

Human genetic determinants of the gut microbiome and their associations with health and disease: a phenome-wide association study

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Background: Recent small-scale studies have suggested a link between the human gut microbiome and highly prevalent diseases. However, the extent to which the human gut microbiome can be considered a determinant of disease and healthy aging has not been well established. In this study, we aimed to determine the spectrum of diseases that are linked to the human gut microbiome through the utilization of its genetic determinants as a proxy for its composition.

Methods: Data from 422,417 unrelated individuals of Caucasian British ancestry with available genotype and matching genetic data from the UK biobank was analysed in this study. 35 single nucleotide polymorphisms (SNPs) known to influence the human gut microbiome were used to perform the phenome-wide association study. Our main outcome was the probability (risk) of health and disease outcomes associated with human genetic determinants of the microbiome.

Results: From the total sample analysed (mean age was 57±8 years),

194,567 (46%) subjects were male. Median exposure was 66-person years (interquartile range 59 to 72). Seven SNPs known to influence the human gut microbiome were significantly associated with 29 health and disease outcomes (false discovery rate <5%, P value <9.14 × 10⁻⁴) including food intake, health status parameters (inflammation, blood pressure and lipid levels), hypertension, type 2 diabetes mellitus, hypercholesterolemia, heart failure, renal failure, and osteoarthritis.

Conclusions: Human genetic determinants of the gut microbiome are associated with 29 specific health and disease outcomes including hypertension, type 2 diabetes mellitus, hypercholesterolemia, heart failure, renal failure, and osteoarthritis. Microbiota and their metabolites play an important role in the interplay between overlapping pathophysiological processes and could be considered as potential targets for the maintenance of health and reduction of disease risk.

