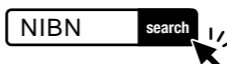




National Institutes of Biomedical Innovation, Health and Nutrition

<https://www.nibn.go.jp/>



National Institutes of Biomedical Innovation, Health and Nutrition



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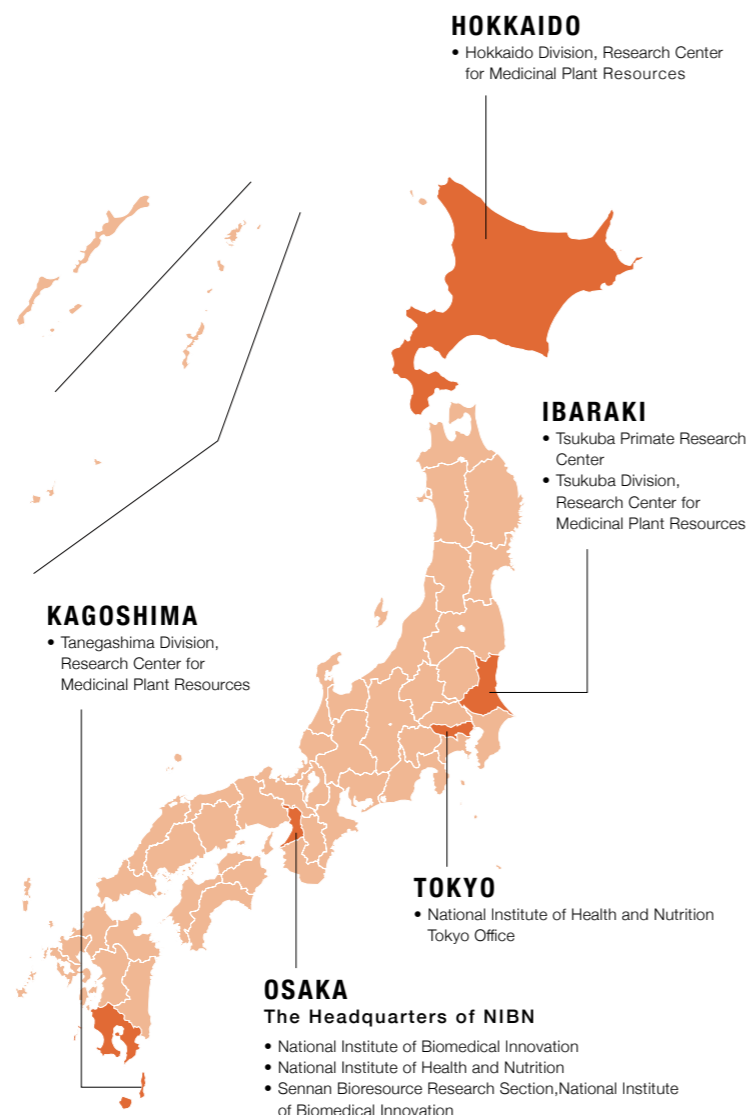
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**INSTITUTE FOR YOUR HEALTH**

WE ARE NIBN

A research institute committed to people's health

Check Our SNS



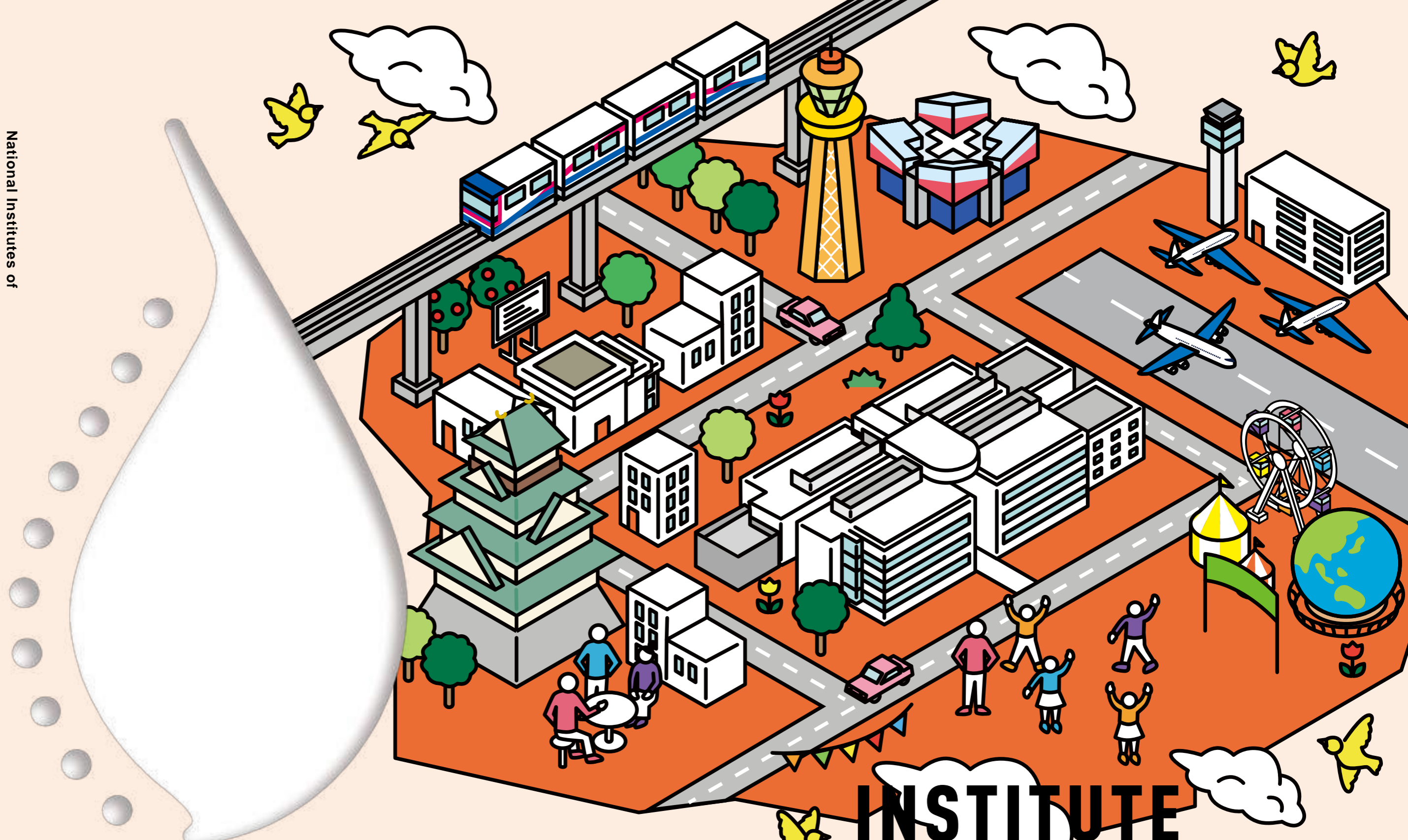
The official YouTube channel



The official X (formerly Twitter) account



The official Instagram account



National Institutes of  
Biomedical Innovation, Health and Nutrition

A research institute committed to people's health

# INSTITUTE FOR YOUR HEALTH

WE ARE NIBN

Living long with healthy conditions has always been a long-standing desire of humankind. For people suffering from illness and their families, living in darkness without hope of a cure or living with even the slightest hope of a cure makes a huge difference on their life.

In order to be a beacon of hope for such people, we are taking on the challenge of interdisciplinary research in both the biomedical and health sciences for drug discovery that leads to new treatment possibilities and researches on nutrition and

physical activity that leads to prevent illness. Always with a spirit of challenges, we are deeply committed to revolutionize Japan and the world from Osaka.

As a research institute committed to people's health, we will not conduct research simply for the sake of research, but rather always aim for new technological innovations, promoting collaborations with medical institutions, private companies, and local and central governments, and conduct research that truly benefits people and society.

# NIBN's Wish

## To Be a Beacon in the Darkness

### The Meaning Behind the Logo

The new NIBN logo is based on the concept of "a beacon of candle". It symbolizes our commitment to research that serves as a beacon of hope, even in the smallest way, to change lives. The ten circles beside the flame represent our mission to provide optimal medical and nutritional solutions tailored to each individual. This logo not only signifies the integration of pharmaceuticals, health, and nutrition but also embodies our role in bringing hope to those battling illness. Our research is driven by the belief that even the smallest light can shine brightly in someone's life.



### NIBN's Philosophy

## Create, Challenge, Achieve ~ Striving for a Healthy and Long-lived Society ~

We contribute to society through a broad range of research activities, including drug discovery based on biomedical and health sciences, studies on nutrition, dietary habits, and physical activity, as well as biological resource research. By strengthening collaboration between industry, government, and academia, we integrate cutting-edge technologies and knowledge to achieve national health and well-being.

### Mission

- Pursuing innovation: We create new knowledge and technology through cutting-edge drug discovery research.
- Promoting health: We challenge ourselves to improve the nation's future well-being through research on nutrition, dietary habits, and physical activity.
- Supporting patients and families: We drive research and development to fulfill the wishes of patients battling various diseases, including rare conditions.

### History

The National Institutes of Biomedical Innovation, Health and Nutrition was established on April 1, 2015, through the merger of the National Institute of Biomedical Innovation and the National Institute of Health and Nutrition.

This integration was part of "the Basic Policy on Reform of Independent Administrative Agencies", approved by the Cabinet in 2013, aiming to advance comprehensive research by merging expertise in pharmaceuticals and food sciences.

National Institute of Health Sciences  
National Institute of Infectious Diseases  
Pharmaceuticals and Medical Devices Agency  
2005 Part of each organization merged National Institute of Biomedical Innovation

### National Institute of Biomedical Innovation

Originally based on the Osaka branch of the National Institute of Health Sciences, this institute integrated parts of the National Institute of Infectious Diseases and the Pharmaceuticals and Medical Devices Agency. Its purpose is to develop a foundation for research and development in pharmaceuticals and biological resources to improve public health.

1920 Institute of Nutrition (established within the Ministry of Interior)  
1938 Jurisdiction transferred to the Ministry of Health and Welfare following its establishment  
2001 Transformed into an independent administrative institution  
National Institute of Health and Nutrition

### National Institute of Health and Nutrition

Founded in 1920 as a Nutrition Research Institute, it became part of the Ministry of Health, and Welfare and later transitioned into an independent administrative agency in 2001. The institute conducts research on public health, nutrition, and national health improvement.

Merged on April 1, 2015

## National Institutes of Biomedical Innovation, Health and Nutrition

Organizational  
Chart



### Greetings



President : Yusuke Nakamura

By walking alongside patients to strengthen collaborating among industry, government, and academia, we aim to accelerate research that contributes to society.

The National Institutes of Biomedical Innovation, Health and Nutrition (NIBN) has been actively engaged in research and development, aiming to transform incurable diseases into curable ones and to realize a society where people live long and healthy lives.

In 2025, the post-war baby boomer generation has reached the advanced age group, ushering in a super-aged society. As a result, the importance of living long and healthy lives has become increasingly significant. Amid this, our second 7-years med- to long-term plan started in 2022, tackling various challenges in anticipation of the "era of 100-year lifespans". Maintaining and improving health through diet and exercise also requires approaches tailored to each individual. Furthermore, in the event of illness, selecting and providing optimal medical care personalized to each person will be essential in the coming era. We aim to further advance drug discovery and nutritional science by leveraging cutting-edge AI analysis and generative AI technologies, ultimately contributing to society.

In recent years, we have been building a platform that supports drug discovery by comprehensively collaborating with the Osaka International Cancer Institute, while also utilizing generative AI to reduce the burden on healthcare professionals and enable real-time, real-world medical data collection and database

development. Building on these foundations, we are working together as one with patients and medical institutions to transform diseases that are currently incurable into ones that can be treated.

As a national research institute guided by the three key domains of biomedical innovation, health, and nutrition, we are committed to addressing challenging areas such as rare and intractable diseases, where private enterprises may struggle to engage. Furthermore, to fully leverage the complementary strengths of the two institutes – from health maintenance to pharmaceutical development – we are placing greater emphasis on the integrated fields that bridge medicine with health and nutrition. In the interdisciplinary domain, we are exploring new possibilities, including research on nutrition, gut microbiota, and immune-related functions.

Moving forward, we will continue our dedicated efforts to develop foundational technologies for innovative drug discovery and to conduct research on food, nutrition, and exercise. Through these initiatives, we aspire to contribute to extending healthy lifespans and strive to become a leading research institute at the forefront of a vibrant and thriving Japan. To bring hope to patients and to Japan as a whole, we would greatly appreciate your continued - and even greater - support and cooperation.



National Institute of Biomedical  
Innovation  
Director, Research Institute :  
Toyomasa Katagiri



National Institute of Health and  
Nutrition  
Director, Research Institute :  
Hidemi Takimoto

The National Institute of Biomedical Innovation is dedicated not only to foundational drug discovery research essential for developing pharmaceuticals to overcome a wide range of diseases, but also to advancing studies on biological resources that support drug discovery, including nonhuman primates and medicinal plants.

To date, we have achieved significant progress: establishing an AI-driven drug discovery platform that accelerates patient stratification and target identification; releasing databases for rare and intractable diseases; developing infectious disease models such as those for COVID-19; and creating antibody, artificial nucleic acid, and peptide therapeutics, as well as innovative imaging systems for drug discovery.

Looking ahead, we will continue to strengthen and expand these foundational capabilities, promote next-generation drug discovery for rare diseases, intractable conditions, and infectious diseases, and deepen collaboration across industry, government, and academia. Through these efforts, we aim to ensure that our research outcomes are returned to society.

With the aspiration to serve as a cornerstone of future medicine, all members of our institute remain committed to taking on new challenges. We sincerely ask for your continued understanding and warm support.

The National Institute of Health and Nutrition is committed to extending healthy life expectancy in Japan through scientific research on nutrition, dietary habits, physical activity, and exercise.

In 2023, we relocated to the Northern Osaka Health and Biomedical Innovation District (KENTO), marking a new stage in which we further strengthen collaboration with local medical institutions and municipalities. We are now advancing practical and novel initiatives, including the development of food environment models that naturally promote healthier choices in partnership with food-related industries, as well as large-scale cohort studies conducted with neighboring local governments.

Going forward, we will continue to enhance and expand our research functions that contribute to public health—such as studies on diet and physical activity for the primary prevention of lifestyle-related diseases, the dissemination of information on functional food components, and communication related to Health Japan 21, a national health policy.

With your continued understanding and support, we remain dedicated to fulfilling our social responsibility as a research institute and to advancing toward a healthier future for all.

# NIBN's Strengths

## Integrating Biomedical Science and Health Science

We are committed to bridging biomedical science, which focuses on treating diseases, and health science, which promotes longevity and well-being. Our daily research covers drug discovery, nutrition, exercise, and biological resources, aiming to contribute to public health from innovative drug development to personalized nutritional and health guidance.

### 01 STRENGTH

#### Drug Discovery Research Leading to Treatment



#### Promoting innovative drug discovery research with new modalities and advanced technologies

National Institute of Biomedical Innovation focuses include developing therapies for rare diseases and infectious diseases using antibodies, nucleic acid-based drugs, and regenerative medicine. By leveraging bioinformatics and AI, we explore drug targets, assess

safety and efficacy, and provide information and resources utilizing rare disease databases. Through collaboration with the Japan Agency for Medical Research and Development (AMED), we aim to bring cutting-edge medical solutions to the world.



### 02 STRENGTH

#### Research on Nutrition, Physical Activity, and Gut Microbiota for Prevention



#### Advanced research on nutrition, physical activity and intestinal bacteria for a healthy and long-lived society

The National Institute of Health and Nutrition is promoting research on the effects of diet and physical activity on health in order to realize a healthy and long-lived society with consideration for reducing environmental impact. Partnering with National Institute of Biomedical Innovation, we utilize AI to develop the "Healthy Human Microbiome Information

Platform" focusing on gut microbiota and circadian rhythms. Our efforts include new prevention and mitigation strategies for lifestyle-related diseases and frailty. Additionally, we assess health impacts of functional foods and dietary ingredients, contributing to evidence-based dietary guidelines and national health policies.



