Moonshot Research and Development Program

MOONSHOT
GOAL-7

To Age 100 without Health Concerns

Japan Agency for Medical Research and Development

AMED

MOONSHOT
RESEARCH & DEVELOPMENT PROGRAM

MOONSHOT

GOAL-7

Realization of sustainable care systems to overcome major diseases by 2040, for enjoying one’s life with relief and release from health concerns until 100 years old

Creating a society in which everyone can stay healthy into old age will not just reduce the burden on medical and social care in a super-aging society, but more importantly will enable us to live fuller and more active lives.
In addition to disease prevention, effective treatment methods mean that many illnesses are expected to become treatable ailments. In this environment, if only we could enjoy life free from the effects of aging!
This is humanity’s universal dream, and the creativity that can imagine achieving this goal and the technologies and newly understood mechanisms that will be developed thanks to this motivating force will provide new impetus to bring us a wonderful future.

Three targets for meeting this goal

TARGET 1

Realization of a society where everyone can prevent diseases spontaneously in daily life

Establish infrastructure to maintain good mental and physical health by developing technologies using regulation of immune systems or sleep, etc. in order to stay healthy and prevent the onset and exacerbation of diseases, and technologies to visualize individual physical and mental state in daily life and urge people to voluntarily take health maintenance actions most suitable for them.

TARGET 2

Realization of medical networks accessible for anyone from anywhere in the world

Establish a medical network functioning regardless of region and even during disasters and emergencies to provide the same level of medical care as normal times by developing diagnostic and treatment devices for simple tests and treatments at home, etc. and diagnosis- and treatment-free technologies for some chronic diseases.

TARGET 3

Realization of drastic improvement of QoL without feeling load

(realization of an inclusive society without health disparity)

Establish a social infrastructure to enable self-reliant life at home without depending on nursing care by developing such technologies as the recovery of body function with rehabilitation without feeling burdened, normalization of ailing biocontrol systems, regeneration or substitution of weakened organs and so forth.

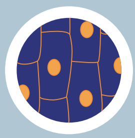
This program aims to achieve the goal established by Japan's Headquarters for Healthcare Policy.
More details are available from the Cabinet Office, Government of Japan website. https://www8.cao.go.jp/cstp/english/moonshot/sub7_en.html

PROJECTS

Improving mitochondrial function to extend life expectancy
Keeping healthy to the best life

Development of method for complex tissue regeneration via tissue embryonization
Regenerating lost limbs

Ended November 2023



Extending healthy lifespan by eliminating senescent cells
Eliminating the cause of aging

Regulating microinflammation: Preventing disease through quantum and neuromodulation technologies
Picking up disease warnings quickly

Deciphering and Engineering Sleep and Hibernation -- The Future of Medical Care
Bringing healthy sleep to people throughout the world

Bring hospital into home toward controlling inflammation at home
Burden-free health management

Understanding and harnessing the role of the gut microbiome in healthy longevity
Harnessing the power of the microbiome for health

A world of zero cancer risk created by rejuvenation using cell lineage conversion
Making cancer a thing of the past

Actualization of a cancer-free society
Bringing the cancer rate down to zero

Study of reservoir functions that support resilience of the brain and its enhancement to overcome dementia
Maintaining brain health and eliminating dementia

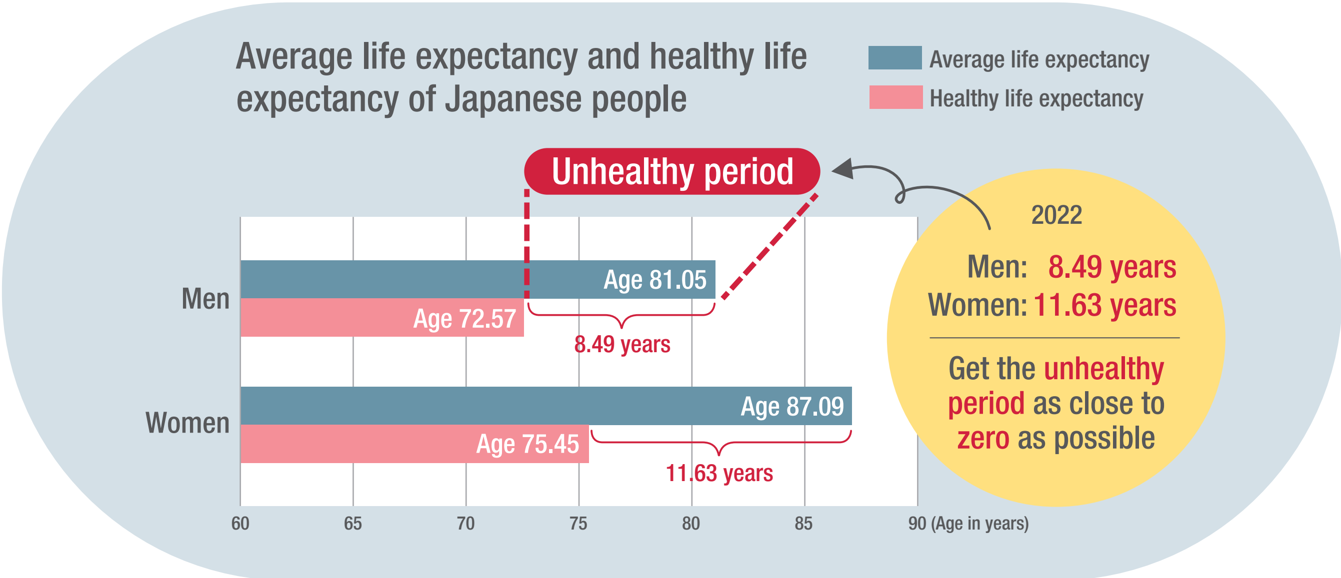
Life course approaches through sleep to protect, nurture, and activate the brain
Aspiring to overcome dementia by improving sleep quality

