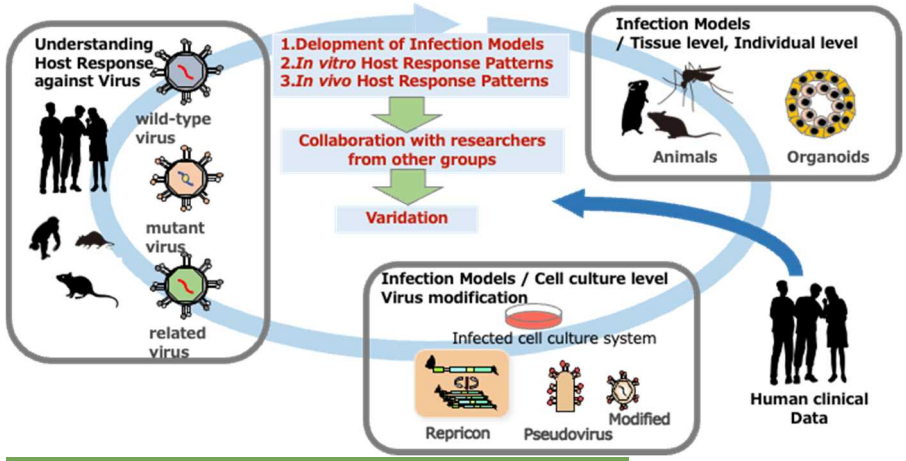
R&D Theme

R & D Project 1: Analysis of virus infection networks

Progress until FY2022

1. Outline of the Project

We establish in vitro or in vivo models for various viral infections, create a database of host response networks after viral infection using various omics analyses, and extract host response patterns in collaboration with researchers in immunology and mathematical sciences. Then, we aim to identify biomarkers that can predict serious pathological changes at an extremely early stage and target molecules that enable therapeutic intervention. Furthermore, through mutual feedback analysis with human clinical data, the results obtained using animal models will be scientifically verified with human clinical data, and human clinical data will be scientifically verified with animal models.

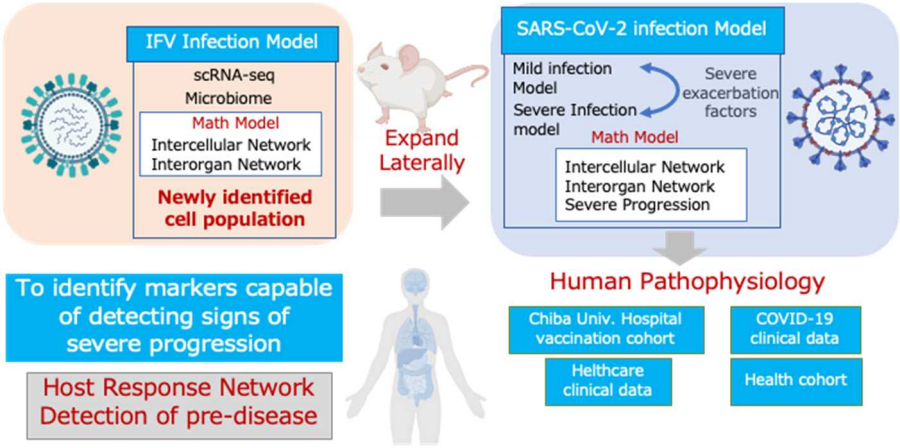


2. Research Achievements

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. A mouse model 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 mouse model. We efficiently conducted the research by laterally expanding the analysis methods and achievements to the newly established SARS-CoV-2 mouse 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 SARS-CoV-2, researchers in Groups 2 and 3 will acquire human clinical data, and through mutual feedback analyses of animal model data and human clinical data, we aim to implement the research results in humans. In addition, we will apply these analytical results to the RSV infection model for respiratory infections, aiming to extract host response patterns common to acute respiratory infections. In addition, we are making good progress in creating mouse models for hemorrhagic fever viruses, intestinal viruses, arthropod-borne viruses, and persistent infection viruses, and we are trying to classify new viruses based on host response patterns.



