

## ***The Effect of the Protein C System On Prostate Tumor Cell Invasion***

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### ***Background and Objective***

We investigated the ability of thrombomodulin (TM), thrombin, protein C, and activated protein C (APC) to affect prostate tumor cell invasion by regulating interactions between plasminogen activator inhibitor-I (PAI-1) and urokinase type plasminogen activator (uPA).

### ***Methods***

Modified Boyden Chambers were used to measure invasion of DU-145 CaP cells in the presence and absence of TM, thrombin, protein C, and APC, uPA, PAI-1 and monoclonal antibodies (MAb) to TM.

### ***Results***

MAb binding to TM's chondroitin sulphate domain increased DU-145 invasion. Addition of thrombin and protein C did not affect invasion. Addition APC at high concentrations slightly decreased invasion. Invasion increased when uPA and PAI-1 were added in the presence of APC.

### ***Discussion and Conclusions***

Binding to TM on CaP cells increased invasion *in vitro*. Addition of thrombin, protein C, and APC did not affect invasion. However, in the presence of uPA and PAI-1, APC competed with uPA for binding to PAI-1, enabling uPA to increase the invasiveness of DU-145 cells. We conclude that in the presence of TM, thrombin, protein C, PAI-1 and uPA, TM regulates tumor cell invasion by generating APC, which can bind to PAI-1, freeing uPA to facilitate tumor cell invasion.

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