

Characteristics of proteins involved in fibrinolysis

Protein	Half-life in vivo	Mol. Weight (Kda)	Plasma concentration	Site of synthesis	Characteristics	Variations & associations with pathology
C1-inhibitor (C1-INH)	2-3 days	106	180 µg/ml	Liver	Single-Chain Glycoprotein	Deficiency, Hyperfibrinolysis : Angioneurotic oedema
Plasminogen	2-3 days	90	200 µg/ml	Liver	Single-Chain Glycoprotein with 5 Kringle domains Complexed with HRGP (50%)	Thrombosis with decreased or abnormal plasminogen Decreased in hepatic diseases and increased in inflammation
Histidin-Rich Glyco-protein (HRGP)	3 days	67	100 µg/ml	Liver	Cystatine superfamily Binds heparin Complexes Plasminogen Calcium dependent Inhibitor of heparin.	Rare deficiencies. Has a similar action to AEAC Hypofibrinolysis with excess of HRGP?
α2 Anti-Plasmin (α2AP)	60 hours	70	70 µg/ml	Hepatocytes	Serine Protease Inhibitor (Serpin)	Bleeding when decreased Deficient in hepatic disorders and DIC
α2 Macroglobulin (α2 M)	3 days	725	2.5 mg/ml	-	Tetramer with 4 identical chains of 160 Kda. Interacts with all classes of proteases	Decreased in situations with high proteolytic activity, such as in pancreatitis (consumption) Elevated in newborns
Factor XII	2-3 days	76	30 ng/ml	Liver	Activates Scu-PA to TcuPA Single-Chain	Deficiencies associated with thrombotic diseases and reduced fibrinolysis
tPA	5 min	68	< 10 ng/ml	Endothelial cells Neurons Microglial cells	Serine Protease with 2 Kringle domains Single-Chain	Increased in cardiovascular disease risk, in respiratory distress syndrome, myocardial infarction, septicemia, liver diseases,... Major role in brain and Nerves synapses
uPA	8 min	55	< 5 ng/ml	Kidney	Serine protease with 1 kringle domain Single-Chain	Decreases in diabetes (IDDM) Secreted by many tumors
PAI-1	5 min	50	< 30 ng/ml	Endothelial cells, Liver, Megacaryocytes	Serine Protease inhibitor (Serpin) Acute phase reactive protein Present in platelets α granules (90%)	Increased in diabetes (NIDDM), hyper-triglyceridemia, liver diseases, inflammation, cancer. Important extra-vascular function
PAI-2	120 min	47	< 10 ng/ml	Placenta, Leucocytes, Macrophages	Serine Protease inhibitor (Serpin)	Highly increased in pregnancy
PAI-3 (Activated Protein C inhibitor)	15 min	57	5 µg/ml	Liver, Male genital tract	Serine Protease Inhibitor (Serpin) Heparin dependent	Also present in urine. No known associated pathology
TAFI	-	60	2.5 µg/ml	Liver	Single-Chain Glycoprotein	Decreased fibrinolytic activity with increased TAFI concentrations
Fibrinogen	3-5 days	330	2-4 mg/ml	Liver	Structure with 2 series of 3 symetric chains (Aα, Bβ, γ)	Bleeding if highly decreased concentrations. Thrombosis with some abnormalities which impair fibrinolysis
MMP-1 to MMP-23	-	60 to 100	-	-	Activated from ProMMP by various mechanisms, including plasmin for MMP1/3/7/9/10/13	Hydrolyse components of the extracellular matrix. Cell remodeling, Cancer
TIMP 1 to 4	-	18 to 30	-	-	Inhibitors and regulators of MMPs	Control matrix degradation
Neuroserpin	-	52	-	-	tPA inhibitor on nerves	Inhibits extracellular fibrinolysis (tPA). Present on nerves
Annexin II	-	35	-	-	Binds tPA and phospholipids. Activates plasminogen. LDL receptor related protein	Induces cell migration and neoangiogenesis
FSAP	-	64	12 µg/ml	-	Single chain glycoprotein. Activated by urokinase. Ca++ dependent	Activates FVII and Pro-Urokinase. Inhibited by α2AP

