

# Anti-infectives

Generating research infrastructure and novel technologies  
for anti-infective drug and vaccine discovery

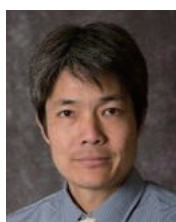
## Research and Development Objectives

### New approaches in drug and vaccine discovery for infectious diseases

The goal of this R&D area is to establish technologies and infrastructure to accelerate basic research in the field of infectious disease drug discovery.

In order to respond immediately to emerging and re-emerging infectious diseases, we need an understanding of the pathogens involved and the interactions with the host as a prerequisite to the development of prophylactic, diagnostic, and therapeutic interventions. Furthermore, there is a need to accelerate the processes required for clinical application. However, the basic research process has become a bottleneck for drug discovery because of the diversity of pathogens, various phases of disease from acute to chronic and latent infections, and the need to respond immediately during a pandemic. These are problems unique to infectious diseases.

This R&D area aims to address the issues in the basic research phase of infectious disease drug discovery by combining existing drug discovery seeds, infrastructure/technologies, research resources for the discovery of drugs against infectious diseases caused by bacteria, fungi, and viruses, etc.; developing an array of robust drug discovery modalities that ultimately translate into clinical application; and strongly promoting interdisciplinary research. We will accumulate research findings that lead to development of new drug discovery modalities, optimization of existing modalities, and development of new platform technologies. The purpose of this R&D area is to accelerate infectious disease drug discovery as part of our efforts to build expertise to respond immediately when new pathogens emerge in the future.



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Started in 2021 • • • 1st period



### Study of the host cell membrane and ion dynamics during virus infection



**OHBA Yusuke**  
Professor, Faculty of Medicine,  
Hokkaido University

In this research and development, we visualize the host cell membrane nano-dynamics that face virus particles during entry using high-speed atomic force microscopy. In addition, we will simultaneously visualize the interactions between virus and host cell molecules and the dynamics of intracellular signaling to understand the host machinery that regulates the virus entry process. Our aim is to decode the "common language" used by viruses to enter host cells and establish the basis for drug discovery targeting such languages.

Started in 2021 • • • 1st period



### Infrastructure for anti-infective drug discovery using a synthetic human body model



**TAKAYAMA Kazuo**  
Junior Associate Professor, Center for iPS Cell Research  
and Application, Kyoto University

To minimize the damage caused by the pandemic of emerging and re-emerging infectious diseases, it is necessary to generate and maintain an infectious disease drug discovery platform that can be used for the rapid development of therapeutic drugs. In this project, we will in vitro evaluation system with high clinical predictability through development of a virtual human body model. This model will be able to evaluate disruption of biological barriers caused by various pathogens including viruses, particularly the causative virus of respiratory tract infections, and subsequent organ dysfunction.

Started in 2021 • • • 1st period



### Generating novel antibacterial capsid technologies toward combating bacterial infection diseases



**CUI Longzhu**  
Professor, School of Medicine,  
Jichi Medical University

Despite the fact that we are facing an imminent crisis caused by antimicrobial resistant (AMR) bacteria, no effective treatment has yet been found. A more serious problem is that the development of antimicrobials is currently at a standstill. In this study, we proposed to produce phage capsid medicines effective against bacterial infections that are difficult to treat with existing antimicrobial agents by using bacteriophage as a new drug discovery modality. Specifically, we will develop new antibacterial agents, detection reagents, and vaccines against refractory bacterial infectious diseases by packaging various foreign gene cassettes on phage capsid.

Started in 2021 • • • 1st period



### Establishment of anti-infective human antibody discovery platform leveraging animals with humanized immune system



**TOMIZUKA Kazuma**  
Professor, Laboratory of Bioengineering,  
Tokyo University of Pharmacy and Life Sciences

On the back of COVID-19 pandemic, there are increasing societal needs for the development of preventive and therapeutic agents. By utilizing our proprietary human antibody-producing animals and mRNA drug discovery technologies we will establish "Express Hu-mAb system" to quickly identify human antibody drug candidates against various infectious diseases. This platform should enable the early implementation of neutralizing antibody therapy that is a key to counter the devastating impact the viruses have in vulnerable populations and in high-risk patients.

Started in 2021 • • • 1st period



### Development of novel antimicrobial adjuvants by innovative compound discovery and synthesis methods



**SUZUKI Masato**  
Senior Research Scientist, AntimicrobialResistance Research  
Center, National Institute of Infectious Diseases

Recently, bacterial infections caused by ESKAPE pathogens and mycobacteria, including nontuberculous mycobacteria, have become a global public health threat. Novel drug discovery for bacterial infections has stalled for decades, which necessitates research and development with different strategies, including re-evaluation of existing compound libraries based on alternative indicators. In this project, we aim to discover and develop novel antimicrobial adjuvants to potentiate the activity of antimicrobials that human beings have developed over a long period of time by using high-content imaging-based compound discovery methods and AI-guided compound synthesis methods.

