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Diverse biological functions of thrombomodulin in cells and wound healing

Thrombomodulin (TM) is a type I transmembrane glycoprotein that was formerly identified as an anticoagulant factor in endothelial cells (ECs) in 1982. It can form a complex with thrombin to facilitate the activation of protein C in the blood circulation. The activated protein C will catalyze the cleavage and inactivation of coagulation factors to constrain the blood coagulation cascade. However, TM was also identified in various cell types which do not have direct contact with blood circulation, indicating that TM may have distinct biological functions in different cell types and contexts.

In our studies we demonstrated that TM was highly concentrated at the cell-cell contact region in ECs and keratinocytes, where it functions as an adhesion protein, in conjunction with cadherin/occludin, to stabilize cell-cell junctions. Moreover, we also demonstrated that lectin domain of TM is essential for cell-cell adhesion and LeY oligo-saccharide is the ligand of the lectin domain. The cytoplasmic domain of TM can be anchored to F-actin through actin linker protein ezrin. In addition, TM expression is involved in the epithelial/mesenchymal transition in cancer cells.

On the other hands, we demonstrated that TM functions as a novel plasminogen (Plg) receptor in migrating cells. The dissociation constant of Plg and TM is about 10-7M as determined by Biacore plasma resonance system. TM, plg and urokinase Plg activator was colocalized at the leading edges in the migrating ECs. It is possible that TM expression can promote Plg activation to facilitate the pericellular proteilysis in front of migrating ECs to facilitate cell migration, invasion and angiogenesis.

Keywords: Thrombomodulin, cell-cell adhesion, angiogenesis, inflammation, vascular disease, and wound healing

Recent Publications

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Biography

Hua-Lin Wu is a chair person and presently working as distinguished professor of department biochemistry and molecular biology in the college of medicine, National Cheng Kung University, Taiwan. He has completed his PhD in Ohio State University. Then he started working as distinguished professor in National Cheng Kung University in 2002 to at present. He has awarded with 24th Wusanlien Award (2001) and also "The 16th National Chair Professorship Award" in 2013. His research interest includes Vascular biology, Haemostasis and fibrinolysis and Protein drug development.

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