Early detection and modulation of the dementia pathogenesis based on the concept evolving from glial pathology to senoinflammation
Making Dementia Prevention and Treatment More Accessible

GOAL-7 KEYWORD

Extending Healthy Longevity

“Healthy longevity” refers to being able to live in the self-awareness of health, without restrictions on activities or chronic disease. The Moonshot Goal 7 aims to make the difference between average life expectancy and healthy life expectancy, that is, the time for which someone is ill or requires social care (the unhealthy period), as close to zero as possible, with the goal of achieving a society in which everyone can stay healthy into old age.



Source: Average life expectancy is from the Ministry of Health, Labour and Welfare’s “2022 Simplified Life Table,” and healthy life expectancy is from the Ministry of Health, Labour and Welfare’s materials from the 4th Health Japan 21 (Third Term) Promotion Expert Committee, 1-1 “Regarding the 2022 Values of Healthy Life Expectancy,” compiled by AMED.

The aim is to build health and social care systems by 2040 that mean people can enjoy living until they turn 100.

Program Director HIRANO Toshio

Our theme is overcoming chronic inflammation, which underlies a whole raft of diseases.

When we catch a cold or injure ourselves, an inflammatory reaction occurs inside our bodies. This inflammation (acute inflammation) is well controlled, and subsides over time. Chronic inflammation, on the other hand, occurs when this control stops working and the inflammation persists long-term. While aging promotes chronic inflammation, the reverse is also true. Chronic inflammation associated with aging is one of the main causes of a raft of age-related diseases, including cancer, arteriosclerosis, diabetes, and dementia. If such chronic inflammation could be controlled, this might help prevent age-related diseases and reduce the gap between average life expectancy and healthy life expectancy. Even under normal circumstances, if BMI calculations show that visceral fat has increased, this can cause chronic inflammation. It is thought that if such chronic inflammation continues to increase, it may become a cause of cancer and many other age-related diseases. Doctors will advise people to reduce their visceral fat by improving their diet and exercising, and patients can be expected to make an effort to follow this advice. In Moonshot Goal 7, we are engaged in research and development that adopts a range of approaches to this process of advice leading to prevention and treatment from the viewpoint of biomedical sciences, including inflammatory substances within the body, mitochondrial function, and senescent cells, with the goal of providing lifestyle advice through medical networks as well as preventive treatment when required, in order to bring the “unhealthy period” during which people are bedridden or otherwise incapacitated to as close to zero as possible. If this goal can be achieved, it would give people the chance to enjoy a new lease of life, which today might not be considered possible because of age-related health concerns. They will be able to pursue their dreams once again in their 60s. That means they get to live life twice over. I am committed to this goal of extending healthy longevity by even a single day because I want everyone’s lives to be bright, enjoyable, and positive right up to the end.

Toward achieving sustainable health and social care systems

Three Targets

1 Everyone can prevent diseases spontaneously in daily life

Smartwatches enabling people to monitor their heart rate and the number of steps they take are already widely available, but to discover the levels of inflammatory substances, sugar, cholesterol, and other substances in their blood, people still need to have blood drawn in a medical institution. If devices can be developed for the simple measurement of these data (biological trends) and to collect urinary and fecal data from toilets, this will enable daily data to be checked on an everyday basis, which would encourage individuals to do something about it, meaning that disease could be prevented before it starts. Presymptomatic disease and aging levels could also be evaluated at the same time. Based on such data, it should be possible to extend healthy longevity not just by improving people's lifestyles from the medical perspective, such as through diet, exercise, and sleep, but also by eliminating senescent cells and nipping chronic inflammation in the bud.

2 Medical networks accessible for anyone from anywhere in the world

Senescent cells are increasing without our knowledge, even in healthy people who are leading normal lives in society. The goal is to create medical networks to prevent disease before it can occur by conducting medical interventions at the pre-disease stage, such as recommending preventive measures such as exercise and diet or sending a message saying "If you go on like this you'll be in trouble" to the individual's smartphone or other device. This means that individuals will be able to receive their normal preventive measures or treatment via these networks wherever they are in the world, or during extraordinary circumstances such as natural disasters. Making this a reality would greatly reduce both the staff and costs required for medical and social care.

