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Relationship between AGE scavenging and angiogenesis in endothelial cell

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Advanced glycation end products (AGEs) are biologically reactive compounds associated with diabetic complications and aging-related disorders. Exposure to AGEs in endothelial cells lead to excess angiogenesis, however, molecular mechanisms underlying AGE-elicited angiogenesis remain unclear. Many types of receptors, such as receptor for AGEs (RAGE), toll like receptor-4 and scavenger receptors, are expressed in endothelial cells and contribute to the AGE-elicited alteration of cell function. Scavenger receptors has been thought to play a significant role in the recognition and elimination of AGEs from the circulation. The involvement of scavenger receptors on the AGE-elicited excess angiogenesis is still unknown. We found that three types of scavenger receptors (CD36, CD163 and lectin-like oxidized LDL receptor-1; LOX-1) contribute to the AGEs-induced enhancement of angiogenesis. The cocktails of neutralizing antibodies against CD36, CD163 and LOX-1 prevented tube formation but not AGE uptake. On the other hand, AGE-RAGE pathway is indirectly involvement in enhancement of tube formation mediated by upregulation of scavenger receptors on cell surface. Fucoidan, which is sulfated polysaccharide derived from brown algae and non-selective scavenger receptors inhibitor, suppressed AGE-elicited tube formation. Our findings propose that therapies drug for AGE-relating disorders need to have capacity inhibiting multiple scavenger receptor in endothelial cells.