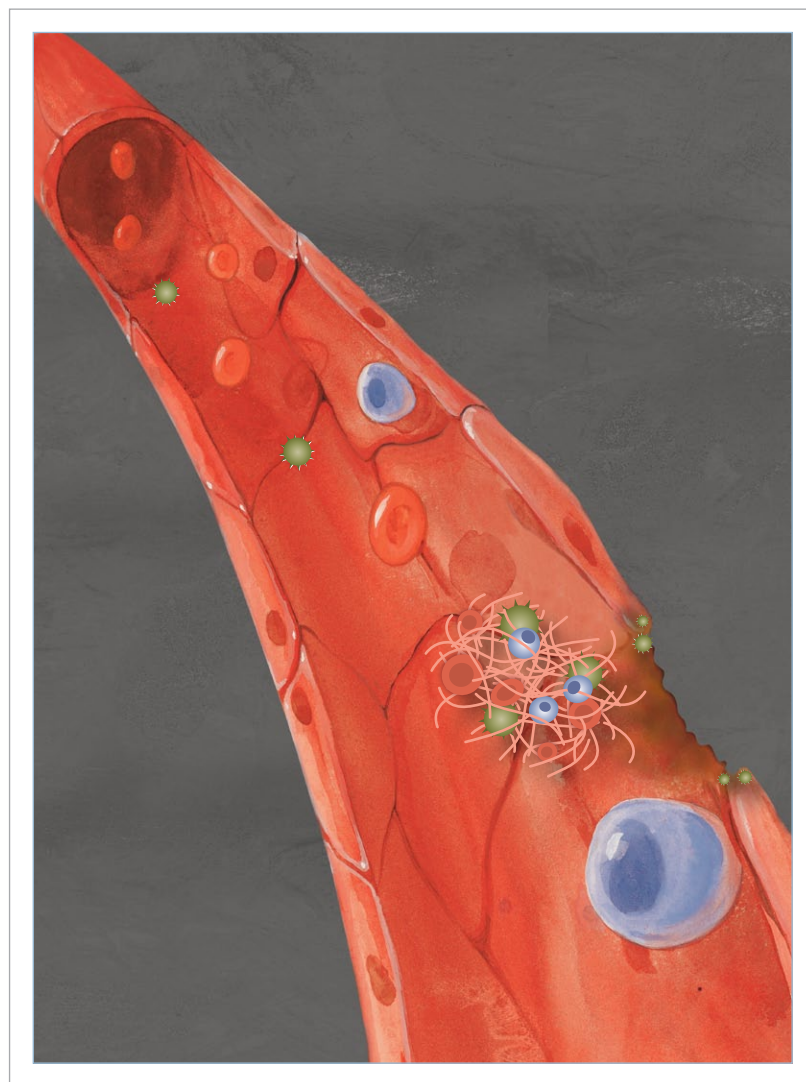
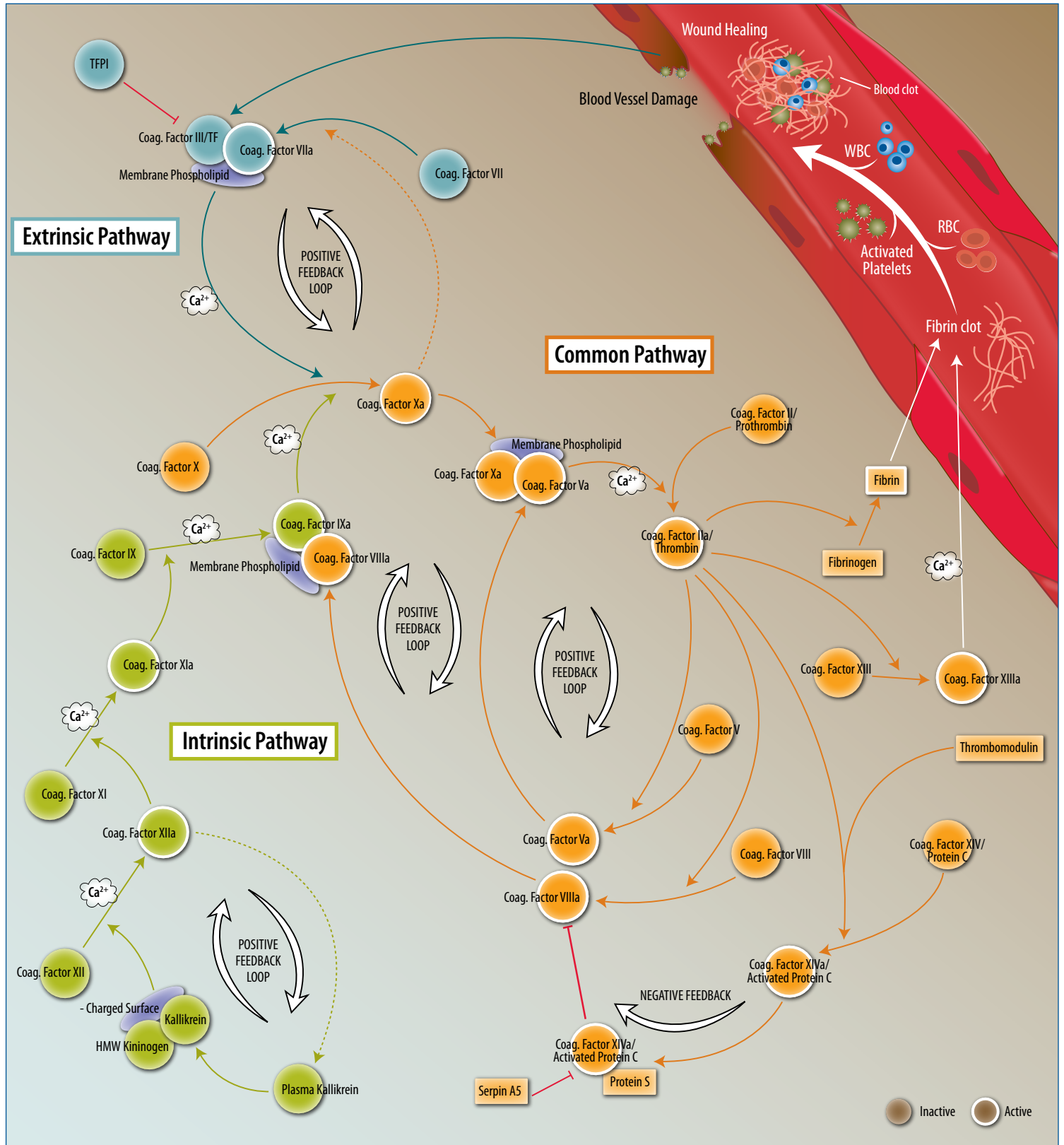


