

Overexpression of miR-183-5p Attenuates Hyperuricemic Nephropathy-Induced Renal Interstitial Fibrosis by Targeting Egr-1 and Inactivating the TGF- β 1/Smad pathway

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Abstract

Background

Hyperuricemic nephropathy (HN) is a major driver of chronic kidney disease characterized by tubulointerstitial fibrosis. MicroRNAs play critical roles in renal disease, yet the precise function of miR-183-5p in HN remains unclear. This study investigated the protective mechanism of miR-183-5p and its downstream target, early growth response-1 (Egr-1), in high uric acid (UA)-induced renal fibrosis.

Methods

Bioinformatics analysis was conducted to predict target genes. Mouse renal tubular epithelial (TCMK-1) cells and C57BL/6J mice were used to establish *in vitro* and *in vivo* HN models. Gains- and loss-of-function experiments, including AAV-mediated overexpression, were performed. Renal function, histological alterations, and expression of Egr-1 and TGF- β 1/Smad signaling markers were evaluated.

Results

Bioinformatics identified Egr-1 as a direct target of miR-183-5p. MiR-183-5p was significantly downregulated in high UA-treated TCMK-1 cells and HN mice. Inhibition of miR-183-5p accelerated fibrotic marker expression. Conversely, overexpression of miR-183-5p attenuated serum creatinine, BUN, and SUA levels, and suppressed collagen deposition and interstitial inflammation in HN mice. Mechanistically, miR-183-5p down-regulated Egr-1 and inhibited the TGF- β 1/Smad pathway. Notably, Egr-1 overexpression counteracted the anti-fibrotic effects of miR-183-5p *in vitro*.

Conclusions

MiR-183-5p protects against hyperuricemia-induced renal interstitial fibrosis by directly targeting Egr-1 and inactivating the TGF- β 1/Smad pathway. Targeting the miR-183-5p/Egr-1 axis represents a promising therapeutic strategy for HN.

‘Clinical trial number: not applicable.’

1. Introduction

Hyperuricemia nephropathy (HN) is a progressive pathological condition resulting from elevated serum uric acid (UA) levels, ultimately leading to renal dysfunction and structural damage [1, 2]. Early in the 20th century, epidemiological studies revealed that approximately 10–30% of the global population suffered from hyperuricemia, a condition showing a strong association with chronic kidney disease (CKD) [3–5]. Driven by modern industrialization and dietary shifts, the incidence of UA-induced nephropathy has escalated rapidly, rendering HN the third most common etiology of CKD, following hypertensive and diabetic nephropathies [6].

Under physiological conditions, systemic UA exists predominantly as urate and is primarily cleared via renal excretion [7]. However, excessive UA production or impaired renal excretion triggers hyperuricemia, subsequently causing renal parenchyma injury [8]. Emerging evidence indicates that sustained hyperuricemia promotes renal fibrosis through the activation of inflammatory cascades and oxidative stress pathways [2, 9, 10]. Fibrosis, characterized by maladaptive tissue repair, abnormal extracellular matrix (ECM) deposition, and structural remodeling, represents an irreversible hallmark of HN and a principal contributor to end-stage renal disease (ESRD) [11–14]. Pathologically, high UA-induced renal fibrosis is marked by tubulointerstitial fibrotic lesions, as well as the proliferation of glomerular mesangial and endothelial cells, accompanied by robust inflammatory cell infiltration and elevated ECM synthesis [15, 16]. These findings underscore the crucial role of fibrosis in driving HN progression.

MicroRNAs (miRNAs)—a class of small non-coding RNAs approximately 22 nucleotides in length—exert post-transcriptional gene silencing by binding to target messenger RNAs (mRNAs) [17, 18]. MiRNAs play pivotal roles in diverse cellular functions, including proliferation, differentiation, and ECM dynamic homeostasis [19]. Notably, recent studies have demonstrated that specific miRNAs participate in modulating hyperuricemic renal fibrosis [28]. Among these, miR-183-5p has emerged as a key regulatory node in diverse human diseases, influencing cell proliferation, migration, and apoptosis by targeting specific signaling cascades [20–23, 31–34]. Specifically, miR-183-5p has been shown to exert protective effects against fibrotic tissue injury by suppressing target gene expression to inhibit cell activation [28, 33].

Transforming growth factor-beta (TGF- β 1) signaling is a canonical pathway driving tissue fibrogenesis [24]. Upon binding to type II receptors, TGF- β 1 recruits and activates type I receptors (such as TGF- β 1RI), which subsequently phosphorylates Smad2/3 to form a transcriptional complex that translocates into the nucleus to induce downstream pro-fibrotic targets, including collagen components and α -smooth muscle actin (α -SMA), thereby directly promoting fibroblast activation, interstitial ECM accumulation, and epithelial-mesenchymal transition (EMT) in renal tubular cells [9, 24, 25, 28]. Furthermore, early growth response factor 1 (Egr-1), a crucial transcription factor, regulates gene networks under diverse pathological stresses [26, 27]. While Egr-1 has been implicated in mediating pulmonary and inflammation-related fibrotic pathways [26], accumulating evidence shows that its expression is significantly upregulated in renal interstitial fibrosis and its deficiency protects against renal dysfunction [26, 30].

Hence, this study aimed to investigate the precise mechanisms by which miR-183-5p and the Egr-1/ TGF- β 1/Smad axis regulate hyperuricemic renal fibrosis, thereby providing theoretical insights and novel therapeutic targets for clinical intervention.

