

## Delayed fibrinolysis in body

### tPA : tissue Plasminogen Activator

The major activator of vascular fibrinolysis, which activates plasminogen onto the fibrin surface. The Zymutest assay measures homogenously tPA as well as its complexes with PAI-1 or other inhibitors. The Zymuphen assay only measures active tPA.

Zymutest tPA:Ag (ARK011A) |  
Zymuphen tPA Activity (A521296)

### uPA: urokinase type Plasminogen Activator

Involved in vascular fibrinolysis, but also in extra vascular fibrinolysis, cell migration and Tissue remodeling. Kallikrein, Factor Seven Activating Protease (FASEP), cathepsins and plasmin activate the single chain uPA (ScuPA) to two chain uPA (Tcu-PA,), the active form, especially when it is bound to its cell receptor uPAR. The assay measures homogeneously the total uPA protein, whether the presentation is (ScuPA, TcuPA, HMW-uPA, LMW-uPA), free or complexed with its inhibitors.

Zymutest uPA:Ag (ARK013A)

### Pro-TAFI and TAFI: Thrombin Activable Fibrinolysis Inhibitor

The zymogen form of Thrombin Activatable Fibrinolysis Inhibitor (pro-TAFI), also known as TAFI, procarboxypeptidase U, or procarboxypeptidase B, is described as a plasma glycoprotein synthesized in the liver. It can be catalysed into its active form, TAFI (TAFIa, carboxypeptidase U or B) by thrombin-thrombomodulin complex. TAFI can potentially inhibit fibrinolysis by removing carboxyterminal lysine residues from partially degraded fibrin, decreasing plasminogen binding onto the fibrin surface, which thereby results in a decrease of fibrinolytic activity. Zymutest pro-TAFI is specific for the intact zymogen form whilst Zymutest TAFI measures all the TAFI molecular forms, including activated and inactivated ones.

Zymutest Pro-TAFI Antigen (ARK037A) |  
Zymutest TAFI:Ag (ARK008A)

### PAI-1: Plasminogen Activator Inhibitor-1

The major inhibitor of tPA and uPA, intravascularly and extravascularly. PAI-1 forms rapidly inactive tPA-PAI-1 and uPA-PAI-1 complexes in presence of tPA or uPA. Most of the blood PAI-1 (>90% in pathology) is in the latent form in platelets. Zymutest PAI-1:Ag measures all the PAI-1 forms, irrelevantly of their presentation. Zymutest PAI-1 Activity only measures active PAI-1, through its binding to tPA.

Zymutest PAI-1:Ag (ARK012A) |  
Zymutest PAI-1 Activity (ARK019A)

