

Original Article

Expression of miR-144, titin-Ab and MAPK signal transduction pathway related proteins in pre-eclampsia patients

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Abstract: Objective: To investigate and analyze the expressions of micro-144 (miR-144), titin antibody (titin-Ab) in peripheral blood and mitogen-activated protein kinase (MAPK) signal transduction pathway related proteins in placenta tissues of pre-eclampsia patients. Methods: Of 58 patients with pre-eclampsia (research group), 31 cases were severe (research group 1) and 27 cases were mild (research group 2), and another 30 normal pregnant women were enrolled as controls. The expression of miR-144 and titin-Ab in peripheral blood and placental tissues in each group was detected and compared. The placental tissues of the subjects were collected after cesarean section, and the expression of MAPK proteins, including p-p38, phosphorylated c-Jun N-terminal kinase (p-JNK), and phosphorylated extracellular regulated protein kinases (p-ERK), was detected by Western Blot. Results: Compared with the control group, miR-144 level in the research group was significantly decreased, while the titin-Ab was significantly increased ($P<0.05$). The miR-144 level in research group 1 was significantly lower than that in research group 2, and titin-Ab level was significantly higher than that in research group 2 ($P<0.05$). The expression level of p-p38 and p-JNK proteins in the research group was significantly higher than that in control group, and the expression level of p-ERK protein was significantly lower than that in control group ($P<0.05$). Compared with research group 2, research group 1 showed significantly higher expression level of p-p38 and p-JNK proteins as well as significantly lower expression level of p-ERK protein ($P<0.05$). Correlation analysis showed that miR-144 in peripheral blood of pre-eclampsia patients was negatively correlated with the expression of p-p38 and p-JNK proteins in placenta tissues, and was positively correlated with the expression of p-ERK protein ($P<0.05$). Whereas titin-Ab was positively correlated with the expression of p-p38 and p-JNK proteins, and was negatively correlated with the expression of p-ERK protein ($P<0.05$). Conclusion: The expression of miR-144 and titin-Ab in the peripheral blood of pre-eclampsia patients is related to the severity of the disease and the MAPK signal transduction pathway in placenta, which plays an important role in the development of pre-eclampsia. The detection of miR-144 and titin-Ab in the peripheral blood can reveal the condition of patients and indirectly reflect the changes of MAPK signal transduction pathway in placenta tissues.

Keywords: Pre-eclampsia, miR-144, titin-Ab, placental tissue, MAPK signal transduction pathway

Introduction

Studies have found that, more than 500,000 women die of pregnancy and childbirth complications every year, of which pre-eclampsia and eclampsia cause more than 70% of maternal deaths [1, 2]. The incidence of pre-eclampsia accounts for about 3.9% of all pregnancies, and may develop into eclampsia in severe cases, which causes generalized convulsions that affect various organ systems. MicroRNA (miRNA) is a non-coding single-stranded small

molecule RNA encoded by endogenous genes with a length of 18-22 nucleotides, which plays an important role in cell proliferation and apoptosis, growth and development, organ formation, hematopoietic process, fat metabolism, antiviral defense and other pathophysiological processes.

Researches showed that, at least 20 miRNAs, including miR-126, miR-141 and miR-210, were differentially expressed in placental tissues of pre-eclampsia patients [3, 4]. Moreover, they

also participate in abnormal proliferation and invasion of trophoblasts and promote the occurrence of pre-eclampsia. Therefore, miRNA level is related to trophoblast abnormalities and pre-eclampsia. What's more, it is suggested that titin antibody (titin-Ab) is differentially expressed in pre-eclampsia, which regulates the abnormal invasion of trophoblast cells and may mediate the occurrence of pre-eclampsia [5, 6]. Previous studies revealed that, with the intervention of cyclosporine A the expression of miR-144 gets down-regulated [7-9]. In addition, according to the prediction of targets can software, there was a specific binding site of miR-144 on the 3'UTR of titin mRNA. After binding, miR-144 could promote the proliferation and migration of trophoblasts and induce pre-eclampsia.

Mitogen-activated protein kinase (MAPK), a serine/threonine protein kinase widely distributed in cells, can transmit cytoplasmic signals to the nucleus. MAPK signal transduction pathway participates in cell proliferation, differentiation, development, apoptosis, inflammatory response and other pathophysiological processes. Scholars have found that the expression of p38MAPK in patients with early-onset severe pre-eclampsia is significantly higher than that in patients with late-onset severe pre-eclampsia or that in control group [10]. Meanwhile, inhibition of MAPK signal transduction pathway promotes the decrease of MMP-9 activity caused by IL-1 β in amniotic cells. Therefore, MAPK signal pathway may be a key to the occurrence of pre-eclampsia. This study speculated that the expression of miR-144 may be related to activation of MAPK signal transduction pathway. In order to further verify the expression of miR-144 and titin-Ab in pre-eclampsia patients and their specific mechanism, this study analyzed the expression of miR-144, titin-Ab in peripheral blood and MAPK signal transduction pathway related proteins in placenta tissues of pre-eclampsia patients.

