

## Role of Tissue Factor Pathway Inhibitor in the Regulation of Tissue Factor-Dependent Blood Coagulation

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### ABSTRACT

Tissue factor pathway inhibitor (TFPI) is a multivalent, Kunitz-type plasma proteinase inhibitor that modulates tissue factor-dependent coagulation *in vivo*. TFPI possesses a peculiar two-step mechanism of action; it directly inhibits activated factor X and subsequently produces feedback inhibition of the factor VIIa/tissue factor catalytic complex in a factor Xa-dependent fashion. TFPI biochemistry and physiology have been extensively studied during the last decade. Its pathophysiologic role in thrombotic disorders has, however, only recently started to be unraveled. In particular, circulating plasma TFPI levels have been found to modulate the activity of the tissue factor-dependent coagulation cascade. In animal models, neutralization of circulating TFPI activity results in restoration of intravascular thrombus formation previously abolished by aspirin. In patients with acute myocardial infarction, TFPI plasma levels measured in blood samples obtained from the coronary sinus were significantly lower than those measured in blood obtained from the ascending aorta, indicating acute consumption of TFPI within the coronary circulation of patients with intracoronary thrombosis. Finally, recent data indicate that transfection of the arterial wall with the gene coding for TFPI is an effective therapeutic intervention to prevent intravascular thrombus formation. Taken together, these observations underline the pathophysiologic importance of TFPI in regulating the procoagulant activity of tissue factor and open new potential therapeutic approaches for the treatment of thrombotic disorders.