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HDL is believed to be protective against cardiovascular disease (CVD) via the reverse cholesterol transport and anti-inflammatory actions in the vessel. Apolipoprotein M (apoM) is an apolipoprotein mainly associated with HDL. Recently ApoM was proven to be the main carrier of Sphingosine 1-phosphate (S1P) in circulation. S1P is a signaling phospholipid involved in the immune system, exerting most of its effects through signaling via 5-G-protein coupled receptors; SIP₁₋₅.

The aim of this thesis is to investigate the role of the apoM/S1P-complex in vascular inflammatory diseases such as atherosclerosis and sepsis. We also want to study the interaction between the apoM/S1P-complex and the S1P-receptors.

We developed a liquid chromatography-tandem mass spectrometry method for S1P-quantification in plasma and cell extracts. We found that plasma levels of S1P and apoM were decreased in sepsis, levels reflecting the severity of the disease. The apoM/S1P-complex contributes to the anti-inflammatory effects exerted by HDL as shown *in vitro* by its inhibiting potential of pro-inflammatory adhesion molecules on the endothelial surface and by its increment of the endothelial barrier function. Plasma levels of apoM and S1P in type-1-diabetes (T1D)- patients (who have increased risk of developing CVD) were not altered compared to healthy controls. However, HDL-particles from T1D showed decreased anti-inflammatory effects which was not related to reduced presence of apoM and S1P. The apoM/S1P-complex could interact with all S1P-receptors as shown by internalization of fluorescently labelled S1P-receptors overexpressed in HEK293-cells. Interestingly, extracellular levels of apoM and S1P could determine which receptor was available at the cellular surface.

In conclusion, our data suggest apoM and S1P to have a role in acute and chronic inflammation. Future research could help us clarify how the apoM/S1P-complex signals through the different S1P-receptors in different inflammatory disorders and hence contribute in developing new therapies against diseases in the vasculature.