

Category : **Sepsis: basic mechanisms**

A239 - Septic shock is associated with a substantial change in the platelet lipidome

M Dechamps¹ ; E de Cartier² ; J De Poortere² ; V Robaux² ; C Des Rosiers³ ; A Forest³ ; J Ambroise⁴ ; L Bertrand² ; S Horman² ; C Beauloye²

¹CARD, IREC, UCLouvain, Brussels, Belgium, ²CARD, IREC, Brussels, Belgium, ³Montreal Heart Institute Research Center, Metabolomic Platform, Montreal, Canada, ⁴IREC, UCLouvain, Centre de technologies moléculaires appliquées, Brussels, Belgium

Introduction:

Sepsis is defined as life-threatening organ dysfunction caused by an impaired host immune response to infection. Sepsis is characterized by major endothelial dysfunction, microvascular alterations, and coagulopathy. In addition to their involvement in pathological hemostatic processes, platelets are key players in sepsis as they promote immunothrombosis. The composition of the platelet lipidome is critical to their function. However, the lipidomic profile of platelets during sepsis has never been studied.

Methods:

Platelets were isolated from 48 septic and 48 control patients. Lipidomic analysis was carried out by untargeted liquid chromatography–mass spectrometry (QTOF).

Results:

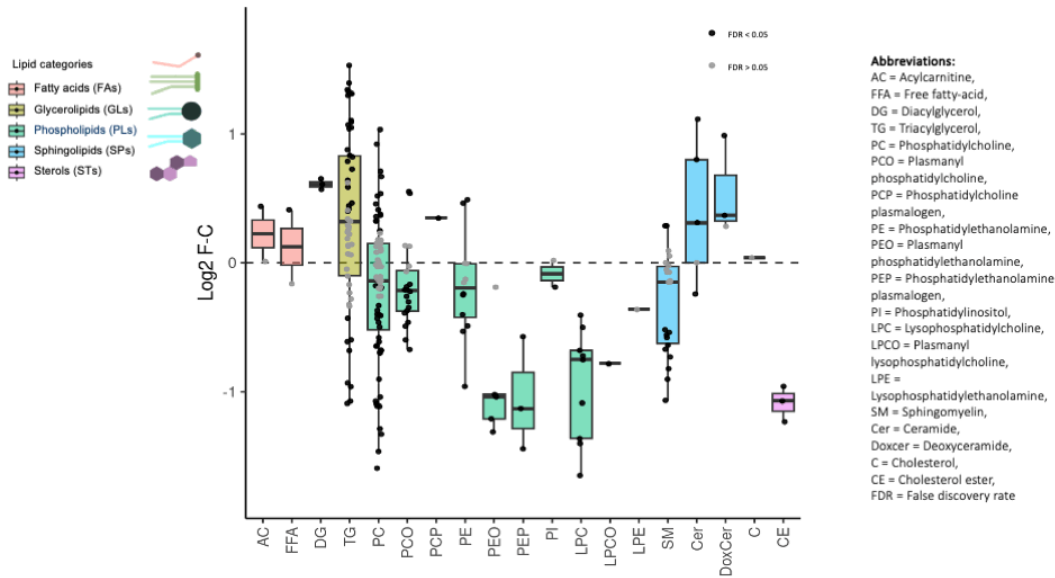
The lipidomic analysis identified 224 species and showed significant changes in the lipid composition of platelets during sepsis. Platelets from patients with septic shock showed increased levels of diacyl and triacylglycerols, as well as ceramides and deoxyceramides. A concordant decrease in sphingomyelin species was also observed. Excessive ceramide formation has been associated with multiple disorders, including atherosclerosis and cardiovascular disease. Regarding phospholipids, patients showed a reduction in lysophospholipids as well as alterations in the composition of fatty acid chains. An increase in short and (un)saturated fatty acid chains was observed and associated with a substantial reduction in phosphatidylcholines and phosphatidylethanolamines containing long polyunsaturated fatty acid chains (ω 3 and ω 6). The latter are key phospholipids for the generation of pro- and anti-inflammatory lipid mediators.

Conclusion:

Critical changes in the platelet lipidome occur during sepsis. Upregulated lipids are mainly glycerolipids and ceramides, while lysophospholipids are drastically reduced. These changes as well as alterations in the composition of the fatty acyl chains of phospholipids might play a role in the pathophysiology of the disease.

Image :

Platelet lipid box plots, comparing patients with septic shock to matched controls



Box-plots of identified lipid classes/subclasses, comparing septic shock patients and controls: The Y-axis displays the Log₂FC of the signal intensity values of each lipid species in septic vs control groups. The X-axis shows the lipid classes/subclasses, classified and color-coded based on their respective categories. Within those classes/subclasses, each dot represents a lipid species. The dot color distinguishes lipids exhibiting a significant difference (black) or not (grey) between the group