


MicroRNA-155-induced T lymphocyte subgroup drifting in IgA nephropathy

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Abstract

Background MicroRNA-155 (miR-155) is an important immune regulator of T lymphocyte subgroup balance and function. This study was performed to explore the relationships between miR-155 expression in peripheral blood mononuclear cells (PBMCs), T lymphocyte subgroups, T lymphocyte regulators, and the clinical manifestations of IgA nephropathy (IgAN) patients.

Methods Sixty biopsy-proven IgAN patients and 25 healthy controls were included in this study. The expression of miRNAs in PBMCs was determined using a microRNA microarray and real-time RT-PCR. T lymphocyte subgroups (Th1, Th2, Treg, and Th17), differentiation regulators (c-Maf, STATA-6, GATA-3, SOCS-1, and Foxp3), cytokines (IFN- γ , IL-5, IL-10, and IL-17), serum IgA1 glycosylation level, and Cosmc expression were examined using flow cytometry, qPCR, and ELISA.

Results Microarray analysis and qPCR suggested that the miR-155 level in PBMCs from IgAN patients was

significantly lower than that in healthy controls (decreased 61%, 0.197 ± 0.068 vs 0.796 ± 0.13 , $p < 0.01$). The expression of GATA-3 (0.08 ± 0.02 vs 0.04 ± 0.01 , $p = 0.035$), SATB-1 (0.12 ± 0.02 vs 0.06 ± 0.01 , $p = 0.036$), and SOCS-1 (0.04 ± 0.01 vs 0.03 ± 0.01 , $p = 0.01$) was significantly higher in IgAN PBMCs compared to healthy controls, while that of Foxp3 (0.013 ± 0.003 vs 0.040 ± 0.01 , $p = 0.026$) and Cosmc (0.08 ± 0.02 vs 0.19 ± 0.04 , $p = 0.024$) was remarkably lower. Flow cytometric analysis revealed that the percentages of peripheral blood Th1 (17.35 ± 1.22 vs 20.89 ± 1.22 , $p = 0.042$) and Treg cells (1.86 ± 0.15 vs 2.48 ± 0.26 , $p = 0.031$) were significantly lower in IgAN patients than in normal controls; however, the percentages of Th2 (1.73 ± 0.29 vs 1.04 ± 0.18 , $p = 0.046$) and Th17 (4.09 ± 0.45 vs 2.06 ± 0.21 , $p < 0.001$) were remarkably higher. ELISA results indicated that serum Th1 cytokine INF- γ (40.77 ± 8.39 vs 83.02 ± 17.4 pg/mL, $p = 0.035$) and Treg cytokine IL-10 (0.77 ± 0.28 vs 4.18 ± 1.34 pg/mL, $p = 0.02$) levels were lower, while Th2 cytokine IL-5 (1.02 ± 0.17 vs 0.65 ± 0.07 pg/mL, $p = 0.04$) and Th17 cytokine IL-17 (53.78 ± 12.20 vs 28.87 ± 4.59 pg/mL, $p = 0.05$) were significantly higher in IgAN patients than in normal controls. Significant correlations were found between miR-155 levels and Foxp3, Cosmc level, 24-h urine protein amount, urine RBC count, serum IgA concentration, and IgA1 dys-glycosylation level. **Conclusion** A remarkably lower expression of peripheral lymphocyte miR-155 was observed in IgAN patients, leading to T lymphocyte subgroup drifting (increases in Th2 and Th17 along with decreases in Th1 and Treg), which inhibits Cosmc gene expression and worsens the aberrant glycosylation of IgA1 in IgAN patients. These results suggest that miR-155 may play an important role in the pathogenesis of IgAN and could serve as a potential disease biomarker.

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Keywords MicroRNA-155 · IgA nephropathy · T lymphocyte subgroups

Introduction

IgA nephropathy (IgAN) is one of the most common forms of glomerulonephritis worldwide [1]. Although this disease has been studied for more than 60 years, its pathogenesis remains unclear. Increasing evidence indicates that disturbed immune reactions such as T lymphocyte homeostasis and an imbalance of circulating T-helper cells and regulatory T cells are involved in the development of IgAN [2–6]. Nevertheless, the mechanism of these immune disorders has not been clarified.

Posttranscriptional regulation by microRNAs (miRNAs) is very important in T cell development. miRNAs regulate gene expression at the posttranscriptional level and play important roles in many physiological and pathological processes [7]. Accumulating evidence suggests that miRNAs are involved in many kidney diseases, such as diabetic nephropathy, polycystic kidney disease, lupus nephritis, and IgAN [8–12]. miR-155 is a multi-functional immune regulatory microRNA that plays distinct roles in mammalian immunity [13, 14], including the fitness of T regulatory (Treg) cells [15] and the Th1/Th2 balance [16, 17]. Therefore, we conducted this study to explore the relationship between miR-155 expression and the T lymphocyte subgroup ratio as well as the clinical manifestations of IgAN.