3 Drastic improvement of QoL without feeling load

When people's health deteriorates, whether by hearing loss or due to illness such as heart disease, this generates a difference between them and healthy people (health disparity). The aim is to reduce this difference to as close to zero as possible. As well as preventing disease, this means maintaining Quality of Life (QoL) from treatment to rehabilitation by providing care and treatment that place as little strain as possible on the body in order to shorten the difference between actual life expectancy and healthy life expectancy. The goal is to maintain QoL until the end of each individual's life.

HIRANO Toshio Program Director

Professor Emeritus, The University of Osaka / President, Osaka International Cancer Treatment Foundation

After graduating from Osaka University Faculty of Medicine in 1972, Hirano studied at the US National Institutes of Health and worked at Osaka Habikino Medical Center before becoming an assistant professor at Kumamoto University. He then moved back to Osaka University as an assistant professor and was then appointed full professor, after which he became Dean of the Graduate School of Frontier Bioscience, Dean of the Graduate School of Medicine and Faculty of Medicine, and eventually the 17th President of Osaka University. He has been a member of the Science Council of Japan, President of the Japan Society of Immunology, a member of the Council for Science, Technology, and Innovation, and President of the National Institutes for Quantum and Radiological Science and Technology, among other positions. His awards include the Sandoz Prize for Immunology, the Fujiwara Prize, the Crafoord Prize, the Japan International Prize, and a Clarivate Citation Laureate 2021 in Physiology or Medicine, and he has received the Medal with Purple Ribbon and the Grand Cordon of the Order of the Second Treasure. He discovered interleukin-6 (IL-6), and identified its mechanism of action and its association with chronic inflammatory disease.

Improving mitochondrial function to extend life expectancy

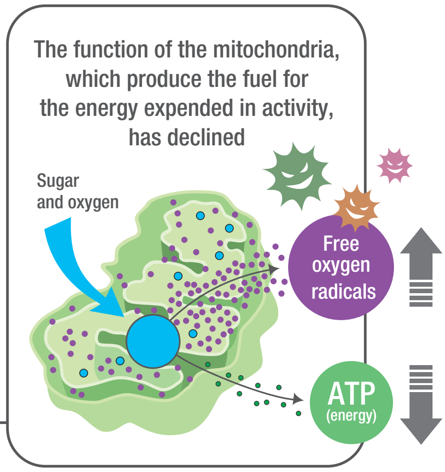
Keeping healthy to the best life

Today's reality

As we age, our physical and mental functions decline (frailty)

- Condition intermediate between good health and requiring social care
- Declining physical and mental function
- Treatment and prevention alone are not enough

Inside the body...

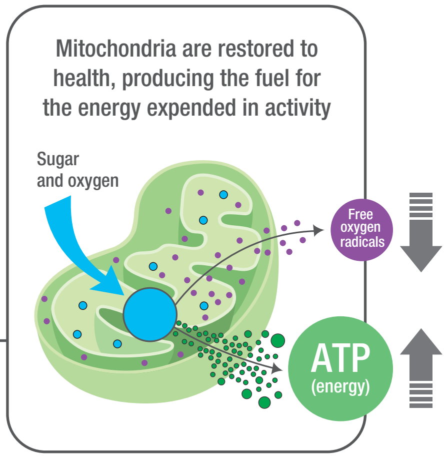


DREAMING POWER

Active, invigorated mitochondria

Our dream

Released from the "aging phenomenon" that weakens the body, while potentially also protected against cancer and dementia



Therapeutic agent MA-5, now in clinical trials

Mitochondrial preemptive medicine

Mitochondria are the organ that produces most of the energy expended in activity. Identifying the relationship between aging and these mitochondria, which are essential to keeping healthy, will be useful for diagnosing mitochondrial function in a way that does not place strain on the body, and for the development of treatment drugs. Our goal is a society in which people can achieve a healthy old age until they turn 100, by enabling the prevention and treatment of a whole raft of diseases including chronic inflammation, which occurs when mitochondrial function declines.

FOR THE FUTURE

Our goal is to detect mitochondrial functional decline as early as possible and provide intervention or treatment in order to build a society in which people stay healthy into old age.

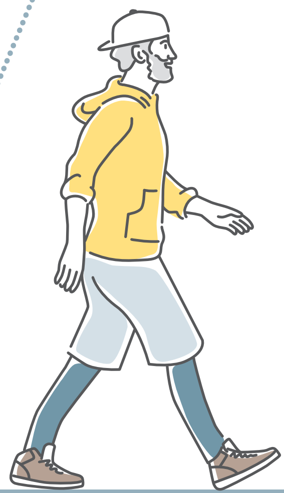
When mitochondrial function goes wrong, it has been shown to be a cause of diseases including deafness, sarcopenia, ALS, and Parkinson's disease. However, a simple method of assessing mitochondrial function has yet to be established. Not only such an assessment method but also ways of improving mitochondrial function with drugs, diet, or exercise are keenly awaited. One pioneering drug is MA-5, which is currently in clinical trials for diseases caused by midochondrial dysfunction.