Materials and methods

Study subjects

Fifty eight patients with pre-eclampsia admitted to General Hospital of Southern Theatre Command of PLA from March to July 2018 were selected as the research group, of which 31 patients with severe pre-eclampsia were taken

as research group 1 and 27 patients with mild pre-eclampsia as research group 2. Inclusion criteria: Meeting the diagnostic criteria for pre-eclampsia and severe pre-eclampsia in the 7th edition of Obstetrics and Gynecology [11]; singleton pregnancy; cesarean section to terminate pregnancy; multipara with no similar medical history in previous pregnancy; aged 24-30 years old, with an average age of 26.1 ± 1.9 years; no history of recurrent spontaneous abortion, teratism, stillbirth and other adverse pregnancy. Exclusion criteria: Complicated with primary hypertension, liver and kidney insufficiency, coronary heart disease, acute inflammation and diabetes; with placental abruption, placenta previa and other pathological pregnancy. Meanwhile, 30 normal pregnant women were selected as control group. All patients had no acute or chronic infectious diseases and malformation fetus during this pregnancy. This study was approved by the Ethics Committee of General Hospital of Southern Theatre Command of PLA. All the subjects signed an informed consent form.

Collection and processing of specimens

Placental specimen: Within 10 min after delivery of the placenta, a 10 g sample of tissue in the central part of the maternal side of the attachment area of placental umbilical cord root was selected. And carefully, the hemorrhagic, necrosis and calcification areas were avoided. After being cleaned with ice phosphate buffer solution (PBS), the tissue was placed in a sterilized frozen tube, quickly frozen in liquid nitrogen, and then transferred to a -80°C refrigerator for storage.

Blood specimen: Before delivery, 2 mL of fasting elbow venous blood was taken from all patients, centrifuged at 1,000 rpm for 10 min to obtain serum specimen. Then the serum was saved in centrifuge tubes and stored in a refrigerator at -80°C for later use.

Detection of miR-144 and titin-Ab levels in serum and placenta tissues by fluorescence quantitative PCR (FQ-PCR)

After collecting serum and placenta tissues of patients, the total RNA of tissues was extracted by Trizol kit (Invitrogen Company, United States). After the purity was detected, the RNA was stored at -80°C. Next, 3 μ L of total RNA was

added to a 20 µL reaction system of 1st strand cDNA synthesis kit (Takara Company, Japan), and reverse transcription was performed at 37°C for 1 h to generate cDNA. The PCR curve was amplified by Bio-Rad quantitative PCR instrument (Bio-Rad Company, USA). The real time (RT) FQ-PCR primer was designed by Shanghai Adicon Company, and the primer sequences were as follows: miR-144 upstream primer: 5'-ATCCAGTCGTGTCGTG-3', downstream primer: 5'-TGCTTATACAGTATAGG-3'; Titin-Ab upstream primer: 5'-GAATTGCGATTAGTACG-3', downstream primer: 5'-GTTGTACTAGTGTCT-3'; Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) upstream primer: 5'-CTTGATGTACGTAGCCTGGA-3', downstream primer: 5'-GTGTGTATGTTACTGTCTGCA-3'. The reaction conditions were as follows: denaturation at 95°C for 5 min, followed by 95°C for 10 sec, 60°C for 20 sec, 72°C for 20 sec, acquiring fluorescence at 78°C for 20 sec, for a total of 40 cycles. The mRNA circulation threshold (Ct) of the target gene was obtained, and the relative expression of target gene was calculated using $2^{-\Delta\Delta Ct}$ ($\Delta\Delta Ct = Ct_{\text{target gene}} - Ct_{\text{internal reference gene}}$).

Detection of expression levels of p-p38, p-JNK and p-ERK in placental tissues with immunohistochemistry

The placenta tissue was collected and placed in 4% paraformaldehyde for 24 h, embedded in paraffin and cut into 5 µm slices. The operation was carried out in accordance with the instruction of Streptavidin Peroxidase Elisa kit, using Rabbit anti-human p-p38, phosphorylated c-Jun N-terminal kinase (p-JNK) and phosphorylated extracellular regulated protein kinases (p-ERK) monoclonal antibodies (Cell Signaling Technology, United States). When in use, antibody diluents containing 59% PBS, 40% Glycerol and 0.05% BSA were used to dilute their concentrations to 1:50. PBS was used as negative control. Diaminobenzidine method was used for staining. Brown-yellow like particles in the cytoplasm or nucleus of placental cells suggested positive staining.

