

## The TNF superfamily member, LIGHT, attenuates fatty acid oxidation and insulin signalling in metabolic cell types and influences glucose tolerance and insulin sensitivity *in vivo*

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A vast number of soluble factors such as the pro-inflammatory cytokine TNF- $\alpha$  have been implicated in the aetiology of obesity and insulin resistance. Our current study focuses on the tumour necrosis factor (TNF) superfamily member, called LIGHT (Lymphotoxin-like, exhibits Inducible expression, competes with Herpes Simplex Virus Glycoprotein D for Herpesvirus Entry Mediator [HVEM] receptor expressed by T lymphocytes) or TNFSF14. Serum levels of LIGHT have been shown to be increased in morbidly obese humans. In addition, the receptors for LIGHT have been demonstrated to be highly expressed in visceral adipose tissue and hepatocytes. We aimed to determine whether LIGHT treatment of hepatocytes and adipocytes may promote inflammation and dysregulate fatty acid oxidation and insulin signalling. To determine the role of LIGHT on signal transduction pathways known to be important in inflammation, fat oxidation and glucose homeostasis, we measured levels of phosphorylation of c-jun amino-terminal kinase (JNK; Thr<sup>183</sup>/Tyr<sup>185</sup>), Acetyl CoA-Carboxylase  $\beta$  (ACCC $\beta$ ; Ser<sup>79</sup>) and Akt (Ser<sup>473</sup>) respectively. Treatment of hepatocytes and adipocytes with LIGHT resulted in decreased phosphorylation of ACC $\beta$ . In addition, treatment of hepatocytes with LIGHT reduced insulin stimulated phosphorylation of Akt and promoted increases in the phosphorylation of the serine threonine kinase JNK. Our data demonstrates for the first time that treatment of hepatocytes and adipocytes with LIGHT may directly inhibit critical signaling pathways involved in lipid homeostasis. Lastly, I will present the results of recent metabolic studies conducted in LIGHT deficient mice.

### Biography

Vance Matthews is an NHMRC Career Development Award Fellow at the Western Australia Institute for Medical Research. Since completing his PhD in 2002, he has completed successful post-doctoral positions in Germany, Western Australia and Melbourne. He has published over 36 manuscripts which have been published in premier journals including Journal of Biological Chemistry, Blood, Hepatology, Journal of Clinical Investigation, Journal of Experimental Medicine, Diabetes and Diabetologia. He regularly reviews for many peer review journals and he is a member of the "World Journal of Gastroenterology" editorial board.

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