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Altered propanoate metabolism and gut Lachnospiriceae composition in lupus nephritis patients

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Objectives: There are growing evidence for the role of gut microbiota in the pathogenesis systemic lupus erythematosus (SLE), especially lupus nephritis (LN). Recently, high abundance of Ruminococcus gnavus belonging to the family Lachnospiraceae has been noticed in fecal sample of LN patients. However, the functional role of gut microbiota and its metabolic pathway which affect host metabolism in LN are less understood.

Methods: Shotgun sequencing of fecal samples from biopsy-proven LN patients and matched controls was performed. We used Kraken2 for taxonomic analysis and humann2 with customized KEGG database for genefamily analysis. Comparison of taxonomic abundance and genefamilies were assessed by Maaslin2.

Results: Control and LN group were included 24 and 20 patients, respectively. Both groups had similar age, sex, and eGFR. In the comparison of relative abundance of major species, Roseburia intestinalis, Butyricimonas faecalis, and Eubacterium eligens were significantly decreased while Ruminococcus gnavus was significantly elevated in LN group, respectively. Interestingly, 3 of these 4 species were included in the same Lachnospiraceae family showing a significantly different composition between the two groups (PERMANOVA $p=0.042$). Furthermore, we found 161 differentially expressed genefamilies including 65 metabolism-associated and 29 carbohydrate metabolism-associated genes. Considering Lachnospiraceae is known to play a role in propanoate (esters of propionate) formation, we further assessed the propanoate pathway (ko00640). As a result, LN patients revealed more prone to propanediol pathway rather than in succinate pathway in the propanoate pathway. This tendency was more pronounce in the contribution to the pduE gene by R. gnavus having well-known pathogenetic linkage with SLE.

Conclusions: LN patients showed altered propanoate metabolism associated with the differential species composition of Lachnospiraceae including R. gnavus. Functional role of this alteration on the pathogenesis of LN should be clarified by further investigations.