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CORRESPONDENCE

Methylation-dependent circulating microRNA 510 in preeclampsia patients

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Preeclampsia (PE), or pregnancy-induced hypertension, is characterized by blood pressure elevation, proteinuria, edema, and organ dysfunction in pregnant women. PE is a complex syndrome that occurs at the twentieth week of gestation or later [1]. PE is associated with high mortality in both the developing and developed worlds. It is also referred to as a hyperdynamic disease associated with endothelial lesions [2]. It has been suggested that PE patients and their babies may develop severe complications, such as metabolic and cardiovascular problems, later in their adult lives [3]. A PE diagnosis depends on the emergence of nonspecific symptoms, and predictions of early onset PE remain challenging. Although novel strategies for controlling or preventing PE have been developed by researchers, no treatment or prediction option is recommended for this disease, and novel prognostic, diagnostic, and therapeutic targets for PE are necessary.

MicroRNAs (miRNAs) are considered to be biomarkers for several diseases, such as hypertension, cardiovascular diseases, and neurological disorders. miRNAs are readily available in blood, serum, saliva, and other body fluids and can be used as a prognostic and diagnostic markers for both communicable and non-communicable diseases [4, 5]. It has been suggested that many miRNAs are involved in the progression of PE [6]. Interestingly, miR-431 participates in the progression of PE by targeting zinc finger E-box-binding homeobox 1 [7], and miR-210 is directly involved in the pathogenesis of PE [8]. According to our previous study, miR-510 participates in hypertension progression through hypermethylation, and its expression is elevated in HTN patient samples [9]. In the present study, we examined miR-510 in PE patient samples and how it correlates with epigenetic regulation, which may be useful in elucidating the molecular mechanism of miR-510 in PE. Our results showed elevated expression of miR-510 in PE compared to normal samples, and methylation analysis of miR-510 corroborates these expression findings. Altogether, the parameters and analysis suggest that miR-510 may be involved in PE and that miR-510 can be a prognostic, diagnostic, and therapeutic target for PE.

miRNAs play very important roles in a wide range of cellular processes and are thought to be emerging biomarkers for communicable and non-communicable diseases [10]. Some miRNAs act as oncomiRs, and some of them act as tumor suppressors for many diseases. In general, many miRNAs are involved in HTN progression, and in our previous publication, we suggested that miR-510 acts as a positive regulator of HTN progression. Therefore, we evaluated this concept in PE blood samples and expected to see a role for miR-510 in PE. To test this hypothesis, we included 50 PE blood samples and 50 normotensive pregnancy blood samples. All samples were processed for expression and methylation analysis. While analyzing the biochemical parameters (data not presented), we found that there were no significant differences between the PE and control samples with respect to age or body mass index (BMI) ($P = 0.23$). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were significantly higher in PE than in the normotensive control. The concentrations of protein in urine protein, or proteinuria, were elevated in PE individuals compared to normotensive individuals ($P < 0.05$).

To determine the molecular mechanism underlying miR-510 actions in PE, we performed qPCR experiments for miR-510 expression in PE samples. Our results showed that

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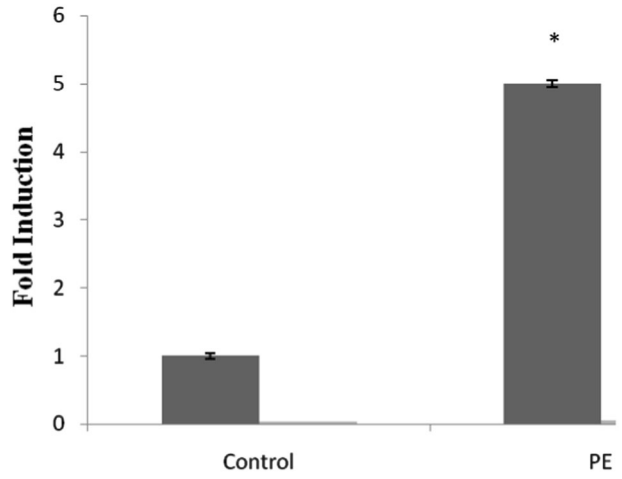

Fig. 1 Expression level of circulating miR-510 in blood samples from individuals with preeclampsia (PE) by quantitative real-time PCR. Unpaired *t*-tests were used to assess the data. $P < 0.05$ vs. control samples

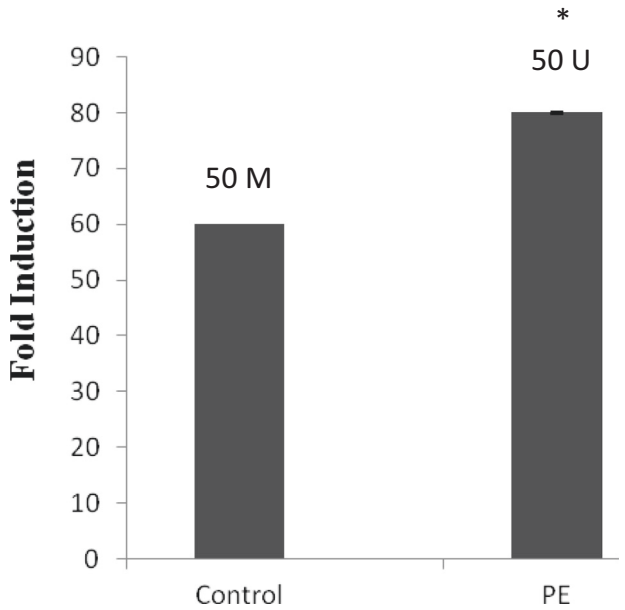

Fig. 2 The methylation frequency in the miR-510 promoter was compared between preeclampsia (PE) and control samples. The number of methylated (M) and unmethylated (U) samples is indicated above the bars. Unpaired *t*-tests were used to assess the data. $P < 0.05$ vs. control samples

the miR-510 level was elevated in PE blood samples compared to normotensive blood samples (Fig. 1). Furthermore, epigenetic regulation is a key component in gene expression analysis, so we analyzed the promoter region of miR-510 in bisulfite-treated PE DNA samples. Our results indicated that the miR-510 promoter region was unmethylated in PE but methylated in the control sample, suggesting that the miR-510 expression data corroborate the methylation analysis. In addition, the methylation frequency analysis of miR-510 showed that PE and normotensive samples had a higher degree of significance ($P < 0.05$) (Fig. 2). Overall, our data suggest that miR-510 expression is higher in PE samples and is correlated with promoter analysis, and future investigations with more samples are needed to confirm the role of miR-510 in PE.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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