DIABETES

IL-13 AND GLUCOSE HOMEOSTASIS

Interleukin 13 (IL-13) has a key role in the regulation of hepatic glucose production in mice, new data reveal.

Novel, insulin-independent therapies for glycaemic management in type 2 diabetes mellitus are needed. Chronic inflammation has been shown to have a detrimental effect on glucose homeostasis in animal models. T helper type 1 (Th1) cytokines are implicated in triggering metabolic stress and chronic inflammation. By contrast, T helper type 2 (Th2) cytokines, such as IL-13, might help mitigate these proinflammatory responses and aid a return to normal glucose homeostasis.

Stanya and co-investigators used mice in which the *IL-13* gene had been deleted to examine the role of IL-13 in metabolic homeostasis. First, the researchers fed *IL-13*^{-/-} mice with the common C57BL/6 genetic background a normal chow diet. These C57BL/6 *IL-13*^{-/-} mice progressively gained weight and developed glucose intolerance and hepatic insulin resistance. The researchers also fed a different genetic strain of *IL-13*^{-/-} mice a high-fat diet. These mice had the BALB/c genetic background, which is characterised by a strong Th2 response and resistance to metabolic disease. The BALB/c *IL-13*^{-/-} mice had elevated concentrations of fasting glucose and triglycerides and increased hepatic glucose production compared with control mice. Although these mice displayed hyperglycaemia, insulin sensitivity was not altered compared with that in the control mice.

Next, the researchers demonstrated that C57BL/6 *IL-13*^{-/-} mice had increased expression of genes involved in hepatic gluconeogenesis. However, recombinant IL-13 treatment in these mice normalized gluconeogenic gene expression. The investigators identified the transcription factor STAT3 as the mediator of the suppressive effect of IL-13 on gluconeogenic gene expression. Furthermore, in hepatocytes in which *Stat3* or IL-13 receptor $\alpha 1$ (*IL-13\alpha 1*) were lacking, the effect of IL-13 on inhibition of glucose production was lost.

The researchers conclude that IL-13 regulates glucose homeostasis via the *IL-13\alpha 1*–STAT3 signalling pathway in the liver, and that this pathway might provide a target for glycaemic control in type 2 diabetes mellitus.

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