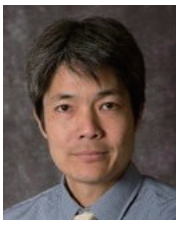
Anti-infectives

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



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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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AMED-CREST Started in 2021 · 1st period

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

OHBA Yusuke
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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.

Generating novel antibacterial capsid technologies toward combating bacterial infection diseases

CUI Longzhu
Professor, School of Medicine,
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Despite the imminent crisis posed by Antimicrobial-resistant (AMR) bacteria, no effective treatment has yet been found. An even more serious concern is that the development of new antimicrobial agents has reached a standstill. In this study, we propose the use of bacteriophages as a novel drug discovery modality to produce phage capsid-based medicines effective against bacterial infections that are difficult to treat with existing antimicrobial agents. Specifically, we aim to develop new antibacterial agents, detection reagents, and vaccines for refractory bacterial infectious diseases by packaging various foreign gene cassettes into phage capsids.

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, Japan Institute for Health Security

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.

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.

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

TAKAYAMA Kazuo
Professor, Medical Research Institute,
Institute of Integrated Research, Institute of Science Tokyo

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 an 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.

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.

AMED-CREST 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.

Creation of new virology research through innovative reverse genetics

FUKUHARA Takasuke
Professor, Faculty of Medical Sciences,
Kyushu 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.

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

MATSUMOTO Sohkichi
Professor, Faculty 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.

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

WATANABE Tokiko
Professor, Research Institute for Microbial Diseases,
The University of Osaka

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.

AMED-CREST 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.

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

SATO Toyotaka
Associate Professor, Fuculty of reterinary 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.

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
Associate Professor, Center for Infectious Disease Research,
Fujita Health University

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.