

# miR-361-3p mitigates lipopolysaccharide-induced inflammation and acute kidney injury by post-transcriptional repression of the myeloid differentiation protein 88/nuclear factor- $\kappa$ B pathway

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## Abstract

**Introduction:** microRNAs (miRs) have been reported to contribute to sepsis-associated acute kidney injury (AKI). Herein, the roles of miR-361-3p and the underlying mechanism were investigated in lipopolysaccharide (LPS)-induced podocyte injury.

**Material and methods:** After podocyte exposure to LPS (1 mg/ml), proinflammatory cytokines were measured using enzyme-linked immunosorbent assay (ELISA); cell apoptosis was evaluated by terminal-deoxynucleotidyl transferase mediated nick end labeling (TUNEL) staining. *In vivo* septic mice, miR-361-3p agonist, agomir-miR-361-3p (20 nM/0.1 ml), was used to treat LPS-induced AKI.

**Results:** Our findings reveal a significant elevation of proinflammatory cytokine production, in addition to the development of podocyte apoptosis after LPS stimulation. However, knockdown of myeloid differentiation primary response protein 88 (MyD88) significantly prevents podocyte death and suppresses the inflammatory response in LPS-stimulated podocytes. More importantly, MyD88 is a direct target of miR-361-3p that can counteract LPS-induced inflammation and podocyte dysfunction via post-transcriptional repression of MyD88. The rescue experiments provide a confrontational phenomenon between miR-361-3p and MyD88 in LPS-stimulated podocytes, reflecting that overexpression of MyD88 neutralizes the protective effect of miR-361-3p on LPS-stimulated podocyte inflammation and apoptosis. Our results also demonstrate that miR-361-3p agonist alleviates LPS-induced renal injury and activation of the toll-like receptor 4 (TLR4)/MyD88/nuclear factor-kappa B (NF- $\kappa$ B) axis.

**Conclusions:** miR-361-3p suppresses LPS-induced inflammation, podocyte apoptosis and AKI by targeting the MyD88/NF- $\kappa$ B pathway. This may provide a novel strategy for the treatment of sepsis-associated AKI.

**Key words:** miR-361-3p, MyD88/NF- $\kappa$ B, sepsis, podocyte, inflammation.

## Introduction

Acute kidney injury (AKI) is one of the decidedly fatal complications and is frequently reported in critically ill patients suffering from sepsis or septic shock [1]. An epidemiological survey indicates that sepsis is an overriding pathogenic factor and is responsible for approximately 50%

of AKI incidents in intensive care units [1]. Mechanically, the pathogenesis of AKI in sepsis may be associated with a persistent inflammatory response, endothelial cell injury, abnormal activation of renal tubular epithelial cells and glomerular filtration barrier (GFB) damage [2, 3]. A podocyte is a terminal differentiated visceral epithelial cell, which is located outside the basement membrane of the glomerulus [4]. As the last line of the GFB, podocytes have frequently been linked with sepsis- or lipopolysaccharide (LPS)-induced AKI [5, 6]. Previous studies have reported that activation of the nuclear factor- $\kappa$ B (NF- $\kappa$ B) pathway by LPS mediates the release of pro-inflammatory cytokines, including tumor necrosis factor (TNF)- $\alpha$ , interleukin (IL)-1 $\beta$  and IL-6, and exacerbates cell apoptosis and dysfunction of podocytes [7, 8]. However, the underlying molecular mechanisms of LPS-induced podocyte injury have not been completely clarified.

Myeloid differentiation primary response protein 88 (MyD88), as a member of the adaptin family, is usually recruited by toll-like receptor 4 (TLR-4), which is an important receptor of LPS [9]. LPS binding with TLR4 contributes to activation of MyD88-dependent intracellular signaling, which can mediate NF- $\kappa$ B activation and promote its translocation from the cytoplasm to the nucleus [10, 11]. Subsequently, activation of NF- $\kappa$ B initiates or enhances the transcription and translation of pro-inflammatory cytokines [10, 11]. At present, the TLR4/MyD88/NF- $\kappa$ B pathway as a classical cascade signaling pathway is persistently reported in inflammation and sepsis-induced renal damage [12, 13].

miRs as a class of small non-coding RNAs with a length of approximately 22 nucleotides have been validated as post-transcriptional repressors to degrade messenger RNA (mRNA) or reduce protein translation via completely or partially binding with the 3'-untranslated regions (3'-UTRs) of target genes in various biological and pathological processes [14, 15]. Diverse differentially expressed miRs have been reported to contribute to sepsis-associated organ damage, including cardiac, hepatic, lung and renal dysfunction [16–19]. In addition, miR-21, miR-30, miR-128 and miR-590-3p are involved in sepsis- or LPS-induced podocyte inflammation, dysfunction and apoptosis [5, 20, 21]. In the present study, the molecular mechanisms of miR-361-3p underlying in LPS-induced podocyte injury and AKI were determined in *in vitro* and *in vivo* septic models.

## Material and methods

### Animal model

Male 8-week-old C57BL/6J mice ( $n = 24$ ) were obtained from the Experimental Animal Center of Jilin University. Mice were allowed to acclimatize to the environment for 1 week. Septic mice were estab-

lished with LPS (20 mg/kg) intraperitoneal injection. Septic mice were treated with agomir-miR-361-3p (20 nM/0.1 ml; RiboBio Co., Ltd., Guangzhou, China) administration by tail-vein injection. The animal experiment was approved by the Ethics Committee of the Second Hospital of Jilin University.

### Cell culture

Mouse renal podocytes were obtained from the National Infrastructure of Cell Line Resource (<http://www.cellresource.cn>; Beijing, China). Podocytes were maintained in RPMI-1640 (Invitrogen, USA) and exposed to LPS (Sigma-Aldrich) with a concentration of 1 mg/ml for 24 h.

### Cell transfection

Podocytes ( $1 \times 10^5$  cells/well) were seeded in 24-well plates and then transfected with miR-361-3p mimics (RiboBio Co., Ltd., Guangzhou, China), short hairpin RNA-MyD88 (sh-MyD88; RiboBio Co., Ltd., Guangzhou, China) or MyD88 expression plasmids (GeneCopoeia, Inc., Rockville, MD, USA) using Lipofectamine 2000 (Invitrogen), according to the manufacturer's protocols.

