

**Abstract Submission No. : 2212**

## **Urinary sediment mRNA as a potent biomarker of IgA nephropathy**

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### **Objectives:**

Quantification of mRNA expression in urinary sediments has emerged as a reliable diagnostic and prognostic modality in various disease conditions. However, few studies have investigated the clinical relevance of urinary mRNA in IgA nephropathy (IgAN). In this study, we investigated the expression of urinary mRNAs and their clinical significance in patients with IgAN.

### **Methods:**

Two hundred biopsy-proven IgAN patients, 48 disease controls (patients with non-IgAN nephropathy), and 79 healthy controls were enrolled in this study. We identified differential expression of mRNAs in renal tissue between IgAN patients and normal subjects using the gene expression omnibus dataset, and selected 15 target mRNAs through meta-analysis and literature review. We compared the expression of mRNAs according to the type of glomerular disease and analyzed the association between mRNAs and clinicopathological parameters in IgAN patients. The predictive value of mRNAs for disease progression is also evaluated.

### **Results:**

The expression of C3, CCL2, CD14, DNMT1, FKBP5, Nephritin, PODXL, and Tfr were significantly upregulated in IgAN patients as compared with healthy controls. DNMT1, FKBP5, and PODXL have good diagnostic accuracy of IgAN (area under curve of the receiver operating characteristic curve > 0.8). C3, GDF-15, Nephritin, and Tfr revealed significant correlation with renal function and urinary protein excretion. During follow-up, 45 (22.5%) IgAN patients experienced disease progression defined as a greater than 25% reduction in estimated glomerular filtration rate (eGFR), decline in eGFR category from the value determined at the time of renal biopsy, or start renal replacement therapy. Nephritin and FLOT1 (HR 1.049, 95% CI 1.012-1.102,  $p = 0.049$ ; and HR 1.050, 95% CI 1.015-1.087,  $p = 0.005$ , respectively) were independently associated with increased risk of disease progression.

### **Conclusions:**

Our results suggest that urinary sediment mRNAs are useful biomarker in patients with IgAN. Further studies with a larger sample size and longer follow-up duration are needed.