IVReD

Protecting People
from Pandemics.

INSTITUTE FOR VACCINE RESEARCH AND DEVELOPMENT

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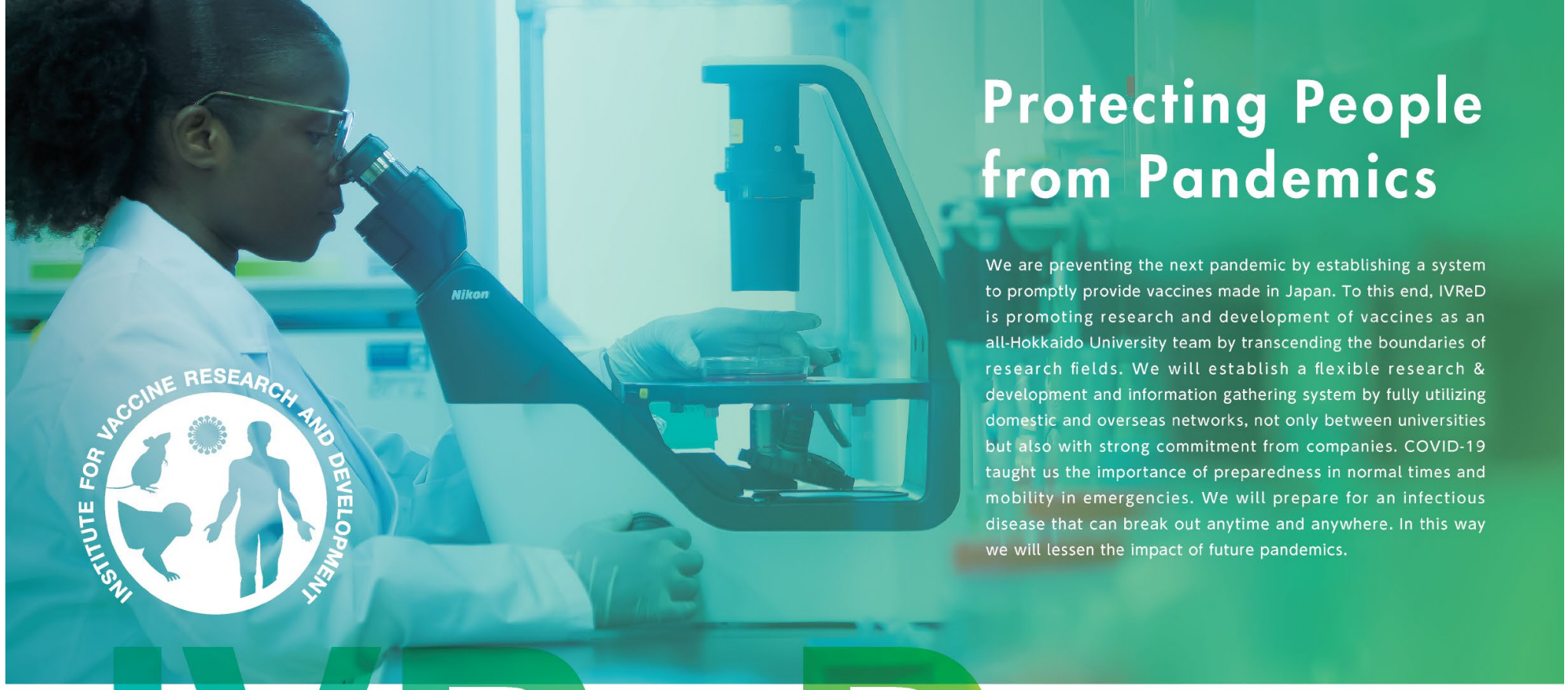
AND DEVELOPMENT

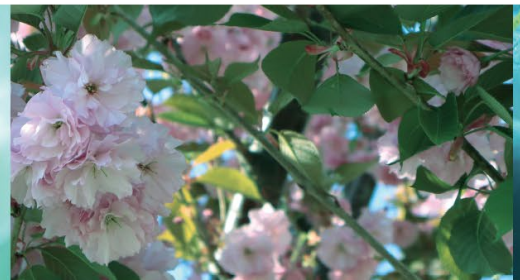


INSTITUTE FOR VACCINE RESEARCH AND DEVELOPMENT

Protecting People from Pandemics

We are preventing the next pandemic by establishing a system to promptly provide vaccines made in Japan. To this end, IVReD is promoting research and development of vaccines as an all-Hokkaido University team by transcending the boundaries of research fields. We will establish a flexible research & development and information gathering system by fully utilizing domestic and overseas networks, not only between universities but also with strong commitment from companies. COVID-19 taught us the importance of preparedness in normal times and mobility in emergencies. We will prepare for an infectious disease that can break out anytime and anywhere. In this way we will lessen the impact of future pandemics.