### Western blotting

Primary antibodies of TLR4 (cat. no: ab217274; dilution: 1 : 1,000; Abcam), MyD88 (cat. no: #50010; dilution: 1 : 1,000; Cell Signaling Technology), NF- $\kappa$ B/p65 (cat.no: 3034; dilution: 1 : 500; Cell Signaling Technology), p-I $\kappa$ B $\alpha$  (cat. no: #2859; dilution: 1 : 1,000; Cell Signaling Technology), I $\kappa$ B $\alpha$  (cat. no: #4814; dilution: 1 : 1,000; Cell Signaling Technology) and nephrin (cat. no: sc-376522; dilution: 1 : 1,000; Santa Cruz Biotechnology) were used for western blotting assay. The protein band was detected with horseradish peroxidase-conjugated secondary anti-rabbit antibodies and developed with an ECL chemiluminescence kit (Santa Cruz Biotechnology). Anti- $\beta$ -actin (cat. no. sc-130065; dilution: 1 : 2,000; Santa Cruz Biotechnology) and anti-histone (cat.no: #9715; dilution: 1 : 2,000; Cell Signaling Technology) signals were used to correct for unequal loading.

### Enzyme-linked immunosorbent assay (ELISA)

Pro-inflammatory cytokines, TNF- $\alpha$ , IL-1 $\beta$  and IL-6 were measured with a mouse ELISA kit (Elabscience Biotechnology Co., Ltd, Wuhan, China) according to the manufacturer's instructions. Malondialdehyde (MDA) level in the supernatant was detected using a commercial kit from the Nanjing Jiancheng Bioengineering Institute (Nanjing, China). 8-hydroxy-2'-deoxyguanosine (8-OHdG) was measured using a DNA damage ELISA kit (Enzo Life Sciences, Farmingdale, NY), according to the manufacturer's instruction.

### RT-qPCR

RT-qPCR for miRs: total RNA was extracted by the miRNeasy Mini Kit (Qiagen, Inc., Valencia, CA, USA). A TaqMan RT kit and TaqMan MicroRNA assay (Applied Biosystems) were used to detect miR-361-3p expression levels using the Applied Biosystems 7300 Real-Time PCR System (Thermo Fisher Scientific, Inc.). miR-361-3p expression levels were calculated using the  $2^{-\Delta\Delta Cq}$  method, as described previously [22], and U6 was used as an internal control.

RT-qPCR for mRNA: Moloney murine leukemia virus reverse transcriptase (Invitrogen) was used to synthesize cDNA with 2  $\mu$ g of total RNA according to the manufacturer's protocol. Real-time PCR was performed using the Applied Biosystems 7300 System with the TaqMan Universal PCR Master Mix (Thermo Fisher Scientific). mRNA expression levels were calculated using the  $2^{-\Delta\Delta Cq}$  method [22], and glyceraldehyde-3-phosphate dehydrogenase (GAPDH) served as the internal control.

### TUNEL staining

After LPS-stimulated podocytes were transfected with sh-MyD88 or miR-361-3p mimics, apoptotic cell proportion was analyzed using TUNEL staining (Roche) according to the manufacturer's protocol.

### Luciferase reporter gene assay

The wild-type (WT) and mutant-type (Mut) 3'-UTR of MyD88 were inserted into the multiple cloning sites of the luciferase-expressing pMIR-REPORT vector (Ambion; Thermo Fisher Scientific, Inc., Waltham, MA, USA). After co-transfection with miR-Con or miR-361-3p combined with WT or Mut 3'-UTR of MyD88 for 48 h, the luciferase activity was measured using a luciferase reporter assay kit (Promega Corporation, Madison, WI, USA) according to the manufacturer's protocols.

### Hematein & eosin (H&E) staining

After fixation with 4% formalin at room temperature for 24 h, kidneys were embedded with paraffin and stained with an H&E kit according to standard histological procedures of the manufacturer (Beyotime Institute of Biotechnology, Haimen, China). H&E staining was visualized with an optical microscope (Olympus BX53, Japan).

### Statistical analysis

Data are presented as the mean  $\pm$  standard deviation. Statistical analysis was performed using GraphPad Prism Version 7.0 (GraphPad Software, Inc., La Jolla, CA, USA). A Student's *t*-test was used to analyze the differences between the two

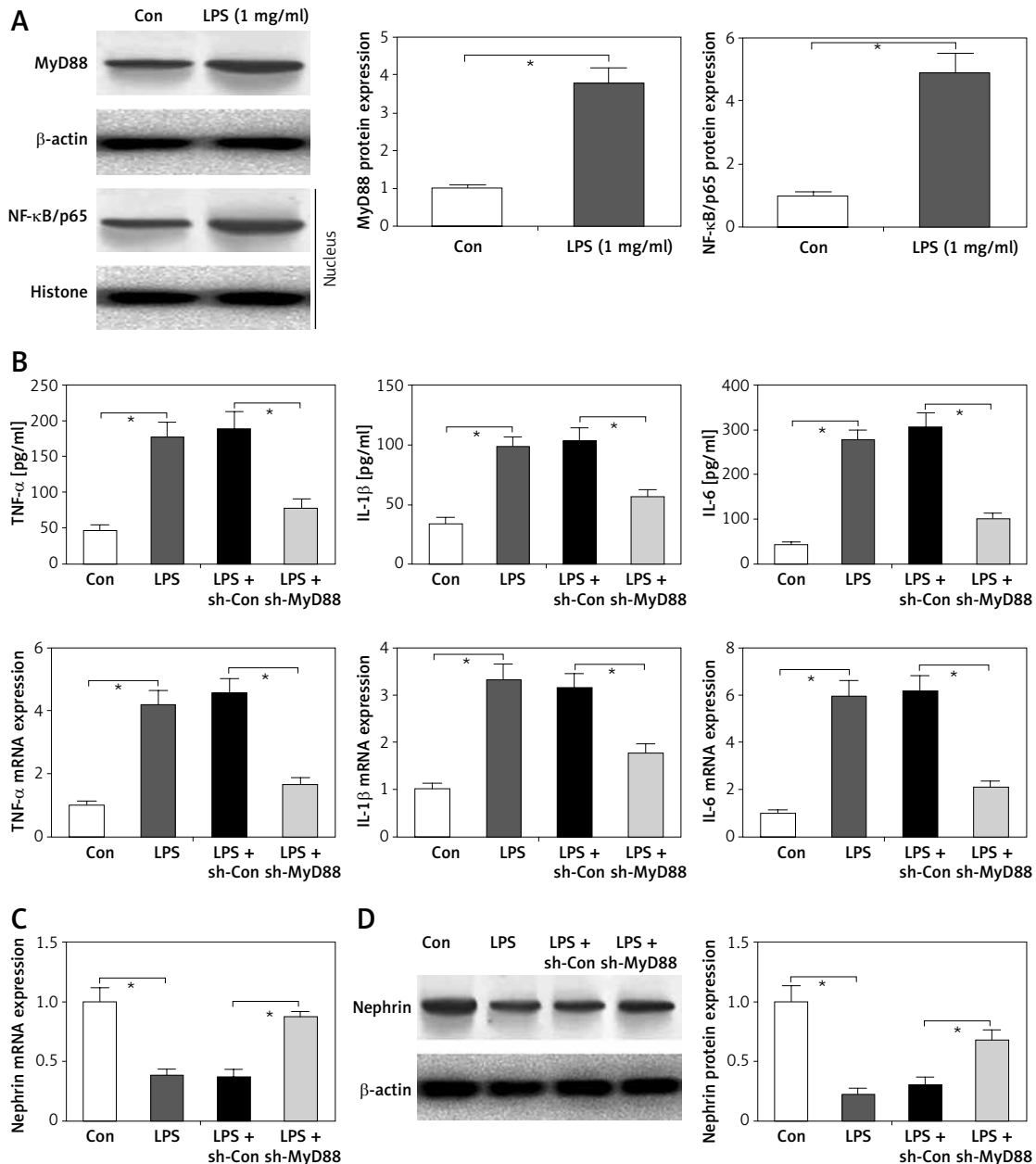
groups. Differences between multiple groups were analyzed by one-way ANOVA.  $P < 0.05$  indicated a statistically significant difference.

