



# Generating Research Infrastructure and Novel Technologies for Anti-infective Drug and Vaccine Discovery

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



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## Research and Development Objective

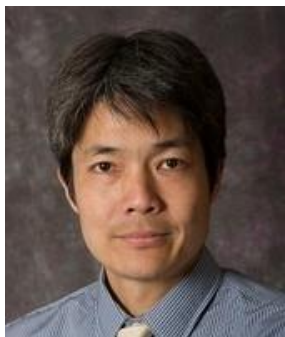
New approaches in drug and vaccine discovery for infectious diseases

## Targets

This Research and Development Objective aims to resolve issues that are the rate-limiting steps in drug discovery research, by building or repurposing drug discovery infrastructure and modalities for infectious disease drug discovery research and developing strategies that ultimately translate to clinical application, as well as strongly promoting interdisciplinary basic research. This Objective aims to achieve three specific goals:

- (1) Development of drug discovery modalities that will contribute to the prevention and treatment of infectious diseases
- (2) Optimization of existing modalities for infectious disease drug discovery
- (3) Generation of technology platforms that will accelerate infectious disease drug discovery leading to innovative preventive and therapeutic agents against infectious diseases

# Program Supervisor (PS)



Yohei Doi, MD, PhD  
Professor, Fujita Health University School of Medicine/  
Professor, University of Pittsburgh School of Medicine

## Profile

Dr. Yohei Doi graduated from Nagoya University School of Medicine in 1998, and after working at the Anjo Kosei Hospital and National Institute of Infectious Diseases, Japan, from 2003 he trained in Internal Medicine at St. Luke's Roosevelt Hospital Center in New York, and from 2005 in Infectious Diseases at the University of Pittsburgh Medical Center in Pennsylvania. He continued to work at the University of Pittsburgh Medical Center as assistant professor from 2008, associate professor from 2016, and a professor from 2021, pursuing basic and clinical research into antimicrobial-resistant bacteria while also engaging in infectious disease clinical care and education. Dr. Doi also serves as professor at Fujita Health University School of Medicine since 2018. He is Chair of the Gram-Negative Committee of the NIH-funded Antibacterial Resistance Leadership Group (ARLG), and a Program Committee member of IDWeek.

## Recent Research Direction

Elucidation of mechanisms underlying antimicrobial resistance and development of inhibitors  
Genomic epidemiological research into drug-resistant bacteria of clinical concern  
Clinical research into the use of new or existing antimicrobials to treat antimicrobial-resistant bacterial infection

# Program Officer (PO)



Yoshiharu Matsuura, DVM, Ph.D  
Director, Center for Infectious Disease Education and Research (CiDER), and SA Professor, Laboratory of Virus Control, Research Institute for Microbial Diseases (RIMD), Osaka University

## Profile

Dr. Yoshiharu Matsuura graduated from the Department of Veterinary Sciences, Faculty of Agriculture at the University of Miyazaki in 1978, and completed the Master's Program in the Graduate School of Veterinary Medicine at Hokkaido University in 1980. He subsequently worked at the Central Research Laboratory of Daiichi Pharmaceutical Co., Ltd., joining the National Institute of Health, Japan in 1982. From 1984 he spent two years studying overseas at Oxford University's NERC Institute of Virology, later becoming Section Chief in the Laboratory of Hepatitis Viruses, Department of Virology II at the National Institute of Infectious Diseases, Japan, in 1992. In 2000 he became a professor at Research Institute for Microbial Diseases in Osaka University, where he subsequently spent four years as Director from 2015. Dr. Matsuura retired from Osaka University in 2021 and was appointed as Director of the Center for Infectious Disease Education and Research (CiDER), which was established the same year at Osaka University. He has chaired the Japanese Society for Virology since 2017. In 2013 he was the recipient of the Hideyo Noguchi Memorial Award for Medical Sciences in recognition of his work on host factors involved in the propagation and pathogenesis of the hepatitis C virus.

## Recent Research Direction

Cell and molecular biological analysis of the mechanisms of viral infection and propagation  
Development of new methods to control viral infectious diseases  
Fostering early career investigators in the field of infectious disease research

# Image of the R&D area

## Research into drug discovery seeds at infectious disease research centers in Japan and overseas



### Current status and challenges in basic research into infectious disease drug discovery

- Require institutions with high-level containment facilities for experiments conducted on pathogens that are infectious, diverse, and capable of mutation, proliferation, and transmission
- Need to respond immediately during pandemics, whose courses may be unpredictable
- Investigators work separately on specific pathogens, the numbers of investigator are on a downward trend, and research still mainly involves outdated research methodologies
- Difficulties in advancing the results of basic research to product development due to withdrawal of companies from the infectious disease field

## Platforms and technologies that will accelerate drug discovery research



# Outline of the Research and Development Area



In order to control emerging and re-emerging infectious diseases, we need to accelerate the processes required for clinical application of prophylactic, diagnostic, and therapeutic interventions based on an understanding of the pathogens involved and the interactions with the host.