Blood Coagulation



Blood Coagulation

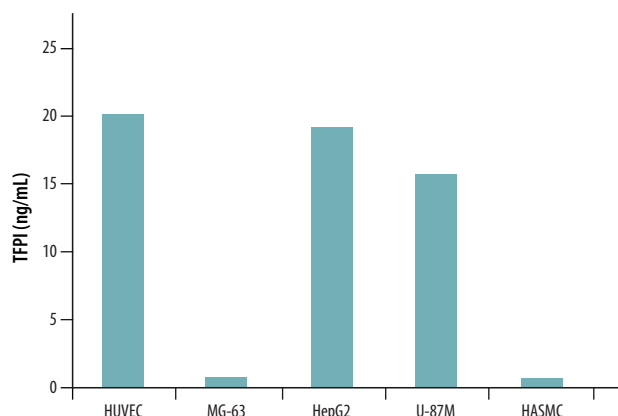


The Blood Coagulation Cascade Promotes the Formation of a Fibrin Clot. Following damage of a blood vessel, the extrinsic pathway of coagulation (blue arrows) is initiated by Coagulation Factor III/Tissue Factor (TF) which forms a complex with Coagulation Factor VIIa and phospholipid, in the presence of Ca^{2+} , to activate Coagulation Factor Xa and rapidly generate Thrombin (IIa). Thrombin cleaves Fibrinogen to produce Fibrin which polymerizes in the presence of Coagulation Factor XIIIa to form a Fibrin clot. The slower, intrinsic pathway of coagulation (green arrows) provides an alternate mechanism for activation of Coagulation Factor Xa. It is initiated by Coagulation Factor XII, Plasma Kallikrein, and high molecular weight Kininogen binding to damaged subendothelial tissue. This results in the cleavage and activation of Coagulation Factor XIIa, which activates Coagulation Factor XIa. This factor then cleaves and activates Coagulation Factor IXa. Coagulation Factor IXa, along with Coagulation Factor VIIIa, activates Coagulation Factor Xa. Events downstream of the activation of Factor Xa are common to both the intrinsic and extrinsic pathways of coagulation (orange arrows). Activated Factor Xa cleaves Prothrombin to generate active Thrombin (IIa) which can then cleave Fibrinogen to produce Fibrin monomers. These monomers are cross-linked by Factor XIIIa to form a Fibrin clot.

