1. **No.**

   FP01902052

2. **Title**

   The Role of Nicotine in Inducing Aortic Aneurysm

3. **Period**

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4. **Summary**

Atherosclerosis induced by hyperlipidemia and abdominal aortic aneurysm is a major problem in our country. In the current research, we have investigated the role of inflammatory signaling involving prostaglandin and its receptor EP4 in the development of atherosclerosis and abdominal aneurysm. In particular, we have investigated the involvement of gaseous components of cigarette smoke in abdominal aneurysm formation. We used vascular smooth muscle cells obtained from human aorta. We investigated the effects of cigarette smoke extract (CSE) or acrolein treatment on changes in EP4 expression. We also investigated the role of prostaglandin receptor EP4 by generating smooth muscle specific overexpression of EP4 mice in development of abdominal aortic aneurysm. Acrolein stimulation (10 micro mol/l) for 24 h increased EP4 mRNA in human aorta smooth muscle cells. CSE stimulation (0.1 mg/ml) for 24 h increased EP4 mRNA, as well. EP4 overexpression mice administered with angiotensin II exhibited abdominal aortic aneurysm, and 75 % of EP4-Tg mice died of AAA rupture within two weeks. However, none of control mice exhibited abdominal aortic aneurysm. Further, vascular smooth muscle cells overexpressing EP4 showed decreased LOX expression in the presence of acrolein. Our data suggest that EP4 signal plays a major role in developing aortic aneurism. A specific component in cigarette smoking may accelerate this process through regulating LOX signal.