THE ASSOCIATION BETWEEN RENAL PARAMETERS AND URINARY MicroRNAs IN PATIENTS WITH IgA NEPHROPATHY

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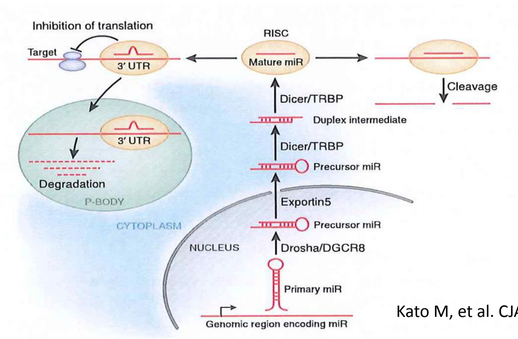
Background & Aim

Background: Renal microRNAs (miR) modulate the development and the progression of renal diseases by regulating various gene expressions in kidney. In this study, we examined whether urinary microRNAs reflect renal lesions and short-term change in renal function in patients with IgA nephropathy.
Aim: To clarify the association between renal parameters and urinary microRNA in IgA nephropathy



Kato M, et al. CJASN 2009

Methods

- We extracted and quantified microRNAs in morning spot urine in 88 patients with IgA nephropathy at biopsy and 5 healthy controls, and examined the relation between clinical and histological parameters (glomerular proliferation, sclerosis and tubulointerstitial changes), one-year changes in eGFR and urinary microRNAs including miR-21, -30c, -133b, -192, and -200c.
- The concentrations of microRNAs were corrected to the concentration of urinary creatinine and were log-transformed for simple correlation analysis. A statistically significant difference was defined as $p < 0.05$.

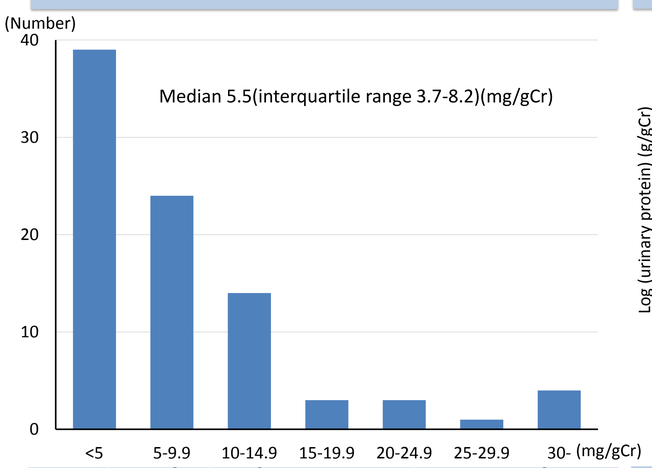
Results

Baseline characteristics

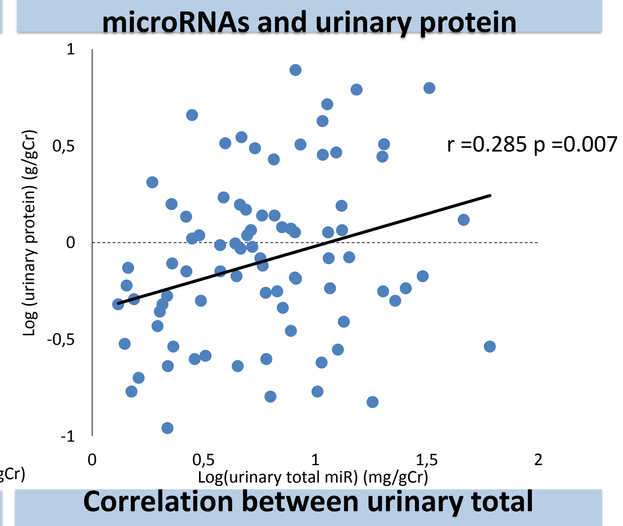
Number	88
Male/Female	42/46
Age (yrs)	41.1±17.8
eGFR (ml/min/1.73m^2)	75.6 ± 31.0
Urine protein (g/gCr)	0.77(0.45-1.46)
Urinary occult blood (-, ±/1+/2+/3+)	8/10/22/48
Urinary β2-MG (μg/gCr)	120(80-257)
Urinary creatinine (g/L)	1.13(0.61-1.61)
Urinary microRNA (mg/gCr)	5.5(3.7-8.2)
Sediment-RBC()	81.8(38.6-196.3)
Sediment-WBC()	10.2(5.4-26.8)
Glomerular proliferation score (0-4)	0.36(0.14-0.58)
Glomerular sclerosis score (0-4)	0.41(0.14-1.00)
Interstitial fibrosis score (0/1/2/3-4)	33/37/13/1

