Cell Adhesion Molecule 1 (CADM1), a Novel Venous Thrombosis Risk Factor, Is Ubiquitously Present in Vascular Endothelium and Smooth Muscle Cells

Tatsumi K[1,], Taatjes DJ[1], Bouchard BA[2], Trotman W[1], Bovill EG[1,3]. University of Vermont College of Medicine, Departments of Pathology[1] and Biochemisry[2] and Fletcher Allen Health Care (FAHC)[3] Burlington VT.

We recently demonstrated that CADM1, interacting with protein C deficiency, is a novel risk factor for venous thrombosis and identified for the first time its expression in endothelial cells. In this study, we have determined the distribution of CADM1 in human vasculature. *Methods*: Human tissue samples representing all organs as well as large vessels were accessioned from archived paraffin blocks from the surgical pathology division of FAHC . Tissue sections were processed for immunoflourescence using antibodies against CADM1, smooth muscle actin (SMA), and Von Willebrand factor (vWF). Intensity of staining was rated as absent, trace or present by three observers. Immunoelectron microscopy (IEM) was performed on cultured human umbilical vein endothelial cells using a post embedding procedure with protein-A gold. Peripheral blood leukocytes were evaluated for the presence of CADM1 using the same antibody following cytospin preparation. *Results*: CADM1 was found ubiquitously in the macro- and micro-vasculature of all organs as well as the aorta and saphenous vein with intensity of staining showing modest variability from organ to organ. CADM1 staining of SMA was observed in both arterial and venous vessels but was considerably stronger on the arterial side. IEM demonstrated cytoplasmic immunogold staining associated with elements of rough endoplasmic reticulum and actin filaments as well as at the membranes of filopodia. In contrast, peripheral blood cells were negative for CADM1expression. *Conclusions*: CADM1 is expressed ubiquitously in endothelial and smooth muscle cells of the macro-and micro-vasculature with IEM evidence for its presence in filopodial cytoplasm and membranes. This is the first report of CADM1 positivity in vascular smooth muscle cells. The biological role of CADM1 remains to be determined but its ubiquitous expression in the endothelium of the macro- and micro-circulation, together with an apparent role in endothelial cell motility, suggests an important role in endothelial barrier function.