2. Materials and Methods

2.1. Animal studies and hyperuricemic nephropathy (HN) model

Male C57BL/6J mice (8–10 weeks old, weighing 20–25 g) were purchased from Changsha Hunan Slike Jingda Experimental Animal Co., Ltd. (Hunan, China). All mice were housed in a specific pathogen-free (SPF) facility under controlled environmental conditions ($22 \pm 2^\circ\text{C}$, 50%–60% relative humidity, and a 12 h light/dark cycle) with *ad libitum* access to standard chow and water. The hyperuricemic nephropathy (HN) model was established by daily intragastric gavage of adenine (0.16 g/kg) and potassium oxonate (2.4 g/kg) suspended in 5% sodium carboxymethyl cellulose (CMC-Na) for 3 consecutive weeks. For *in vivo* gene delivery, recombinant adeno-associated virus serotype 9 expressing miR-183-5p (AAV9-miR-183-5p) or empty vector (AAV9-NC) was administered via tail vein injection two weeks prior to model induction. At the end of the experimental period, blood samples were collected for serum biochemical analysis. All animals were anesthetized by intraperitoneal injection of pentobarbital sodium (100 mg/kg) at the end of the experiment. After complete anesthesia, the mice were euthanized by cervical dislocation. Kidney tissues were harvested, weighed, and immediately processed for histological examination or frozen in liquid nitrogen for Western blot analysis. All animal procedures were approved by the Institutional Animal Care and Use Committee of Hainan Medical University (Approval No. Med-Eth-Re[2025] 599) and performed in strict compliance with the NIH Guide for the Care and Use of Laboratory Animals.

2.2. Cell culture and *in vitro* treatments

The mouse renal tubular epithelial cell line (TCMK-1) was obtained from Hunan Fenghui Biotechnology Co., Ltd. (Hunan, China). Cells were cultured in Minimum Essential Medium (MEM; Gibco, USA) supplemented with 10% fetal bovine serum (FBS; Gibco, USA) and 1% penicillin-streptomycin (PS) at 37°C in a humidified atmosphere containing 5% CO_2 . To establish a hyperuricemic cell model, TCMK-1 cells were exposed to uric acid (UA; 0.8 mM) for 24 h or 48 h.

2.3. Cell transfection and AAV transduction

For gain- and loss-of-function studies *in vitro*, lentiviral vectors encoding miR-183-5p mimic (H-miR-183), miR-183-5p inhibitor (L-miR-183), or corresponding negative control (NC) were constructed and transfected into TCMK-1 cells at a multiplicity of infection (MOI) of 50. Transfection efficiency was evaluated 48 h post-transfection by fluorescence microscopy and quantitative real-time PCR (RT-qPCR). To perform rescue experiments, TCMK-1 cells were co-transfected with an Egr-1 overexpression plasmid (oe-Egr-1) alongside miR-183-5p mimic.

2.4. Histological, immunohistochemical (IHC), and pathomorphological assays

Kidney tissues were fixed in 4% paraformaldehyde, embedded in paraffin, and cut into 4- μm -thick sections. Hematoxylin and Eosin (H&E), Masson's trichrome, and Periodic Acid-Schiff (PAS) stainings were performed according to standard protocols to assess renal structural injury, collagen deposition, and glycogen accumulation, respectively. For IHC analysis, tissue sections were deparaffinized, rehydrated, and subjected to heat-induced antigen retrieval. Sections were incubated with primary antibodies against Egr-1 (1:200; Affinity Biosciences, AF0589) and α -SMA (1:200; Proteintech, 10494-1-

AP) overnight at 4°C, followed by incubation with HRP-conjugated secondary antibody. Stained sections were visualized under a light microscope and quantified using ImageJ software.

2.5. Western blot analysis

Total protein was extracted from TCMK-1 cells and mouse renal cortex tissues using RIPA lysis buffer supplemented with 1 mM PMSF and a protease/phosphatase inhibitor cocktail. Protein concentrations were quantified using a BCA assay kit. Equal amounts of protein (30 µg/lane) were separated by SDS-PAGE and transferred onto PVDF membranes. Membranes were blocked with 5% non-fat milk in TBST for 1 h at room temperature and incubated overnight at 4°C with primary antibodies against Egr-1 (Affinity Biosciences, AF0589), TGF-β1 (Proteintech), p-Smad2/3 (Walleibio, WL02510), t-Smad2/3, α-SMA (Proteintech, 10494-1-AP), Vimentin, and GAPDH (Proteintech). After washing with TBST, membranes were incubated with HRP-conjugated goat anti-rabbit IgG secondary antibody (1:5000; Proteintech, SA00001-2) for 1 h. Protein bands were visualized using an enhanced chemiluminescence (ECL) detection system and quantified using ImageJ. GAPDH served as an internal control.

2.6. RNA isolation and quantitative real-time PCR (RT-qPCR)

Total RNA was extracted from cells and tissue samples using TRIzol reagent according to the manufacturer's instructions. RNA concentration and purity were measured using a NanoDrop spectrophotometer. For miRNA detection, reverse transcription was performed using a miRNA First-Strand cDNA Synthesis Kit. RT-qPCR was conducted on a Real-Time PCR System using SYBR Green Master Mix. U6 was used as an internal normalization control for miR-183-5p. Relative gene expression was calculated using the $2^{-(\Delta\Delta Ct)}$ method.

2.7. Serum biochemical assays

Serum levels of serum creatinine (SCr), blood urea nitrogen (BUN), and serum uric acid (SUA) were measured using commercial enzymatic assay kits according to the manufacturer's protocol.

2.8. Statistical analysis

Data are presented as mean ± standard deviation (SD). Statistical analyses were performed using GraphPad Prism Aofware (version 9.0). Comparisons between two groups were analyzed using Student's *t*-test, while comparisons among multiple groups were evaluated using one-way analysis of variance (ANOVA) followed by Tukey's post-hoc test. A *P*-value < 0.05 was considered statistically significant.

