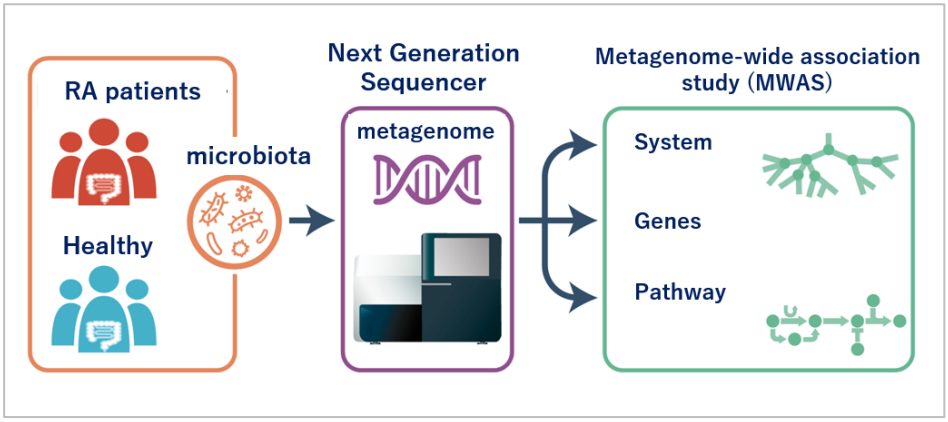
A metagenome-wide association study of gut microbiome revealed novel etiology of rheumatoid arthritis in the Japanese population.

Keywords: microbiota, metagenome-wide association study (MWAS), big data analysis

The research group led by Yukinori Okada (Statistical Immunology, IFReC/Graduate School of Medicine) conducted metagenome-wide association study (MWAS) of the RA gut microbiome in the Japanese population (ncase = 82, ncontrol = 42) by utilizing whole-genome shotgun sequencing of high depth (average 13 Gb per sample).

The Phylogenetic case–control association tests showed high abundance of multiple species belonging to the genus Prevotella (e.g., Prevotella denticola) in the RA case metagenome. The non-linear machine learning method efficiently deconvoluted the case–control phylogenetic discrepancy. Gene functional assessments showed that the abundance of one redox reaction–related gene (R6FCZ7) was significantly decreased in the RA metagenome compared to controls. A variety of biological pathways including those related to metabolism (e.g., fatty acid biosynthesis and glycosaminoglycan degradation) were enriched in the case–control comparison. A population-specific link between the metagenome and host genome was identified by comparing biological pathway enrichment between the RA metagenome and the RA genome-wide association study (GWAS) results. 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 gutmicrobiome, host genome, and pathology of RA, which contributes to our understanding of the microbiome's role in RA etiology.



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