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Titel des Beitrags:
TIMP-1 creates a pre-metastatic niche in the liver through SDF-1/CXCR4-dependent neutrophil recruitment in mice.

Abstract:
Due to its ability to inhibit pro-metastatic matrix metalloproteinases, tissue inhibitor of metalloproteinases (TIMP)-1 has been thought to suppress tumor metastasis. However, elevated systemic levels of TIMP-1 correlate with poor prognosis in cancer patients suggesting a metastasis-stimulating role of TIMP-1. In colorectal cancer patients, tumor as well as plasma TIMP-1 levels were correlated with synchronous liver metastasis or distant metastasis-associated disease relapse. In mice, high systemic TIMP-1 levels increased the liver susceptibility towards metastasis by triggering the formation of a pre-metastatic niche. This promoted hepatic metastasis independent of origin or intrinsic metastatic potential of tumor cells. High systemic TIMP-1 led to increased hepatic SDF-1 levels, which in turn promoted recruitment of neutrophils to the liver. Both inhibition of SDF-1-mediated neutrophil recruitment and systemic depletion of neutrophils reduced TIMP-1-induced increased liver susceptibility towards metastasis. This indicates a crucial functional role of neutrophils in the
TIMP-1-induced pre-metastatic niche. Conclusion: Our results identify TIMP-1 as an essential promoter of hepatic pre-metastatic niche formation. (Hepatology 2014).