Transposable element signature in plasma as an early predictor of preeclampsia and pregnancy complications

Applications

Early Risk Stratification: Enables the identification of mothers at high risk for preeclampsia weeks before traditional diagnostic methods.

Precision Medicine: Supports personalised prenatal care plans by providing actionable insights into maternal and fetal health at an earlier stage.

Benefits

Improved Outcomes: Earlier detection allows for timely interventions, potentially reducing severe complications for both mother and baby.

Non-Invasive & Convenient: Utilises maternal blood samples, ensuring a safe and accessible testing process during pregnancy whilst compatible with existing prenatal care workflows.

Deregulated transposable elements (TEs) are associated with increased inflammation in maternal placentas. A machine learning approach was utilised to produce a TE signature from cell-free RNA (cfRNA) from maternal plasma. This represents a novel and robust way of predicting PE at an early gestation period, before the onset of clinical symptoms.

Background

Preeclampsia (PE) is a severe pregnancy complication affecting 5–10% of pregnancies globally, contributing to 14% of maternal deaths and significant preterm births. PE stems from placental inflammation and abnormal artery development, leading to foetal growth restriction, placental abruption, seizures, organ damage, and long-term cardiovascular risks. Effective management hinges on early detection and timely intervention, including corticosteroids to enhance foetal lung maturity, antihypertensives to control blood pressure, and anticonvulsants to prevent seizures, balancing maternal health with optimal timing for delivery. TEs are mobile DNA sequences that are abundant in the human genome, and they can be used in diagnosis by detecting their abnormal activity or expression levels.

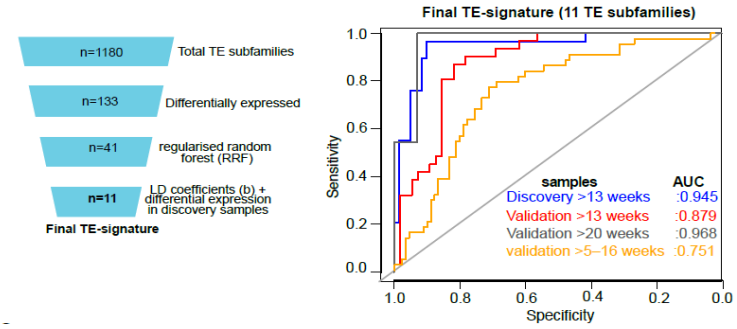
The problem

- PE is typically diagnosed in the second half of pregnancy, often after the 20th week
- Current diagnostic methods often identify the condition only after symptoms appear
- This poses significant health risks to both mother and baby

Invention: Benefits and application

TE-focused analysis of maternal cell-free RNA (cfRNA) data revealed differential levels of TE transcripts in PE compared to healthy controls. A machine learning approach was applied to maternal cfRNAseq datasets, and a TE transcript signature was identified that could predict PE early in pregnancy. Using transposable elements-based signatures to predict PE showed much higher accuracy and positive and negative predictive values than recent PE predictions based on maternal features, mRNA and noncoding RNAs and cfDNA-based prediction.

Figure 1. Schematics (left) showing the training models used to identify the final TE signature that predicts PE. Area under the curve (AUC) with 95% confidence interval (right) for >13, >20 and 5–16 week gestation age (GA) showing sensitivity (y-axis) and specificity (x-axis) for PE prediction model using the final list of 11 TEs for discovery (blue) and validation (red, grey and orange) samples.



This novel approach utilising TE signatures in plasma as an early prediction (between 5-16 weeks) from a single test can fit directly into the current standard of care practice. This method can diagnose PE early and determine the risk of a subject developing severe symptoms, significantly improving the current late-stage and ambiguous diagnosis process. The discovered TE signature in cell-free RNA is an exciting approach for early diagnosis before symptoms appear and can improve obstetric and neonatal outcomes by enabling targeted surveillance and early interventional obstetric care.

Patents

A UK patent application has been filed (Application no. 2409378.3).

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Key publication

Patel *et al.* Early Prediction of Preeclampsia Based on Transposable Elements signature in cell-free RNA. https://www.biorxiv.org/content/10.1101/2024.11.08.622691v1