Unveiling alterations in plasma and blood lipidomic signatures in Systemic Lupus Erythematosus and Systemic Sclerosis patients for metabolic biomarkers discovery

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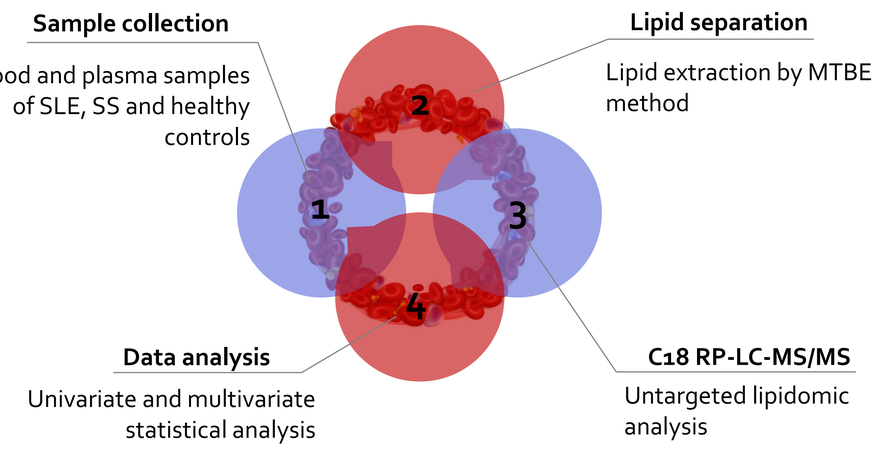
1 Introduction

Systemic lupus erythematosus (SLE) and systemic sclerosis (SS) are two of the most prevalent autoimmune disease (AID) that severely impact the patients` life, society and health care systems. The immunological parameters used to diagnose SLE and SS have low specificity and predictive value of their own, which makes the diagnosis of these AID a hard task[1]. Thus, it is imperative to find new biomarkers that can ease the diagnosis and be used in the prognosis and disease management processes. The lipid metabolism has been reported to be dysregulated in patients with SLE and SS, showing the importance of lipid regulation in the pathogenesis of these AID. Some molecular lipid species in SLE, such as plasmalogens, fatty acids (FA), and oxidized phospholipids, have been reported to be altered, however the results are inconsistent and contradictory between studies[2]. Concerning SS, there are few reported investigations on lipid alterations, nonetheless, phospholipids (PL), sphingolipids, plasmalogens, FA and carnitines (CAR) have been reported to be altered. This way, it is urgent the improvement of the screening methodologies to evaluate lipidic changes in SLE and SS. Having said that, lipidomics is the best approach to study the lipidome of AID and its modifications. The identification of the healthy lipidomic signature at the molecular level and its variations in a pathological state sheds light on the contribution of lipids to disease development and its molecular mechanisms.

2 Objectives

- **Lipidomic signature of SLE and SS**
  - Comprehensively assess and compare the lipid profile of SLE, SS and healthy controls (CT) by using an untargeted C18 RP-LC-MS lipidomic approach in both whole blood and plasma
- **Simplify the lipidomic analysis in clinical settings**
  - Analysis of whole blood eliminating the need for centrifugation to collect the plasma
- **Determine if lipids at the cellular level experience specific changes with AID**

3 Methods



4 Results

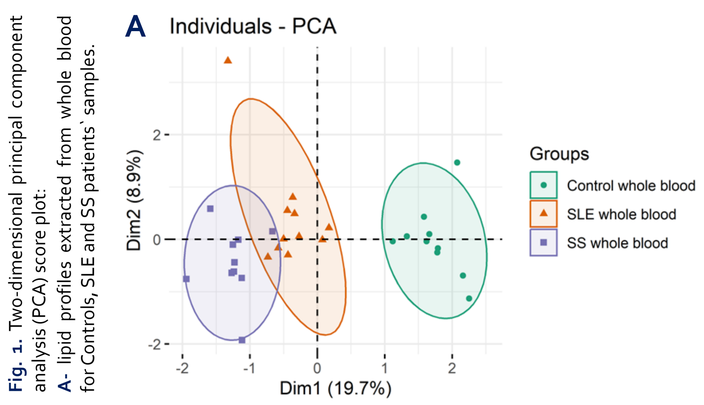


Fig. 1. Two-dimensional principal component analysis (PCA) score plot: **A-** lipid profiles extracted from whole blood for Controls, SLE and SS patients` samples.

- ✓ Plasma and blood samples from AID differ from controls and are similarly clustered.
- ✓ The lipid profiles of SLE and SS exhibit partial overlap
  - Inherent biological heterogeneity associated with human samples
  - Inflammatory conditions characteristic of AID diseases

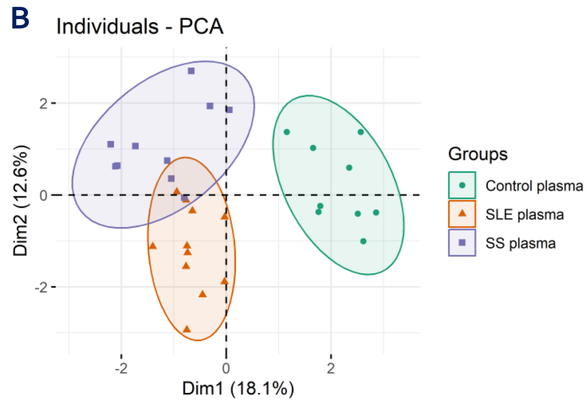


Fig. 1. Two-dimensional principal component analysis (PCA) score plot: **B-** lipid profiles extracted from plasma for Controls, SLE and SS patients` samples.

