

Figure 1. Schematic diagram of the study design.

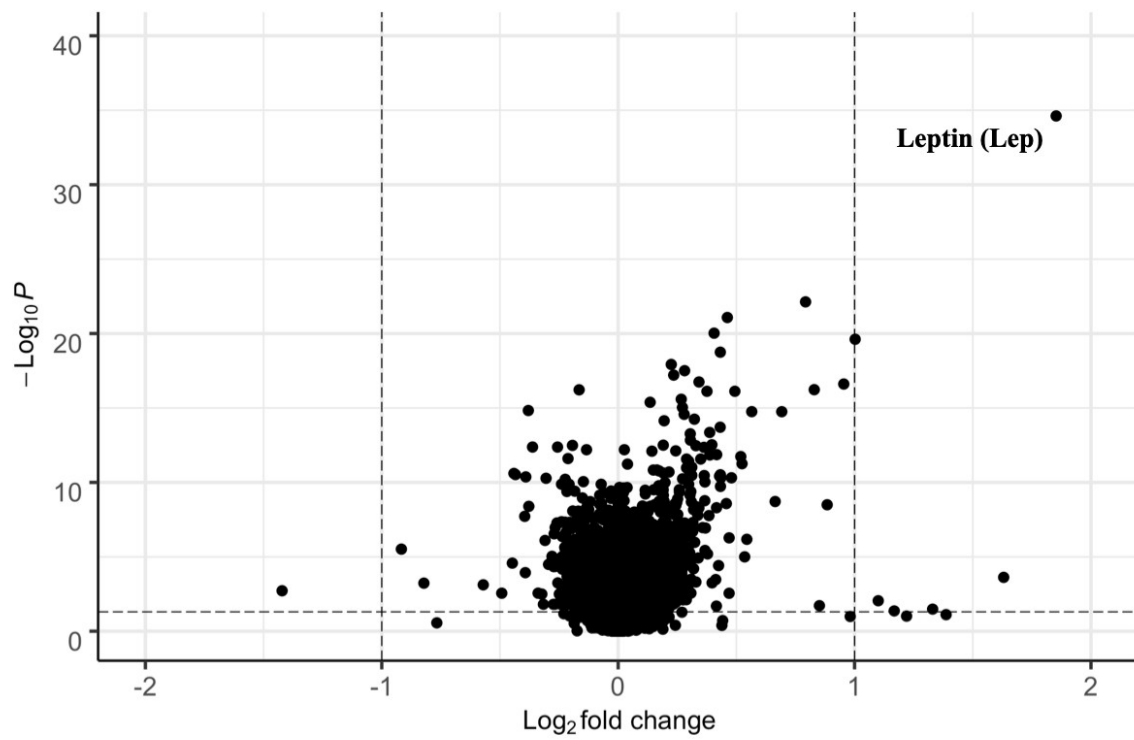


Figure 2. Meta-analysis identified differentially expressed genes in placentas from preeclamptic (PE) women. Volcano plot, fold changes (FC) on the X-axis and $-\log(P)$ on the Y-axis, was used to evaluate the performance of each placental gene that differentiates PE from non-preeclamptic (non-PE) women.

