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Urinary exosomal micro-RNAs are potential diagnostic and prognostic biomarkers in patients with IgA nephropathy

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Objectives:

Micro-RNAs (miRNAs) are small non-coding RNA molecules which regulate disease pathophysiology by modulating target gene expression. miRNAs are derived from tissues and biofluids such as serum, saliva, and urine. Recently, emerging evidence suggests urinary exosomal miRNAs as non-invasive biomarkers of various kidney diseases. However, few studies investigated clinical relevance of miRNA in IgA nephropathy (IgAN). In this study, we evaluated urinary exosomal miRNA expression and analyzed its clinical significance in patients with IgAN.

Methods:

Urine samples were collected from 93 patients with biopsy-proven IgAN and 20 normal controls. We identified mRNA differential expression of renal tissue between IgAN and normal subjects in the gene expression omnibus dataset, and selected 884 glomerular and 67 tubulointerstitial genes through meta-analysis. We then used the miRTarBase, TargetScan, micorRNA database to predict potential miRNA targets. Finally, 11 urinary exosomal miRNAs were selected. We observed urinary exosomal expression of miRNAs and analyzed their diagnostic and prognostic accuracy for IgAN.

Results:

The expression of miR-16-5p, miR-29a-3p, miR-29c-3p, miR-126-3p, miR-199a-3p, miR-615-3p, and miR-29b-3p were significantly upregulated in IgAN patients as compared with control. miR-16-5p, miR-29a-3p, miR-126-3p, and miR-199a-3p have good diagnostic accuracy of IgAN (area under curve of the receiver operating characteristic curve > 0.8). Proteinuria significantly correlated with miR-16-5p, miR-29a-3p, miR-124-3p, miR-199a-3p, and miR-335-3p. Baseline renal function significantly correlated with miR-199a-3p and miR-29b-3p. During follow-up period, 15 (16.1%) IgAN patients experienced rapid progression defined as a sustained decline in estimated glomerular filtration rate of more than 5ml/1.73m^2/year. miR-16-5p and miR-29a-3p were independently associated with increased risk of rapid progression (HR 1.841; 95% CI, 1.058-3.202, p = 0.031 and HR 1.363; 95% CI 1.047-1.773, p = 0.021, respectively).

Conclusions:

Urinary exosomal miRNAs might be potential non-invasive biomarkers for diagnosis and prediction of disease progression of IgAN. Further studies are needed to clarify our results and ascertain the underlying mechanisms.