TODAY

- Establish drugs to treat the diseases caused by a decline in mitochondrial function
- Develop sensors to measure mitochondrial function
- Link the data from the sensors to a database, and establish systems to suggest measures such as rehabilitation, oral care, diet, and medications that are appropriate to the individual concerned to improve their weakened mental and physical state

2030
TARGET

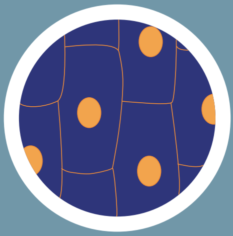
- Establish methods of diagnosing and treating the various diseases caused by a decline in mitochondrial function
- Enable the simple detection at home of age-related mitochondrial functional decline from breath, urine, saliva, or similar samples, and help improve their weakened mental and physical state by indicating the optimum diet and exercise for that person



2040
BREAKTHROUGH

ABE Takaaki Project Manager
Professor, Graduate School of Biomedical Engineering, Tohoku University

After graduating from Tohoku University, Abe continued to study at Tohoku University Hospital and Kyoto University Graduate School of Medicine, gaining a doctorate in medicine. He went on to a postdoctoral fellowship (PD) at the Japan Society for the Promotion of Science, before moving to Harvard Medical School as a postdoctoral fellow in the Human Frontier Research Program. On his return to Japan he conducted research into kidney disease and hypertension as a JST PRESTO project while working in the Division of Nephrology, Endocrinology, and Hypertension of Tohoku University Medical School. Since 2008 he has been a professor in the Tohoku University Graduate School of Bioengineering and Tohoku University Graduate School of Medicine. He was appointed an AMED Moonshot Project Manager in 2020.

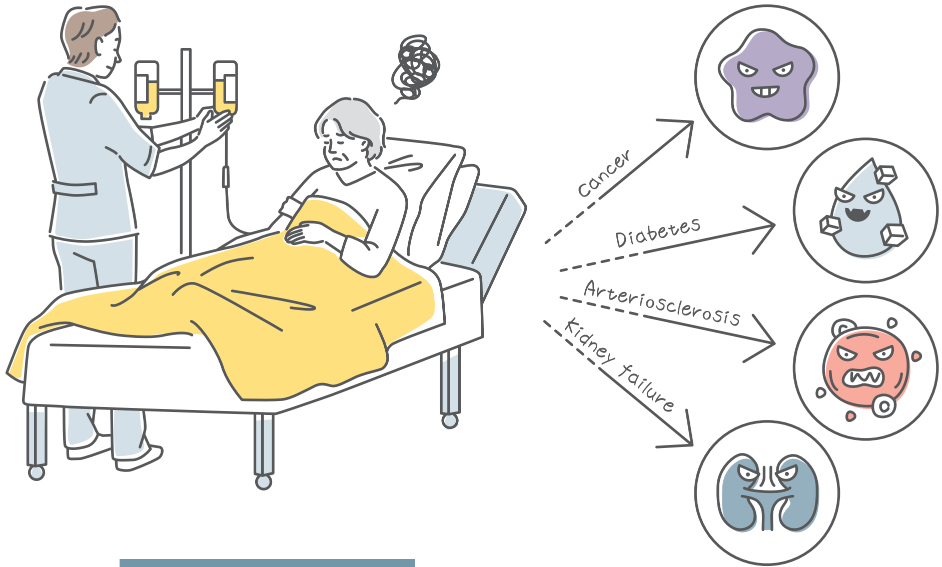


Extending healthy lifespan by eliminating senescent cells

Eliminating the cause of aging

Today’s reality

- The body ages as we grow older, both in ways we can see and in ways we can’t
- Aging and its associated diseases must be treated individually



DREAMING POWER

Develop the technology to eliminate senescent cells

Our dream

- Prevent age-related changes in the body
- Overcome every type of disease for which age is a cause

Callianthemum hondoense, found near mountain peaks in the Southern Alps of Japan. They date back to the glacial period, and have fresh, vibrant flowers.

Senescent cells

Chronic inflammation due to the accumulation of “inflammation-inducing cells”, such as senescent cells, causes aging and diseases of old age. Our goal is to prevent and treat the entire range of diseases for which age is a cause by eliminating senescent cells, which increase with age, from the body and suppressing inflammation.

FOR THE FUTURE

Improve aging and eradicate the entire range of age-related diseases by removing the senescent cells that cause chronic inflammation.

