miR-128-3p enhances the protective effect of dexmedetomidine on acute lung injury in septic mice by targeted inhibition of MAPK14

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Abstract

Background: To investigate the mechanism of miR-128-3p and MAPK14 on the protective effect of dexmedetomidine on acute lung injury in septic mice.

Methods: SPF C57BL/6 mice were divided into 8 groups. The pathological changes and wet/dry weight ratio (W/D), PaO₂, PaCO₂, MDA, SOD and MPO levels in lung tissue and the serum levels of inflammation factors were observed. Dual luciferase reporter assay was used to verify the targeting relationship between miR-128-3p and MAPK14. qPCR and WB were used to detect the expression of miR-128-3p and MAPK14.

Results: Compared with the Normal group, other groups had lower MDA, MPO, inflammatory factors levels and the expression level of MAPK14, while the content of SOD and the expression level of miR-128-3p was significantly decreased. DEX treatment and up-regulation of miR-128-3p could significantly decrease the contents of MDA, MPO, inflammatory factor levels and significantly increase the SOD content in model mice, however, MAPK14 over-expression had opposite effects. miR-128-3p up-regulation enhanced the changes of above indicators caused by DEX treatment and MAPK14 over-expression could block the protective effect of DEX on acute lung injury in septic mice. miR-128-3p up-regulation reversed the effects of MAPK14 over-expression in model mice.

Conclusion: miR-128-3p can further enhance the protective effect of dexmedetomidine on acute lung injury in septic mice by targeting and inhibiting MAPK14 expression.

Background

Sepsis is the most common systemic clinical complication of severe trauma, burns and major surgery, which can deteriorate into multiple organ dysfunction syndrome, becoming the leading cause of death in these patients [1]. Traditionally, sepsis is considered to be an organ failure syndrome caused by immune disorders in the case of severe infection [2]. Excessive inflammatory response induced by sepsis can lead to multiple organ damage and failure. Acute respiratory distress syndrome (ARDS) is a common complication of sepsis as lung is particularly sensitive to sepsis damage [3]. ARDS is characterized by progressive hypoxemia, enhanced vascular permeability, edema, neutrophil infiltration and lung accumulation, which greatly increases patient morbidity and mortality [4]. Therefore, the researches on the new targets for the treatments of sepsis are hotspot [5].

Dexmedetomidine (DEX), a α_2 -adrenergic receptor agonist, has an imidazole structure and sedative, analgesic and hemodynamic stabilization effects [6]. A good anti-inflammatory effect of DEX has been discovered on important organs in mice with spinal cord injury, myocardial ischemia-reperfusion and sepsis, etc. [7]. Moreover, DEX can improve ARDS, reduce pathomorphological changes, inhibit oxidative stress damage, inflammatory response and apoptosis in lung epithelial cells by inhibiting TLR-4/NF- κ B pathway [8].

P38 mitogen-activated protein kinase (p38MAPK) is an important signal regulating cell proliferation and apoptosis. Its phosphorylated form can activate a variety of physiological processes, and MAPK14 is a member of the MAPK family [9]. ARDS is often mediated by a variety of intracellular signaling pathways, such as PI3K/Akt, c-Jun N-terminal protein kinase, mitogen-activated protein kinase, and p38 activation, which play a role in inflammatory responses, cell death, and alveolar epithelial cell damage in ARDS [10, 11].

MicroRNAs (miRNAs) are endogenous small non-coding RNAs with a length of 21-23 nucleotides. miRNAs inhibit translation or induce the degradation of targeted mRNA by binding to the 3' untranslated region (UTR) [12]. Increasing number of evidences have proved that miRNAs associated with certain inflammatory lung diseases. For example, up-regulation of miR-125b significantly reduced lipopolysaccharide (LPS)-induced lung inflammation in mice [13]. miR-212-3p inhibits LPS-induced inflammatory responses by targeting high mobility group box -1 in mouse macrophages [14]. miR-128-3p plays an important role in Dox-induced liver injury by targeting Sirt1 [15]. However, whether miR-128-3p participates in the anti-inflammatory activity of dexmedetomidine in ARDS remains unclear.

