PLASMA LIPIDS AND AMINOACIDS LINKED TO LOW SARS-COV-2 SUSCEPTIBILITY

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Through the analysis of plasma samples by LC & GC-MS, we aim to delineate new mechanisms of SARS-CoV-2 susceptibility and progression to severe disease that may help find better therapies for COVID-19.

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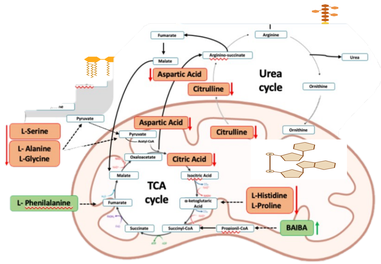
OBJECTIVE

Exploration of metabolomic and lipidomic hallmarks of COVID-19 progression in plasma samples from heavily exposed unvaccinated healthcare workers

BACKGROUND

- Host factors have been shown drive SARS-CoV-2 susceptibility and COVID-19 disease severity.
- Metabolic profiles related to SARS-Cov-2 infection have been described. However, a combination of metabolomic techniques provides a broader picture.
- The specific effects of host factors in abnormal immune response to SARS-Cov-2 infection and the effect of comorbidities in the disease are still being studied.

Why some unvaccinated individuals with repeated high-risk exposures to SARS-CoV-2 did not show evidence of COVID-19?



Albóniga OE et al. Metabolic Snapshot of Plasma Samples Reveals New Pathways Implicated in SARS-CoV-2 Pathogenesis. J. of Proteome Research. 2021

STUDY DESIGN

Cohort of unvaccinated people from April 2020

Susceptible: asymptomatic healthcare workers with a positive IgG for SARS-CoV-2 or previous COVID-19 confirmed by PCR

Non-susceptible: healthy healthcare workers who reported at least three high-risk exposures to SARS-CoV-2 without having experienced symptoms suggestive of SARS-CoV-2 infection and were negative by PCR an Ab testing

COVID-19+: hospitalized patients with confirmed PCR within the first 7 days from the onset symptomps.

- **Mild** disease
- **Moderate** disease
- **Severe** disease

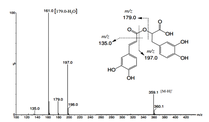
COVID-19-:asymptomatic with a negative PCR

METHODOLOGY

Liquid Chromatography–Mass Spectrometry (LC-MS) and Gas Chromatography–Mass Spectrometry (GC-MS)



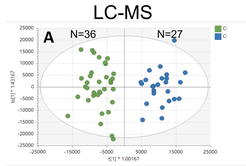




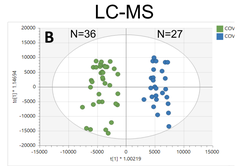
Schematic representation of typical metabolomic results

ANALYSIS

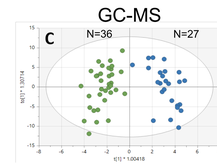
PCA analysis of LC-MS and GC-MS data allowed identifying lipids differentially abundant in the COVID-19+ group compared with the COVID-19- group.



Positive ionization mode

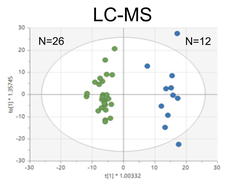


Negative ionization mode

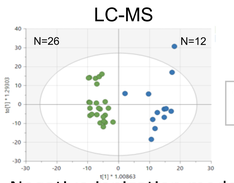




PCA analysis of LC-MS data allowed identifying lipids differentially abundant in the non-susceptible group compared with the susceptible group.



