

## What your gut bacteria can tell you about type 2 diabetes

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Identifying changes in the types and activities of microorganisms that live in the human gut could help early diagnosis of type 2 diabetes (T2D), a study by researchers from the Broad Institute in the US and Seoul National University, South Korea, has found.

The work, published in the open access journal *Genome Medicine*, examined variations in composition and function of the <u>gut microbiota</u> in relation to existing clinical T2D indicators like Body Mass Index (BMI) or Fasting Blood Sugar (FBS, the amount of glucose found in the blood after an overnight fast). The researchers showed that changes in the gut microbiota that can be observed in clinical T2D are already present at sub-clinical and pre-onset stages of the condition. The ability to detect changes like this before T2D symptoms develop might be useful for early diagnosis and intervention, thus providing a new way to potentially reduce the time between detection of T2D and onset and thus mitigate the effects of the disease.

While imbalances in the gut microbiota have been linked with T2D, previous research only compared cases of those with established T2D to healthy individuals. It was not clear whether changes in the microbiota occur before T2D can be detected with current markers like BMI and FBS. To find out whether this is the case and to identify links between T2D biomarkers, changes in the gut microbiota, and host genetics, the researchers examined a cohort of 20 identical (monozygotic) healthy Korean twins aged 30-48 years who were enrolled in the Healthy Twin Study in South Korea. As identical twins share the same genes, they



present a unique opportunity to identify aspects of disease linked to the gut microbiome - the collection of microorganisms living in the gut - separately from causes due to human genetic variation.

Curtis Huttenhower, the corresponding author, said: "Previous studies of the microbiome in T2D have examined extreme cases - individuals with established disease as compared to particularly healthy individuals - in order to identify imbalances in the gut microbiota linked to the disease. We set out to determine whether these microbial changes occur early on, in tandem with preclinical variation in typical T2D biomarkers such as BMI. It was also possible for us to take into account genetic contributions and temporal variation in the microbiome thanks to the participation of a group of twins who generously provided multiple samples over time."

The researchers collected physiological data like age, height and weight; clinical data like BMI and FBS; information on lifestyle and dietary habits; and 36 fecal samples with which to assess microbial community structure. For most individuals (16), one sample each was collected at the start of the study period and one sample each between 12 and 44 months later. For two pairs of twins (four individuals), only one time point's samples were available. This longitudinal sampling method allowed the researchers to observe changes in the microbiota between individuals and over time.

None of the individuals studied were yet diagnosed with full T2D, but the wide range of disease markers and the different levels at which they presented - from healthy to near-clinical - enabled the researchers to investigate for the first time how the function and composition of the microbial community in the gut vary at different stages before onset of the condition. Since other recent work has begun to catalog changes that occur in the gut after T2D onset, assessing whether these changes can be detected before the condition becomes apparent may enable early



diagnosis and aid our understanding of whether microbial or immune responses are also causal in disease development, which was not a part of this study

The methods used in this study could potentially be used in other twin cohorts to identify early microbial markers of other conditions at the presymptomatic stage, according to the researchers. Due to the small sample size of this study (20 individuals), further research needs to be done in larger cohorts to confirm these findings.

The twin-based design also led to an unexpected finding of the study: while twins had the same species of microorganisms living in their guts, these species were present as different strains. Curtis Huttenhower, said: "It suggests that twins are initially colonized by the same bugs in infancy - due perhaps to shared environment or genetics - and then retain those organisms long enough to begin to diverge through short-term evolution. If true, this can be studied directly in larger twin cohorts, and it would help us understand how the microbiome develops beyond diabetes alone in a wide variety of conditions."

**More information:** Moran Yassour et al. Sub-clinical detection of gut microbial biomarkers of obesity and type 2 diabetes, *Genome Medicine* (2016). DOI: 10.1186/s13073-016-0271-6

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