1. No.
   2019T006

2. Title
   Mechanism of suppression / treatment of progression of chronic kidney disease through nicotinic receptor

3. Period
   2019-2021

4. Summary
   In the first year, we examined the effects of vagus nerve stimulation on a model of chronic kidney disease (kidney fibrosis) using unilateral ischemia-reperfusion injury (ischemia for 26 minutes), but were unable to obtain reproducible results. We are currently improving the optogenetics method to establish a method for noninvasive and repeated vagus nerve stimulation, and will conduct another study as soon as the method is established.

   In the second year, we were able to demonstrate for the first time in the world the effects of vagus nerve stimulation after kidney injury using a cisplatin nephropathy model. Plasma cytokine levels were evaluated, and it was found that CCL2, a chemokine involved in the migration of monocytes and macrophages induced by cisplatin administration, was suppressed by vagus nerve stimulation, resulting in decreased macrophage infiltration into the kidney.

   In the final year, the significance of α7 nicotinic acetylcholine receptor-positive macrophages i*n vivo* was clarified using the macrophage-specific α7 nicotinic acetylcholine receptor knockout mice that were generated. In addition, by combining single-cell RNA-seq of the spleen, ligand-receptor analysis, Transwell migration assay, and splenectomy experiments, we found that α7 nicotinic acetylcholine receptor stimulation enhances macrophage-macrophage interactions and exerts anti-inflammatory and kidney protective effects.