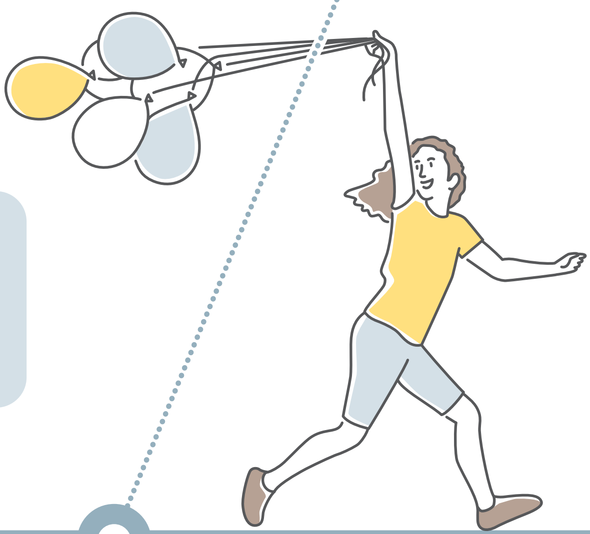
Currently, age-related decline in physical function and a diverse range of diseases are all dealt with by treating them individually. However, if the senescent cells that cause chronic inflammation could be eliminated, this might enable the entire range of age-related diseases to be overcome. We are engaged in research to prevent senescent cells from accumulating within the body despite advancing age. Our ultimate goal is to achieve the ultimate in preventive medicine by enabling the degree of progression of aging to be easily measurable at home and for this information to be shared with family doctors, so that senescence can be dealt with before disease symptoms appear.

TODAY

- Implement the world's first clinical trials of chemical substances that remove senescent cells
- Build the technology to measure the level of aging and its speed

2030
TARGET

- Develop the technology to remove senescent cells, so getting rid of age-associated disease and organ failure
- Establish techniques for measuring the level of aging and its speed, and construct systems for measuring the effects of removing senescent cells



2040
BREAKTHROUGH

NAKANISHI Makoto Project Manager
Professor, The Institute of Medical Science, The University of Tokyo

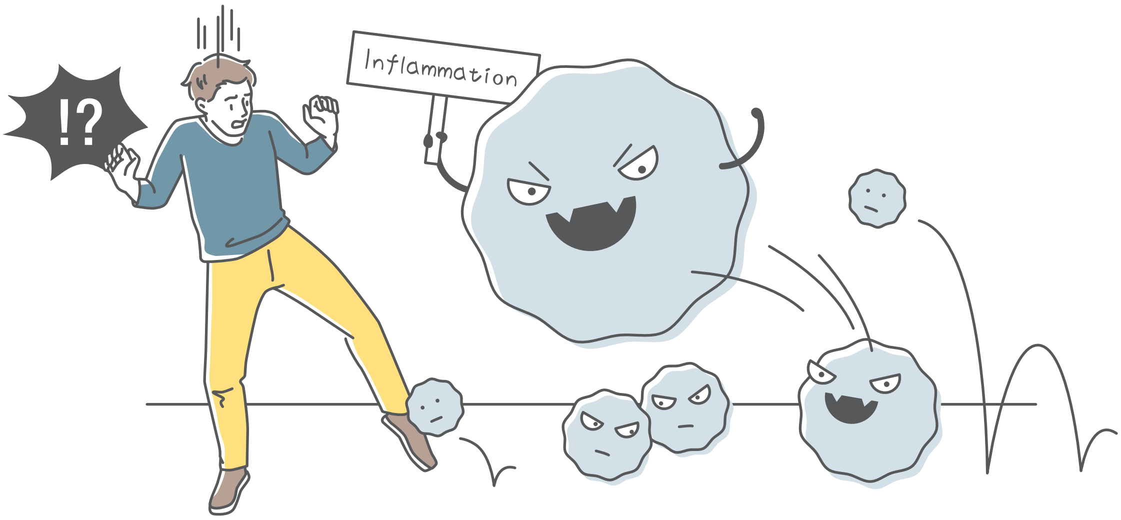
After graduating from university, Nakanishi spent a year in clinical research before embarking on a career in basic research to pursue his interest in the aging of individuals. In 1993 he went to study in the United States, where he began studying cellular senescence in detail. From 2000 he joined the Nagoya City University Graduate School of Medical Sciences, where he started studying the induction mechanism of cellular aging by DNA damage. He then moved to the Institute of Medical Science of The University of Tokyo in 2016, where he put together a laboratory to engage in research with the goal of identifying the regulatory mechanism of individual aging. Since 2023 he has been the Director of The Institute of Medical Science, with responsibility for leading the entire institution.

Regulating microinflammation:
Preventing disease through quantum and neuromodulation technologies

Picking up disease warnings quickly

Today's reality

- Disease-causing microinflammation is undetectable
- Microinflammation is impossible to eliminate



DREAMING POWER

Unleash the power of quantum and neuromodulation technologies

Our dream

- Detect microinflammation at a very early stage by quantum tech
- Prevent disease by eliminating microinflammation by neuromodulation tech

Members of Professor Murakami's lab, award celebrations

Immune cells and IL-6 amplification

Inflammation causes a wide range of diseases, but this requires the activation of both immune cells in the blood and non-immune cells in tissues. Factors and other substances from activated immune cells act to activate IL-6 amplification in non-immune cells in tissues, and the overproduction of IL-6 and migration factors may induce inflammation, resulting in disease.

