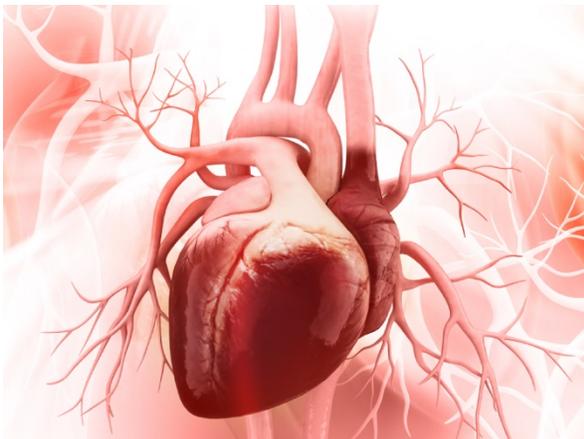


Lifelong SIRT-1 Overexpression Attenuates Large Artery Stiffening With Advancing Age

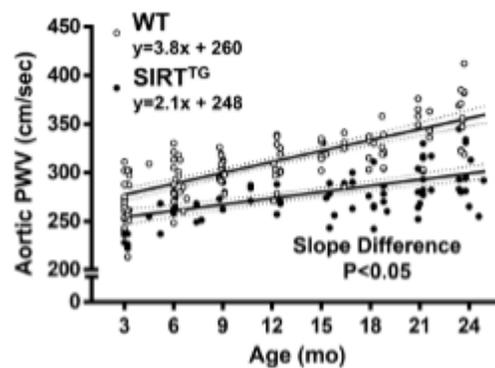
In the United States, there is a progressive increase in cardiovascular diseases (CVDs) related to aging. The prevalence of advancing age-related deaths associated with CVDs has highlighted the important research efforts to understand the cause, treatment, and prevention of age-related CVD.

One cause/consequence of CVDs in aging is the change of arterial phenotype from elastic to stiffened arteries. Arterial stiffness is a non-invasive indicative measure of CVD severity and progression and is associated with an increased risk of cardiovascular events. So, reversing age-related arterial stiffening is a priority target of treatment. Aortic stiffness is typically assessed using ultrasound Doppler flow velocity measurements to determine pulse wave velocity (PWV) in a particular vessel. Research has shown that advanced-age aortic stiffening is associated with decreasing sirtuin-1 (SIRT-1) expression. Previous caloric restriction studies have shown that SIRT-1 KO ameliorates the caloric restriction protective effect of vascular stiffening with aging. Reciprocally, would increasing SIRT-1 expression amend age-related aortic stiffness?



Daniel R. Machin in Anthony J. Donato's lab at the University of Utah, published that SIRT-1 overexpression attenuates stiffening of the major vasculature with aging. They did this in 3-24 months SIRT-1 transgenic overexpressing and control mice.

The primary outcome measure was the change in aortic PWV over time through parallel non-invasive measurements with ultrasound Doppler flow velocity at 3-month intervals. Generally, increased velocity is associated with increased stiffening of the blood vessel. Histology of the aorta, for both morphology and composition, was assessed to corroborate the *in vivo* findings at approximately 6, 12, and 24 months of age.



The study suggests that with aging (3-24 mo), PWV increase in presence of SIRT-1 overexpression is about 40% lower compared to control. Histology further showed that aortic elastin content decrease was ameliorated in the SIRT-1 overexpressing mice. Conversely, the age-associated increase in aortic collagen, advanced glycation end products, and calcification seen in controls were similarly ameliorated in the SIRT-1 overexpressing mice. As permanent SIRT-1 overexpression can reduce age-related aortic stiffening, it can be highlighted as a viable interventional target for further investigation.

Reference:

Machin DR, Auduong Y, Gogulamudi VR, Liu Y, Islam MT, Lesniewski LA, Donato AJ. Lifelong SIRT-1 overexpression attenuates large artery stiffening with advancing age. *Aging (Albany NY)*. 2020 Jun 20;12(12):11314-11324. doi: 10.18632/aging.103322. Epub 2020 Jun 20. PMID: 32564006; PMCID: PMC7343505.