3. Results

3.1. Bioinformatic identification of miR-183-5p target genes and Egr-1 binding sites in HN

To explore the potential miRNA-gene interactions involved in hyperuricemic nephropathy (HN), transcriptomic data from renal tubular cells in a rat model of HN-associated fibrosis (GSE214358) were analyzed. A total of 1,761 differentially expressed genes (DEGs) satisfying the criteria ($|\log_2FC| > 1$, adjusted $p < 0.05$) were identified and displayed in a volcano plot (Fig. 1B). Furthermore, target prediction using the TargetScan database retrieved 378 potential target genes for miR-183. Cross-overlap analysis between the DEGs and predicted targets identified 25 differentially expressed genes regulated by miR-183 in HN (Fig. 1A). Notably, sequence alignment via TargetScan revealed that the 3' untranslated region (3' UTR) of early growth response-1 (*Egr-1*) contains a highly conserved binding site for miR-183-5p (Fig. 1C).

3.2. Downregulation of miR-183-5p in HUA-stimulated TCMK-1 cells

To investigate the expression pattern of miR-183-5p under hyperuricemic conditions, TCMK-1 cells were exposed to high concentrations of uric acid (UA, 800 μ M) for 24 h and 48 h. Quantitative RT-PCR analysis demonstrated that miR-183-5p expression was significantly downregulated in UA-treated TCMK-1 cells compared with the control group in a time-dependent manner (Fig. 2). Specifically, miR-183-5p level exhibited a noticeable decrease at 24 h and reached its lowest expression level at 48 h (Fig. 2). Based on these observations, exposure to 800 μ M UA for 48 h was selected as the optimal condition for subsequent *in vitro* functional assays.

3.3. Inhibition of miR-183-5p promotes renal interstitial fibrosis activation *in vitro*

To evaluate the functional role of miR-183-5p loss-of-function in renal fibrosis, TCMK-1 cells were transfected with a miR-183-5p inhibitor (L-miR-183) or exposed to high UA. Western blotting analysis revealed that knock-down of miR-183-5p markedly upregulated the expression of its predicted target, *Egr-1*, along with key profibrotic markers, including TGF- β 1, p-Smad2/3, α -SMA, and vimentin, compared with the negative control group (Fig. 3A). Densitometric analysis confirmed that the protein levels of α -SMA and vimentin in the L-miR-183 group were substantially elevated ($p < 0.05$ vs. NC group), closely mimicking the profibrotic effects induced by high UA exposure (Fig. 3B). These results indicate that inhibition of endogenous miR-183-5p alone is sufficient to trigger ECM accumulation and promote the activation of renal interstitial fibrosis.

(A) Representative Western blot analysis showing the protein expression levels of *Egr1*, TGF- β 1, phosphorylated Smad2/3 (p-Smad2/3), total Smad2/3 (t-Smad2/3), α -SMA, and Vimentin in the indicated experimental groups (CON, HUA, CON + NC, and CON + L-miR183). GAPDH was used as the internal loading control. **(B)** Quantitative densitometric analysis of *Egr1*, TGF- β 1, p-Smad2/3 relative to t-Smad2/3, α -SMA, and Vimentin expression levels normalized to GAPDH. Data are presented as mean $\pm$ SD (n = 3 or 6 per group). $P < 0.01$, *** $P < 0.001$, **** $P < 0.0001$.

3.4. Overexpression of miR-183-5p attenuates high UA-induced renal damage and fibrosis *in vitro* and *in vivo*

To determine whether restoring miR-183-5p expression could suppress fibrosis, both *in vitro* and *in vivo* gain-of-function experiments were performed. In TCMK-1 cells, transfection with the miR-183-5p overexpression vector (H-miR-183) significantly suppressed the high UA-induced upregulation of Egr-1, TGF- β 1, and p-Smad2/3 (Fig. 4A). In the C57BL/6J mouse model of HN, tail vein injection of AAV-miR-183-5p was administered to overexpress miR-183-5p. Serum biochemical analysis demonstrated that mice in the high UA group exhibited significantly increased levels of serum creatinine (SCr), blood urea nitrogen (BUN), and serum uric acid (SUA) compared to control mice; however, miR-183-5p overexpression markedly restored renal function and reduced serum levels of SCr, BUN, and SUA (Fig. 4B). Histopathological evaluation via HE, Masson, and PAS staining revealed prominent renal interstitial inflammation, collagen deposition, and glycogen accumulation in HN mice, all of which were noticeably mitigated by AAV-miR-183-5p treatment (Fig. 4C). Consistent with these histological improvements, immunohistochemical (IHC) staining showed reduced expression of Egr-1 and α -SMA in renal tissues of miR-183-5p-overexpressing mice (Fig. 4D). Furthermore, Western blotting of renal tubular tissue confirmed that miR-183-5p overexpression substantially inhibited the protein levels of Egr-1, TGF- β 1, p-Smad2/3, α -SMA, and vimentin (Fig. 4E). Taken together, these findings demonstrate that miR-183-5p overexpression effectively alleviates high UA-induced renal interstitial fibrosis and functional impairment.

(A) Representative Western blot analysis of Egr-1, TGF- β 1, and p-Smad2/3 protein expression in TCMK-1 cells transfected with miR-183-5p overexpression vector (H-miR-183) under high UA conditions. (B) Serum levels of creatinine (SCr), blood urea nitrogen (BUN), and serum uric acid (UA/SUA) in HN mice following AAV-mediated miR-183-5p overexpression, measured by commercial serum assays. (C) Representative H&E, Masson's trichrome, and PAS staining of kidney tissues evaluating renal interstitial inflammation, collagen deposition, and glycogen accumulation. (D) Representative immunohistochemistry (IHC) images showing expression levels of Egr-1 and α -SMA in renal tissues. (E) Western blot analysis and quantitative normalization of Egr-1, TGF- β 1, p-Smad2/3, total Smad2/3, α -SMA, and Vimentin protein levels in renal tissues. GAPDH was used as the loading control. Data are presented as mean $\pm$ SD (n = 3 or 6 per group). P < 0.01, *** P < 0.001, **** P < 0.0001.