## Results

### Knockdown of MyD88 attenuates LPS-induced inflammation and podocyte dysfunction

The MyD88/NF- $\kappa$ B signaling cascade is a crucial regulatory pathway to activate the inflammatory response in various inflammatory cell and animal models, including the sepsis-associated inflammatory response [12, 13]. Srivastava *et al.* have corroborated that the mRNA of MyD88 and NF- $\kappa$ B are dramatically up-regulated in podocytes after 1 h with LPS stimulation [23]. Our findings indicated that a significant increase in MyD88 and NF- $\kappa$ B protein expression levels is confirmed in LPS-stimulated podocytes (Figure 1 A). In addition, LPS exposure enhances the transcription and secretion of pro-inflammatory cytokines, including TNF- $\alpha$ , IL-1 $\beta$  and IL-6, while the silencing of MyD88 significantly antagonizes the LPS-induced increase of mRNA and secretory product of pro-inflammatory cytokines (Figure 1 B). Nephrin, as an adhesion protein, is expressed at the podocyte intercellular junction in the glomerulus and is indispensable for podocyte recovery following damage [24]. The previous study suggests that high glucose-induced podocyte injury is accompanied by the reduction of nephrin mRNA and protein expression [25]. Our results revealed that the mRNA and protein expression levels were markedly reduced in the LPS-stimulated podocytes. Interestingly, knockdown of MyD88 restores the LPS-induced down-regulation of nephrin mRNA and protein expression in podocytes (Figures 1 C, D).

To further elucidate the role of MyD88 loss of function in LPS-triggered podocyte damage, the yield of MDA and 8-OHdG in cell supernatant liquid was evaluated. MDA, as a lipid peroxidation product, is a marker of cell membrane damage [26]. As shown in Figure 2 A, LPS incubation increases MDA production, which is reduced following MyD88 loss of function in the podocyte. We also found that LPS stimulation elevates the 8-OHdG level, which is a marker reflecting the degree of DNA oxidative damage [27]. However, knockdown of MyD88 significantly reverses the LPS-induced elevation of 8-OHdG level in podocytes (Figure 2 B). Furthermore, the apoptotic cell proportion (Figures 2 C, D) and the ratio of BAX to Bcl-2 mRNA expression level (Figure 2 E) are significantly elevated in LPS-stimulated podocytes compared with those cells in the control group. However, blocking of the MyD88/NF- $\kappa$ B signaling by sh-MyD88 transfection attenuates LPS-induced



**Figure 1.** Knockdown of MyD88 attenuates LPS-induced inflammation and podocyte dysfunction. After stimulation of podocytes with LPS (1 mg/ml), protein expression of MyD88 and NF- $\kappa$ B/p65 was detected by western blotting (A). After transfection with sh-MyD88 into LPS-stimulated podocytes, proinflammatory cytokine levels were measured using ELISA assays (B; upper) and RT-qPCR (B; below); nephrin mRNA and protein levels were evaluated using RT-qPCR (C) and western blotting (D), respectively

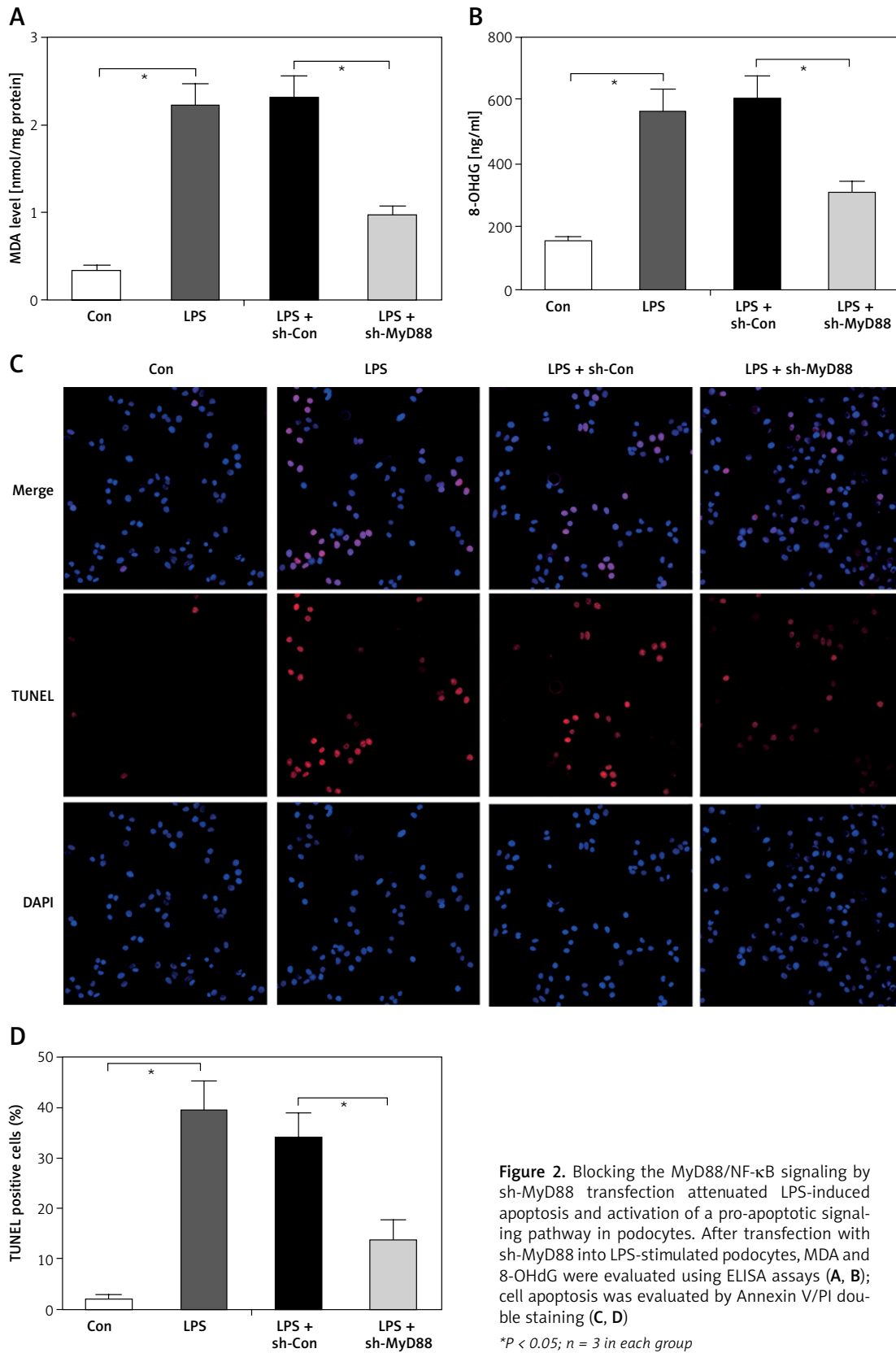
\* $P < 0.05$ ;  $n = 3$  in each group.