### 03 STRENGTH

#### Biological Resource Research Supporting Drug Discovery in Japan



#### Bringing innovation to drug development through bioresource research

Our research centers, including Center for Drug Discovery Resources Research, Research Center for Medicinal Plant Resources, and Tsukuba Primate Research Center, engage in research and development of biological resources. These

include human tissues, cell lines, disease model animals, medicinal plants, and experimental primates. Through genetic data integration and quality enhancement, we aim to advance research on drug discovery for intractable diseases.



### Japan's Pharmaceutical Industry Facing an Era of Major Transformation and Challenges

As Japan's trade deficit in pharmaceuticals continues to grow each year, the country's pharmaceutical industry is required to address the following challenges:

#### Challenges

- Shortage of drug discovery seeds
- Low success rates in clinical proof-of-concept trials
- Paradigm shift towards biopharmaceuticals
- Risk of financial strain due to high-cost drugs
- Need for integration and organization of big data and IT workforce development
- Weaknesses in pandemic infectious disease countermeasures
- Risk of supply chain collapse due to country-specific risks

#### Initiatives Required to Address These Challenges

- Integrating and organizing big data to efficiently identify drug discovery targets using AI and conduct clinical trials with patient stratification.
- Developing innovative biopharmaceutical creation technologies and accelerating vaccine and therapeutic drug development.
- Establishing a national economic security framework through public-private collaboration.



# NIBN's Challenges

## Translating Research Outcomes into Societal Benefits Through Diverse Partnerships

We are expanding collaborations to realize a healthier society. Through partnerships with medical institutions, municipalities, and businesses, we support clinical research, urban development, and product innovation. Our collaborative efforts also extend internationally.

Promote open innovation with the region at the core.

Convergence of research infrastructures will also develop fusion areas.

In March 2023, National Institute of Health and Nutrition relocated to "Northern Osaka Health and Biomedical Innovation Town" (Kento), situated across Suita and Settsu cities. This move enhances open innovation with neighboring institutions, including the National Cerebral and Cardiovascular Center and Suita Municipal Hospital. Strengthening cooperation with the National Institute of Biomedical Innovation in Saito, we aim to advance integrated research themes.

Through these initiatives, we foster collaborations between researchers and industries in Osaka and Kansai area, promoting evidence-based policies and accumulating valuable research data.



National Institute of Biomedical Innovation  
International Culture Park  
(Saito: Ibaraki City, Osaka Prefecture)



National Institute of Health and Nutrition  
Northern Osaka Health and Biomedical Innovation Town  
(Kento: Suita and Settsu Cities, Osaka Prefecture)



## NIBN's Expanding International Network

In September 2024, NIBN signed a Memorandum of Understanding (MOU) with Institut Pasteur du Japon to initiate collaboration in pharmaceuticals and vaccine development. This partnership enhances research on biological resources and health sciences, facilitating global expansion of research findings and fostering opportunities for researchers.

Additionally, in June 2024, a delegation led by Dr. Wen-Chang Chang from Taipei Medical University (TMU) visited NIBN, leading to an MOU in September 2024.



Signing ceremony  
with Institut Pasteur du Japon



Signing ceremony with Taipei Medical  
University (TMU)

## Bringing Together Knowledge Across Fields for a Healthier Society

### Collaboration with Medical Institutions



#### Creating Value through the Integration of Medicine and Nutrition

We are strengthening research partnerships with advanced medical institutions, integrating clinical research insights and patient data to develop nutrition and health guidance that enhances post-treatment quality of life.



Osaka International Cancer  
Institute

Providing and developing advanced cancer treatment, while also promoting support for cancer survivors.



Osaka Women's and  
Children's Hospital

Providing advanced perinatal and pediatric medical care, actively engaging in research and maternal-child health initiatives.



National Cerebral and  
Cardiovascular Center

A research and development hub for the prevention and treatment of cardiovascular diseases, offering advanced medical care.

Collaboration between NIBN and Each Center

- Sharing research outcomes and clinical information
- Exchange of opinions in regular meetings
- Conducting joint research

### Collaboration with Local Communities



#### Promoting Healthy and Sustainable Urban Development

We promote sustainable urban development that supports healthy lifestyles. Through collaboration with local governments and citizens, we establish systems linking diet and physical activity, aiming to create an environment where everyone can live healthily.

##### Development of a Web Application for Supporting Nutritional Balance and Sustainability-Conscious Food Choices

We are developing a web application to support healthy eating habits, aiming to increase the utilization of products that consider both health and environmental aspects.

##### Research for the Development of a Japanese Nutritional Profiling System

We are conducting validation studies on the Japanese nutritional profiling system developed in FY 2024 to facilitate its utilization.

##### Research on Personalized Physical Activity Levels Based on Life Course and Lifestyle

By creating energy expenditure and physical activity profiles using doubly labeled water, we enable personalized recommendations for physical activity levels.

##### Research Evaluating Food-Related Companies' Health Initiatives Using International Standards

We assess corporate efforts to promote healthier products, aiming to create a food environment where healthy choices come naturally.

## Toward the Realization of a Naturally Healthy Diet

### Collaboration with Industries



#### Innovation in Food Environments Based on Scientific Evidence

We are building a platform in collaboration with food companies to support a healthy diet for the Japanese population. Our initiatives focus on developing products that consider nutritional balance and sustainability and examining effective information dissemination methods based on scientific evidence.

##### Database

##### Establishment and Utilization of a Processed Food and Recipe Database

We have created a database that displays nutritional information for processed foods and recipes, and have published it on the NIBN website. Going forward, we will further enhance it with data provided by companies and universities, and advance data analysis.



##### Feedback

##### Effective Collaboration System with Companies and Local Communities

We promote information sharing among participating companies and municipalities, supporting the optimization of the nutritional balance of processed foods and meals.



##### Social Implementation

##### Creating a Food Environment that Encourages Healthy Eating

We explore effective ways to provide and sell nutrition-conscious products to both health-conscious and non-health-conscious consumers.



##### Simulation

##### Predicting and Validating Effects Through Simulation

We predict the impact of promoting and practicing healthy eating through simulations, evaluating health, medical, and economic benefits.



# Center for Intractable Diseases and ImmunoGenomics (CiDIG)

MESSAGE

## A professional's commitment to research

Since my student days, I have consistently focused on human immunology research. Before joining the National Institutes of Biomedical Innovation, Health and Nutrition, I had the opportunity to hone my expertise at leading infectious disease research institutions in Japan, France and the United States, working at the forefront of translational research. However, I have always aspired to contribute to drug and vaccine development originating from Japan. Receiving an invitation from this institute, a leading center for translational research, solidified my decision to return to Japan and take on this challenge.

Director Takuya Yamamoto



Informing patients in a timely manner and contributing broadly to people's health and longevity through interdisciplinary research involving experts in the fields of intractable disease, genome and immunology

Exploring approaches to intractable diseases, cancer and infectious diseases by elucidating the hidden connections between genomic and immune information

With advancements in computer science, life sciences have undergone a paradigm shift toward research and development utilizing big data. However, the practical implementation of these benefits for patients remains a work in progress. To bridge this gap, omics analysis—which systematically structures and analyzes diverse human phenotypic data—plays a crucial role. Since human phenotypes vary widely, it is essential to capture biological samples as temporally and spatially interconnected data at high resolution and analyze them with advanced expertise.

To maximize the potential of valuable biological samples for patient benefit, we must ensure the collection and structured organization of high-quality biospecimens linked to clinical data. Additionally, the entire process—from data generation through experimental analysis to high-level data interpretation—must be conducted with scientific rigor. Against this backdrop, our center was established in April 2023 to advance research and development that integrates clinical information with genomic and immune data, ultimately driving the diagnosis, prevention, and treatment of rare diseases, cancer, and infectious diseases.

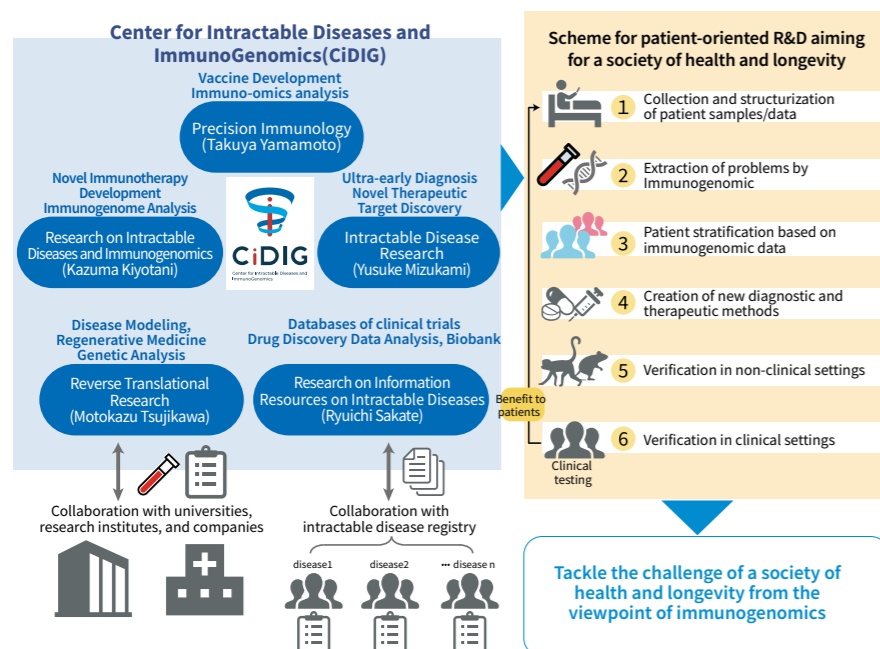


Figure 1: Development of higher-dimensional immunological analysis platform

## Utilizing platforms for high-dimensional immunological analysis seamlessly connecting clinical and non-clinical data

The Center is dedicated to realizing precision medicine through immunological approaches. By understanding individual immune characteristics and identifying disease- and population-specific challenges, we have established a comprehensive, high-resolution platform to analyze differences in immune systems and their responses to antigens across individuals.

This platform enables us to elucidate disease-specific immune responses and develop novel biomarkers and immunotherapies. Specifically, we conduct research on immunotherapies for pancreatic cancer and chronic persistent infections, as well as preclinical and clinical trials for vaccines targeting acute infectious diseases such as influenza and COVID-19.

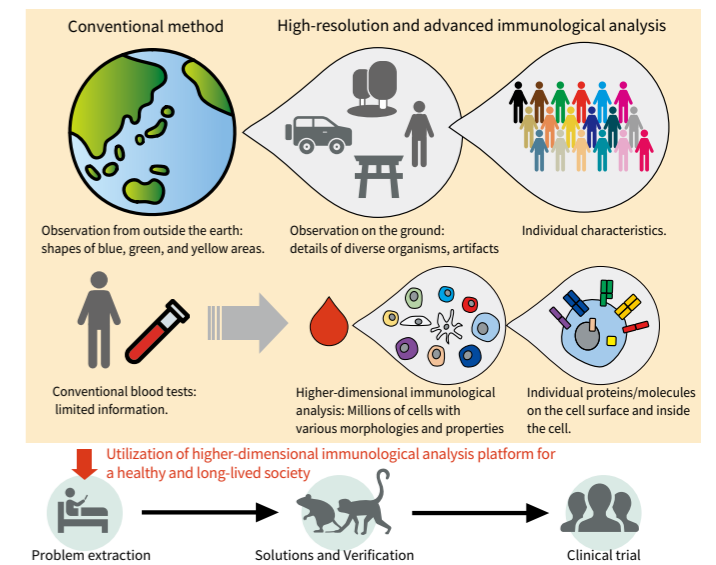


Figure 2: Metaphorical illustration of higher-dimensional immunological analysis

## Developing cancer immunotherapies based on genomic information

We focused on developing personalized immunotherapy based on the patients' cancer genome. We have established a system for efficiently predicting cancer-specific neoantigens from genome information. Using this system, we are conducting clinical research to develop personalized neoantigen-targeted cancer vaccines as well as novel T-cell therapies. In pancreatic cancer, we have identified abnormal KRAS gene activation at early stages and are actively investigating immune evasion mechanisms. Although KRAS has long been considered "undruggable", the recent emergence of KRAS inhibitors has opened new possibilities. We aim to develop more effective treatments by combining these inhibitors with immunotherapy.

## What are intractable diseases? Why should we find a cure?

Intractable diseases refer to conditions that are difficult to cure or lack established treatments. Many designated intractable diseases are classified as rare diseases, making research and development particularly challenging and necessitating government support.

At our institute, we are committed to enhancing research resources for rare diseases, utilizing omics analysis to study disease mechanisms, and developing new treatments and drugs. As of April 2025, Ministry of Health, Labour and Welfare has designated 348 diseases as intractable diseases, affecting approximately one million patients. We also advance research that supports drug discovery by widely providing information and resources through platforms such as the clinical trials database "Nanryo Chiken Web", the drug discovery information database "DDrare", and the Rare Disease Bank.

## Collaborating with experts from research on intractable diseases, cancer and infectious diseases to social implementation

Realizing innovation through big data utilization and solving real-world health challenges requires a series of highly specialized processes, including: 1. proper collection, management, and structuring of relevant biological samples and clinical information 2. well-designed preclinical and clinical trials, and 3.

high-quality and high-volume omics data analysis. At the Center, teams with deep expertise collaborate organically to tackle rare diseases, cancer, and infectious diseases. Through timely translation of research findings into clinical applications, we contribute broadly to public health and longevity.

## Center for Intractable Diseases and ImmunoGenomics (CiDIG)

### Laboratory of Precision Immunology

We aim to achieve personalized and stratified medicine using immunological approaches to overcome refractory diseases, including cancer and chronic infectious diseases. By advancing the accurate understanding of individual donor immune status changes through high-parameter flow cytometry data and multi-layered immune omics analysis, we conduct disease-specific surrogate marker exploration and develop vaccines and immunotherapies.

### Laboratory of Immunogenomics

To realize precision medicine for individual patients, we conduct multi-omics analyses, including genomic and immunogenomic approaches, to explore pathogenesis and biomarkers of diseases. We also aim to develop novel immunotherapies based on patients' genomic information.

### Laboratory of Rare Disease Information and Resource Library

We have newly launched the "Nanryo Chiken Web", a platform designed to provide patients with easy-to-understand information about clinical trials for the intractable diseases. We also conduct research to support drug discovery for rare and intractable diseases by analyzing target genes and pathways, developing "DDrare" database to provide this information, and operating a biobank in collaboration with patient registries.

### Laboratory of Molecular Diagnostics and Therapeutics

We leverage molecular pathology platforms and biological analyses of early carcinogenesis and tumor progression to investigate the fundamental mechanisms of cancer development using human clinical specimens. Our ultimate objectives are to establish surveillance strategies and ultra-early diagnostic methods for high-risk populations, identify novel therapeutic targets, and translate our findings into effective cancer prevention.

### Reverse Translational Research Project

We conduct reverse translational research by transforming various clinical questions into basic research themes for resolution. This includes elucidating the pathology of rare diseases and applying machine learning to analyze rare disease data, utilizing research findings to address clinical challenges.



# Microbial Research Center for Health and Medicine

An Introduction to Major Research Project MICROBIAL RESEARCH CENTER FOR HEALTH AND MEDICINE



**MESSAGE**

**Why I Became a Researcher and My Future Goals**

Originally, I had wanted to work for a trading company, but became a researcher after I found myself fascinated by new discovery through scientific research. Currently, I am working diligently to expand my research to create a new and healthier society.

Director Jun Kunisawa

## A Near-Future Vision for a Healthy Society from the Perspective of Gut Environment: Individualized and Stratified Dietary Guidance, Development of New Drugs, Vaccines, and Functional Foods

### Integrating the medical and health sciences

When you hear the term "intestinal bacteria", you might imagine its relationship to bowel movements, but have you ever heard that intestinal bacteria may be involved in immune responses, allergies, or obesity?

The merger of the National Institute of Biomedical Innovation with the National Institute of Health and Nutrition has created a framework where we can study both medical science (after illness occurs) and health science (before illness occurs and after recovering from illness), and our project, focused on gut health, aims to maximize the benefits of this integration.

Components consumed through food are absorbed in the gut and become part of the body, so the content and quantity of food can influence various health conditions, such as obesity and brain function.