Materials and methods

Patients and healthy controls

Sixty biopsy-proven IgAN patients were examined in this study. Patients were diagnosed with IgAN if glomerular mesangial proliferation was present with IgA as the sole or predominant immunoglobulin deposition. Patients were excluded if they had other systemic diseases such as Schonlein–Henoch purpura, systemic lupus erythematosus, Sjogren syndrome, rheumatoid arthritis, diabetes mellitus,

or liver cirrhosis. No patients had received corticosteroids or other immunosuppressants before biopsy. Clinical data were collected, including BP, urinalysis, serum creatinine, albumin, blood urine nitrogen (BUN), cystatin C, and 24-h urine protein. A renal biopsy was performed in every patient recruited in this study. Twenty-five healthy volunteers without any known disease or a family history of genetic disease were selected as controls. BP, urinalysis, and serum creatinine were measured.

This study was approved by the Ethics Committee of West China Hospital of Sichuan University in accordance with the Declaration of Helsinki. Written informed consent was obtained from each participant.

Lymphocyte isolation and RNA extraction

Lymphocytes were isolated according to a method previously reported [18]. Briefly, peripheral blood mononuclear cells (PBMCs) were separated from EDTA-anticoagulated venous blood by density gradient centrifugation using Lymphocyte-H Lymphocyte Isolation Media (Cedarlane Laboratories, Canada). Monocytes were depleted by the wall sticking method for 2 h. Total RNA was extracted using TRIzol reagent (Invitrogen, USA) according to the manufacturer's instructions. RNA quality and quantity were measured using a NanoDrop spectrophotometer (ND-1000, Nanodrop Technologies). RNA integrity was determined by gel electrophoresis.

RNA labeling and microRNA microarray

The microRNA microarray was performed separately in five IgAN patients and five healthy controls. MicroRNA labeling was performed using a miRCURY™ Hy3™/Hy5™ Power Labeling Kit (Exiqon, Denmark) according to the manufacturer's guidelines. After labeling, samples were hybridized onto miRCURY™ LNA Array (version 16.0) (Exiqon, Denmark) slides in a 12-Bay Hybridization System (Nimblegen Systems, USA). Thereafter, slides were scanned using an Axon GenePix 4000B microarray scanner (Axon, USA). Images were analyzed by GenePix Pro 6.0 software (Axon, USA) for data extraction.

Table 1 qPCR primers used in this study

	Forward	Reverse
GAPDH	GCACCGTCAAGGCTGAGAAC	TGGTGAAGACGCCAGTGGA
Foxp3	CTGACCAAGGCTTCATCTGTG	ACTCTGGGAATGTGCTGTTC
c-Maf	CATGCATTACGATGCTTGCT	TGGATGTCATGCGCTAAGTC
STAT-6	CCTCGTCACCAGTTGCTT	TCCAGTGCTTTCTGCTCC
GATA-3	CAATGCCTGTGGGCTCTACTAC	GGCTGAAGGGCGAGATGTG
SOCS-1	ACCTTCTTGGTGC GCGAC	TCAAATCTGGAAGGGGAAGG

Table 2 Baseline clinical characteristics of participants

	IgAN patients (<i>n</i> = 60)	Controls (<i>n</i> = 25)
Age (years)	34.7 ± 4.4	31.5 ± 4.7 ^a
Male/female	30/30	13/12
Disease duration (months) ^a	20.2 ± 11.7	NA
Blood pressure systolic (mmHg)	110.7 ± 27.8 ^a	103.5 ± 12.5 ^a
Blood pressure diastolic (mmHg)	74.1 ± 7.9 ^a	60.9 ± 10.8 ^a
Urine RBC (per view)	29.7 ± 13.6	NA
24-h urine protein (g)	2.21 ± 0.24	NA
Serum albumin (g/L)	35.6 ± 5.3	NA
Serum BUN (mmol/L)	6.57 ± 1.78	NA
Serum creatinine (μmol/L)	107.7 ± 21.6	NA
Serum cystatin C	1.12 ± 0.33	NA

^a Expressed as the mean ± standard deviation

Measuring IgA1 dys-glycosylation level and T lymphocyte cytokines

The serum IgA1 dys-glycosylation level was measured using an IgA1 dys-glycosylation ELISA kit (Shanghai, China) according to the manufacturer's guidelines. Briefly, samples were added to 96-well plates in duplicate and incubated for 30 min at 37 °C. After incubation for an additional 30 min at 37 °C with detecting solution, color was developed and detected at 450 nm. Serum T lymphocyte cytokines (IFN-γ, IL-5, IL-10, and IL-17) were measured using multiplex immunoassay kits (Millipore Corporation, USA) and detected with a multiplex detection platform (Luminex[®] 100/200[™] System, USA) according to the manufacturer's guidelines.

Flow cytometric analysis on T lymphocyte subgroup

The cellular phenotypes of peripheral T cells (Th1, Th2, Th17, and CD4⁺CD25⁺Foxp3⁺ Treg) were defined by multicolor flow cytometry. Anti-human CD4-FITC, CD3-PE, CD25 a-APC, IL4-PE-Cy7, IL17-PE-Cy7, and Foxp3-PE were purchased from Becton Dickinson Biosciences (San Diego, USA). The human Treg staining kit and anti-human IFN-γ-Percp-Cy5 antibodies were obtained from eBioscience (San Diego, USA). Cells were stained according to the manufacturer's recommendations. Stained cells were run on a FACSCalibur cytometer (BD Bioscience, USA), and data were analyzed using FACS Diva software (BD Bioscience, USA).