Blood Coagulation

Injuries that damage blood vessels promote blood coagulation, a rapid response to initiate hemostasis and protect the host from excessive blood loss. Blood coagulation results from a series of proteolytic reactions involving the step-wise activation of coagulation factors. Subsets of these factors can be activated by two distinct pathways, the extrinsic, or tissue damage pathway (blue arrows), and the intrinsic, or contact pathway (green arrows). Each is initiated by different factors, but both converge upon a single common pathway (orange arrows) that leads to the activation of Coagulation Factor Xa, and the conversion of Prothrombin/Coagulation Factor II to active Thrombin/Coagulation Factor IIa. Thrombin converts Fibrinogen to Fibrin monomers which polymerize to form a Fibrin clot. The Fibrin clot acts in concert with activated platelets at the site of the injury to form a blood clot that stabilizes the damaged tissue and prevents further blood loss.

In addition to directly generating active Fibrin, Thrombin activates Coagulation Factor XIII, which stabilizes Fibrin and promotes its polymerization. Thrombin also activates Coagulation Factors V, VIII, and Protein C. These factors enhance or inhibit Thrombin production through positive or negative feedback. Factors Va and VIIIa promote Thrombin production by positively regulating either the cleavage of Prothrombin itself, or the cleavage and activation of Coagulation Factor Xa, respectively. In contrast, activation of Protein C by Thrombin binding to Thrombomodulin leads to the degradation of Factors Va and VIIIa, and inhibits the cleavage of Prothrombin. These forms of feedback regulation, along with the sequential activation of clotting factors, allow precise control of the blood coagulation cascade. This tight regulation is critical to prevent excessive blood loss associated with too little clotting, or too much clotting, which could result in the blockage of a blood vessel and lead to a heart attack or a stroke. Identifying other regulatory mechanisms may reveal additional molecular targets for exogenous control of clotting activity. R&D Systems offers a variety of research reagents useful for the characterization of molecules involved in blood coagulation pathways.



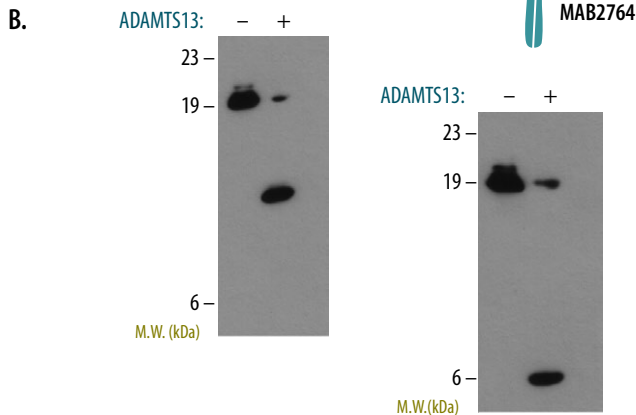
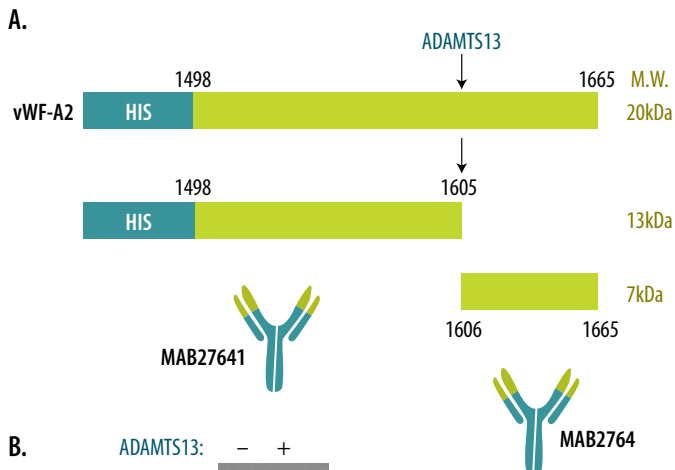
Determination of the Levels of Tissue Factor Pathway Inhibitor (TFPI) in Cell Culture Supernates using the Quantikine® ELISA. Aliquots of cell culture supernates removed from human umbilical vein endothelial cells (HUVEC), MG-63 osteosarcoma cells, HepG2 liver cells, U-87M glioblastoma/astrocytoma cells, or human aortic smooth muscle cells (HASMC) were assayed for levels of TFPI using the human TFPI Quantikine ELISA Kit (Catalog # DTFP10).