Moreover, as many immune cells exist in the gut, intestinal bacteria also influence immune-related diseases like infectious disease, allergies and rheumatoid arthritis. Recently, the role of gut bacteria has been gaining attention.

The outcomes of this research on gut health will promote precision nutrition, personalized and stratified dietary guidance, drug discovery targeting gut health, and the development of vaccines and functional foods, expanding the possibilities of the healthcare industry.

### Informatics analysis of human big data set and elucidation of mechanisms by animal models

In collaboration with institutions across Japan, we collect human data and use the latest information science to generate hypotheses from these datasets. These hypotheses are then tested and underlying mechanisms are elucidated through basic research using animal models and other approaches, with the findings fed back into human studies. By repeating this cycle, we continuously advance research aimed at promoting health and preventing or improving diseases from the perspective of the gut environment (see Figure 1).

### Research on humans and practical applications in society

We gather information on lifestyle habits (such as diet) and health (such as health checkup data) from participants, along with blood, stool, and saliva samples. We measure parameters such as gut microbiota, oral microbiota, metabolites derived from diet, and immune system markers. By the end of fiscal year 2025, we will have collected data from more than 15,000 individuals, and we are building one of the world's largest microbiome databases.

As feedback to participants, we provide data-driven dietary guidance tailored to their gut microbiota profiles. As a result, we have begun to observe changes such as an increase in butyrate-producing bacteria, which are attracting attention for their health benefits. Furthermore, to compensate for the commonly insufficient intake of dietary fiber, our research has shown that consuming glutinous barley helps create an environment with a diverse range of gut bacteria, which is associated with a reduced risk of various diseases.

### Discovery of useful gut bacteria that may alleviate obesity and diabetes, and elucidation of their mechanism of action

Using the integrated analysis platform "MANTA," developed in collaboration with our Artificial Intelligence Center for Health and Biomedical Research, we have successfully identified beneficial bacteria and metabolites that exhibit preventive and therapeutic effects against various diseases. For example, we discovered *Blautia wexlerae* (hereinafter referred to as "*Blautia*"), a gut bacterium that may help prevent and improve obesity and diabetes. This bacterium produces compounds with anti-inflammatory and fat-accumulation-suppressing effects, suggesting its potential to contribute to the prevention and improvement of these metabolic disorders. Building on this discovery, we are currently advancing initiatives aimed at promoting a healthier society, including drug development targeting *Blautia* and the creation of functional foods.

### Exploring interactions among microbes

In addition to discovering individual beneficial bacteria such as *Blautia*, we are also advancing research that focuses on the relationships

among microbes. For example, we have found that short-chain fatty acids—used as an energy source in the gut and known to regulate immune function and help build a body less prone to fat accumulation—are produced from dietary fiber through the cooperative actions of multiple gut bacteria. Based on these findings, we have proposed the concept of a "microbial relay". At the same time, our studies have revealed that microbes in the gut do not always act cooperatively; rather, there also exist new types of relationships in which certain bacteria suppress others, functioning almost like "natural enemies".

### Relationship between cooking oil consumption and allergy or inflammation

Through research focusing on the cooking oils we consume in daily life, we are exploring active metabolites produced after oil intake that help suppress allergies and inflammation. Animal model studies have shown that after consuming flaxseed oil, specific enzymes in various tissues produce compounds such as 17, 18-EpETE and 12-HEPE, each of which suppresses allergic and inflammatory responses in the gut, respiratory system, and skin through distinct mechanisms.



*Blautia*

Furthermore, we have discovered that microorganisms found in the gut microbiota and in fermented foods produce anti-allergic and anti-inflammatory compounds such as  $\alpha$ KetoA and *trans*-10-*cis*-15-octadecadienoic acid, using dietary oils as substrates. For example,  $\alpha$ KetoA has been shown to suppress inflammatory

responses in macrophages, thereby reducing allergic dermatitis and diabetes. These findings hold promise for the development of new drugs and functional foods.

### Social implementation of diet and gut environment using AI and visualization technologies

By leveraging these data platforms, we are developing an AI system that can predict the health benefits of foods traditionally considered good for well-being. In addition, to make it easier to assess the state of the gut microbiota, we are generating antibodies against representative gut bacteria and applying them to visualization technologies. This approach is expected to enable personalized dietary recommendations and health management by allowing individuals to easily examine their own gut environment. Some elements of this technology have already been implemented at the Osaka-Kansai Expo, and its social deployment and practical application just around the corner.



Next-generation Sequencer (MiSeq) for intestinal microbiota analysis

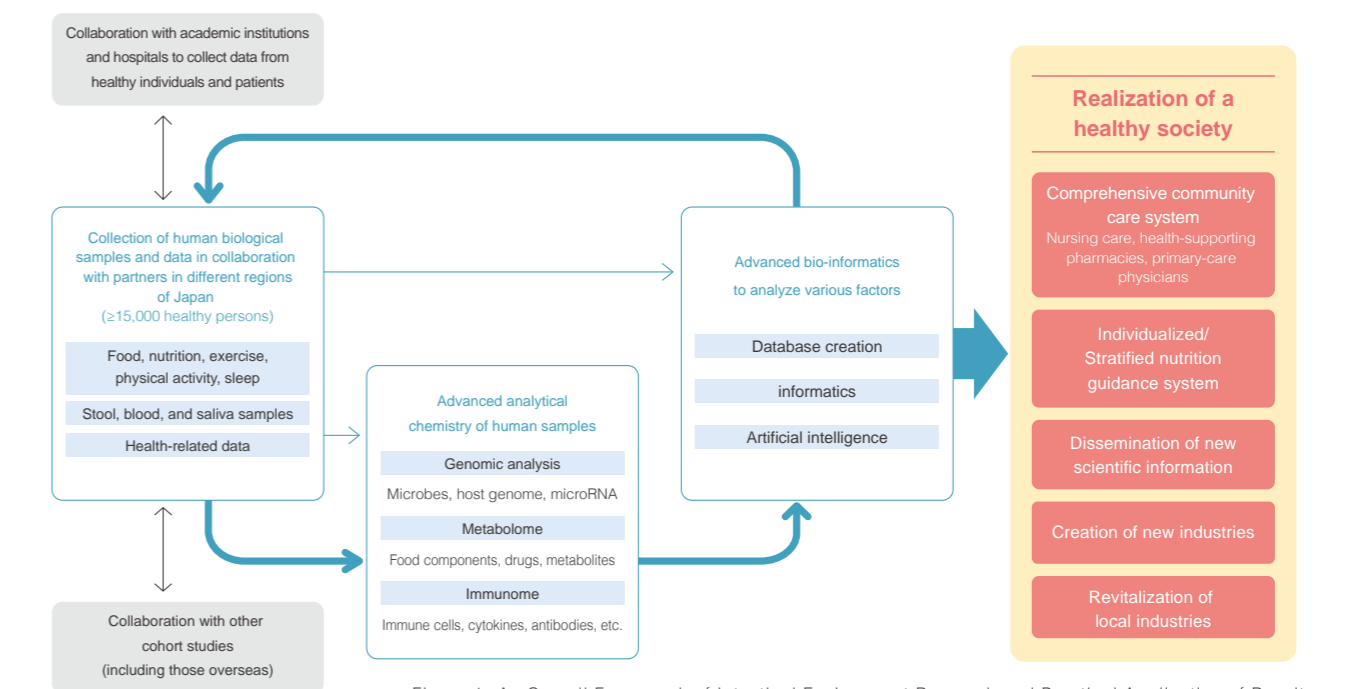


Figure 1: An Overall Framework of Intestinal Environment Research and Practical Application of Results

## Microbial Research Center for Health and Medicine

### Laboratory of Vaccine Materials

Focusing on the immune system of mucosal tissues, we conduct research to develop vaccines, immunotherapies, and healthcare products that prevent and improve infectious diseases, allergies, inflammatory diseases, and lifestyle-related diseases. Examples include vaccines and diagnostic systems for bacterial food poisoning and adjuvants utilizing gut microbiota components.

### Laboratory of Gut Microbiome for Health

We clarify the role of human gut microbiota in the relationship between lifestyle habits, lifestyle-related diseases, and frailty by integrating findings from both observational and interventional studies. By integrating perspectives on metabolism and chrono-nutrition, we aim to build scientific evidence that contributes to extending healthy life expectancy, while promoting social implementation through the development of stratified and personalized nutrition and behavioral programs, as well as healthcare products.

### Laboratory of Gut Environmental System

Focusing on the gut environment formed by symbiotic microorganisms, such as intestinal bacteria, and dietary components, we study their relationship with health and disease through human research and animal models. We apply our findings to drug discovery and healthcare product development such as diagnostic systems.

### Laboratory of Microbial Informatics

We elucidate the pathogenic mechanisms of infectious diseases while conducting research to develop vaccines and pharmaceuticals contributing to infection control. Additionally, we aim to develop pharmaceuticals and healthcare products by elucidating the relationship between the microbiome and health/disease, and by exploring valuable genetic resources.

An Introduction to Major Research Project MICROBIAL RESEARCH CENTER FOR HEALTH AND MEDICINE

# Center for Drug Design Research (CDDR)



MESSAGE

## Wishes as a Center Director

Our center is dedicated to the mission of the National Institutes of Biomedical Innovation, Health and Nutrition: "Transforming Incurable Diseases into Curable Ones". To achieve this goal, we are engaged in the development of fundamental technologies for innovative drug discovery, with a particular focus on methodologies and techniques for designing novel modalities such as antibody, nucleic acid, and peptide therapeutics. With a united effort, our center remains committed to overcoming diseases.

Director Toyomasa Katagiri

## The Challenge to Conquer Diseases: Integrating Cutting-Edge Technology to Boost Innovative Drug Discovery

### What is CDDR ?

The Center for Drug Design Research (CDDR) was established in 2015 to strengthen the technological support of the "Drug Discovery Support Network", a research support program that bridges fundamental academic research outcomes from universities and research institutions to practical applications. CDDR aims to develop foundational technologies for an advanced drug discovery platform that addresses challenges faced by the Japanese pharmaceutical industry.

Currently, CDDR not only utilizes established technologies and expertise but also serves as a key technical support hub for the "Drug Discovery Support Network Project", an all-Japan initiative that connects various research efforts to pharmaceutical development. Furthermore, CDDR promotes research and development in drug design, focusing on drug target discovery, candidate compound screening, in silico drug discovery, and optimization technologies, with the goal of creating biopharmaceuticals, vaccines, and other new modality drugs. In particular, in FY 2024, CDDR established a world-class multiphoton excitation microscopy-based drug discovery imaging platform to advance the development of diagnostic and therapeutic methods. Through these activities, we aim to contribute to drug discovery for disease treatment.

CDDR consists of six projects, categorized into the following three areas:

1. Projects for Drug Target Discovery and Functional Analysis (Proteomics for Drug Discovery, Drug Target Proteomics, and

2. Projects for Drug Development (Antibody Design and XNA Screening and Design)
  3. Projects for Drug Efficacy Evaluation (Drug Discovery Imaging and Advanced Biopharmaceuticals).
- By integrating the highly competitive technologies of each project, we aim to establish a drug discovery platform that addresses unmet medical needs.



Inside the Research Center

### Training the Next Generation of Researchers and Strengthening External Collaborations

CDDR aims to enhance the level of drug discovery research while strengthening collaborations with universities, research institutions, and industry to improve research efficiency and success rates. The development of highly skilled research personnel is essential for fostering

productive collaborations. To achieve this, we actively engage in personnel exchanges and joint research with graduate schools at institutions such as Kyoto University, University of Osaka, Kobe University, Nagoya City University, Asahikawa Medical University, and Tokushima University.

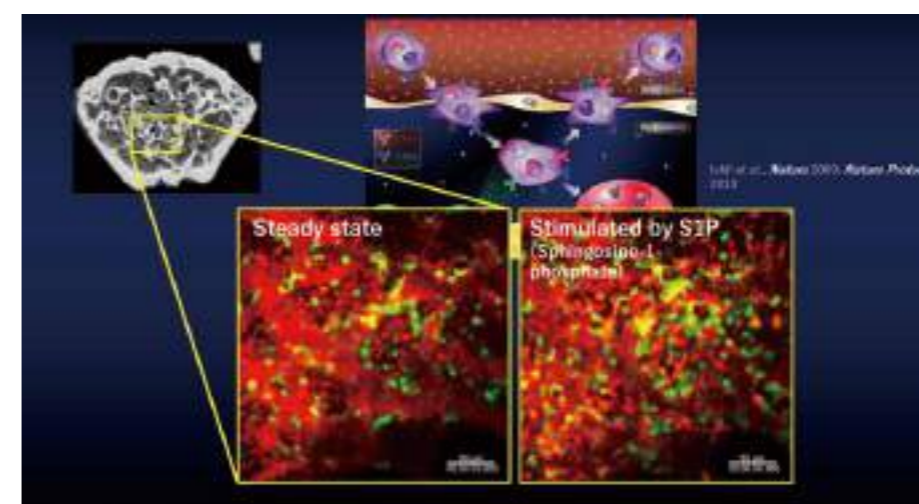
## Platform Launched as a Global Hub for Bioimaging Drug Discovery Research

Bioimaging is an advanced technology that uses multiphoton excitation microscopy to visualize structures and functions in living organisms at high resolution for a deeper understanding of biological phenomena. Multiphoton excitation microscopy uses near-infrared light to achieve high penetration into deep tissue, allowing non-invasive acquisition of three-dimensional images. This technology provides more realistic and reliable data than in vitro experiments because cell dynamics and intercellular interactions can be observed in real time under natural physiological conditions. In addition, side effects and systemic effects can be evaluated over time, making it an innovative tool in drug discovery research.

In FY 2025, we launched the Next Generation Intravital Imaging-based Drug Discovery Platform, a contract analysis service utilizing the world's highest resolution multiphoton excitation microscope. This platform provides a pharmaceutical-regulatory

compliant data management and quality assurance system and ensures confidentiality of research through contract research agreements with pharmaceutical and healthcare-related companies. Furthermore, we are promoting research and development in imaging-based quantitative analysis and drug probe technologies, and developing the platform as an international research center. We are also focusing on technical guidance and human resource development, fostering new experts and promoting the dissemination of technology.

In addition, the bioimaging technology is expected to be applied to cancer screening because it enables in-situ evaluation of malignancy and metastatic invasiveness of cancer cells without the need for biopsy. This technology provides rapid and quantitative diagnosis while reducing patient burden, and is expected to further develop in the medical field.



World's first successful bioimaging in bone



Multiphoton excitation microscopy



Chromatographic system

## Center for Drug Design Research

### Laboratory of Proteomics for Drug Discovery

We develop sensitive and scalable proteome analysis platform for clinical specimens to identify novel biomarkers and therapeutic targets useful for disease diagnosis and treatment.

### Laboratory of Drug Discovery Imaging

Focusing on the dynamic network of immune cells, we aim to uncover the fundamental principles maintaining organ and tissue integrity and develop innovative drugs to regulate these mechanisms.

### Laboratory of Advanced Biopharmaceuticals

We develop basic technologies for the creation of new biopharmaceutical modalities using protein engineering, antibody engineering and organic synthetic chemistry. Our focus is on the development of engineered antibodies with enhanced functions compared to conventional antibody drugs.

### Laboratory of XNA Screening and Design

We work on synthesizing artificial nucleic acids (xeno nucleic acids: XNA), designing sequences, screening target-specific nucleic acid molecules and optimizing them for different applications to create nucleic acid drugs.