3.5. Egr-1 reversal counteracts the anti-fibrotic effect of miR-183-5p

To confirm whether miR-183-5p exerts its protective effects directly by targeting Egr-1, a rescue experiment was performed by co-transfecting an Egr-1 overexpression plasmid (oe-Egr-1) into UA-stimulated TCMK-1 cells overexpressing miR-183-5p. As expected, co-transfection of oe-Egr-1 successfully restored Egr-1 protein expression that had been suppressed by the miR-183-5p mimic (Fig. 5A). Importantly, Western blotting and quantitative analyses demonstrated that restoration of Egr-1 significantly counteracted the therapeutic benefits of miR-183-5p, as evidenced by the re-elevation of

downstream TGF- β 1/Smad signaling components and fibrotic markers (α -SMA and vimentin) (Fig. 5B). Collectively, these rescue findings provide compelling evidence that miR-183-5p attenuates high UA-induced renal interstitial fibrosis primarily through the targeted repression of Egr-1.

4. Discussion

In hyperuricemic nephropathy (HN), renal tubulointerstitial damage serves as a hallmark pathological feature that significantly drives progressive fibrosis, impairs kidney function, and ultimately leads to end-stage renal failure [9, 16]. Accumulated evidence demonstrates that interstitial fibrosis originates from the abnormal deposition of extracellular matrix (ECM), a process intimately linked to the aberrant activation and injury of renal tubular epithelial cells (RTICs) [9]. In addition, hyperuricemic stimuli and elevated soluble uric acid trigger complex cellular cascades, including oxidative stress, epithelial-to-mesenchymal transition (EMT), and NLRP3 inflammasome activation in renal cells [5, 9, 16]. Therefore, strategies aimed at attenuating tubulointerstitial fibrosis and rescuing renal function are paramount for the clinical management of HN.

In the present study, we observed a marked upregulation of Early Growth Response-1 (Egr-1) in the renal tissues of HN mouse models, consistent with previous reports regarding its profibrotic role. Egr-1 is a key zinc-finger transcription factor that regulates diverse cellular responses, including proliferation, differentiation, and apoptosis. Pathological activation of Egr-1 accelerates the transdifferentiation of fibroblasts into myofibroblasts, increases ECM protein synthesis, and amplifies local inflammatory pathways, thereby exacerbating interstitial fibrosis [26, 30].

Emerging research highlights microRNAs (miRNAs) as pivotal post-transcriptional regulators in renal pathophysiology and fibrotic diseases. Among various candidate miRNAs, miR-183-5p has been identified as a critical regulator across various pathological contexts, including cardiovascular injury, inflammation, and oncogenesis [20–22, 28, 34]. However, its precise functional role and downstream targets in hyperuricemia-induced renal interstitial fibrosis remained largely uncharacterized. Our experimental data revealed that endogenous miR-183-5p levels were significantly diminished in the kidneys of HN models, suggesting that its downregulation may be closely implicated in the pathogenesis and progression of renal interstitial fibrosis.

To elucidate the functional impact and mechanistic pathways of miR-183-5p *in vivo*, we administered an adeno-associated virus (AAV) vector expressing miR-183-5p to hyperuricemic mice. Notably, AAV-mediated overexpression of miR-183-5p significantly preserved renal function and attenuated interstitial collagen deposition and fibrotic lesions. Bioinformatic analysis using the TargetScan database further identified potential target genes regulated by miR-183-5p. Crucially, the 3'-untranslated region (3'-UTR) of Egr-1 mRNA contains complementary binding sites for miR-183-5p. Given that Egr-1 drives pathological RTIC activation and fibrogenesis, we hypothesized that miR-183-5p exerts its anti-fibrotic action by directly targeting and suppressing Egr-1 expression.

Subsequent Western blot analysis confirmed that miR-183-5p upregulation markedly suppressed Egr-1 protein expression, thereby inhibiting downstream profibrotic and inflammatory cascades. These observations substantiate the hypothesis that the miR-183-5p/Egr-1 signaling axis plays a protective role against hyperuricemia-induced renal damage.

Nevertheless, several limitations of this study should be acknowledged. First, although our in vitro experiments demonstrated the protective role of miR-183-5p in renal tubular epithelial cells (TCMK-1), renal interstitial fibrosis involves complex cross-talk between multiple cell types. Future in vitro studies employing primary interstitial fibroblasts and co-culture systems are warranted to further delineate its cell-type-specific mechanisms and potential paracrine effects. Second, human renal biopsy samples were not included to validate the clinical relevance of miR-183-5p expression levels. Future investigations employing transcriptomic profiling and translational clinical cohorts will be essential to fully elucidate the broader regulatory networks of miR-183-5p.

In conclusion, the present study demonstrates for the first time that miR-183-5p protects against hyperuricemia-induced renal interstitial fibrosis by directly targeting Egr-1 and suppressing the dysregulated activation of RTICs. These findings expand our understanding of miRNA-mediated mechanisms in HN pathogenesis and suggest that targeted modulation of the miR-183-5p/Egr-1 axis represents a potential therapeutic strategy for preventing renal fibrosis and managing hyperuricemic nephropathy.