Positive ionization mode

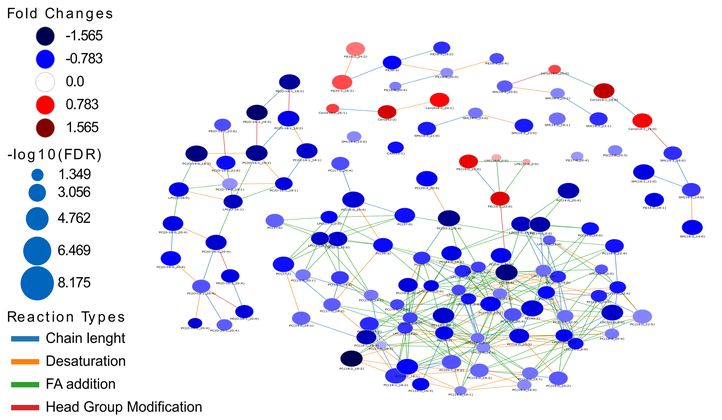


Negative ionization mode



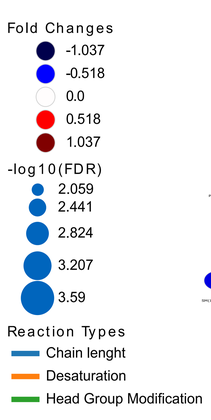
RESULTS

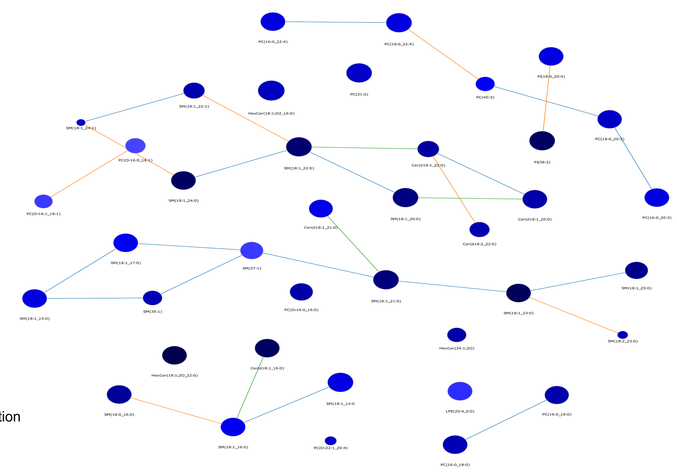
LINEX lipid network and heatmap from LC-MS show differentially expressed lipid classes when comparing *COVID-19+ vs COVID-19-* groups.



Main lipid classes: Ceramides (Cer); Phosphatidylinositols (PIs, and LPIs); phosphatidyl-Ethanolamines (PEs, PE-Os, LPEs, and LPE-Os).
Main connections: chain length, FA addition and desaturation.
Function: cell membrane components that mediate numerous **cell-signaling events** (some have been previously described)

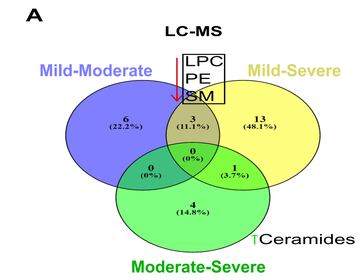
LINEX lipid network and heatmap from LC-MS show differentially expressed lipid classes when comparing *Susceptible vs Non-susceptible* groups.

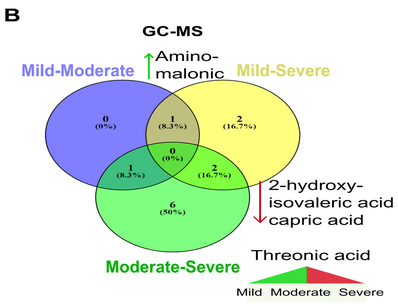




Main lipid classes: Ceramides (Cer); Phosphatidylinositols (PIs, and LPIs); phosphatidyl-Ethanolamines (PEs, PE-Os, LPEs, and LPE-Os).
Main connections: chain length, FA addition and desaturation.
Function: decreased blood lipids might be related with an increase of **lipid rafts** due to viral infection. This has been associated before to COVID-19 **comorbidities** (obesity and cardiovascular - related conditions)

There are differentially abundant metabolites depending on disease progression status





CONCLUSIONS

--Non-susceptible individuals showed a unique lipidomic pattern characterized by the upregulation of most lipids, especially ceramides and sphingomyelin, representing candidate predictors of susceptibility to SARS-CoV-2 infection.

--Since lipid composition can affect the cell membrane structure and virus infectivity, our study encourages further research on the role of ceramides and sphingomyelin in the frontline against SARS-CoV-2 infection.

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