

OSTEOSCOOP

News on current events in osteoporosis and rheumatology

Osteocalcin: a skeleton key to metabolism

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A link between energy metabolism and bone has long been suspected but poorly defined. Obesity protects against osteoporosis, and maturity-onset (type 2) diabetes is associated with increased bone mineral density and fewer fractures. A direct link was made with the discovery that the adipocyte-derived hormone leptin acts on the osteoblasts to inhibit bone formation through hypothalamic and sympathetic nervous system relays. Working on the hypothesis that endocrine regulation requires feedback control, the same investigators complete a previously unknown endocrine circuit with their discovery [1] that the skeleton is a ductless gland, whose osteoblasts secrete osteocalcin, a protein that profoundly influences insulin production and sensitivity and fat metabolism.

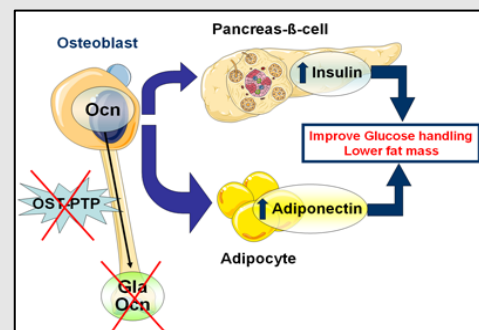
Lee et al. [1] examined the phenotype of mice lacking the protein tyrosine phosphatase OST-PTP, an enzyme which induces a post-translational modification of osteocalcin whereby glutamic acid residues are carboxylated to form γ -carboxyglutamic acid (Gla) residues. Gla residues confer to osteocalcin a high affinity for mineral ions and potentiate the role of this protein in extracellular matrix mineralization. Mice lacking OST-PTP are hypoglycemic and are protected from obesity and glucose intolerance because of an increase in pancreatic β -cell proliferation, insulin secretion, and peripheral insulin sensitivity. In contrast, mice lacking the osteoblast-secreted molecule osteocalcin display decreased β -cell proliferation and insulin secretion, and increased insulin resistance. Removing one osteocalcin allele from OST-PTP-deficient mice corrects their metabolic phenotype. Ex vivo experiments revealed that osteocalcin can stimulate insulin expression in β -cells and adiponectin, an insulin-sensitizing adipokine, in adipocytes; in vivo osteocalcin can improve glucose tolerance.

By revealing that the skeleton exerts an endocrine regulation of sugar homeostasis this study expands the biological importance of this organ and the role of osteoblasts and our understanding of energy metabolism.

1. Lee NK et al. *Cell*. 2007;130: 456-469.

Osteocalcin: a skeleton key to metabolism

Osteocalcin is normally converted into its Gla-derivative through the action of the tyrosine phosphatase OST-PTP. In the absence of this enzyme, the endocrine Osteocalcin increases the secretion of insulin by pancreatic β -cells and of adiponectin by adipocytes. These effects result in improved glucose handling and in lowering of fat mass.



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