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Osteocalcin differentially regulates β -cell and adipocyte gene expression and affects the development of metabolic diseases in mice

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The osteoblast-specific secreted molecule osteocalcin behaves as a hormone regulating glucose metabolism and fat mass in two mutant mouse strains [1]. In a recent study [2], the authors asked two questions: is the action of osteocalcin on β -cells and adipocytes elicited by the same concentrations of the molecule, and more importantly, does osteocalcin regulate energy metabolism in wild-type mice? Cell-based assays using isolated pancreatic islets, a β -cell line, and primary adipocytes showed that picomolar amounts of osteocalcin are sufficient to regulate the expression of the insulin genes and β -cell proliferation markers, whereas nanomolar amounts affect adiponectin and Pgc1 α expression in white and brown adipocytes, respectively. *In vivo* the same difference exists in osteocalcin's ability to regulate glucose metabolism on the one hand and affect insulin sensitivity and fat mass on the other hand. Furthermore, long-term treatment of wild-type mice with osteocalcin can significantly weaken the deleterious effect on body mass and glucose metabolism of gold thioglucose-induced hyperphagia and high-fat diet.

These results establish in normal, wild-type mice the importance of this novel molecular player in the regulation of glucose metabolism and fat mass and suggest that osteocalcin may be of value in the treatment of metabolic diseases.

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

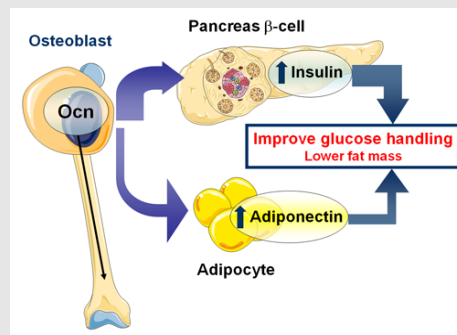
2. Ferron M et al. *Proc Natl Acad Sci USA*. 105: 5266-70, 2008.

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Beyond its local effects on bone, osteoblast-specific osteocalcin behaves as a hormone regulating glucose metabolism and fat mass in mutant mice. Picomolar amounts of osteocalcin are sufficient to regulate the expression of the insulin genes and β -cell proliferation markers, whereas nanomolar amounts affect adiponectin expression in adipocytes.

Long-term treatment of wild-type mice with osteocalcin can significantly weaken the deleterious effect on body mass and glucose metabolism of toxic-induced hyperphagia and high-fat diet.

Therefore, osteocalcin may be of value in the treatment of metabolic diseases.



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