Gut microbiota
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Akkermansia muciniphila induces gut microbiota remodelling and controls islet autoimmunity in NOD mice

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Abstract

Objective Intestinal microbiota is implicated in the pathogenesis of autoimmune type 1 diabetes in humans and in non-obese diabetic (NOD) mice, but evidence on its causality and on the role of individual microbiota members is limited. We investigated if different diabetes incidence in two NOD colonies was due to microbiota differences and aimed to identify individual microbiota members with potential significance.

Design We profiled intestinal microbiota between two NOD mouse colonies showing high or low diabetes incidence by 16S ribosomal RNA gene sequencing and colonised the high-incidence colony with the microbiota of the low-incidence colony. Based on unaltered incidence, we identified a few taxa which were not effectively transferred and thereafter, transferred experimentally one of these to test its potential significance.

Results Although the high-incidence colony adopted most microbial taxa present in the low-incidence colony, diabetes incidence remained unaltered. Among the few taxa which were not transferred, *Akkermansia muciniphila* was identified. As *A. muciniphila* abundancy is inversely correlated to the risk of developing type 1 diabetes-related autoantibodies, we transferred *A. muciniphila* experimentally to the

high-incidence colony. *A. muciniphila* transfer promoted mucus production and increased expression of antimicrobial peptide *Reg3γ*, outcompeted *Ruminococcus torques* from the microbiota, lowered serum endotoxin levels and islet toll-like receptor expression, promoted regulatory immunity and delayed diabetes development.

Conclusion Transfer of the whole microbiota may not reduce diabetes incidence despite a major change in gut microbiota, but single symbionts such as *A. muciniphila* with beneficial metabolic and immune signalling effects may reduce diabetes incidence when administered as a probiotic.

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Footnotes

Contributors: AH and WMDV designed the work; AH analysed data and wrote the first version of the manuscript; RT, SAP, CB, HP, PDC, JPO and RE performed experiments and/or analysed data; WMDV and PDC reviewed the manuscript and wrote parts of the final version, which all authors approved.

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