The gut microbiota plays a key role in treatment with classic diabetes medication

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A clearer picture of how the classic diabetes medication metformin works has emerged. A recent study at Sahlgrenska Academy and University of Girona indicates that the clinical effect – control of blood

glucose – is achieved through modulation of the gut microbiota.

"It is fascinating that it is not entirely clear how metformin works, although it has been used clinically for 60 years," says Fredrik Bäckhed, Professor of Molecular Medicine, and the leading researcher behind the study published in *Nature Medicine*.

The human body contains more bacteria than human cells. Most of these bacteria exist in the gut, which is the most densely populated ecosystem known today, where their genes (microbiome) complements our own genome with 1000-fold more genes.

Improved blood glucose control

Fredrik Bäckhed's research group at Sahlgrenska Academy has previously shown that the gut microbiota is altered in patients with type 2 diabetes and after bariatric surgery. By conducting a clinical study in patients with new onset diabetes, the group could clarify how the gut microbiomeis affected by metformin.

Sequencing of the microbiome of 22 patients before and after treatment compared with a placebo treated group of patients showed that the gut microbiome was altered dramatically within two months of treatment. Through experiments in the laboratory, the researchers demonstrated that metformin increases the growth of several bacterial species that are linked to improved metabolism.

"Transplantation of the gut microbiota from patients before and after treatment to bacteria-free mice showed that the metformin-modified microbiota may at least partially explain the good effects of metformin on blood glucose control," says Fredrik Bäckhed.

Some patients with type 2 diabetes can control their disease with

metformin, while others are not helped. Perhaps this is due to their microbiome configuration. Moreover, the most common adverse events are intestinal problems such as diarrhoea and abdominal pain.

"Imagine if we can change the intestinal flora in the future so that more people respond to treatment, and that adverse events can be reduced by changing the gut microbiota of patients who will take metformin," concludes Fredrik Bäckhed.

More information: Hao Wu et al. Metformin alters the gut microbiome of individuals with treatment-naive type 2 diabetes, contributing to the therapeutic effects of the drug, *Nature Medicine* (2017). DOI: 10.1038/nm.4345

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