In this study, we found a targeting relationship between miR-128-3p and MAPK14 via bioinformatics prediction. Since p38MAPK is involved in the ALL, we hypothesized that miR-128-3p may down-regulate the expression of MAPK14, thereby inhibiting p38 signaling pathway to alleviate ARDS in septic mice.

Methods

Animals and model establishment

A total of 120 healthy SPF (specific pathogen free) C57BL/6 mice (purchased from Zhejiang Experimental Animal Center), clean grade, body weight 35 ± 5 g, were used for experiment in this study. Mice were divided into 8 groups: Normal group (healthy mice without treatment), Model group (model mice), DEX group (model mice treated with dexmedetomidine), miR-128-3p mimic group (model mice treated with miR-128-3p overexpression vectors), oe-MAPK14 group (model mice treated with MAPK14 overexpression (oe) vectors), miR-128-3p mimic+oe-MAPK14 group (model mice treated with miR-128-3p and MAPK14 overexpression vectors), miR-128-3p mimic+DEX group (model mice treated with miR-128-3p overexpression vector and dexmedetomidine), DEX+oe-MAPK14 group (model group mice treated with MAPK14 overexpression vector and dexmedetomidine), with ten mice in each group.

The sepsis model was established by cecal ligation and puncture. Briefly, the mice were fixed in table and anesthetized with 3% pentobarbital sodium (50 m/kg). After eyeball blood collection, the mice died of excessive blood loss, and lung tissue samples were retained. A 1 cm long surgical incision was made in the central part of the anterior abdominal cavity of the mice to separate out the cecum end, then the root of the cecum was ligated and punctured with a 4-gauge needle, and the contents in cecum were extruded out. Finally, the cecum and incision were sutured. Pre-warmed saline was injected postoperatively. Except for no ligation and puncture, the other steps in the Normal group were the same as those in the model

group. Thirty-two animals died, so the success rate of model establishment was 70.90%, of which 70 were taken for the following experiments.

After the operation, immediately, mice intraperitoneally injected with DEX (12.5 µg/kg, GLP BIO, America) and miR-128-3p mimic, MAPK14 overexpression vectors (The NC, miR-128-3p and MAPK14 overexpression adenoviral vectors were constructed by GenePharma, Suzhou). The treatment dosage of virus was 20 mg/kg. Three days after modeling and treatment, mice were euthanized for sample collection and analysis. After anesthetization by 0.3% pentobarbital sodium solution (30 mg/kg), 5 mice in each group was used to collect venous blood and other 5 mice was used for blood gas analysis. Fresh lung tissues of all mice were collect. This study was performed in The People's Hospital of Yinzhou, and experimental studies in accordance with the Basel declaration have been approved by the ethics committee of The People's Hospital of Yinzhou (No. D20181103).

Dual luciferase reporter system assay

The targeting relationship and binding site of miR-128-3p and MAPK14 was analyzed via the biological prediction website (www.targetscan.org), when was next verified by the dual luciferase reporter system assay. The MAPK14 (PGL3-MAPK14wt) and mutants that bind to the miR-128-3p (PGL3-MAPK14mut) dual luciferase reporter vectors were separately constructed. The Rellina plasmids and the two reporter plasmids were co-transfected into HEK293T cells with the miR-128-3p plasmid and the NC plasmid, respectively. After 24 h of cell transfection, dual luciferase assays were performed according to the instruction of the dual luciferase reporter kit (Promega). Relative luciferase activity = firefly luciferase / Renilla luciferase [8].

