Abstract Type : Poster exhibition
Abstract Submission No.: A-0637
Abstract Topic : Glomerular and Tubulointerstitial Disorders

Blautia Enrichment and Enhanced Butyrate Production in IgA Nephropathy: A Multicenter Cohort Analysis

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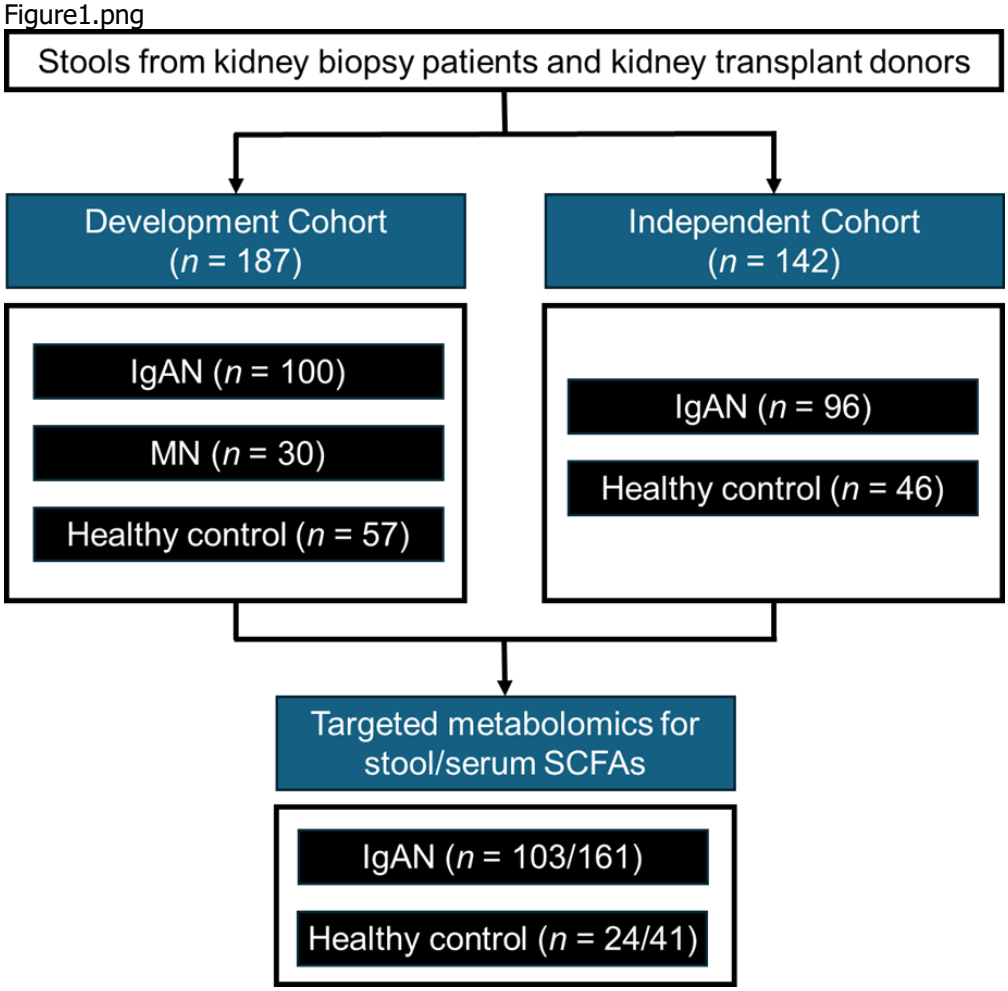
Objectives : The mucosal immune system is implicated in the pathogenesis of immunoglobulin A nephropathy (IgAN), but alterations of the gut microbiota and their contributions to the pathophysiology are not fully understood. We investigated the characteristics of gut microbiota in IgAN in a multicenter cohort.
Methods : We analyzed fecal samples from 187 patients (100 IgAN, 30 membranous nephropathy, 57 healthy controls) and an independent validation cohort of 142 patients (96 IgAN, 46 healthy controls) recruited from six tertiary hospitals. Gut microbiota was profiled via 16S rRNA sequencing (Illumina MiSeq). Alpha and beta diversities were assessed with Shannon indices and Bray-Curtis distances. Differential abundance analyses of microbial genera and PICRUSt2-derived predicted metagenome functions were conducted with MaAsLin2. Serum and fecal short-chain fatty acids (SCFAs) were quantified via targeted metabolomics using liquid chromatography-mass spectrometry.
Results : Compared to controls, IgAN patients exhibited significant differences in beta diversity ($p = 0.001$) but not alpha diversity ($p = 0.67$). Among the nine microbial genera associated with IgAN, Blautia and Ruminococcus gnavus group were consistently enriched in IgAN upon validation ($p = 0.008$ and 0.011, respectively). Especially, in IgAN patients, Blautia abundance positively correlated with systolic blood pressure, diastolic blood pressure, serum creatinine, and urine protein creatinine ratio ($p < 0.05$). Metagenomic analysis identified 31 KEGG pathways associated with IgAN, with pyruvate metabolism (ko00620) consistently elevated in both cohorts ($p = 0.005$). Serum SCFA profiles in IgAN patients showed elevations in lactate ($p < 0.001$) and butyrate ($p = 0.017$) levels compared to controls, while fecal SCFA levels did not differ significantly.
Conclusions : IgAN patients exhibited distinct gut microbiome profiles, with enriched Blautia and Ruminococcus gnavus group, elevated pyruvate metabolism, alongside increased serum butyrate levels. As key acetate producers, these taxa may influence butyrate synthesis, potentially influencing IgAN pathogenesis.

THE KOREAN SOCIETY OF NEPHROLOGY
KSN 2025 SEOUL, KOREA
June 19 (Thu) – 22 (Sun), 2025 Coex, Seoul, Korea
Beyond Challenges, Towards Healthier Kidney

Figure1.png



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