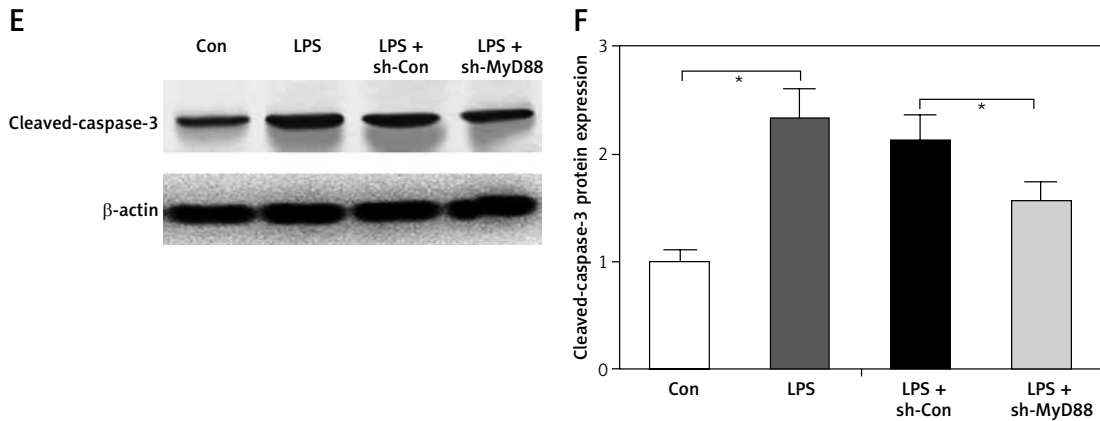
apoptosis and the activation of the pro-apoptotic signaling pathway in podocytes.

### MyD88 is a potential target of miR-361-3p

miRs, as post-transcriptional gene silencers, can repress protein translation via binding with the 3'-UTR of the target gene in mammals [14, 15]. Using the on-line bioinformatics tool TargetScan ([www.targetscan.org](http://www.targetscan.org)), we found that miR-361-3p interacts with the 3'-UTR of MyD88 by a sequence

of complementary base pairing, as shown in Figure 3 A. Luciferase reporter gene assay was performed to validate whether MyD88 is a potential target of miR-361-3p. Reconstructed WT or Mut 3'-UTR of MyD88 was co-transfected with miR-Con or miR-361-3p mimics into podocytes, and the results demonstrated that the luciferase activity is significantly reduced in podocytes containing the WT 3'-UTR of MyD88 after transfection with miR-361-3p mimics, which has no obvious effect on luciferase activity in podocytes containing Mut





**Figure 2.** Cont. Cleaved-caspase-3 protein levels were evaluated using western blot analysis (E) and quantitative analysis (F)

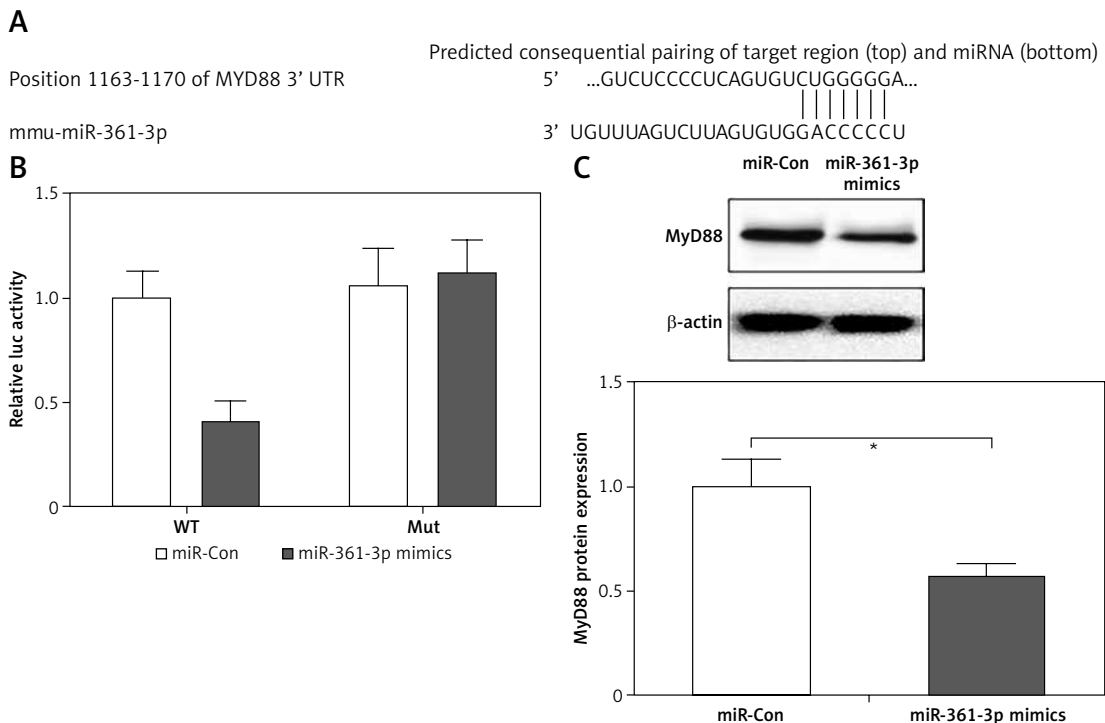
\**P* < 0.05; *n* = 3 in each group.

