# Plasma-derived and synthetic HDL inhibit tissue factor in endothelial cells and monocytes

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*Background and aim* - High density lipoproteins (HDL) exert anti-thrombotic activities by preventing platelet adhesion and activation, by stimulating the anticoagulant protein C pathway and by promoting fibrinolysis. Aim of the study was to assess the effect of plasma-derived and synthetic HDL on endothelial and monocyte expression of tissue factor (TF), the primary initiator of coagulation in physiological and pathological conditions.
*Methods and Results* - HDL inhibited TF expression in TNFalpha-stimulated human umbilical vein endothelial cells and in thrombin-stimulated monocytic cells at physiological concentrations and in a dose-dependent way. Prebeta-migrating HDL particles were not responsible for the inhibitory effect, since their selective removal did not alter HDL-mediated TF inhibition; $HDL_2$ and $HDL_3$ subclasses were equally effective. Synthetic HDL made of apoA-I and phosphatidylcholine fully retained the ability to inhibit TF expression in a dose-dependent manner; lipid-free apoA-I was not effective nor was sphingosine-1-phosphate involved. HDL-mediated TF inhibition was due to a modulation of cell cholesterol content through the interaction with SR-BI, but not ABCG1; downstream, HDL inhibited the activation of p38 MAPK and the repression of PI3K pathway responsible for TF expression. In vivo, human apoA-I transgenic mice displayed a reduced aortic expression of TF than wild-type animals. In addition, plasma levels of TF were increased in subjects with low HDL-C levels when compared to high HDL-C subjects.
*Conclusions* - The anti-thrombotic activity of HDL can also be mediated by the inhibition of TF expression and activity in endothelial and monocytic cells; sHDL retain the inhibitory activity of plasma-derived HDL, strengthening the rationale for sHDL infusion in acute coronary syndromes.