

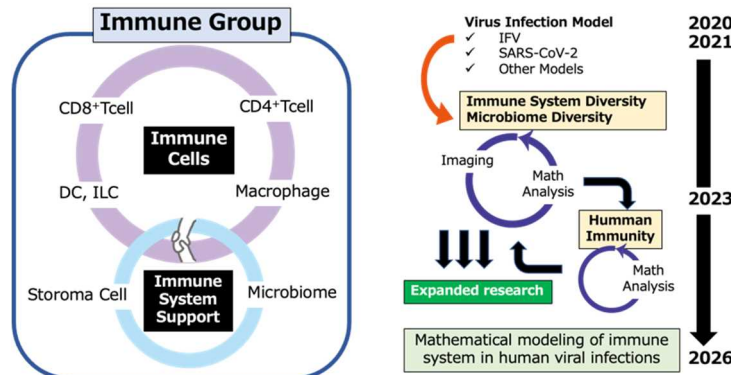
R & D Project 2: Analysis of Host Response Network

Progress until FY2022

1. Outline of the Project

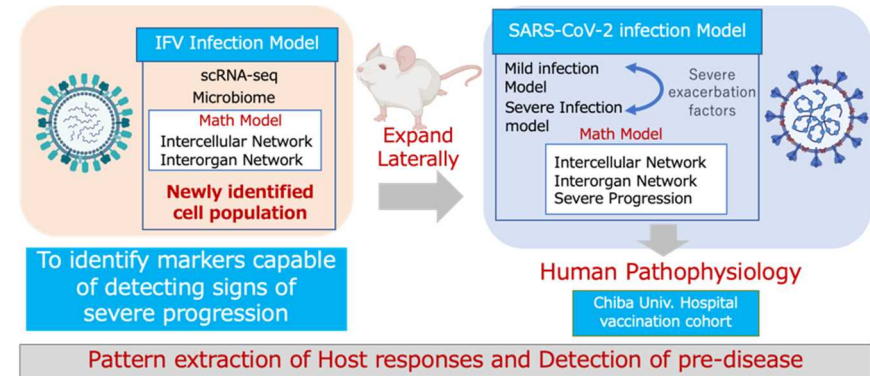
Using animal models infected with various viruses, gene expression of innate immune cells such as effector and memory T cells, macrophages, dendritic cells, and innate lymphocytes in the acute and chronic stages are analyzed at the single cell level and visualize gene expression patterns in collaboration with researchers in molecular imaging. Through this research, 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. In addition, we will identify the key molecules and networks of immune cells against each viral infection and investigate the gene expression patterns of immune-supporting cells in lymph nodes and bone marrow, cells in the respiratory tract and blood vessels, and their roles in viral infection responses. In addition, we will examine changes in the microbiome of the intestinal tract, respiratory tract, etc., and their role in viral infection response. In collaboration with mathematical and imaging researchers, we will examine 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 immune-supporting cells to viral infections.



2. Research Achievements

Among viral infections, the most likely to cause pandemics are respiratory viruses such as IFV and coronaviruses. In this project, the analysis of SARS-CoV-2, an urgent issue, was given top priority. Animal models for SARS-CoV-2 had not been established at the start of the research, and the research progress would take time, such as the need for a BSL3 laboratory. We proceeded with the analysis using the existing IFV infection model. We efficiently conducted the research by laterally expanding the analysis method and achievements to the newly established SARS-CoV-2 infection model. As a result, we found cells and molecules that exhibit characteristic dynamics common to IFV and SARS-CoV-2 infections and identified candidate targets that would enable ultra-early diagnosis and therapeutic intervention.



3. Future Plans

Regarding the in vivo and in vitro models of viral infection created in Group 1, we will comprehensively analyze the host response to viral infection in collaboration with researchers in Group 3 and proceed with extracting host response patterns. By comprehensively analyzing host responses, including innate immune cells, adaptive immune cells, immune-supporting cells, and body microbiota, using new measurement and mathematical analysis techniques, we can identify targets that enable ultra-early intervention and diagnosis.