Real-time RT-PCR

Real-time RT-PCR analysis of miR-155 was performed using the TaqMan microRNA assay kit (Applied Biosystems, USA) with U6 as an endogenous control. Real-time RT-PCR of Foxp3, c-Maf, STATA-6, GATA-3, SOCS-1, Foxp3, and GAPDH was performed using Bio-Rad iQ SYBR Green Supermix with Opticon2 (Bio-Rad, USA); GAPDH served as an endogenous control. The primers used are listed in Table 1. qPCR products were purified and sequenced directly by Invitrogen (Shanghai, China) to confirm the consistencies with GenBank records.

Statistical analysis

Data obtained from this study were expressed as the mean ± SEM and were analyzed using SPSS 19.0 statistical software (Chicago, USA). *P* < 0.05 was considered statistically significant.

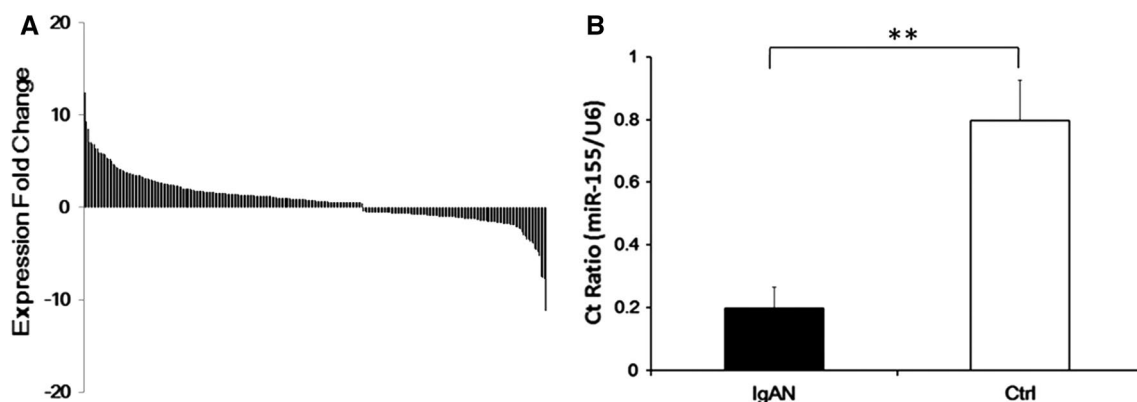


Fig. 1 **a** MicroRNA microarray results. In the 1032 microRNAs successfully analyzed, 533 microRNAs are up-regulated and 499 are down-regulated compared to normal controls. **b** miR-155 expression

in peripheral lymphocytes of IgAN patients and healthy controls (Ct ratio 0.197 ± 0.068 vs 0.796 ± 0.130, *p* < 0.01)

Table 3 Expression profile of several immune-related microRNAs in the peripheral lymphocytes of IgAN patients (shown as fold changes or percent decrease)

Up-regulated			Down-regulated		
ID	Fold	<i>p</i>	ID	% Decrease	<i>p</i>
miR-29c	13.43	0.12	miR-146a	20	0.07
miR-142-3p	10.29	0.08	miR-146b-3p	21	0.12
miR-223	6.86	0.43	miR-152	27	0.31
miR-145	4.83	0.24	miR-181a	30	0.06
miR-150	4.61	0.54	miR-191	31	0.84
miR-491-3p	3.93	0.10	miR-137	34	0.58
miR-17*	2.30	0.09	miR-92b	38	0.43
miR-374c	2.10	0.58	miR-132	52	0.09
miR-23b*	2.02	0.13	miR-155	61	0.04
miR-23a	1.87	0.11	miR-148a	73	0.07
miR-26a	1.14	0.08	miR-26b*	89	0.09

Bold values indicate the difference with significance

* Part of the name of specific microRNA

Results

Clinical characteristics of participants

IgAN patients and healthy controls did not differ significantly in age, sex, or ethnological background ($p > 0.05$) (Table 2).

MicroRNA microarray and qPCR indicate miR-155 deficiency in the PBMCs of IgAN patients

We first examined the total miRNA expression profile in the PBMCs of IgAN patients by microarray. In the microarray analysis, 1032 microRNAs were successfully measured; among them, 533 were up-regulated and 499 were down-regulated compared to healthy controls (detailed results are provided in the supplemental material). A threshold of an increase or a decrease more than 50% that of normal controls was used to identify up- or down-regulated miRNAs (Fig. 1a). Fold changes of several important microRNAs

