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## Addition of high-density lipoprotein3 and Apo A-I antagonize the platelet storage lesion and the release of platelet extracellular vesicles

Gerd Schmitz<sup>1</sup>, Evelyn Orsó<sup>1</sup> and Helmut Meyer<sup>2</sup>

<sup>1</sup>University of Regensburg, Germany

<sup>2</sup>Leibniz-Institut, Germany

During activation and senescence, platelets release increased amounts of platelet extracellular vesicles (PL-EVs). We established an *in vitro* model for size, proteomic, lipidomic and transcriptomic characterization of PL-EVs over 5 days in platelet concentrates to better understand the platelet storage lesion. After 5 days standard blood banking, PL-EVs were isolated by filtration and differential gradient ultracentrifugation into 5 platelet microvesicle subfractions (PL-MV F1-F5) and platelet exosomes (PL-EXs) and subjected to Nanoparticle Tracking Analysis, Flow Cytometry, proteomic/lipidomic mass spectrometry, miRNA-microarray profiling and deep sequencing. PL-EVs showed overlapping particle mean sizes of 180-260 nm, but differed significantly in composition. Less dense (F1-3), intermediate and dense (F5-EX) PL-EVs, are enriched in lipidomic and proteomic markers for plasma membrane, intracellular membranes/platelet granules and mitochondria. F1-F4 is enriched in free cholesterol, sphingomyelin(SM), dihydroSM and glycerophospholipids. F4-F5 are enriched with phosphatidylinositol, ceramides, lysophosphatidic acid, phosphatidylserine and cardiolipin species. Alpha-synuclein (81% of total expression) accumulated in F1-F2, amyloid beta precursor protein in F3-F4 (84%) and ApoE (88%) and ApoJ (92%) in F3-5. PL-EXs are enriched in lipid-raft and adhesion markers. During platelet senescence, HDL3/apoA-I significantly reduce PL-EVs by 62%, and the decrease correlates with the concentration of added apoA-I, and is mediated by SRB-I and CD36. Compared to platelets, PL-EVs enriched miRNAs related to neurodegenerative diseases. Different lipid and protein compositions of PL-EVs suggest their unique cellular origins, partly overlapping with platelet granule secretion. Dense PL-EVs might represent autophagic vesicles released during platelet activation/apoptosis and PL-EXs resemble lipid rafts, with a possible role in platelet coagulation and immunology. Segregation of alpha-synuclein and amyloid beta precursor protein, ApoE/J into less dense and dense PL-MVs, respectively, show their differential carrier role of neurological disease-related cargo. HDL3/apoA-I influences membrane homeostasis of platelets by reduction of PL-EV release during platelet senescence, improving intracellular lipid processing/vesicle transport and increasing cholesterol CE-efflux.

### Biography

Gerd Schmitz has completed his MD from the University of Cologne and Postdoctoral studies from the University of Münster, Germany. Until end of 2014, he was the director of the Institute of Laboratory Medicine and Transfusion Medicine at the University of Regensburg, Germany. Since then he started his own consulting company < [www.lipoconsult.org](http://www.lipoconsult.org) >. He has published more than 350 papers in reputed journals and has been serving as an Editorial Board Member of several journals.

[Gerd.schmitz@ukr.de](mailto:Gerd.schmitz@ukr.de)

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