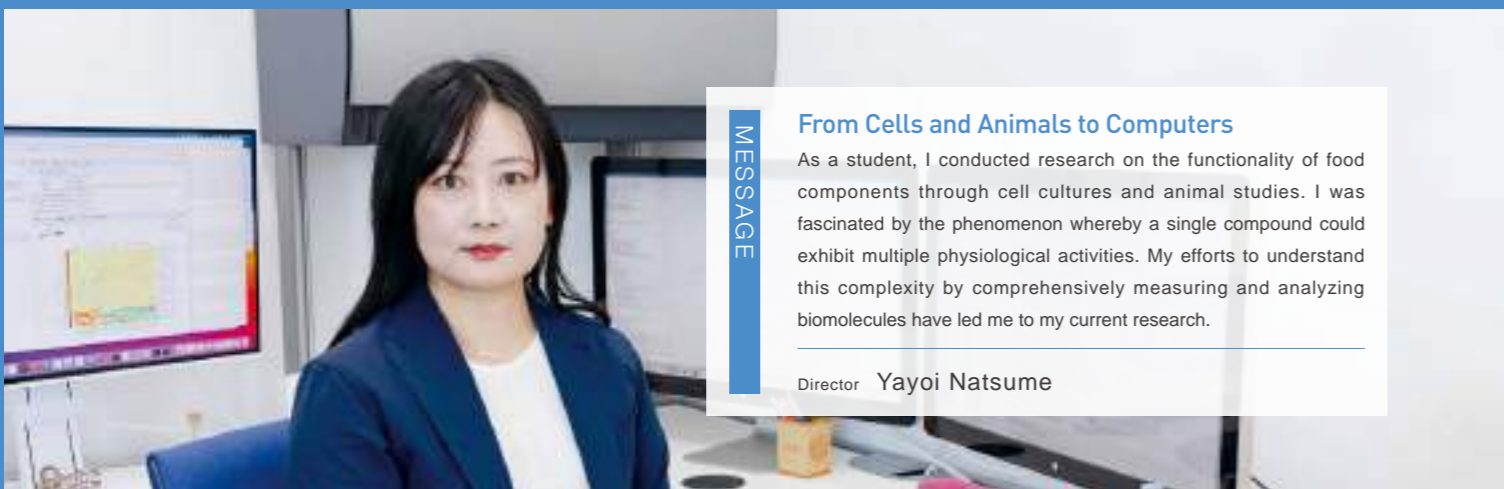
### Laboratory of Antibody Design

We focus on designing next-generation antibody-based pharmaceuticals to maximize therapeutic efficacy. By exploring the binding modes (epitope) of various antibody-based drugs across molecular boundaries, we aim to develop clinically applicable, innovative, and high-performance antibody therapeutics.

### Laboratory of Biofunctional Molecular Medicine

Through comprehensive cancer omics analysis, we identify "cancer-related genes" and clarify their in vivo functions, aiming to uncover the molecular mechanisms underlying development, progression, and treatment resistance. Furthermore, we are studying the development of therapeutic strategies by functional regulation of these genes in vivo.

# Artificial Intelligence Center for Health and Biomedical Research



MESSAGE

## From Cells and Animals to Computers

As a student, I conducted research on the functionality of food components through cell cultures and animal studies. I was fascinated by the phenomenon whereby a single compound could exhibit multiple physiological activities. My efforts to understand this complexity by comprehensively measuring and analyzing biomolecules have led me to my current research.

Director Yayoi Natsume

## Approaching Invisible Life Phenomena Through Data : The Future of Drug Development Woven with AI

### The Establishment of Artificial Intelligence Center for Health and Biomedical Research

The Artificial Intelligence Center for Health and Biomedical Research was established on April 1, 2019, within the National Institutes of Biomedical Innovation, Health and Nutrition (NIBN). Its mission is to integrate AI-related activities and expand research capabilities in the fields of drug discovery and health sciences. AI has seen rapid advances and integration across various fields, including biology and chemistry. These disciplines, with their long histories, have witnessed technological innovations that have enabled the acquisition of diverse data. Additionally, as theoretical foundations continue to be established, large-scale simulations based on vast computational outputs have become possible. This evolution has led to the fusion of biology, chemistry, and information science, giving rise to fields like bioinformatics and cheminformatics. These disciplines, which have developed alongside computers, are now entering a new phase with the advancements in machine learning and natural language processing. At our center we strive to fulfill the aspirations of those who seek effective treatments and long, healthy lives by harnessing cutting-edge AI technologies to drive research in the areas of drug discovery and human longevity.



Figure 1 : Data-Driven Drug Target Discovery



## Visualizing the Invisible: Understanding the World Through Computational Data

Drug development involves multiple processes, each presenting unique challenges—ranging from the depletion of viable drug targets and rising medical costs due to biopharmaceuticals to high attrition rates in clinical trials. The development of pharmaceuticals relies on the collective expertise of biology, chemistry, and various other scientific fields.

One of our key research initiatives at the center is data-driven drug target discovery. The term "data-driven" signifies making decisions based on data. Traditionally, researchers identify biologically significant molecules associated with a disease and, through analysis, determine the most effective drug targets. In contrast, data-driven drug target discovery involves collecting disease-related data and utilizing AI technologies to propose drug targets. By identifying potential drug targets directly from patient data, we hope to reduce the risk of new drug candidates failing at the clinical trial stage.

Another crucial aspect of drug development is identifying compounds (molecules) that bind to drug targets and modulate their function efficiently. Our center promotes research and development that harnesses AI-related technologies and molecular simulation techniques to rapidly and accurately generate candidate compounds for a wide range of drug discovery targets, through both data-driven and logic-based approaches. These research outcomes are expected to serve as a driving force in addressing the rising healthcare costs associated with biopharmaceuticals, as well as the increasing resource and time-related costs in drug development.

**Conventional *in silico* screening**

Design and evaluation of small molecule drugs

- Ligand-based drug design (LBDD)
- Structure-based drug design (SBDD)

**Enhancement using physicochemical methods**

Incorporation of molecular motion (medium and large polymers)

**Molecular Dynamics: MD simulation**

$$m_i \frac{d^2 \mathbf{r}_i(t)}{dt^2} = \mathbf{F}_i(t) = - \frac{dU(\mathbf{r}^N)}{d\mathbf{r}_i}$$

**Epitope prediction combining physical chemistry and informatics**

Highly accurate prediction with explicit consideration of glycan dynamics

**Bioinformatics (existing methods)**

Input: Sequence / Structure

- Predictive modeling by machine learning (sequence-based)
- Three-dimensional structural analysis (structure-based)

**MD Simulation**

**Epitope Prediction Results**

Existing Methods

This time

Experiment

Successfully achieved significant narrowing

Figure 2 : Advanced *in silico* design using physicochemical methods

## Advancing Drug Discovery with AI and Human Collaboration

AI adoption in academic research is no longer a novelty. However, at our center, we focus on applying the most suitable AI technologies to specific challenges in drug development and healthy longevity. By utilizing AI in practical and meaningful ways, we aim to bridge fundamental discoveries with real-world applications. We are building a research framework that connects knowledge extracted from patient data with the physical entities at the core of drug development. Our mission is to demonstrate the new possibilities of AI-driven drug discovery.

Moreover, by collaborating closely with other research institutions that collect and manage extensive biological and chemical datasets, we play a vital role in deepening insights and strengthening partnerships. Through these collaborations, we achieve a scale and precision of analysis that would be impossible through independent research alone, creating new value and opportunities.



## Our Vision for the Future of the Artificial Intelligence Center for Health and Biomedical Research

Our goal is to leverage AI technologies to solve challenges in drug development and healthy life extension - discovering innovative solutions that were previously unattainable. However, our vision extends beyond simply applying existing AI technologies.

At the Center, we aim to contribute to the advancement of AI itself - developing truly groundbreaking AI innovations that will drive the future of drug discovery and health sciences.



## Artificial Intelligence Center for Health and Biomedical Research

### Laboratory of Bioinformatics

To support data-driven drug target discovery, we conduct research on analyzing various disease-related data (such as clinical and omics data) and developing novel analytical methods using cutting-edge technologies, including machine learning.

### Laboratory of *In Silico* Design

To rapidly identify and create pharmaceutical compounds across diverse therapeutic targets, we develop structure-based drug discovery technologies using molecular simulation and informatics. By applying this technology, we aim to understand complex molecular recognition mechanisms within the human body, develop design strategies based on that understanding and create novel therapeutic drugs.

# Center for Drug Discovery Resources Research



**MESSAGE**

**Why did I focus on cell biology?**

While synthesizing compounds on my own under the Faculty of Pharmacy at university and analyzing the effects they have on cells and animals from a chemical structure-based perspective, I became fascinated by the mystery of cells as a research tool.

Director Arihiro Kohara

## Supporting Drug Discovery Research by Providing High-Quality Biological Resources

### Establishment and provision of drug discovery resources for immediate response in emergencies

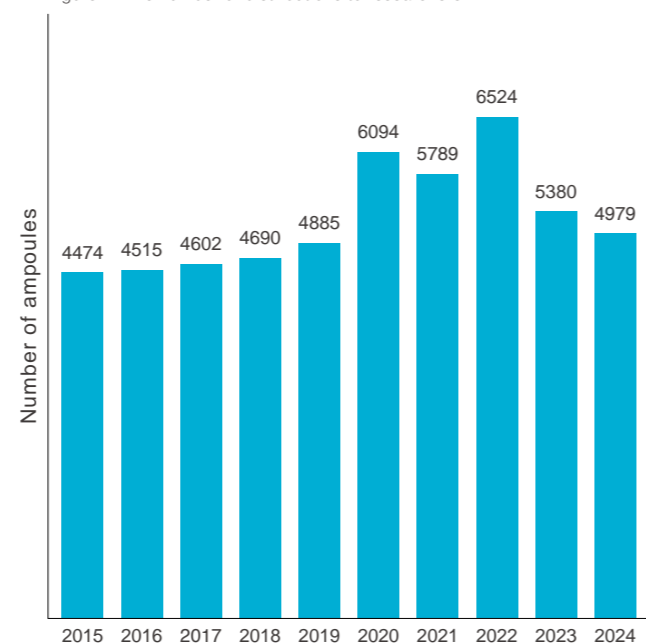
Since its inception in 1985, the Center has been collecting and registering various biological resources, including cultured cell lines, to support basic research in Japan, particularly in drug discovery. To date, we have established a system to provide over approximately 2,000 types of cell lines and continue to add more than 40 new biological resources annually to meet the needs of researchers. Researchers can easily request resources via the "JCRB Cell Bank" website, and requested cell lines are delivered within a week to ensure swift initiation of research. This initiative has now grown to reliably provide approximately 5,000 cell lines annually, serving as a foundation for advancing research.

Our well-structured supply system enabled a rapid response to the COVID-19 pandemic. As early as February 2020, in collaboration with the National Institute of Infectious Diseases, we became the first in the world to provide a useful cell line (JCRB1819: VeroE6/TMPRSS2) for isolating and propagating the SARS-CoV-2 virus. This contribution greatly facilitated the development of vaccines and therapeutics.

Figure 1: Changes in the number of newly catalogued cultured cell resources

FY	Number of cell lines collected	Number of cell lines catalogued
2015	79	70
2016	43	93
2017	73	56
2018	106	40
2019	47	42
2020	88	40
2021	66	44
2022	65	46
2023	52	62
2024	106	64
Total	725	557

Figure 2: The number of distributions to researchers.



## Commitment to high-quality and reliable resources

Advancements in cell characterization and quality testing technologies are occurring. While the global standard for cell banks mandates the absence of microbial contamination and misidentification in human-derived cells, our center goes beyond these minimum requirements by implementing additional quality assessments and characterizations. Our goal is to provide safe and reliable biological resources for researchers.

One of our key initiatives includes a proprietary virus screening technology capable of detecting 20 different DNA and RNA viruses. This method addresses virus infections in cells, an aspect often overlooked by researchers. Additionally, we offer specialized cell collections, such as bioluminescent

cancer cells incorporating firefly luciferase genes for in vivo imaging in mouse transplantation models. Another important collection involves cells derived from patients with highly tumorigenic genetic disorders, such as xeroderma pigmentosum, with comprehensive characterization data provided to researchers.

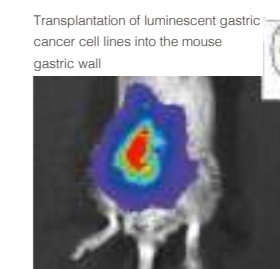


Figure 3: Visualization of bioluminescent cancer cells transplanted into mice

## Development of new drug discovery resources through advanced technologies

Drug discovery resources evolve with changing research needs. Initially, cancer cell lines were categorized based on their organ of origin. Today, researchers demand detailed profiling of oncogene mutations, verification of target molecule expression, and quantitative expression data, reflecting a significant increase in complexity and



Figure 4: Facilities for preparation/storage of biological resources

precision. Our center actively develops new biological resources to meet these emerging needs.

Traditional cell banks predominantly store cancer cell lines cultured on flat surfaces in containers, which may not be possible to accurately mimic the three-dimensional nature of tumors in the human body. The selective expansion of highly proliferative and easily manageable cancer cells in culture has been a major limitation. While these cell lines have been

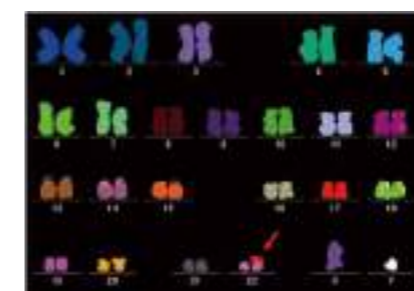


Figure 5: Identification of abnormal chromosomes via a chromosomal analysis.

widely utilized as standardized research tools due to their reproducibility, they do not fully support drug development. There is a growing demand for more physiologically relevant research models.



Figure 6: Organoids prepared from the intestinal tract

To address this, our center operates a "Human Tissue Bank" initiative, where, with appropriate patient consent, we provide researchers with previously discarded cancer tissues and adjacent normal tissues. This effort has successfully established human intestinal models, and our blood-brain barrier model, developed using endothelial cells, holds promise for central nervous system drug development.

Furthermore, leveraging our expertise in cell bank, we are actively researching and developing freezing technologies for preserving three-dimensional cell aggregates while maintaining their original functionality. This includes the development of cell cryoprotectants and freezing devices that ensure optimal preservation of these valuable resources for future research applications.

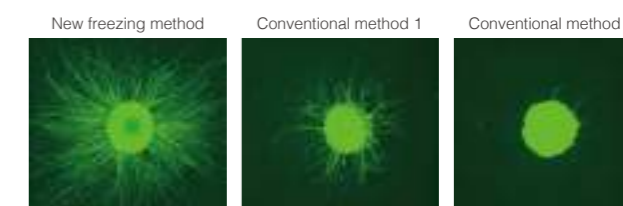


Figure 7: Neurite outgrowth of iPS cell differentiation-induced neurons after thawing

## Center for Drug Discovery Resources Research

### Laboratory of Drug Discovery Resources Research

We operate the JCRB Cell Bank, which has the largest number of registered cell lines in Japan, and the Human Tissue Bank, which provides surgical residual tissues to domestic researchers. By offering high-quality biological resources, we support the foundation of drug discovery research both domestically and internationally. Additionally, we are engaged in the development of essential cell tools for drug discovery research.

### Laboratory of Drug Discovery Resources Research Collaboration Promotion Office

To promote the development of model cell evaluation systems, such as functional maintenance cells and disease model cells necessary for drug discovery research, as well as freezing technologies for biological resources, we facilitate collaboration both within and outside the institute, aiming for efficient resource and technology development.

### Laboratory of Cell Model for Drug Discovery

We are developing efficient differentiation methods to induce stem cells into target cells from the perspectives of developmental biology and molecular biology. Using the functional cells obtained, we are establishing screening systems and other foundational technologies for drug discovery.

### Laboratory Animal Resource Bank (LARB)

We develop disease model small animals that are essential for research on intractable diseases and therapeutic development while also operating an experimental animal research resource bank. By developing, analyzing, collecting, preserving, and supplying spontaneous and genetically modified model animals, we support and promote disease and drug discovery research.



# Research Center for Medicinal Plant Resources

An Introduction to Major Research Project RESEARCH CENTER FOR MEDICINAL PLANT RESOURCES



**MESSAGE**

**The Fascination of Plant Research**

Unlike animals, plants do not exhibit obvious changes before our eyes, but sometimes, unexpected transformations occur without notice. The joy of discovering a new and unprecedented change is truly exceptional.