3'-UTR of MyD88 (Figure 3 B). After transfection with miR-361-3p mimics into podocytes, the protein expression of MyD88 is significantly inhibited compared with the control group (Figure 3 C).

### Overexpression of miR-361-3p overturns the LPS-evoked MyD88/NF-κB pathway and podocyte injury

Firstly, we found a significant decrease in miR-361-3p expression level in LPS-exposed podocytes (Figure 4 A). To investigate the function of

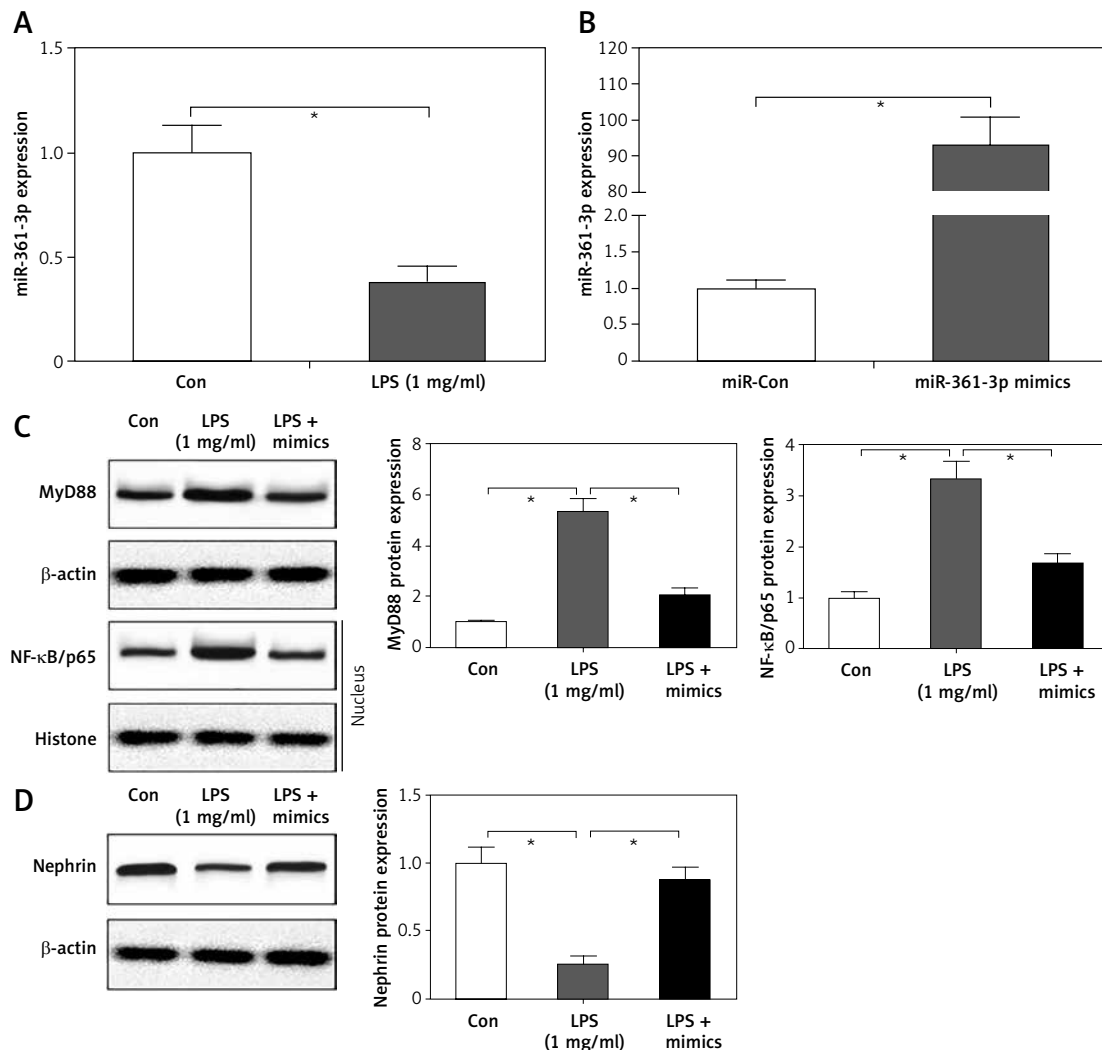
miR-361-3p in LPS-induced podocyte dysfunction, miR-361-3p mimics were transfected into podocytes, and the results showed that miR-361-3p expression was increased approximately 96-fold after transfection with miR-361-3p mimics into podocytes (Figure 4 B). Concomitantly, the LPS-induced up-regulation of MyD88 and NF-κB protein expression was muted when cells were transfected with miR-361-3p mimics (Figure 4 C). Moreover, the LPS-induced down-regulation of nephrin protein expression level was markedly elevated after



**Figure 3.** MyD88 is a potential target of miR-361-3p. **A** – Bioinformatics algorithms predicted that miR-361-3p targeted the 3'-UTR of MyD88, and the complementary base pairing sequences were highly conserved. **B** – When WT-MyD88 or Mut-MyD88 plasmid was co-transfected with miR-361-3p mimics, the luciferase activity was measured. **C** – After transfection with miR-361-3p mimics into podocytes, the protein expression of MyD88 was measured using western blotting assays

\**P* < 0.05; *n* = 3 in each group.





**Figure 4.** Overexpression of miR-361-3p oververts the LPS-evoked MyD88/NF- $\kappa$ B pathway and podocyte injury. **A** – After LPS (1 mg/ml) stimulation of podocytes, miR-361-3p expression was evaluated using RT-qPCR. **B** – After transfection with miR-361-3p mimics into podocytes, miR-361-3p expression was evaluated using RT-qPCR. **C** – After transfection with miR-361-3p mimics into LPS-stimulated podocytes, protein expression of MyD88 and NF- $\kappa$ B/p65 was detected by western blotting. **D** – Nephrin protein level was evaluated using western blotting

\* $P < 0.05$ ;  $n = 3$  in each group.

transfection with miR-361-3p mimics into podocytes (Figure 4 D).

