Plasminogênio. Ativadores do plasminogênio (tPA e uPA) aumentam a angiogênese, a invasividade as metástases no câncer

The plasminogen activator system and cancer.
Division of Hematology and Oncology, Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL 60611, USA.

Abstract
The fibrinolytic system, more appropriately referred to as the plasminogen activator system, controls not only the intravascular fibrin deposition but also participates in a wide variety of physiologic and pathologic processes. In cancer, the components of this system are involved in tumor growth, invasion and metastasis, through their effect on angiogenesis and cell migration. These components are found in most tumors and their expression signifies not only their function but also carries a prognostic value. Their expression is in turn modulated by cytokines and growth factors, many of which are up-regulated in cancer. Though both plasminogen activators, tPA and uPA, are expressed in tumor cells, uPA with its receptor (uPAR) is mostly involved in cellular functions, while tPA with its receptor Annexin II on endothelial surface regulates intravascular fibrin deposition. Among the inhibitors of fibrinolysis, PAI-1 is a major player in the pathogenesis of many vascular diseases as well as in cancer. Therapeutic intervention, either using plasminogen activators or use of experimental inhibitor agents against PAI-1, has shown encouraging results in experimental tumors but not verified clinically. Information provided in this brief review is aimed to promote greater interest in the role of the plasminogen activator system in cancer.

PMID: 19176991

The role of plasminogen-plasmin system in cancer.
Division of Hematology and Oncology, Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, USA. h-kwaan@northwestern.edu

Abstract
Components of the plasminogen-plasmin system participate in a wide variety of physiologic and pathologic processes, including tumor growth, invasion and metastasis, through their effect on angiogenesis and cell migration. These components are found in most tumors and their expression not only signifies their function but also carries a prognostic value. Their expression is in turn modulated by cytokines and growth factors, many of which are up-regulated in cancer. Though both tPA and uPA are expressed in tumor cells, uPA with its receptor (uPAR) is mostly involved in cellular functions, while tPA with its receptor Annexin II on endothelial surface, regulates intravascular fibrin deposition. Among the inhibitors of fibrinolysis, PAI-1 is a major player in the pathogenesis of many vascular diseases as well as in cancer. Therapeutic interventions, either using plasminogen activators or experimental inhibitor agents against PAI-1, have shown encouraging results in experimental tumors but not been verified clinically.

PMID: 19377918

Urokinase plasminogen activator system: a multifunctional role in tumor progression and metastasis.
Choong PF, Nadesapillai AP.
Department of Orthopaedics, The University of Melbourne, Melbourne, Australia.

Abstract
The urokinase plasminogen activator (uPA) system is central to a spectrum of biologic processes including fibrinolysis, inflammation, atherosclerotic plaque formation, matrix remodeling during wound healing, tumor invasion, angiogenesis, and metastasis. Binding of uPA with its receptor (uPAR) initiates a proteolytic cascade that results in the conversion of plasminogen to plasmin. Plasmin through its own proteolytic function degrades a range of extracellular basement membrane components and activates others such as the metalloproteinases. Independent of catalytic activity, uPAR also is involved in cell signaling, interactions with integrins, cell motility, adhesion and invasion, and angiogenesis. Over expression of uPA or uPAR is a feature of malignancy and is correlated with tumor progression and metastasis. In contrast, inhibition of expression of these components leads to a reduction in the invasive and metastatic capacity of many tumors. Strategies that target uPA or its receptor with the aim of disrupting the interaction between the two or the ligand independent actions of uPAR include antisense technology, monoclonal antibodies, cytotoxic antibiotics, and synthetic inhibitors of uPA. Targeted therapy is a goal of future cancer treatment and the uPA system is a likely candidate for manipulation.

PMID: 14600592