Director **Kayo Yoshimatsu**

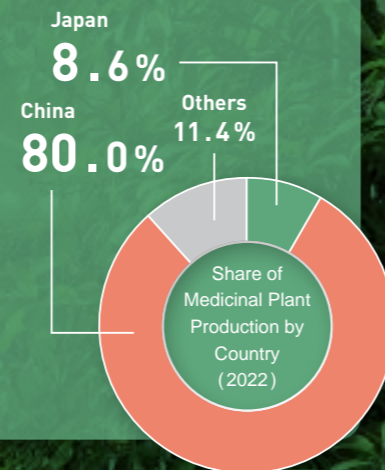
## Importance of Domestic Cultivation and Conservation of Resources for the Stable Supply of Crude Drugs

Under the Convention on Biological Diversity, medicinal plants are classified as "genetic resources". Due to this convention and other international treaties such as the Washington Convention, obtaining plant seeds and seedlings from abroad is extremely difficult. As of 2022, the share of crude drugs produced in Japan was only about 9%, compared to 80% from China (See the figure on the right, Cited from Shoyakugaku Zasshi 79 (1), 18-62 (2025)).

The promotion of domestic cultivation of raw medicinal plants faces three main challenges.

- (1) Securing Seeds and Seedlings – The supply system for seeds and seedlings remains underdeveloped.
- (2) Training of Cultivators and Instructors – The rapid aging of skilled farmers poses a significant challenge.
- (3) Improving Production Efficiency and Sustainability – The technical infrastructure, including mechanization and appropriate pesticide use, is insufficient.

In addition to (1) to (3) above, there are other challenges in maintaining and managing medicinal plants. These include the large number of herbal medicines used in Japan, the diversity in origin, growing environment, life style, and growth period, and the fact that even within a single plant species, the constituents contained often differ depending on the origin and environment. In addition, the maintenance and management of medicinal plants requires multiple locations and methods (e.g., conservation cultivation in fields and greenhouses, seed preservation, and culture preservation) in order to disperse hazards. Under these circumstances, the challenge is how to achieve stable cultivation and supply of medicinal plants in one's own country.



## Maximizing the Potential of Medicinal Plants to Benefit People's Health in the Future

### Enabling the broad use of medicinal plants in Japan

Medicinal plants have been used in pharmaceuticals since ancient times. They are also indispensable for the research and development of pharmaceuticals, including Western medicines. The Center cultivates and preserves more than 4,000 strains of medicinal plants according to vegetation at three locations in Japan (subarctic, temperate, and near subtropics) (Figure 1). We regard medicinal plants as important assets and believe that it is our responsibility to make them available when needed and to pass them on to future generations. We are conducting various research to achieve this. In addition, we supply seeds and seedlings to research institutes in Japan and provide instructions on their cultivation techniques.

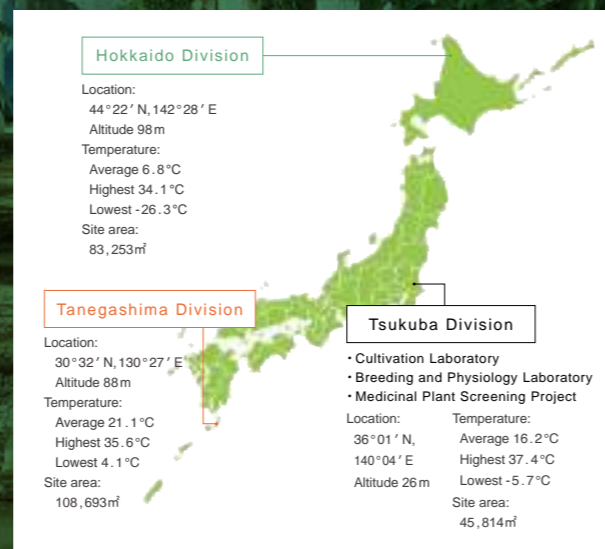


Figure 1: Locations (temperature in 2024)

## Research Center for Medicinal Plant Resources Introduction of Research Divisions, Laboratories, and a Project

### Hokkaido Division

Focusing on medicinal plants that thrive in cold regions, we have planted over 1,000 strains in our medicinal plants garden, arboretum, useful plants garden for the Ainu people, and research fields. Additionally, we conduct research and development on breeding medicinal plant cultivars suitable for pharmaceutical raw materials, optimizing cultivation conditions, and implementing measures against weeds, pests, and diseases while disseminating these technologies to production areas.

### Tsukuba Division - Cultivation Laboratory

We conduct research on the cultivation and quality evaluation of medicinal plants. Additionally, as part of international academic cooperation, we engage in low-temperature preservation of valuable plant seeds and carry out seed exchange programs with botanical gardens abroad. Preserved seeds undergo periodic germination tests, and those with decreased germination rates are regenerated to ensure the continuous conservation of genetic resources.

### Medicinal Plant Screening Project

We store and manage over 10,000 plant extracts, primarily derived from plants growing in Japan, as Dimethyl sulfoxide (DMSO) solutions at -20°C. These extracts are provided to companies and research institutions in various fields, including pharmaceuticals, cosmetics, health foods, and agrochemicals, with the aim of facilitating their application and commercialization. From FY 2024, we have also started providing Kampo prescription extracts.

### Tsukuba Division - Breeding and Physiology Laboratory

We conduct research on the maintenance, preservation, and quality improvement of medicinal plant resources, as well as their application to production, using plant biotechnology. By utilizing plant tissue culture techniques, we cultivate and maintain various plant species as genetically identical "clones" under sterile conditions.

### Tanegashima Division

Since Tanegashima Island is a habitat for many plant species at their southern or northern limits, as well as rare species, we conserve and propagate medicinal plant species. In the respect of medicinal plants that are difficult to obtain from abroad, we aim to establish a sustainable production system by improving efficiency across all processes, from seed propagation to crude drug production, using locally acclimatized plant strains.

## Preserving Northern Plants and Breeding of Superior Medicinal Plant Cultivars Using an Expansive Field

We have been working on breeding medicinal plant cultivars suitable for the production of pharmaceuticals. So far, we have bred and registered a total of seven medicinal plant cultivars such as coixseed, peony, glycyrrhiza, and perilla (Figure 2). A medicinal cultivar of coixseed known as 'Kitanohato', which can be cultivated even in cold regions, has been successfully produced in Hokkaido. It is widely used not only for pharmaceuticals, but also for quasi-drug lotions and edibles. A medicinal cultivar of peony called 'Benishizuka' is actually produced in Okayama Prefecture, and 'Yumesaika' in Akita Prefecture.



Figure 2: The latest issue of the Guidelines for the Cultivation of Medicinal Plants (left) and medicinal plants bred and registered at the Center (right)

## Research on Germination Conditions of Medicinal Plants

In recent years, the genetic resources of wild plants have been rapidly declining. To address this issue, we have been storing seeds under low-temperature conditions. Since optimal storage conditions vary by seed type, we preserve them in tin cans or styrofoam bottles at 10 °C, -1 °C, and -20 °C, continuously studying the best storage methods. Regular germination tests are conducted, and if germination rates decline, seeds are regenerated to maintain genetic resources. We have also continued seed exchange programs with botanical gardens worldwide for over 70 years (Figure 3).



Figure 3: Seed storage (top left, bottom left), germination test (top right), Index Seminum (seed list) sent to overseas botanical gardens (bottom right)

## Plant Biotechnology Contributing to Stable Supply of Medicinal Plant Resources

To ensure the safe, secure and stable supply of important medicinal plant resources, we utilize plant biotechnology for their preservation. Plant tissue culture is a key biotechnology technique that employs the plant's ability to regenerate a complete plant from any part, a property known as totipotency. Using this technology, we cultivate and maintain various medicinal plants as genetically identical "clones". These cloned plants serve as a vital source of high-quality seedlings for medicinal plants expected to be cultivated domestically (Figure 4).



Figure 4: Plant tissue culture maintained under LED light (left) and planting work in a clean bench (right)

## Preserving Tropical, Subtropical and Temperate Medicinal Plants and Leading Commercial Production of those Difficult to Obtain

*Rauvolfia serpentina* (Rauvolfia) is a medicinal plant used in Ayurveda and known for its blood pressure-lowering effects. However, due to resource depletion in India, it has been listed under CITES Annex II, making international procurement difficult. Our center has been preserving and cultivating *Rauvolfia* since the 1950s, with the aim of ensuring a stable supply of its pharmaceutical formulations for hypertension treatment.



Figure 5: *Rauvolfia serpentina* in flowering season (top) and its roots used as herbal medicine (bottom)

## Medicinal Plant Screening Project

It is estimated that there are 270,000 species of plants growing worldwide. However, the use of natural resources from overseas is becoming increasingly difficult due to the Convention on Biological Diversity and other regulations. Our plant extracts and Kampo prescription extracts are expected to lead to new developments in underused domestic plant resources, crude drugs, and Kampo medicines.



Figure 6: Collection of wild plants (left), extraction equipment (middle), biological activity evaluation using plant extract library (right)

An Introduction to Major Research Project RESEARCH CENTER FOR MEDICINAL PLANT RESOURCES

# Tsukuba Primate Research Center



**MESSAGE**

**Day-to-day Research activities**

Research using Nonhuman Primates (NHP) covers many areas, from basic research to practical applications in medicine, with the ultimate goal being disease control. In this way, medical science research using NHP aims to control diseases from basic research and shed light on the final phase of disease overcome. To reach this future goal, we are developing the drug discovery technology platforms, establishing the research on the creation of animal models for human diseases using NHP, and furthermore, the development of vaccines with the best possible effects on global public health.

Acting Director **Toyomasa Katagiri**

## Issues with Primate Imports Caused by the COVID-19 Pandemic

Due to the COVID-19 pandemic, the import of laboratory primates from China was suspended, making their procurement extremely difficult. As a result, contract testing has become challenging, and drug development has faced significant delays.

As of the 2023 fiscal year, primates are primarily being imported from Vietnam and Cambodia. However, from 2012 to 2023, the import prices of laboratory primates have risen sharply, increasing approximately tenfold compared to 2013 (see Figure 1).

Given the rising import costs and regulatory restrictions, the demand for domestic production of laboratory primates is growing. Therefore, the key challenge now is how to establish a stable domestic system for breeding and supplying these essential animals for pharmaceutical development.

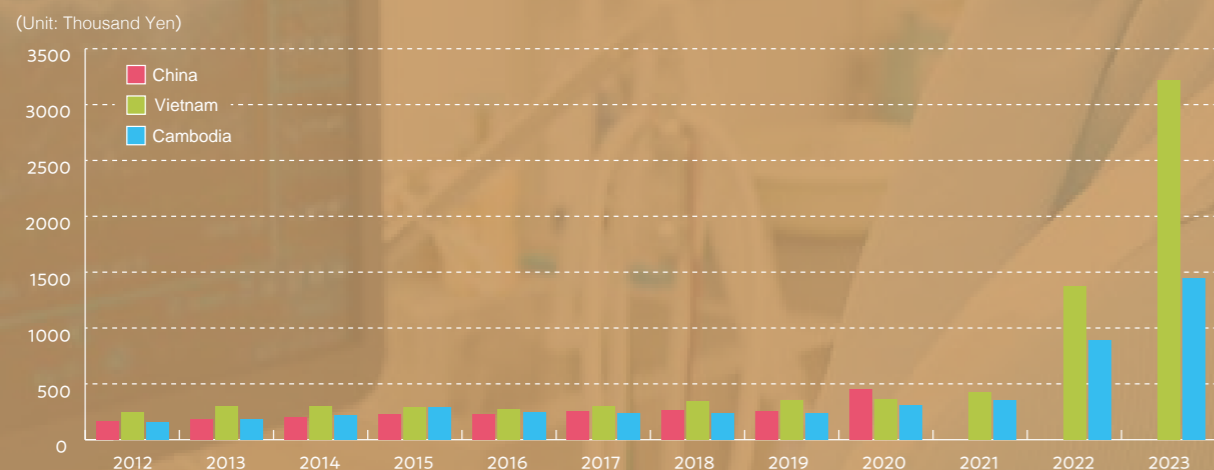


Figure 1: Trends in CIF Import Price per Primate in the Ministry of Finance's Simplified Trade Statistics  
Quoted from the FY 2023 Comprehensive and Collaborative Research Report of the Ministry of Health, Labour and Welfare Scientific Research Grant (Reference No. 202306010A).

## Supplying Quality Nonhuman Primates for Medical Research and Using them to Conduct Independent Medical Research

NHP for medical experiments are essential for drug discovery

A variety of evidence is needed, from drug development and research to the provision of those drugs to society. Among these, experiments for confirming efficacy in animals before clarifying it in humans are an indispensable part of that process. Testing in NHP, which are closely related to humans, is particularly crucial to drug discovery. As the export of laboratory NHP from other countries has ground to a halt since the pandemic, NHP for medical experiments are becoming increasingly important to drug discovery in Japan.

## Breeding SPF monkeys with an unparalleled in the world pedigree to secure a population of elderly monkeys

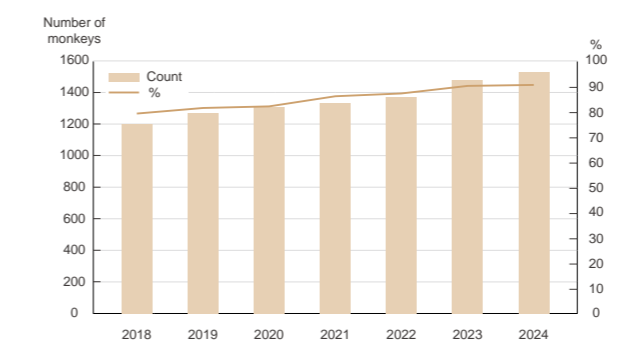
Our center is the only medical research primate center in Japan, dedicated to enhancing the quality of cynomolgus macaques as research resources while establishing a system for their maintenance and supply. Additionally, we promote biomedical research using non-human primates, spanning from the individual to the genetic level.

In our center, we breed Specific Pathogen-Free (SPF) monkeys and provide animals with clear backgrounds, including lineage, medical history, and test results. The proportion of SPF monkeys in our breeding facilities was 14.0% in FY 2007, whereas it has remained above 90% since the end of FY 2023, reaching a level close to the upper limit (Figure 2).

Furthermore, in the context of an accelerating aging society, aged individuals housed under completely controlled conditions are an essential research resource. The aged primates at our center are unparalleled in the world in both quality and quantity on a global scale.

Table 1: Number of Cynomolgus Monkeys Produced and Supplied Each Year

	Category	2018	2019	2020	2021	2022	2023	2024
Number of monkeys produced	Normal monkeys	143	196	163	154	206	170	187
	Special monkeys	15	4	10	10	2	0	7
Total		158	200	173	164	208	170	194



The proportion of SPF monkeys in our breeding facilities was 14.0% in FY 2007, but has remained above 90% since the end of FY 2023, reaching a level close to the upper limit.

Figure 2: Chronological Changes in the Numbers and Percentages of High-Quality SPF Cynomolgus Monkeys Produced

## Providing experimental animals and technological support to help streamline drug discovery

We do more than simply supply monkeys to academia and other institutions. We thoroughly review submitted experimental protocols, and only those that are fairly evaluated and approved by our review committee are conducted and completed within our center. In other words, we provide not only monkeys but also a full range of resources, including hard resources such as CT scanners and dissection rooms, as well as soft resources such as experimental expertise and highly skilled researchers. This comprehensive support enables faster and more cost-effective drug development.