Abbreviations

Hyperuricemic nephropathy (HN)

early growth response

1 (Egr-1) uric acid (UA) Mouse renal tubular epithelial (TCMK-1) chronic kidney disease

(CKD) extracellular matrix (ECM) end-stage renal disease (ESRD) MicroRNAs (miRNAs) messenger

RNAs (mRNAs) Transforming growth factor-beta (TGF-β1) TGF-β1 recruits and activates type I

receptors (such as TGF-β1RI) α-smooth muscle actin (α-SMA) epithelial-mesenchymal transition

(EMT) specific pathogen-free (SPF) carboxymethyl cellulose (CMC-Na) adeno-associated virus

serotype 9 expressing miR-183-5p (AAV9-miR-183-5p) recombinant adeno-associated virus serotype 9

empty vector (AAV9-NC) negative control (NC) multiplicity of infection (MOI) Egr-1 overexpression

plasmid (oe-Egr-1) differentially expressed genes (DEGs) 3' untranslated region (3' UTR)

Declarations

Ethics approval and consent to participate

All animal procedures were approved by the Institutional Animal Care and Use Committee of Hainan Medical University (Approval No. Med-Eth-Re[2025] 599) and performed in strict compliance with the NIH Guide for the Care and Use of Laboratory Animals.

Consent for publication

Agreed to be published in BMC Urology

Availability of data and materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Competing Interests

No potential conflict of interest was reported by the author(s).

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Authors' contributions

All authors contributed to the study conception and design. Jiali Wei conducted the overall conception and guidance of this study. Jiachang Li, Yuhan Ma, Qiong Yuan, Zhanle Chen, Junheng Zhao, Ying Yang collected all data and wrote the manuscript.

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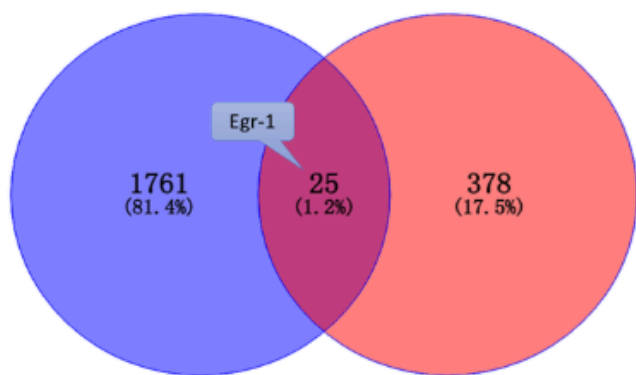
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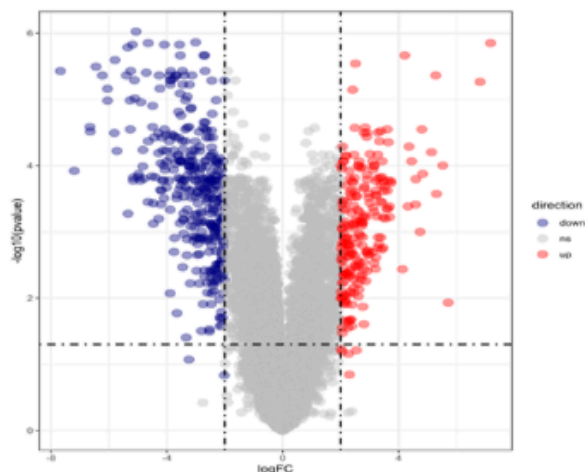
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Figures



■ Differential genes in hyperuricemic nephropathy ■ miR-183-5p Target Gene



Differential genes in hyperuricemic nephropathy

Human Position 411-417 of EGR1 3' UTR
[hsa-miR-183-5p.1](#)
 5' ... CCUUGUACAGUGUCU**GUGCCAUG**...
 3' UCACUUAAGAUGGU**CACGGUAU**

Mouse Position 403-409 of EGR1 3' UTR
[mmu-miR-183-5p](#)
 5' ... CUUUGUACAGCAUCU**GUGCCAUG**...
 3' UCACUUAAGAUGGU**CACGGUAU**

Rat Position 402-408 of EGR1 3' UTR
[rno-miR-183-5p](#)
 5' ... CUUUGUACAGCAUCU**GUGCCAUG**...
 3' UCACUUAAGAUGGU**CACGGUAU**

* The EGR-1 3' UTR miR-183-5p target site is highly conserved and expressed in humans, mice, and rats, showing high similarity.

Figure 1

Validation of miR-183-5p targeting Egr-1. (A) Venn diagram showing overlap between miR-183-5p target genes and DEGs in HN. (B) Volcano plot illustrating significant gene expression variations associated with HN. (C) TargetScan analysis indicating miR-183-5p binding sites within the 3' UTR of Egr-1.

