

KSN 2016 Abstract Submission

Glomerular disease

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Systems metabolomic study identifies robust biomarker panel and characterizes the metabolic dysfunctionality for different primary nephrotic syndromes

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Background: Nephrotic syndrome (NS) is a nonspecific kidney disorder, characterized by proteinuria, hypoalbuminemia, dyslipidemia, and edema. It is mostly represented by minimal change disease (MCD), focal segmental glomerulosclerosis (FSGS), and membranous glomerulonephritis (MGN). Since urine metabolites may mirror disease-specific functional perturbations in kidney injury, we examined urine samples for distinctive metabolic changes to identify biomarkers for clinical applications.

Methods: A total of 48 urine samples (12 healthy controls, 12 MCD, 12 FSGS, and 12 MGN) were analyzed using mass spectrometry-based metabolite profiling. We developed multi-component covarianced models based on the disease-specific metabolic modulation to discriminate three different types of NS. To extensively validate their diagnostic potential, new batch from 54 patients with primary NS were independently analyzed and examined for the robustness and reliability of the biomarker panel a year after.

Results: In independent validation set, the model including citric acid, pyruvic acid, fructose, ethanolamine, and cysteine effectively discriminated FSGS from the others (area under the curve [AUC]: 0.812 against MCD and 0.802 against MGN), but not MCD from MGN. Thus, we developed an additional metabolite multi-composite, including methionine, cysteine, citrulline, and pyruvic acid, which successfully discriminated between MCD and MGN (AUC 0.843). Furthermore, we proposed the re-constructed metabolic network characteristically dysregulated by the different NS that may deepen comprehensive understanding of the disease mechanistic.

Conclusion: Our study could help the enhanced identification of NS and therapeutic plans for future

Keywords: biomarker, Metabolomics, nephrotic syndrome