qRT-PCR

Trizol (Thermo Fisher Scientific, New York, USA) was used to extract total RNAs from lung tissue. The cDNA was synthesized by reverse transcription using TaqMan MicroRNA Assays Reverse Transcription Primer (Thermo scientific, USA). SYBR[®] Premix ExTaq[™] II Kit (Xingzhi Biotechnology Co., Ltd., China) was used for quantitative PCR detection. The following components were added in sequence: 25 µL of SYBR Premix ExTaq[™] II (2×), 2 µL of PCR upstream and downstream primers, ROXReferenceDye (50×) 1 µL, 4 µL DNA template, and 16 µL of ddH₂O. Fluorescence quantitative PCR was performed in ABI PRISM[®] 7300 (model Prism[®] 7300, Shanghai Kunke Instrument Equipment Co., Ltd., China). The reaction conditions were: pre-denaturation at 95 °C for 10 min, denaturation at 95 °C for 15 s, annealing at 60 °C for 30 s, 32 cycles, extending at 72 °C for 1 min. miR-128-3p with U6 as internal reference, and MAPK14 used GAPDH as internal reference. The relative expression amount of each gene of interest was calculated by $2^{-\Delta\Delta C_t}$. Primer sequences are shown in Table 1.

Western blot

Total protein in lung tissue was extracted using RIPA lysate containing PMSF (Phenylmethanesulfonyl fluoride, R0010, solarbio). The protein concentration was determined by BCA kit (thermo, USA). The

protein sample was mixed with the loading buffer, boiled for 10 min. Then 50 µg of protein sample was electrophoresed at 70 V for 3 h and transferred onto a PVDF membrane (ISEQ00010, Millipore, Billerica, MA, USA) with constant flow 150 mA. The membrane was then blocked by 5% skim milk at 4 °C for 2 h, washed with TBST, and incubated with anti-rabbit anti-mouse MAPK14 (ab31828, 1:500, Abcam, UK), GAPDH (ab22555, 1:2,000, Abcam, UK) overnight at 4 °C. After washing with TBST thrice, the membrane was incubated with HRP-labeled goat anti-rabbit IgG antibody (Beijing Zhongshan Biotechnology Co., Ltd., diluted 1:5,000) for 2 h and wash TBST thrice. ECL fluorescence detection kit (Cat. No. BB-3501, Ameshame, UK) was used for color development and the membrane was photographed by Bio-Rad image analysis system (BIO-RAD, USA) and the results were analyzed by Image J software. The relative protein content = the gray value of the corresponding protein band / the gray value of the GAPDH protein band.

Blood gas analysis and lung tissue wet / dry weight ratio (W/D)

Three days after modeling and treatment, mice were anesthetized by 0.3% pentobarbital sodium solution (30 mg/kg), and the carotid artery blood was taken for blood gas analysis to observe arterial oxygen partial pressure (PaO₂) and carbon dioxide partial pressure (PaCO₂) by an automatic blood gas analyser, with 29% oxygen inhalation. The wet / dry weight ratio (W/D) was calculated to reflect the degree of edema of the lung. The left lung of the mouse was removed by thoracotomy, and the wet weight was weighed after clearing the lung surface by filter paper. After drying in an incubator at 80 °C for 48 h, the sample in constant weight was weighted as the dry weight. Lung tissue wet / dry weight (W/D) = (lung wet weight / lung dry weight) * 100%.

HE staining

Three days after modeling and treatment, some lung tissues were fixed in 10% neutral formalin solution for 24 hours, and was dehydrated by gradient alcohol, embedded in paraffin and sliced. Then slice was treated with xylene transparent, hydrated by gradient alcohol and washed with distilled water for 1 min. Subsequently, the slice was stained with hematoxylin for 3 min, flushed with tap water, immersed in alcohol containing 0.5% hydrochloric acid for 10 s, stained with eosin dye solution for 5 min. Finally, the slice was conventionally dehydrated, transparentized and sealed with neutral gum. Each slice was observed under an optical microscope (XP-330, Shanghai Bingyu Optical Instrument Co., Ltd., Shanghai, China). Five random fields of view in slices of each mice were chosen for quantification by two lab assistants who are blind for the information of slices. Tissue damage index of each mice was scored 0-5: 0 score, no or few tissue abnormal could be observed in the fields; 1 score, slight tissue damage could be observed in the fields; 2 scores, middle degree of tissue damage could be observed in the fields; 3 scores, severe issue damage could be observed in the fields. Mean tissue damage index of all slices in this group indicates the damage degree of lung tissue in this group.