IVReD



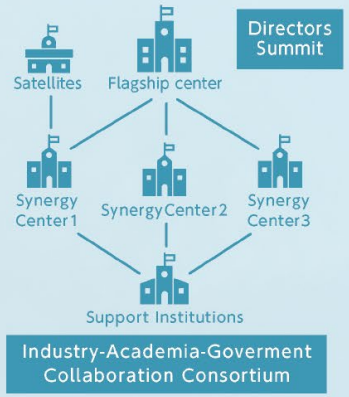
IVReD

ABOUT THE CENTER

The Institute for Vaccine Research and Development (IVReD) was established in October 2022 at the Creative Research Institution, Hokkaido University, as a synergy center along with the University of Tokyo (flagship center), Osaka University, Chiba University, and Nagasaki University (synergy centers) under the support by the Japan Agency for Medical Research and Development (AMED)'s "Japan Initiative for World-leading Vaccine Research and Development Centers" projects.
IVReD will promote basic research for vaccine development and establish a system to employ pre-developed vaccines in the population in cooperation and alignment with institutions, companies, and universities.

The "Japan Initiative for World-leading Vaccine Research and Development Centers"

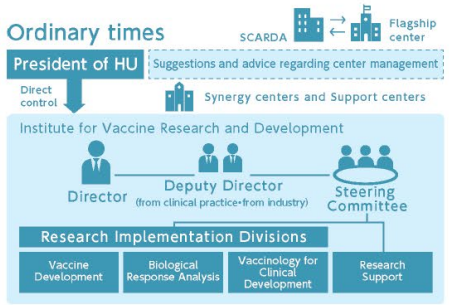
Based on the "Strategy for Strengthening Vaccine Development and Production Systems" (approved by the Cabinet on June 1, 2021), the project aims to establish unprecedented world-class R&D institutes (flagship and synergy institutes), the centers to support the institutes, and to strengthen and promote related research from the inter-pandemic period by focusing on the practical application of vaccines.

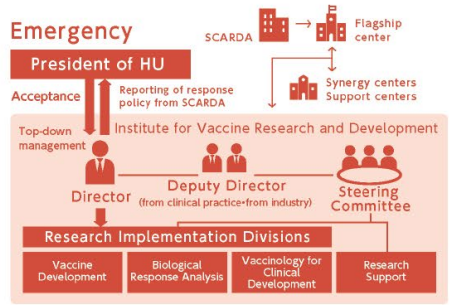


Vaccine R&D System by All-Hokkaido University

IVReD will contribute to the establishment of a system for the development and production of Japanese vaccines through the cooperation with Hokkaido University Hospital, Graduate School of Medicine, Institute for Genetic Medicine, Graduate School of Pharmaceutical Sciences, Graduate School of Veterinary Medicine, and International Institute for Zoonosis Control at the same campus.

During an infectious disease emergency, IVReD will contribute to the rapid development of vaccines through the integrated research system.





MESSAGE

Message from Director

Protect human beings from infectious diseases and their pandemics

As of July 14, 2024, it is reported that there are approximately 766 million people infected with COVID-19 worldwide and approximately 7.5 million deaths. The international community has been hit hard by the COVID-19 pandemic.

Dr. Taylor from the University of Edinburgh in the United Kingdom reported in 2001 that 61% of infectious microorganisms and 75% of emerging infectious disease pathogens are zoonotic pathogens. Hence, it is considered important to understand the infection route of the pathogens. Five pandemics declared by the World Health Organization (WHO) in the past 100 years have been caused by respiratory pathogens, either influenza viruses or coronaviruses. Respiratory infectious diseases have more diverse transmission routes than other infectious diseases, such as droplets, air, contact, oral, and environment, and the transmission speed is high. Hence, the next pandemic will likely be caused by influenza viruses, coronaviruses, or other respiratory pathogens. Apparent from the experience of COVID-19, rapid development of vaccines and therapeutics is essential to overcome the pandemic. Therefore, establishing the system to rapidly develop vaccines and to practically apply these within the community is an urgent need.

Hokkaido University established, ahead of the world, the "Research Center for Zoonosis Control", the predecessor organization of the current "International Institute for Zoonosis Control (IIZC)", as the only institution specializing in zoonosis control. IIZC is maintaining an influenza A virus library storing all subtypes. In addition, as a countermeasure against COVID-19, Hokkaido University is performing environmental, basic and clinical research throughout the University which has led to significant findings to lessen the disease burden. In addition, Hokkaido University is working on tuberculosis, which kills about 1.5 million people every year, through an established international collaboration network for tuberculosis. Based on the results of surveys on the prevalence of drug-resistant strains, new diagnostic methods have been developed and are being implemented in society.