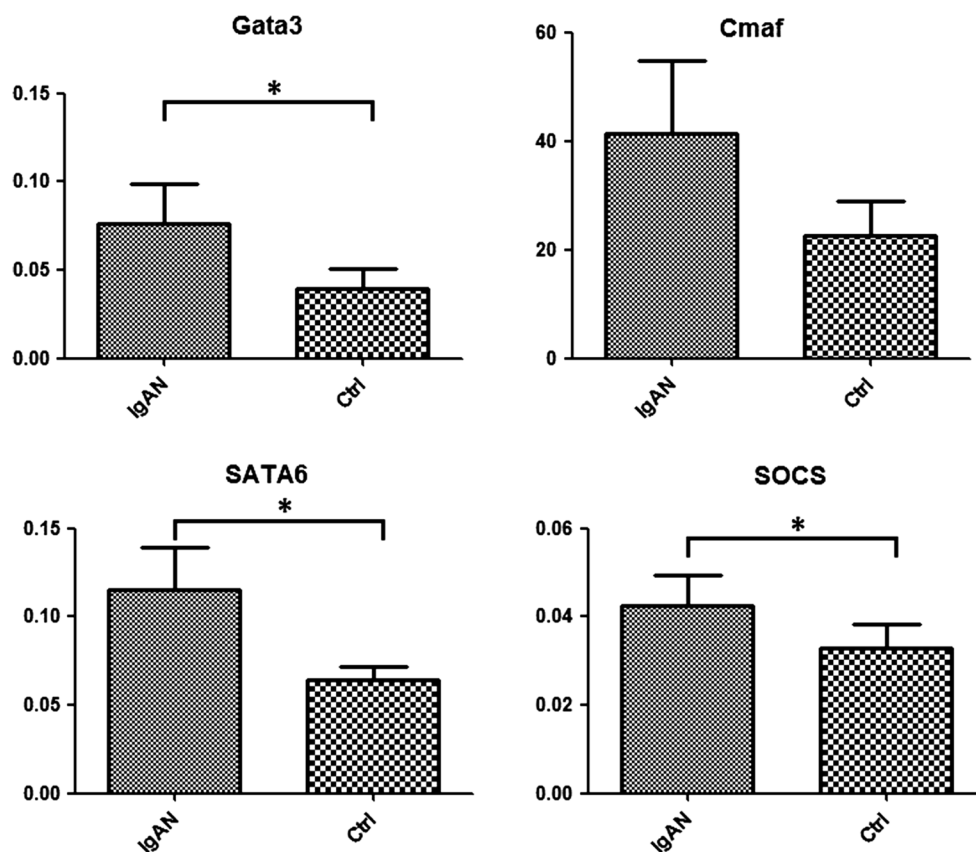


Fig. 2 Real-time RT-PCR of PBMCs indicates that the expression spectrum of T lymphocyte differentiation regulators in IgAN patients is remarkably different than those in normal controls. IgAN patients

had significantly higher expression levels of GATA-3, SATA-6 and SOCS-1, but not c-Maf

related to lymphocyte development, differentiation, and regulation are listed in Table 3. Although the expression levels of most microRNAs were not significantly different relative to normal controls, the miR-155 level in the PBMCs of IgAN patients was dramatically decreased compared to healthy controls (decreased 61%), which was confirmed by real-time RT-PCR (Ct ratio 0.197 ± 0.068 vs 0.796 ± 0.130 , $p < 0.01$, Fig. 1b).

qPCR, flow cytometry, and ELISA reveal that lymphocyte differentiation regulatory expression disorder leads to T lymphocyte subgroup drifting in IgAN patients

Quantification of real-time RT-PCR results indicated that the mRNA expression levels of T lymphocyte differentiation regulators in the PBMCs of IgAN patients are remarkably different than those in normal controls. The expression levels of GATA-3 (Ct ratio 0.08 ± 0.02 vs 0.04 ± 0.01 , $p = 0.035$), SAT-6 (Ct ratio 0.12 ± 0.02 vs 0.06 ± 0.01 , $p = 0.036$), and SOCS-1 (Ct ratio 0.04 ± 0.01 vs 0.03 ± 0.01 , $p = 0.01$)

were significantly higher in IgAN patients than in healthy controls; however, the expression level of c-Maf did not differ between IgAN patients and controls (Fig. 2). Furthermore, flow cytometric analysis demonstrated that the percentages of peripheral blood Th1 (17.35 ± 1.22 vs 20.89 ± 1.22 , $p = 0.042$) and $CD4^+CD25^+Foxp3^+$ Treg (1.86 ± 0.15 vs 2.48 ± 0.26 , $p = 0.031$) cells were significantly lower in IgAN patients than in normal controls. However, the percentages of Th2 (1.73 ± 0.29 vs 1.04 ± 0.18 , $p = 0.046$) and Th17 (4.09 ± 0.45 vs 2.06 ± 0.21 , $p < 0.001$) cells were remarkably higher in IgAN patients compared with normal controls (Fig. 3). Serum T lymphocyte cytokines (IFN- γ , IL-5, IL-10, and IL-17) were measured using multiplex immunoassay kits, which indicated that Th1 cytokine INF- γ (40.77 ± 8.39 vs 83.02 ± 17.4 pg/mL, $p = 0.035$) and $CD4^+CD25^+Foxp3^+$ Treg cytokine IL-10 (0.77 ± 0.28 vs 4.18 ± 1.34 pg/mL, $p = 0.02$) levels were lower, while Th2 cytokine IL-5 (1.02 ± 0.17 vs 0.65 ± 0.07 pg/mL, $p = 0.04$) and Th17 cytokine IL-17 (53.78 ± 12.20 vs 28.87 ± 4.59 pg/mL, $p = 0.05$) were significantly higher in IgAN patients than in normal controls (Fig. 4).

