

Validation of Preeclampsia on the Lipidyzer™ Platform

Accurate Lipid Analysis with less Quantitative Bias

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INTRODUCTION

Preeclampsia is the leading cause of maternal perinatal morbidity and mortality. This is manifested by a shallow invasion of cytotrophoblast (CTB) cells into mother's uterus. Failed vascular transformation of the spiral arteries is the hallmark of the placental defects in preeclampsia. The response: high blood pressure & proteinuria. There are several studies reporting lipid changes in preeclampsia so a pilot study was used to validate these known changes and further explore lipid biology in normal CTB development. Also, the pilot study will determine whether the Lipidyzer™ Platform could be used for a larger scale study to find early serum/plasma lipid biomarkers for preeclampsia risk.

METHODS

In this pilot study, plasma samples from women in preterm labor (n=12, study controls) and women with preeclampsia (n = 12) were evaluated, gestational age (GA)-matched at 25-37 weeks. The Lipidyzer™ Platform chemical standards kits were used for simplified sample extraction and preparation and more accurate lipid quantitation. The Lipidyzer™ Platform (SCIEX) was used for targeted profiling of over a thousand lipid species from 13 different lipid classes, providing extensive lipid coverage. Two methods were used covering thirteen lipid classes using a flow injection analysis (FIA); one injection with SelexION® Technology ON and another with the SelexION Technology turned OFF. The lipid molecular species were measured using MRM and both positive and negative polarities were used for analysis.

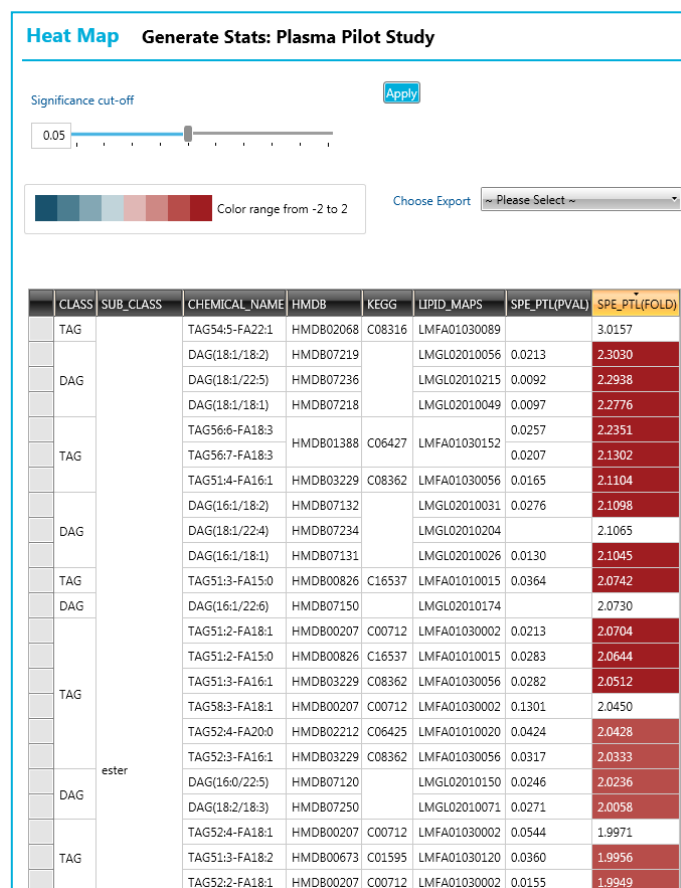


Figure 2. Heat Map Generated using the Lipidomics Workflow Manager. Here, the plasma samples were classed according to their phenotype, SPE for the severe preeclamptic women and PTL for the women at preterm labor (acting as the controls). All species in red were being upregulated in the SPE group relative to the PTL group.

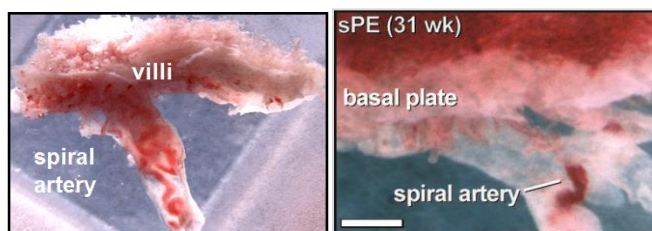


Figure 1. Preeclampsia: A Two-Step Disease. (Left) A Normal, healthy spiral artery and placenta at 16 weeks. (Right) Poor formation of the spiral artery at 31 wks.

