Exome sequencing in pooled DNA samples to identify maternal pre-eclampsia risk variants

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SUPPLEMENTARY INFORMATION

Clinical definitions

Pre-eclampsia was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg with new-onset proteinuria (≥0.3g/24h) after 20 weeks of gestation[1]. Pre-eclampsia was defined early-onset when diagnosed before 34+0 weeks of gestation, and severe in the presence of systolic blood pressure ≥160 mmHg, diastolic blood pressure ≥110 mmHg, proteinuria ≥5 g/24h or clinically severe symptoms of preeclampsia, including clonus or respiratory distress. Birth weights below −2.0 SD units (birth weight relative to sex and length of gestation) according to Finnish standards[2] were classified as SGA. Placental insufficiency was defined as uterine artery resistance index or pulsatility index >+2 SD units. In the FINNPEC cohort, the diagnoses were determined based on medical records and verified independently by a research nurse and a study physician.

Sample collection and DNA extraction

A venous blood sample of 36 ml was drawn from each study participant, and genomic DNA was extracted from whole blood using the NucleoSpin Blood XL DNA extraction kit (Macherey-Nagel GmbH & Co.) or Chemagic Magnetic Separation Module I –machine (Chemagen). The extracted DNA was stored at -20°C.

Exome sequencing

Exome sequencing was performed at the Science for Life Laboratory, Stockholm, Sweden. DNA libraries were prepared from 3 µg of input material sheared to 300 bp using a Covaris S2 instrument (Covaris, MA, USA) using SureSelectXT kits (Agilent, CA, USA) and an Agilent NGS workstation according to the manufacturer's instructions (SureSelectXT Automated Target Enrichment for Illumina Paired-End Multiplexed Sequencing, version A). The SureSelectXT Human All Exon 50 Mb capture kit was used for the targeted enrichment. The clustering was performed on a cBot

cluster generation system using a HiSeq paired-end read cluster generation kit according to the manufacturer's instructions. The samples were sequenced on an Illumina HiSeq 2000 as paired-end reads to 100 bp following the manufacturer's instructions. Base conversion was performed using Illumina's OLB v1.9.

Supplementary Table S1. Phenotypes per pool in the exome sequencing

Pool	Phenotype
PE 1	Early-onset, severe pre-eclampsia
PE 2	Early-onset, severe pre-eclampsia
PE 3	Severe pre-eclampsia, proteinuria >6g/24h
PE 4	Severe pre-eclampsia, proteinuria >6g/24h
PE 5	Severe pre-eclampsia, previous miscarriage(s)
PE 6	Severe pre-eclampsia, proteinuria >3g/24h
PE 7	Severe pre-eclampsia
PE 8	Severe pre-eclampsia
PE 9	Severe, recurrent pre-eclampsia
PE 10	Familial pre-eclampsia

References

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