Mean±SD, Median (interquartile range)

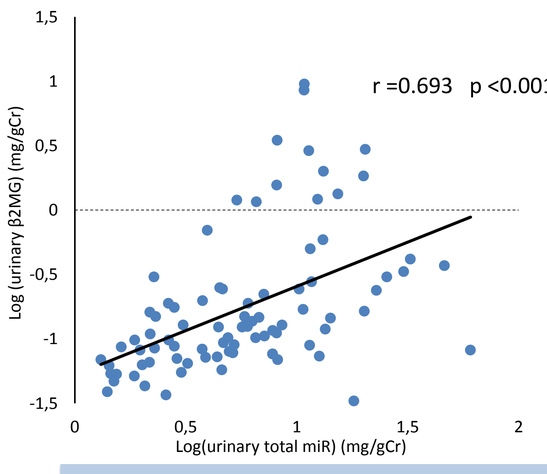
Urinary total microRNAs



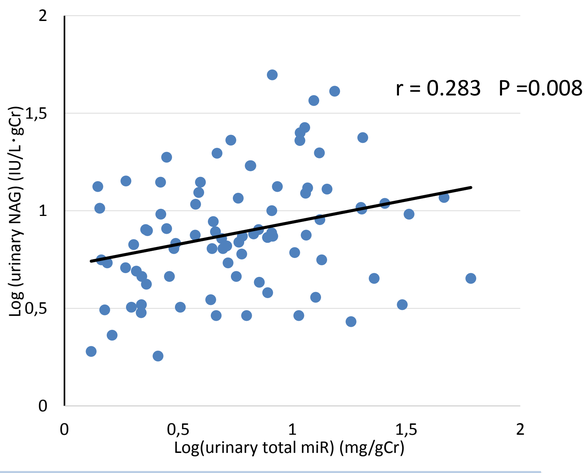
Correlation between urinary total microRNAs and urinary protein



Correlation between urinary total microRNAs and urinary β2MG



Correlation between urinary total microRNAs and urinary NAG

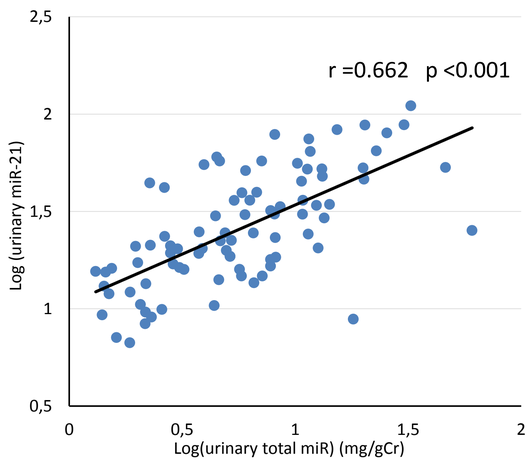


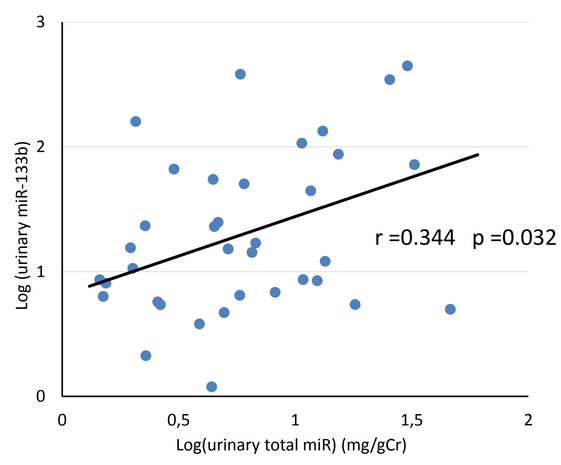
Multiple linear regression analysis to predict the values of urinary microRNAs

