Editorial

Kidney Res Clin Pract 2023;42(5):539-540
pISSN: 2211-9132 • eISSN: 2211-9140
https://doi.org/10.23876/j.krcp.23.129

KIDNEY RESEARCH AND CLINICAL PRACTICE

Metabolomics profiling: a potential tool for predicting immunoglobulin A nephropathy progression

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Immunoglobulin A nephropathy (IgAN) is the most prevalent primary glomerulonephritis and one of the leading causes of end-stage kidney disease globally [1,2]. Identifying reliable biomarkers of disease progression is crucial for timely intervention and improved patient outcomes in IgAN. Despite the variable prognosis, there are currently no definitive biomarkers that accurately predict the outcomes of the disease. In recent years, rapid advancements in high-throughput omics technologies have empowered researchers to extract vast quantities of data from limited samples, such as blood, urine, or kidney tissue. These technologies have emerged as powerful tools for biomarker discovery in glomerular diseases, including IgAN [3].

Metabolomic analysis has shown promise in the field of nephrology, as it allows for a comprehensive assessment of various factors influencing complicated pathophysiology of kidney diseases. Metabolites can provide a real-time snapshot of systemic and local kidney metabolic status, thereby offering potential insights into disease progression and therapeutic responses. The human metabolome is the end product of numerous influences, including genetic variability, environmental factors, internal biochemical processes, and their complex interactions [4]. Consequently, the multifaceted pathophysiological mechanisms of IgAN, characterized by multiple pathologic hits, are likely to result in related shifts in the concentrations of specific metabolites. Thus, metabolites could serve as pathognomonic biomarkers, capable of linking the dots between the sequential pathological hits of IgAN [5].

^{1}H-NMR spectroscopy offers a unique advantage in metabolomics analysis. It provides quantitative results, offering absolute concentration values for metabolites. This technique detects a broad range of metabolites, and its excellent reproducibility makes it suitable for high-throughput analysis. It can detect a wide spectrum of metabolites, including small organic molecules and metabolites of lipids, amino acids, and carbohydrates, offering a comprehensive view of the metabolic shifts in disease. Also, the non-destructive nature of ^{1}H-NMR allows potential re-analysis of samples, making it particularly useful for lon-

Received: May 22, 2023; **Accepted:** June 15, 2023
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*The KOrea Renal biobank NEtwoRk System TOward NExt-generation analysis (KORNERSTONE), supported and reviewed by the Korea Centers for Disease Control and Prevention, is a large, multicenter biobank and prospective cohort study for glomerular disease with extensive clinical data collection, biospecimens, and digital pathologic images.

gitudinal studies to monitor disease progression and treatment response. Furthermore, the presence of high-abundance metabolites might overshadow the detection of less abundant, yet potentially significant ones [6]. In terms of ^{1}H-NMR spectroscopy, although it provides broad metabolite coverage, its sensitivity is lower compared to other techniques like mass spectrometry, requiring high-quality samples and careful data interpretation. Moreover, variability in urine metabolite concentrations due to diet, lifestyle, volume status, medications, and other factors necessitates rigorous study design and data normalization strategies.

Jeon et al. [7] investigated the metabolomic profiles in the serum and urine of patients with IgAN to identify potential biomarkers for disease progression. The study included 20 IgAN patients, of whom a proportion exhibited disease progression, with higher urine protein/creatinine ratios than the non-progressor group. Through ^{1}H-NMR spectroscopy, distinct clusters were observed between the control and IgAN groups, as well as between progressors and non-progressors. Pathway enrichment analysis identified several altered metabolic pathways associated with IgAN progression, including glycerolipid metabolism, aminoacyl-tRNA biosynthesis, valine, leucine, isoleucine biosynthesis, and glycine, serine, and threonine metabolism. Predictive models incorporating these identified metabolites and proteinuria showed improved prognostic power for IgAN progression. In the serum, the combination of glycerol, threonine, and proteinuria had an area under the curve (AUC) of 0.923 for disease progression, while in urine, the combination of leucine, valine, and proteinuria had an AUC of 0.912. These results highlight the potential of metabolomic profiling in predicting IgAN progression and in revealing altered metabolic pathways in IgAN patients. Further studies involving a larger patient cohort are warranted to validate these findings and explore the mechanistic links between the altered metabolic pathways and IgAN progression.

Conflicts of interest

The author has no conflicts of interest to declare.

Data sharing statement

The data presented in this study are available on request from the corresponding author.

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