Complement components, proteolysis-related, and cell communication-related proteins detected in urine proteomics in IgA nephropathy.

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INTRODUCTION AND AIMS

IgA nephropathy (IgAN) is the most common primary glomerulonephritis. The first symptoms of IgAN are erytrocyturia or hematuria, proteinuria, and decline in renal function, or any combination thereof. One of the promising diagnostic methods is urine proteomics.

METHODS

We studied urine proteomics in 30 patients with IgAN and 30 age-and sex-matched healthy controls. Demographic characteristics and renal function of IgAN and control groups are presented in the Table. Thirty urine samples of the IgAN group were divided into 3 disease pooled samples (DPS I, II, and III) and 30 urine samples of the control group were divided into 3 control pooled samples (CPS I, II, and III). We used isoelectric focusing/liquid chromatography–mass spectrometry/mass spectrometry (IEF/LC-MS/MS) to detect all proteins larger than 10 kDa. To minimize the risk of protein degradation, we proposed a new protocol for urine collection and preparation.

RESULTS

We identified 761, 951, and 956 proteins in each of the 3 IEF/LC-MS/MS experiments. The results were combined, yielding a dataset with 1238 proteins identified by at least 2 peptides. The statistical analysis of the quantitative results revealed 18 proteins that were differently populated in the urine of IgAN patients compared with healthy controls. All identified proteins were searched in the STRING database, which defines a metric called „confidence score" to describe interaction confidence. We fetched all interactions for our dataset, which had a medium confidence score of 0.4 and higher.

CONCLUSIONS

We found increased urinary concentrations of complement components, coagulation factors, extracellular matrix, intracellular, transmembrane and other proteins with IgAN. Some of them have never been linked to IgAN before.

	IgAN group (n = 30)	Control group (n = 30)
sex, male / female	15 / 15	15 / 15
age, y	39.8 (20–60)	39.3 (20–62)
body mass, kg	76.1 (46–135)	75.7 (45–105)
serum creatinine, µmol/l	94.5 (40.2–279.9)	120.1 (51.5–365.6)
GFR (CKD-EPI formula), ml/min	66.3 (17.5–127.6)	99.3 (66.6–132)
proteinuria, g/d	1.19 (0–3.9)	0

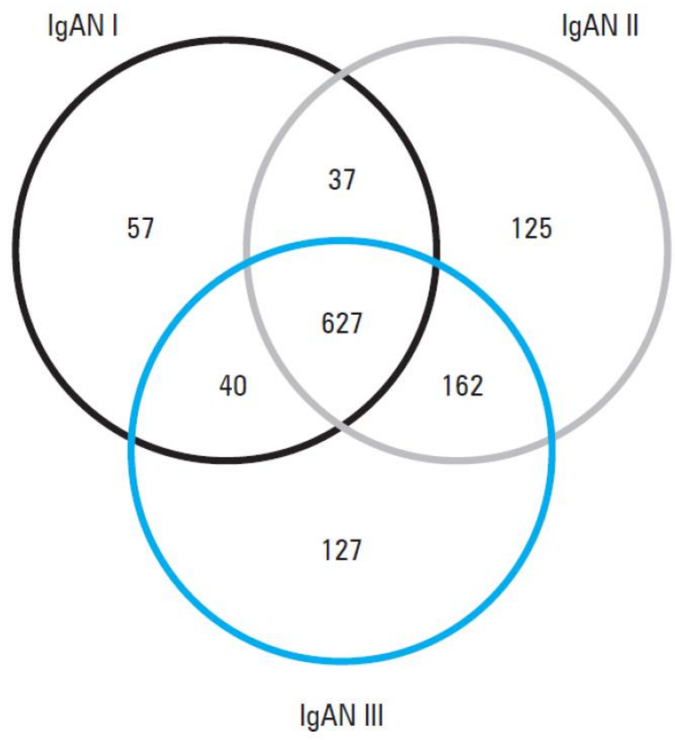

FIGURE 1 Results of qualitative analysis: a Venn diagram representing the number of proteins identified by 2 or more peptides in 3 biological replicates of the isobaric tags for relative and absolute quantitation experiment (3 isoelectric focusing gel strips); 627 proteins are common in all 3 experiments
Abbreviations: IgAN – IgA nephropathy

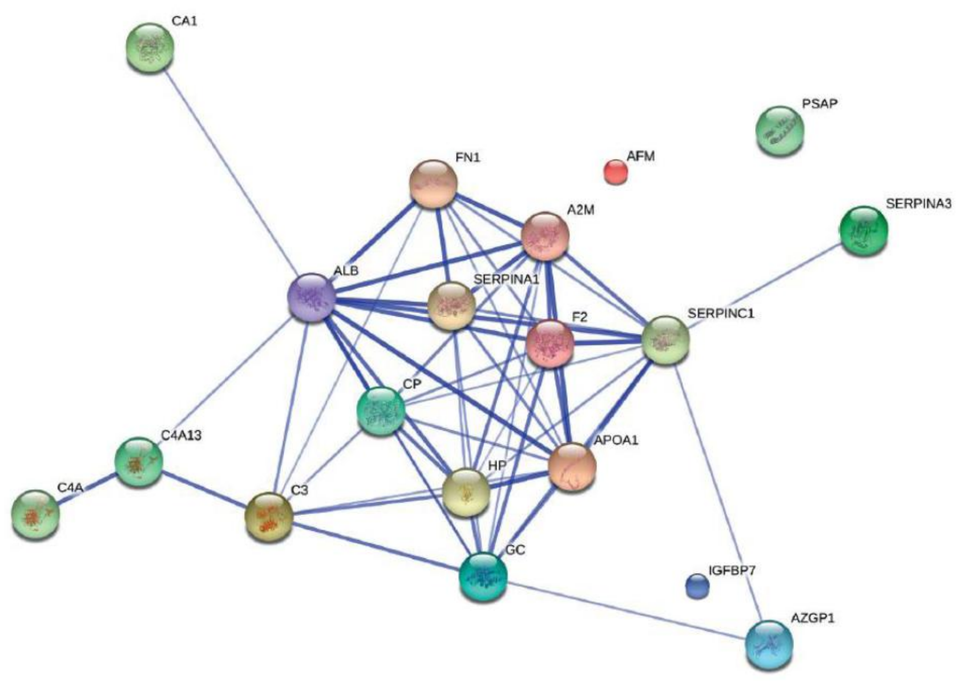

FIGURE 2 Network topology of the protein––protein interactions of our protein dataset as extracted from the STRING database

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