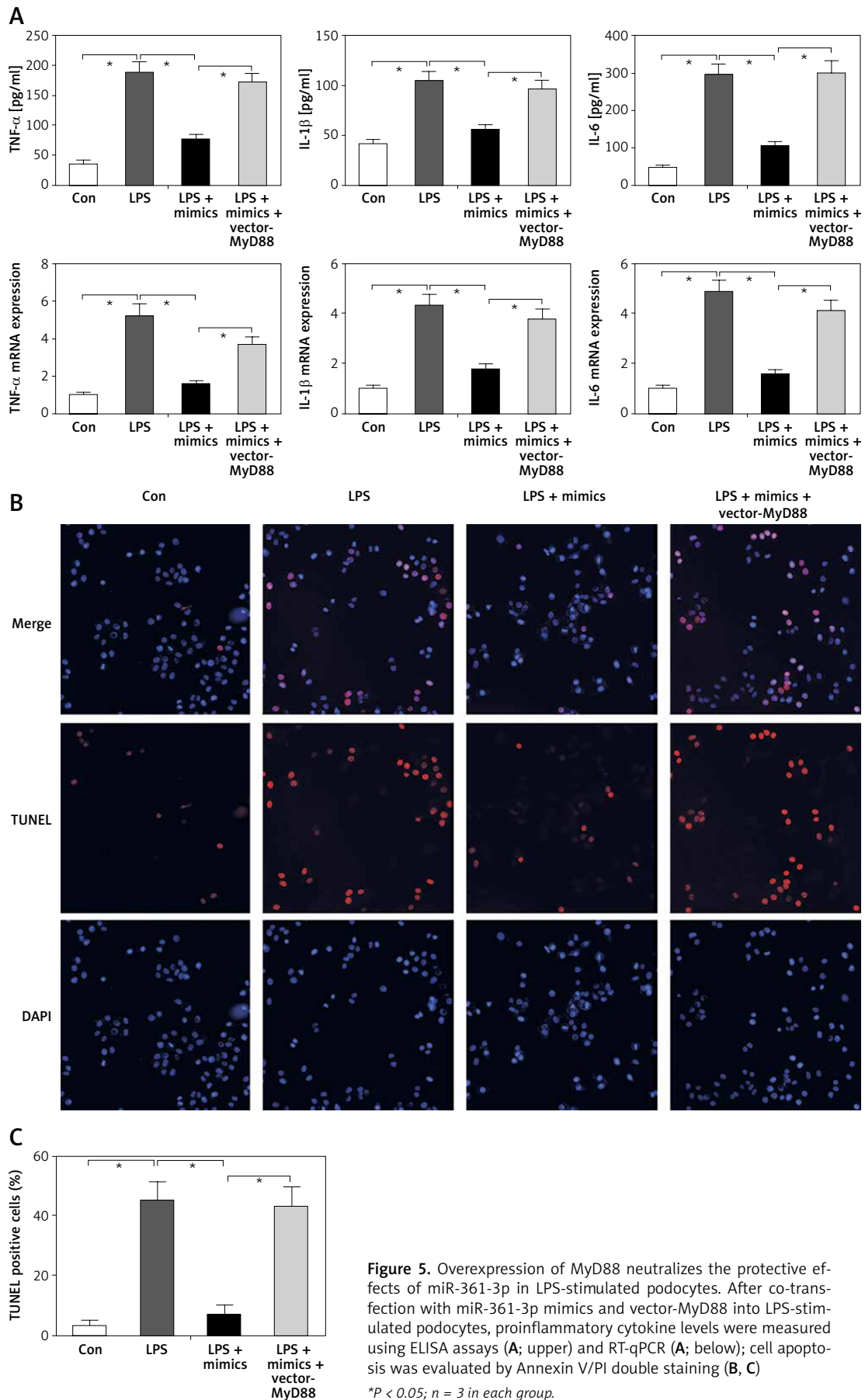
#### Overexpression of MyD88 neutralizes the protective effects of miR-361-3p in LPS-stimulated podocytes

As presented in Figure 5 A, the LPS-induced increase of mRNA and secretory products of pro-inflammatory cytokines, including TNF- $\alpha$ , IL-1 $\beta$  and IL-6, were down-regulated by overexpression of miR-361-3p. However, the anti-inflammatory activity of miR-361-3p weakened after transfection with MyD88 overexpressed plasmids into podocytes. In addition, LPS-induced apoptosis (Figures 5 B, C) and the up-regulation of MDA (Figure 5 D) and 8-OHdG (Figure 5 E) in podocytes were reversed by overexpression of miR-361-3p.

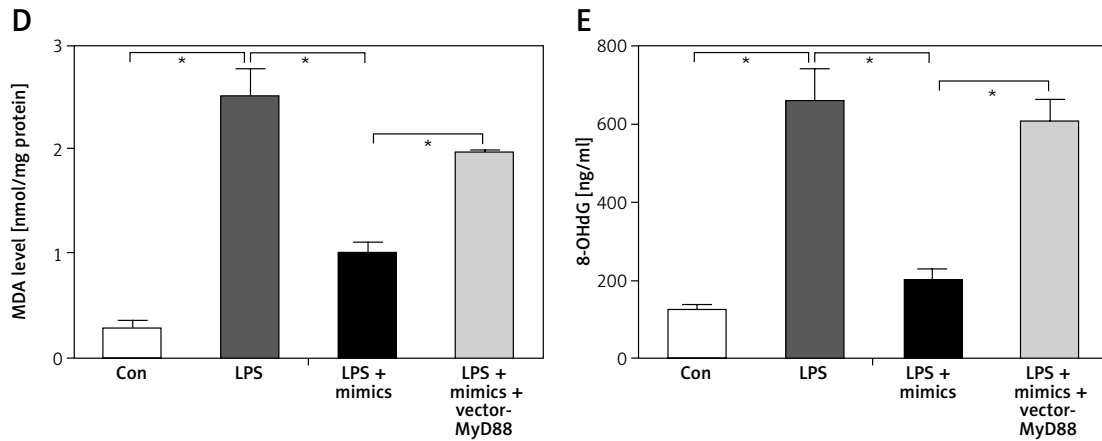
Additionally, the suppressive effects of miR-361-3p on LPS-induced podocyte dysfunction were abrogated by overexpressed MyD88.

