The potential for solid tumors to activate the coagulation system and to induce venous thrombosis is referred to as Trouseau's syndrome. There has been considerable advancement in the understanding of how cancer affects the coagulation system. On other side, a body of evidence has emerged suggesting the coagulation system has important effects on tumors.

Haemostasis is controlled by the balance of forces that cause blood to solidify or to remain fluid. The process is very delicate and involves several interacting systems. Tissue factor (TF) and thrombomodulin (TM) are transmembrane receptors involved in the regulation of procoagulant and anticoagulant reactions.

Recently, the roles of these receptors other than as coagulant receptors, have been investigated and both have been demonstrated to have multiple functions beyond coagulation. Either targeted gene disruption or knockout studies of these two receptors suggested additional roles for TF and TM beyond the coagulation pathway in embryogenesis. TF and TM are expressed in tumors. Clinical findings show that TF expression by tumor cells is positively correlated with tumor associated angiogenesis, whereas TM is negatively correlated with tumor cell proliferation.

In this work, the two transmembrane receptors, TF and TM, who are playing opposite roles in the control of haemostasis, were studied with regards to functions distinct from coagulation.

By introducing mutations to the wildtype cDNAs and subsequent overexpression in tumor cells, we demonstrated:

1. TF induces VEGF.
1a. TF induce transcription of VEGF, a potent angiogenic factor;
1b. TF exerts this role independent from binding of its ligand, factor VIIa;
1c. TF exerts this role via its cytoplasmic tail, which can be phosphorylated in vitro, having the potential to transduce intracellular signals.
2. TM negatively regulates tumor cell proliferation.
2a. TM expression in tumor cells reduces $H^3$-thymidine incorporation and proliferation;
2b. TM reduces proliferation independent of its anticoagulant property;
2c. The lectin-like domain and cytoplasmic tail are required for its role in modulating tumor cell proliferation.

In conclusion, TF and TM, who have opposing activities in the coagulation cascade, also have distinct yet opposing properties in tumor cell biology. These cell biologic properties are independent of coagulation. The *in vitro* findings correlate well with clinical observations.