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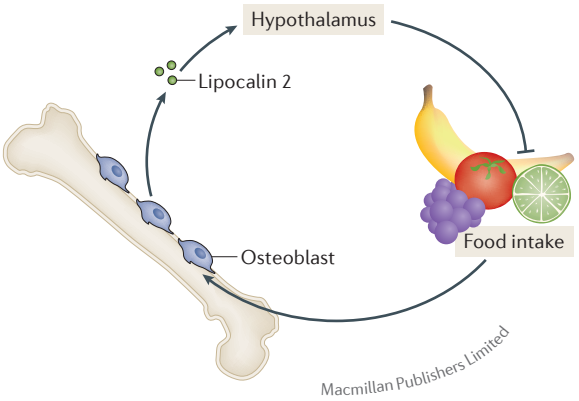
BONE

Osteoblast-derived lipocalin 2 suppresses appetite

> …upregulation of *Lcn2* … in osteoblasts after feeding seems to limit appetite…

The endocrine actions of bone have been expanded to include regulation of appetite by new findings published in *Nature*.

Lipocalin 2 is associated with obesity and was previously thought to be mainly secreted by adipose tissue; however, Stavroula Kousteni and colleagues now show that osteoblasts express lipocalin 2 at levels tenfold higher than in white adipose tissue. To determine the metabolic function of osteoblast-derived lipocalin 2, the investigators generated mice lacking lipocalin 2 in osteoblasts, adipocytes or globally.



Deletion of lipocalin 2 in adipocytes had no effect. By contrast, mice lacking lipocalin 2 in osteoblasts had increased appetite, as well as decreased glucose tolerance and insulin sensitivity. Mice with a global deletion of lipocalin 2 had a similar phenotype to mice lacking lipocalin 2 in osteoblasts. Re-feeding experiments in wild-type mice showed that serum levels of osteoblast-derived lipocalin 2 increased 1–3 h after re-feeding following an overnight fast, and food intake was suppressed 1–3 h after food intake. Thus, upregulation of *Lcn2*, the gene that encodes lipocalin 2, in osteoblasts after feeding seems to limit appetite after a meal. "This finding broadens our understanding of the control of appetite and expands the endocrine functions of bone," explains Kousteni.

The researchers were able to show that lipocalin 2 crossed the blood–brain barrier and bound to melanocortin 4 receptor (MC4R) in the hypothalamus, which activated the MC4R-dependent appetite-suppressing pathway. "This observation identifies a new ligand for MC4R," says Kousteni.

Interestingly, exogenous administration of lipocalin 2 in lean wild-type mice and leptin-deficient obese mice led to a chronic suppression of appetite. Lipocalin 2 could, therefore, ameliorate the deleterious consequences of leptin deficiency.

The researchers are now planning to examine the function of lipocalin 2 in humans. "Lipocalin 2 might be a new tool to explore the control of obesity and insulin resistance," concludes Kousteni.

Claire Greenhill

ORIGINAL ARTICLE Mosialou, I. *et al.* MC4R-dependent suppression of appetite by bone-derived lipocalin 2. *Nature* http://dx.doi.org/10.1038/nature21697 (2017)