Detection of expression of MAPK related proteins in placenta tissues by western blot

MAPK related proteins included p38, JNK, ERK, p-p38, p-JNK and p-ERK. Placenta tissue homogenate was prepared on ice. Pre-cooled phenylmethylsulfonyl fluoride (PMSF) and radio

immunoprecipitation assay (RIPA) reagents were added to extract the total proteins, and phosphatase inhibitor was added to phosphorylated proteins (PMSF, RIPA and phosphatase inhibitor were all purchased from Cambridge, MA, USA). After being cleaved and centrifuged at 4°C, the proteins were added with loading buffer and denatured by boiling, in order to prevent phosphatase from degrading phosphate protein. The proteins were quantified by bicinchoninic acid assay, loaded with a volume of 30 µL per well, then boiled for 10 min to carry out protein denaturation. Next, 10% polyacrylamide gel was prepared, and the electrophoresis voltage of concentrated gel and separating gel was 100 V and 120 V, respectively. The proteins were transferred to a polyvinylidene fluoride (PVDF) membrane by semi-dry method, with a current of 70 mA for 35 min. Afterwards, the membrane was washed with tris buffered saline tween (TBST) buffer for 10 min, 3 times, then blocked with 10% skimmed milk at room temperature for 3 h. And p38, JNK, ERK, p-p38, p-JNK and p-ERK antibody (Cell Signaling Technology Company, United States) were added in a PBS with a dilution ratio of 1:400. The membrane was washed with TBST buffer for 10 min, 3 times, and incubated overnight at 4°C. Following washing with TBST buffer for 10 min, 3 times, horseradish peroxidase (HRP)-labeled goat anti-rabbit secondary antibody (1:3,000; Wuhan BOSTER Biological Technology Co., Ltd., China) was added. After that, the membrane was rinsed with TBST for 10 min, 3 times. The protein bands on the membrane were developed and exposed using the enhanced chemiluminescence kit. Gel-ProAnalyzer software analysis system (United Bio Company, United States) was used to measure the gray value of the target band.

Outcome measures

Main outcome measures: The mRNA expression of miR-144, titin-Ab in peripheral blood and placenta tissues, and the protein expression of p38, JNK, ERK, p-p38, p-JNK and p-ERK in placenta tissues.

Secondary outcome measures: The correlation between the mRNA expression of miR-144, titin-Ab in peripheral blood and placenta tissues and the protein expression of p-p38, p-JNK and p-ERK in placental tissues.

Table 1. Comparison of general information ($\bar{x} \pm sd$, n)

Group	Research group 1 (n=31)	Research group 2 (n=27)	Control group (n=30)	t	P
Age (year)	25.9 \pm 3.1	26.9 \pm 2.7	25.7 \pm 2.9	1.126	0.329
Gestational age (week)	34.5 \pm 3.7	35.2 \pm 3.5	35.1 \pm 3.7	0.323	0.725
Gravidity parity (time)	2.1 \pm 1.2	2.5 \pm 1.3	2.2 \pm 1.5	0.685	0.507
Body mass index (kg/m ²)	24.58 \pm 1.62	25.19 \pm 1.73	24.66 \pm 1.25	1.304	0.277
Birth weight (g)	2672.55 \pm 89.41	2591.72 \pm 81.45	3057.32 \pm 217.88	86.409	0.000

Table 2. mRNA expression of miR-144 and titin-Ab in peripheral blood ($\bar{x} \pm sd$, n)

Group	miR-144	Titin-Ab
Research group (n=58)	0.96 \pm 0.22**	1.53 \pm 0.64**
Severe pre-eclampsia (n=31)	0.84 \pm 0.18**	1.82 \pm 0.77**
Mild pre-eclampsia (n=27)	1.22 \pm 0.24**##	1.22 \pm 0.41**##
Control group (n=30)	1.92 \pm 0.72	0.81 \pm 0.21

Note: Compared with control group, **P<0.01; compared with severe pre-eclampsia group, ##P<0.01. Titin-Ab, titin antibody.

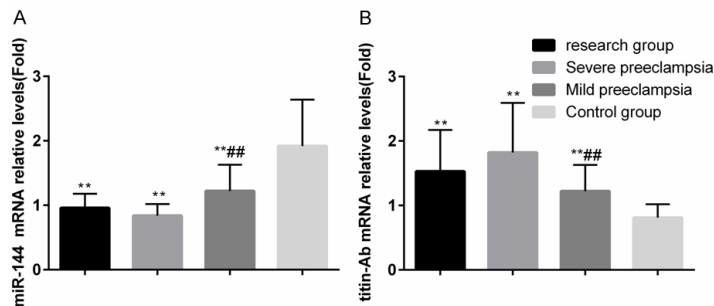


Figure 1. mRNA expression of miR-144 and titin-Ab in peripheral blood. A: Expression of miR-144; B: Expression of titin-Ab. Compared with control group, **P<0.01; compared with severe pre-eclampsia group, ##P<0.01. Titin-Ab, titin antibody.

Statistical analysis

The data obtained from this study were analyzed by SPSS19.0 statistical software. The measurement data were expressed as $\bar{x} \pm sd$ and analyzed by t-test. The counting data were expressed by number of cases/percentage (n/%) and analyzed by χ^2 test. Pearson correlation analysis was used for data correlation. A value of $P<0.05$ indicated statistical significance.

Results

Comparison of clinical data

There was no significant difference in age, gestational age, gravidity parity and body mass

index among the three groups ($P>0.05$). However, the difference in birth weight was statistically significant ($P<0.05$). See **Table 1**.

