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Unique signatures of gut microbiome in non-alcoholic fatty liver disease

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Non-alcoholic fatty liver disease (NAFLD) is one of the most prevalent liver disorders globally, affecting up to 25% of the adult population. With the increasing prevalence of metabolic disorders worldwide, NAFLD has emerged as a major public health concern. Recent evidence suggests that the gut microbiome plays a critical role in the progression of NAFLD by influencing metabolic dysregulation and immune responses. In this study, we performed shotgun metagenomic sequencing on 196 fecal samples from non-NAFLD and NAFLD (NAFL and NASH) individuals in Korea to identify unique gut microbiome signatures associated with NAFLD. Beta diversity analysis using PERMANOVA revealed distinct compositional differences among non-NAFLD, NAFL, and NASH groups. Additionally, significant differences in gut microbiome composition were observed across obesity, diabetes, and age groups, indicating a strong association between NAFLD and metabolic factors. Differential abundance analysis identified species X from the Erysipelotrichaceae family as enriched in NAFLD patients, suggesting its potential as a diagnostic marker. Other microbial features showed a trend of depletion in NAFLD patients compared to healthy controls, pointing to possible dysbiosis within the gut microbiome. We further conducted a meta-analysis using public datasets from five countries across three continents. The results revealed cohort-specific microbiome patterns, suggesting that functional roles of the gut microbiome may be more consistent than compositional features across populations. These findings highlight unique gut microbiome characteristics in Korean NAFLD patients and underscore the importance of considering cohort-specific microbiome patterns in understanding the role of the microbiome in NAFLD progression.