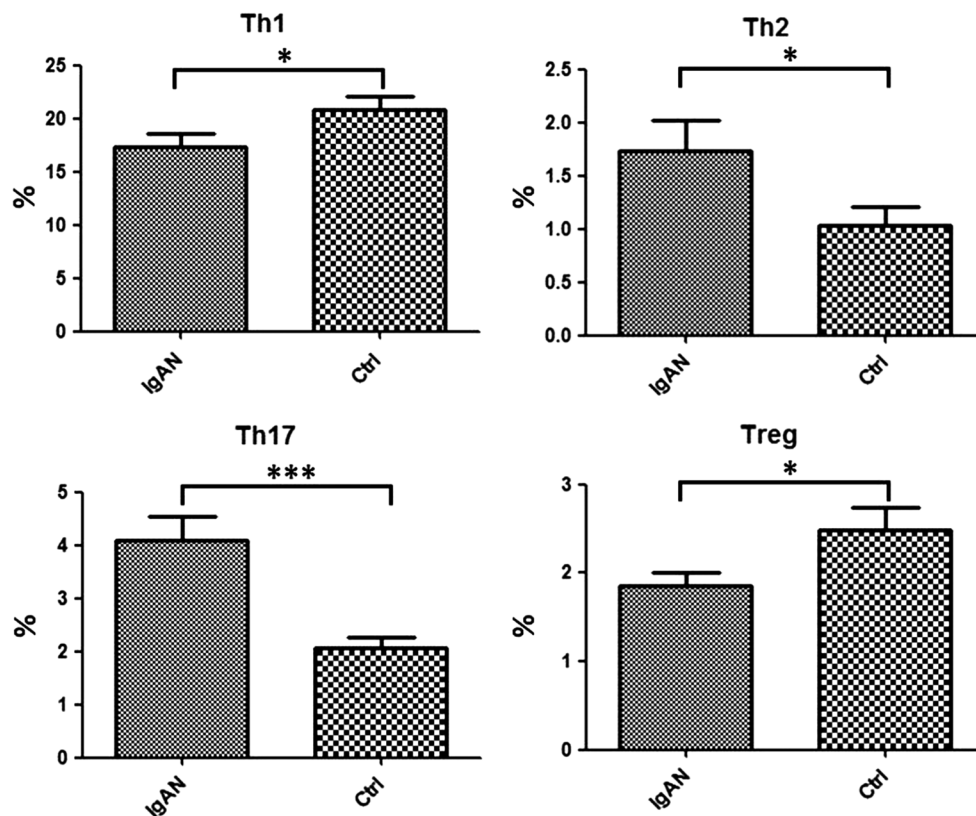


Fig. 3 Flow cytometric analysis of PBMCs indicates remarkable subgroup drifting in IgAN patients compared with normal controls. The percentages of peripheral blood Th1 and $CD4^+CD25^+Foxp3^+$

Treg cells in IgAN patients were significantly lower than in normal controls; however, the percentages of Th2 and Th17 cells were remarkably higher

miR-155 level is related to Foxp3 and Cosmc expression as well as IgA1 glycosylation levels in IgAN patients

We also performed a qPCR analysis on Foxp3 and Cosmc genes, which indicated that the expression of Foxp3 (Ct ratio 0.013 ± 0.003 vs 0.040 ± 0.01 , $p = 0.026$) and Cosmc (Ct ratio 0.08 ± 0.02 vs 0.19 ± 0.04 , $p = 0.024$) in peripheral lymphocytes of IgAN patients was remarkably decreased compared with those of the healthy controls (Fig. 5). ELISA analysis revealed that the serum IgA1 dys-glycosylation level was higher in IgAN patients than in normal controls (OD value 0.34 ± 0.04 vs 0.20 ± 0.03 , $p = 0.01$). Moreover, significant correlations were found between miR-155 levels and Foxp3 ($R^2 = 0.46$, $p < 0.001$) and Cosmc ($R^2 = 0.18$, $p = 0.033$) expression, as well as IgA1 dys-glycosylation ($R^2 = 0.187$, $p = 0.044$) levels (Fig. 5).

miR-155 expression is related to clinical manifestations

Potential correlations between peripheral lymphocyte miR-155 level and clinical manifestations such as 24-h proteinuria, hematuria, serum creatinine, BUN, and cystatin C were

analyzed in IgAN patients. We found that peripheral lymphocyte miR-155 level was significantly correlated with 24-h urine protein level ($r = -0.726$, $p < 0.001$), urine RBC count ($r = -0.796$, $p < 0.001$), and serum IgA level ($r = -0.499$, $p = 0.003$), but not with serum creatinine ($r = 0.075$, $p = 0.68$), BUN ($r = 0.087$, $p = 0.64$), or cystatin C ($r = 0.171$, $p = 0.35$) (Fig. 6).

Discussion

To our knowledge, the present study is the first performed in the PBMCs of IgAN patients to clarify the role of T lymphocyte-related microRNAs in the pathogenesis of IgA nephropathy. In the microarray analysis, 1032 microRNAs were successfully measured; among them, 533 were up-regulated and 499 were down-regulated compared with normal controls (Fig. 1a). The microarray (decreased 61%) and real-time RT-PCR (0.197 ± 0.068 vs 0.796 ± 0.130) analyses revealed that the miR-155 expression level was significantly lower in peripheral lymphocytes of IgAN patients than in healthy controls ($p < 0.001$).