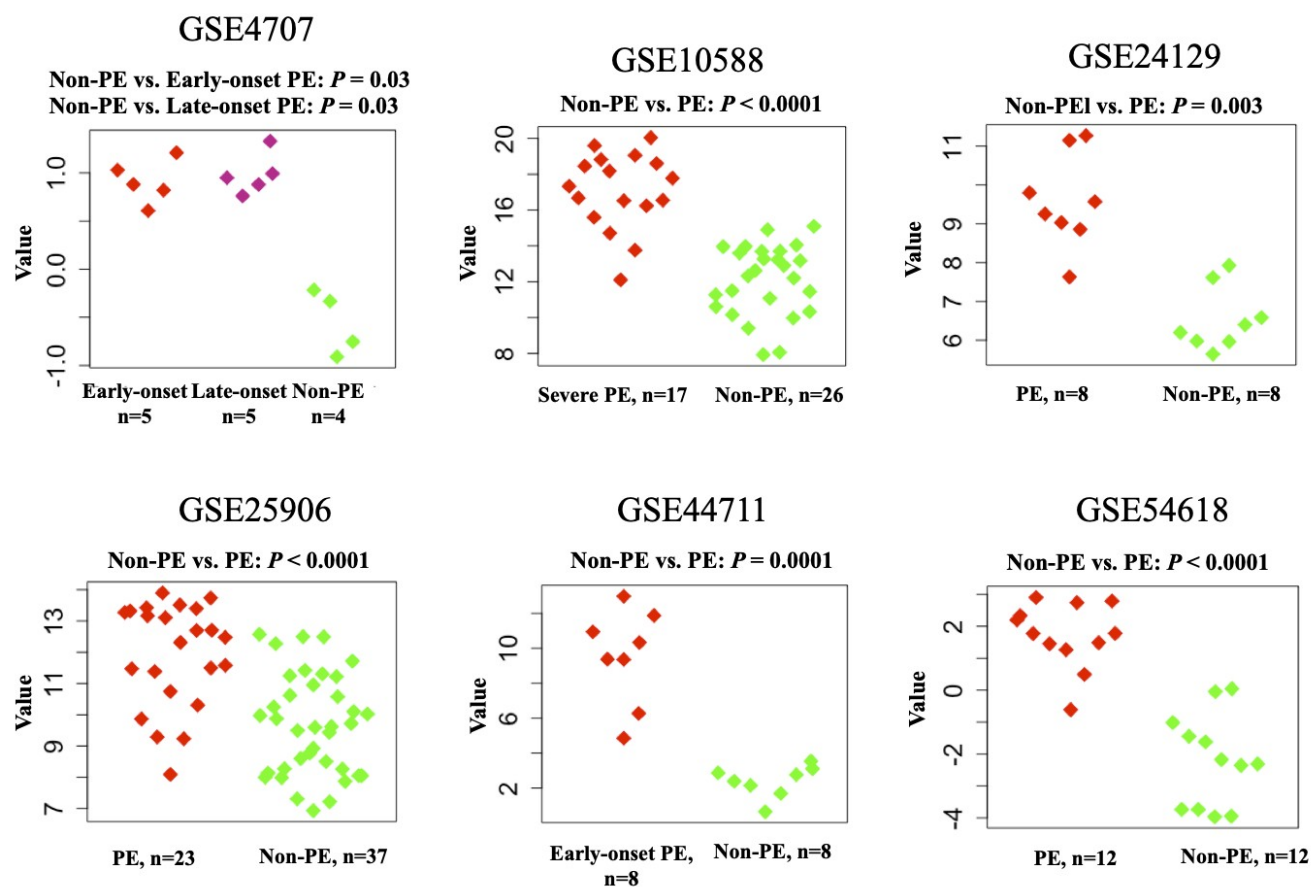


Figure 3. Transcriptional quantification of leptin (Lep) genes: a comparison between non-preeclamptic (PE) and preeclamptic (PE) placental expressions at delivery.

