

Adipocyte-secreted factors and higher bone mass in obese people

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Several studies have reported controversial results about the positive correlation between the body fat mass and bone mineral density. It remains unclear whether some adipocyte-secreted factors can act on bone metabolism, directly on osteoblasts, to favor bone formation or osteoclasts, which control bone resorption. The authors of this study [1] investigated the effect of fat cell secreted molecules on proliferation and differentiation of preosteoblasts.

They showed that fat cell secretion factors increased proliferation of murine preosteoblast cells by almost 3-fold. This proliferation was reduced by inhibiting FGFR1, the receptor of FGF. Accordingly, the authors evidenced that human adipocytes secreted bFGF. This molecule alone is sufficient to induce preosteoblast proliferation. When preosteoblasts were stimulated to proliferate by adipocyte-secreted factors, the OPG/RANKL ratio increased 9-fold in a PI3K-dependant manner. OPG (osteoprotegerin) is a well-known inhibitor of osteoclast differentiation and bone resorption. On the other hand, RANKL promotes osteoclast differentiation. Moreover, stimulated pre-osteoblasts inhibited the formation of mature osteoclasts.

In conclusion, human adipocytes secrete factors that directly act on preosteoblasts and alter their crosstalk with osteoclasts. This study highlights the effects of adipocytes on bone metabolism and argues in favor of the positive relationship between body fat mass and bone mineral density. It could explain the higher bone mass in obese people.

1. Kühn MC et al. *Mol Cell Endocrinol.* 2011; Doi :10.1016/j.mce.2011.10.018.

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Adipocytes produce basic fibroblast growth factor (bFGF) which interacts with its receptor (FGFR1) at the surface of preosteoblastic cells. This interaction activates phosphoinositide 3-kinase (PI3K). This activation triggers preosteoblast proliferation but has no direct effect on osteoblast differentiation that occurs after proliferation. PI3K activation also leads to increased expression of osteoprotegerin (OPG), a strong inhibitor of osteoclast differentiation and to decreased expression of RANKL, an osteoclast differentiation inducer. The resulting increase in OPG/RANKL ratio affects osteoclast differentiation. These data provide a rationale for the positive relationship between body fat mass and bone mineral density.