## Combating intractable diseases, rare diseases and infectious diseases with no established therapy!

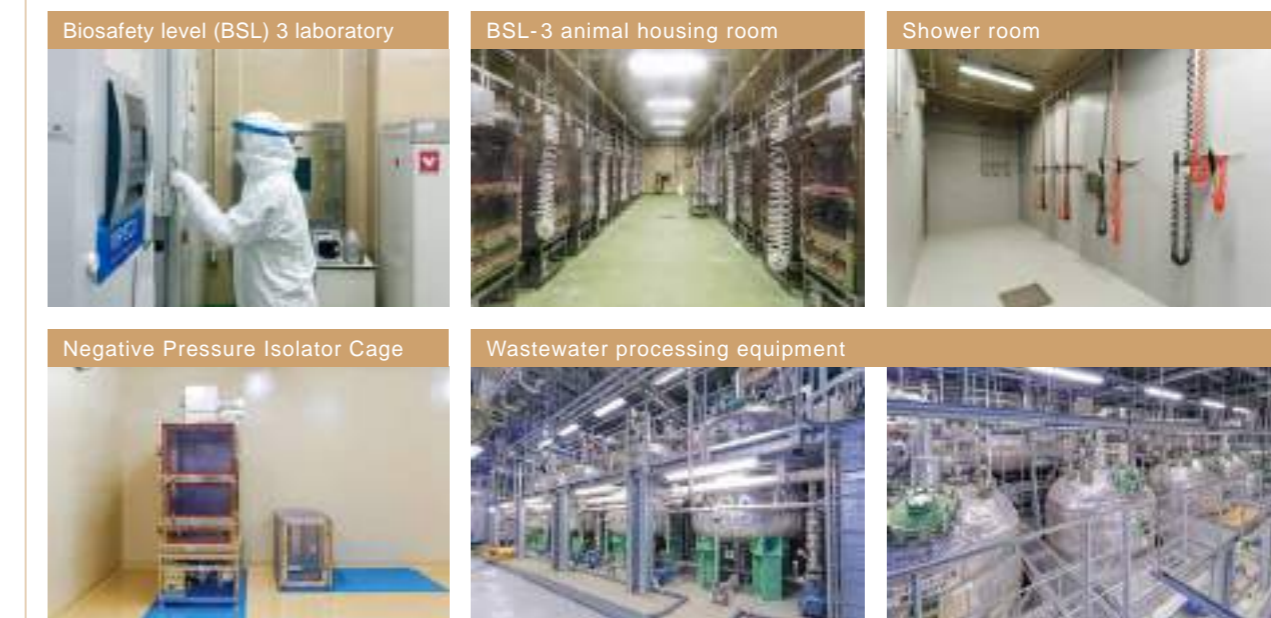
We primarily focus on researching intractable diseases for which no established treatments exist, as well as diseases that public institutions are responsible for addressing. Using primate models that allow us to investigate disease onset at the genetic level, we have been able to track and analyze the pathophysiology of rare disease models such as macular degeneration and dilated cardiomyopathy from the pre-symptomatic stage. In 2024, we initiated whole-genome analysis of cynomolgus macaques. This unique approach, conducted using strictly controlled and clean primate populations, has earned high international recognition.

One of our recent achievements is the establishment of a COVID-19 evaluation system, where we successfully developed and reported an effective treatment for the Omicron variant using primate models. In 2024, within 100 days of the WHO's declaration of a Public Health Emergency of International Concern (PHEIC), we were the only institution in Japan to create and evaluate an Mpx model. This has helped establish a system for the rapid development of vaccines against emerging infectious diseases.

Additionally, we have advanced research on HTLV-1, becoming the first in the world to successfully develop an HTLV-1 infection model in primates. This research aims to uncover the mechanisms of mother-to-child transmission through breast milk, which is essential for developing treatments and vaccines.

Furthermore, we have developed a vaccine technology incorporating an adjuvant antigen into an attenuated AIDS virus, which has demonstrated high efficacy in primate-based evaluations. Human clinical trials are planned within the next few years, raising hopes for the realization of an HIV cure.

## Infectious Disease Experimental Facility to Support Advanced Basic Research: Animal Biosafety Level (ABSL)-3



# Center for Nutritional Epidemiology and Policy Research



MESSAGE

## Why I Started This Research

I studied food science at university, and as I delved deeper into the field, I became increasingly interested in the relationship between "food and health", which led me to pursue a medical degree. Along the way, I encountered the field of "epidemiology" and began my journey as an epidemiologist.

Director Mieko Nakamura

By investigating and analyzing the "nutrition" and "diet" of the Japanese people, we aim to show society how to create lifelong health through "food".

## Exploring the "Scientific Evidence" for Nutrition for a Healthy Tomorrow

At our center, we primarily conduct nutrition research using epidemiological methods to clarify the relationship between nutrition, diet, and health, as well as to contribute to the development and evaluation of nutrition policies. Among our activities, the aggregation and analysis of the "National Health and Nutrition Survey" (an annual nationwide survey conducted by the Ministry of Health, Labour and Welfare) serve as a foundation for research at our center. The results of this survey are used to establish dietary reference values — guidelines indicating the types and amounts of nutrients Japanese people should consume for a healthy life — as well as to inform policy recommendations and provide scientific evidence to support them. For example, the findings are used to monitor target values set in the "Health Japan 21 (the third term)", a national health promotion policy by the government, and also serve as representative values in international collaborative research.

Additionally, we conduct research to improve the accuracy of nutritional survey methods for the ongoing implementation of the National Health and Nutrition Survey. We also carry out research on Japanese dietary habits and behavioral factors, as well as reviews and related studies aimed at enhancing dietary and nutrition guidelines.

In a cross-disciplinary project on "Promoting the Improvement of Food Environments through Industry-Academia-Government Collaboration", we have built database of processed foods and recipes and conducted simulation research, collaborating with companies. The database has been made publicly available as the "Branded Food and Recipe Co-operation Data Bank Japan (FRDB)" (see Figure 1). We will continue working to enrich and utilize the database through collaboration with a growing number of companies and experts.

Furthermore, in health economics research assessing the impact of policies that promote sustainable and healthy diets on health, society, and the economy, we are creating an environment where individuals, businesses, and local governments can effectively use simulation models and scientific evidence for decision-making. By utilizing public statistical data including the National Health and Nutrition Survey and collaborating with organizations like WHO, we contribute to global epidemiological data creation, thereby supporting the dissemination of information to society.



Figure 1: Branded Food and Recipe Co-creation Data Bank Japan (FRDB)

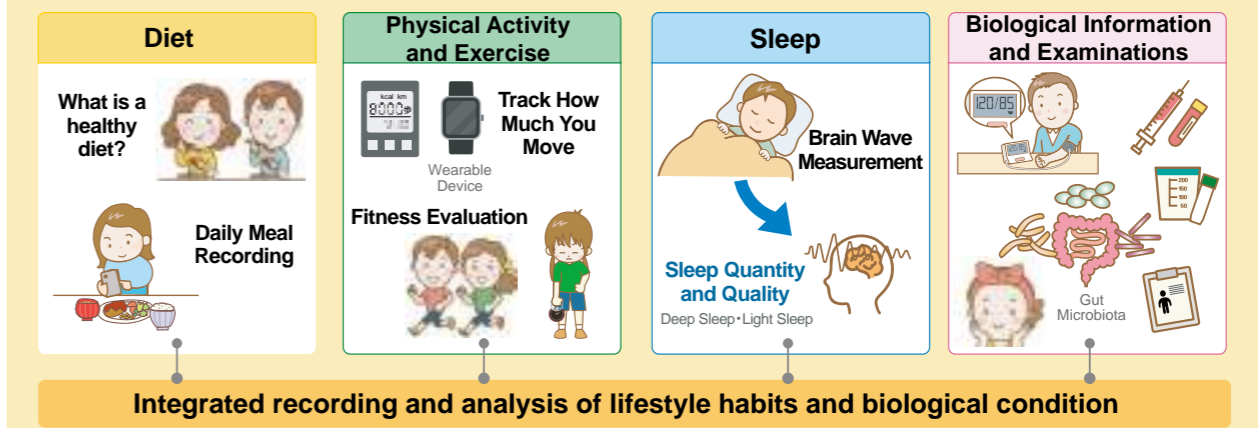
## Life Course Approach Looking Ahead to the "100-Year Life" Era

When considering the "100-Year Life" era, it is not just about extending average life expectancy, but focusing on extending healthy life expectancy, ensuring independence throughout one's lifetime. Nutritional priorities vary across different life stages. We carry out research focused on infants, pregnant and lactating women, working-age populations, and the older adults, with the aim of contributing to the resolution of nutritional issues

across all stages of life. In 2025, with the cooperation of Settsu City, we launched the "Settsu Health Survey" in collaboration with the Clinical Nutrition Research Center and external research institutions (see Figure 2). We conduct detailed assessments of nutrition, physical activity, sleep patterns, and biological markers to promote public health and generate new scientific evidence.

## Settsu Health Survey ~ Toward developing Future Health Together ~

We are conducting research with the people of Settsu City to collect data on "diet, exercise, sleep, and biological information" to help everyone live happier lives!



To establish personalized healthy lifestyle habits for everyone, from children to adults

This project is jointly conducted by the Center for Nutritional Epidemiology and Policy Research, the Center for Clinical Nutrition and Research institutions outside the NIBN.

Figure 2: Settsu Health Survey (Joint Research Project of the Center for Nutritional Epidemiology and Policy Research, the Center for Clinical Nutrition, and External Research Institutions)

## From Scientific Evidence to Social Implementation ~Toward Social Contribution~

Scientific evidence on nutrition, physical activity, and related fields becomes truly meaningful when it supports the daily practices of the public. In addition to generating scientific evidence on nutrition, dietary habits and health, we are committed to ensuring that this evidence informs the policies and practices of individuals and organizations, with a view to contributing to society.



## Center for Nutritional Epidemiology and Policy Research

### Laboratory of the National Health and Nutrition Survey

We conduct statistical aggregation and analysis of the National Health and Nutrition Survey, which is conducted annually by the Ministry of Health, Labour and Welfare of Japan. In addition, we conduct research on dietary intake and eating behaviors among the Japanese population using data from this survey, with the aim of contributing to the development and promotion of national and local health policies, such as *Health Japan 21 (the Third Term)*.

### Laboratory of Nutrition Guidelines

We conduct research on the scientific evidence necessary for the formulation, dissemination, and implementation of dietary and nutrition guidelines. In particular, we focus on developing a nutritional care model aimed at preventing frailty in older adults in collaboration with the Taipei Medical University.

### Laboratory of Nutritional Epidemiology

In collaboration with domestic and international research institutions and large-scale cohort studies, we conduct nutritional epidemiology research to clarify the relationship between diet, nutrition, and non-communicable diseases, as well as research on improving food environments. We aim to translate scientific evidence on diet, nutrition, and health into societal benefits.

### Laboratory of Nutrition and Social Science

To support the development of effective policies, our laboratory conducts research on the social aspects of population health and nutrition through two main approaches: (1) international collaborative epidemiological studies using official statistics to examine the control of risk factors for noncommunicable diseases, and (2) policy evaluation research employing methods such as simulation modeling and health economic analysis.

MESSAGE

## Future Research Directions

Our center has conducted extensive research on the characteristics of physical activity, exercise, sedentary behaviour, and physical fitness that contribute to health and well-being among healthy individuals. Moving forward, we aim not only to further advance these lines of research but also to explore appropriate physical activity for people with various health conditions and for those living in specific environments, such as post-disaster settings.

Director **Hidemi Takimoto**



## Improving the Public's Physical Activity and Exercise Habits Through Physical Activity Guide and Accurate Assessment of Physical Activity

To promote greater people's physical activity through physical activity guide and accurate assessment of physical activity

In Japan, the National Health and Nutrition Survey using pedometers has been conducted since 1989 to assess the level of physical activity among the population. The survey is a large-scale international initiative and has become a globally significant source of trend data on physical activity. The Center for Physical Activity Research has been engaged in two major initiatives to further encourage increased step counts among participants in the National Health and Nutrition Survey.

First, we conduct public outreach to promote physical activity and to prevent prolonged sitting among the public. The *Physical Activity Guide for Health Promotion 2023*, which was announced by the Ministry of Health, Labour and Welfare in January 2024, outlines the overall direction of physical activity and exercise recommendations as follows: "Consider individual differences, adjust the activity intensity and amount, and start with feasible activities and goals. Move the body more than before, even if only slightly more." The guide encourages people to incorporate physical activity into their daily lives. Furthermore, it urges them to be mindful of and make efforts to move the body as much as possible, avoid sedentary behaviour (e.g., prolonged sitting), and avoid long inactivity periods. The history of physical activity and exercise guidelines in Japan began with the *Exercise Requirement for Health Promotion 1989*, and the current guide represents the fourth edition. Our laboratory has played a major role in developing these guidelines and continues to communicate the importance of physical activity and regular exercise habits to the public.

In order to update physical activity recommendations for the public, it is necessary to comprehensively collect academic papers worldwide (systematic review) and synthesizing the results (meta-analysis). Currently, we are launching and conducting a participatory systematic review project aimed at updating and generating scientific evidence for the planned revision of the guidelines in ten years.

The second effort is to develop and validate methods of assessing the level of physical activity. Over the last few years, assessment of the level of physical activity has been based on values obtained by processing signals

from an accelerometer built into each activity tracker. However, pedometers and activity trackers can be located in various places on or near the body, such as one worn on the waist, on the arm, or built into a smartphone. In other words, even if the number of steps can vary depending on the device and its placement, it remains unclear whether the displayed count accurately reflects the actual number of steps. Our center conducts validation studies on the accuracy and reliability of various devices. This supports the ongoing evaluation of step count trends in the National Health and Nutrition Survey and contributes valuable knowledge applicable to physical activity research across diverse fields.

### Identification of modifiable factors to prevent frailty, from research to implementation in society at large

The world is looking to see how Japan, a rapidly aging country, will cope with a super-aged society. As people age, their physical and psychological abilities (e.g., motor and cognitive functions) decline, and these abilities can be affected by the presence of multiple chronic diseases. This can lead to impaired daily functions and greater susceptibility to physical and psychological frailty. This condition is known as frailty. While frailty is primarily characterized by a decline in functional ability often observed in later life, early identification combined with appropriate intervention and support can help preserve or enhance daily functioning. Our center has reported research findings elucidating the relationship between physical activity, exercise, and frailty. These insights are being applied to real-world practice, including the development of strategies for frailty prevention through the promotion of physical activity and exercise.

Furthermore, while frailty is commonly perceived as a condition unique to later life, recent findings indicate that a notable proportion of individuals in their 40s and 50s—those in the workforce—also exhibit signs of frailty. In collaboration with Osaka Prefecture, our center is developing a lifestyle modification program aiming at preventing frailty. As part of industry-

specific health checkups, we offer frailty screenings and analyze both the proportion of workers identified as frail and the factors contributing to frailty. Our findings also indicated that individuals who were familiar with the term 'frailty' were less likely to be classified as frail compared to those who were not. Based on these findings, we aim to raise awareness of frailty among working-age adults to support long-term prevention efforts.

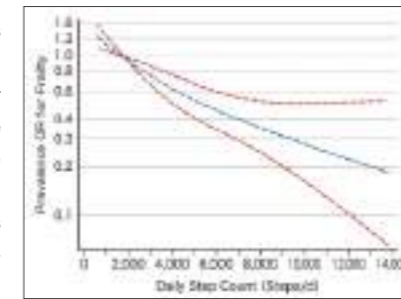


Figure 1: Association between daily steps and frailty (Watanabe et al., 2020)

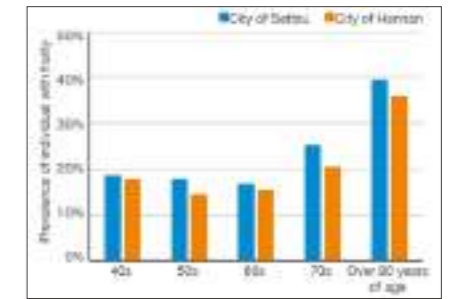


Figure 2: Prevalence of Frailty by Age Group (Yoshida et al., 2021)

## Research that contributes to preparedness for health crises such as large-scale disasters

Engaging in physical activity is influenced not only by demographic characteristics such as age and sex, but also by the surrounding physical environment—for example, the presence of well-maintained sidewalks—and by how people perceive that environment, such as being aware of walkable paths nearby. People tend to adapt to their surroundings and engage in daily physical activity accordingly, but unexpected changes in the environment can lead to significant shifts in activity levels. Disasters are the most impactful events that can bring about changes in our living environment.

In the areas affected by the Great East Japan Earthquake of March 2011, many residents were forced to evacuate. During this process, evacuees had little or no control over choosing their living environment. It has been reported that evacuees experienced reduced physical activity due to the lack of supportive environments for exercise. Insufficient physical activity

is thought to lead to muscle loss and lifestyle-related diseases, which may in turn raise the risk of older adults needing long-term care. Alongside natural disasters, the outbreak of COVID-19 in Japan resulted in large-scale behavioural restrictions across the population. When a crisis impacts people's health, reduced physical activity and the resulting long-term deterioration in health can be seen as a 'secondary health impact'.