It is with this background that Hokkaido University established the Institute for Vaccine Research and Development (IVReD), which consists of Hokkaido University Hospital (clinical research core hospitals), Graduate School of Medicine, Graduate School of Pharmaceutical Sciences, Graduate School of Veterinary Medicine, Institute for Genetic Medicine, and International Institute for Zoonosis Control, all within the same campus, together with multiple companies such as Denka Company Limited, Shionogi & Co., Ltd., and NB Health Laboratory Co. Ltd. IVReD also incorporates an international research and education network which includes the University of Melbourne and others. IVReD will promote basic research that can contribute to the establishment of vaccine development and production systems by utilizing respiratory pathogens and others detected and isolated by epidemiological studies and stored in the pathogen library in accordance with the flagship vaccine institute of the University of Tokyo.

Prof. Hirofumi Sawa, MD, Ph.D.

Director, Institute for Vaccine Research and Development (IVReD) Hokkaido University

MISSION

After 5 Years Development of vaccines for respiratory infectious diseases

Building a management system for vaccine research and development under the "preemptive strategy" utilizing multiple new modalities

Our strategy

System

- Setting up the clinical specimen collection system
- Streamline R&D system toward social implementation
- Establishing systems for human resource development, international alliances, and research support

Research

- Establishment of Structural Vaccinology
- Promotion of basic research for vaccine development
- Establishment of novel methods to evaluate vaccine efficacy (host response/pathogen detection)
- Development of vaccines for respiratory infectious diseases

After 10 Years Establishing rapid vaccine development systems for respiratory infectious diseases and practical application of vaccines based on the research results

Resolving issues to speed up R&D, and establishing alignments among flagship and synergy vaccine institutes

System

- Establishing a system for rapid vaccine development

Research

- Introducing vaccines for respiratory infections to the community, based on 5 years' achievements

We will promote a **"preemptive strategy"** through basic research that can contribute to vaccine development and practical application of products to contribute to society.

Leading the development of domestic vaccines employing the "preemptive strategy"

Infectious Diseases and Pandemics	System for promptly providing domestically produced vaccines
Emerging infectious diseases → Zoonoses Animal / Human Pandemics likely to be triggered by respiratory infections	"Preemptive Strategies" Library of pathogens with the potential to cause zoonoses Target: Zoonoses → Isolation → Library (A, B; 1, 2, 3) → Vaccine Seeds

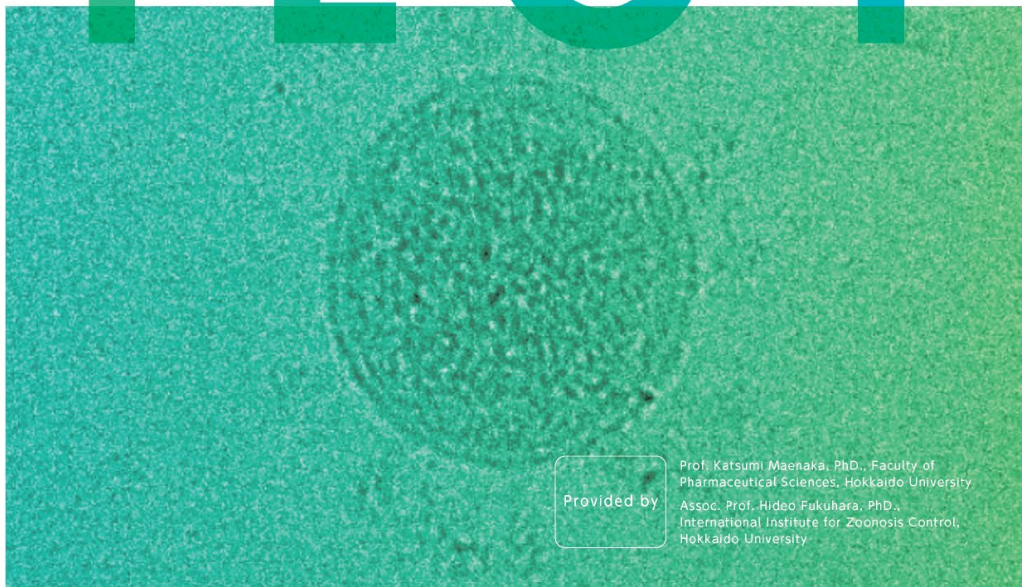
Basic research contributing to the establishment of vaccine development and production system in Japan

STRATEGY

Cryogenic Electron Microscopy (CryoEM) for BSL3 pathogens

Research and Development Goals

IVReD will conduct the "preemptive strategy" to establish a library of microorganisms that could cause infectious diseases in humans, promote basic research that can contribute to vaccine development, and implement products for the community. Specifically, IVReD will isolate and identify microorganisms that may cause infectious diseases in humans from humans, wild animals, domestic animals, arthropods, etc., store them in a pathogen library, analyze their pathogenicity and transmissibility, and select candidates for vaccine development. In addition, IVReD will establish a system that can promptly provide domestically produced vaccines including preparation of vaccine seed viruses, trial production of pandemic model vaccines, and preclinical trials.