Gateway reflex and inflammatory reflex

Stress, pain, and other environmental stimuli each activate different neural circuits. These activated neural circuits create gateways for immune cells in the blood to invade tissues, activating IL-6 amplification at specific vascular sites and causing disease. This mechanism of disease induction by neural circuits is called the "gateway reflex". The phenomenon whereby activated vagus neural circuits suppress the immune system is known as the "inflammatory reflex".

FOR THE FUTURE

Use the power of quantum and neuromodulation technologies to achieve the ultra-early discovery and elimination of disease.

We are engaged in research to identify signs of disease from the expression levels of specific genes in immune cells in the blood and non-immune cells in tissues, and to investigate the activation of IL-6 amplification to assess organs that are inflamed, with the aim of understanding “microinflammation” before it reaches the stage of chronic inflammation. For example, we are attaching stick-on electrodes to the body to control the activation of neural circuits where the gateway reflex or the inflammatory reflex occurs, with the aim of blocking the invasion of tissues and organs by inflammatory cells that attack their own body and nipping disease-causing microinflammation in the bud, which may help prevent autoimmune diseases and perhaps even dementia and arteriosclerosis.

TODAY

2030 TARGET

- Establish a method for the ultra-early/ultra-sensitive detection of microinflammation by using genetic analysis or molecular sensors to investigate blood, urine, and tissues
- Validate the effectiveness of technologies to pick up signs of disease by artificially stimulating specific neural circuits
- Develop AI technology to predict the onset of microinflammation on the basis of big data gathered by means such as sensors

2040 BREAKTHROUGH

- Develop technology for the detection and elimination of microinflammation based on research on the inflammatory reaction and various forms of big data analysis
- Connect small wearable devices to AI-controlled big data analysis systems, and develop a system for eliminating systemic microinflammation wherever a person may be.

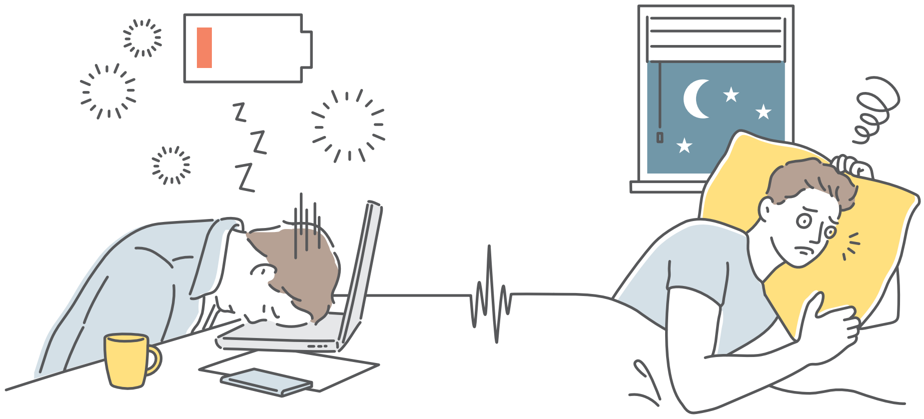
MURAKAMI Masaaki Project Manager
Professor, Institute for Genetic Medicine, Hokkaido University

After graduating from the Faculty of Veterinary Medicine of Hokkaido University, Murakami obtained a PhD from Osaka University on the IL-6 signal transduction mechanism. He subsequently studied T-cell immunology at Hokkaido University and in the U.S. and conducted research at Osaka University on the relationship between IL-6 and disease, in which he discovered IL-6 amplification and the gateway reflex. He is currently affiliated with the Hokkaido University Institute for Genetic Medicine, while also pursuing the elucidation of the mechanism of onset of rheumatoid arthritis and other inflammatory diseases in laboratories at the National Institutes for Quantum Science and Technology and the National Institute for Physiological Sciences.

Bringing healthy sleep to people throughout the world

Today's reality

- Accumulated sleep debt causes a range of different disorders
- One in four people is troubled by insomnia or feeling sleepy during the day



DREAMING POWER

Unlock the mystery of sleep to control sleeping

Our dream

- Prevent disease through high-quality sleep
- A world in which everyone is happy with how they sleep

Device for measuring brainwaves during sleep

Sleep debt

Although the amount of sleep needed for physical and mental health varies between individuals, on average Japanese people sleep much less than people in other nations, and the great majority of students and those of working age are not getting sufficient sleep in Japan. The accumulated sleep deficits lead to "sleep debt", and as this can be a cause of depression, metabolic syndrome, and dementia, hopes are growing for the development of technology capable of controlling sleep at need.

