

OSTEOSCOOP

News on current events in osteoporosis and rheumatology

Modulation of osteoclastogenesis by fatty acids

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Clinical studies have shown that total body fat mass is related to both bone density and fracture risk and that fat ingestion reduces bone turnover. These effects are at least partially mediated by endocrine mechanisms, but it is possible that lipids might act directly on bone. This study [1] assessed the effects of broad fractions of milk lipids in osteoblasts, bone marrow, and neonatal mouse calvariae.

Several milk fractions and their hydrolysates inhibited osteoclastogenesis in bone marrow cultures, so the effects of free fatty acids were assessed in this model. Saturated fatty acids (0.1–10 µg/ml) inhibited osteoclastogenesis in bone marrow cultures and osteoclast-like RAW264.7 cells. This effect was maximal for C14:0 to C18:0 fatty acids. The introduction of greater than 1 double bond abrogated this effect; ω3 and ω6 fatty acids had comparable low activity. Osteoblast proliferation was modestly increased by the antiosteoclastogenic compounds, ruling out a nonspecific toxic effect. Active fatty acids did not consistently change expression of RANKL or osteoprotegerin in osteoblastic cells nor did they affect the activity of key enzymes in the mevalonate pathway. However, receptors known to bind fatty acids were found to be expressed in osteoblastic (GPR120) and osteoclastic (GPR40, 41, 43, 120) cells. A synthetic GPR 40/120 agonist mimicked the inhibitory effects of fatty acids on osteoclastogenesis.

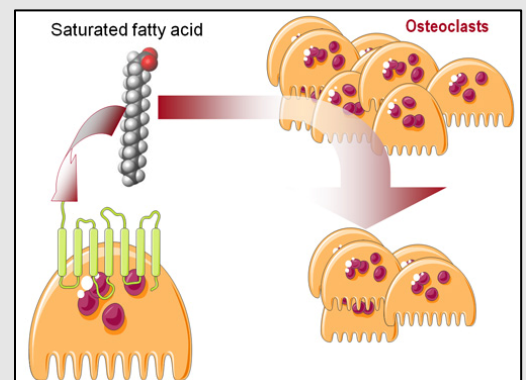
These findings provide a novel link between lipid and bone metabolism, which might contribute to the positive relationship between adiposity and bone density as well as provide novel targets for pharmaceutical development.

1. Cornish J et al. *Endocrinology*. 2008;149:5688-5695.

Modulation of osteoclastogenesis by fatty acids

Because several milk fractions and their hydrolysates inhibited osteoclastogenesis in bone marrow cultures, the effects of free fatty acids were assessed in this model. Saturated fatty acids (0.1–10 µg/ml) inhibited osteoclastogenesis in bone marrow cultures and osteoclast-like cells. This effect was not related to a change in the RANK ligand - osteoprotegerin balance. Instead, free fatty acids interact with membrane receptors to inhibit osteoclastogenesis. Pharmacological agonists of these receptors mimic the effect of fatty acids.

These findings provide a novel link between lipid and bone metabolism, which might contribute to the positive relationship between adiposity and bone density.



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