

### Can worm-induced eosinophils prevent obesity?

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The hygiene hypothesis suggests that the absence of exposure to microorganisms in modern societies is responsible for the rise in chronic inflammatory diseases such as allergies and autoimmune diseases. However, can this be extended to the similar dramatic rise in metabolic disorders such as the metabolic syndrome and type 2 diabetes? Recent evidence has emerged that helminth infection can be important in preventing obesity and the glucose intolerance associated with the metabolic syndrome.



Picture of *Nippostrongylus* taken by Claire Hoving University of Cape Town, SA.

A recent publication in *Science* by Wu *et al.* (1) has shown that eosinophils, a cell type increased in allergies and helminth infection, can affect the activation state of adipose tissue macrophages. In obese mice the macrophages associated with adipose tissues are classically activated. They produce inflammatory mediators such as tumour necrosis factor  $\alpha$  (TNF $\alpha$ ) and a molecule called resistin, which in concert with an obesity associated reduction in adiponectin produced by the adipose tissue, results in cells becoming resistant to insulin and glucose intolerance. In lean mice, however, adipose tissue macrophages are of the alternatively activated phenotype characterised by the expression of peroxisome proliferator-activated receptor- $\gamma$  (PPAR $\gamma$ ) and arginase 1. Alternatively activated macrophages are induced by Interleukins (IL-4 and IL-13) the production of which is also classically associated with helminth infection. The authors used IL-4 reporter mice (where cells expressing IL-4 are fluorescent) to show that tissue dwelling eosinophils were the source of the IL-4 that induced alternatively activated macrophages in adipose tissue. The proof that this finding can relate to obesity and metabolic disorders was shown in two ways: hypereosinophilic mice had less adipose tissue and an improved response to glucose challenge. Conversely mice deficient in eosinophils were more obese and glucose resistant when fed the same diet than their respective wild type counterparts.

All of these experiments were carried out in infection free animals, so what happens when animals are infected by helminths? When the authors infected mice, which had been fed on a high fat diet, with the number of adipose tissue eosinophils increased and glucose tolerance improved. Importantly, these findings persisted long after the parasite was cleared.

Obesity is now being considered as an inflammatory disease and the disciplines of physiology and immunology are clearly more interlinked than previously thought. The vertebrate immune system has evolved with the constant presence of worms, and it seems that not only might being infected by these organisms be important in modulating the immune system, but also in preventing the common metabolic problems associated with a westernised life style. Perhaps we should revisit the Victorian procedure of selling pills containing tapeworm eggs as a weight reduction aid?

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3144160/?tool=pubmed>

Wu, D *et al.* 2011 Eosinophils sustain adipose alternatively activated macrophages associated with glucose homeostasis. *Science* **332**: 243-247