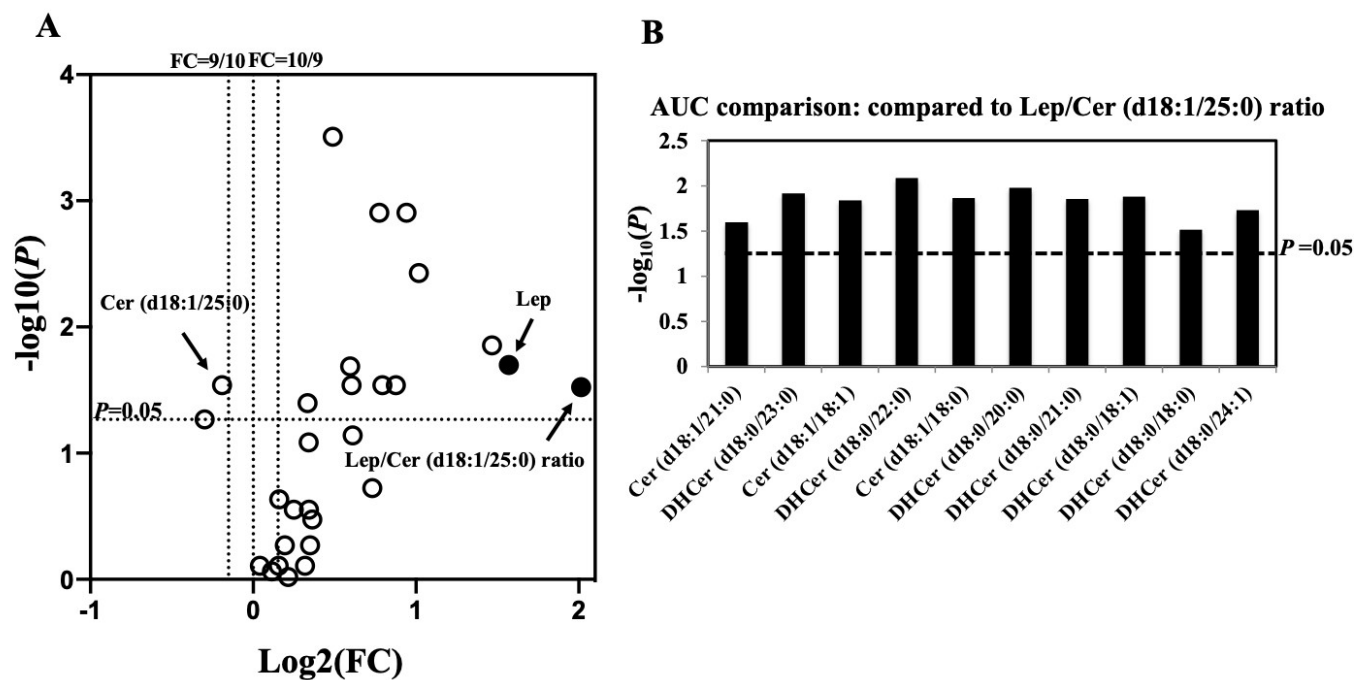


Figure 4. Comprehensive mass spectrometric analyses of 26 Cers/DHCers for preeclampsia (PE) diagnosis in the testing cohort. A: Fold change of each analyte between non-preeclamptic (non-PE) and preeclamptic (PE) women. A total of 11 Cers had $P < 0.05$. B: Area under curve (AUC) comparison between Lep/Cer(d18:1/25:0) ratio and other Lep-Cer combinations using each of the significant Cers in conjunction with Lep. DeLong test P were calculated (the y-axis). Lep: leptin. Cer: ceramide. DHCer: dihydroceramide.

