Identifying biomarkers associated with type 2 diabetes using longitudinal microbiome data

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The human microbiome, consisting of symbiotic microorganisms, plays a crucial role in shaping human health and impacting the development of diseases. Recent advances in 16S rRNA gene sequencing have accelerated our understanding of the microbiome's role in conditions like type 2 diabetes (T2D). Notably, altered miRNA profiles within urine extracellular vesicles are associated with the development of diabetic nephropathy in T2D patients. The aim of this study is to identify microbiome biomarkers associated with T2D using urine microbe-derived extracellular vesicles obtained from urine samples. This study makes use of genus-level longitudinal microbiome data from the Korea Association REsource (KARE) project, collected over three phases in 2013, 2015, and 2017. The longitudinal study design is used in microbiome studies to examine the dynamic changes in microbial abundance over time. To identify the T2D related microbiome biomarkers, we analyze the longitudinal data by five statistical methods: linear mixed model (LMM), generalized estimating equations (GEE), negative binomial mixed model (NBMM), zero-inflated negative binomial mixed model (ZINBMM), and zero-inflated Gaussian mixed model (ZIGMM). We find that both NBMM, and ZINBMM reveal more genera as biomarkers compared to other methods. Several markers commonly identified by all these approaches include *Blautia*, *Brevibacterium*, *Campylobacter*, *Enhydrobacter*, *Enterococcus*, *Finegoldia*, *Massilia*, *Peptoniphilus*, and *UCG-005*. Among these genera, the microbes *Brevibacterium*, *Campylobacter*, *Enterococcus*, *Finegoldia*, and *Peptoniphilus* were found to be associated with T2D in previous research studies.