastogenesis

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The differentiation of multipotent stemcells of mesodermal origin results in the formation of adipocytes, chondrocytes, osteoblasts, and myoblasts. In humans, osteoporosis and age-related osteopenia are associated with an increase in marrow fat tissue and osteoblast numbers correlated negatively with the number of adipocytes. Osteoblastic differentiation is driven by *runx2*, and then characterized by the expression of alkaline phosphatase, osteocalcin, and eventually by the mineralization of the extracellular matrix. Differentiation of adipocytes is initiated through C/EBP α and C/EBP β that activate expression of peroxisome proliferator-activated receptor γ (PPAR γ), a member of the nuclear hormone receptor family. PPAR γ regulates adipocyte-specific gene expression and is critical for the formation of mature lipid-filled adipose cells. Recent studies have demonstrated that PPAR γ ligands, thiazolidinediones, induce changes in bone mineral density in elderly patients with type 2 diabetes. Because a lack of mechanical information favors the development of adipocytes at the expense of osteoblasts, a recent study [1] tested the hypothesis that the PPAR γ -dependent balance between osteoblasts and adipocytes is affected by mechanical stimuli through in vivo rodent osteogenic exercise, in vitro cyclic loading of cancellous haversian bone samples, and cyclic stretching of primary stromal cells and C3H10T1/2 cells, a pluripotent mesenchymal cell line.

The authors found that running rats exhibit a decreased marrow fat volume associated with an increased bone formation, presumably through recruitment of osteoprogenitors. In the tissue culture model and primary stromal cells, cyclic loading induced higher Runx2 and lower PPAR γ 2 protein levels. Given the proadipocytic and antiosteoblastic activities of PPAR γ , the effect of cyclic stretching was evaluated in C3H10T1/2 cells, treated either with a PPAR γ activator (rosiglitazone), or antagonist (GW9662). On rosiglitazone, cyclic stretch partially overcomes the induction of adipogenesis and is still able to favor osteoblast differentiation. Conversely, cyclic stretch has additive effects with GW9662 in inducing osteoblastogenesis.

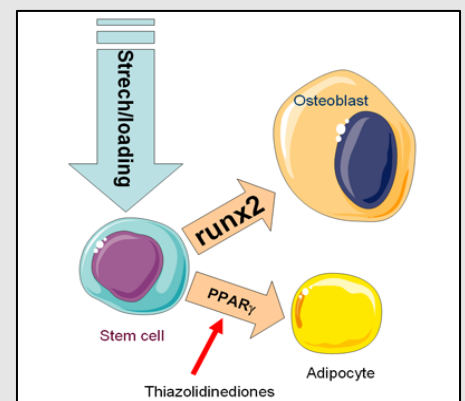
This study provides evidence that mechanical stimuli are potential PPAR γ modulators counteracting adipocyte differentiation and inhibition of osteoblastogenesis.

1. David V et al *Endocrinology*. 2007;148: 2553–2562.

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