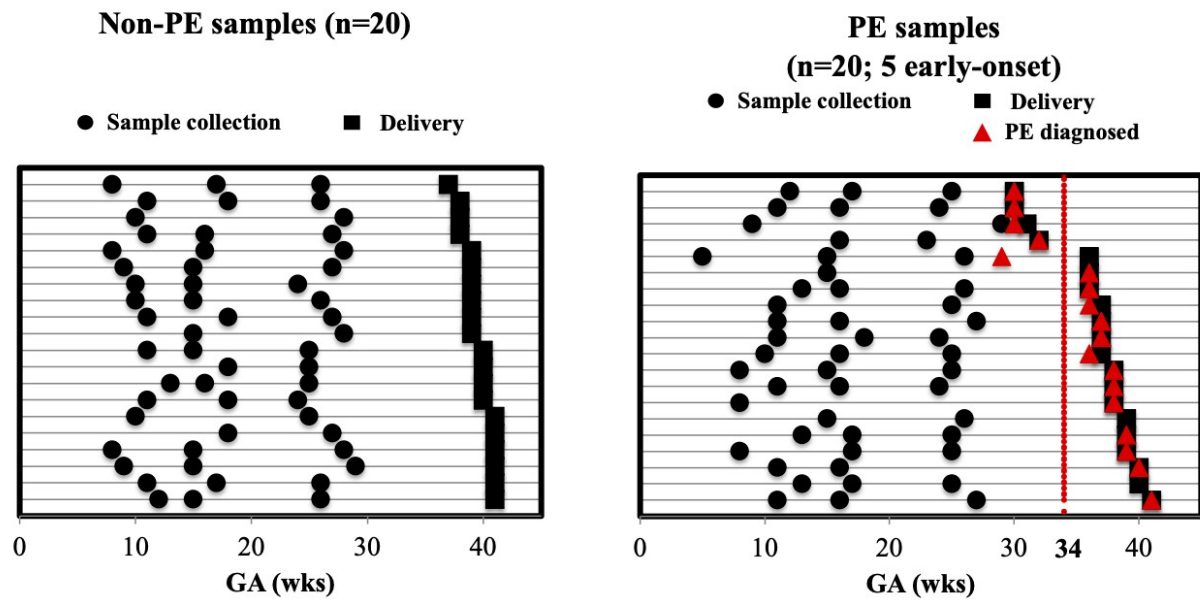


Figure 5. Sample collection timelines from the validation cohort: Serial blood sampling from each non-preeclamptic (PE) and preeclamptic (PE) woman at different gestational ages (GAs). Times of sample collection, delivery, and confirmatory PE diagnosis of each woman (denoted by each row) are represented by black circles, black squares, and red-filled triangles, respectively.

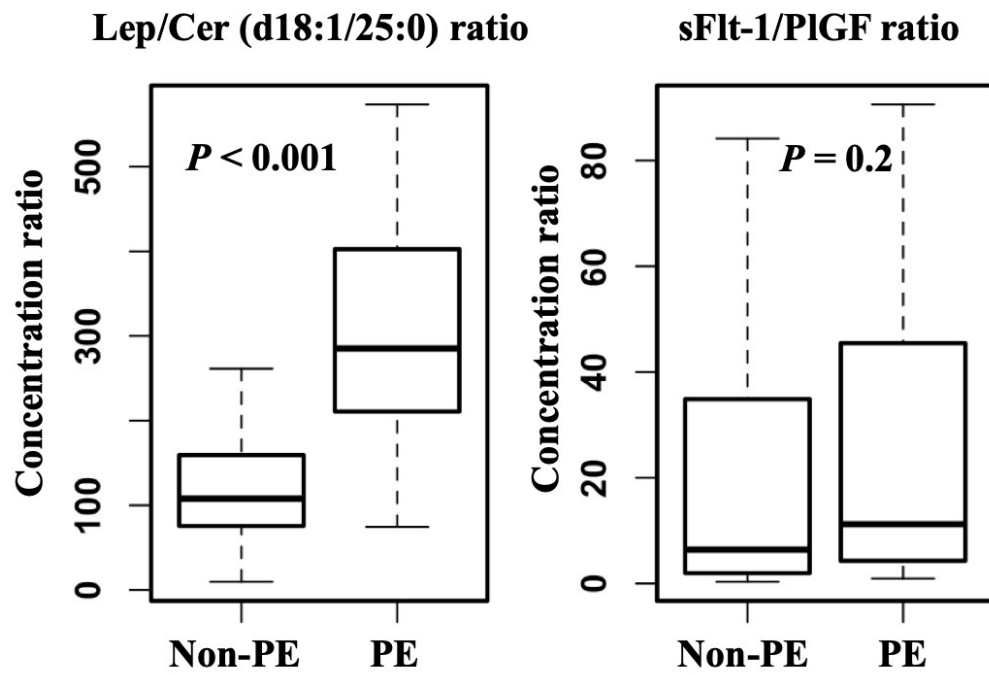


Figure 6. Comparisons of maternal serum levels between non-preeclamptic (PE) and preeclamptic (PE) pregnancies in the validation cohort. Left: Lep/Cer (d18:1/25:0) ratio; Right: sFLT-1/PlGF ratio. Lep: leptin. Cer: ceramide.