国立研究開発法人 科学技術振興機構 Japan Science and Technology Agency

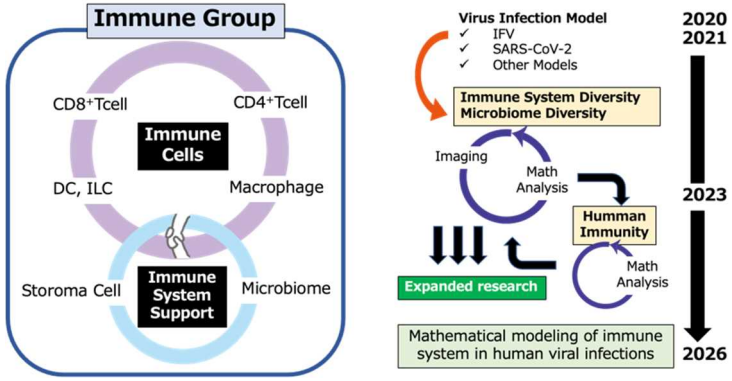
R&D Theme

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

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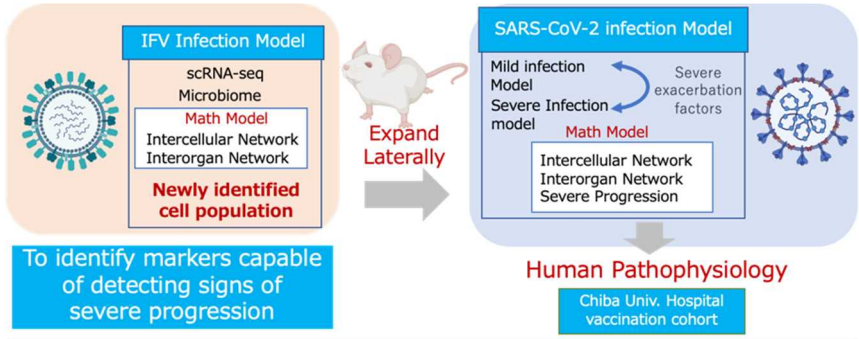


3. Future Plans

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.

R&D Theme

R & D Project 3: Development of analysis frameworks for imaging and math analysis to comprehend Virus-Human Interaction Networks.

Progress until FY2022

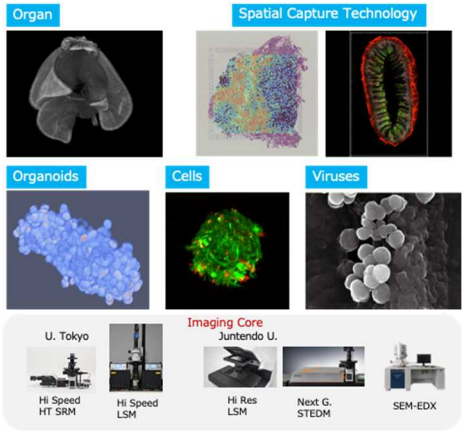
1. Outline of the Project

By advancing imaging technology and combining it with omics technology, we will promote the development of comprehensive and chronological next-generation measurement technology. We also aim to achieve high scalability through advanced multiplexing of measurements, focusing on the parallelism of imaging technology. As a method for analyzing the large-scale, high-dimensional data obtained, we use tensor analysis to estimate dynamic time-varying intercellular interaction networks from comprehensive time-series data. Furthermore, we apply network motif analysis and network topology analysis to the cell-cell interaction network and decompose it into modules that reflect the dynamics of the entire network. We construct a multi-layered mathematical model based on modularized cell-cell interaction networks and perform simulations and sensitivity analyses. Combining multi-layered mathematical models with generative models such as generative adversarial networks (GANs), we generate fictitious time-series data based on experimental data and use it to stratify immune response patterns.

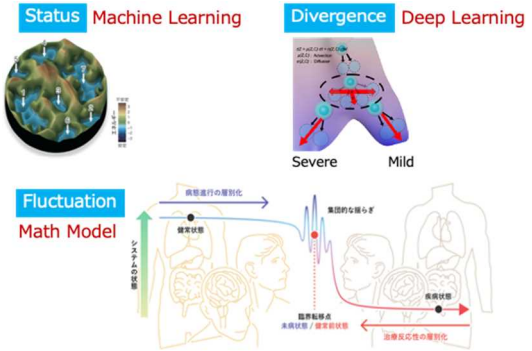
2. 2022年度までの成果

The imaging group is working on a technology that enables a three-dimensional spatial understanding of protein localization and gene expression dynamics at various levels of viruses, cells, organs, and organoids to measure host responses after virus infection, especially immune cell responses. We also provided technology and analysis support for these technologies to other Moonshot projects.

The mathematics group has developed analytical methods for extracting host response network patterns after virus infection and has conducted research with researchers in Groups 1 and 2 to capture signs of severe changes in virus infection. In addition, to accelerate the interdisciplinary study of experimental and mathematical science, we actively carried out joint research and researcher exchanges with Aihara PJ.



Imaging Group



Mathematical Group

3. 今後の展開

In the Imaging Group, we will advance the measurement and visualization of biological data to understand host response networks in established infection animal models comprehensively. In the Mathematical Group, we will develop models and extract patterns based on the comprehensive and inclusive data of host responses after viral infections. Additionally, we will expedite the original plan and focus on identifying and detecting pre-disease states of infectious diseases based on clinical data.