Goal2 Realization of ultra-early disease prediction and intervention by 2050.

Understanding and Control of Virus-Human Interaction Networks



#### R&D item

# 2. Analysis of Host Response Network

## Progress until FY2023

#### 1. Outline of the Project

Using mice infection models, gene expression of innate immune cells such as effector and memory T cells, macrophages, dendritic cells, and innate lymphocytes in the acute and chronic stages are analyzed at the single cell level and visualize gene expression patterns in collaboration with researchers in molecular imaging. We will acquire information essential for classifying the response patterns of immune cells to viral infection, create a mathematical model of immune response patterns in collaboration with mathematical researchers, and construct a database. Furthermore, we will identify the key molecules and networks of immune cells against each viral infection, investigate the gene expression patterns of immune-supporting cells in lymph nodes and bone marrow and those of cells in the respiratory tract and blood vessels, and clarify their roles in viral infection responses. In addition, we will examine the microbiome to clarify their roles in the host response to viral infection. In collaboration with mathematical and imaging researchers, we will explore the networks of immune cells, immune-supporting cells, and the microbiome and elucidate the molecular mechanisms that control the

networks between groups. Regarding the microbiome, we aim to identify critical bacterial groups in the response of immune cells and immunesupporting cells to viral infections.



### 2. Research Achievements

We conducted comprehensive gene expression analysis focusing on immune cells using infection models of influenza virus and SARS-CoV-2. In collaboration with researchers from Project 3, we identified molecules involved in exacerbating the diseases. Furthermore, we examined the effects of the inhibitors against identified molecules in mouse models, assessing their validity as biomarkers and molecular targets for therapeutic intervention. To facilitate the application of our research findings to humans, we analyzed the correlation between viral infections and human conditions, such as obesity, aging, and allergies. Additionally, we obtained clinical data from various cohorts, including

the Chiba University Corona Vaccine Center staff cohort. We analyzed the immunological characteristics related to the maintenance of a presymptomatic state.



#### 3. Future Plans

2020

2021

2023

2026

From the host response patterns extracted from infection models, we aim to identify markers and molecular targets that enable ultra-early

treatment and prevention before severe pathological changes such as exacerbation occur. We will advance scientific validation and analysis towards their implementation in humans. Additionally, we will define a new classification of viruses based on the obtained host response patterns and develop prevention and treatment methods according to these patterns. We aim to create a society capable of preventing infectious disease outbreaks before a pandemic occurs.



