1. No.
   2023G023

2. Title
   Role of Brain-Gut Axis via Vagus Nerve in Depression-Like Behaviors of α7 nAChR KO Mice

3. Period
   2023-2025

4. Summary

   During the entire study period, we investigated the role of the α7 nicotinic acetylcholine receptor (α7 nAChR) in systemic pathophysiology, with a particular focus on the interplay among the gut, immune system, bone, and brain. In the first year, we examined female *Chrna7* knock-out (KO) mice and found that bone mineral density (BMD) was significantly lower in these mice than in wild-type controls. Furthermore, ovariectomy (OVX) caused a greater reduction in BMD in *Chrna7* KO mice, suggesting that α7 nAChR is involved in maintaining bone homeostasis in females. These findings raised the possibility that loss of *Chrna7* contributes to osteoporosis-related phenotypes through the gut microbiota–bone axis.

   In the second year, we used a cuprizone (CPZ)-induced demyelination model to investigate the role of vagal signaling and α7 nAChR-mediated neuroimmune interactions in demyelinating pathology. CPZ feeding induced demyelination in multiple brain regions, and our findings suggested that α7 nAChR deficiency and vagotomy influence the severity of demyelination. These results support the idea that a vagus nerve–dependent neuroimmune network contributes to central nervous system pathology.

   Taken together, this research demonstrates that α7 nAChR plays a broad regulatory role across peripheral and central systems, linking bone metabolism, immune regulation, and brain pathology. Our findings provide an integrated framework for understanding how body–brain communication pathways may contribute to both somatic and neuropsychiatric disorders.