R&D item

3. Development of analysis frameworks for imaging and math analysis to comprehend Virus-Human Interaction Networks.

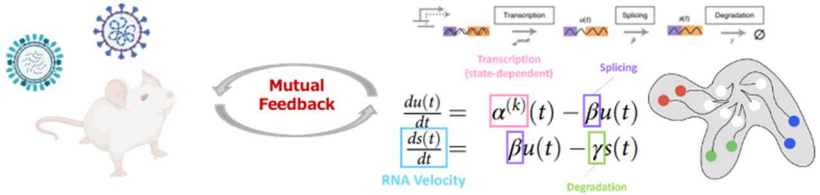
Progress until FY2023

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. Research Achievement

The Imaging Group, in collaboration with researchers from Project 1 and 2, developed measurement techniques and conducted imaging analysis using influenza virus and SARS-CoV-2 infection models. We performed spatial transcriptome analysis, three-dimensional lung observations, virus particle detection in tissue section by EM, and imaging technology development. These efforts visualized host responses to viral infection from various perspectives. Additionally, we began planning for the commercialization of our microscopy technology. The Mathematical Group developed a technique to integrate bulk RNA-seq and scRNA-seq data, enabling the extraction of host network models and identifying factors linked to severe disease. These findings were shared with Project 1 and 2 for experimental validation.
We also used a multi-layered mathematical model to replicate time-series data from SARS-CoV-2 and influenza virus infections, considering the impact of various immune cells. We especially performed Single-cell colocalization analysis using a deep generative model named “DeepCOLOR” and published it in Cell Systems.



3. Future Plan

Imaging Group: Establish measurement techniques to visualize host response networks after virus infection. Collaborating with Project 1 and 2, we will improve these techniques to understand host responses to viral infections comprehensively.
Mathematical Group: The Mathematical Group will enhance the elucidation of host response networks using developed analytical techniques, identifying molecular targets and biomarkers for early disease prediction. We will also analyze human clinical data and integrate it with animal model data, advancing the implementation of our research findings in humans.