

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

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Research and Development Objective

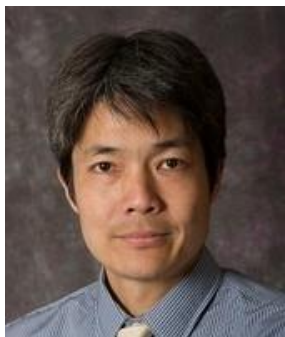
New approaches in drug and vaccine discovery for infectious diseases

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, in 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 participating 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, ASM Microbe and the annual meeting of the Japanese Association for Infectious Diseases.

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), 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 Osaka University's Research Institute for Microbial Diseases, where he subsequently spent four years as Director from 2015. Dr. Matsuura retired from Osaka University in 2021 and assumed the office of Director of the Center for Infectious Disease Education and Research (CiDER), which was established the same year at Osaka University. He has been Chairman of 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
- Difficult to advance 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 the development of new drug discovery modalities, the optimization of existing modalities, and the support of the 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 to application, develop strategic combinations of infectious disease drug discovery research, technologies, and seeds.

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



- Basic research that may lead to the discovery of new preventive and/or therapeutic agents, based on insights of pathogenesis, from pathogen entry into the body to arrival at the target tissues, interactions with intracellular organelles, and the pathway by which infection is established including proliferation within the cells.
- Establishment of novel therapeutic concepts and development of modalities through elucidation of epigenetic control governing pathogen proliferation, the role of the microbiome, and pathogen-specific host defense mechanism.
- Exploratory research aimed at the 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.
- Development of technology platforms for antiviral agents, 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 to build exploratory infrastructure to search for innovative protective antigens against the pathogens for which no effective vaccines are currently available or more effective vaccines are needed and develop suitable vaccine modalities.

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



- 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 relating to rational drug design for compound optimization. In addition, research to dramatically shorten infectious disease drug discovery research periods by demonstrating the correlation between in silico and wet studies.
- Development of an infectious disease drug discovery AI platform 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, optimization of natural host symbiosis, and predictions of emergence of variant or resistant strains. Also, development of modalities to enable immediate response.

Points to Note When Submitting a Proposal (1)



- Clearly state the research hypothesis and 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.
- We encourage collaborations between different scientific disciplines that are logical and innovative.

Points to Note When Submitting a Proposal (2)



- 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 (entire direct costs)	Up to 5.5 years	Around 4–6 projects

Message from PS and PO

- Although this project has arisen because of the coronavirus crisis, the objective is to build drug discovery and development platforms and to create strong networks of investigators in order **to keep our citizens safe and protect them** not only from COVID-19 but also **from other infectious diseases expected to emerge or become more prevalent 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.**

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..