Provided by

Prof. Katsumi Maenaka, PhD., Faculty of Pharmaceutical Sciences, Hokkaido University

Assoc. Prof. Hideo Fukuhara, PhD., International Institute for Zoonosis Control, Hokkaido University

IVReD promotes research on vaccine development for zoonotic pathogens with a focus on respiratory infections

◎ Outline of research and development plan

IVReD will conduct research and development targeting 1) influenza, 2) coronavirus infections, and 3) tuberculosis, which are respiratory infections with a high potential to cause the next pandemic or are currently spreading, especially because of the diverse routes of transmission including droplets, air, poor hygiene, oral and environment, and a higher speed of transmission than for other infections.

IVReD will also collect specimens of zoonotic pathogens from wild animals and humans, utilizing the domestic and international collaborative research networks established by the members of the institute. Furthermore, IVReD will artificially create viruses based on the genome information obtained from the database. Additionally, IVReD will construct a library of zoonotic pathogens, mainly respiratory tract infections, and analyze their pathogenicity and transmissibility.

IVReD will promote research on vaccine development for the zoonotic pathogens by selecting those that have the potential to cause future pandemics.

FLOW Flow of Research and Development at IVReD

1 Research on viruses and other pathogens

- Establishment of pathogen libraries
- Collection and provision of information on cutting-edge R&D trends

2 Structural Biology Research

- Analysis of pathogens by cryo-electron microscopy in BSL3 facility
- Determination of structures of complexes between pathogen proteins and antibodies

3 Basic research on vaccines (Division of Biological Response Analysis)

- Analysis of innate immune response in vaccination and infection
- Analysis of acquired immune responses using mouse and human specimens

4 Basic research on vaccines (Division of Vaccinology for Clinical Development)

- Research to improve existing vaccines
- Research for Drug Delivery Systems (DDS) development

5 Research on evaluation systems

- Establishment of evaluation systems (*in vivo*, *in vitro*) for infections
- Development of new diagnostic techniques

6 Clinical research

- Promotion of "reverse translational research" by feeding back the results obtained by efficacy and safety evaluation to clinical trials

IVReD
HOKKAIDO UNIVERSITY

Constructing a World-leading Vaccine Research and Development Center in collaboration with companies and clinical sites

Institute for Vaccine Research and Development

IVReD is closely aligning and cooperating with the flagship institute, the University of Tokyo, and other synergy institutes, and in direct collaboration with industry and clinical sites under the management of the Strategic Center of Biomedical Advanced Vaccine Research and Development for Preparedness and Response (SCARDA) at AMED. IVReD consist of 4 divisions, Vaccine Development, Biological Response Analysis, Vaccinology for Clinical Development, and Research Support, that take actions under the leadership of Director Hirofumi Sawa, Deputy Director Tomio Ikeda, and Deputy Director Norihiro Sato.

Director :
Hirofumi Sawa, M.D., Ph.D.

Deputy director (Industry) :
Tomio Ikeda,
DVM., PhD., EMBA.
(Denka Company Limited)

Denka

IFV Vaccine

Deputy director (Clinic) :
Norihiro Sato, M.D., Ph.D.
(Hokkaido University Hospital Clinical Research and Medical Innovation Center)

World-class researchers belong to each division

Division of Vaccine Development

- Isolation of pathogens, establishment of libraries, and elucidating transmission routes
- Structural analysis of pathogens and complexes of vaccine-produced antibodies and proteins in pathogens
- Development of novel drug delivery systems and whole virus particle vaccines

Hideyoshi Harashima, PhD.
(DDS)

Hiroshi Kida, DVM., PhD.
(IFV vaccine)

Tomio Ikeda, DVM., PhD., EMBA.
(Denka Company Limited)
(IFV Vaccine)

Katsumi Maenaka, PhD.
(CryoEM)

Toshihiro Ito, DVM., PhD.
(IFV vaccine)

Division of Biological Response Analysis

- Analysis of pathogenicity of zoonotic pathogens
- Analysis of host innate immunity in response to infection and vaccination
- Analysis of host acquired immunity in response to infection and vaccination

Koichi Kobayashi, M.D., Ph.D.
(Innate immunity)

Hirofumi Sawa, M.D., Ph.D.
(Virology, Vaccinology)

Masaaki Murakami, DVM., PhD.
(Acquired immunity)

Katherine Kedzierska, PhD.
(Immune response to viral infection)

Division of Vaccinology for Clinical Development

- Development of novel adjuvants
- Construction of *in vitro and in vivo* infection experimental systems for pathogens
- Establishment of clinical specimen collection system

Satoshi Konno, M.D., Ph.D.
(Clinician for respiratory infectious diseases)

Akihiko Sato, DVM., PhD.
(*In vitro* evaluation system)

SHIONOGI

Norihiro Sato, M.D., Ph.D.
(Clinical research)

Kazuhiro Matsuo, Ph.D.
(CTL adjuvants)

Kiyoshi Takayama, PhD.
(*In vivo* evaluation models)

