**Abstract**

Cancer is spread by the plasminogen activation system which is also responsible for biological processes including clearance of fibrin clots, cell migration, and activation of growth factors. The key role is played by urokinase plasminogen activator receptor (uPAR) which is a tethered membrane protein receptor having three domains, one of which is critical in activating its substrate, the serine protease urokinase plasminogen activator (uPA). uPA activation begins when two of uPA’s domains (an N-terminal growth factor domain (GFD) and a kringle domain) interact with domain one of uPAR, creating a tight bond which converts uPA to its active form. The proteolytic cascade reaction continues when activated uPA converts inactive plasminogen to the active protease plasmin. Plasmin is a multi-use protease that can activate several matrix metalloproteinases, which along with plasmin, leads to digestion of extracellular matrix (ECM) and enhanced cell migration. The binding of uPA to uPAR localizes these proteolytic cascades to the migrating edge of the cell, thereby clearing a path in the extracellular matrix that the cells can move through. Tumor cells often express high levels of uPA and uPAR, facilitating metastasis. uPA-uPAR expression can change a benign tumor into a malignant tumor. The activity of uPAR can be regulated by the proteolytic removal of its N-terminal D1 domain. When uPAR’s N-terminal D1 domain is disabled or removed it cannot bind to uPA, therefore the cancer cells lack the ability to metastasize. This prevention technique could lead to the cure for cancer.

**Background**

A number of factors can cause tumors, including environmental carcinogens and inherited genetic mutations. Tumors are classified as either benign or malignant. Malignant cells have the ability to spread throughout the body and metastasize. The inactivation of uPA can be achieved by cleaving D1 from uPAR.

**Deterioration of Extracellular Matrix (ECM) in Tumor Cells Leads to Cancer Cell Metastasis**

**References**


SMART Teams are supported by the National Institutes of Health (NIH)- National Center for Research Resources/Science Education Partnership Award (NCRR-SEPA), and an NIH CTSA Award to the Medical College of Wisconsin.