1. No.
   2018T001

2. Title
   New Therapeutic Strategy to AD/HD Targeting Nicotinic Aetylcholine Receptors

3. Period
   2018-2022

4. Summary

   Attention-deficit/hyperactivity disorder (AD/HD) is a neurodevelopmental disorder which main symptoms are inattention and hyperactivity. In the present, its pathogenesis is not well understand and there is no medicine to cure. In this project, to investigate the relationship between neuroinflammation and AD/HD onset, we examined (i) whether prenatal (E14-E15) nicotine exposure (PNE) induces inflammatory cytokines in the fetal brain, and whether those could be used as biomarkers for AD/HD onset. Next, we investigated (ii) whether galantamine (a cholinesterase inhibitor and α7 nicotinic acetylcholine receptor (nAChR) allosteric modulator) ameliorates AD/HD-like behaviors in 2 animal models developed by us.

   PNE significantly increased the expressions of inflammatory markers such as iNOS protein, TNF-α and IL-10 mRNA in the forebrain of fetal mice. Additionally, in AD/HD patients, plasma IL-6 levels were significantly increased compared to healthy controls. Therefore, it suggests that inflammatory response is involved in the pathogenesis of AD/HD and that blood IL-6 may be useful as a diagnostic biomarker for AD/HD onset. Furthermore, galantamine alleviated AD/HD-like behaviors (attentional impairment in the object-based attention test and enhanced impulsivity in the cliff avoidance test) in 2 AD/HD models such as PNE and Shati/Nat8l-deficient mice via α7 nAChR. These data suggest that galantamine may be useful as a novel drug repositioning for AD/HD and α7 nAChR will be potential target for AD/HD therapy.