NB HEALTH LABORATORY

Division of Research Support

- Liaison to industry and other partners
- Public Relations
- Collection and analysis of cutting-edge information on R&D and infection outbreak trends
- Administrative support for researchers

Yasuhiko Suzuki, PhD.
(Tuberculosis diagnosis, Protein mass production)

Keiichi Yamamoto, M.S.
(Project Manager, Intellectual property)

Gabriel Gonzalez, PhD.
(Bioinformatics)

MEMBERS

Division of Vaccine Development

Division of Vaccine Development

Tomio Ikeda, DVM., PhD., EMBA.
(Denka Company Limited) (IFV Vaccine)

Denka

◎Research and development of pandemic influenza vaccine

- As part of a proactive strategy against zoonotic diseases, this research aims to develop and ready to commercialize a pandemic influenza vaccine that induces priming and cell-mediated immunity. As a research and development co-investigator, promote the following research subjects:
- Virus strains that may cause pandemic influenza in the future are being analyzed and pandemic vaccine candidate strains will be selected by these accumulated informations such as HA and NA gene sequences, antigenicity, proliferation ability.
- Inactivated intact virus particle vaccines of the pandemic vaccine candidate strains will be prototyped, and their antibody-inducing ability, infection-suppressing effect, and safety will be evaluated in animals. Suitable vaccine candidate strains that show better results will be prepared and stored as seed virus strains at GMP level. In parallel, a P3 laboratory equipped with cell culture equipment will be set up to prepare for rapid vaccine production in the event of a pandemic.

Division of Vaccine Development

Hideyoshi Harashima, PhD.
(DDS)

◎Basic research on vaccines
◎Development of novel lipid libraries and their optimization for mRNA vaccines

- Aiming to develop a novel Drug Delivery System (DDS), construct a novel lipid library and optimize it for mRNA vaccines.
- We synthesize more than 30 types of pH-responsive cationic lipids which greatly affect mRNA transfer efficiency and helper lipids which greatly affect in vivo disposition and intracellular trafficking of lipid nanoparticles, which are components of new lipid libraries.
- Using these lipids, various lipid compositions and mRNA are packaged into LNP using a microfluidic device. LNP are optimized by 1) physical properties, 2) the balance between transfection efficiency and toxicity, 3) route of administrations.
- We also establish a novel loading methodology of BCG components as adjuvants into LNP.
- Based on these studies, we will develop mRNA-loaded lipid nanoparticles that maximize vaccine efficacy and minimize side effects, and create mRNA vaccines for influenza viruses and coronaviruses.

Division of Vaccine Development

Hiroshi Kida, DVM., PhD.
(IFV vaccine)

◎Research and Development of Pandemic Influenza Vaccine

- The aim of the present study is to develop pre-pandemic influenza vaccines of global standard in Japan as the preparedness for future pandemics in the world.
- Virus strains that may cause pandemic influenza in the future are selected from the Hokkaido University Influenza Virus Library, and procedure of vaccine manufacturing such as conditions of cultivation, inactivation and purification of candidate viruses shall be established. After that, inactivated intact virus particle vaccines shall be prepared as pre-pandemic model vaccines of which effectiveness and safety are ensured.
- Especially it is seriously concerned that H5N1 highly pathogenic avian influenza viruses spread all over the world due to misuse of vaccine to poultry in a few countries. Misuse of avian influenza vaccine led to silent spread of the H5N1 highly pathogenic avian influenza viruses because of the failure to detect and cull inapparently infected poultry birds. At present, the H5N1 virus has been entrenched in the nesting lakes of migratory ducks in the northern regions, especially in Siberia. The migratory ducks carry and spread the highly pathogenic H5N1 virus to poultry and wild birds all over the world. Therefore, it is concerned if pigs are coinfected with avian H5 viruses and seasonal human influenza H1N1 or H3N2 viruses and produce genetic reassortants, resulting in the production of pandemic influenza viruses. The objective of the present study is to develop H5 influenza virus vaccines to counteract pandemic influenza caused by the reassortant virus with dangerous H5 HA with furin-cleavage site is inserted.

Division of Vaccine Development

Katsumi Maenaka, PhD.
(CryoEM)

◎Structural analysis using cryo-electron microscopy facilities including BSL3 microscope to establish of rational design for vaccine design (Structural Vaccinology)

- Based on the COVID-19 pandemic, we aim to establish a rational vaccine design method based on three-dimensional structures for the next pandemic.
- Using structural biology techniques including cryo-electron microscopy, we will analyze the HA and particles of the selected influenza viruses and the S protein particles of SARS-CoV-2 variants.
- Complexes of viral proteins and particles with monoclonal antibodies obtained from vaccinated animals will be analyzed using cryo-electron microscopy. We will evaluate the profiling of the binding mode to the epitope from the three-dimensional structures.
- The relationship between structure and pathogenicity,and the identification of antibody-binding epitopes, will be examined with vaccine efficacy. We aim to establish "Structural Vaccinology", which can infer the effect of vaccines from the binding structures of monoclonal antibodies.