Activity detection of myeloperoxidase (MPO), mitochondrial superoxide dismutase (SOD) and malondialdehyde (MDA)

The lung tissue in size of 125 mm³ was homogenized with 1 mL of PBS, centrifuged at 4 °C, 12,000 xg for 10 min, and the supernatant was taken. The myeloperoxidase (MPO), which reflects the degree of neutrophil accumulation in lung tissue, was detected in strict accordance with the kit instructions (K744-100, Biovision, US). MDA and SOD in lung tissue were detected by MDA (A003-1-2) and SOD (A001-3-2) assay kits purchased from Nanjing Jiancheng Reagent Co., Ltd., respectively.

Enzyme-linked immunosorbent assay (ELISA)

Blood taken from mouse eyeballs were stand at room temperature for a while and at 4 °C overnight, centrifuged at 3,500 xg/min to collect serum and the samples were preserved at -80 °C. The level of inflammatory factors was measured by according the ELISA kit instructions (kit numbers: 69-21138, 69-22800, 69-25328, 69-40133; Wuhan Merck, China).

Statistical analysis

All data were processed by SPSS21.0 statistical software. The measurement data were expressed as mean ± standard deviation. One-Way ANOVA and Tukey post- Hoc test was used for comparison between groups. $p < 0.05$ indicates that the difference is statistically significant.

Results

DEX alleviate the lung tissue damage in sepsis mice and its effects affected by miR-128-3p and MAPK14 gene regulation

HE staining was used to detect the pathological changes of lung tissue in mice (Fig. 1). Lung tissue of Normal group was in regular structure without obvious pathological damage. Sepsis model mice without treatment and those treated with MAPK14 overexpression or miR-128-3p up-regulation had different degrees of inflammatory cell infiltration in the alveoli and interstitial; there was effusion in the cavity and thickened alveolar septum, meanwhile, some alveoli were collapsed, atelectasis, and formed transparent membrane and alveolar structure was damaged. However, DEX could alleviate the lung tissue damage and miR-128-3p up-regulation could enhance the protective effect, but MAPK14 over-expression could reverse the effect of DEX.

miR-128-3p targets and negatively regulates the gene expression of MAPK14 and expression of miR-128-3p and MAPK14

The biological prediction website (<http://www.microrna.org/microrna/home.do>) predicted that miR-128-3p and MAPK14 have specific binding sites (Fig. 2a), which was verified by the dual luciferase report system assay (Fig. 2b). The luciferase activity of the Wt-MAPK14 and miR-128-3p mimic transfected group was significantly lower than that in the Wt-MAPK14 and NC mimic group ($p < 0.05$). However, the luciferase activity of the group transfected with Mut-MAPK14 and miR-128-3p mimic or Mut-MAPK14 and

NC mimic group showed no significant difference ($p > 0.05$). Therefore, miR-128-3p could target and negatively regulate MAPK14 gene expression.

