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DIABETES

Genetically engineered *Lactobacilli* reprogram intestinal cells to secrete insulin and ameliorate hyperglycaemia

Oral administration of *Lactobacilli* engineered to secrete the inactive full-length form of glucagon-like peptide 1 (GLP-$1_{1–37}$) markedly reduces blood glucose levels, according to a new study in rats. The findings have potential implications for the treatment of patients with type 1 diabetes mellitus (T1DM).

Numerous strategies to replace β cells destroyed by autoimmune attack in T1DM have been proposed, including the reprogramming of pancreatic non-β cells and other tissue-specific cells into β cells or cells with insulin-secreting potential. Previously, the researchers showed that genetically engineered commensal bacteria could deliver GLP-$1_{1–37}$ to human intestinal carcinomas and stimulate glucose-responsive insulin secretion. In the current study the investigators tested whether similar bacteria could reduce hyperglycaemia in rats with streptozotocin-induced T1DM. "Our goal was to reprogram rat intestinal cells into glucose-responsive insulin-secreting cells through daily oral administration of GLP-$1_{1–37}$-secreting bacteria," explain the authors in their report.

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Diabetic rats fed GLP-$1_{1–37}$-secreting *Lactobacilli* daily for 50 days had higher levels of insulin and were more glucose-tolerant following an oral glucose tolerance test than those fed wild-type *Lactobacilli*; no significant difference was observed in levels of blood glucose and plasma insulin between diabetic rats fed genetically engineered *Lactobacilli* and nondiabetic control rats. Reduced hyperglycaemia in rats fed GLP-$1_{1–37}$-secreting *Lactobacilli* was accompanied by the appearance of insulin-secreting intestinal epithelial cells that expressed key β-cell markers (pancreas/duodenum homeobox protein 1, transcription factor MafA and forkhead box protein A2) indicative of reprogramming to an insulin-producing phenotype.

"These results provide evidence of the potential for a safe and effective nonabsorbed oral treatment for diabetes [mellitus] and support the concept of engineered commensal bacterial signalling to mediate enteric cell function *in vivo*," the authors conclude in their report.

David Holmes

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CORRECTION

Diabetes: Genetically engineered *Lactobacilli* reprogram intestinal cells to secrete insulin and ameliorate hyperglycaemia

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