Microbe-derived acetate suppresses NAFLD/NASH development via hepatic FFAR2 signalling in mice

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Video Byte

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Abstract

In the US and east Asia, non-alcoholic fatty liver disease (NAFLD) affects at least a quarter of the population. This disease is the manifestation of metabolic syndrome in the liver and can progress to non-alcoholic steatohepatitis (NASH). The gut microbiome is likely a contributing factor in NAFLD development and progression. Recently, researchers sought to identify the mechanisms that link the two together. They used a high-fat/fructose/cholesterol diet (HFC) to induce NALFD-like symptoms in mice and found that adding the prebiotic inulin to their diet ameliorated these symptoms. Inulin-fed mice had global changes to their microbiome, particularly elevated levels of the bacterial groups Bacteroides and Blautia. Inulin supplementation also increased their gut concentrations of short-chain fatty acids, like acetate. Further experiments found that species from Bacteroides and Blautia had a synergistic effect on acetate production. and that it was acetate, not other short-chain fatty acids like butyrate or propionate, that protected against NAFLD/NASH. Reducing the expression of the acetate receptor FFAR2 reduced the protective effect of inulin and may increase insulin resistance in the liver. These results suggest that there is a commensal microbiome-acetate-FFAR2 molecular circuit that improves liver insulin sensitivity and prevents the development of NAFLD/NASH.