FETAL GENOME INCREASES THE RISK OF PRE-ECLAMPSIA IN PREGNANCY, RESULTS OF THE INTERPREGGEN STUDY OF EC 7FP "GENETIC STUDY OF PRE-ECLAMPSIA IN CENTRAL ASIAN AND EUROPEAN POPULATIONS"

G. Svyatova*, G. Berezina, D. Salimbayeva on behalf of the InterPreg Gen Consortium
The Scientific Centre of obstetrics, gynecology and perinatology (Almaty, Kazakhstan)
respmgk@mail.ru

Keywords: GWAS study, pre-eclampsia, fetal genome, InterPregGen, deCODE, GOPEC, ALSPAC.

Introduction: Pre-eclampsia (PE) affects up to 5-10% of pregnancies and has serious complications: fits, stroke, liver and blood problems and can leads to the death of mother and baby. The problems in identifying genetic aspects of PE are the limited statistical power due to the small study size and ethnic heterogeneity. To solve this problem, InterPregGen study was established, which involved teams from the UK, Iceland, Finland, Norway, Kazakhstan and Uzbekistan. The aim of study was to investigate the genetic basis of PE in European and Central Asian populations.

Methods: GWAS meta-analysis tested 7,476,169 sequence variants in 2,658 offspring of preeclamptic pregnancies and 308,292 controls of European descent from Iceland (deCODE cohort) and the UK (GOPEC and ALSPAC cohorts). DNA samples were analysed by Illumina HumanOmni 2.5-8 v1.1 BeadChips (2,400,000 snps) at the Sanger Institute (UK) and deCODE Genetics (Iceland). We carried out QC using PLINK. Cases and controls were imputed together with IMPUTE2 (impute_v2.3.0) and SHAPEIT23 using the pre-phasing workflow against the 1000 Genomes Phase 1 reference panel.

Results: Our results of the European descent from Iceland deCODE and the UK GOPEC and ALSPAC cohorts were published in Nature Genetics, 49, 1255-1260, (2017). The first genome-wide significant susceptibility locus (rs4769613; P = 5.4x10-11) was discovered in 4380 cases and 310,238 controls. The locus is near the gene encoding Fms-like tyrosine kinase 1 (FLT1), providing biological support since an isoform (sFlt-1) of placental origin is implicated in the pathology of preeclampsia. The strongest association is in pregnancies where preeclampsia developed in the late gestation and offspring birth weights exceeded the 10th centile. An additional nearby variant, rs12050029, associates with preeclampsia independent of rs4769613. DNA from a further 4,220 babies from pre-eclamptic pregnancies in Kazakhstan and Uzbekistan is currently being analysed in an extended study to reveal the same changes near sFlt-1.

Conclusion: InterPregGen study discovered sequence variants in the fetal genome that increases the risk of PE. The new insights from this study could form the basis for more effective prevention and treatment of PE and improve the outcome of a pregnancy for a mother and a child.

Research leading to these results was conducted as part of the InterPregGen study, which received funding from the European Union Seventh Framework Programme under grant agreement no. 282540.