**Increased Aortic Stiffness and Attenuated Lysyl Oxidase Activity in Obesity**

**Aortic stiffness** has been proposed as an indicator of **vascular aging**. One potential mechanism through which obesity exerts adverse effects on the vascular system is by increasing aortic stiffness, a change known to be predictive of increased cardiovascular mortality. The aim of this study was to investigate the pathophysiology that links obesity to aortic stiffening. We found that ob/ob mice had increased aortic pulse wave velocity (PWV) and tissue rigidity. ob/ob aorta exhibited decreases of lysyl oxidase (LOX) activity and cross-linked elastin, and increases of elastin fragmentation and elastolytic activity. The aortas of ob/ob mice were surrounded by a significant amount of proinflammatory and pro-oxidative perivascular adipose tissue (PVAT). In *in vitro* studies revealed that the conditioned medium from differentiated adipocytes or the PVAT of ob/ob mice attenuated LOX activity. Furthermore, inhibition of LOX in wild-type lean mice caused elastin fragmentation and induced a significant increase in PWV. Finally, we found that obese humans had stiffer arteries and lower serum LOX levels than do normal-weight humans. In conclusion, our results demonstrated that obesity resulted in aortic stiffening in both humans and mice, and established a causal relationship between LOX downregulation and aortic stiffening in obesity.

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**Fig.1. Higher aortic PWV and stiffness in obese mice**

**Fig.2. Decreased LOX activity and elastin cross-linking, and increased elastolytic activity in the ob/ob aorta**

**Fig.3. Increased perivascular adipose tissue (PVAT) in ob/ob mice**

**Fig.4. Higher inflammatory cytokine expression and oxidative stress in the PVAT and aortas of ob/ob mice**

**Fig.5. Increased aortic stiffness and elastin fragmentation by inhibition of LOX activity**

**Fig.6. Arterial stiffening and lower LOX levels in obese humans**

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**Hypothesis**

- Observation
  1. Elastin fragmentation
  2. Lysyl oxidase ↓
  3. PVAT releasing factors

**Arterial stiffness**

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**Conclusion**

- Obesity resulted in aortic stiffening in both humans and mice
- A causal relationship between LOX downregulation and aortic stiffening in obesity
- LOX downregulation and proinflammatory, pro-oxidative PVAT as key mediators of aortic stiffening in obesity

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