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The Protective Role of Endothelial SIRT1 Against Vascular Aging and Hypertension

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Background

Introduction: SIRT1 is a gene that regulates aging. In the inner lining of blood vessels, called the endothelium, SIRT1 promotes healthy aging of blood vessels and regulates the endothelial function of blood pressure regulation. Aging hardens blood vessels and increases the risk of hypertension and other cardiovascular complications. When endothelial SIRT1 is expressed, endothelial function is enhanced, smooth muscle cell proliferation and remodeling are prevented, vascular contraction and dilatation are properly regulated, and cardiovascular diseases are ultimately avoided. **Objectives**: This study investigated the beneficial effects of SIRT1 in the vascular endothelium against vascular aging and hypertension. **Methods**: three types of mice were studied; normal mice without any genetic modification, known as wild-type (WT) mice, mice with overexpression of human vascular endothelial SIRT1, known as EC-SIRT1 mice, and mice with overexpression of a mutant and non-functional SIRT1 in the vascular endothelium, known as EC-H363Y mice. Body weight and circulating blood glucose of mice were measured. Systolic blood pressure was measured from the tail of mice. Vascular function analysis was done with a wire myography system. Senescence staining of full length aorta was done and protein expression of endothelial nitric oxide synthase, the enzyme responsible for promoting vasodilatation, was measured in the aorta of mice.

Results 1: Body weight & blood glucose

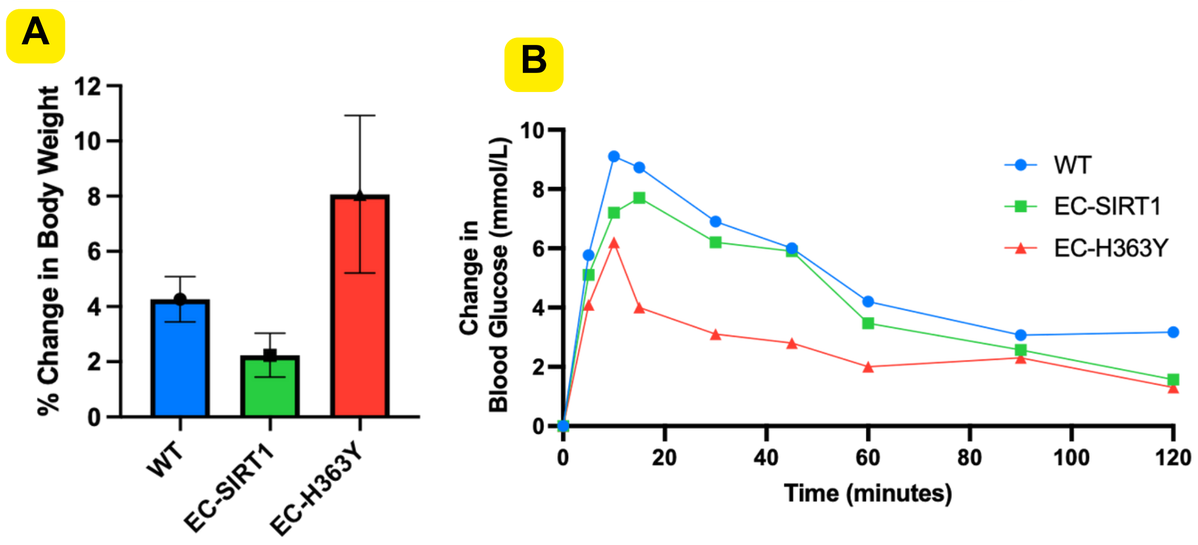


Figure 1: Body weight (A) and glucose metabolism profile (B) were measured in WT, EC-SIRT1 and EC-H363Y mice at ~20 and ~30 weeks old. Data are presented in mean ± SEM.

Results 2: Blood pressure & vascular function

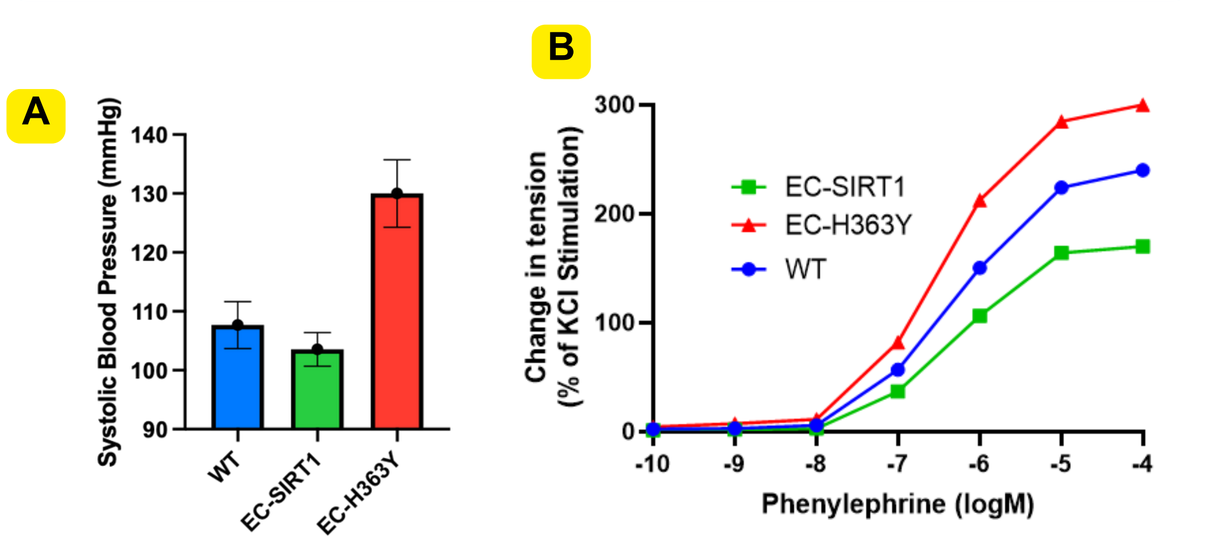


Figure 2: Blood pressure (A) and aortic contraction (B) were measured in ~30 weeks old WT, EC-SIRT1 and EC-H363Y mice. Data are presented in mean ± SEM.