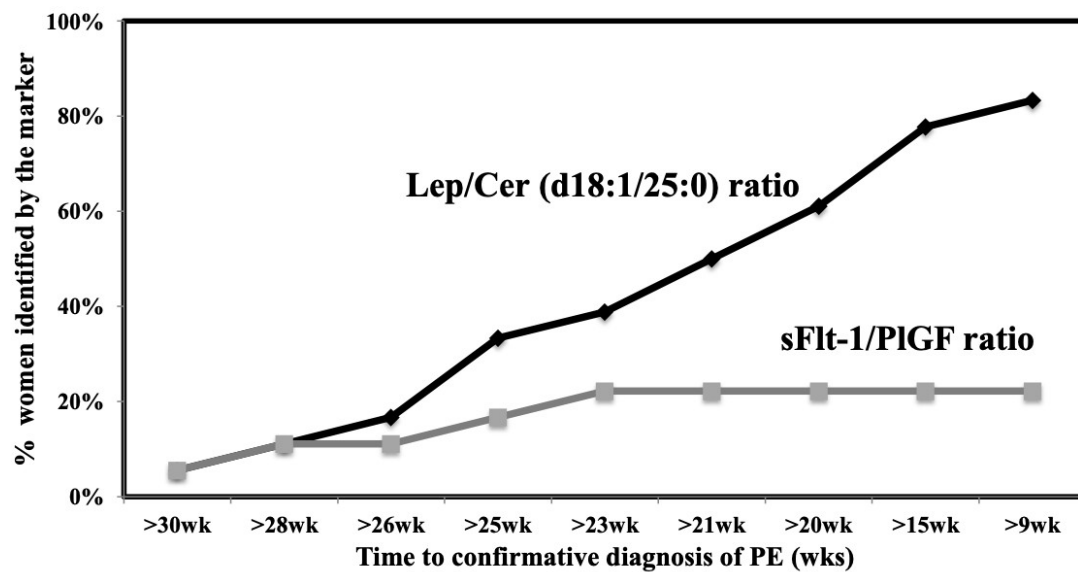


Figure 7. Comparative analysis between the ratios of Lep/Cer (d18:1/25:0) and sFLT-1/PlGF in predicting impending preeclampsia (PE). X-axis: the duration of time (wks) from the sampling to PE confirmatory diagnosis. Y-axis: the percentage of the PE women who were identified as high-risk within the specified duration before a confirmatory diagnosis. Lep: leptin. Cer: ceramide. wks: weeks.

Lep/Cer (d18:1/25:0) ratio		
	PE	Non-PE
Classified as PE	17	2
Classified as Non-PE	3	18

Predictive performance at 5-25 weeks

Marker	Sample GA (wks)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Lep/Cer (d18:1/25:0) ratio	5-25	0.85 (0.62-0.97)	0.90 (0.68-0.99)	0.89 (0.69-0.97)	0.86 (0.68-0.95)
sFLT-1/PlGF ratio	5-25	0.40 (0.19 -0.64)	0.45 (0.23-0.68)	0.42 (0.27-0.59)	0.43 (0.29-0.58)

Figure 8. Individual-level performance of the Lep/Cer (d18:1/25:0) ratio in predicting impending preeclampsia (PE). A: 2x2 table. B: Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Lep: leptin. CI: confidence interval. GA: gestational age. Cer: ceramide.