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ABSTRACTS OF THE 57TH SCIENTIFIC SESSIONS

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's-GravenhageINHIBITION OF TISSUE TYPE PLASMINOGEN
ACTIVATOR INHIBITOR ACTIVITY BY ACTIVATED
PROTEIN C

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Confluent cultures of EC from human umbilical cord, when incubated in serum free medium, produce t-PA antigen, t-PA inhibitor activity, and F VIIIIRAg. Addition of highly purified APC ($\leq 0.2\%$ thrombin) did not effect protein synthesis in general or the production of t-PA antigen and F VIIIIRAg. However, APC -but not protein C or DIP-APC- significantly inhibited the accumulation of t-PA inhibitor activity in the cell supernatant (33% inhibition at 60 nM APC in 5 different cell cultures); this effect of APC was dose-dependent and sensitive to anti-protein C IgG. Subsequent studies revealed that APC also inhibits the activity of t-PA inhibitor in EC-conditioned medium. From the other proteases tested (Xa, IXa, thrombin) only thrombin -at relatively high concentrations- gave inhibition of the t-PA inhibitor activity. It is concluded that APC has no direct effect on the production of t-PA and F VIIIIR:Ag in EC cultures; however, APC might contribute to the regulation of fibrinolysis by its inhibitory action on t-PA inhibitor. The physiological significance of this reaction needs further evaluation.