Expression of miR-144 and titin-Ab in peripheral blood

Compared with the control group, miR-144 level in peripheral blood of the patients in the research group was significantly decreased ($P<0.05$), and that in research group 1 was significantly lower than that in research group 2 ($P<0.05$). The titin-Ab level in peripheral blood of the patients in the research group was significantly increased ($P<0.05$), and that in research group 1 was significantly higher than that in research group 2 ($P<0.05$). See **Table 2** and **Figure 1**.

Expression of miR-144 and titin-Ab in placental tissue

Compared with the control group, miR-144 level in placenta tissue of the patients in the research group was significantly decreased ($P<0.05$), and that in research group 1 was significantly lower than that in research group 2 ($P<0.05$). The titin-Ab level in placenta tissue of the patients in the research group was significantly increased ($P<0.05$), and that in research group 1 was significantly higher than that in research group 2 ($P<0.05$). See **Table 3** and **Figure 2**.

Expression of MAPK pathway related proteins in placenta tissues by immunohistochemistry

p-p38, p-JNK and p-ERK were mainly expressed in the cytoplasm of cytotrophoblasts in placental tissues. Optical microscope showed that

Table 3. mRNA expression of miR-144 and titin-Ab in placental tissue ($\bar{x} \pm sd, n$)

Group	miR-144	Titin-Ab
Research group (n=58)	1.02 \pm 0.29**	1.95 \pm 0.66**
Severe pre-eclampsia (n=31)	0.91 \pm 0.20**	2.14 \pm 0.81**
Mild pre-eclampsia (n=27)	1.39 \pm 0.35**##	1.36 \pm 0.37**##
Control group (n=30)	2.03 \pm 0.66	0.93 \pm 0.24

Note: Compared with control group, **P<0.01; compared with severe pre-eclampsia group, ##P<0.01. Titin-Ab, titin antibody.

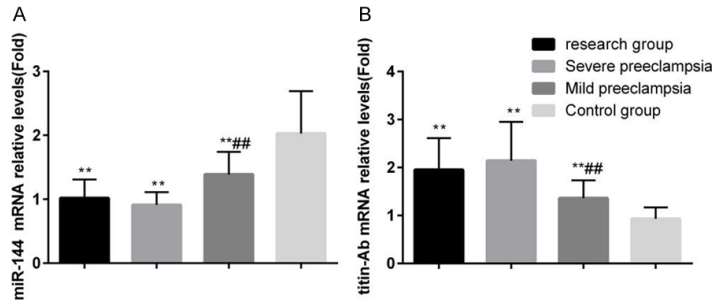


Figure 2. mRNA expression of miR-144 and titin-Ab in placental tissue. A: Expression of miR-144; B: Expression of titin-Ab. Compared with control group, **P<0.01; compared with severe pre-eclampsia group, ##P<0.01. Titin-Ab, titin antibody.

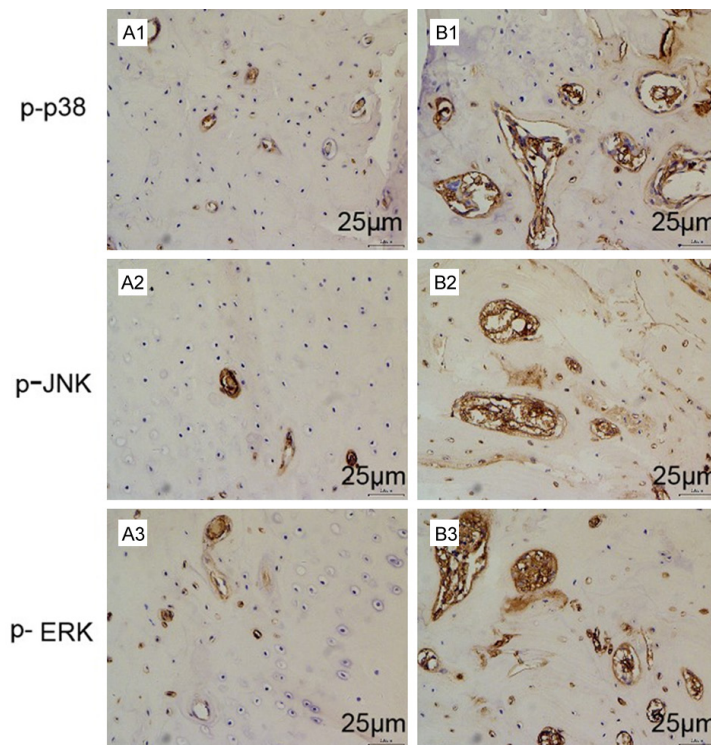


Figure 3. Expression of MAPK pathway related proteins in placenta tissues by immunohistochemistry (50 \times). A: Control group; B: Pre-eclampsia group. p-JNK, phosphorylated c-Jun N-terminal kinase; p-ERK, phosphorylated extracellular regulated protein kinases.

only a small number of positive fine particles of p-p38, p-JNK and p-ERK were expressed in the cytotrophoblasts in control group, while a large number of brown and yellow particles appeared in the pre-eclampsia patients. See **Figure 3**.

