

DYSLIPIDAEMIA

**ACTIVE BAT REDUCES
ATHEROSCLEROSIS**

Activating brown adipose tissue (BAT) increases plasma lipoprotein metabolism and accelerates clearance of their remnants by hepatic tissue according to new research published in *Nature Communications*. In turn, this process limits atherosclerosis and might be useful in developing therapies for this disease.

The investigators fed *APOE*3-Leiden.CETP* transgenic mice, a model of atherosclerosis that has human-like lipoprotein metabolism, with a diet that induces hyperlipidaemia and atherosclerosis. BAT was then activated using subcutaneous injections of a β 3-adrenergic receptor (β 3AR) agonist that mimics the effect of cold exposure and induces thermogenesis. Control mice received the same diet, but were injected with phosphate buffered saline.

Overall, mice receiving the β 3AR agonist lost weight (by up to –8% from their initial weight), and had less total gain of fat mass (–81%) than controls over 10 weeks. This effect was attributed to increased fatty acid oxidation (+67% over controls on the day of injection). Mice treated with the β 3AR agonist also had increased white adipose tissue browning compared with controls.

Activation of BAT reduced plasma levels of triglycerides and total cholesterol (approximately –54% and –23%, respectively). This effect was attributed to faster plasma turnover and increased hepatic uptake of lipoprotein remnants in β 3AR agonist-treated mice as measured using glycerol tri[3 H]oleate and [14 C] cholesteryl oleate-labelled particles that mimic VLDL.

Furthermore, mice treated with the β 3AR agonist had fewer atherosclerotic lesions (mean lesion area 43% lower than in control mice), which was correlated with reduced total plasma cholesterol exposure. Importantly, this antiatherogenic effect was abrogated in mice deficient in apolipoprotein E (apoE) and LDL receptor, which are essential for hepatic clearance of triglyceride-rich lipoprotein remnants.

The investigators comment that, “these findings demonstrate that activation of BAT reduces plasma (V)LDL-cholesterol through enhanced LDLR-mediated hepatic clearance of apoE-containing lipoprotein remnants and subsequently reduces atherosclerosis development.”

Tim Geach

Original article Berbée, J. F. P. *et al.* Brown fat activation reduces hypercholesterolaemia and protects from atherosclerosis development. *Nat. Commun.* doi:10.1038/ncomms7356