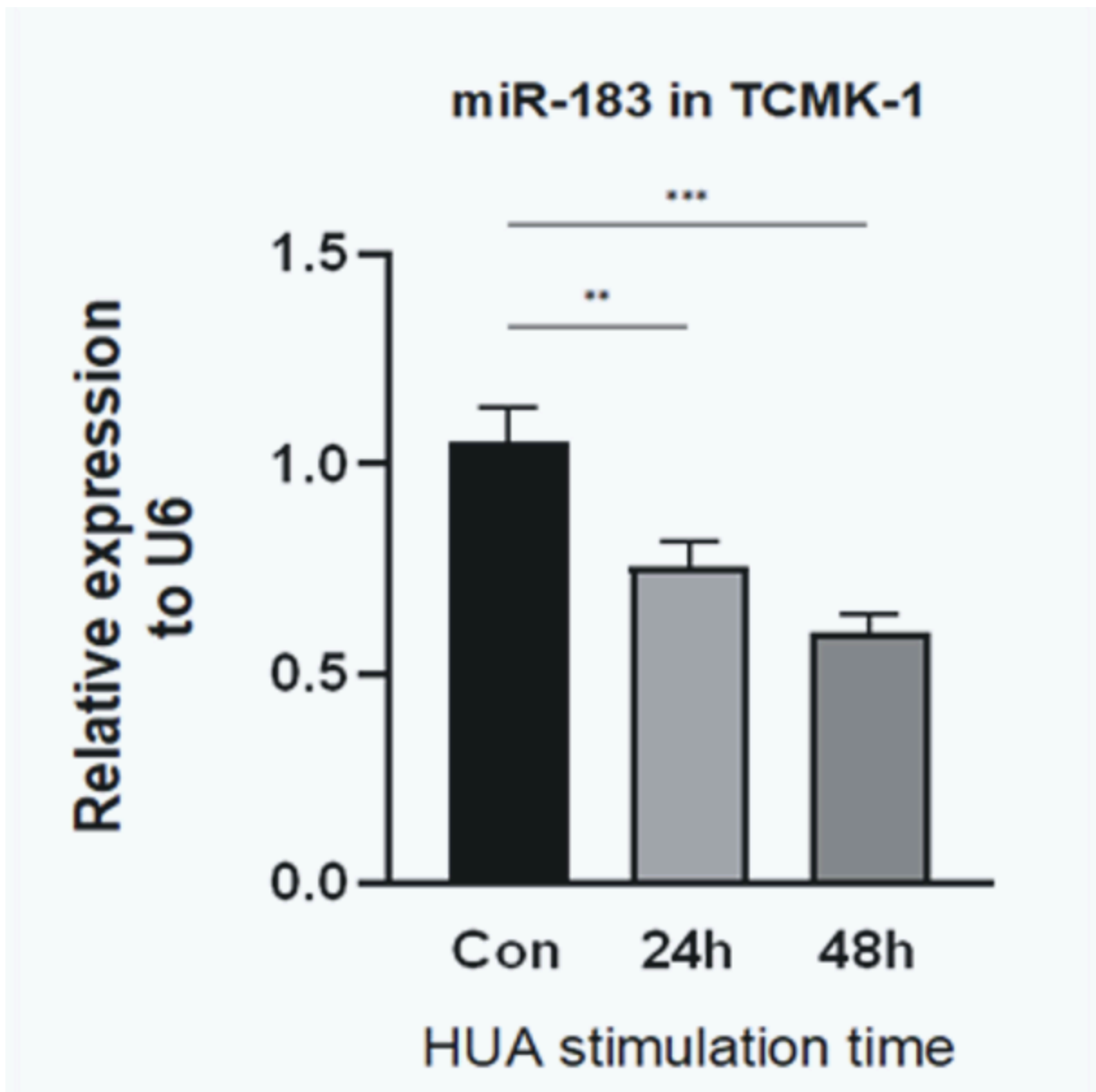


Figure 2

Expression of miR-183-5p in hyperuricemic nephropathy. Changes in miR-183-5p levels measured by RT-PCR in the control group, 24h and 48h hyperuricemia stimulation groups .*** P <0.001. Data are presented as mean $\pm$ SD. One-way ANOVA was used. HUA: hyperuricemia.