Division of Vaccine Development

Toshihiro Ito, DVM., PhD.
(IFV vaccine)

◎Investigation of practical application of inactivated virus complete particle vaccine against pandemic influenza

- Select candidate strains of vaccines against influenza viruses that have the potential to cause pandemics in the future, and establish their vaccine seed systems by examining the culture and inactivation conditions.
- Evaluate the efficacy of the trialed whole particle vaccine (WPV) in terms of immunogenicity and safety, etc., with the aim of early commercialization of inactivated virus WPV against pandemic influenza.

MEMBERS

Division of Biological Response Analysis

Division of Biological Response Analysis

Hirofumi Sawa, M.D., Ph.D.
(Virology, Vaccinology)

◎Establishment of library of zoonotic pathogens
◎Selection of vaccine candidates from zoonotic pathogens

- To collect zoonotic pathogens, including influenza viruses, corona viruses and Mycobacterium tuberculosis from wildlife and humans by using an international research network.
- To make recombinant viruses based on genomic data.
- To establish a library of zoonotic pathogens
- To analyze pathogenicity and transmissibility of obtained pathogens for selection of vaccine candidates
- To perform basic research for vaccine development for selected pathogens

Division of Biological Response Analysis

Koichi Kobayashi, M.D., Ph.D.
(Innate immunity)

◎Development of vaccine platform using bacteria
◎Vaccine development against viral infections

- We will develop a new genetically modified bacterial vaccine platform by combining the original technology successfully developed in our laboratory with the technology developed by our collaborators. This vaccine platform is safe for human use, has excellent adjuvant potential (immunogenicity), is highly capable of presenting antigens in both MHC class I and class II pathways, and induces long-lasting immunological memory. It is stable and can be stored at room temperature. By incorporating specific antigens, it can be used as a vaccine against infectious diseases such as specific viruses, but it also has a non-specific immunity-inducing ability, so it has a certain effect even against infectious diseases with mismatched antigens.
- Develop viral vaccines by incorporating antigens such as coronavirus into the vaccine platform.
- Create a pan-coronavirus vaccine to prepare for a possible third novel coronavirus epidemic in the future by using antigens that are widely conserved in coronaviruses as antigens.

Division of Biological Response Analysis

Masaaki Murakami, DVM., PhD.
(Acquired immunity)

◎Comprehensive analysis of immune cells and tissue non-immune cells during respiratory infection and vaccination
◎Establishment of pathogen detection technology with high sensitivity using quantum technology

- We will establish an analytical platform covering cellular, expression, and genetic analyses in immune cells and tissue non-immune cells during the development of respiratory infections such as coronaviruses and influenza viruses in clinical specimens, model animals, and at the time of vaccination.
- Using this analysis platform, identify immune cell fractions including novel cell fractions that are correlated with specific aggravation, sequelae, and vaccine efficacy at the onset of respiratory infections and vaccination, perform detailed analysis, identify diagnostic markers, and drug discovery targets.
- We will establish a diagnostic platform that can diagnose types of pathogens including mutations with ultra-high speed and ultra-high sensitivity using quantum technology such as AI nanopores and diamond nanosensors.
- In collaboration with the Department of Respiratory Medicine, Hokkaido University Hospital, we will build a system that collects and stores specimens from hospitalized patients with respiratory infections and those who have been vaccinated, and analyzes them on the above platform.

Division of Biological Response Analysis

Katherine Kedzierska, PhD.
(Immune response to viral infection)

◎Understanding immune responses to respiratory infections and vaccinations

- We facilitate the research on immune responses to respiratory virus infections, such as SARS-CoV-2 and influenza viruses using human clinical or animal samples. In particular, we aim to elucidate the mechanisms of T cell-mediated immune responses and establishment of immune memory which are effective against pandemic viruses.
- To identify the factors that correlate with recovery speed and milder symptom in patients with mild to moderate infection or factors that correlate with severity of infections. Furthermore, we also aim to elucidate the induced immune responses by those factors.
- We aim to elucidate the mechanisms of viral immune evasion and mechanisms of induction of cross immunity against those viruses. In particular, we will evaluate the proportion and longevity of specific CD8+ T cells induced by influenza virus or SARS-CoV-2 infection, as well as the cross-reactivity of such CD8+ T cell responses using SARS-CoV-2 and influenza A and B viruses. To immunologically evaluate the vaccine developed in this project, we will use the comprehensive immune evaluation platform that we have established.
- The results of our studies will be applied to the establishment of rapid and close global infectious disease research network for clinical and basic research in the event of a pandemic outbreak.

