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METABOLISM

New insights into the BAT–liver–gut axis

Cold-induced brown adipose tissue (BAT) activation increases appetite and food intake, which can result in an excess of dietary cholesterol. Until now, however, the way the body adapts to this excess was unclear. New research reveals how the body maintains systemic cholesterol homeostasis under conditions of BAT activation and how these processes affect the composition of the gut microbiome.

"The increased uptake of dietary ingredients, such as cholesterol, following BAT activation was thought to promote the development of atherosclerosis," explains Joerg Heeren, corresponding author on the study. "Surprisingly, however, in previous studies we have shown the opposite — in mice, the activation of BAT is protective against atherosclerosis." In the present study, the authors investigated how the body adapts to the excess of dietary cholesterol after BAT activation to maintain cholesterol homeostasis.

To determine the cholesterol derivatives in various tissues, the authors performed lipidomic analyses of mice that had been exposed to cold to stimulate BAT activity. The authors found that cold-induced BAT activation had an enormous effect on the alternative bile acid synthesis pathway and specifically the key enzyme CYP7B1. Mechanistically, BAT activation resulted in increased hepatic expression of CYP7B1, as well as increased hepatic synthesis and faecal excretion of bile acids.

Next, the authors profiled the faecal microbiome of warm-housed and cold-housed mice by analysing the DNA sequence encoding the 16S ribosomal rDNA. The team reported that the cold-induced changes to cholesterol homeostasis altered the bacterial composition of the gut.

"Our study supports the concept that the processing of cholesterol to bile acids by the host, but not the diet per se, determines the composition of the gut microbiome," explains lead author Anna Worthmann. "We believe that targeting the activation of CYP7B1 might be a novel strategy to treat metabolic diseases by reducing levels of cholesterol and/or by enhancing energy expenditure via BAT activation or via changing the gut bacteria."

Alan Morris

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