ABSTRACT

Identifying CD36 as a Receptor for Albumin Transcytosis by Dermal Microvascular Endothelial Cells

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Albumin is the most abundant serum protein and its accumulation in the interstitial space leads to tissue edema. The movement of albumin from the vascular lumen to the interstitial space is not well characterized, but under resting conditions is thought to involve transcytosis. Little is known regarding the mechanism of endothelial albumin transcytosis and how it varies across the tissue beds. Using a novel assay based on TIRF microscopy, in this present study I have shown that albumin transcytosis is saturable in the skin but not the lung microvascular endothelial cells, implicating a receptor-mediated process. I have identified the scavenger receptor CD36 as being necessary for albumin transcytosis across the dermal microvascular endothelium, in contrast to the lung where macropinocytosis dominates. Mutations in the apical helical bundle of CD36 prevented albumin internalization by cells. A modified Miles assay in mice deficient in CD36 in endothelial cells exhibited a lower basal permeability to albumin and less basal tissue edema in the skin but not in the lung. Finally, these mice also exhibited a smaller subcutaneous fat layer despite having comparable total body weights and circulating fatty acid levels as wild-type animals. These findings shed light on the mechanism and functional importance of albumin transcytosis, which holds implications both for better understanding fatty acid transport and enhancing tissue-specific drug delivery.