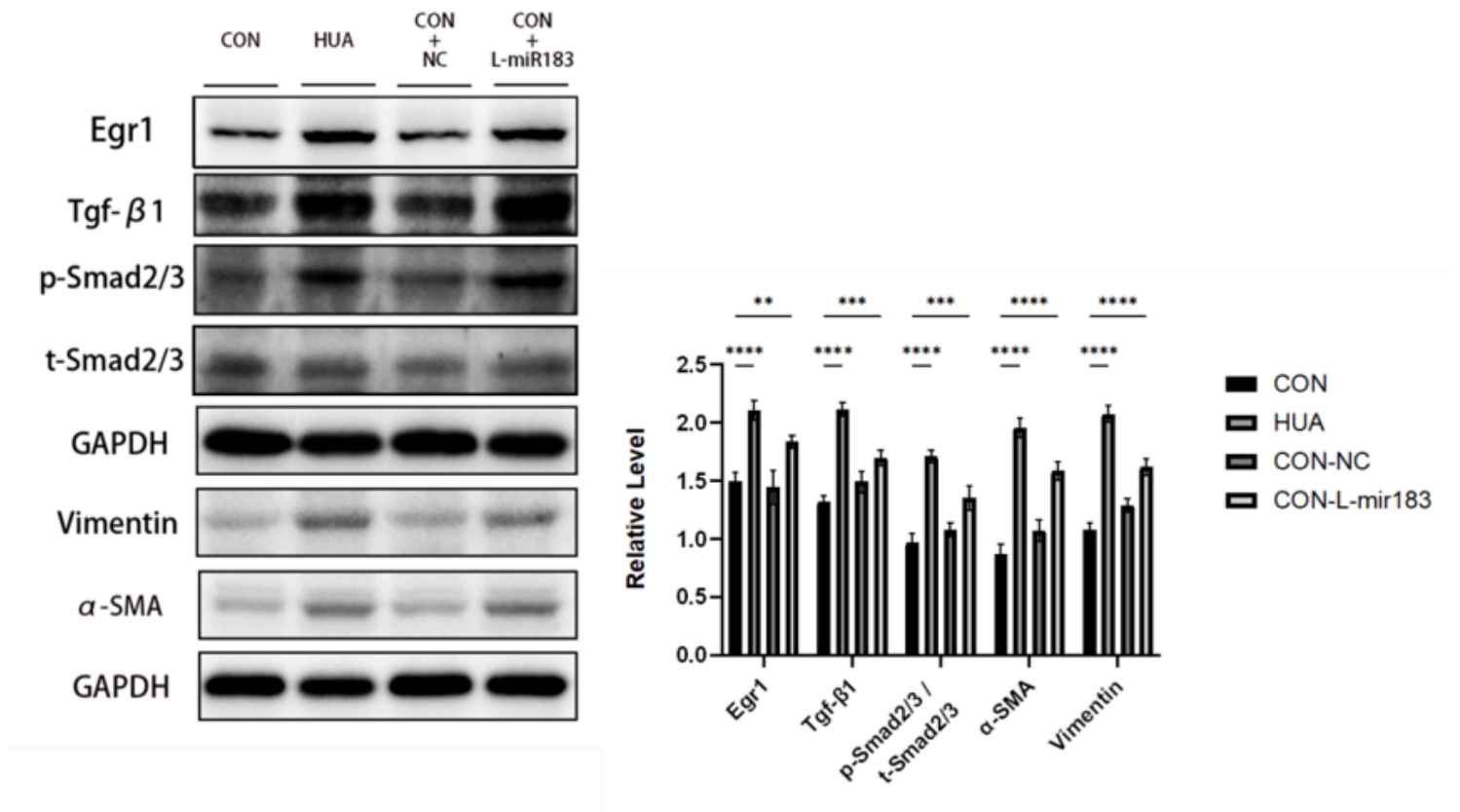


Figure 3

Effects of miR-183 inhibition on the TGF-β1/Smad signaling pathway and renal fibrosis markers.

(A) Representative Western blot analysis showing the protein expression levels of Egr1, TGF-β1, phosphorylated Smad2/3 (p-Smad2/3), total Smad2/3 (t-Smad2/3), α-SMA, and Vimentin in the indicated experimental groups (CON, HUA, CON + NC, and CON + L-miR183). GAPDH was used as the internal loading control. **(B)** Quantitative densitometric analysis of Egr1, TGF-β1, p-Smad2/3 relative to t-Smad2/3, α-SMA, and Vimentin expression levels normalized to GAPDH. Data are presented as mean ± SD (n = 3 or 6 per group). P < 0.01, *** P < 0.001, **** P < 0.0001.

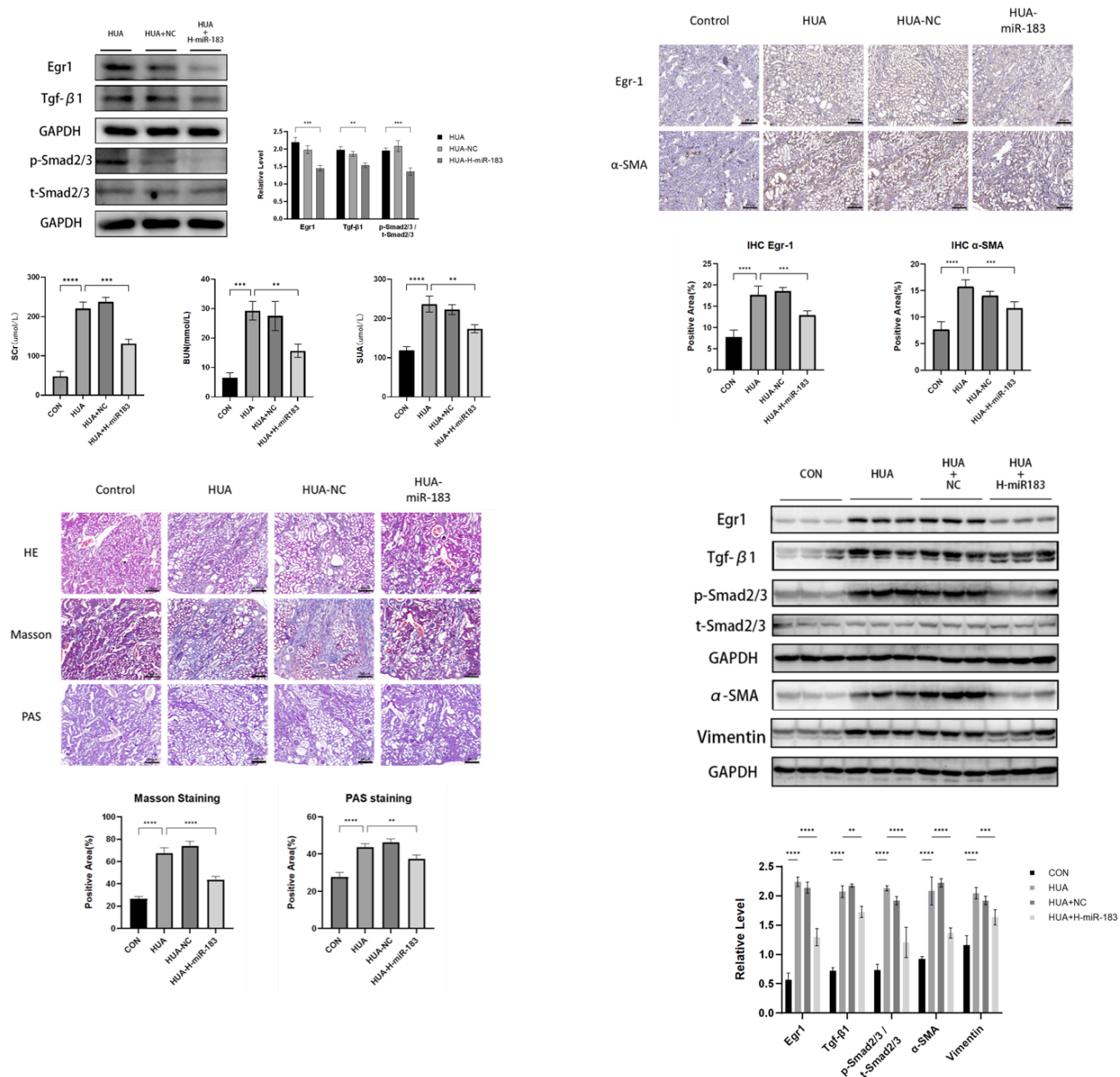


Figure 4

Overexpression of miR-183-5p attenuates high uric acid (UA)-induced renal dysfunction, inflammation, and fibrosis *in vitro* and *in vivo*.