To further verify the above prediction and investigate if miR-128-3p and MAPK14 affected the effect of DEX on lung of sepsis mice, we detected the gene expression of miR-128-3p and MAPK14 in lung tissues of mice by qRT-PCR and Western blot (Fig. 2 c-e). Model mice had down-regulated miR-128-3p and upregulated MAPK14 when compared with the normal mice and DEX treatment could partly reverse these changes (all $p < 0.05$). In mice treated with miR-128-3p up-regulation, the expression levels of MAPK14 and p-MAPK14 were significantly decreased and miR-128-3p up-regulation could enhance the changes caused by DEX ($p < 0.05$). MAPK14 overexpression could reverse the gene expression trend in DEX treated mice ($p < 0.05$).

miR-128-3p and MAPK14 affect the effects of DEX on Blood gas analysis and lung W/D of sepsis model mice

The W/D of the lung tissue, PaO₂ and PaCO₂ of each group are shown in Fig. 3. Model mice had significantly higher W/D, PaCO₂ and lower PaO₂ when compared with the normal mice (all $p < 0.05$). In sepsis mice treated with DEX or miR-128-3p mimic, the levels of W/D and PaCO₂ were significantly decreased and PaO₂ level was increased. miR-128-3p up-regulation could enhance the effects of DEX ($p < 0.05$). MAPK14 overexpression could reverse the changes of indicators in DEX treated mice ($p < 0.05$).

miR-128-3p and MAPK14 affect the effects of DEX on serum levels of inflammatory factors of sepsis model mice

The serum levels of inflammatory factors in each group were detected by ELISA (Fig. 4). Model mice had significantly higher inflammatory factors (interleukin (IL)-8, IL-17, IL-6 and tumor necrosis factor (TNF)- α) when compared with the normal mice (all $p < 0.05$). In sepsis mice treated with DEX or miR-128-3p mimic, the levels of inflammatory factors were significantly decreased. miR-128-3p up-regulation could enhance the effects of DEX ($p < 0.05$). MAPK14 overexpression could reverse the changes of inflammatory factors in DEX treated mice ($p < 0.05$).

miR-128-3p and MAPK14 affect the effects of MPO, SOD and MDA contents in lung tissues of sepsis model mice

The contents of MPO, SOD and MDA in lung tissue of each group showed in Fig. 5. Model mice had significantly higher MPO and MDA contents and lower SOD content when compared with the normal mice (all $p < 0.05$). In sepsis mice treated with DEX or miR-128-3p mimic, the MPO and MDA contents were significantly decreased and SOD content was increased. miR-128-3p up-regulation could enhance the effects of DEX ($p < 0.05$). MAPK14 overexpression could reverse the changes of inflammatory factors in DEX treated mice ($p < 0.05$).

Discussion

DEX is a $\alpha 2$ -adrenergic drug used in clinic, which can be used as an anti-oxidative drug before anesthesia, reducing the concentration of cytokines in kidney tissue and can also reduce lung damage caused by LPS, ischemia-reperfusion and ventilation in animal models [16-18]. DEX has also been shown to reduce oxidative stress and apoptotic lesions in lung tissue [19]. In addition, it can reduce lung tissue fibrosis in rats after acute lung injury [20]. In our study, we established sepsis model and treated the model mice with DEX and we observed the pathological changes in lungs. The results showed that DEX had the protective effect on sepsis-induced lung injury. In addition, DEX could alleviate lung edema, improve respiratory function and inhibit inflammatory factor release and oxidative stress reaction in sepsis mice. All these results were consisted with the results of previous studies, proving that DEX does have a good protective effect in sepsis mice with ARDS.

The effect of miR-128-3p is frequently observed in a variety of human diseases, including myocardial failure, diabetes, etc. [21, 22]. It has been reported that the p38 MAPK signaling pathway is involved in the inflammatory response and mediates the production of many cytokines, including IL-1 β , TNF- α and IL-6 in ARDS [23, 24]. Many anti-inflammatory drugs act by targeting p38 MAPK [25]. In this study, we also found the intervention of gene expression of miR-128-3p and MAPK14 in sepsis mice could affect the effects of DEX. We found that there may be a target relationship between miR-128-3p and MAPK14 via bioinformatic website, which then verify by dual-luciferase reporter system assay. In lung tissue of sepsis mice, this target relationship was verified again. Interestingly, miR-128-3p up-regulation could enhance the protective effect of DEX, while MAPK14 over-expression plays a negative role in DEX protection. Therefore, we conclude that overexpression of miR-128-3p in lung of septic mice can target and inhibit P38 MAPK signaling pathway to improve the protective effect of dexmedetomidine (Fig.6).

