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Titel des Beitrags: SASH1, a new potential link between smoking and atherosclerosis.

Abstract: We have previously reported that SASH1 expression is increased in circulating human monocytes from smokers and was positively correlated with the number of carotid atherosclerotic plaques. The aim of this study was to further validate the link between smoking, SASH1 and atherosclerosis within the vascular wall and to assess the impact of SASH1 expression on endothelial cell functions. Human carotids with atherosclerotic plaques were obtained from 58 patients (45 of them with known smoking status: smoker, non-smoker, ex-smokers), and were processed for gene expression analyses and immunostaining. To investigate its function, SASH1 was silenced in human aortic endothelial cells (HAECs) using two different siRNA and subcellular localization of SASH1 was determined by immunostaining and subcellular fractionation. Subsequently the transcriptomic analyses and functional experiments (wound healing, WST-1 proliferation or Matrigel assays) were performed to characterize SASH1 function. SASH1 was expressed in human vascular cells (HAECs, smooth muscle cells) and in monocytes/macrophages. Its tissue expression was significantly higher in the atherosclerotic carotids of smokers compared to non-smokers (p < 0.01).
In HAECs, SASH1 was expressed mostly in the cytoplasm and SASH1 knockdown resulted in an increased cell migration, proliferation and angiogenesis. Transcriptomic and pathway analyses showed that SASH1 silencing results in a decreased CYP1A1 expression possibly through the inhibition of TP53 activity. We showed that SASH1 expression is increased in atherosclerotic carotids in smokers and its silencing affects endothelial angiogenic functions; therefore we provide a potential link between smoking and atherosclerosis through SASH1 expression.