



Congress Abstract

Comprehensive Urinary Proteomics Identifies Novel eGFR-Related Biomarkers Unique to Chronic Kidney Disease

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Proceedings of Central Asian Congress of Nephrologists with International Participation, October 9-10, Aktau, Kazakhstan

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ABSTRACT

Introduction: Chronic kidney disease (CKD) is a progressive condition characterized by declining kidney function and altered urinary protein excretion. However, relationships between individual urinary proteins and kidney function remain incompletely understood. We aimed to compare urinary proteomic profiles between patients with CKD and healthy controls (HC) and identify proteins associated with estimated glomerular filtration rate (eGFR).

Methods: Urinary proteomics was performed in 79 patients with CKD and 54 HC using diaPASEF on a timsTOF Pro 2 platform. DIA-NN data were processed with MSstats using log₂ transformation, median normalization, and Tukey's median polish without missing-value imputation. Differential abundance was assessed using limma models adjusted for log₁₀ urinary creatinine and LC-MS run order with robust empirical-Bayes moderation. Protein associations with eGFR were evaluated separately in CKD and HC using Spearman correlation. Benjamini-Hochberg false-discovery rate (BH-FDR) <0.05 was used to define significance.

Results: CKD participants had lower eGFR and higher urine albumin-to-creatinine ratio than HC (both $P < 0.001$). Summed MaxLFQ intensity was higher in CKD (8.0 [7.7-8.2] vs 7.5 [7.4-7.6] log₁₀; $P < 0.001$), despite fewer detected protein groups (4,338 vs 4,553) (Table 1).

Values are median (IQR), mean $\pm$ SD, n (%), or detected protein-group counts, as appropriate. P values compare HC with patients with CKD. Sex was compared using the Pearson chi-square test. Age, serum creatinine, urine ACR, and summed MaxLFQ intensity were compared using the Wilcoxon rank-sum test. Estimated GFR was compared using Welch's two-sample t-test. Detected protein groups were reported descriptively and were not statistically tested. ACR, albumin-to-creatinine ratio; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HC, healthy controls; IQR, interquartile range; MaxLFQ, maximum label-free quantification.

Creatinine-adjusted differential abundance analysis showed broad bidirectional changes in the CKD urinary proteome. Among the most significantly upregulated proteins were A1AG1, TRFE, AFAM, A1AG2, and A1AT, whereas MUC18, BCAM, CD248, ROBO4, and IBP7 were among the most significantly downregulated proteins (Figure 1).

No protein-eGFR association remained significant after BH-FDR correction in HC (3,316 proteins tested). In CKD, 125 of 1,905 tested proteins showed significant associations with eGFR. The strongest FDR-ranked associations included positive associations for F16P1 ($q = 0.60$) and UROK ($q = 0.49$), and negative associations for

CFAD ($q = -0.59$), VSIG4 ($q = -0.57$), SH3L1 ($q = -0.65$), FABP4 ($q = -0.62$), PEDF ($q = -0.50$), RET4 ($q = -0.50$), B2MG ($q = -0.49$), and FHR4 ($q = -0.67$) (Figure 2).

Conclusions: CKD was characterized by a distinct urinary proteomic profile and numerous proteins associated with kidney function. The presence of 125 eGFR-associated proteins in CKD, with none surviving FDR correction in HC, suggests disease-related variation in the urinary proteome. These findings support further evaluation of urinary proteins as potential CKD biomarkers.

Keywords: Proteomics; Chronic Kidney Disease; Biomarkers

Table 1

General Characteristics of Study Population

Parameter	HC, n = 54	CKD, n = 79	P value
Sex, female	27 (50%)	46 (58%)	0.349
Age, years	32.2 (29.1–47.7)	35.6 (27.0–48.1)	0.747
eGFR, mL/min/1.73 m ²	104.3 ± 14.0	85.8 ± 30.2	<0.001
Serum creatinine, µmol/L	77.8 (66.8–92.1)	82.9 (68.7–104.8)	0.044
Urine ACR, mg/mmol	0.3 (0.1–0.6)	53.9 (13.2–200.5)	<0.001
Detected protein groups, n	4553	4338	
Summed MaxLFQ intensity, log ₁₀	7.5 (7.4–7.6)	8.0 (7.7–8.2)	<0.001

