

Metagenome-wide association study of gut microbiome revealed novel aetiology of rheumatoid arthritis in the Japanese population

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We conducted a comprehensive metagenome-wide association study (MWAS) of the gut microbiome in an RA case-control cohort of the Japanese population ($n_{\text{case}} = 82$, $n_{\text{control}} = 42$) by using whole-genome shotgun sequencing. Phylogenetic case-control association tests showed a high abundance of multiple species belonging to the genus *Prevotella* (e.g., *Prevotella denticola*) in the RA case metagenome. Gene functional assessments showed that the abundance of one redox reaction-related gene (R6FCZ7) was significantly decreased in the RA metagenome compared with controls. A population-specific link between the metagenome and host genome was identified by comparing biological pathway enrichment between the RA MWAS and the RA genome-wide association study. No apparent discrepancy in alpha or beta diversities of metagenome was found between RA cases and controls. Our shotgun sequencing-based MWAS highlights a novel link among the gut microbiome, host genome, and pathology of RA, which contributes to our understanding of the microbiome's role in RA aetiology.