MEMBERS

Division of Vaccinology for Clinical Development

Division of Vaccinology for Clinical Development

Norihiro Sato, M.D., Ph.D.
(Clinical research)

◎Support from research and development to practical application in the medical and health science fields

- A support organization has been established within Hokkaido University Hospital to link the results of basic research in the medical and health science fields to the practical application of medical care. Hokkaido University is certified as a translational research support institution established by the Ministry of Education, Culture, Sports, Science and Technology.
- In addition, Hokkaido University Hospital is certified as a clinical research core hospital selected by the Ministry of Health, Labor and Welfare based on the Medical Care Law.
- The Institute of Health Science Innovation for Medical Care (HELIOS) is organized at Hokkaido University Hospital as an organization to operate these, and I am the director of that organization.
- HELIOS supports the development of pharmaceuticals, medical devices, regenerative medicine products, and in-vitro diagnostics, as well as the implementation of clinical research such as the utilization of real-world data and other medical information. It is leading to practical application such as approval and establishment of standard treatment.

Division of Vaccinology for Clinical Development

Satoshi Konno, M.D., Ph.D.
(Clinician for respiratory infectious diseases)

◎Construction of a network of core hospitals related with respiratory infectious disease in Hokkaido
◎Development of Phase 1 study at Hokkaido University Hospital

- Respiratory physicians are responsible for treating respiratory infections such as COVID-19 and tuberculosis in Hokkaido. From the perspective of infection, host reaction/immunity, and comorbidity and differentiation of other diseases, it can be seen as an advantage for patients, and it will also facilitate the construction of a network of main hospitals in Hokkaido.
- Our department have already been conducted many collaborative studies among several hospitals, including Sapporo City General Hospital, which is first-class infectious disease designated medical institution, and Japan Community Health care Organization (JCHO) Hokkaido hospital and National Hospital Organization Hokkaido Medical Center, which are Tuberculosis designated medical institution in Sapporo City.
- In this research, we can take advantage of strong relationships among many hospitals, and can be possible for collecting a variety of clinical specimens, such as serum, sputum, saliva, and TB culture from these hospitals.
- Our hospital has the only Phase 1 unit in Hokkaido, and we have already established a system for developing clinical research on new vaccines in the future. At the same time, in order to respond swiftly to epidemics of new respiratory infections that we will face for a long time to come, we plan to make efforts to train respiratory physicians who specialize in respiratory infections.

Division of Vaccinology for Clinical Development

Kazuhiro Matsuo, Ph.D.
(CTL adjuvants)

◎Research and development of preventive vaccines for adult tuberculosis and COVID-19 using novel CTL adjuvant and its application

- Although BCG is widely used as a vaccine against tuberculosis in infant, efficacy against the pulmonary disease in adults is limited. Development of a tuberculosis vaccine for adults has been underway around the world. However, there has been no practical vaccine yet to solve the problem. In addition, it has been reported that BCG suppresses various diseases other than tuberculosis by its off-target effect. It was reported in 2022 that the BCG Tokyo strain showed effective suppression for the onset of COVID-19 due to its excellent induction of innate immunity. However, it remains unclear what kind of immune response is responsible for such off-target effects.
- Various adjuvant molecules have been purified and identified from the BCG Tokyo strain. Among them, we will identify molecules that enhance the induction of cytotoxic T lymphocyte (CTL) and apply them to preventive vaccines against infectious diseases in which CTL plays a critical role in protection against infection and onset of the diseases. Using the novel adjuvant, we will aim to develop a tuberculosis vaccine to enhance the CTL response by BCG, which has a weak CTL priming ability, and a universal coronavirus vaccine that can cover a variety of mutant strains by induction of CTL against conserved regions of SARS-CoV2 antigens.

Division of Vaccinology for Clinical Development

Kiyoshi Takayama, PhD.
(In vivo evaluation models)
NB HEALTH LABORATORY

◎Development of novel vaccines and therapeutic agents against influenza and coronavirus infections

- Estabilish models of influenza and coronavirus infections in rodents and monkeys that reflect human symptoms.
- Using the constructed animal model, we will verify the efficacy of newly created vaccines and acquire basic data for clinical research. At the same time, we explore target molecules that control host immunity involved in sever symptons after infection.
- Based on this knowledge, we will discover novel therapeutic drug seeds (antibodies, low-molecular-weight drugs) that universally prevent severe virus infection regardless of virus strains.

Division of Vaccinology for Clinical Development

Akihiko Sato, DVM., PhD.
(In vitro evaluation system)
SHIONOGI

◎Research and development of pandemic influenza vaccine
◎Research and development of vaccines against COVID-19

- In order to manufacture a virus-inactivated whole-particle model vaccine using the current seasonal influenza vaccine-producing strain, a large-scale influenza virus culture method is examined. We aim to establish a production method suitable for rapid vaccine production in the event of a pandemic by setting up a P3 laboratory equipped with a roller-type rotary culture device or a large-capacity bioreactor.
- Build a coronavirus vaccine evaluation system. Neutralization measurement methods using various corona mutant strains have already been established. Coronaviruses are constantly mutating, so we will establish a system to stably implement neutralization measurement methods using various cells and virus strains so that we can select an evaluation system suitable for new coronavirus vaccines.
- As a preparation for using an adjuvant, we will mainly construct a cell evaluation system by analyzing the adjuvant effect by measuring Th1/cytotoxic T cell activation.