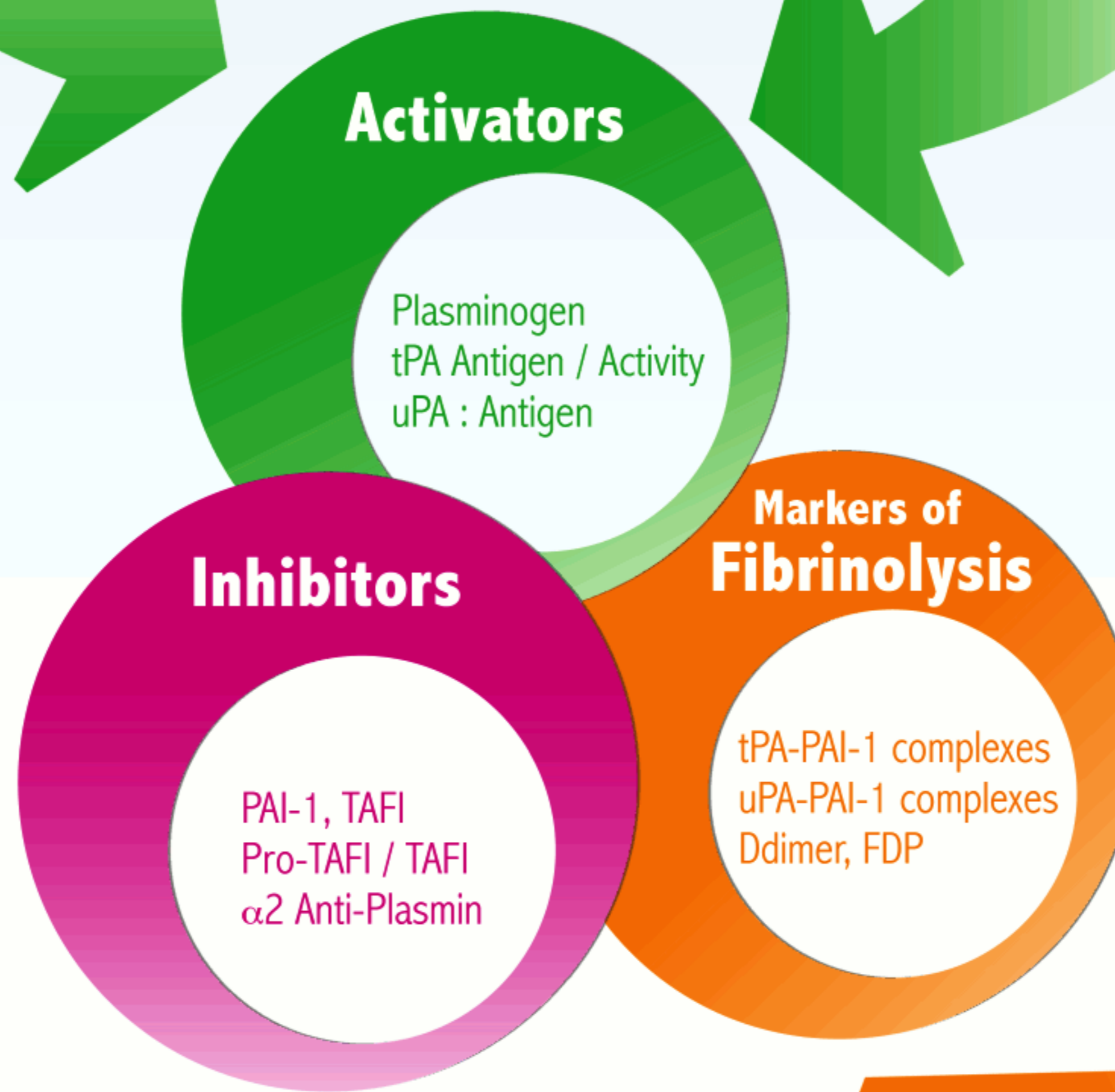
### $\alpha$ 2-Anti-Plasmin

The major fast acting plasmin inhibitor in plasma, which deficiency induces hyperfibrinolysis and bleeding risk.  $\alpha$ 2 Anti-Plasmin is measured with a functional assay, through its rapid plasmin inactivation.

BIOPHEN  $\alpha$ 2-AP (A220502)

## Equilibrium between activators & inhibitors

## A key system in thrombosis malignancy & neurology



### Plasminogen

Plasminogen is the inactive precursor of plasmin, a potent serine protease involved in the dissolution of fibrin blood clots. Both hereditary and acquired forms of plasminogen deficiency have been described. These are usually associated with either a thrombotic or a hyperfibrinolytic condition. Plasminogen binding to fibrin clot is modulated by Histidin Rich Glyco- Protein (HRGP) and  $\alpha$ 2 Anti-plasmin. Plasminogen is usually measured using a chromogenic assay.

Biophen Plasminogen (A221502) Chromogenic assay

### Fibrinogen

Fibrinogen, when clotted to fibrin, triggers and regulates fibrinolysis functions. Fibrin binds  $\alpha$ 2- AP, tPA, plasminogen (in a regulated manner) and is a substrate for TAFIa and plasmin. Fibrinogen can be measured using functional clotting assays, such as Clauss Method (Fibriphen), or with immunoassays.

Zymutest Fibrinogen (ARK024A) |  
Liaphen Fibrinogen (A120102)

### Ddimer

The circulating enzyme, plasmin, cleaves the fibrin gel in a number of places. The resultant fragments, "high molecular weight polymers", are digested several times more by plasmin to lead to intermediate forms and then to small polymers (fibrin degradation products or FDPs). The crosslink between two D fragments remains intact however, and these are exposed on the surface when the fibrin fragments are sufficiently digested. The typical Ddimer fragment contains two D domains and one E domain of the original fibrinogen molecule and is present in blood when a blood clot forms and is degraded by fibrinolysis.

Zymutest DDimer (ARK023A)

### uPA-PAI-1 complexes

Can be generated in blood circulation when increased levels of uPA and PAI-1 are present, but these complexes are usually formed extravascularly. Can be a marker of some cancer types (especially breast tumors), as a prognosis of disease evolution, when measured in tumor extracts or exsudates.

Zymutest uPA-PAI-1 complexes (ARK018A)

### tPA-PAI-1 complexes

Generated in blood circulation when fibrinolysis is stimulated, and increased levels of tPA and PAI-1 are present. Elevated concentrations of tPA-PAI-1 complexes reflect the involvement of fibrinolytic mechanisms in circulation.

Zymutest tPA-PAI-1 complexes (ARK017A)