COMPLEMENT MASP-1 INDUCES ENDOTHELIAL CELLS TO ATTRACT AND BIND NEUTROPHIL GRANULOCYTES

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Background and objectives
The complement system and neutrophil granulocytes (PMNs) are substantially important in immune response against bacteria and fungi. Endothelial cells, besides many other functions, can also participate in antimicrobial immunity through their cytokine production and homing regulation by adhesion molecules. We previously demonstrated that complement mannan-binding lectin associated serine protease 1 (MASP-1) is able to activate Ca-, NFκB and p38 MAPK signaling pathways in endothelial cells by cleaving protease activated receptors (PARs). Moreover, MASP-1 stimulated endothelial cells produce IL-6 and IL-8. However, the results of the downstream events have not been studied so far. Therefore, we aimed to assess if endothelial cells induced by MASP-1 have the capability to attract and bind PMNs.
Methods
We used human umbilical vein endothelial cells, freshly prepared PMNs and PLB-985 cell line (as a model for PMNs) for our experiments. ELISA, immunofluorescence and quantitative PCR were used to determine the level of cytokines and adhesion molecules, transwell and plate-based adhesion test were utilized to assess chemotaxis and adhesion.

Results
The unique cytokine pattern induced by MASP-1 may have an important role in the activation of PMNs, since we demonstrated that supernatant of MASP-1 treated endothelial cells triggered PMN chemotaxis. MASP-1 did not influence the expression of ICAM-1 and VCAM-1, whereas ICAM-2 was moderately down-regulated and E-Selectin expression was significantly increased. Furthermore, PLB-985 cells differentiated towards PMNs were able to adhere better to MASP-1 treated endothelial cells than to non-treated ones.

Conclusions
The expression of VCAM-1 is required for the transmigration of T cells and monocytes, while for PMNs E-selectin may be sufficient (in the presence of basal levels of ICAMs). MCP-1 and IL-8 are very potent chemotactic factors for monocytes and PMNs, respectively. The expression of E-selectin together with increased production of IL-6 and IL-8 suggests that MASP-1 stimulation of endothelial cells selectively favors the activation of neutrophils. Our findings suggest a novel connection between the two antibacterial/antifungal immune mediators – the complement system and neutrophil granulocytes.