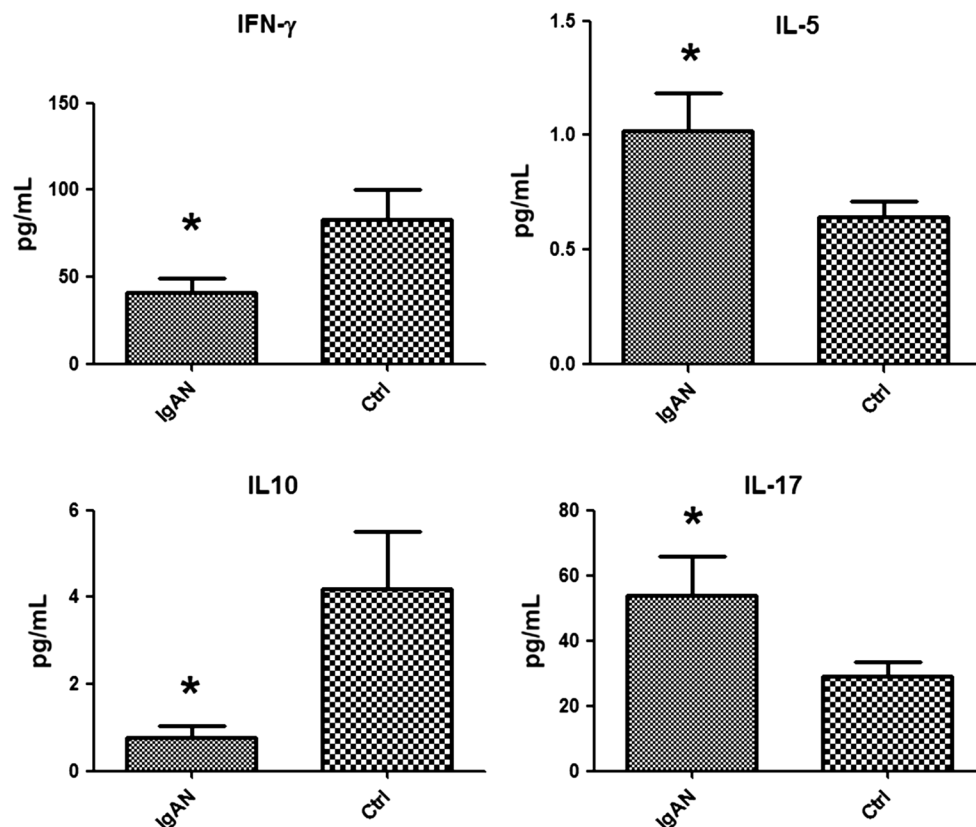


Fig. 4 ELISA analysis indicates that T lymphocyte cytokines in IgAN patients are remarkably different than those in normal controls. Th1 cytokine INF- γ and CD4⁺CD25⁺Foxp3⁺ Treg cytokine IL-10

levels were lower, while Th2 cytokine IL-5 and Th17 cytokine IL-17 were significantly higher in IgAN patients than in normal controls

miR-155 participates in the regulation of differentiation and activation of T and B lymphocytes as well as lymphocyte homeostasis [13]. Significant lymphocyte immune disorders and drifting of the Th1/Th2 balance have been observed in miR-155 knockout mice. Moreover, miR-155 inhibits the transcription of c-Maf, STATA-6, and GATA-3, which in turn affects the expression of IL-4 [17]. It was also reported that miR-155 promotes the maturation and differentiation of Treg cells through the regulation of SOCS-1 [16]. The Th2 polarization of CD4⁺ T cells and the decrease in Treg cells is observed when there is miR-155 deficiency. In this study, we found that mRNA expression levels of T lymphocyte differentiation regulators (GATA-3, SATA-6 and SOCS-1) in the PBMCs of IgAN patients are remarkably higher than those in normal controls while Foxp3 is much lower. Furthermore, flow cytometric analysis revealed that the percentages of peripheral blood Th1 and CD4⁺CD25⁺Foxp3⁺ Treg cells are significantly lower in IgAN patients than in normal controls; however, the percentages of Th2 and Th17 cells are remarkably higher in IgAN patients. A multiplex immunoassay also indicated that Th1 cytokine INF- γ and CD4⁺CD25⁺Foxp3⁺ Treg cytokine IL-10 levels are lower, while Th2 cytokine IL-5 and Th17 cytokine are significantly higher in IgAN patients than in normal controls. These results suggest that the miR-155 deficiency observed in IgAN patients may result in Th2 polarization and a decreased Treg/Th17 ratio.

Several studies have shown that T lymphocyte subgroup members participate in the regulation of IgA molecular glycosylation. It was reported that the Th2 cytokine IL-4 inhibits the expression of β 1, 3GT, and Cosmc, leading to dys-glycosylation of IgA. Meanwhile, Treg cells can alter the Th1 and Th2 ratio by promoting Th2 cell apoptosis and may influence IgA glycosylation [3, 19]. In the current study, we found significant correlations between miR-155 levels and Foxp3 ($R^2 = 0.46$, $p < 0.001$) and Cosmc ($R^2 = 0.18$, $p = 0.033$) expression, as well as IgA1 dys-glycosylation ($R^2 = 0.187$, $p = 0.044$) (Fig. 5).