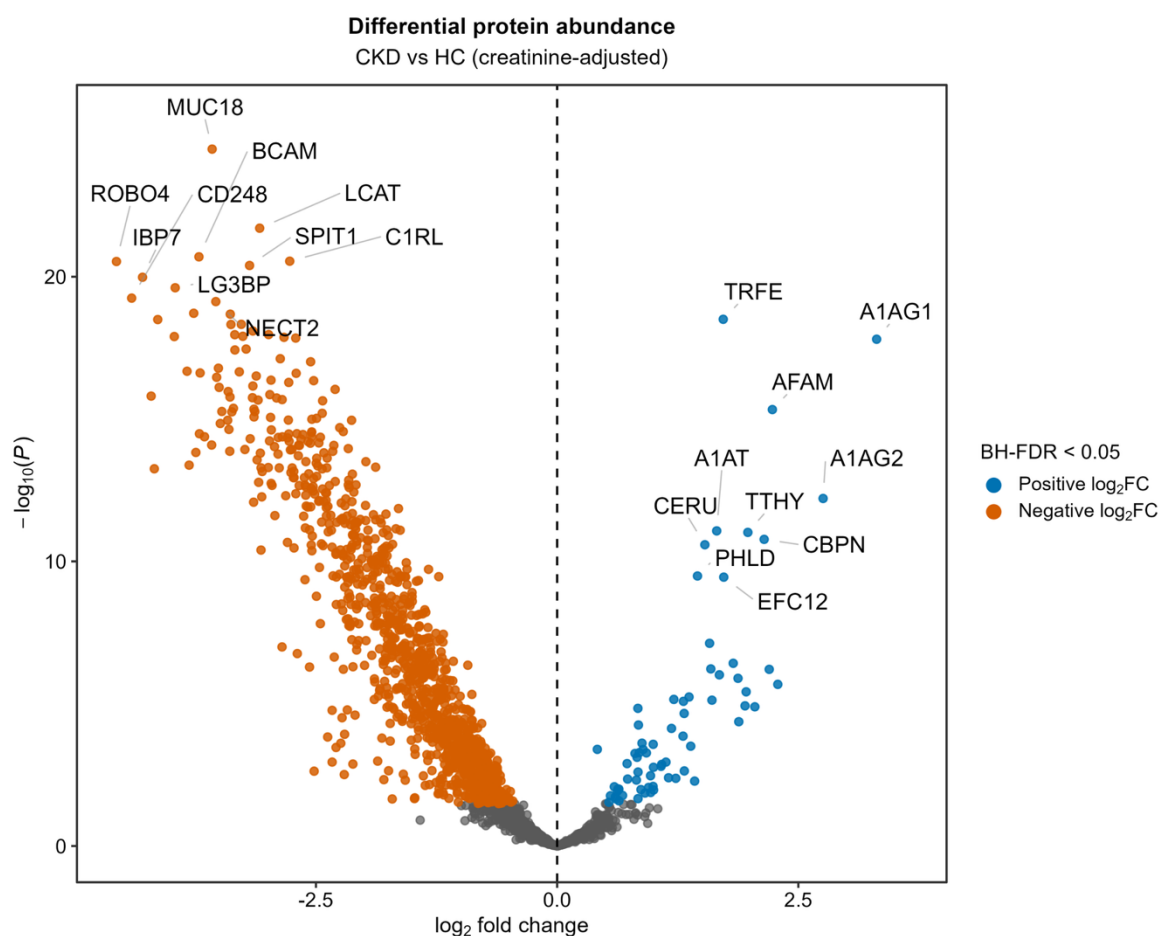


Figure 1

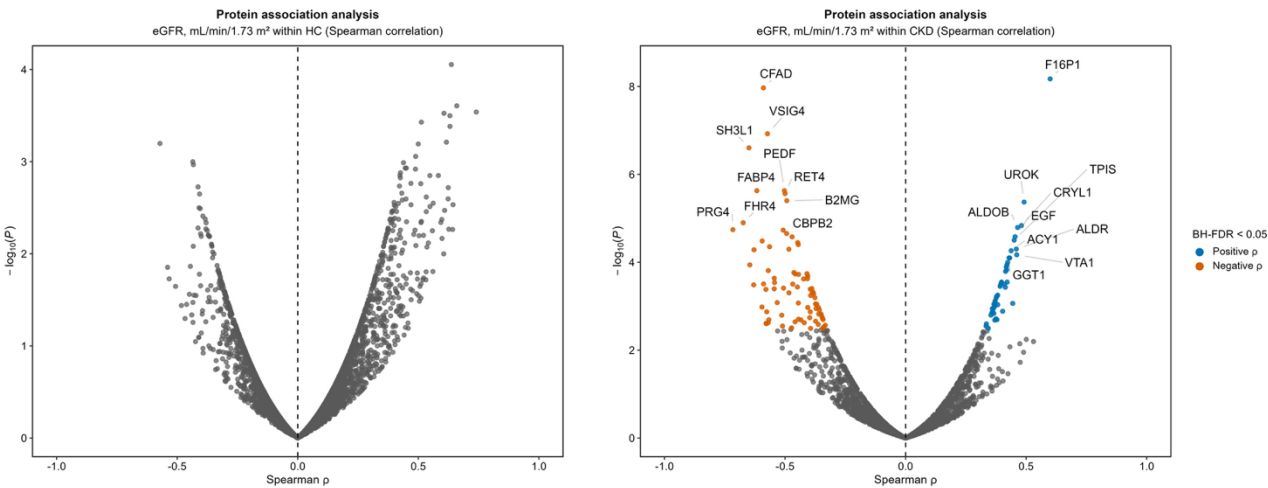


Figure 2