Platelet lipidomics, atherosclerosis and coronary artery disease

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Introduction: Platelets play a key role in the pathophysiology of atherogenesis. Patients with coronary artery disease (CAD) reveal enhanced activity of circulating platelets. Platelet hyperactivity is associated with adverse clinical outcome in CAD. Dyslipoproteinemia is associated with enhanced platelet activation. Experimental studies showed that plasma lipids modulate platelet function. LDL binds to platelets and stimulates platelet activation. Further, platelets internalize LDL and metabolize the lipoprotein by oxidation and peroxidation. Ox-LDL laden platelets are phagocytosed by monocytes/macrophages and induce formation of foam cells promoting formation of atherosclerotic plaques. Further, enhanced content of oxLDL within platelets is associated with a prothrombotic phenotype of platelets. Recently, the murine and human platelet lipidome has been characterized. Activation of platelets results in significant changes of platelet lipidome. The platelet lipidome in patients with CAD may disclose patients at risk for adverse clinical outcome.

Methods: We investigated the platelet lipidome in a large cohort of patients with symptomatic CAD by untargeted liquid chromatography-mass spectrometry. Furthermore, we examine the impact of significantly altered lipids in ACS on platelet-dependent thrombus formation and aggregation.

Results: In a consecutive study, we characterized the platelet lipidome in a CAD cohort (n = 139) and showed significant changes of lipids between patients with ACS and CCS. We found that among 928 lipids, seven platelet glycerophospholipids were significantly up-regulated in ACS, whereas 25 lipids were down-regulated compared to CCS. The most prominent up-regulated lipid in ACS, PC18:0 (PC 10:0-8:0), promoted platelet activation and ex vivo platelet-dependent thrombus formation.

Conclusion: Our results reveal that the platelet lipidome is altered in ACS and up-regulated lipids embody primarily glycerophospholipids. Alterations of the platelet lipidome, especially of medium chain lipids, may play a role in the pathophysiology of ACS and provide the basis of novel biomarkers to identify patients at risk for adverse cardiovascular events.