FOR THE FUTURE

Unlock the secrets of “sleep” and “hibernation” for a life untroubled by sleep-related issues

Sleep insufficiency and chronic inflammation are known to have a causal relationship with each other, and as well as identifying its specific mechanisms, predicting the health risk due to sleep deficits, such as the development of chronic inflammation in the form of metabolic syndrome, and elucidating how this works will be the key.
To achieve this, the goal is to build sleep big data to understand the whole picture of Japanese people’s sleep and to clarify the control mechanisms and functions of sleep. Through this, our aim is to resolve a range of sleep-related issues and realize a society where everyone can prevent diseases through sound sleep in daily life. Making artificial hibernation practicable could also save lives otherwise lost during emergency situations, which would revolutionize emergency medicine.

TODAY

- Discover clues to drugs that can adjust the optimum sleeping time
- Discover clues to drugs that can adjust the REM sleep needed to refresh the brain
- Use big data analysis to develop a system for predicting sleep-debt risk
- Discover clues to drugs and technologies that enable artificial hibernation

2030 TARGET

- Prevent the onset and exacerbation of diseases caused by sleep problems by developing the technology to regulate non-REM and REM sleep, and sleep deficit by devising sleep-debt risk prediction systems
- Revolutionize emergency medicine through artificial hibernation technology, dramatically reducing mortality and morbidity

2040 BREAKTHROUGH

YANAGISAWA Masashi Project Manager
Director/Professor, International Institute for Integrative Sleep Medicine, University of Tsukuba

Yanagisawa obtained MD and PhD degrees at the University of Tsukuba. He is the discover of the endothelial vasoconstrictor endothelin and of orexin, a neurotransmitter that regulates the sleep/wake cycle. In 1991, aged 31, he moved to the United States, as a professor at the University of Texas Southwestern Medical Center and an investigator of the Howard Hughes Medical Institute. In 2010 he also established a research laboratory in the University of Tsukuba. Since 2012 he has been Director and Professor of the World Premier International Research Center Initiative-International Institute for Integrative Sleep Medicine (WPI-IIIS). He is also the CEO of S’UIMIN and a member of the U.S. National Academy of Sciences. He was awarded the 2023 Breakthrough Prize in LIfe Sciences.

Bring hospital into home toward controlling inflammation at home

Burden-free health management

Today's reality

Diabetes, cancer, and other lifestyle-related diseases are managed in hospital

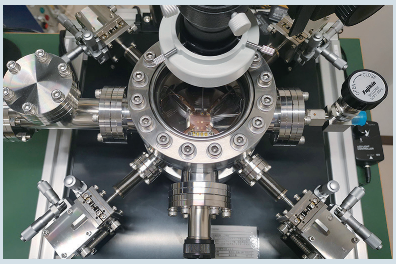
- People attend hospitals for detailed tests and large-scale treatment
- There are limits on the number of hospital visits, and getting to the hospital is a strain in itself
- Patients who live a long way from hospital may not be seen until too late

DREAMING POWER

Develop "medical networks"

Our dream

- Easily collect physical data at home, and discover and treat lifestyle-related diseases at the pre-disease stage
- Eliminate healthcare disparities between regions, and establish healthcare services that are equally accessible from anywhere in the country



Ultra-low-concentration gas analyzer measuring simulated skin gas

Medical networks

Use data on "skin gases" (the vapor emitted from the surface of the skin) collected at home using smart digital devices for analysis and diagnosis in hospital. Networks connecting homes and medical institutions will enable people who find it difficult to get to hospital to undergo tests and receive medical care. This mechanism will revolutionize remote medicine and help build a society in which lifestyle-related diseases are no longer a concern.

FOR THE FUTURE

Connect hospitals and homes via digital devices, to build a society in which everyone can overcome lifestyle-related diseases

The development of smart digital devices to measure “skin gases”, which are an indicator of health, will enable the at-home diagnosis of the chronic inflammation that causes lifestyle-related diseases, and the very early discovery of disease. As well as building medical networks to connect hospitals and homes via digital devices, research and development is also underway on treatment methods such as electromagnetic stimulation and drugs that have effects similar to those of exercise. Making remote medicine a reality and enabling inflammation to be controlled at home will help to overcome lifestyle-related diseases, something that is highly significant for Japan’s ultra-aging society.

