4D-lipidomics profiling in ALD using VIP-HESI and trapped ion mobility time-of-flight mass spectrometry

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BRUKER

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Introduction

- Adrenoleukodystrophy (ALD) is a genetic metabolic disorder characterized by accumulation of very long-chain fatty acids (VLCFA)

- In depth characterization of the ALD lipidome is needed to elucidate the complex disease pathology and understand the highly unpredictable clinical course of ALD

Method

- We performed 4D-lipidomics (retention time, m/z, ion mobility and fragmentation) using an UHPLC-MS platform employing timsTOF Pro (Bruker) in fibroblasts from ALD patients and healthy controls.

- A vacuum-insulated probe heated ESI source was used and ions were separated and fragmented using Parallel Accumulation Serial Fragmentation (PASEF).

- Lipid Annotation was done using an in-house bioinformatics pipeline in combination with MetaboScape (Bruker).
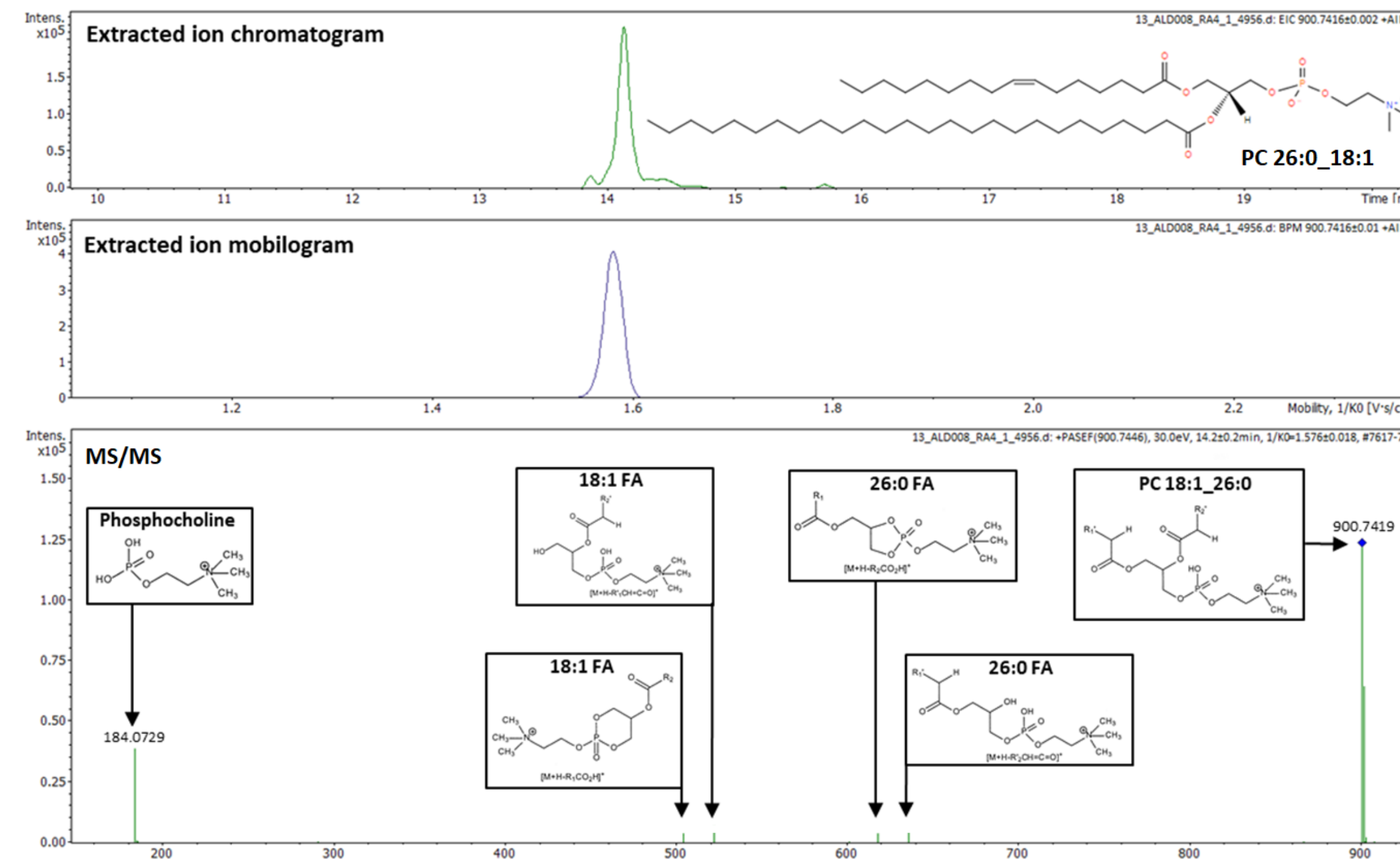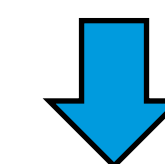
Results