Expression of MAPK pathway related proteins in placenta tissue of pre-eclampsia patients

The expression level of p-p38 and p-JNK proteins in placenta tissue of the patients in the research group was significantly higher than that in the control group (P<0.05), and that in research group 1 was significantly higher than that in research group 2 (P<0.05). The expression level of p-ERK protein in the research group was significantly lower than that in the control group (P<0.05), and that in research group 1 was significantly lower than that in research group 2 (P<0.05). See **Figure 4**.

Correlation between miR-144 and p-p38, p-JNK proteins in pre-eclampsia patients

Correlation analysis showed that miR-144 in peripheral blood of pre-eclampsia patients was negatively correlated with the expression of p-p38 and p-JNK proteins in placenta tissues, and was positively correlated with the expression of p-ERK protein (P<0.05). miR-144 in placenta tissues was negatively correlated with the expression of p-p38 and p-JNK proteins in placenta tissues, and was positively correlated with the expression of p-ERK protein (P<0.05). See **Figure 5**.

Correlation between titin-Ab and p-p38, p-JNK proteins in pre-eclampsia patients

Titin-Ab in peripheral blood of pre-eclampsia patients was negatively

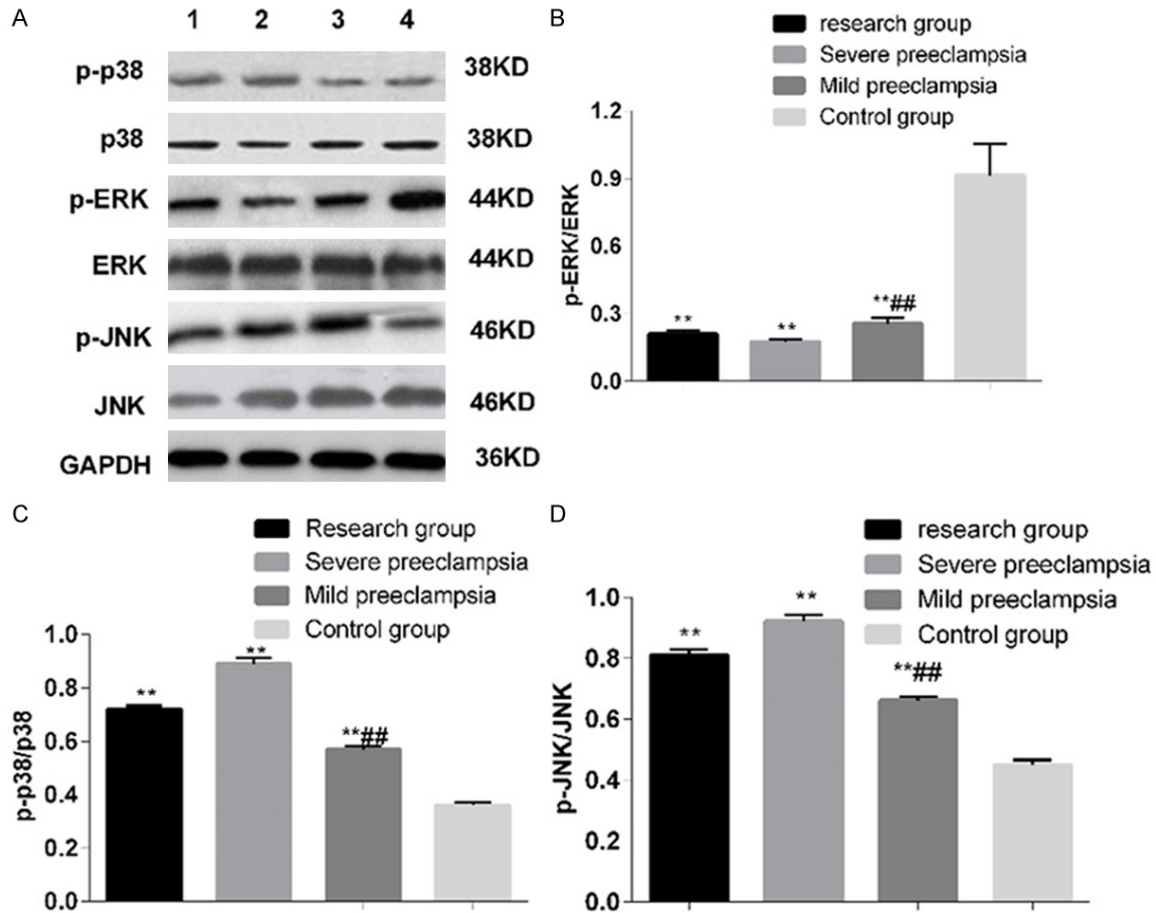


Figure 4. Expression of MAPK pathway related proteins in placenta tissue of pre-eclampsia patients. A: Protein bands of MAPK pathway related proteins in western blot; B: Relative protein expression of p-ERK; C: Relative protein expression of p-p38; D: Relative protein expression of p-JNK. Compared with control group, ** $P < 0.01$; compared with severe pre-eclampsia group, ## $P < 0.01$. p-JNK, phosphorylated c-Jun N-terminal kinase; p-ERK, phosphorylated extracellular regulated protein kinases.

correlated with the expression of p-ERK protein in placenta tissues ($P < 0.05$), and was positively correlated with the expression of p-p38 and p-JNK proteins. Titin-Ab in placental tissues was negatively correlated with the expression of p-ERK protein in placental tissues, and was positively correlated with the expression of p-p38 and p-JNK proteins ($P < 0.05$). See **Figure 6**.