RESULTS

We validated the known triglycerides (TAGs) and diglycerides (DAGs) changes already reported in the literature which were being upregulated in the severe preeclampsia (SPE) group (Figure 2). This positive result encouraged us to plan a follow up study of 300 samples of women who did (33) or did not (67) develop preeclampsia collected at many time points across their pregnancy and at delivery.

CONCLUSIONS

A plasma data set with biological variation was used to validate findings already known in preeclampsia on the Lipidyzer™ Platform. Both triglycerides and diglycerides were up-regulated in SPE, consistent with previous reported findings (Figure 2 and 3). Novel findings were also made in the cholesteryl esters which will be further validated in a larger study. The platform enables facile lipid analysis with less quantitative bias.

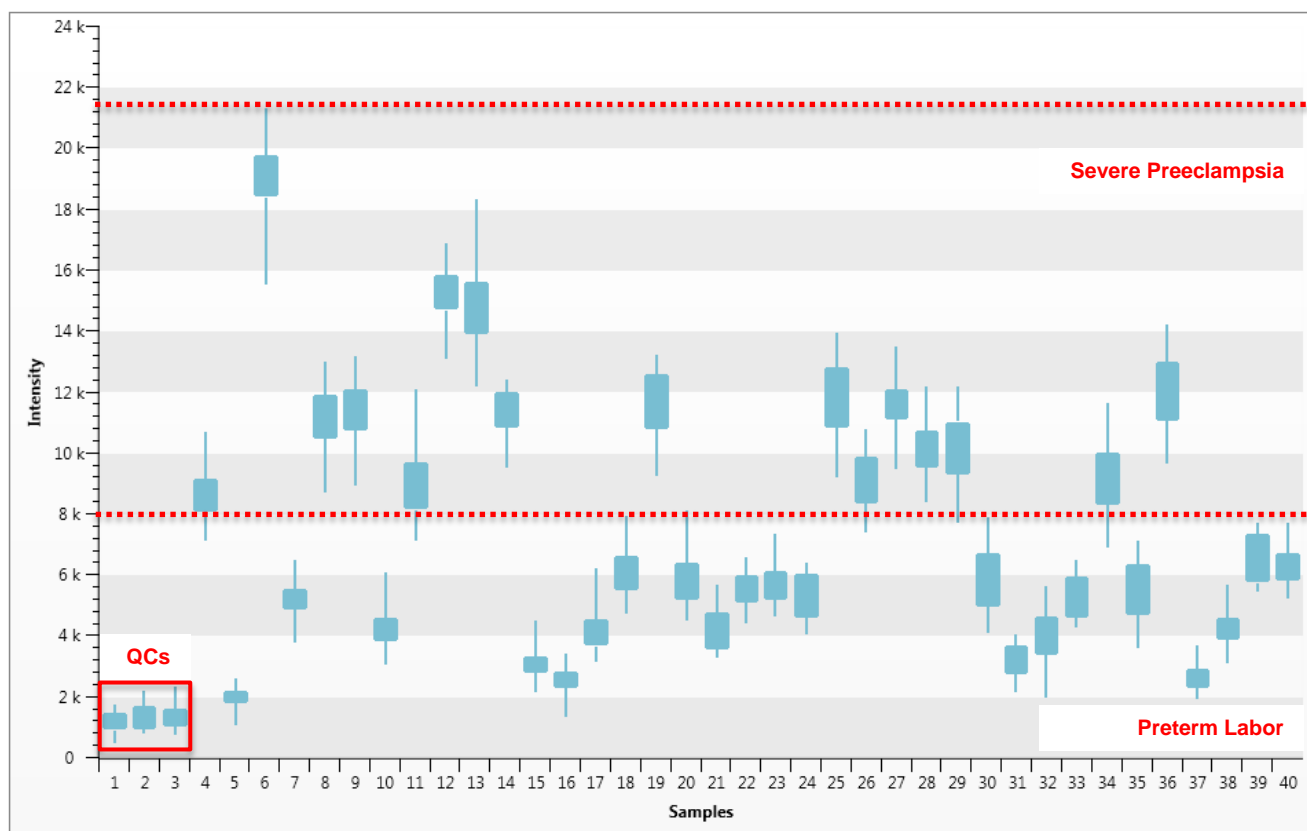


Figure 3. Track Changes in Specific Lipids Across Samples. Data is automatically processing in Lipidomics Workflow Manager Software and results can be easily visualized. A box and whisker plot is viewed for the DAG(18:1/18:2) species, highlighting the changes in intensity of this lipid across all samples acquired across a batch. A user can very quickly see if a sample has an abnormally high/low lipid species concentration. The QCs can be visualized this way; here the QCs are the first three samples 1-3. There is differentiation when you look across the samples, the SPE group display higher concentrations than the PTL.

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