1. Principal Researcher  
   Name: Sanae Ishii  
   Title: Associate Professor at Kyorin University  
   Affiliation: Faculty of Health Sciences, Pathology Research Team

2. Research Title:  
   Nasal inflammation-induced depression-like behavior via dual routes: degeneration of olfactory  
   neurocircuit and activation of meningeal immunity

3. Japanese Group Organization  
   Principal Researcher  
   Name: Sanae Ishii  
   Title and Affiliation: Associate professor at Kyorin University  
   Collaborating Researcher  
   Name: Yuko Mishima  
   Title and Affiliation: Lecturer at Kyorin University  
   Collaborating Researcher  
   Name: Hinami Asano  
   Title and Affiliation: Student at Department of Medical technology, Faculty of Health Sciences of  
   Kyorin University (master course)

   Principal Researcher  
   Name: Geoffroy Laumet  
   Title and Affiliation: Assistant Professor at Michigan State University, College of Natural Science,  
   Neuroscience Program, East Lansing, MI, 48824, USA  
   Collaborating Researcher  
   Name: Robert Dantzer  
   Title and Affiliation: Professor at MD Anderson Cancer Center, Department of Symptom  
   Research, Division of Internal Medicine, Houston, TX, 77030, USA

5. Research Period, from/to (yyyy/mm/dd) and total number of years.  
   From 2020/04/01 to 2023/03/31 (3 years)

6. Abstract, Results, and Research Significance (300 words):  
   Olfactory system is a unique pathway that can affect the brain by bypassing the blood brain barrier, since  
   the olfactory sensory neurons (OSNs) project their axons to the olfactory bulb (OB). Our previous studies  
   indicate that chronic nasal inflammation causes loss of OSNs, neuroinflammation and synaptic loss in the OB within 3  
   weeks, and degeneration of projection neurons and atrophy of the OB within 10 weeks, indicating that nasal  
   inflammation affected the OB through the olfactory pathway. In addition, nasal cavity connects to the subarachnoid  
   space via olfactory nerves, so that the nasal inflammation may affect the meningeal immunity. In this study, we aimed  
   1) to determine the changes in the meningeal immunity and OB microenvironment following nasal inflammation by  
   immunohistochemistry, real time RT-PCR, and spectral flow cytometry. The other aim was 2) to determine whether  
   nasal inflammation triggers sickness and/or depression-like behavior. U.S. group taught us the experimental techniques  
   for examining meningeal immunity and for behavioral studies and performed spectral flow cytometry of the OB and  
   meninges after nasal inflammation.
Histological and spectral flow cytometric analyses indicated that a variety of peripheral immune cells transiently infiltrated the OB and the ratio of peripheral immune cells in the OB increased at 24 hours after intranasal LPS administration, however, the ratio did not change in the meninges. Real time RT-PCR indicated that pro-inflammatory cytokines were upregulated in the OB and meninges, and anti-inflammatory cytokines were upregulated only in the OB. At 24 hours after intranasal administration, food and water intake and the body weight decreased in LPS-treated mice, but the immobility time of tail suspension test and forced swim test was not different in saline- and LPS-treated mice, suggesting that acute nasal inflammation caused sickness behavior, but not depression-like behavior.

7. Other (Research-related concerns, particular points of note):
It is very sorry that we could not visit US group during the first 2 years because of the pandemic of corona virus.

*Please attach any reference materials as necessary.