Severe COVID-19 in pregnancy has a distinct metabolomic profile which defines clinical outcomes

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Background

- Pregnancy is associated with increased risk for more severe COVID-19
- Alterations in protein and metabolite expression may underly the increased risk of more severe COVID-19 in pregnancy

Objective

- Investigate the pathophysiology behind various clinical trajectories in pregnant patients diagnosed with COVID-19 using multi-omics profiling

Study Design

Prospective cohort study of 30 pregnant patients with varying COVID-19 severity

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Maternal serum analyzed via LC-MS-based mutiomics analysis (profiling of proteins, lipids, electrolytes, and metabolites)

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Assessed how COVID-19 severity related to analyte levels while adjusting for participant age, race, run order, total protein signal, and total compound signal via multivariate regressions, PCA analysis, and DAVID Functional enrichment analyses

Results

- 30 participants: 7 asymptomatic, 12 mild/moderate, 6 severe, 5 controls
- 99 proteins were significantly associated with severe/critical COVID, with 42 increased and 57 decreased in severe/critical infections (FDR < 0.05,).
- 103 lipids were associated with severe COVID, with 61 increased and 103 decreased (FDR < 0.05)
- Functional terms: Complement Activation, Regulation of Immune Response, and Immunoglobulin V-set (FDR < 0.05)

Conclusion

- Similar to general population, severe COVID-19 in pregnancy demonstrates altered complement activation and dysregulation of plasma lipids.

Severe COVID-19 in pregnancy is associated with specific proteomic signatures and altered metabolites, including **greater inflammation, complement activation, and dysregulation of plasma lipids**

Protein/Metabolite	Beta	FDR
Inter-alpha-trypsin inhibitor heavy chain H2	-0.17	1.13×10^{-4}
Plasmenyl-PC	-0.89	1.49×10^{-4}
Transthyretin	-0.18	2.16×10^{-4}
LysoPC 22:0	-0.65	2.22×10^{-4}
Putative uncharacterized protein C6orf99	0.32	3.68×10^{-4}
Plasmanyl-PC	-0.59	5.67×10^{-4}
Leucyl-cystinyl aminopeptidase	-0.67	5.67×10^{-4}
Serum amyloid A-1 protein	0.79	6.58×10^{-4}
BPI fold-containing family B member 1	0.44	6.58×10^{-4}
Alpha-1-antichymotrypsin	0.21	6.58×10^{-4}
C3/C5 convertase	0.15	6.58×10^{-4}
Peptidase inhibitor 16	-0.33	6.58×10^{-4}
Inter-alpha-trypsin inhibitor heavy chain H1	-0.11	9.01×10^{-4}
Intercellular adhesion molecule 1	0.31	9.90×10^{-4}
Gelsolin	-0.11	1.16×10^{-3}
Protein HEG homolog 1 (fragment)	-0.18	1.16×10^{-3}
Lipopolysaccharide-binding protein	0.32	1.18×10^{-3}
Coagulation factor X1	-0.27	1.19×10^{-3}
C-reactive protein	0.96	1.23×10^{-3}

Table 1: Top genes coding for various inflammatory mediators significantly upregulated or downregulated in pregnant patients with severe COVID-19

Questions?
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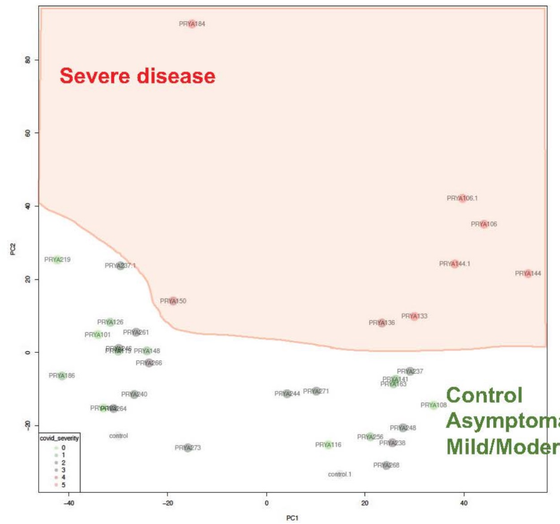

Figure 1: Principal components analysis showing clear separation of severe COVID-19 cases vs. all others

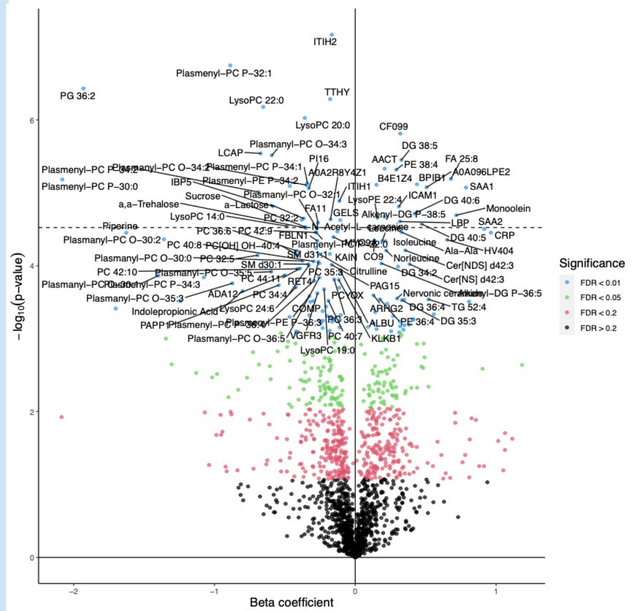

Figure 2: Volcano plot illustrating proteins altered in severe SARS-CoV-2 positive pregnancies