MEMBERS

Division of Research Support

Division of Research Support

Yasuhiko Suzuki, PhD.

(Tuberculosis diagnosis, Protein mass production)

◎Research and development of vaccines using novel CTL-inducing adjuvants and their applications

- In order to commercialize a novel tuberculosis vaccine using a novel CTL-inducing adjuvant derived from Mycobacterium bovis, it is necessary to produce vaccine antigens in large quantities.
- Optimizing the antigen protein production by examining the culture method of recombinant M. smegmatis. Furthermore, we will establish a system that can purify a large amount of recombinantly expressed proteins in fewer steps.
- We will attempt to combine immune checkpoint inhibitor antibodies or their analogues with the aim of enhancing the effects of novel adjuvants in our research.
- The company uses its proprietary technology to express glycosylated proteins using Chinese hamster ovary (CHO) cells to create CHO cells that can express large amounts of immune checkpoint inhibitor antibodies or their analogues.
- Establish a system that can purify a large amount of recombinantly expressed proteins in fewer steps.

Division of Research Support

Keiichi Yamamoto, M.S.

(Project Manager, Intellectual property)

◎Efficient intellectual property of research results

- The ultimate goal of IVReD is to protect people from infectious diseases and their pandemics. In addition to aiming for the early development of vaccines for respiratory infections, we are establishing a system to realize this development and promote the social implementation of vaccines for respiratory tract infections based on the results of basic research in academia.
- Additionally, we will contribute to the "rapid development and production system for Japanese vaccines" in outbreaks of infectious diseases by flexible responses.To achieve this goal, it is essential to cooperate and collaborate with numerous internal and external research institutions, industry, and government agencies.
- As a multifaceted approach to infectious diseases, techniques and concepts from various academic fields are necessary.Therefore, we aim to achieve our goals as early as possible by centrally confirming and coordinating the R&D status of such a wide variety of related divisions to facilitate cooperation among them. In addition, from the viewpoint of providing incentives to researchers and increasing their motivation, we will actively promote the rights of research results and licensing activities.

Division of Research Support

Gabriel Gonzalez, PhD.

(Bioinformatics)

◎Risk assessment and prediction of the amino acid substitutions effects in the vaccines effectivity against respiratory pathogens.

- To maximize the protective effects of the vaccines, constant validation of their effectivity to neutralise the circulating variants of a pathogen is required.
- An approach to provide constant validation of the efficacy of vaccines despite the genetic diversity of pathogens is by in silico analysis and prediction of amino acid substitutions structural effects in the epitope determinants.
- The continuous advances in protein modelling are not a substitute for wet-bench experiments, but a great complement to explore a higher number of scientific and clinical hypotheses and narrow the targets with predicted results for laboratory validation and exploration.
- We are also exploring the simulation of multiple conditions that can affect the interaction of pathogens with the host, such as pH, temperature, etc.
- Additionally, we analyse databases of pathogens sequences in search for recurrent amino acid substitutions that could indicate uncharacterised sites under selection and a future risk.

NETWORK

Gathering and sharing information on the latest research trends through domestic and international networks

IVReD aims to achieve results by flexibly building research systems in response to domestic and international trends. Progress in research will utilize a wide range of domestic and international networks established by co-investigators. Specifically, IVReD will prepare for the emergence of infectious diseases by collecting worldwide information on outbreaks of infectious diseases from the Hokudai Center for Zoonosis Control in Zambia (HUCZCZ), overseas partner institutions, WHO, and GOARN.
In promoting basic research for vaccine development, IVReD will collaborate with the University of Oxford, Texas A&M University, the University of Melbourne, and other institutions to collect information on research trends around the world and share it with SCARDA, its flagship institute, and synergistic institutes.

Flexible R&D and information collection system utilizing networks with overseas research institutions

International organizations cooperating in infection disease control

- World Health Organization (WHO)
- Office International des Epizooties (OIE)
- GOARN※ ※Network made up of numerous public health institutions, research institutes, NGOs, etc. that works closely with the WHO to monitor and counter infectious diseases that pose a threat.
- Food and Agriculture Organization of the United Nations (FAO)

ACCESS

Institute for Vaccine Research and Development (IVReD)

Division of Research Support, Hokkaido University
Institute for Vaccine Research and Development,
North 21, West 11, Kita-ku, Sapporo, Hokkaido, Japan,
001-0021
Email: kyotenjimu@ivred.hokudai.ac.jp
https://www.ivred.hokudai.ac.jp/

Route from the Main Gate

Route from the North 18 Gate