Blood Coagulation Research Reagents Available from R&D Systems

Molecule	Recombinant & Natural Proteins	Antibodies	ELISAs/Assays
ADAMTS13	H	H	
Angiostatin		H	
Annexin A2		H M R	
Annexin A6	H		
Annexin V	H	H	Ms
Apolipoprotein H/ApoH		H	
Coagulation Factor II/Thrombin	H	H	
Coagulation Factor III/Tissue Factor	H M	H M	
Coagulation Factor VII	H M	H M	
Coagulation Factor X	H	H	
Coagulation Factor XI	H M	H	
Coagulation Factor XIV/Protein C	H M	H M	
Collagen I	B R		Ms
Collagen II		M	
Collagen IV	M		Ms
Collagen XXV α 1		H	
EPCR		H M	H
Glycoprotein V/CD42d		H	
GPIIb α	H	H	
GPVI	H	H	
Kininogen	H M	H M	
α_2 -Macroglobulin	H	H	
PAR1		H	
PAR2		H	
Plasma Kallikrein/KLKB1	H M	M	
Plasminogen	H	H	
Plasminogen Kringle 5		M	
Protein S/PROS1		H	
SDNSF/MCFD2		H M	
Serpin A1/ α 1-Antitrypsin	H M	H	
Serpin A5/Protein C Inhibitor	H	H M	
Serpin C1/Antithrombin III	H	H M	
Serpin D1/Heparin Cofactor II	H M	H M	
Serpin E1/PAI-1	H	H M	H
TFPI	H M	H M	H
TFPI-2	H	H M	
Thrombomodulin/CD141	H M	H M	
uPA	H	H	H
uPAR	H M	H M	H
vWF-A2	H	H	

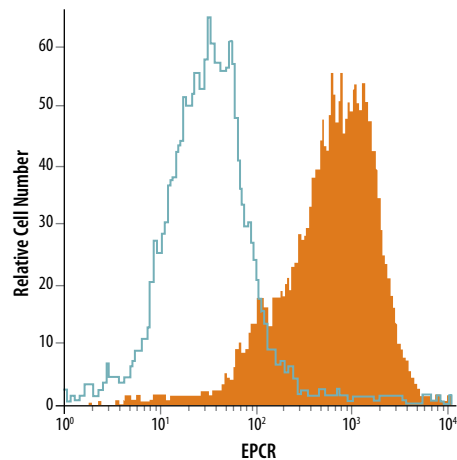
KEY: H: Human M: Mouse R: Rat B: Bovine Ms: Multi-species

For a complete listing of R&D Systems products available for Blood Coagulation research, please visit our website at www.RnDSystems.com/go/Coagulation

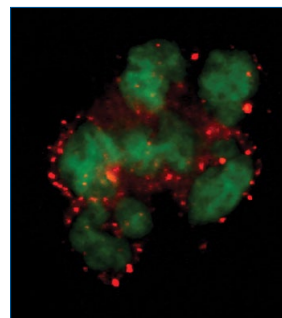


Detection by Western Blot of ADAMTS13-cleaved von Willebrand Factor.

A. Schematic representation of the proteolytic cleavage of His-tagged recombinant human vWF-A2 (Catalog # 2764-WF) by ADAMTS13 (Catalog # 4245-AD). B. Following cleavage by ADAMTS13, the N-terminal fragment of vWF-A2 was detected by Western blot using anti-human vWF-A2 monoclonal antibody (Catalog # MAB27641) and the C-terminal fragment was detected using anti-human vWF-A2 monoclonal antibody (Catalog # MAB2764).



Detection of Endothelial Protein C Receptor (EPCR) in Mouse bEnd.3 Cells by Flow Cytometry. Mouse bEnd.3 endothelial cells were stained with biotinylated anti-mouse EPCR polyclonal antibody (Catalog # BAF2749; filled histogram) or biotinylated normal goat IgG (Catalog # BAF108; open histogram) followed by APC-conjugated streptavidin (Catalog # F0050).



Detection of Coagulation Factor VII in Human Peripheral Blood Mononuclear Cells (PBMC). Coagulation Factor VII was detected in PHA-stimulated human PBMC using anti-human Coagulation Factor VII monoclonal antibody (Catalog # MAB2338). Cells were stained using a Rhodamine Red™ X-conjugated anti-mouse IgG secondary antibody (red) and counterstained with FluoroNissl™ Green (green).

Rhodamine Red and FluoroNissl™ are trademarks of Invitrogen.



R&D Systems, Inc.

614 McKinley Place NE

Minneapolis, MN 55413

TEL: (800) 343-7475

(612) 379-2956

FAX: (612) 656-4400

www.RnDSystems.com

PRSR STD

U.S. POSTAGE

PAID

R&D SYSTEMS



Printed on recyclable paper 10% post consumer waste.