	Regression coefficient	SE	t value	p value
Log(urinary β2MG/Cr)	0.344	0.088	3.91	＜0.01
Male	-0.110	0.039	-2.85	＜0.01
Log(S-RBC)	-0.124	0.061	-2.04	0.04
eGFR	0.003	0.002	1.74	0.09
Age	0.002	0.003	0.53	0.60
Log(UP/C)	0.054	0.130	0.42	0.68
Log(S-WBC)	0.040	0.071	0.57	0.57
Glomerular proliferation score(0-4)	-0.004	0.112	-0.04	0.97
Glomerular sclerosis score(0-4)	-0.063	0.061	-1.04	0.30
Interstitial fibrosis score(0-4)	0.049	0.063	0.78	0.44

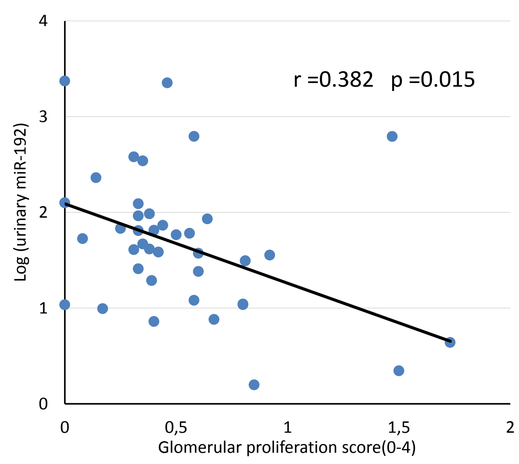
- The urinary excretion of total microRNAs in patients with IgA nephropathy was non-significantly higher than those in controls (9.7±11.9 vs. 4.4±2.8 [mean±SD] μg/gCr, p= 0.21) .
- Urinary total microRNAs was correlated positively with urinary excretion of protein (r= 0.26), beta2-microglobulin (r= 0.48), N-acetyl-beta-D-glucosaminidase (NAG) (r= 0.28), but not with urinary red blood cells and white blood cells, eGFR and renal histological changes.

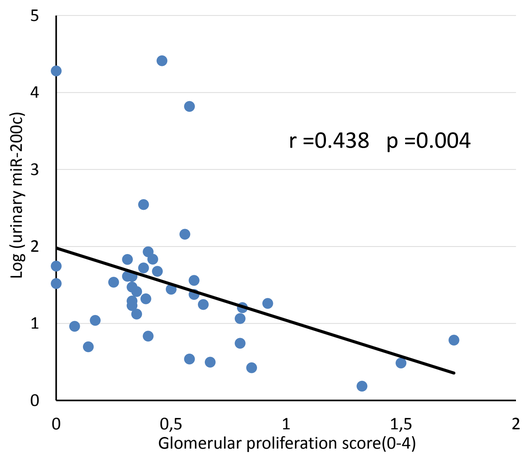
Correlation between the type of microRNA and total microRNAs



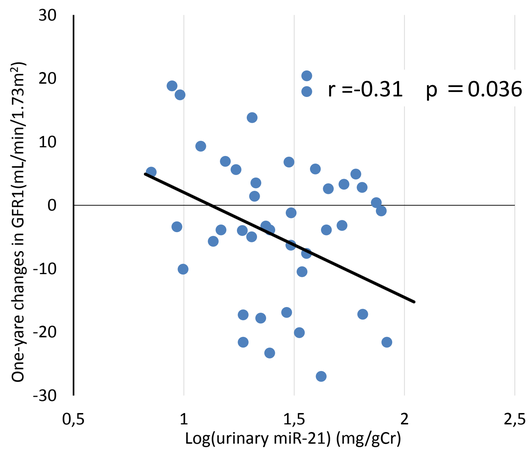


Correlation between the type of microRNA and glomerular proliferation





Correlation between the one-year changes in eGFR and urinary microRNA-21



- There was a significant correlation between the type of microRNA and specific renal parameters.
  - ➢ miR-21 related positively with urinary protein (r= 0.40), beta2-microglobulin (r= 0.62), and NAG (r= 0.37)
  - ➢ miR-192 and miR-200c related inversely with glomerular proliferative changes (r= -0.38, -0.44, respectively)
  - ➢ miR-30c and miR-192 related inversely with urinary red blood cells (r= -0.38, -0.44, respectively)
  - ➢ miR-21 and miR-30c related inversely with urinary white blood cells (r= -0.24, -0.39, respectively)
- Furthermore, the one-year changes in eGFR after biopsy showed a significant inverse correlation with urinary concentration of miR-21 (r= -0.31).

Conclusions

In this study urinary microRNAs were related with clinical and pathological parameters and one-year changes in renal function in patients with IgA nephropathy, suggesting that it might be used as a biomarker of IgA nephropathy.

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