1. No.
   2020T004

2. Title
   Role of Cigarette Smoking in the Gut-Brain-Axis in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS)

3. Period
   2020-2024

4. Summary
   [Background] Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a chronic, intractable disorder, characterized by post-exertional malaise, sleep disorders, cognitive impairment, muscle weakness and other symptoms. Recent works have indicated the involvement of neuroinflammation in ME/CFS. The aim of this project is to elucidate pathogenesis by focusing on gut-brain axis.
   [Methods] We apply combined analysis of microbiome, immunological assessment and brain imaging. We performed 16SrRNA and metagenomic analysis of 30 fecal samples from ME/CFS patients of NCNP hospital, obtained peripheral blood to evaluate lymphocyte subset analysis and to measure anti-autonomic nerve receptor antibody titers. In addition, brain MRI imaging such as free water diffusion imaging are applied.
   [Results] Compared with age and healthy subjects, ME/CFS samples showed dysbiosis. By both 16SrRNA sequencing and metagenomic analysis, we detected differences in abundance between patients and controls.in phylum/genus/species levels including several specific bacteria correlated with clinical severity. Of note, we revealed a significant reduction of tryptophan-related genes in the feces of the patients. We further showed the reduction of tryptophan-related metabolites in the feces and in the blood of the patients, which were not only related to the frequency of specific bacterial species but also to the clinical severity of the patients. Brain imaging study revealed that significant negative correlations between the serum levels of several autoantibody titers and DTI indices were identified, mainly in the right frontal operculum (J Neuroimaging. 2023;33(5):845-851).
   [Conclusions] The evaluation of gut-brain axis of ME/CFS patients though our method will help to understand the pathogenesis of ME/CFS.