Results 3: Endothelial senescence & protein expression

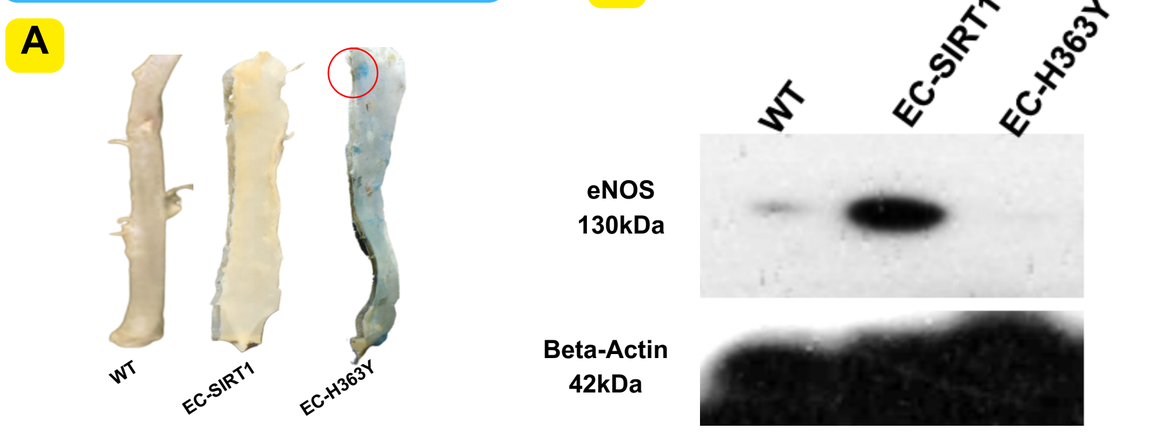
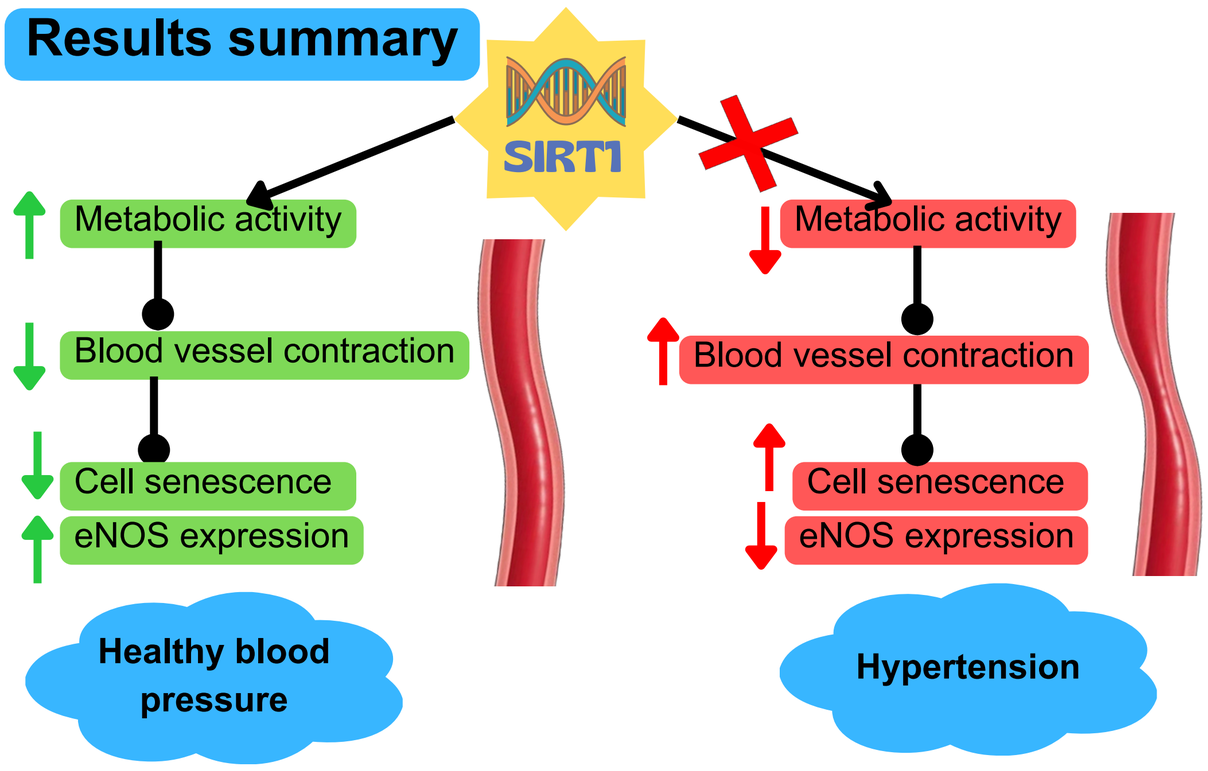


Figure 3: Aortae of ~30 weeks old WT, EC-SIRT1 and EC-H363Y mice were stained for senescent endothelial cells. Blue marks indicate senescence (A). Western blotting was performed to measure protein expression of endothelial nitric oxide synthase (eNOS) of the same aged mice.

Results summary



Conclusion

This study demonstrated that overexpression of SIRT1 in the vascular endothelium is protective against vascular aging and hypertension. Dysfunctional negative dominant SIRT1 expression in the endothelium promoted vascular aging and increased blood

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