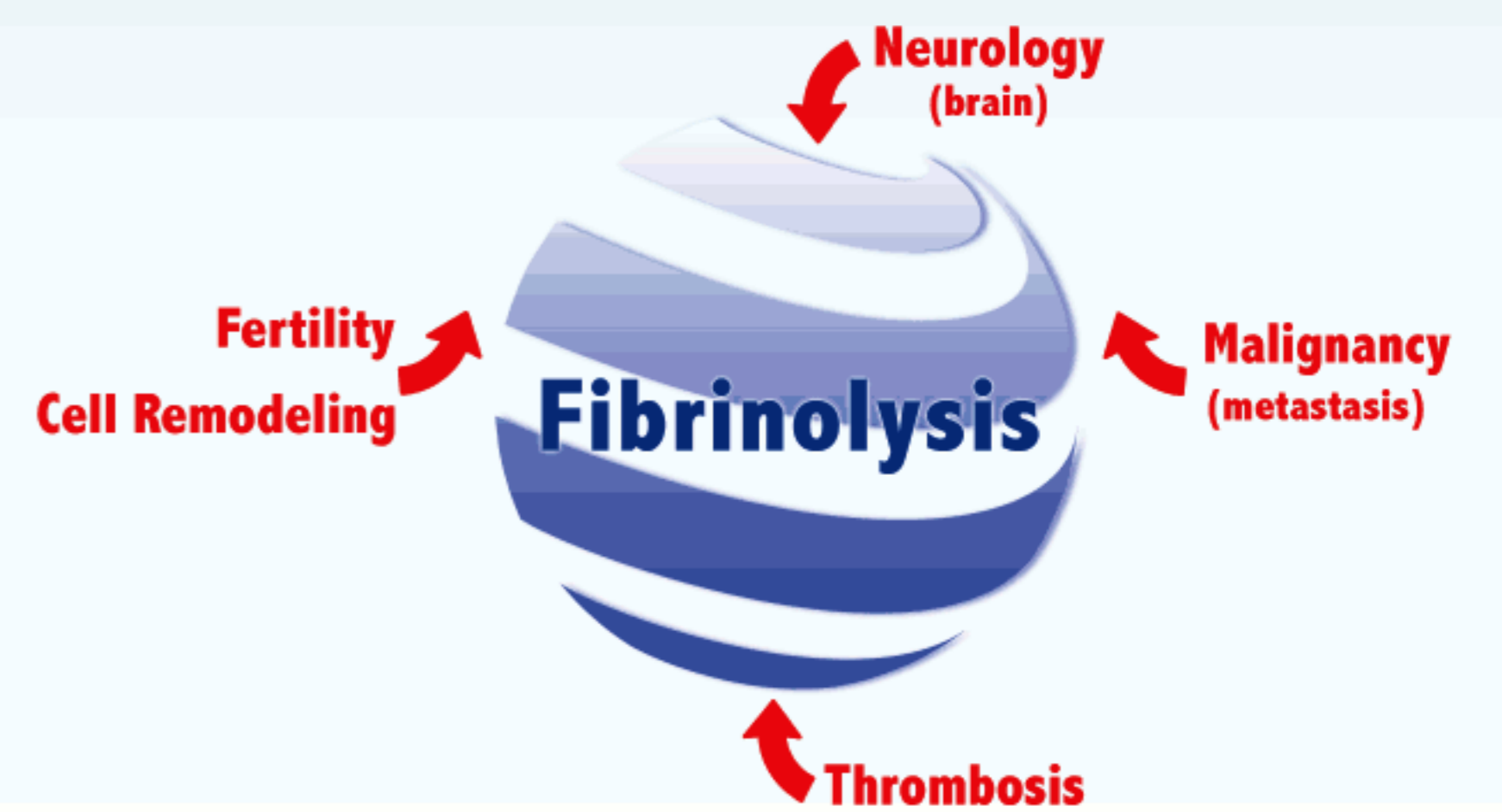
Fibrinolysis mechanisms



Highly regulated biological system



Updated technologies for investigating fibrinolysis



A major body biological mechanism, involved in many processes, and which if dysfunctions can kill...

... but Silently !!!

- ⚡ Intra vascular clot dissolution
- ⚡ Brain & neurological functions
- ⚡ Extra-vascular matrix degradation
- ⚡ Development of cancer

... and with a delayed mode of action !!!