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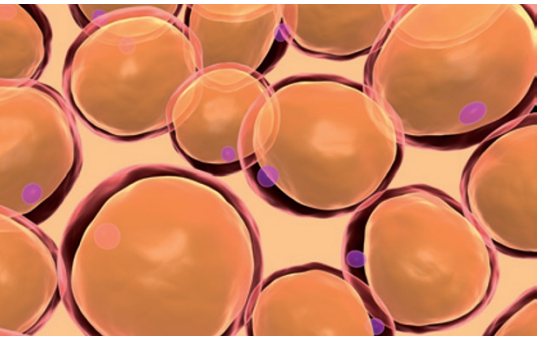
OBESITY

Rethinking inflammation and adipocyte homeostasis

New research published in *Cell Metabolism* reveals a role for 'healthy inflammation' in adipose tissue, which is required for adipocyte remodelling and expansion.

It is widely accepted that chronic systemic low-grade inflammation is associated with the development of obesity and metabolic dysfunction. Now, researchers from the Touchstone Diabetes Center at the University of Texas South Western Medical Center, USA, have uncovered a surprising role for localized acute inflammation in adipose tissue expansion, which is an important process for protecting against harmful deposition of lipids in tissues such as the liver.

"We thought that inflammation leads to metabolic disease, but actually we need some localized inflammation to prevent metabolic disease," explains senior researcher, Philipp Scherer.



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Preliminary studies demonstrated that injection of lipopolysaccharide into adipose tissues stimulated adipogenesis *in vivo*, which suggested that acute inflammation might have a positive role in adipocyte remodelling and homeostasis. The investigators assessed the effects of a high-fat diet (HFD) in mouse models of anti-inflammation to better understand the relationship between localized inflammation and adipocyte differentiation.

Feeding a HFD to mice that constitutively expressed a dominant-negative form of tumour necrosis factor (TNF) resulted in lower body weights and fat mass, as well as reduced glucose tolerance, in these animals compared to littermates fed a regular chow diet. Similarly, feeding a HFD to RID tg mice (in which multiple proinflammatory pathways, including toll-like receptor 4, TNF and IL-1β, were specifically blocked in adipocytes) led to reductions in fat pad mass, blunted responses to lipopolysaccharide, systemic insulin resistance and metabolic inflexibility.

In both models HFD feeding resulted in the development of severe hepatic steatosis, which was indicative of increased ectopic lipid deposition—a phenomenon that might explain the more pronounced metabolic disease in these mice compared with control mice fed a HFD.

White adipose tissue in the mesenteric fat pads of RID tg mice lacked the ability to sense and respond to proinflammatory stimuli (such as bacteria-derived toxins), which resulted in impaired intestinal barrier function, development of 'leaky gut' and subsequent chronic systemic inflammation and metabolic dysfunction.

These findings might explain the failure of anti-inflammatory therapeutic strategies to combat metabolic disease.

"A healthy immune system is essential for proper metabolic function," says Ingrid Wernstedt Asterholm, lead author of the study, "rather than trying to block inflammation in the context of metabolic disease, we should be seeking ways to improve the immune response."

Jennifer Sargent

Original article Wernstedt Asterholm, I. *et al.* Adipocyte inflammation is essential for healthy adipose tissue expansion and remodeling. *Cell Metab.* doi:10.1016/j.cmet.2014.05.005