- Using 4D-lipidomics we were able to generate an in-depth characterization of the ALD lipidome in a four-dimensional data space consisting of >1300 lipids.

- Our results demonstrate that VLCFA are incorporated into multiple complex lipid species including (lyso)phosphatidylcholines and neutral lipids

- Acquisition of MS/MS spectra using PASEF enabled the identification of individual fatty acid moieties of VLCFA incorporated complex lipids.
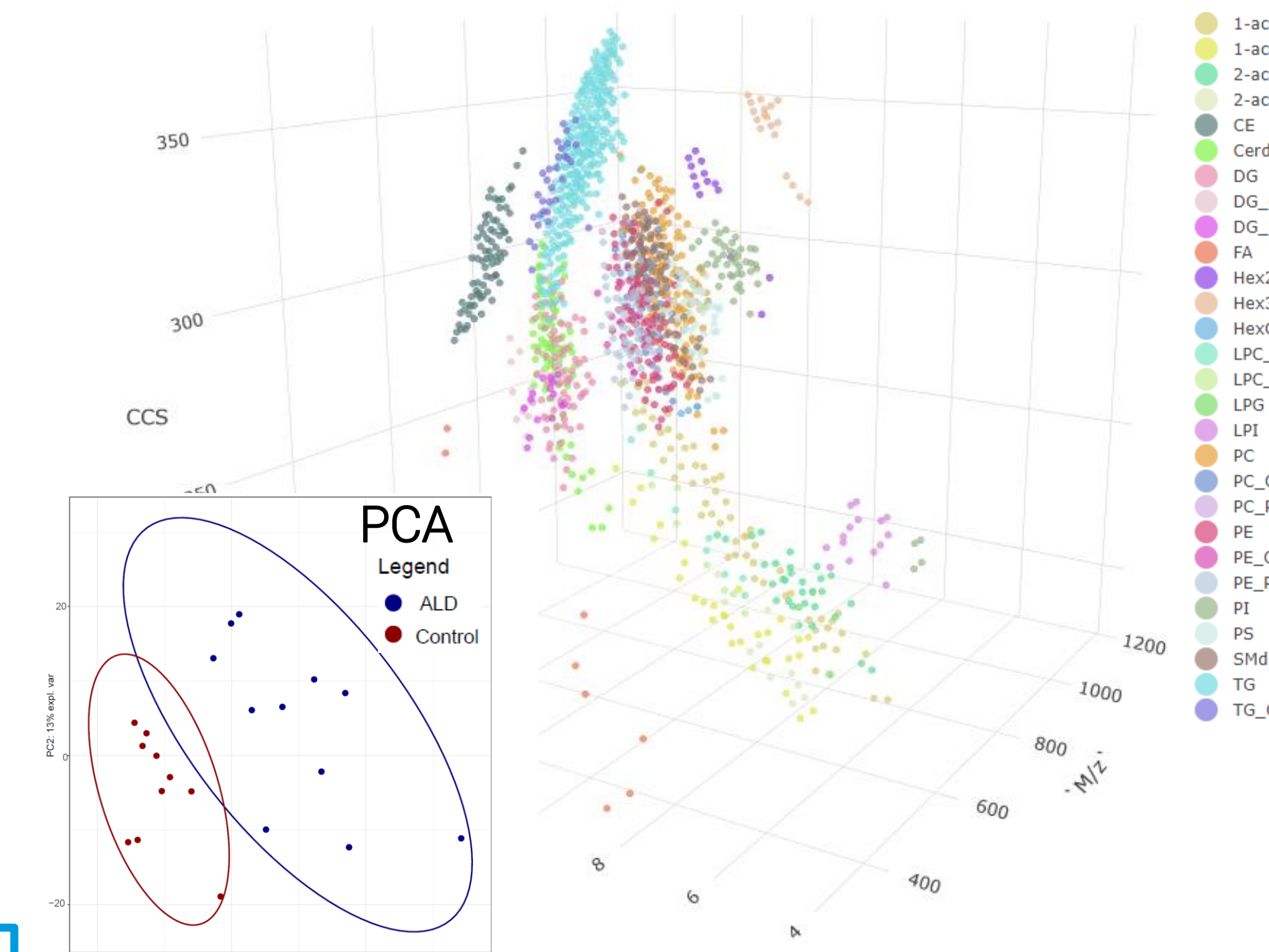
Data analysis

