EMMPRIN (CD147/basigin) mediates platelet-monocyte interactions in vivo and augments monocyte recruitment to the vascular wall.

Abstract:
Platelets play a central role in hemostasis, in inflammatory diseases such as atherosclerosis, and during thrombus formation following vascular injury. Thereby, platelets interact intensively with monocytes and enhance their recruitment to the vascular wall. To investigate the role of the extracellular matrix metalloproteinase inducer (EMMPRIN) in platelet-monocyte interactions. Isolated human monocytes were perfused in vitro over firmly adherent platelets to allow investigation of the role of EMMPRIN in platelet-monocyte interactions under flow conditions. Monocytes readily bound to surface-adherent platelets. Both antibody blockade and gene silencing of monocyte EMMPRIN substantially attenuated firm adhesion of monocytes to platelets at arterial and venous shear rates. In vivo, platelet interactions with the murine monocyte cell line ANA-1 were significantly decreased when ANA-1 cells were pretreated with EMMPRIN-silencing small interfering RNA prior to injection into wild-type mice. Using intravital microscopy, we showed that recruitment of EMMPRIN-silenced ANA-1 to the injured carotid artery was significantly reduced as compared with control cells. Further silencing of EMMPRIN resulted in significantly fewer ANA-1-platelet aggregates in the
mouse circulation as determined by flow cytometry. Finally, we identified glycoprotein (GP)VI as a critical corresponding receptor on platelets that mediates interaction with monocyte EMMPRIN. Thus, blocking of GPVI inhibited the effect of EMMPRIN on firm monocyte adhesion to platelets under arterial flow conditions in vitro, and abrogated EMMPRIN-mediated platelet-monocyte aggregate formation in vivo. EMMPRIN supports platelet-monocyte interactions and promotes monocyte recruitment to the arterial wall. Therefore, EMMPRIN might represent a novel target to reduce vascular inflammation and atherosclerotic lesion development.