KSN 2017 Abstract

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Identification of urinary biomarkers for recurrence of IgA nephropathy after kidney transplantation using proteomic methods

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Objectives : Immunoglobulin (Ig) A nephropathy is one of the most common primary glomerulonephritis worldwide causing end stage renal disease, and has a strong tendency to recur after kidney transplantation. Since graft survival has been improved by more potent immunosuppressive agents, the rates of IgA nephropathy recurrence and graft loss due to recurrence are expected to increase. The aim of this study was to identify a novel set of urinary proteomic profiles which could distinguish recurrence of IgA nephropathy in kidney transplant recipients.

Methods : This study included 10 renal transplant patients with histologically proven recurrence of IgA nephropathy (Rec group), and 20 renal transplant patients with normal kidney function (control group). To identify potential urinary biomarkers, we performed SDS-PAGE followed by liquid chromatography-mass spectrometry (LC-MS/MS). SWATH (Sequential Window Acquisition of all THeoretical Mass Spectra) was utilized in protein quantification. The data were normalized and receiver operating characteristic (ROC) curve was used in statistical analysis.

Results : A total of 96 proteins differentially expressed in urine samples between two groups were identified. Among protein profiles identified, SERPINA1 had high association with Rec group compared to control group (area under the curve [AUC] 0.805 (0.617-0.993)). Transferrin was also associated with Rec group significantly (AUC 0.790 (0.564-1.000)). APOA4 and RBP4 had high distinguishable capacity to differentiate Rec group from control group (AUC 0.550 (0.181-0.719) and 0.660 (0.391-0.929), respectively). The combined set of above mentioned 4 proteins had higher discriminating value of Rec group compared to control group (AUC 0.940)

Conclusions : These results suggest that SERPINA1, Transferrin, APOA4, and

KSN 2017 Abstract

RBP4 allow the detection of recurrence of IgA nephropathy and could be used as urinary biomarkers for predicting IgA nephropathy recurrence after kidney transplantation. Further validation in a larger population is required to determine if these biomarkers provide a potential noninvasive method of diagnosing recurrence of IgA nephropathy in a clinical setting.

Keywords : Kindey transplantation, IgA nephropathy recurrence, urinary biomarker, proteomics