GUT MICROBIOTA

Mucin-munching bacteria modulate glucose metabolism

“*Akkermansia muciniphila* ... has a key role in systemic glucose metabolism

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The gut microbiota has a crucial role in metabolic health, but researchers are only just determining the mechanisms underpinning this effect. In two new papers, investigators have found that *Akkermansia muciniphila*, a bacteria that degrades mucin in the gut lining and can have beneficial effects on metabolic disorders, has a key role in systemic glucose metabolism and mediates the effect of the antidiabetic drug, metformin.

In one study, published in *Nature Communications*, Natalia Shulzhenko and her colleagues sought to determine if the inflammatory cytokine IFN γ influences the gut microbiota, both of which can modulate glucose homeostasis. The team found that, in IFN γ -deficient mice, which have improved glucose tolerance, the abundance of *A. muciniphila* was significantly increased, an effect that could be reversed by reintroduction of the cytokine. This effect was dependent on the presence of *A. muciniphila*, as mice lacking both IFN γ and this specific gut bacteria did not have improved glucose tolerance.

The team also identified a gene expressed in the ileum of the mouse that regulates the levels of *A. muciniphila* in response to IFN γ . “We computationally predicted a gene that is important for the control of this microbe in the gut and validated it experimentally,” add Shulzhenko and study co-author Andrey Morgun. “We found that *Irgm1* is a crucial mediator of the effect of IFN γ on *A. muciniphila*.”

Finally, the association between IFN γ , glucose tolerance and *A. muciniphila* was also found in humans, suggesting that a fundamental, conserved mechanism exists that could be therapeutically exploited in the future.

In another article in *Diabetes Care*, a team led by Juan Escobar examined the effect of metformin on the gut microbiota composition in 28 patients with type 2 diabetes mellitus (T2DM), 14 of whom were receiving metformin. Faecal samples were collected from each participant and from 84 control individuals who did not have T2DM. Microbial DNA was isolated from the faecal samples and subjected to 16S rRNA sequencing to determine the abundance of different microbiota communities.

The team found that metformin altered the composition of the gut microbiota. “We detected a higher relative abundance of *A. muciniphila* and a collection of bacteria involved in short-chain fatty acid production,” clarifies Escobar.

The team also found increased abundance of microbiota known to produce short-chain fatty acids such as butyrate and propionate, which can improve glucose homeostasis and have beneficial effects on hepatic glucose production, appetite and body weight.

“Metformin is a beautiful example of a molecule able to modulate the gut microbiota in positive ways,” highlights Escobar, who hopes that his work will help clinicians to enhance treatments to promote microbial health and improve patient welfare.

Tim Geach

ORIGINAL ARTICLES Greer, R. L. *et al.* *Akkermansia muciniphila* mediates negative effects of IFN γ on glucose metabolism. *Nat. Commun.* <http://dx.doi.org/10.1038/ncomms13329> (2016) | de la Cuesta-Zuluaga, J. *et al.* Metformin is associated with higher relative abundance of mucin-degrading *Akkermansia muciniphila* and several short-chain fatty acid-producing microbiota in the gut. *Diabetes Care* <http://dx.doi.org/10.2337/dc16-1324> (2016)