Differential regulation of LPS-mediated VE-cadherin disruption in human endothelial cells and the underlying signaling pathways: a mini review

ABSTRACT

Endothelial cells lining the inner vascular wall form a monolayer that contributes to the selective permeability of endothelial barrier. This selective permeability is mainly regulated by an endothelium-specific adherens junctional protein, known as vascular endothelial-cadherin (VE-cadherin). In endothelial cells, the adherens junction comprises of VE-cadherin and its associated adhesion molecules such as p120, α-catenin, and β-catenin, in which α-catenin links cytoplasmic tails of VE-cadherin to actin cytoskeleton through β-catenin. Proinflammatory stimuli such as lipopolysaccharide (LPS) are capable of attenuating vascular integrity through the disruption of VE-cadherin adhesion in endothelial cells. To date, numerous studies demonstrated the disruption of adherens junction as a result of phosphorylation-mediated VE-cadherin disruption. However, the outcomes from these studies were inconsistent and non-conclusive as different cell fractions were used to examine the effect of LPS on the disruption of VE-cadherin. By using Western Blot, some studies utilized total protein lysate and reported decreased protein expression while some studies reported unchanged expression. Other studies which used membrane and cytosolic fractions of protein extract demonstrated decreased and increased VE-cadherin expression, respectively. Despite the irregularities, the results of immunofluorescence staining are consistent with the formation of intercellular gap. Besides that, the overall underlying disruptive mechanisms of VE-cadherin remain largely unknown. Therefore, this mini review will focus on different experiment approaches in terms of cell fractions used in different human endothelial cell studies, and relate these differences to the results obtained in Western blot and immunofluorescence staining in order to give some insights into the overall differential regulatory mechanisms of LPS-mediated VE-cadherin disruption and address the discrepancy in VE-cadherin expression.

Keyword: Endothelial; VE-cadherin; Protein; Vascular