

This invention relates to novel fusion proteins which are comprised of a targeting protein that binds tissue factor (TF), which is operably linked to the thrombomodulin (TM ) EGF456 domain alone or in combination with at least one other TM domain selected from the group consisting of the N-terminal hydrophobic region domain, the EGF123 domain, the interdomain loop between EGF3 and EGF4, and the O-glycosylated Ser/Thr-rich domain, or analogs, fragments, derivatives or variants thereof. The fusion protein binds at the site of injury and prevents the initiation of thrombosis. The fusion protein can be used to treat a variety of thrombotic conditions including but not limited to deep vein thrombosis, disseminated intravascular coagulation, and acute coronary syndrome.