Bruker MetaboScape
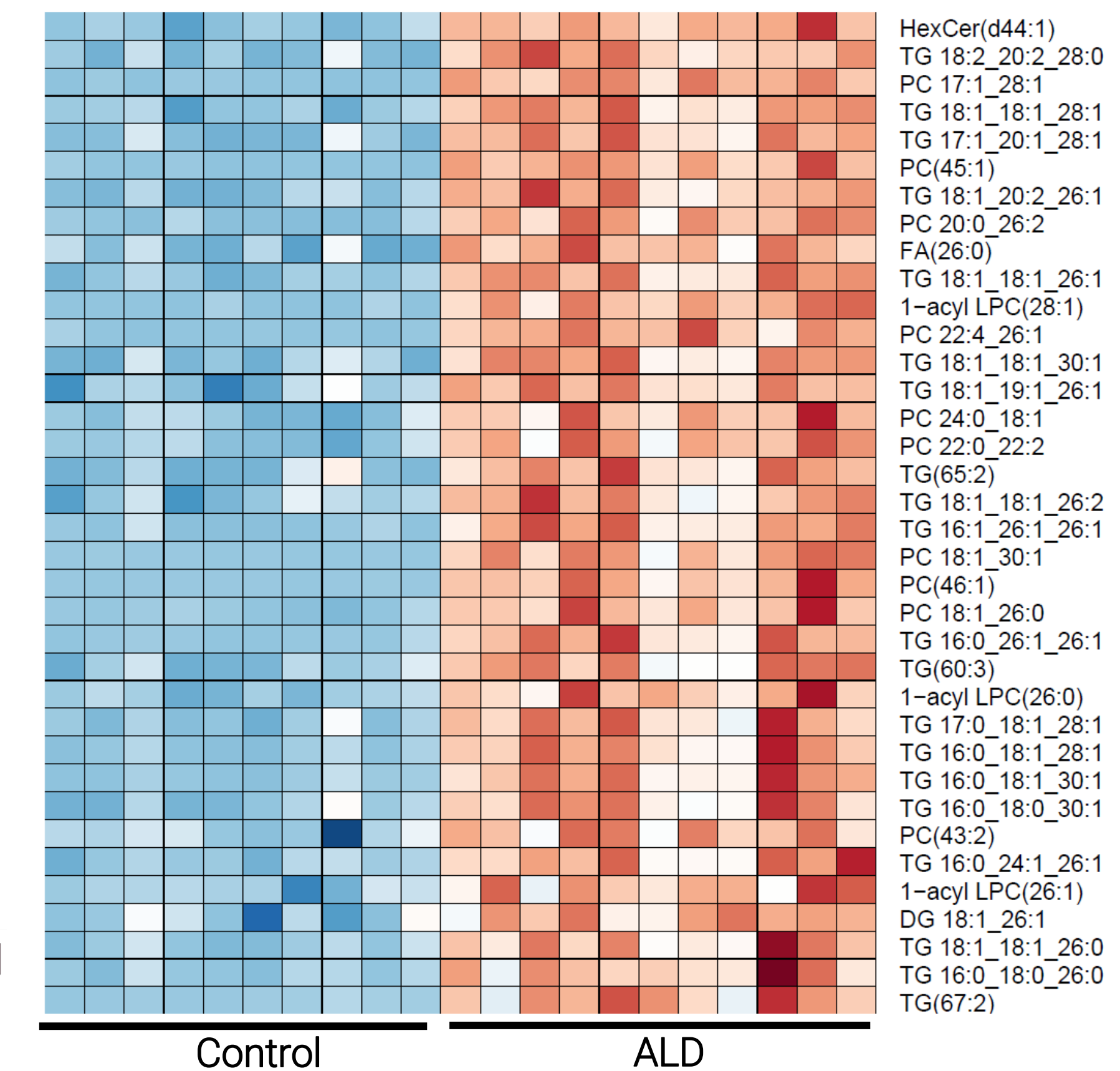

Note: Fatty acid annotation with the highest MS/MS score is shown.

