

A novel link between inhibition of angiogenesis and tolerance to vascular stress

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The vascular endothelium forms the interface against blood stream. Functional integrity of the vascular endothelium is essential for the maintenance of vascular health, counteracting the occurrence of vascular diseases including atherosclerosis and diabetic vascular complications. In light of its important role, the vascular endothelium should have a self-defense system. One candidate of such a system is vasohibin-1 (VASH1), a protein preferentially expressed in vascular endothelial cells (ECs). We have isolated VASH1 as a novel angiogenesis inhibitor synthesized by ECs. Unique features of VASH1 are its anti-angiogenic activity as well as ability to promote stress tolerance of ECs and their survival. When ECs are exposed to cellular stresses, the synthesis of VASH1 protein in ECs is enhanced through posttranscriptional mechanism, and that makes ECs resistant to stress-induced premature senescence via the expression of superoxide dismutase 2 (SOD2) and sirtuin 1 (SIRT1).

We have recently found that the expression of VASH1 is decreased during the replicative senescence of ECs. The mechanism and significance of age-related down-regulation of VASH1 will be discussed in the meeting.