Abstract: **P542**

**Human monocyte subsets differentially express tissue factor in vivo and in vitro**

**Authors:**
B Thaler¹, KA Krychtiuk¹, PJ Hohensinner¹, M Lenz¹, K Huber², G Heinz¹, J Wojta¹, W Speidl¹, ¹Medical University of Vienna, Cardiology - Vienna - Austria, ²Wilhelminen Hospital - Vienna - Austria,

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Human monocytes can be divided into a classical (CM, CD14++CD16-), a non-classical (NCM, CD14+CD16++), and an intermediate subset (IM, CD14++CD16+) whereby CM are mainly phagocytes, NCM patrol along the endothelium and IM exhibit pro-inflammatory properties and are associated with inflammatory diseases such as atherosclerosis. Besides their inflammatory properties, these subsets are also involved in coagulation. Especially, in pathologies like sepsis where bacteria induces a systemic inflammatory response leading to uncontrolled coagulation, monocytes are known to be major contributors through the production of tissue factor (TF). Tissue factor, as the main initiator of the extrinsic coagulation pathway, induces the activation of thrombin. We hypothesized that besides their known characteristic inflammatory potential, monocyte subtypes exhibit specific coagulatory profiles.

120 consecutive patients admitted to the ICU were enrolled. Blood samples were taken at admission and stained for CD14, CD16 and TF expression was measured. Furthermore, whole blood obtained from healthy controls was stimulated with TNF-a or LPS for 4 hours and subset specific TF-expression was analyzed. In addition, TF mRNA was measured in sorted monocyte subsets. Moreover, blood samples from healthy controls were incubated with dimethyl fumarate (DMF) to block NF-kB for 30 minutes prior to stimulation with LPS for 4 hours. Subset specific TLR4 and TNFR expression was measured in blood samples from healthy donors. Clotting assays were performed with LPS stimulated and unstimulated monocyte subsets.

At ICU admission, IM showed significantly higher TF expression as compared to CM (p<0.0001), while NCM showed the lowest TF expression (p<0.0001 compared to CM and IM). Moreover, in vitro stimulation of sorted monocyte subsets with LPS induced only in IM a significant increase in mRNA levels (p<0.05).

Monocytes from healthy controls showed no difference in TF expression. Incubation with LPS and TNF-a showed a significantly higher increase of TF surface expression in all subsets, but only LPS induced significant more TF in IM compared to CM and NCM (p<0.05).The presence of DMF blocked the induction of TF expression through LPS in all subsets indicating a signal transduction via NF-kB. Measurement of TRL4 and TNFR showed that IMs express significantly more TLR4 compared to CMs and NCMs and all three subsets have equal levels of TNFR. Clotting experiments confirmed the ability of activated IMs to induce clotting to greater extent than CMs and NCMs.

In conclusion, monocyte subsets show a distinct coagulatory phenotype besides their well-characterized inflammatory properties.