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Titel des Beitrags: Clinical Relevance of the Plasminogen Activator Inhibitor Type1 -- a Multifaceted Proteolytic Factor

Abstract: The plasminogen activator inhibitor type-1 (PAI-1) is a multifaceted proteolytic factor. It not only functions as an inhibitor of the protease uPA (urokinase-type plasminogen activator), but also plays an important role in signal transduction, cell adherence, and cell migration. Thus – an apparent paradox considering its name –, although it inhibits uPA during blood coagulation, it actually promotes invasion and metastasis. In the early 1990s, clinical evidence associated elevated PAI-1 levels in tumor tissue with poor clinical outcome in primary breast cancer. These clinical data have since been supported by experimental evidence that the concerted action of uPA, its cell surface receptor uPA-R, and PAI-1 facilitates invasion and metastasis. The strong prognostic impact of PAI-1 in primary breast cancer has been validated by international research groups assessing fresh tumor tissue extracts by ELISA. There is clinical evidence that high-risk patients with elevated PAI-1 in their tumor benefit from adjuvant systemic therapy. uPA also has a strong prognostic impact in primary breast cancer. In node-negative breast cancer, risk-group selection for adjuvant systemic therapy based on tumor levels of both PAI-1 and uPA is close to routine clinical use. Also in other malignancies such as ovarian, esophageal, gastric, colorectal or...
hepatocellular cancer, elevated PAI-1 is associated with tumor aggressiveness and poor patient outcome. This abundant clinical evidence implicating PAI-1 as a key factor for tumor invasion and metastasis renders it a promising target for tumor therapy. Novel therapeutic approaches targeting the PAI-1/uPA interaction are already in pre-clinical testing.