1. No.
   2022Y013

2. Title
   The Novel Mechanism of Smoking/Atherosclerosis with Focus of Streptococcus

3. Period
   2022-2024

4. Summary
   This three-year study aimed to test the hypothesis that the translocation of *Streptococcus*, a dominant genus in the oral microbiota, to the gut contributes to the progression of smoking-induced atherosclerosis. In the first year, fecal samples from Japanese health check-up participants were analyzed using 16S rRNA amplicon sequencing. Contrary to previous findings in the duodenal mucosa, no increase in fecal *Streptococcus* was observed in smokers, suggesting that smoking-induced microbiota alterations may differ between mucosal and fecal compartments. In the second year, long-term treatment with streptolysin O, a *Streptococcus*-derived exotoxin, to Wistar rats resulted in elevated blood pressure and impaired vascular reactivity. These effects were suppressed by a TLR4 inhibitor, indicating a TLR4-mediated mechanism. In the final year, the impact of cardiolipin, a structural component of *Streptococcus*, on endothelial function was investigated. Long-term exposure reduced acetylcholine-induced vasorelaxation and decreased endothelial nitric oxide synthase (eNOS) expression. Collectively, these findings suggest that *Streptococcus*-derived components can impair vascular endothelial function and may contribute to the development of hypertension and atherosclerosis.