Another important finding of this study is that the peripheral lymphocyte miR-155 level is related to the clinical manifestations of IgAN patients, such as 24-h urine protein level ($r = -0.726$, $p < 0.001$), urine RBC count ($r = -0.796$, $p < 0.001$), and serum IgA concentration ($r = -0.499$, $p = 0.003$), but not with renal function indices such as serum creatinine ($r = 0.075$, $p = 0.685$), BUN ($r = 0.087$, $p = 0.637$), and cystatin C ($r = 0.171$, $p = 0.351$). Considering that severe proteinuria and hematuria indicate a poor prognosis of IgAN [21], lower miR-155 expression may also suggest a poor prognosis of the disease. Correlations found in the current study indicate a potential use of microRNA as a biomarker of IgA nephropathy, which may aid in the diagnosis, treatment, and prognosis prediction of the disease.

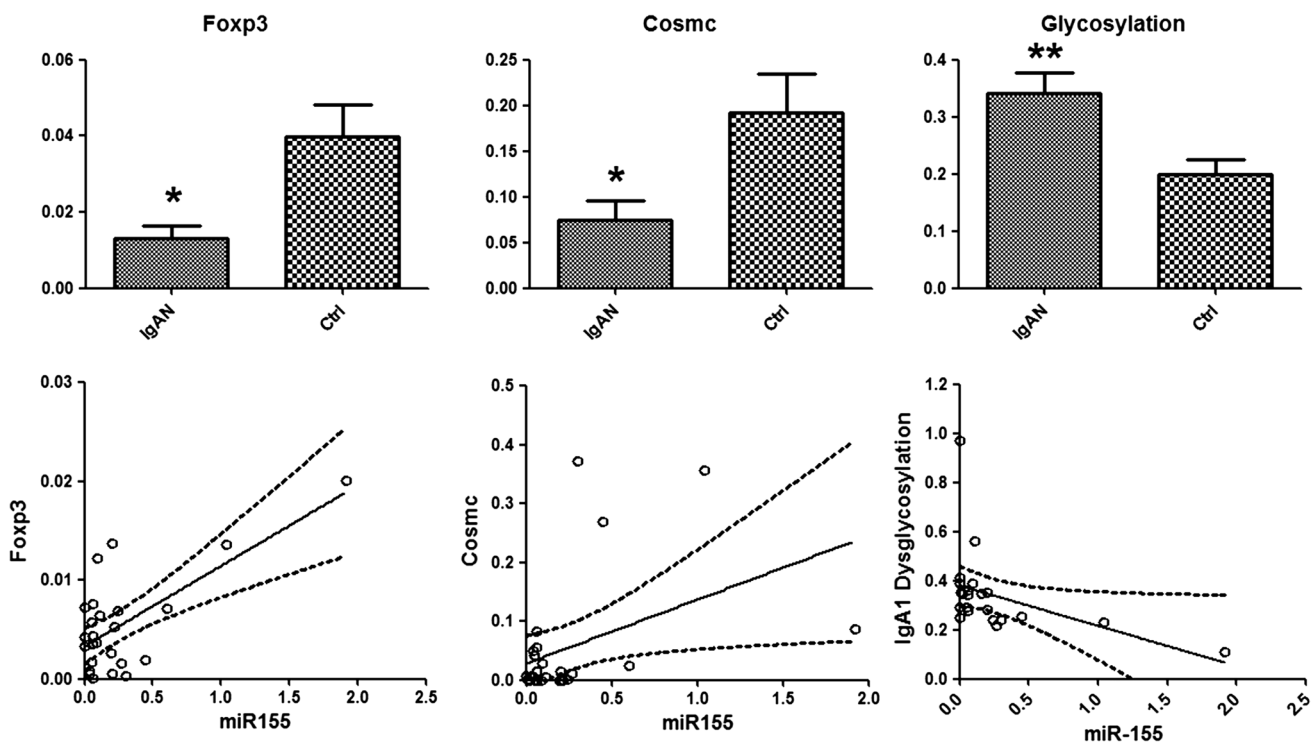


Fig. 5 Correlation between miR-155 and Foxp3 and Cosmc expression and IgA dys-glycosylation

