1. No.
   2021G017

2. Title
   Cigarette smoking reduces prevalence of Parkinson's disease by modulating intestinal microbiota!?

3. Period
   2021-2023

4. Summary
   More than 60 epidemiological studies point to the notion that smoking reduces the risk of Parkinson's disease (PD) by ~40%. In addition, smoking is the most prevalent feature that reduces the risk of PD. Accumulating evidence suggests that, in about a half of PD patients, abnormal aggregation of alpha-synuclein fibrils (Lewy bodies) in the substantia nigra in PD starts from the intestinal neural plexus. Smoking potentially affects intestinal microbiota and subsequently reduces the risk of PD. Stool samples of PD patients and healthy cohabitants were subjected to 16S rRNA-seq and shotgun-seq analyses. Random forest modeling to predict the progression of PD in two years using 16S rRNA-seq data failed to make a dependable model for non-smokers, but was able to make a decent model for smokers. Decreased *Escherichia coli* and increased *Erysipelatoclostridium* were hallmarks of rapid progression of PD, both of which may also account for the low prevalence of PD in smokers. Shotgun-seq analysis revealed that intestinal bacteria producing short-chain fatty acids (SCFAs) and polyamines were reduced in PD. In addition, fecal concentrations of SCFAs and polyamines were reduced in PD. However, analysis of the sub-dataset of the current and past smokers showed that smoking did not affect these features. Requirement of a large number of samples for shotgun-seq analysis was likely to have prevented us from elucidating the differences between smokers and non-smokers in the shotgun-seq analysis.