#### Agomir-miR-361-3p protects against LPS-induced renal injury

In the *in vivo* septic model, H&E staining was used to assess pathological changes of the kidney from septic mice. Histologic examination by H&E staining revealed constrictive glomerulus accompanied with distensible glomerular lumina and tubular loss in LPS-treated mice, while the miR-361-3p agonist agomir-miR-361-3p obviously reserved LPS-induced pathological changes (Figure 6 A). In addition, nephrin protein expression was significantly repressed in the kidney of septic mice compared with normal mice. However, ago-







**Figure 5.** Cont. MDA and 8-OHdG were evaluated using ELISA assays (D, E)

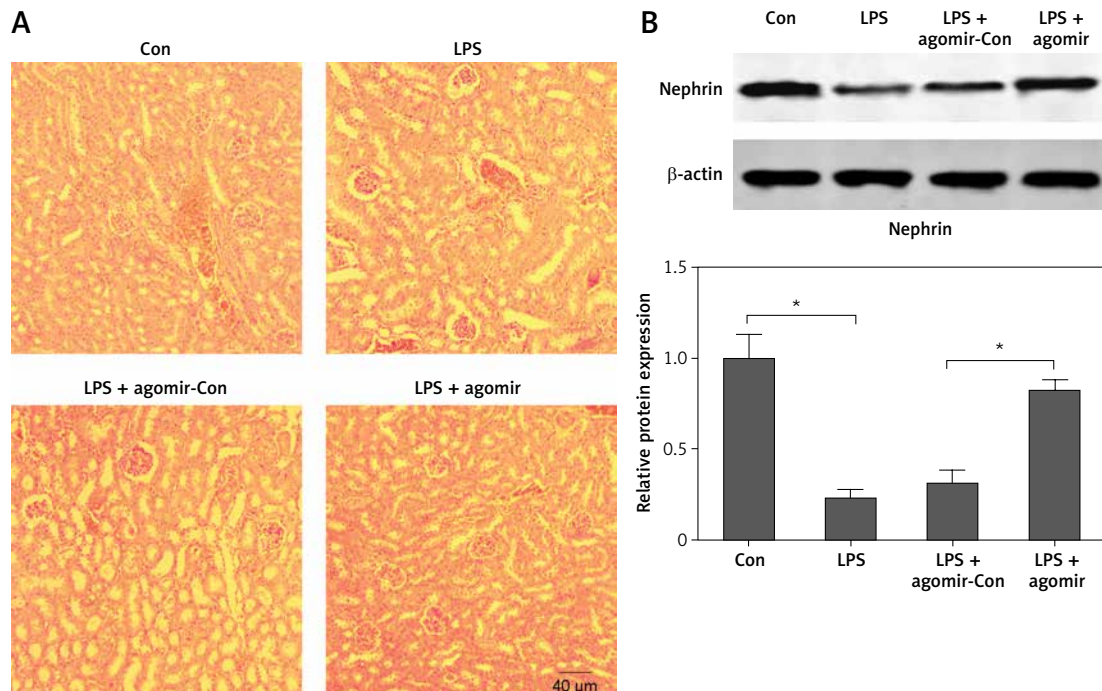
\* $P < 0.05$ ;  $n = 3$  in each group

miR-361-3p administration restored nephrin protein expression in the kidney of septic mice (Figure 6 B), suggesting that the elevation of miR-361-3p expression in the kidney has a protective effect against LPS-induced renal damage.

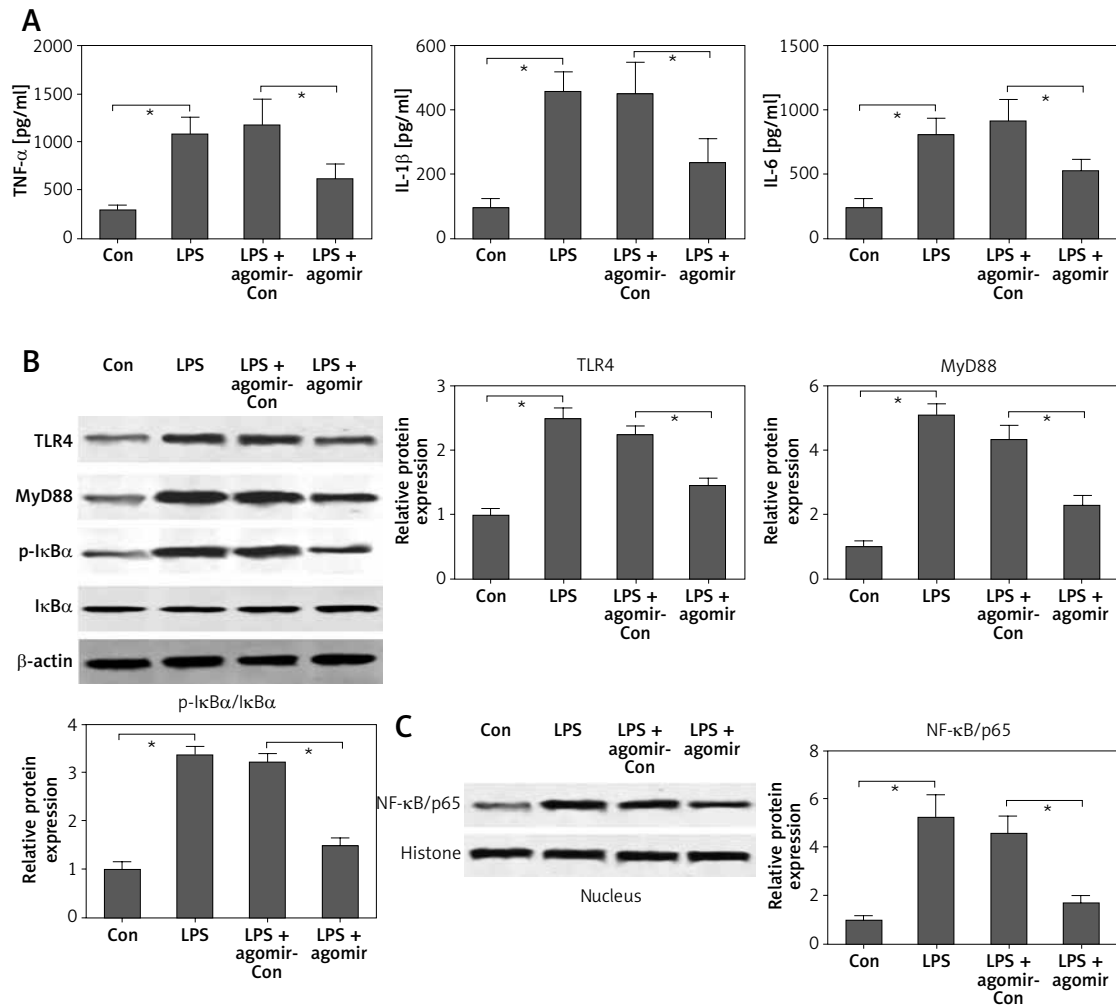
#### Agomir-miR-361-3p inhibits the MyD88/NF- $\kappa$ B pathway in septic mice