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.

- Leverage various research methodologies and resources, and networks of investigators and domestic infectious disease research sites supported by AMED and other bodies
- Promote interdisciplinary research through coordinated collaborations between research institutions and pharmaceutical companies, etc. in Japan and overseas and active participation of investigators in a wide range of fields not limited to infectious diseases or microbiology
- Accumulate research findings that can lead to development of new drug discovery modalities, optimization of existing modalities, and development of new platform technologies

- (1) Develop new approaches, including drug discovery modalities, that will contribute to the prevention and treatment of infectious diseases
- (2) Optimize existing modalities for infectious disease drug discovery
- (3) Develop technology platforms that will accelerate infectious disease drug discovery and generate innovative preventive and therapeutic agents against infectious diseases

## 【AMED-CREST】

The goal is to resolve issues that are bottlenecks in the basic research phase of infectious disease drug discovery by combining existing drug discovery seeds, infrastructure/technologies and research resources for the discovery of drugs against infectious diseases caused by bacteria, fungi, and viruses, etc., and developing an array of robust drug discovery modalities that ultimately translates to clinical application, as well as by strongly promoting the participation of investigators from various fields to vitalize interdisciplinary cutting-edge research and organic collaboration between research institutions and pharmaceutical companies in Japan and overseas.

We expect early career investigators to be proactive in submitting proposals and participating in the research, and we welcome proposals that are designed to include collaborations with overseas institutions engaged in advanced research.

\* For this R&D area, we are only calling for unit type (AMED-CREST) proposals, in order to lay the groundwork for research organizations to promote interdisciplinary research and, with a view towards application, develop strategic combinations of infectious disease drug discovery research, technologies, and seeds.

# FY 2021 Awarded Projects



Project	Principal Investigator	Affiliation	
Study of the host cell membrane and ion dynamics during virus infection	OHBA Yusuke	Hokkaido University	Professor
Generating novel antibacterial capsid technologies toward combating bacterial infection diseases	CUI Longzhu	Jichi Medical University	Professor
Development of novel antimicrobial adjuvants by innovative compound discovery and synthesis methods	SUZUKI Masato	National Institute of Infectious Diseases	Senior Research Scientist
Study of the molecular mechanism of persistent infection and identifying novel privileged molecular structures for the next-generation antibacterial drug discovery	TAKAYA Akiko	Chiba University	Associate Professor
Infrastructure for anti-infective drug discovery using a synthetic human body model	TAKAYAMA Kazuo	Kyoto University	Junior Associate Professor
Establishment of anti-infective human antibody discovery platform leveraging animals with humanized immune system	TOMIZUKA Kazuma	Tokyo University of Pharmacy and Life Sciences	Professor



# FY 2022 Awarded Projects



Project	Principal Investigator	Affiliation	
Frontier of New Middle Molecule Drug Discovery Field by Targeting Pathogens' Intrinsically Disordered Proteins (IDPs)	MATSUMOTO Sohkichi	Niigata University	Professor
Natural product 2.0 for a new modality of drugs for infectious diseases	ASAI Teigo	Tohoku University	Professor
Establishment of platforms for drug discovery and development of novel drugs with broad-spectrum antiviral activity	WATANABE Tokiko	Osaka University	Professor
Creation of new virology research through innovative reverse genetics	FUKUHARA Takasuke	Hokkaido University	Professor

# Examples of R&D Proposals (1) \*Excerpt from Application Guidelines



- Establishment of novel therapeutic concepts and development of modalities through elucidation of epigenetic control governing pathogen proliferation, the role of microbiome, and pathogen-specific host defense mechanism.
- Exploratory research aimed at development of novel antimicrobials (small molecules, natural substances, other entities) that target the pathogens' virulence, such as control of the bacterial toxin secretion system or quorum sensing transcription factors.
- Elucidation of the mechanisms of drug resistance in bacteria, fungi, or viruses that cause sexually transmitted and other infectious diseases, as well as research into the mechanisms of long latency and persistent infections, and the use of these findings to establish new therapeutic concepts.
- Development of technology platforms for antimicrobial drugs, including nucleic acid therapeutics, peptides, nanobodies, and compounds that induce targeted protein degradation.
- Development of research platforms aimed at understanding the mechanism of drug resistance and development of pharmaceutical agents to inhibit or counter relevant mechanisms of resistance.
- Research of drug discovery infrastructure targeting drug-resistant fungal infections.

