Lipidomics profiling of plasma samples from patients with SARS-CoV-2 by timsTOF Pro 2 PASEF

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Introduction

The coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread throughout the world. One of the key pathways regulating the immune response to COVID-19 infection is the release of regulatory lipid mediator which leads the dysregulation of lipid metabolism and causes the alteration of blood cholesterol and lipoprotein homeostasis, all suggested lipids can be involved in SARS-CoV-2 pathogenesis [1-3]. In this work, a non-targeted LC-timsTOF Pro 2 PASEF lipidomics workflow was performed to profile lipids and their changes within plasma samples.

Method

About 110 plasma samples were collected from 15 female and male patients up to 10 days of admission with laboratory-confirmed SARS-CoV-2 infection at UC Davis Medical Center. Metabolomics samples were prepared by aliquot 50 µL plasma samples to 100µL methanol, vortexed and centrifuged at 10,000 rpm for about 10 minutes, the supernatant was then transfer into sample insert vials for injection; Lipidomics samples were prepared by aliquot 30 µL plasma into 225 µL cold methanol, 750 µL MTBE, 190 µL water, vortexed and shaken for 60 min at room temperature, centrifuged at 10,000 rpm for 10 min, the non-polar layer or supernatant was collected and evaporated to dry in a SpeedVac, reconstituted with 50 µL of methanol to dichloromethane (9:1 v/v) and transferred into sample insert vial for injection. Sample analysis was performed by Elute UHPLC timsTOF Pro 2 (Bruker) with PASEF data acquisition under ESI positive and negative modes. Data analysis was conducted in DataAnalysis 5.3 and MetaboScape 2022 (Bruker).

Results and Discussions

The parallel accumulation serial fragmentation (PASEF) provides very fast MS/MS acquisition speed at full sensitivity following ion mobility separation to deeply profile low abundant lipids using data dependent acquisition. Data analysis and feature findings of the SARS-CoV-2 plasma samples were performed in MetaboScape 2022 with the T-ReX®4D algorithm applied for automatic feature extraction and retention time alignment. Under optimized selection criteria, about 5637 feature compounds were generated where 4776 compounds were selected for MS/MS accounting about 84.7% total features coverage. In addition, the ion mobility (1/K0) and collisional cross sections (CCS) of each feature were calculated and listed in the generated feature table (Figure 1A).

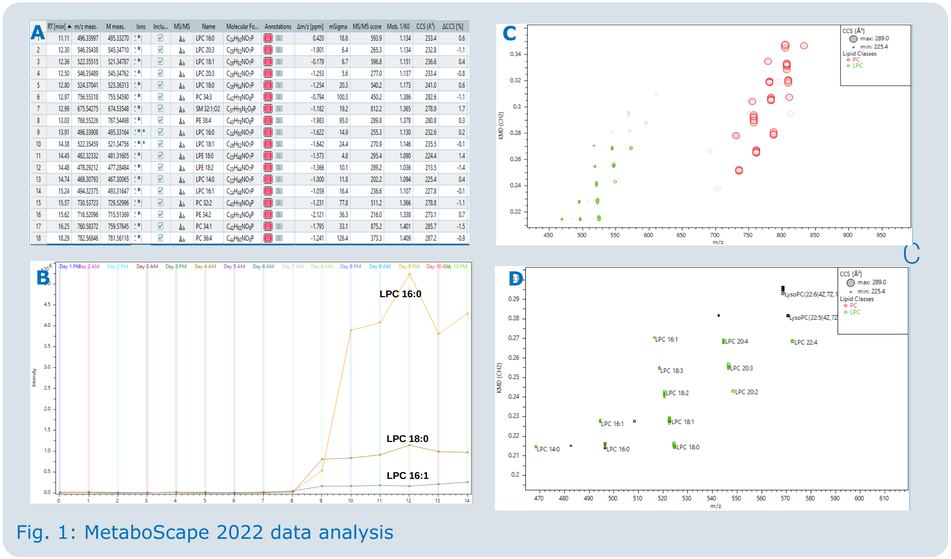

Fig. 1: MetaboScape 2022 data analysis

Features could be annotated with rule-based lipid class annotation, LipidBlast MS/MS spectral library annotation, and CCS annotation which provide additional confidence based on the predicted CCS from the machine-learning models. Annotated results could be further evaluated based on mass accuracy, isotope pattern matching, MS/MS score and ΔCCS to exclude redundant and false results. Furthermore, Kendrick Mass Plot could be used to give an overview on annotated lipid classes to quickly identify false annotations, analyze lipid series and perform deep analysis of the homologous lipid series (Figures 1C, 1D).

The lipid profile of patients in this time series administration period up to 10 days could be plotted in MetaboScape 2022 to visually check the change of feature concentration level over time (Figure 1B).

Statistical analysis is part of MetaboScape 2022 including PCA, PLS, T-test/ANOVA and new Clustering. A PCA plot of subject 3 from 10-days plasma sample analysis were listed in Figure 2.

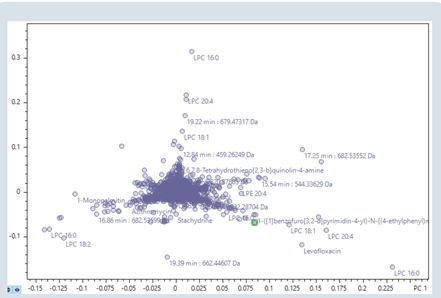

Fig. 2: MetaboScape 2022 statistical analysis

High ion mobility separation resolution on lipid isomers together with outlier detection in MetaboScape 2022 provide highly confident results on lipid profiling .

Summary

The use of Trapped Ion Mobility Spectrometry (TIMS) and MetaboScape 2022 for data processing and analysis is a fast lipid profiling approach allows for increased unknown lipid annotation ID and reliable quality results

References

(1) Robert Nardacci et al.; Cell Death and Disease (2021) 12: 263

(2) Marianna Caterino et al.; Nature (2021) 11: 2941

(3) Cindy B McReynolds et al.; Frontiers in Physiology (2021) 12: Article 663869

Conclusions

- The use of Trapped Ion Mobility Spectrometry (TIMS) and MetaboScape 2022 data processing and analysis allows for increased unknown annotation speed
- TIMS allows to achieve more confident annotation due to cleaner spectra, better reliable data interpretation and separation of possible lipid isomers
- MetaboScape 2022 data processing and analysis provides a comprehensive tool for fast and reliable lipid identification with easy reporting.

timsTOF Pro 2 and MetaboScape 2022