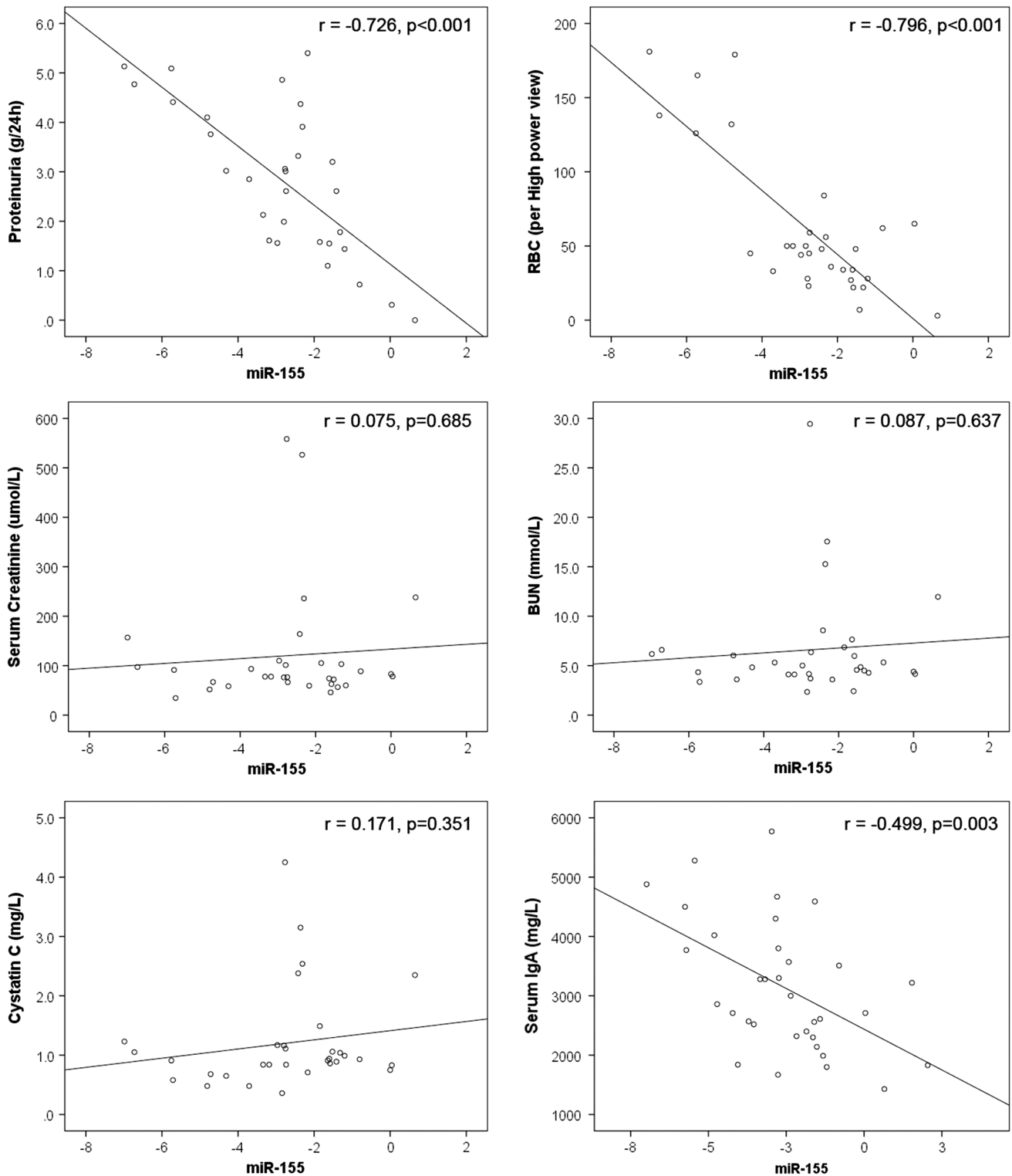


Fig. 6 Correlation of peripheral lymphocyte miR-155 expression level (Ln Ct ratio) with 24-h urine protein level, urine RBC count, serum creatinine, BUN, cystatin C, and serum IgA (the horizontal axis represents the natural logarithm of the miR-155 Ct ratio)

Our findings are remarkably different from those of recent studies that reported that intra-renal expression and urinary miR-155 are increased in IgAN patients [11]. This

difference may be explained by the fact that the micro-RNA expression pattern varies by tissue and organ. On the other hand, given that IgA secretion and glycosylation

disorders are the main pathogenesis of IgAN, lymphocytes are believed to be the initial site of the pathogenic process. We speculated that examination of the microRNA expression profile in kidney tissue would only identify downstream responders rather than upstream disease initiators and could only provide information on in situ miRNAs related to mesangial proliferation or the fibrotic process rather than microRNAs related to the underlying causes of IgAN. The decreased miR-155 expression level in peripheral lymphocytes may reflect the functional deficiency of T cell immunity, which was reflected by a higher serum IgA level as well as renal deposition level in our study, whereas the increased miR-155 level in kidney tissue and urine may reflect intra-renal fibrotic inflammatory responses.

In previous studies, we found that a defect in IgA₁ glycosylation caused by *Cosmc* gene expression is one of the key pathogenic causes of IgAN [18, 21]. Based on the findings of this study, we suspect that decreased miR-155 expression in the peripheral lymphocytes of IgAN patients results in T lymphocyte subgroup drifting, i.e., an increase in Th2 and Th17 along with a decrease in Th1 and Treg. This “drifting” induces suppression of the *Cosmc* gene and thus results in aberrant IgA₁ glycosylation and ultimately kidney IgA deposition and IgAN.

Although some interesting findings were found in the current study, there are still several limitations. Firstly, microRNA analysis was performed on PBMCs rather than isolated lymphocyte subgroups because we were unable to extract a sufficient amount of RNA for the microRNA microarray from lymphocyte subgroups. Further studies may be needed to clarify our findings using isolated T lymphocyte subgroups. Secondly, although we determined that the expression levels of several immune-related microRNAs in IgAN patients differed from those in normal controls, most differences were not statistically significant. Furthermore, qRT-PCR studies with more patients will be performed to confirm these preliminary results.

Conclusion

Remarkably lower expression of peripheral lymphocyte miR-155 was observed in IgAN patients, leading to T lymphocyte subgroup drifting (an increase in Th2 and Th17 along with a decrease in Th1 and Treg), which inhibits *Cosmc* gene expression and worsens the aberrant glycosylation of IgA1 in IgAN patients. These results suggest that miR-155 may play an important role in the pathogenesis of IgAN and could serve as a potential disease biomarker.

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Compliance with ethical standards

Conflict of interest The authors report no conflicts of interest.

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