Discussion

The pathophysiological process of pre-eclampsia may involve maternal, placental and fetal factors [12, 13]. Some studies show that, abnormal invasion of trophoblast may be an important cause of pre-eclampsia [14, 15]. Trophoblast mainly refers to the trophoblastic layer outside the embryo, which is the fetal cell directly contacting the maternal-fetal interface

and the maternal immune system. It provides essential nutrients for the development of egg cells and constitutes the basic barrier for the exchange of substances between mother and fetus [16, 17]. The abnormal invasion of trophoblast can lead to incomplete dilation of spiral arterioles, abnormal stenosis of spiral arterioles in myometrium, placental hypoperfusion and hypoxia, thus inducing pre-eclampsia. It is suggested that titin, an important regulatory protein in the process of trophoblast invasion, is abnormally expressed in pre-eclampsia, which indicates the abnormal invasion of trophoblast [7, 18]. In our previous study, miR-144 may play an important role in the pathogenesis of pre-eclampsia, but its specific mechanism has not been reported.

In order to verify the relationship between miR-144 and the onset of pre-eclampsia, its expres-

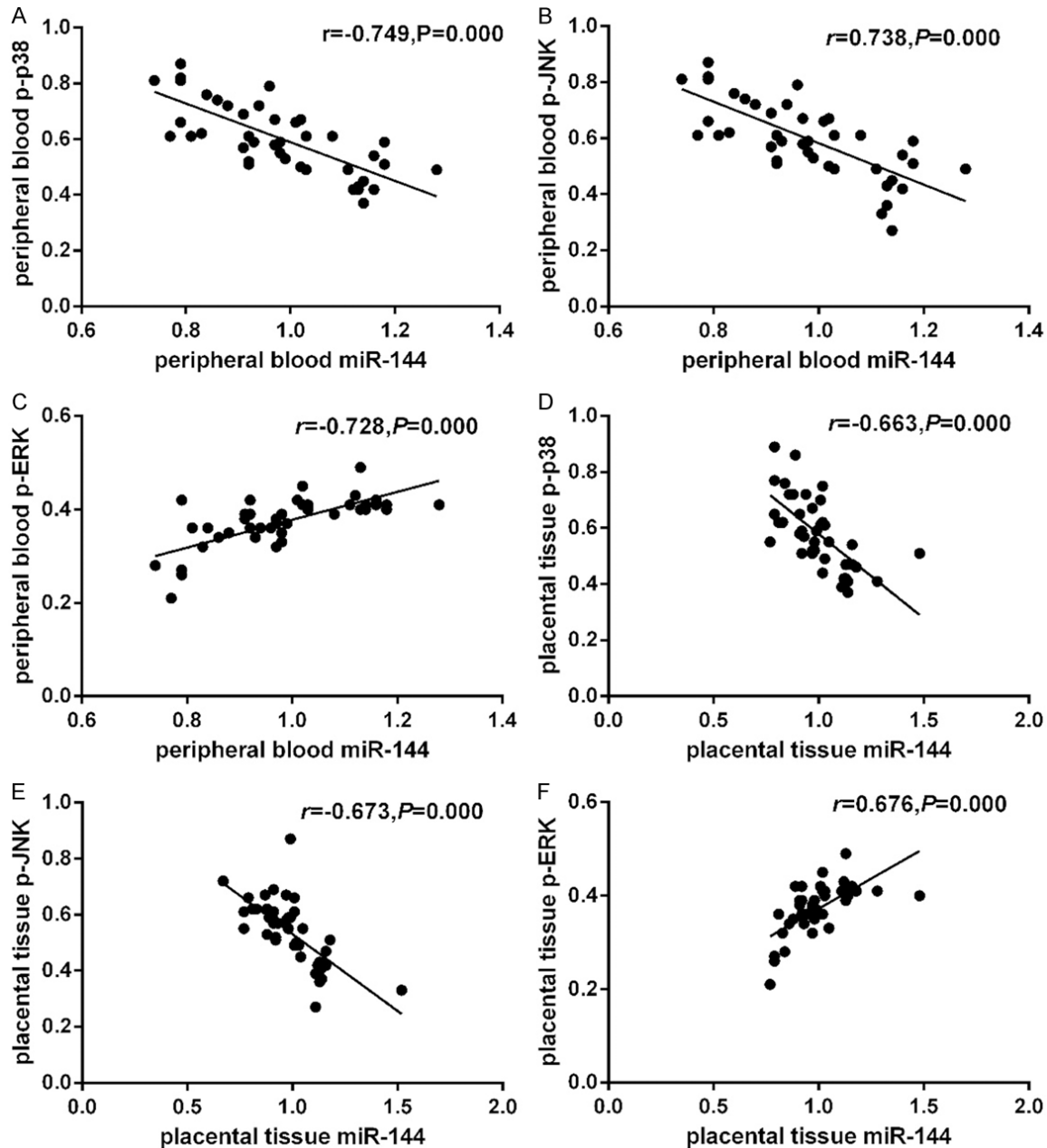


Figure 5. Correlation between miR-144 and p-p38, p-JNK proteins in pre-eclampsia patients. A: Correlation between peripheral blood miR-144 and p-p38; B: Correlation between peripheral blood miR-144 and p-JNK proteins; C: Correlation between peripheral blood miR-144 and p-ERK; D: Correlation between placental tissue miR-144 and p-p38; E: Correlation between placental tissue miR-144 and p-JNK proteins; F: Correlation between placental tissue miR-144 and p-ERK. p-JNK, phosphorylated c-Jun N-terminal kinase; p-ERK, phosphorylated extracellular regulated protein kinases.

sion in pre-eclampsia patients was first analyzed. The results showed that miR-144 level in peripheral blood and placental tissue of pre-eclampsia patients was significantly lower than that of normal individuals, and the expression level in severe patients was significantly lower than that in mild patients. It is suggested that the expression level of miR144 is decreased in

the plasma of pre-eclampsia patients. And statistical analysis reveals that miR-141 expression in pre-eclampsia patients is down-regulated and is correlated with the disease condition. At the same time, by detecting the expression of titin-Ab, it was found that the titin-Ab level in peripheral blood and placenta tissue of pre-eclampsia patients was significantly higher