To determine the effect of agomir-miR-361-3p on the production of inflammatory cytokines, serum TNF- $\alpha$ , IL-1 $\beta$  and IL-6 were measured using ELISA assays. As shown in Figure 7 A, up-regulation of serum TNF- $\alpha$ , IL-1 $\beta$  and IL-6 was observed in septic mice, while agomir-miR-361-3p treat-

ment attenuated the over-activation of the inflammatory response in septic mice. To investigate the underlying molecular mechanism by which miR-361-3p inhibits the inflammatory response, the effects of miR-361-3p on the protein expression of MyD88/NF- $\kappa$ B signaling components were examined in the kidney of septic mice. As shown in Figures 7 B and C, the protein expression of TLR4, MyD88, p-I $\kappa$ B $\alpha$  and nuclear NF- $\kappa$ B/p65 was elevated in the kidney following LPS treatment. However, agomir-miR-361-3p administration inhibited the activity of the TLR4/MyD88/NF- $\kappa$ B axis, with accompanying downregulation of TLR4, MyD88, p-I $\kappa$ B $\alpha$  and nuclear NF- $\kappa$ B/p65 protein expression.



**Figure 6.** Agomir-miR-361-3p protects against LPS-induced renal injury. H&E staining was used to assess pathological changes of the kidney from septic mice (A; magnification 100 $\times$ ; scale bar = 40  $\mu$ m). Nephrin protein expression in the kidney was analyzed using western blot (B). \* $P < 0.05$ ;  $n = 6$  in each group



**Figure 7.** Agomir-miR-361-3p inhibits the MyD88/NF-κB pathway in septic mice. Serum TNF-α, IL-1β and IL-6 were measured using ELISA assays (A). The protein expression levels of TLR4, MyD88, p-IκBα (B) and nuclear NF-κB/p65 (C) in the kidney were analyzed using western blot (B)

\*P < 0.05; n = 6 in each group.

## Discussion

MyD88 has been recognized as a key mediator in the bacterial endotoxin-activated innate immune response and is responsible for acute or chronic inflammatory disorders by reinforcing the transcription factor-modulated release of inflammatory cytokines that can cause systemic multi-organ damage, and AKI is a common cause of death from sepsis [10, 11, 28]. Studies on molecular mechanisms also document that MyD88 is a notorious indicator in sepsis- or LPS-caused AKI, and destruction of the MyD88 signaling pathway can block AKI in *in vivo* and *in vitro* experimental models [29, 30]. Interestingly, MyD88 is also identified as a novel anti-AKI drug target by traditional Chinese medicine, natural active components and synthetic drugs and gene delivery (gene-based medicine) [30–32]. Consistent with previous studies [5, 7, 12], our findings uncovered a significant elevation of proinflammatory cytokine produc-

tion, in addition to the development of podocyte damage and AKI after LPS stimulation in an *in vitro* and *in vivo* septic model. However, knockdown of MyD88 significantly improved podocyte function and suppressed the inflammatory response in LPS-exposed podocytes. More importantly, MyD88 is a direct target of miR-361-3p. RT-qPCR corroborates that miR-361-3p is significantly down-regulated in LPS-stimulated podocytes and in the kidney of septic mice. Overexpression of miR-361-3p counteracts LPS-induced inflammation, podocyte dysfunction and AKI via post-transcriptional repression of MyD88.

During podocyte damage, inflammation and apoptosis are the two main pathologic processes, and over-activation of inflammation can exacerbate apoptosis in podocytes [33]. Therefore, interdiction of inflammation-related signal cascades may be a potential therapeutic strategy to protect against toxicant-induced podocyte death. Previous studies have shown that MyD88 interaction

with NF- $\kappa$ B contributes to high glucose-induced inflammation and apoptosis in podocytes [34]. In the diabetic mouse model, the MyD88/NF- $\kappa$ B signaling pathway modulates renal damage and inflammation [35]. Srivastava *et al.* also suggest that the MyD88/NF- $\kappa$ B signaling pathway is involved in LPS-induced podocyte injury [36]. Unfortunately, the molecular mechanism underlying MyD88/NF- $\kappa$ B mediated podocyte injury has not been mentioned in the case of the LPS-stimulated podocyte. In our study, we aimed to determine the role of miR-361-3p in LPS-stimulated podocyte inflammation and apoptosis, whether it was post-transcriptional repression of MyD88. Bioinformatics algorithms and experimental measurements revealed that MyD88 was a direct target of miR-361-3p that could repress the protein expression of MyD88 in podocyte transfection with miR-361-3p mimics. The rescue experiments provided a confrontational phenomenon between miR-361-3p and MyD88 in LPS-stimulated podocytes, reflecting that overexpression of MyD88 neutralized the protective effect of miR-361-3p on the LPS-stimulated inflammatory response and apoptosis in podocytes.

At present, miR-361-3p is closely correlated with insulin resistance, diabetes, and multiple cancer types [37, 38]. Moreover, several studies have reported that deregulation of miR-361-3p is closely associated with inflammation-related dysfunction, such as spondyloarthritis, inflammatory endothelial damage and enteritidis [39–41]. However, the precise molecular mechanism of miR-361-3p has not been investigated in LPS-induced inflammation and AKI. Based on the above-mentioned finding of miR-361-3p as a potential post-transcriptional regulator of MyD88-mediated inflammation, the expression of miR-361-3p was measured in LPS-stimulated podocytes. Our results demonstrated that LPS stimulation for 24 h leads to a significant decrease in miR-361-3p expression in podocytes. To further determine the role of miR-361-3p in LPS-treated podocytes, miR-361-3p mimics were transfected into podocytes to augment the expression of miR-361-3p. Our findings indicated that miR-361-3p gain of function inhibited inflammation and apoptosis, and improved podocyte damage, as well as down-regulating the protein expression of MyD88 and NF- $\kappa$ B in LPS-stimulated podocytes. In the *in vivo* septic model, miR-361-3p agomir prevents LPS-evoked renal histologic damage and inhibits the TLR4/MyD88/NF- $\kappa$ B-mediated inflammatory response. Based on these findings, we conclude that miR-361-3p ameliorates LPS-induced podocyte dysfunction and AKI via repressing the MyD88/NF- $\kappa$ B signaling pathway.

In conclusion, miR-361-3p exhibits a novel function to weaken LPS-induced AKI and podocyte

dysfunction that may involve its inhibition of the target gene MyD88. Our findings suggest that miR-361-3p may be a possible therapeutic target in sepsis-related AKI.

### Conflict of interest

The authors declare no conflict of interest.

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