4D-Lipidomics

Detected lipids

PCA

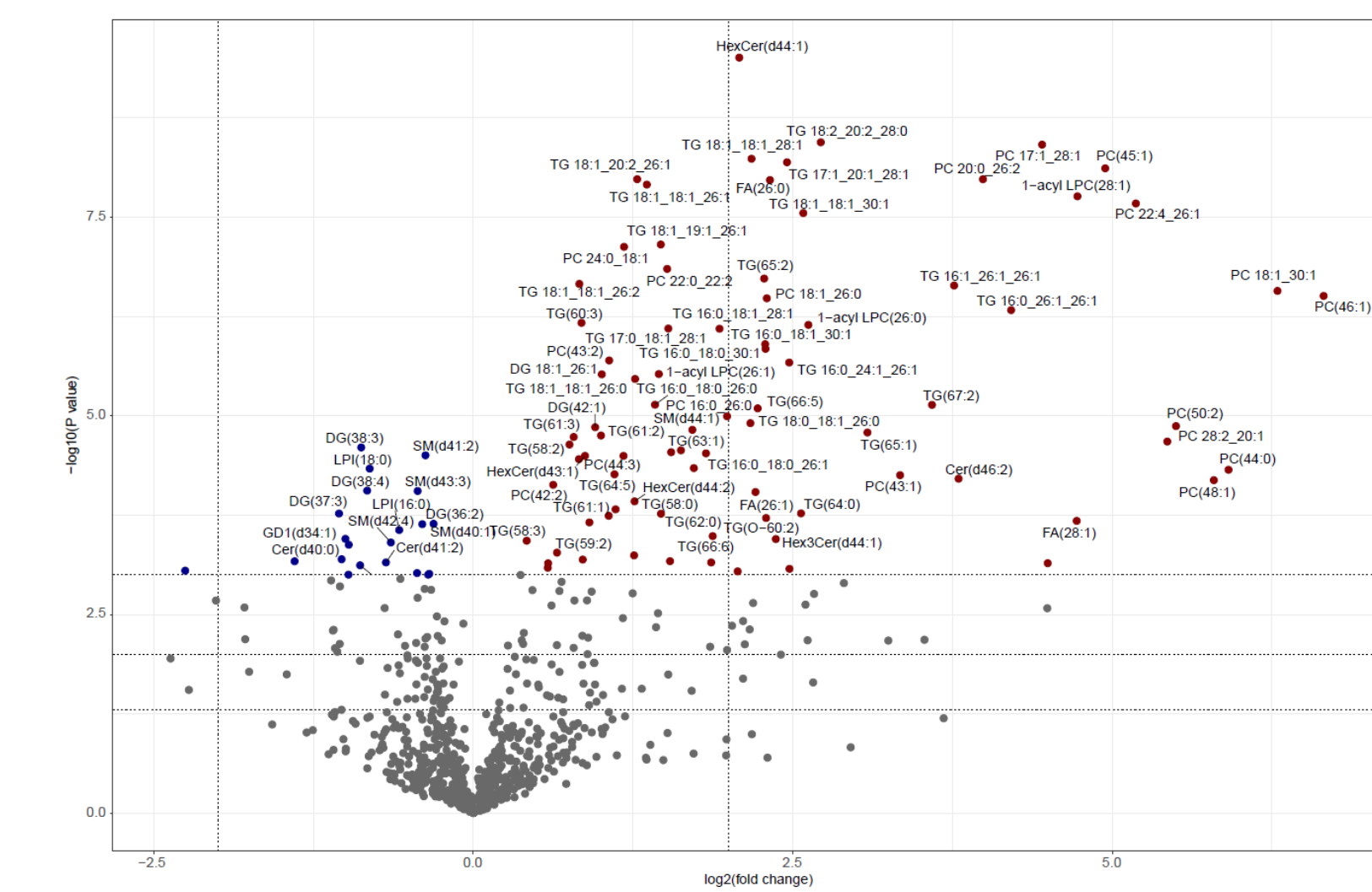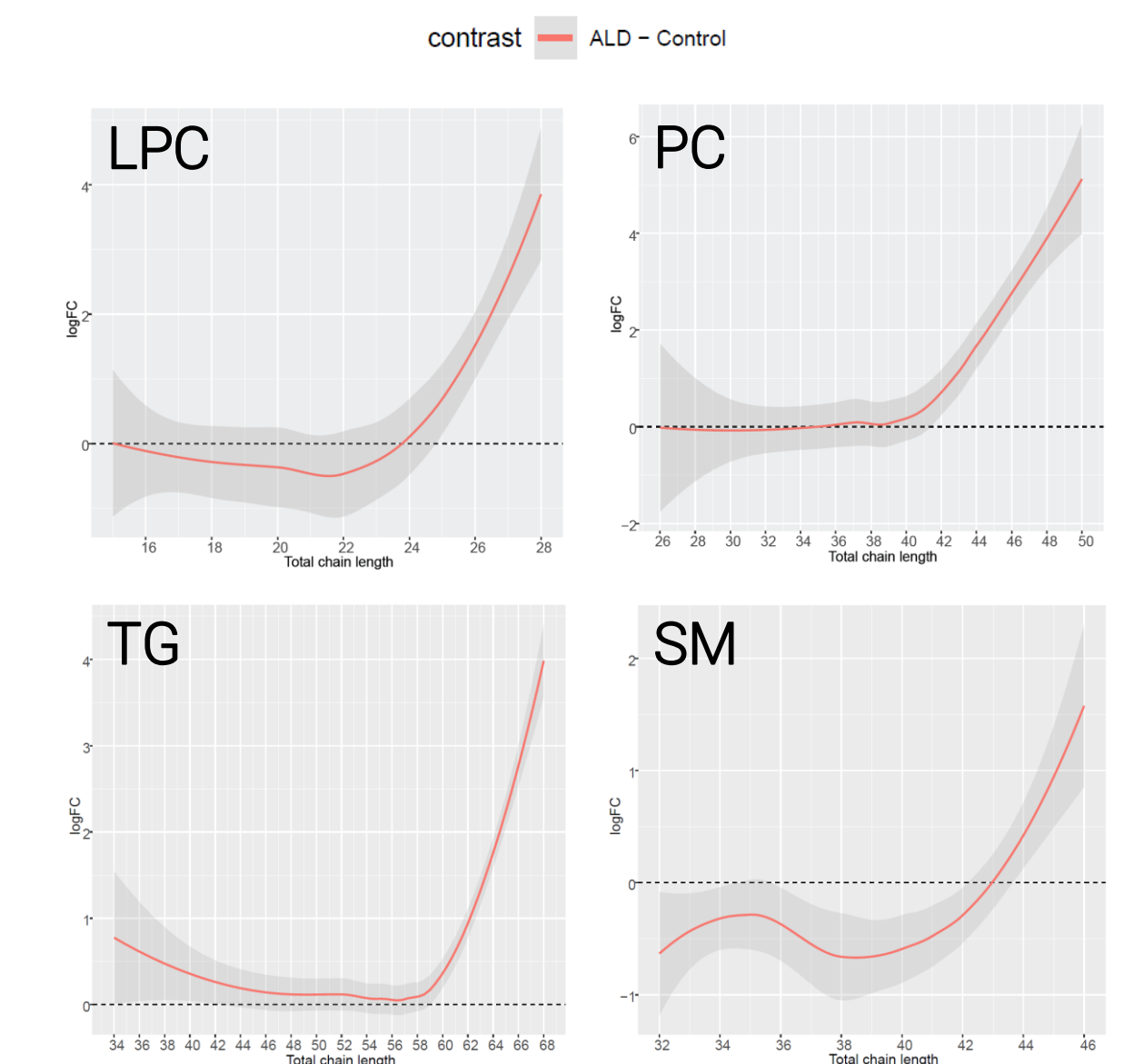### Heatmap sorted on VIP score

Volcano plot

Trend: logFC vs Chain length

Conclusion

- 4D-lipidomics using PASEF is a promising technique to enhance the characterization of the lipidome.

- VLCFA are incorporated into multiple complex lipid species thereby profoundly altering the ALD lipidome.

- Further investigation is needed to analyse whether these systemic lipidome changes can be tied to the multiform pathology of ALD.

Technology

For Research Use Only. Not for use in diagnostic procedures.

Innovation with Integrity