(A) Representative Western blot analysis of Egr-1, TGF- β 1, and p-Smad2/3 protein expression in TCMK-1 cells transfected with miR-183-5p overexpression vector (H-miR-183) under high UA conditions. (B) Serum levels of creatinine (SCr), blood urea nitrogen (BUN), and serum uric acid (UA/SUA) in HN mice following AAV-mediated miR-183-5p overexpression, measured by commercial serum assays. (C) Representative H&E, Masson's trichrome, and PAS staining of kidney tissues evaluating renal interstitial inflammation, collagen deposition, and glycogen accumulation. (D) Representative

immunohistochemistry (IHC) images showing expression levels of Egr-1 and α -SMA in renal tissues. (E) Western blot analysis and quantitative normalization of Egr-1, TGF- β 1, p-Smad2/3, total Smad2/3, α -SMA, and Vimentin protein levels in renal tissues. GAPDH was used as the loading control. Data are presented as mean $\pm$ SD (n = 3 or 6 per group). P < 0.01, *** P < 0.001, **** P < 0.0001.

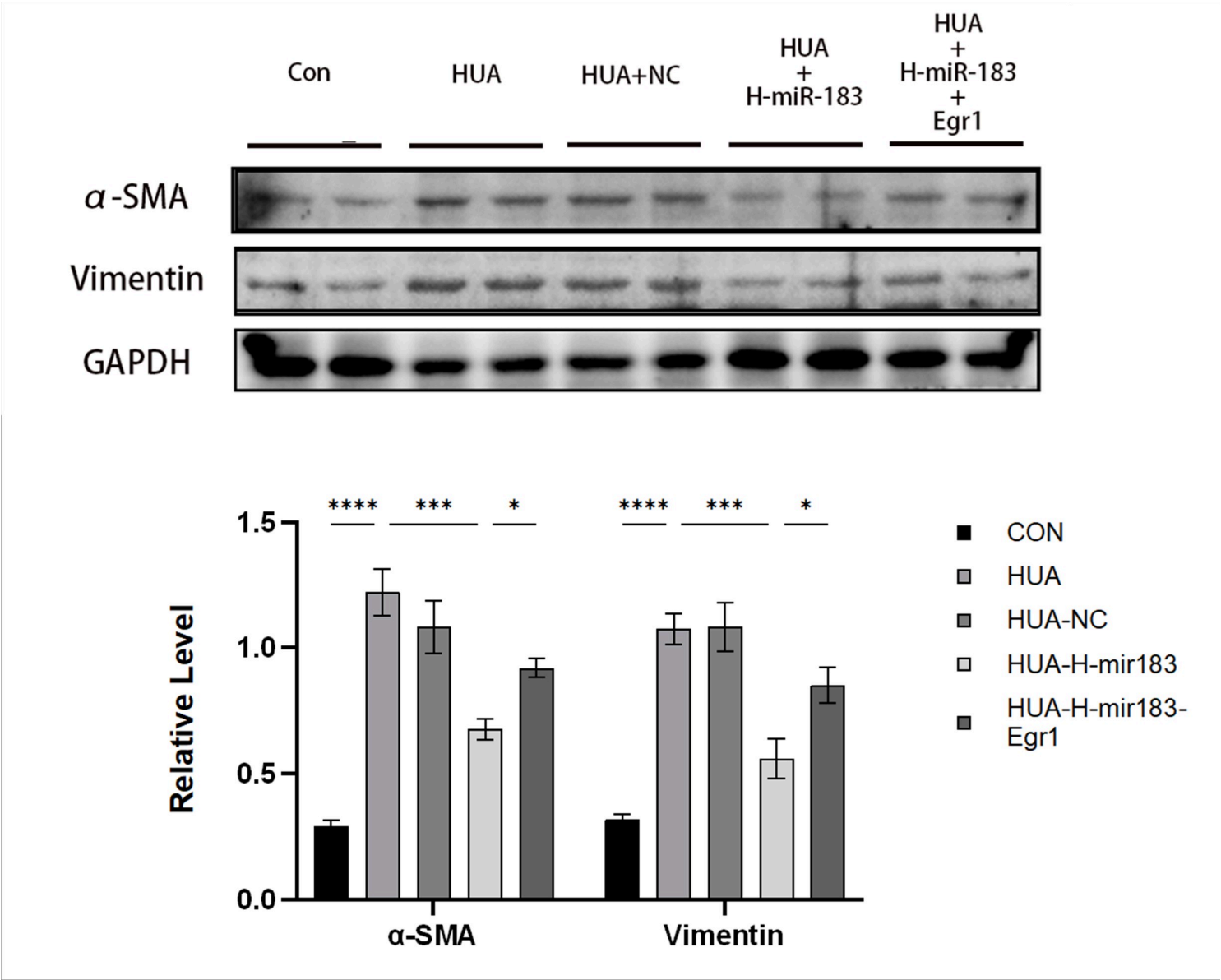


Figure 5

Egr-1 overexpression reverses the renal fibrosis suppression effect of miR-183 overexpression. Expression of α -SMA and vimentin were measured by WB.

Supplementary Files

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