Mother and maternal grandmother were heterozygous for the F8 variant. It is possible that the two additional variants were either de novo mutations or inherited from the father.

Conclusions: The clinical phenotype noted may represent a compound heterozygous state associated with atypical lyonization and characterised by a novel mutation in the F8 gene accompanied by two additional mutations also associated with low factor VIII levels on the alternate allele.

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CRITICAL ILLNESS IN PRETERM INFANTS IS ASSOCIATED WITH DIFFERENTIAL EXPRESSION OF STRESS-ACTIVATED PROTEIN KINASE SIGNALLING AND DRUG METABOLIZING CYP450 GENES

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Background: Preterm infants often suffer from critical conditions involving stress that requires advanced treatment including increased oxygen supply. We aimed to examine the influence of critical illness at the molecular level represented by gene expressions.

Methods: 20 premature infants in a level III NICU at Oslo University Hospital, Rikshospitalet, were studied. Inclusion criteria was critical illness defined by conditions requiring surgical procedures and severe drop in oxygen saturation, SaO_2 (< 60%), following more than 80% oxygen supply. For peripheral blood preparation we used RiboPure™-Blood, GLOBINclear™-Human protocol, and NugeneOvation RNA-Amplification system. Gene expressions were assessed using GeneChipHumanGenome-U133 Plus2.0-arrays from Affymetrix. Ethical approval was granted by the Regional Committees for Medical and Health Research Ethics in Norway.

Results: A total of 107 peripheral blood samples were assessed. Thirteen samples at the time of critical illness from 7 infants showed significant differential expression for 6000 genes. Further investigation identified higher expression levels in a group of genes related to oxidative stress and stress activated protein kinase (SAPK) signalling pathway. We also found significant differential expression of CYP450 genes involved in drug metabolism, including CYP1A2, CYP2D6, and CYP3A4. Interestingly, CYP1A2 was standing out with more than a 6 fold increased level.

Conclusion: This is the first study on simultaneously expressed genes in preterm babies. Our results highlight the significance of critical illness, pathophysiological mechanisms following stress and their effect on gene expression levels. Thus, molecular biomarkers are important to understand the impact of stress on gene expression, including CYP450 genes, in preterm infants.

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EXPRESSION OF CYTOCHROME P450 METABOLIZING ENZYMES IN PRETERM INFANTS DEPENDS ON AGE, BUT NOT GENDER

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Background: The neonatal period is a critical time for premature born infants. Variability in drug response may be due to differences in expression of the metabolizing CYP450 genes. Comprehensive studies of CYP450 gene expression at clinical relevant time points are lacking. We aimed to compare the gene expression levels of all CYP450 genes simultaneously in relation to gestational age (GA) and gender.

Materials: Peripheral blood at subsequent time points was withdrawn from premature born infants between GA 25.2-37.0, in a level III NICU at Oslo University Hospital, Rikshospitalet. We used the RiboPure™-Blood-, GLOBINclear™-Human protocol, NugeneOvation RNA Amplification system, and GeneChip HumanGenome U133 Plus 2.0 arrays from Affymetrix to analyse global gene