Whole blood

✓ In whole blood PE(36:4) and PS(40:4)
- ↑ in SLE
- ↓ in SS

→ Possible discriminatory markers for each disease

Both matrices

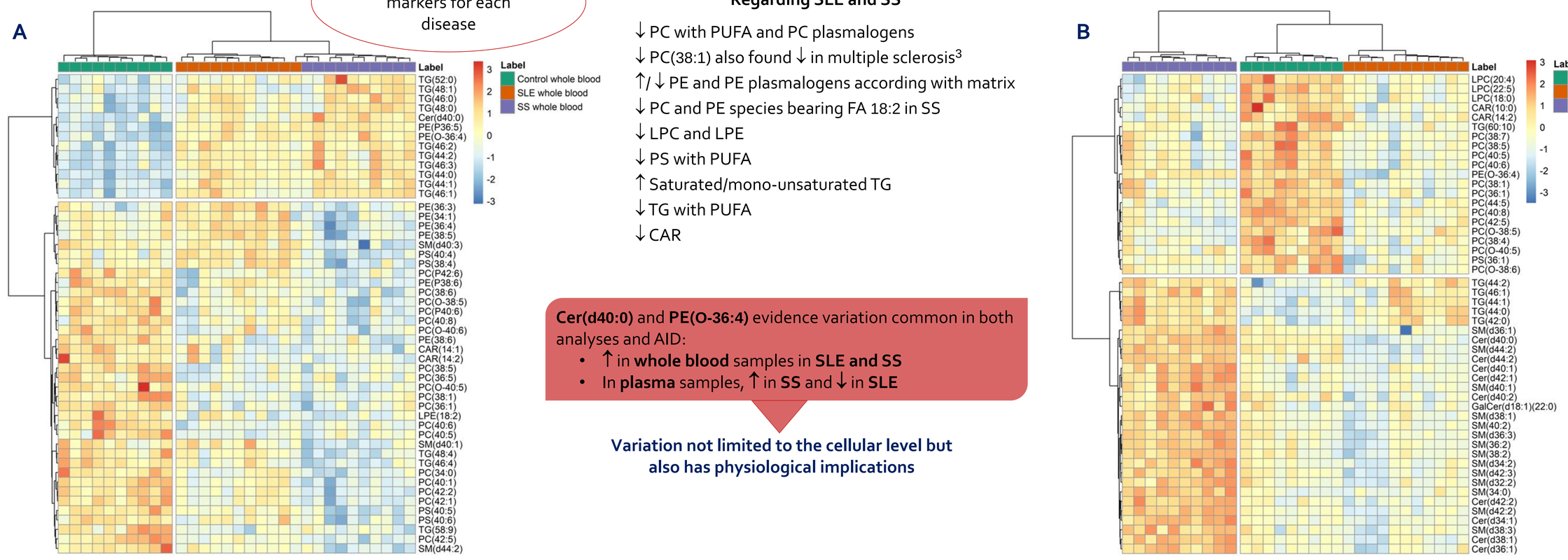
Regarding SLE and SS

- ↓ PC with PUFA and PC plasmalogens
- ↓ PC(38:1) also found ↓ in multiple sclerosis[3]
- ↑/↓ PE and PE plasmalogens according with matrix
- ↓ PC and PE species bearing FA 18:2 in SS
- ↓ LPC and LPE
- ↓ PS with PUFA
- ↑ Saturated/mono-unsaturated TG
- ↓ TG with PUFA
- ↓ CAR

Plasma

↑ SM in SS

↑ Cer in SS



Cer(d40:0) and **PE(O-36:4)** evidence variation common in both analyses and AID:
- ↑ in **whole blood** samples in **SLE and SS**
- In **plasma** samples, ↑ in **SS** and ↓ in **SLE**

Variation not limited to the cellular level but also has physiological implications

Fig. 2. Two-dimensional hierarchical clustering heatmap of the 50 most discriminating lipid molecular species in whole blood (A) and plasma (B) of Control, SLE and SS groups. Relative abundance levels are indicated on the colour scale, with the numbers indicating the fold difference from the overall mean. The clustering of the control and disease groups is represented by the dendrogram at the top. The clustering of individual lipid molecular species is represented by the dendrogram on the left.

5 Conclusions[4]

- SLE and SS lipidomic signature is significantly different from that of a healthy state, particularly in SM, Cer and PL bearing PUFA species.
- The increased levels of particular SM and Cer molecular species in the plasma of SS patients make them putative lipid biomarkers of SS.
- PC(38:1) may be considered a potential plasma biomarker for AID due to its variations in SLE, SS and multiple sclerosis (previously reported).

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7 References

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