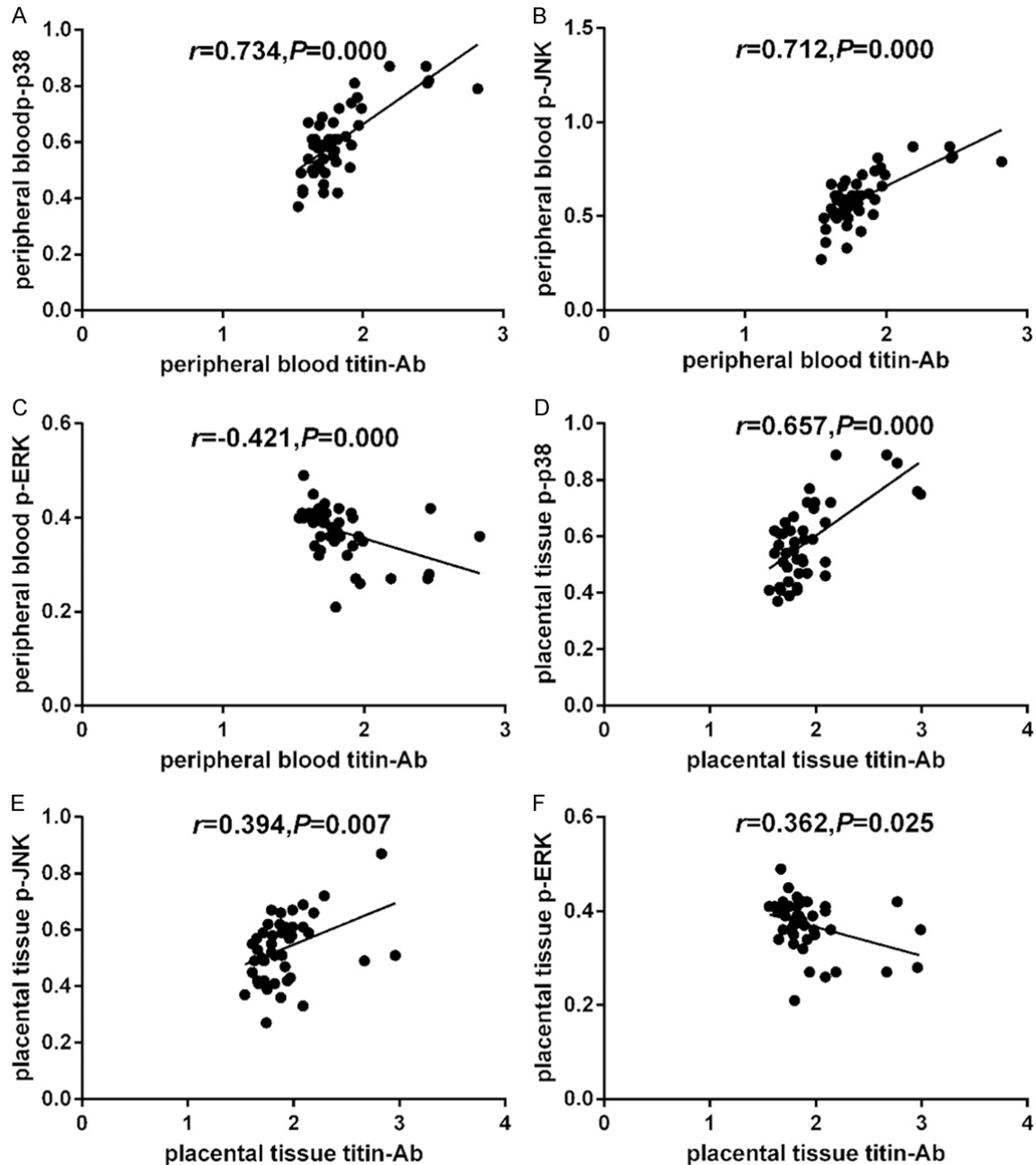


Figure 6. Correlation between titin-Ab and p-p38, p-JNK proteins in pre-eclampsia patients. A: Correlation between peripheral blood titin-Ab and p-p38; B: Correlation between peripheral blood titin-Ab and p-JNK proteins; C: Correlation between peripheral blood titin-Ab and p-ERK; D: Correlation between placental tissue titin-Ab and p-p38; E: Correlation between placental tissue titin-Ab and p-JNK proteins; F: Correlation between placental tissue titin-Ab and p-ERK. titin-Ab, titin antibody; p-JNK, phosphorylated c-Jun N-terminal kinase; p-ERK, phosphorylated extracellular regulated protein kinases.

than that of normal individuals, and the expression level in severe patients was significantly higher than that in mild patients. As suggested, the expression level of titin-Ab is up-regulated in the plasma of pre-eclampsia patients, and is higher in severe patients.

MAPK signal transduction pathway plays an important role in the regulation of eukaryotic cell proliferation, differentiation, apoptosis and other life cycle activities. Shin et al. believe that the expression of phosphorylated MAPKs (p-ERK, p-JNK, p-p38) is significantly increased

in fetal membranes near the cervix of preterm pregnant women, while MAPK signal transduction pathway up-regulates IL-1 β -induced MMP-9 activity in amnion cells, thus playing an important role in preterm labor [19, 20]. Another study shows that, the expression of TNF- α and IL-6 in serum of pre-eclampsia patients is increased, and the expression of p-p38 and p-JNK in placenta tissue of pre-eclampsia patients is higher than that in normal pregnancies, suggesting the critical role of MAPK signal transduction pathway in the pathogenesis of pre-eclampsia [21]. The results of this study showed that the expression level of p-p38 and p-JNK proteins was up-regulated in placenta tissue of pre-eclampsia patients, while the expression level of p-ERK protein was down-regulated, and the expression level of each index in severe patients was significantly higher than that in mild patients. These results are consistent with those of literature reports, indicating that MAPK signal transduction pathway is involved in the pathogenesis of pre-eclampsia.

We further studied the correlation between miR-144, titin-Ab and p-p38, p-JNK proteins in pre-eclampsia patients. The correlation analysis showed that miR-144 in peripheral blood of pre-eclampsia patients was negatively correlated with the expression of p-p38 and p-JNK proteins in placenta tissues, and was positively correlated with the expression of p-ERK protein. Similarly, miR-144 in placenta tissues had a negative correlation with the expression of p-p38 and p-JNK proteins in placenta