As RNA therapy is increasing popular now, we hope that our findings could provide some new insights for the drug research and development as well as the new treatment strategy development of sepsis and acute lung injury cause by sepsis. However, some of the patients who develop pulmonary injury associated with sepsis do not die from respiratory dysfunction, but from the development and impairment of multiple organ dysfunction. In this study, we only observed the changes of biomarkers in lung and serum inflammatory factors. An important mechanism and effect to be evaluated of therapy in Lung injury associated with sepsis is the impact on mortality over time. Therefore, we need a further research to explore if our therapy prevents or treats the injury in other organs and decreases the mortality.

Conclusions

miR-128-3p mediates the P38 signaling pathway by targeting the MAPK14, thereby inhibiting inflammatory factor release and oxidative stress damage.

Declarations

Ethics approval

This study was performed in The People's Hospital of Yinzhou, and was approved by the Ethics Committee of The People's Hospital of Yinzhou (No. D20181103).

Consent for publication

Not applicable.

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

Not applicable.

Authors' contributions

LD and LFS were responsible for data collection and data process. XG and SHY contributed to statistical analysis and data analysis. LD was responsible for manuscript concept, guidance and editing. All authors read and approved the final manuscript.

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Not applicable.

Abbreviations

ARDS, acute respiratory distress syndrome; DEX, dexmedetomidine; miRNAs, microRNAs; UTR, untranslated region; LPS, lipopolysaccharide; p38MAPK, p38 mitogen-activated protein kinase; MAPK14, mitogen-activated protein kinase 14; SPF, specific pathogen free; NC, negative control; oe-MAPK14, MAPK14 overexpression; PMSF, phenylmethanesulfonyl fluoride; PVDF, polyvinylidene fluoride; W/D, wet/dry weight ratio; PaO₂, arterial oxygen partial pressure; PaCO₂, carbon dioxide partial pressure; HE, hematoxylin; MPO, myeloperoxidase; SOD, superoxide dismutase; MDA, malondialdehyde; ELISA, enzyme-linked immunosorbent assay; ICU, intensive care unit; IL, interleukin; TNF, tumor necrosis factor; ANOVA, analysis of variance.

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Table

Table 1 Primer sequences

Gene	Sequence
miR-128-3p	F: 5'-GGTCACAGTGAACCGGTC-3'
	R: 5'-GTGCAGGGTCC GAGGT-3'
MAPK14	F: 5'-CTGACCGACGACCACGTTC-3'
	R: 5'-CTTCGTTACAGCTAGGTTGC-3'
U6	F: 5'-CTCGCTTCGGCAGCACA-3'
	R: 5'-AACGCTTCACGAATTTGCGT-3'
GAPDH	F: 5'-TTCAACGGCAGTCAAGG-3'
	R: 5'-CACCAGTGGATGCAGGGAT-3'

Figures

Figure 1

Pathological changes in lung tissue of mice in each group (400×, n=3). (a) Representative images in each group; (b) Tissue damage index of each group. Sepsis model mice without treatment and those treated with MAPK14 overexpression or miR-128-3p up-regulation had different degrees of inflammatory cell infiltration in the alveoli and interstitial; there was effusion in the cavity and thickened alveolar septum, meanwhile, some alveoli were collapsed, atelectasis, and formed transparent membrane and alveolar structure was damaged. Compared with Normal group, * $p < 0.05$; compared with Model group, # $p < 0.05$; compared with DEX group, % $p < 0.05$; compared with miR-128-3p mimic group, & $p < 0.05$; compared with oe-MAPK14 group, \$ $p < 0.05$; compared with miR-128-3p mimic+oe-MAPK14 group, @ $p < 0.05$; compared with miR-128-3p mimic+DEX group, Δ $p < 0.05$. DEX, dexmedetomidine. UTR, untranslated region. DEX, dexmedetomidine.

