1. No.
   2017T005

2. Title
   Role of Inflammasomes in the Pathogenesis of Inflammation-madiated Atherosclerosis due to Smoking Habit

3. Period
   2017-2021

4. Summary
   We investigated the link between smoking and NLRP3 inflammasome in macrophages but observed that cigarette smoke extract (CSE) and related compounds had little or no effects on NLRP3 inflammasome activation. On the other hand, we found that CSE markedly induced cell death in vascular smooth muscle cells (VSMCs) and identified that CSE-induced VSMC death is an iron-dependent cell death, known as ferroptosis. VSMC ferroptosis was induced by acrolein (ACR) and methyl vinyl ketone (MVK), major constituents of CSE. In addition, CSE caused arterial VSMC ferroptosis and medial cell loss in *ex vivo* murine aortas. These findings suggest that CSE-induced ferroptosis contributes to the development of aortic aneurysm/dissection. We also found that CSE induced ferroptosis in macrophages through a PKC-dependent pathway. Moreover, PKC was involved in ACR-induced ferritin degradation (ferritinophagy) and intracellular Fe2+ elevation. Taken together, our findings demonstrate that ferroptosis is responsible for CSE-induced cell death and provide new insights into the role and mechanism of smoking-induced cell and tissue damage.