## Examples of R&D Proposals (2) \*Excerpt from Application Guidelines



- Research to build exploratory infrastructure to search for innovative protective antigens against pathogens for which no effective vaccines are currently available or more effective vaccines are needed and develop suitable vaccine modalities.
- Development of infectious disease animal models that can be used for clinical prediction and alternative humanized models, including in humanized mice, chimeras, and human tissues of iPS cell origin.
- Refinement of in silico screening using pathogen protein structural analysis and protein science, and research aimed at rational drug design for compound optimization. In addition, research to dramatically shorten infectious disease drug discovery by demonstrating correlation between in silico and wet studies.
- Development of infectious disease drug discovery AI platforms through the use of big data that can draw on Reverse Translational Research (rTR), multi-omics analysis, and other relevant areas.
- Development of analytical methods using biostatistics and biomathematics and of platform technologies for prevalence prediction, through the use of databases on pathogen evolution and genome mutations to identify pathogen immune evasion mechanisms, optimize natural host symbiosis, and predict emergence of variant or resistant strains. Also, development of modalities to enable immediate response.

# Points to Note When Submitting a Proposal (1)

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- Clearly state the research hypotheses, goals and objectives.
- Clearly indicate how the various research projects run by the PI and the Co-Investigators could generate synergistic effects and how this will contribute to the goals and objectives for the overall research proposal.
- Formulate a research plan that can be executed within the R&D period and include specific steps to be taken if the research does not progress as planned.
- While drug discovery research targeting a specific infectious disease is not the main scope of this R&D area, applicants may include such research plans as proof of concept in the proposal.
- For research based on SARS-CoV-2, design the research proposal with a focus on applications in other emerging pathogens.

## Points to Note When Submitting a Proposal (2)

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- We encourage collaborations between different scientific disciplines that are logical and innovative.
- We strongly encourage proposals where early career investigators take on leading roles.
- We welcome proposals designed to include collaborations with investigators at overseas research institutions engaged in advanced research via existing or new networks.
- This program does not include development phases beyond non-clinical studies, but research can be progressed through out-licensing to other programs according to the status of R&D progress.
- Given the goals of the R&D, we recommend participation of physician scientists involved in clinical practice in the relevant field.

# R&D costs and R&D period



In order to select a wide variety of R&D projects to generate research infrastructure and novel technologies for anti-infective drug and vaccine discovery, AMED is soliciting research proposals according to the following conditions.

Type of proposal	R&D funds	R&D period	No. of projects to be selected
AMED-CREST (unit-type)	300 million yen or less (direct costs over entire period)	Up to 5.5 years	Around 2–4 projects

# Message from PS and PO

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- Although this project was initiated in response to the coronavirus crisis, the objective is to build drug discovery and development platforms and to create strong networks of investigators in order **to ensure the health and safety of residents and protect them from infectious diseases that are expected to emerge or propagate in Japan in the future.**
- We strongly encourage research proposals that acknowledge the current status of the field, where infectious disease drug discovery has stagnated, and aim **to create new drug discovery modalities or optimize modalities that are successful in other fields.**
- This project runs for 5.5 years, but the threat posed by infectious diseases will continue into the future. We will therefore prioritize proposals that include **measures to continue and develop the work further in relevant fields after the project has ended, including the personnel, technologies, and research infrastructure.**
- We particularly welcome proposals **where early career investigators serve as principal investigators.**
- The focus is on basic research, but AMED-CREST projects include an emphasis on research targeted at strategic outcomes, so we are interested in proposals that emphasize potential **clinical significance or utility.**

## Collaboration with other programs

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This R&D area has provided opportunities for research exchanges with researchers selected under AMED's Japan Program for Infectious Diseases Research and Infrastructure (Interdisciplinary Cutting-edge Research) since FY2021, promoting discussions between projects and the launch of joint research, as well as active collaborations between programs.



We seek research proposals that aim to establish creative and original research platforms and the development of innovative technology platforms that facilitate infectious disease drug discovery.

We also look for the participation of collaborative multidisciplinary teams.

We look forward to reviewing your applications..