Figure 2

miR-128-3p negatively regulates gene expression of MAPK14 and the expression of miR-128-3p and MAPK14. (a) The sequence of the 3'-UTR region in which miR-128-3p binds to MAPK14; (b) Dual luciferase assay to detect luciferase activity, $n=3$. (c) The mRNA levels of miR-128-3p and MAPK14 in lung tissue of each group, $n=4$; (d) Representative protein bands of MAPK14 and p-MAPK14 in lung tissue of each group; (e) Quantification results of the protein level of MAPK14 and p-MAPK14 in lung tissues of each group, $n=4$. Compared with Normal group, $*p < 0.05$; compared with Model group, $\#p < 0.05$; compared with DEX group, $\%p < 0.05$; compared with miR-128-3p mimic group, $\&p < 0.05$; compared with oe-MAPK14 group, $\$p < 0.05$; compared with miR-128-3p mimic+oe-MAPK14 group, $@p < 0.05$; compared with miR-128-3p mimic+DEX group, $\Delta p < 0.05$. DEX, dexmedetomidine. UTR, untranslated region.

Figure 3

The W/D, PaO₂, PaCO₂ of each group of mice. (a) W/D of mouse lung tissue, n=3; (b) PaO₂ in mice, n=5; (c) PaCO₂ in mice, n=5. Compared with Normal group, *p < 0.05; compared with Model group, #p < 0.05; compared with DEX group, %p < 0.05; compared with miR-128-3p mimic group, &p < 0.05; compared with oe-MAPK14 group, \$p < 0.05; compared with miR-128-3p mimic+oe-MAPK14 group, @p < 0.05; compared with miR-128-3p mimic+DEX group, Δp < 0.05. DEX, dexmedetomidine. W/D, wet tissue mass ratio; PaO₂, arterial oxygen partial pressure; PaCO₂, carbon dioxide partial pressure.

Figure 4

The W/D, PaO₂, PaCO₂ of each group of mice. (a) W/D of mouse lung tissue, n=3; (b) PaO₂ in mice, n=5; (c) PaCO₂ in mice, n=5. Compared with Normal group, *p < 0.05; compared with Model group, #p < 0.05; compared with DEX group, %p < 0.05; compared with miR-128-3p mimic group, &p < 0.05; compared with oe-MAPK14 group, \$p < 0.05; compared with miR-128-3p mimic+oe-MAPK14 group, @p < 0.05; compared with miR-128-3p mimic+DEX group, Δp < 0.05. DEX, dexmedetomidine. W/D, wet tissue mass ratio; PaO₂, arterial oxygen partial pressure; PaCO₂, carbon dioxide partial pressure.

Figure 5

MPO, SOD, MDA content in lung tissue of mice in each group (n=3). (a) MPO content in mice; (b) SOD content in mice; (c) MDA content in mice. Compared with Normal group, * $p < 0.05$; compared with Model group, # $p < 0.05$; compared with DEX group, % $p < 0.05$; compared with miR-128-3p mimic group, & $p < 0.05$; compared with oe-MAPK14 group, \$ $p < 0.05$; compared with miR-128-3p mimic+oe-MAPK14 group, @ $p < 0.05$; compared with miR-128-3p mimic+DEX group, Δ $p < 0.05$. MPO, myeloperoxidase; SOD, superoxide dismutase; MDA, malondialdehyde; DEX, dexmedetomidine.

Figure 6

miR-128-3p inhibits MAPK14 pathway to enhance the protective effect of dexmedetomidine on acute respiratory distress syndrome in septic mice. DEX, dexmedetomidine; ARDS, acute respiratory distress syndrome.

Supplementary Files

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