1. **No.**

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2. **Title**

   The Effect of Smoking on the Development of Aortic Aneurysms: an Innovative Approach Using a Novel Mouse Model.

3. **Period**

   2016-2020

4. **Summary**

   The purpose of this study is to clarify the relationship between thoracic aortic aneurysm and smoking substances using a mouse model. Thoracic aortic aneurysm has less inflammatory findings than abdominal aortic aneurysm and has been reported to be caused by disruption of extracellular matrix and activation of TGFβ signaling, however, the association between thoracic aneurysm and smoking and its potential mechanism are not clear. We identified exacerbating factors of aortic aneurysm, TSP1, using our mouse model, and found that TSP1 was increased in smooth muscle cells by smoking-related substances (nicotine and oxidative stress). Furthermore, cell experiments confirmed that oxidative stress impaired endothelial cell-cell junctions. It was suggested that smoking-related substances may exacerbate aortic aneurysm by causing endothelial dysfunction. Therefore, we created another mouse model of thoracic aneurysm that causes endothelial dysfunction and investigated the relationship with aortic aneurysm. We found that aortic aneurysm exacerbates when endothelial dysfunction does occur. Based on these findings, we propose that smoking-related substances promote the growth of thoracic aneurysms by inducing aortic exacerbation factors as well as causing endothelial dysfunction.