

MiR-148a affects the expression of MMP-9 in trophoblast cells by targeting PTEN.

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Abstract

This study aimed to investigate the role of microRNA-148a in the development of placenta and in the pathogenesis of preeclampsia (PE), and to explore the underlying molecular mechanism. The expression level of miR-148a in the placenta of 20 preeclamptic patients was detected by qRT-PCR, and we found miR-148a was significantly decreased in the preeclamptic placentas. To investigate the role of miR-148a in trophoblast cells, miR-148a mimic/inhibitor was used. The results suggested that miR-148a over-expression enhanced JEG-3 cell proliferation, migration and invasion, while miR-148a down-regulation inhibited JEG-3 cell proliferation, migration and invasion. In addition, we revealed that miR-148a directly targets PTEN in JEG-3 cells. Moreover, miR-148a mimic could decrease PTEN expression, thereby enhancing the expression of matrix metalloproteinase-9 (MMP9). While miR-148a inhibitor increased PTEN expression, and decreased MMP-9 expression. Also we found that PTEN-siRNA could reverse the decrease of MMP9 induced by miR-148a inhibitor. Taken together, the results suggested that miR-148a affects MMP-9 expression in trophoblast cells by targeting PTEN, which influences the trophoblast cell invasion ability and participates in the pathogenesis of PE.

Keywords: Preeclampsia (PE), miR-148a, PTEN, Matrix metalloproteinase-9 (MMP-9).

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Introduction

Preeclampsia (PE) is a human pregnancy-specific multi-system involvement of the disease. The main clinical manifestation is in the pregnancy weeks after the emergence of high blood pressure and protein urine retention [1,2]. PE endothelium damage and vascular spasm caused by reduced organ perfusion can cause acute renal failure, cerebral hemorrhage, pulmonary edema, syndromes and other serious complications [3,4]. About 5-8% of all pregnancies were complicated by this pregnancy-related disease and this disease mixed both the morbidity and mortality of maternal and neonatal in the world [5]. Although studies of the etiology and prevention of PE have made some progress, the clinical treatment in addition to conventional antispasmodic, anti-hypertensive, termination of pregnancy has not yet the most effective prevention and treatment. At present, it is generally recognized that the placenta is "shallow bed" that is due to the infiltration of gestational trophoblastic cells caused by superficial uterine spiral small artery recast insufficient [6]. Studies have shown that the occurrence of severe PE was associated with the decrease of trophoblast invasion ability [7].

MicroRNAs (miRNAs), a kind of endogenous small non-coding RNAs (22 nucleotides in length), play important roles in the post-transcriptional regulation of various physiological activities *via* targeting mRNAs for cleavage or translational prevention [8]. MiRNAs can regulate one-third of all mammalian genes expression. A growing number of evidence revealed that miRNAs play an important role in regulating cell growth, proliferation, apoptosis, differentiation, migration and metabolism, etc. [9]. Evidence has indicated that compared with the normal placentas, a number of miRNAs are abnormally expressed in the preeclamptic placentas [10]. Some miRNAs have been found to play critical roles in the regulation of trophoblastic invasion *in vitro* [11]. MiR-148a has been well studied in tumor growth, metastasis, and invasion [12-14]. Studies have suggested that miR-148a inhibits the epithelial-to-mesenchymal transition of the non-small cell lung cancer cells [15,16]. To date, the role of miR-148a in trophoblast biology is still unclear.

In this study, we first detected the expression level of miR-148a in preeclamptic placentas, and the results suggested that miR-148a was decreased in the preeclamptic placentas. Then, the role of miR-148a in trophoblast proliferation,