THE KOREAN SOCIETY OF NEPHROLOGY
APCN & KSN 2024
June 13(Thu) - 16(Sun), 2024 Coex, Seoul, Korea
APSN
Promoting Sustainable Kidney Health: The Asia-Pacific and Beyond

Abstract Submission No.: A-0554

Multi-omics Studies Unveil the Relationship between Systemic Microbiota and Metabolites with IgA Nephropathy

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Objectives : IgA nephropathy (IgAN) is the most common primary glomerulonephritis. Microbiota have long been thought to be involved in the pathogenesis of IgAN, but the microbiome profile of IgAN patients is not fully understood. In this study, multi-omics analysis was conducted to explore the the microbiota composition and metabolite profiles of IgAN patients, elucidating potential associations between microbial and metabolites.
Methods : We recruited a total of 316 IgAN patients and 197 healthy controls. IgAN patients underwent two follow-up visits. Serum, urine, and fecal samples were collected from each participant. Fecal samples underwent shotgun sequencing, while metabolite profiling was conducted on fecal, serum, and urine samples. Bioinformatic analysis of sequencing results was performed to compare differences between the IgAN group and the HC group.
Results : In IgAN patients, we observed a significant increase in the abundance of strains from Proteobacteria-Gammaproteobacteria-Enterobacterales-Enterobacteriaceae-Escherichia, which was significantly downregulated in individuals who experienced clinical remission following treatment. Coprococcus exhibited a marked reduction in IgAN patients, while their relative abundance significantly increased in those achieving clinical remission. In clinical correlation analysis, Escherichia showed a significant positive correlation with serum IgA concentration and a significant negative correlation with eGFR. Untargeted metabolomic profiling revealed 74, 97, and 120 differential metabolites in serum, feces, and urine, respectively. Notably, in IgAN patients, Indole-3-carboxaldehyde was significantly upregulated in urine, while N6-Acetyl-L-lysine was significantly downregulated. Moreover, metabolites that were significantly upregulated were significantly downregulated in individuals achieving clinical remission. Notably, Erysipelatoclostridium in the gut exhibited a significant negative correlation with Retinal, highlighting the significance of gut microbiota and metabolites as influential factors in the development and progression of IgAN.
Conclusions : The composition of gut microbiota and the profiles of serum, urine, and fecal metabolites underwent significant alterations in IgAN patients. Furthermore, upon achieving treatment-induced remission, the microbial and metabolic compositions tended to resemble those of healthy individuals.

Fig 1.png

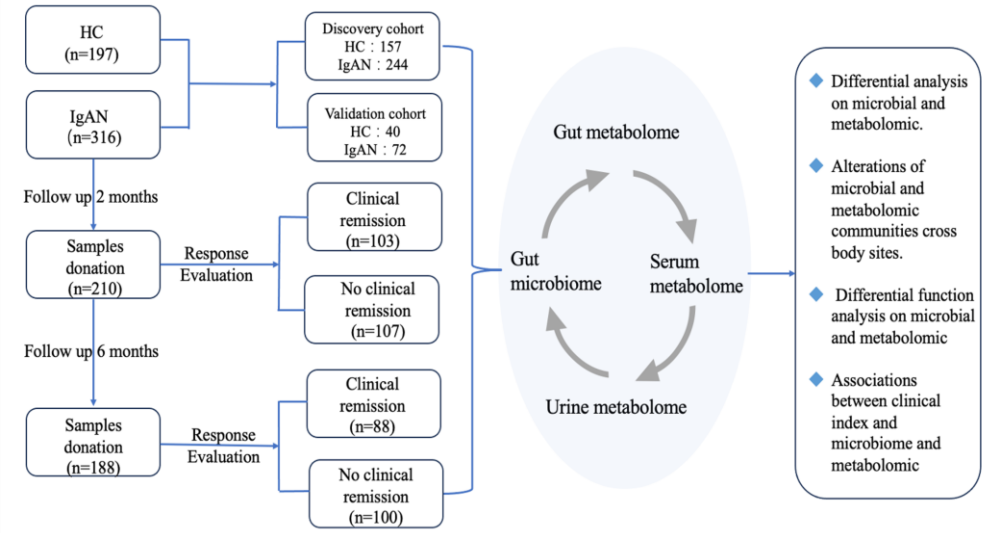
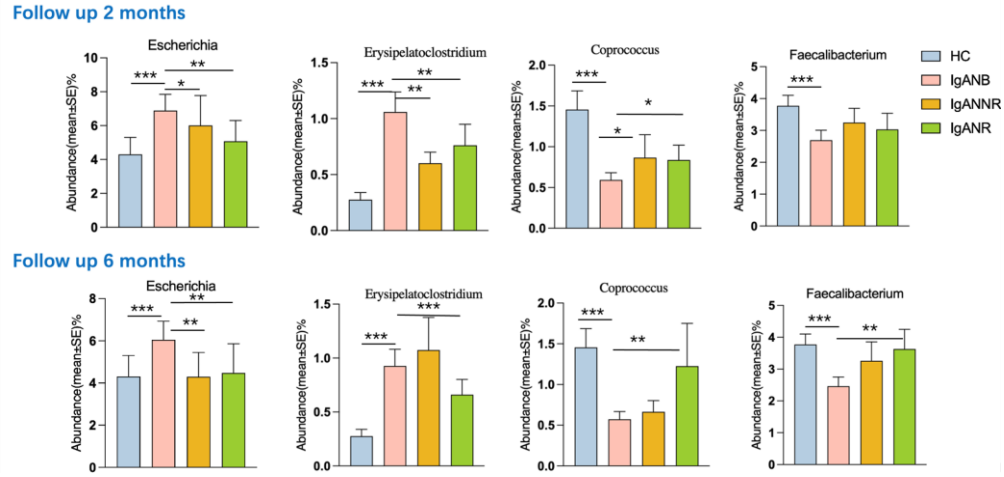

HC (n=197)
IgAN (n=316)
Discovery cohort HC : 157 IgAN : 244
Validation cohort HC : 40 IgAN : 72
Follow up 2 months
Samples donation (n=210)
Response Evaluation
Clinical remission (n=103)
No clinical remission (n=107)
Follow up 6 months
Samples donation (n=188)
Response Evaluation
Clinical remission (n=88)
No clinical remission (n=100)
Gut metabolome
Gut microbiome
Serum metabolome
Urine metabolome
Differential analysis on microbial and metabolomic.
Alterations of microbial and metabolomic communities cross body sites.
Differential function analysis on microbial and metabolomic
Associations between clinical index and microbiome and metabolomic

Fig 1.png


Follow up 2 months
Escherichia
Erysipelatoclostridium
Coprococcus
Faecalibacterium
Abundance(mean±SE)%
HC
IgANB
IgANNR
IgANR
Follow up 6 months
Escherichia
Erysipelatoclostridium
Coprococcus
Faecalibacterium
Abundance(mean±SE)%