In recent years, Japan has experienced increasingly frequent and severe disasters, putting everyone at risk of being affected. Therefore, in addition to protecting lives during disasters, it is becoming increasingly important to consider strategies that help affected people maintain health in post-disaster environments. Our center aims to contribute to disaster preparedness by exploring how to support active lifestyle among affected individuals in the aftermath of health crises.

## Longitudinal Study on Health, Nutrition, and Well-being (Settsu Study)

Society is becoming more complex, as individuals face the combined pressures of a rapidly aging population, declining birth rates, and the need to balance work with caregiving responsibilities. As society undergoes major changes, promoting health across all generations and creating livable communities requires implementing effective health strategies tailored to each age group. In 2024, we carried out a survey of Settsu City residents aged 18 and over, exploring topics such as physical activity, nutrition, well-being, and social engagement. Over the next 20 years, by obtaining official data such as long-term care certification records and medical and long-term care insurance claims for study participants, and linking these with questionnaire responses, we will be able to track the onset of diseases and the need for long-term care. By identifying key health issues among residents through the survey results and proposing effective strategies for health promotion and community development, we aim to create a livable environment for people of all generations. The data from the Settsu Study can be made available for research use by any organization, including industries, upon review and approval. We hope to actively promote collaborative research through this resource.

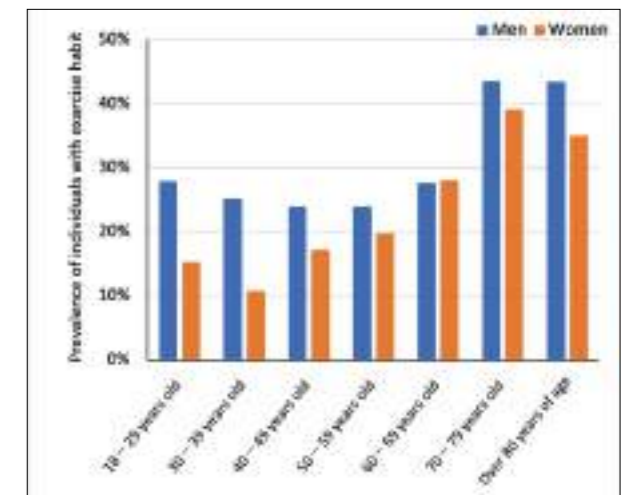


Figure 3: Prevalence of those who have an exercise habit by gender and age group

## Center for Physical Activity Research

### Laboratory of Physical Activity Guideline

Working together with universities and research institutions, we build a body of evidence on how physical activity and sedentary behaviour affect health. Our goal is not only to raise awareness of the importance of staying active, but also to apply these insights to real-world practices—through updated guidelines and tailored approaches for different age groups and genders—so that everyone can enjoy a healthier life.

### Laboratory of Well-Being

Amid changes in social structures and values, enhancing not only health but also well-being has become a critical issue. Grounded in epidemiological methods and enriched by insights from psychology and information science, we aim to clarify the relationships between physical activity, exercise, sedentary behaviour, physical fitness, sports, and well-being and to propose vibrant, active societies tailored to each generation.

### Laboratory of Exercise Epidemiology

Through field studies and analysis of public data, we conduct epidemiological research on the relationships between physical activity, sedentary behaviour, disease prevention, healthy life expectancy, and well-being. We also identify factors contributing to the gap between scientific evidence and real-world behaviour, aiming to bridge this gap through social implementation efforts.



MESSAGE

### Current research and vision

Our research focuses on addressing health issues such as obesity, diabetes, and fatty liver disease, as well as age-related conditions like sarcopenia and frailty. We aim to develop nutritional guidance and intervention methods based on precise nutritional assessments. By integrating analyses of gut microbiota and genetic predispositions, we seek to establish "personalized nutritional assessments". This approach enables us to provide optimal nutrition and dietary recommendations tailored to each individual's constitution and health status, contributing to disease prevention and health maintenance. Through our research, we are committed to supporting the public in leading healthy and high-quality lives.

Director Yuichi Yoshida

## Advancing Health and Disease Prevention through Personalized Nutrition

### Assessing Energy Expenditure for Highly Accurate Personalized Nutrition

Personalized nutrition aims to provide nutritional support tailored to an individual's constitution and lifestyle, with precise evaluation of energy requirements at its core. Energy requirements must be determined based on factors such as age, sex, physical activity level, and health conditions, as their accuracy directly affects dietary management and health maintenance. To establish estimation methods for daily energy expenditure, we utilize human calorimeter and the doubly-labeled water method, contributing to the formulation of "Estimated Energy Requirements" in the Dietary Reference Intakes for Japanese.

Additionally, our research focuses on energy metabolism and the appropriate intake of major nutrients, including protein, fat, and carbohydrate, to aid in establishing dietary reference intakes for Japanese. We also investigate the mechanisms behind obesity and lifestyle diseases caused by excessive or insufficient nutrient intake and explore prevention strategies.

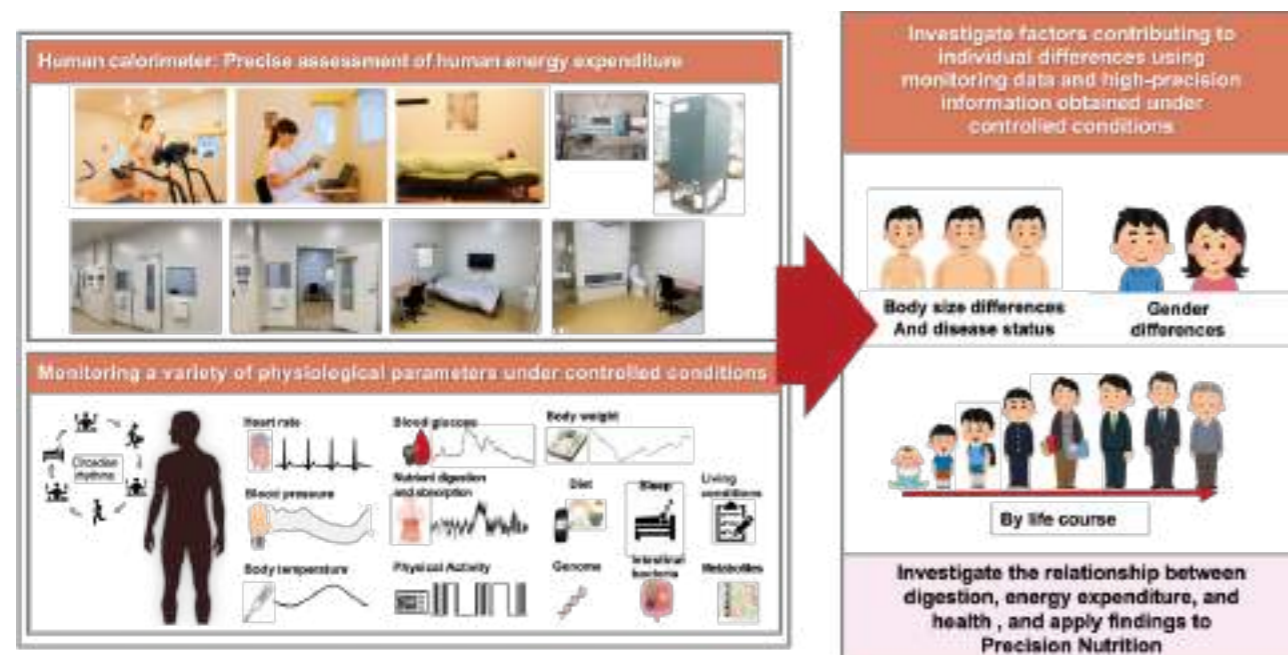


Figure 1: Research using a human calorimeter to investigate individual differences in digestion, absorption, and metabolism

### Longitudinal Study on the Nutrition and Dietary Habits of Pregnant Women in Settsu City (PANCAKE Study)

In collaboration with the Center for Nutritional Epidemiology and Policy and Center for Physical Activity Research, we conduct a longitudinal study on nutrition and dietary habits. Using internationally recognized techniques such as the doubly labeled water method, we comprehensively analyze body composition and energy intake during pregnancy, which have not been fully understood in Japanese pregnant women. Based on these data, we aim to establish scientific evidence for dietary and nutritional recommendations that support maternal health and healthy fetal development.

### Research on Individual Differences in Digestion and Absorption Rates

The "energy" values displayed for foods and meals represent the estimated energy absorbed by the body, excluding energy lost through feces, urine, and sweat.

Since human digestion and absorption rates significantly impact required energy intake, we investigate individual differences in digestion and absorption and their determining factors to advance personalized nutrition. Our studies in young adults have revealed significant individual variations in digestion and absorption rates, influenced by energy loads. Future research will explore sex-based differences, body composition, aging, and disease-related effects.

### Research Utilizing a Large-Scale Japanese Cohort for Personalized Nutrition

Using large-scale cohort data from Japanese populations, we analyze lifestyle habits, health status, gut microbiota, and genetic factors to develop dietary recommendations for disease prevention and mitigation. Since food intake involves multiple nutrients that interact synergistically, we investigate how nutrition affects the onset of lifestyle diseases, frailty, and sarcopenia. We also focus on intestinal bacteria as a key factor in individual differences in dietary effects. With a database of over 15,000 individuals, we collaborate with industry partners to further our research.

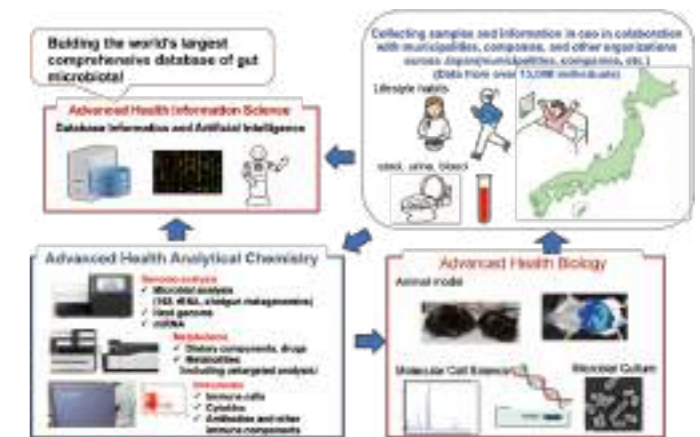


Figure 2: Building a Microbiome Information Infrastructure for Advancing Health Sciences

### Does Protein Requirement Vary Based on Physical Activity and Life Course?

Establishing the Indicator Amino Acid Oxidation (IAAO) method in Japan is a critical step toward scientifically determining protein requirements.

The IAAO method, recommended by WHO, is a highly reliable technique, but its reports on protein requirements have been limited to only two countries worldwide. Developing and applying this method in Japan has been a significant challenge. This method utilizes <sup>13</sup>C-labeled phenylalanine to measure amino acid oxidation. When protein intake is insufficient, unutilized amino acids are oxidized, increasing <sup>13</sup>CO<sub>2</sub> excretion in breath, allowing for accurate determination of protein needs.

Currently, we are using this method to verify protein requirements in healthy young adults and the elderly. In the future, we will explore how physical activity levels, life course differences, and conditions like frailty and sarcopenia affect protein requirements. Our findings are expected to contribute to revisions of Japan's dietary reference intakes and the development of more effective health policies.

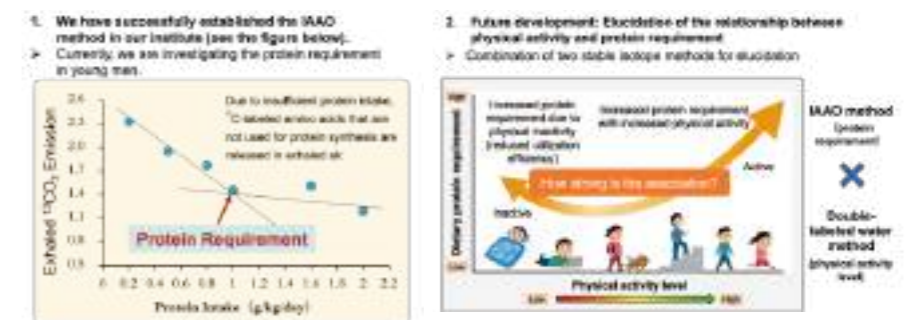


Figure 3: Evaluation of Protein Requirements in Japanese Using the Indicator Amino Acid Oxidation Method

## Center for Clinical Nutrition

### Laboratory of Nutrition Metabolism

We conduct research to explore individual differences and influencing factors in the digestion and adsorption rates of energy and nutrients, as a foundation for advancing personalized nutrition.

### Laboratory of Nutritional Therapy

Focusing on energy and key nutrients, our aim is to identify what and how much should be consumed throughout the life course to support and improve health. Through cohort and intervention studies involving human participants, we conduct multifaceted research into the relationships between nutrition, lifestyle habits, and disease risk factors.

### Laboratory of Behavioral Physiology

We validate assessment methods for lifestyle behaviors (diet and physical activity) and conduct research to clarify their relationship with health. Human behavior is influenced by a complex interplay of genetic, physical, and psychological factors. We investigate these relationships using diverse research methodologies, including genetics, physiology, and epidemiology.



**MESSAGE**

**Looking Ahead to Future Research**

I have been collaborating with various fields and conducting research on the health functions of agricultural products and food. By utilizing the center's technologies and research results, we aim to steadily connect our research with the proposal of a delicious, enjoyable, and healthier diet tailored to each individual.

Director Masuko Kobori



## Science of Food through Chemical Analysis and Nutrition/Functionality Research for Safe and Healthy Eating Habits

### Our Goal

We conduct research on the nutrition, health functions, and safety of food in order to contribute to the health and longevity of people through dietary habits. Diet plays a major role in maintaining and promoting health, and a balanced diet is the foundation of that. Additionally, it is becoming increasingly clear which foods are most appropriate for each individual and their current state. We will continue our research to make it possible for everyone to enjoy a diet that suits their preferences and is also beneficial to their health.



Inside the Experimental Room

## Contributing to the Maintenance and Enhancement of the Reliability of Nutritional Labels as Experts in Analytical Chemistry

"Foods with Health Claims" such as "Foods for Specified Health Uses (FOSHU)", "Foods with Function Claims", and "Food with Nutrient Function Claims" are health-functional foods that meet the standards set by the government and are the only types of food that can display health-related functions. Both "FOSHU" and "Foods with Function Claims" can show functions that help maintain or enhance health, with the former being approved by the government, while the latter is the responsibility of the business to report information on safety and evidence of functionality. "Food with Nutrient Function Claims" is that containing a certain amount of specified nutrients and can display their function using government-defined expressions without the need for notification. All of these foods are based on a balanced diet, and if consumed in the recommended amounts, they are expected to contribute to health. However, it is crucial that the ingredients and nutrients are correctly included as displayed. "Food for special dietary uses" is the food that can display specific uses, such as for infants, pregnant women, or individuals with swallowing difficulties,

with government approval. At our center, we work in collaboration with the Consumer Affairs Agency to conduct actual measurements of functional ingredients and nutrient content in "health-functional foods" and "special use foods" available on the market, verifying whether they meet the required standards. Our research efforts aim to ensure that the foods people consume remain safe and continue to contribute to health maintenance and promotion.

Additionally, processed foods are required to have mandatory nutritional labeling for energy, protein, fat, carbohydrates, and sodium (equivalent to salt), with optional labeling for dietary fiber and vitamins/minerals. Nutritional content must generally be displayed based on actual product measurements, so analytical institutions must always obtain accurate analytical values. To promote proper nutritional labeling and improve the reliability of food composition analysis methods, we conduct annual external quality control surveys and work to maintain and enhance analytical techniques.

## Scientifically Clarifying the Risks of "Health Foods" and Providing Reliable Information

In addition to health-functional foods, there are other foods claiming to be beneficial to health, collectively referred to as "so-called health foods". In response to health issues associated with Foods with Function Claims, there is a strong demand for reliable information about the risks of "health foods". Our center operates the "Health Food Safety and Efficacy Information" website and social media platforms, providing information on health risks and alerts in a timely and easy-to-understand manner. We also gather daily information on health foods, from basic information to topics currently in the spotlight, and communicate it clearly to a broad audience, working to spread correct knowledge and prevent health issues related to the use of "health foods".