tissues, and positive correlation with the expression of p-ERK protein. However, conversely, titin-Ab in the peripheral blood of pre-eclampsia patients was negatively correlated with the expression of p-ERK protein in placenta tissues, and was positively correlated with the expression of p-p38 and p-JNK proteins. There was a negative correlation between titin-Ab in placental tissues and the expression of p-ERK protein in placental tissues, and a positive correlation between titin-Ab in placental tissues and the expression of p-p38 and p-JNK proteins. Ma et al. point out that the expression of p-p38 in placental tissue of patients with pre-eclampsia is higher than that of normal pregnancies, and it also may be involved in the pathogenesis of pre-eclampsia with positive feedback [22]. Moreover, MAPK signal transduction pathway related proteins play an important role in the pathogenesis of pre-eclampsia. The study of Luo et al. also shows that the expression of

p-p38 MAPK protein in placental tissues in control group, mild pre-eclampsia group and severe pre-eclampsia group was 0.13 ± 0.05 , 0.59 ± 0.12 and 1.16 ± 0.18 respectively, showing an increasing trend [23]. In addition, immunohistochemistry shows that in severe group, syncytial nodules in placental villi are increased. Obliterative endarteritis of microvessels, obvious hyperplasia of vascular mid-layer fibers and myometrial tissues, hyperplasia of intimal fiber tissues, and occlusion of vascular lumen occur. The results of the above studies are consistent with ours, suggesting that MAPK signal transduction pathway may be involved in the pathogenesis of pre-eclampsia, and miR-144 and titin-Ab in peripheral blood and placenta tissues may mediate the pathological process of pre-eclampsia by regulating MAPK signal transduction pathway. This study was a preliminary study that only obtained the correlation between miR144, titin-Ab and MAPK signal transduction pathway. However, MAPK signal transduction pathway may involve the activity of multiple signal molecules, and the impact of upstream and downstream molecules on pre-eclampsia was not systematically discussed. Therefore, cell experiments and animal experiments will be conducted to further explore the specific mechanism of miR144, titin-Ab and MAPK signal transduction pathway.

In summary, miR144 expression is down-regulated and titin-A expression is up-regulated in pre-eclampsia patients. Both of them are closely related to the development of pre-eclampsia, and the mechanism may be related to the regulation of MAPK signal transduction pathway.

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Disclosure of conflict of interest

None.

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