S52-3 Signaling mechanism involved in regulation of endothelial cell-cell junctions

◯Shigetomo FUKUHARA[1], Naoki MOCHIZUKI[1]

[1]Dept. of Structural Analysis, NCVC

Endothelial cells lining blood vessels tightly contact with each other, thereby maintaining vascular integrity. Compromising vascular integrity leads to an increase in vascular permeability, which is associated with chronic inflammation, edema and tumor angiogenesis. Vascular endothelial (VE)-cadherin is an endothelium-specific cell-cell adhesion molecule involved in endothelial barrier functions. We have previously reported that cyclic AMP-elevating agonists such as prostaglandins and adrenomedullin potentiate VE-cadherin-dependent cell adhesion by inducing activation of Rap1 small GTPase through Epac.

We further investigated the mechanism whereby Rap1 potentiates VE-cadherin-dependent cell adhesions, and found that Rap1 induces formation of circumferential actin bundles along the cell-cell junctions. Although it has been believed that α-/β-catenins anchor cadherin to actin cytoskeleton to stabilize cadherin at cell-cell junctions (Static model), Nelson's group has recently suggested a new dynamic model that α-/β-catenins does not stably connect actin to cadherin. However, our study clearly indicated that the circumferential actin bundles anchor VE-cadherin to the cell-cell junctions through α-/β-catenins. Thus, it is revealed that Rap1 potentiates endothelial cell-cell junctions through the mechanism based on the static model. In this symposium, we will also discuss how angiopoietin-1/Tie2 receptor signal regulates endothelial cell-cell junctions.