In fact, more than 30% of Japanese people habitually consume supplements and other so-called "health foods", and it is essential to consider nutrient and functional ingredient intake from supplements when evaluating the nutrition of a person's diet. Therefore, we are also working on developing dietary survey methods to estimate nutrient intake from supplements.



Figure 1: A website and social media platform that provides information on so-called "health food" in an easy-to-understand manner, and an original character "Sappurin"

## Towards Achieving a Healthier Diet

To achieve a healthier diet, we are developing technologies to estimate the type of diet a person is consuming based on the food components excreted in urine. While it is well known that a balanced diet is important for health maintenance and promotion, it has been reported that less than 50% of people maintain a balanced diet. Our goal is to use this technology to detect imbalances in diet through simple urine tests and suggest diets that are healthy and suitable for each individual. Furthermore, based on the techniques and insights gained from our research on food component analysis and nutrition/function, we are developing a Japanese Nutrient Profiling Model (a system for categorizing or ranking foods according to their nutrient content and evaluating their overall nutritional value) for both processed foods and recipes. By applying these research results and technologies, we aim to lead to a future where people can freely enjoy a healthy diet from a wide range of options.



## Center for Food Function and Labeling

### Laboratory of Food Analysis and Labeling

We verify whether foods collected under the Food Labeling Act and specially designated foods approved under the Health Promotion Act contain the stated nutrients and ingredients through actual measurements. We also conduct research to improve the accuracy and effective utilization of nutritional labeling.

### Laboratory of Food Safety and Function

To promote the appropriate use of health foods within dietary contexts, we conduct research on health impact assessments and scientific evidence building for highly utilized food materials and components in health foods. Additionally, we research strategies to optimize dietary balance.

### Laboratory of Food and Health Information

Based on scientific evidence, we continuously collect health-related information on foods and provide it to experts and the public. We conduct risk communication activities and related research to eliminate health hazards caused by so-called health foods and to promote accurate knowledge.

# Center for Private-Public-Academic Collaboration Research



MESSAGE

## Aiming to Serve as a Hub for Private-Public-Academic Collaboration Research

The implementation of research findings from the National Institute of Health and Nutrition, with its long history, is becoming increasingly important in realizing Japan's vision of a "100-year life era". Against this backdrop, the first research center within the National Institute of Health and Nutrition dedicated to Private-Public-Academic collaboration has been established and begun its research activities toward societal implementation.

Director Hideyuki Ito

## Bridging Private-Public-Academic Collaboration through Health and Nutrition Research

### Contributing to Global Health as a WHO Collaborating Centre

Our center promotes collaboration with various national and international institutions, companies, and governments. As the only WHO Collaborating Centre in East Asia that commit to address significant public agendas in both nutrition and physical activity, we are building an international network to lead efforts in improving nutrition and physical activity, particularly in the Asia-Pacific region. Through this network, we support researchers in the Asia-Pacific region, enhance surveillance on nutrition and physical activity, and contribute to addressing regional health and nutrition challenges (coexistence of undernutrition and overnutrition).

Through the NIHN Fellowship Program for Asian Researchers, we invite overseas researchers engaged in health and nutrition research to enhance their expertise and skills. This initiative strengthens the research capabilities of participating scientists and fosters international cooperation. Between FY 2004 and FY 2025, we have invited 36 researchers from 15 countries, resulting in several research outcomes through collaborative researches.

The Asia Nutrition Network Symposium on Nutrition, held biennially since 2004, addresses major health and nutrition challenges in Asia. Based on the key themes, we facilitate in-depth discussions, including keynote lectures from the technical lead of nutrition at WHO Western Pacific Regional Office and country reports from speakers across countries in the Asia-Pacific region. These discussions address issues such as the double burden of malnutrition and health disparities.

Starting in FY 2024, we organize workshops to develop a training program for researchers in the Asia-Pacific region, focusing on surveillance of nutrition and physical activity.

Through these initiatives, we aim to foster new research advancements and contribute to improving nutrition in the Asia-Pacific region.

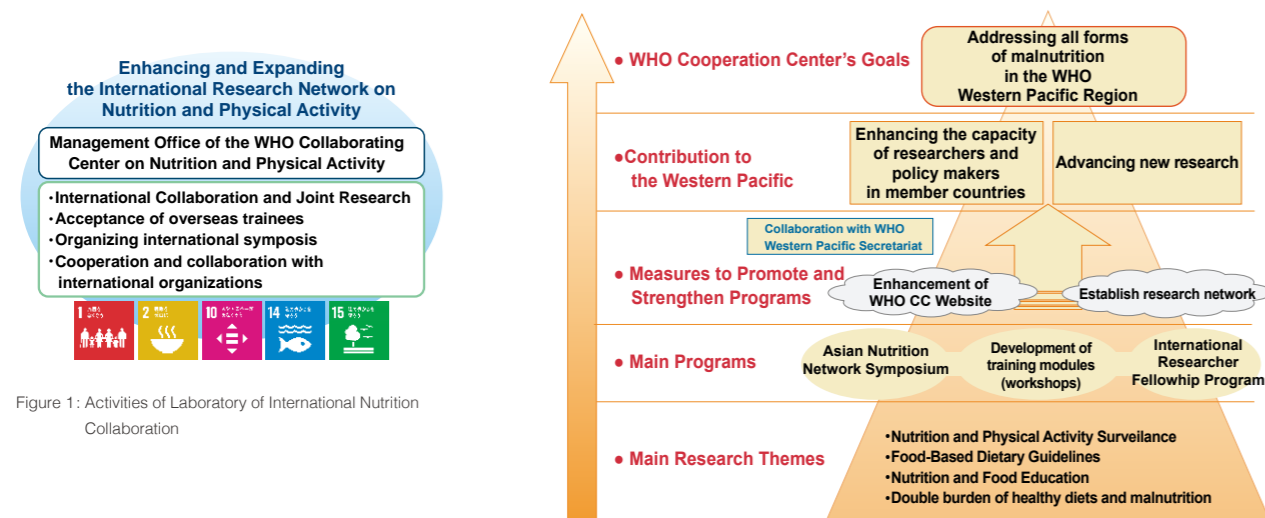


Figure 1: Activities of Laboratory of International Nutrition Collaboration

Figure 2: Action Plan of the WHO Collaborating Centre on Nutrition and Physical Activity

## Toward Zero Health and Nutrition Challenges in Times of Disasters

Japan is a country highly prone to natural disasters. To mitigate malnutrition, health disparities, and health risks caused by disasters—including disaster-related deaths—we have initiated Japan's first government-backed research program specializing in "Disaster and Nutrition". Drawing on our experiences as a disaster-prone country and the lessons learned, we aim to build evidence through research, translate it into guidelines and policy recommendations, and implement actions such as Logistics support during emergencies.

A cohort study of approximately 10,000 individuals affected by the Great East Japan Earthquake revealed that higher consumption of dairy products was associated with a lower risk of hypertension. Additionally, prolonged evacuation led to an increase in obesity, but a study found that men who consumed seafood more frequently had a lower risk of obesity after two years.

Additionally, we collaborate with the Center for Physical Activity Research and local governments to conduct research aimed at preventing health problems after disasters from the perspectives of both nutrition and physical activity.

The findings from these studies are incorporated into various guidelines and related documents, and we also provide logistics support to disaster-affected areas when emergencies occur.

Through collaboration among government, industry, and academia, we translate research findings into practical applications—such as logistics support during emergencies—to help sustain lives saved and promote the development of food environments essential to maintaining health.

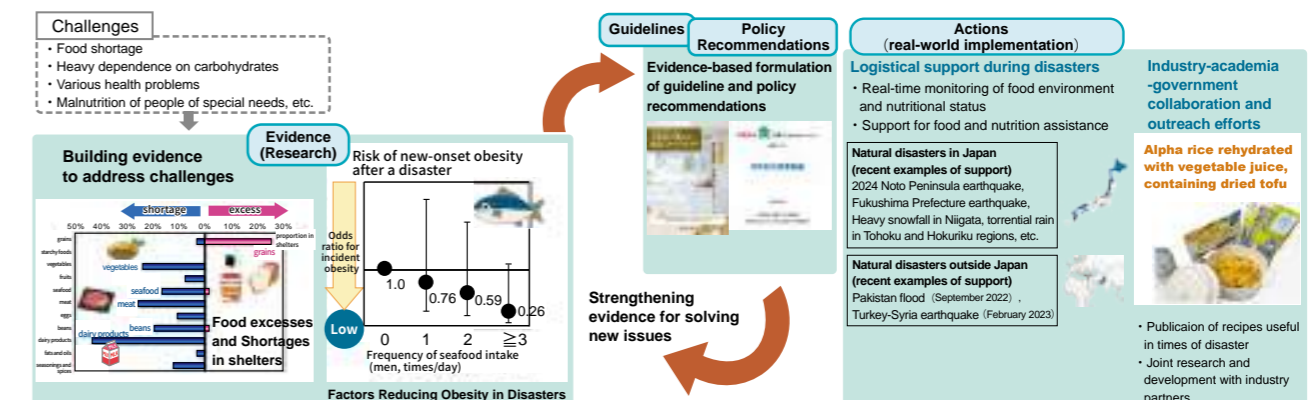


Figure 3: Activities of Laboratory of Disaster Nutrition and Information

## Creating a Sustainable and Naturally Healthy Food Environment

Our center strives to establish a sustainable food environment that naturally promotes health, leaving no one behind. To achieve this, we collaborate with food manufacturers, the restaurant industry, academic institutions, and various stakeholders to build scientific evidence and conduct research on social implementation.

Utilizing our expertise in dietary habits and physical activity, we work with other research institutions to analyze public statistics and research data to address health and nutrition issues and reduce health disparities. Additionally, to contribute to the formulation and revision of national guidelines, we conduct research on the relationship between nutrition, diet, and health. Our findings aim to provide efficient and effective solutions to societal challenges and be translated to the social implementation.

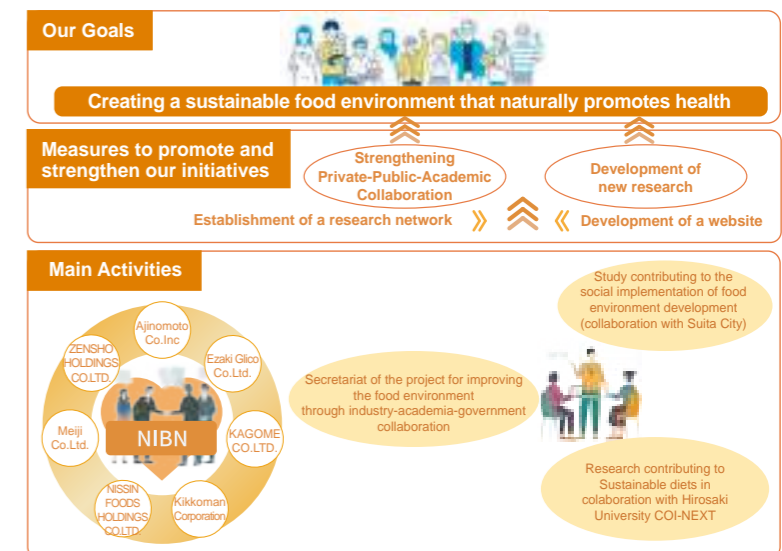


Figure 4: Activities of Section of Research Collaboration and Partnership

## Center for Private-Public-Academic Collaboration Research

### Laboratory of International Nutrition Collaboration

With the goal of eliminating all forms of malnutrition, we collaborate with WHO and other international organizations, conduct joint research with research institutions in Asia-Pacific region. We promote international collaboration through the fellowship program, international symposiums, and initiatives to improve nutrition and physical activity surveillance.

### Laboratory of Disaster Nutrition and Information

We share information domestically and globally based on Japan's experiences and lessons as a disaster-prone country. Our research aims to improve food and nutrition issues during disasters, reduce nutritional disparities, and mitigate health damage while providing evidence-based logistical support.

### Section of Research Collaboration and Partnership

To realize a sustainable, healthy, and enjoyable diet, we lead a cross-center collaborative research project—partnering with multiple food companies through a project for improving the food environment through industry-academia-government collaboration. Our goal is to develop a food environment model that naturally promotes health for all, not just for those with high health awareness.

# Industry-Government-Academia Collaboration

Research Seeds and Industry-Government-Academia Collaboration Needs Collection

Visit here for a collection of seeds 

## To Companies and Research Institutions

- Want to learn more about our research?
- Interested in joint research?
- Want to utilize our patents and research achievements?
- Need technical consultation?

Please feel free to contact  
Industry-Government-Academia Collaboration Team  
from Department of Strategy and Research Support  
(see contact information below).

## Collaboration Process

### STEP 01

#### Inquiry / Hearing

Industry-Government-Academia Collaboration Team from Department of Strategy and Research Support will listen to your needs and organize a general policy based on your request.

### STEP 02

#### Consultation

We match researchers according to individual needs, allowing for detailed consultations.

### STEP 03

#### Joint Research and Other Collaborations

Upon agreement, necessary contracts are concluded to proceed with joint research and other collaboration.



For inquiries regarding

industry-government-academia collaboration, please contact  
Industry-Government-Academia Collaboration Team, Planning Division,  
Department of Strategy and Research Support,  
National Institutes of Biomedical Innovation, Health, and Nutrition

TEL (+81)72-641-9832 mail sangakukan@nibn.go.jp

# Public Relations Activities

Visit here to see the results 

## Purposes of Our Public Relations (PR) Activities

We conduct research daily to serve as a beacon of hope for patients battling illness, their families, and those wishing for a long, healthy life. To become a beacon of hope for many people, we actively engage in public relations, sharing our research achievements and initiatives while collaborating with various sectors.

- 1 Realizing Two-Way Communication with Society (Implementing research with social applications in mind)
- 2 Fulfilling our accountability as a public institution
- 3 Ensuring the public accessibility of research findings
- 4 Supporting funding acquisition

## Introducing Our Research Through Easy-to-Understand Videos

To dispel the impression that our institute's work is difficult or inaccessible, we have created a series of videos that clearly explain our research activities. These videos are available on our official YouTube channel (accessible via the QR code on the back cover). We warmly invite not only those with an interest in our research, but also anyone who simply wishes to learn "what kind of research we do," to enjoy these videos at your convenience.

## Outreach Activities for Local Communities

To contribute to society through our research, we actively engage in outreach activities, particularly in Osaka and Kansai area, where we are based. We participate in science classes and accept lecture requests for events. If you are interested in our activities and research, please feel free to contact us.

For PR inquiries, please contact

PR Team, Planning Division, Department of Strategy and Research Support,  
National Institutes of Biomedical Innovation, Health, and Nutrition

TEL (+81)72-641-9832 mail pr@nibn.go.jp

## Support Us Through Donations, Supporting a Future of Healthy Living

The National Institutes of Biomedical Innovation, Health and Nutrition (NIBN) aims to:

1. Conduct foundational technology research and biological resource studies to contribute to the development of innovative pharmaceuticals and medical devices.
2. Improve national health through research and information dissemination related to nutrition, dietary habits, and physical activity for health maintenance, enhancement, and disease prevention.

To enhance research in pharmaceuticals, health, and nutrition, we seek financial support from companies and individuals. We deeply appreciate your understanding and support in advancing our research activities.

## Types of Donations

There are two types of donations based on their purpose, and funds are used according to the designated purpose:

Donations supporting the overall activities of the institute

Donations designated for specific projects or research activities

## Tax Benefits

Donations to our institute qualify as contributions to a "Specified Public Interest Promotion Corporation", making them eligible for tax benefits.

## Acknowledgment of Donors

As a token of our gratitude, we publish the names of donors who have given consent on our website.

## How to Donate

### Online Donations

You can easily donate online! Fill in the required information and complete your donation smoothly.



### Donations by Form

Fill out the required details in the form and submit it. Donations can be completed with simple procedures.

For inquiries, please call us. Our donation team will provide guidance.

For donations inquiries, please contact

Fundraising Team, Planning Division, Department of Strategy and Research Support,  
National Institutes of Biomedical Innovation, Health, and Nutrition

TEL (+81)72-641-9832 mail fundraising@nibn.go.jp