Started in 2022 • • • 2nd period



### Natural product 2.0 for a new modality of drugs for infectious diseases



**ASAI Teigo**  
Professor, Graduate School of Pharmaceutical Sciences,  
Tohoku University

Natural products are one of the most attractive sources for drug discovery, especially in the field of infectious diseases. In this R&D, we aim to generate unprecedented natural product-based screening sources by leveraging vast genetic resources encoding novel natural products and useful biocatalysts through awaking of silent biosynthetic genes, genome mining, synthetic biology, and chemo-enzymatic synthesis. Our goal is to establish "Natural Products 2.0", a new modality that will be a fundamental technology for sustainable development of drugs for infectious diseases.

Started in 2021 • • • 1st period



### Study of the molecular mechanism of persistent infection and identifying novel privileged molecular structures for the next-generation antibacterial drug discovery



**TAKAYA Akiko**  
Associate Professor, Graduate School of Pharmaceutical  
Sciences, Chiba University

The generation of antimicrobial-tolerant cells called persisters is a strategy used by bacteria to develop antimicrobial resistance. However, the molecular mechanisms by which bacteria as persister cells survive by avoiding antibiotics and host immune responses are still unknown. This project aims to elucidate the molecular mechanisms that enable persister cells to survive in harsh environments, determine the activity and efficacy of compounds targeting persister regulators for the treatment of bacterial infections, and identify novel privileged molecular structures for antimicrobial drug discovery.

Started in 2022 • • • 2nd period



### Creation of new virology research through innovative reverse genetics



**FUKUHARA Takasuke**  
Professor, Faculty of Medicine,  
Hokkaido University

The main objective of this research is to develop and improve rapid and simple reverse genetics methods for various viruses to enable swift production of recombinant viruses in the event of an outbreak of any emerging/re-emerging viruses. With the following five concepts: comprehensiveness, speed, simplicity, application, and library construction - we aim to establish a system that enables not only our own group but also all researchers to start drug discovery rapidly and vaccine development using various recombinant viruses when emerging/re-emerging viruses threaten public health.

Started in 2022 ●●● 2nd period



### Frontier of New Middle Molecule Drug Discovery Field by Targeting Pathogens' Intrinsically Disordered Proteins (IDPs)



**MATSUMOTO Sohkiichi**  
Professor, School of Medicine,  
Niigata University

Intrinsically disordered proteins (IDPs), which are changing the concept of proteins, are mostly untapped as drug targets since they deviate from the traditional lock and key model of drug discovery. In this proposal, the IDPs of *Mycobacterium tuberculosis*, which slows down growth and induce dormancy, will be used as a model target, and will be the subject of a research project that combines "Biophysics," "Structural Biology," "Molecular Dynamics Calculation," "Organic chemistry," and "Microbiology." We aim to establish a practical framework to discover anti-IDPs drugs and also develop a therapeutic agent against intractable mycobacterial diseases.

Started in 2023 ●●● 3rd period



### Bio-hysteresis-based identification of treatment resistance factors in refractory infectious diseases and its application to discovery of universally effective next-generation antimicrobial agents



**MINATO Yusuke**  
Senior Assistant Professor, Department of Microbiology,  
Fujita Health University School of Medicine

Development of novel treatment options for chronic bacterial infections, such as nontuberculous mycobacterial infections, for which therapeutic efficacy is difficult to predict, is desperately needed. We will characterize bacterial and host factors using a unique approach we designated "bio-hysteresis analysis" to comprehensively identify treatment resistance factors. Furthermore, we will establish drug target evaluation models that reflect the therapeutic resistance factors and develop a target identification platform for developing new antimicrobial agents that show universal efficacy against a wide variety of refractory cases.

Started in 2022 ●●● 2nd period



### Establishment of platforms for drug discovery and development of novel drugs with broad-spectrum antiviral activity



**WATANABE Tokiko**  
Professor, Research Institute for Microbial Diseases,  
Osaka University

Emerging diseases like Ebola, avian influenza, and COVID-19, threaten the global economy and public health. Many of these diseases are caused by RNA viruses; therefore, it is imperative that we prepare for outbreaks of the various types of RNA viruses. In this project, we aim to establish platforms for the development of innovative drugs with broad-spectrum antiviral activity to combat viral diseases. We propose to identify host factors that play universally important roles in the interactions between hosts and various RNA viruses as potential drug targets, and to develop mid-sized molecules (e.g., nucleic acid- and glycan-based drugs) as next-generation antivirals.

Started in 2023 ●●● 3rd period



### Development of novel modalities to rejuvenate aged immunity against infectious diseases



**OSHIUMI Hiroyuki**  
Professor, Faculty of Life Sciences,  
Kumamoto University

Aging is the most significant risk for infectious diseases, so vaccination is recommended, but vaccines are less effective in preventing infections in older people. In this study, we will develop novel modalities to rejuvenate aging immunity to better protect the elderly from various infection. We will then investigate the effectiveness and mechanisms of candidate modalities in mouse models with the ultimate goal of solving the aging problem.

Started in 2023 ●●● 3rd period



### Study of the development of new modality creation technology against bacterial infections using non-antimicrobial substances



**SATO Toyotaka**  
Associate Professor, Faculty of Veterinary Medicine,  
Hokkaido University

This research aims to establish a highly original modality for treating bacterial infections that utilizes substances with physical properties and actions that are different from those of conventional antimicrobial agents. Specifically, we will leverage "non-antimicrobial active substances" and develop a new approach for treating bacterial infections through a new technology that confers antimicrobial activity to these substances.