1. No.
   2022Y010

2. Title
   Exploring the molecular mechanisms of smoking-induced exacerbation of heart failure

3. Period
   2022-2023

4. Summary
   Smoking increases the risk of heart failure, yet its direct effects on cardiac tissue remains unclear. We tested our hypothesis that smoking induces cellular senescence in macrophages and causes dysregulation in macrophage polarization which mediates cardiomyocyte hypertrophy, cardiac fibrosis and inflammation. We have previously reported that CSE induces both nuclear and mitochondrial DNA damage leading to activation of innate immune response via a cytosolic DNA sensor called the cGAS-STING pathway in vascular endothelial cells. We investigated whether CSE induced inflammation in a similar mechanism in the component cells of the heart. The results from the study conducted previous year using murine bone marrow-derived macrophages suggested that CSE caused dysregulation of polarization and induced cellular senescence in macrophages. We investigated the effects of CSE on cellular senescence and inflammation in cardiomyocytes using murine cardiac cell line derived (HL-1). The results indicated that CSE induced cellular senescence and inflammation. However, CSE-induced DNA double-strand breaks were not detected in HL-1 cells. Previous reports suggests that smoking induces various types of DNA damage, thus CSE-induced increases of IL-6 and MCP1 mRNA levels are possibly due to DNA single-strand breaks, oxidative damage or mitochondrial DNA damage. In future studies, it needs to be identified that CSE causes which type of DNA damage in cardiomyocytes. In addition, the effects of CSE on cellular interaction between macrophages and cardiomyocytes needs to be investigated.