- The collection of skin gas data means that the state of inflammation can be checked without obvious intervention, imposing no burden on the body
- Working toward a society in which therapies and drugs with similar effects to those of exercise are revolutionizing remote medicine

- Build systems to collect and analyze skin gases, and use this information in conjunction with data on exercise, sleep, and diet
- Develop smart digital devices capable of measuring the state chronic inflammation in daily life
- Develop therapies as alternatives to exercise, and implement the appropriate treatment for individuals at home

TODAY

2030 TARGET

2040 BREAKTHROUGH

NANGAKU Masaomi Project Manager
Professor, Graduate School of Medicine, The University of Tokyo

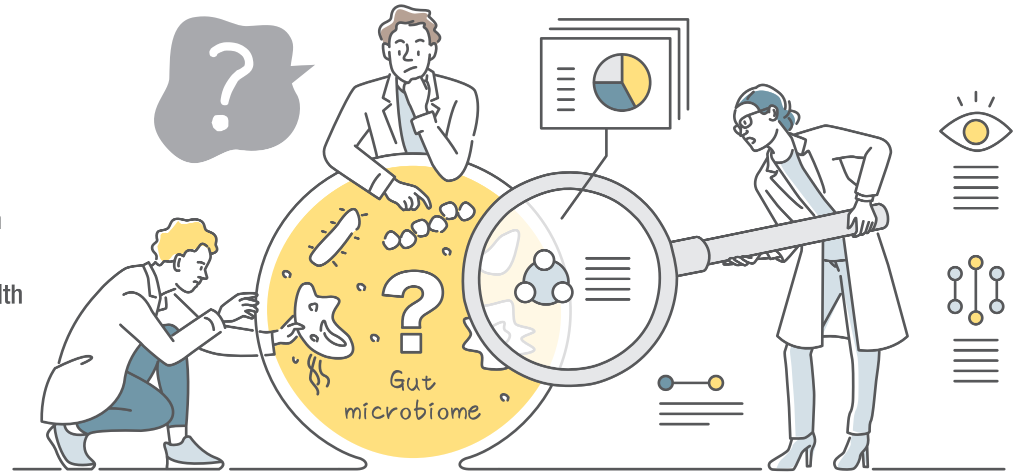
Having graduated from The University of Tokyo School of Medicine in 1988, in 1994 Nangaku went on to work in the Department of Nephrology of the University of Washington before becoming a professor in the Division of Nephrology and Endocrinology of the Graduate School of Medicine of The University of Tokyo in 2012. In 2023 he was appointed Dean of the Graduate School of Medicine and Faculty of Medicine of The University of Tokyo. He is the current President of the International Society of Nephrology, President of the Japanese Society of Internal Medicine, and President of the Japanese Society of Nephrology. He is currently engaged on elucidating the pathophysiology of kidney disease on the basis of oxygen biology and developing treatment methods, as well as working for the innovative development of remote medicine by providing a range of advice to the Japanese Medical Science Federation on the right way to extend these services.

Understanding and harnessing the role of the gut microbiome in healthy longevity

Utilizing the power of the microbiome for health

Today's reality

- Much remains unknown about how the gut microbiome affects health
- Chronic inflammation, Alzheimer's disease, and Parkinson's disease are difficult to cure



DREAMING POWER

Understand the mechanisms and actions of gut microbiome metabolites

Our dream

- Use gut microbiome metabolites to control the immune system and chronic inflammation
- Achieve the prevention and treatment of chronic inflammation, Alzheimer's disease, and Parkinson's disease

Full staff meeting in May 2023

The gut microbiome

Our intestines are host to around 1000 species of gut bacteria, and their roles include maintaining the body in a certain state. There are known to be between 100,000 and 200,000 gut microbiome metabolites, and if simple tests to measure these could be developed by identifying the changes they cause in the body and their chemical structures, these would immediately provide large quantities of data that would be useful for the early discovery and prevention of disease.

FOR THE FUTURE

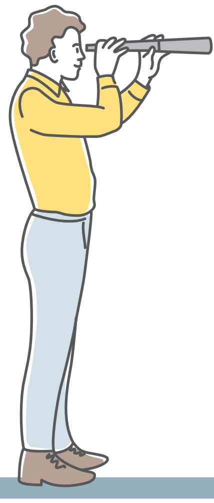
Discover gut bacteria involved in the control of chronic inflammation, and make use of them for prevention and treatment to achieve a society with healthy longevity.

Gut microbiome metabolites can act directly on the networks that link the intestinal tract and the brain. Artificially regulating these actions may help control chronic inflammation and lead to treatments for neurological diseases such as Alzheimer's disease and Parkinson's disease. Gut microbiome metabolites also function to activate and inhibit the immune system, and we are researching immune system interventions using both bacteria themselves and their metabolites. Our goal is to be able, for example, to put together a "microbial cocktail" and supplement metabolites that are lacking in order to treat particular diseases.

TODAY

2030 TARGET

- Unravel the actions and mechanisms of the tens of thousands of gut microbiome metabolites
- Identify gut bacteria and gut microbiome metabolites that extend healthy longevity
- Understand and utilize the mechanism that connects the gut and the brain
- Discover gut bacteria that control chronic inflammation, and develop methods of intervening in the neurological and immune systems.



2040 BREAKTHROUGH

- Enable health management through the analysis of gut microbiome metabolites
- Intervene in the gut microbiome by direct action or dietary improvements
- Prevent and treat chronic inflammation and neurological diseases with microbial cocktails

HONDA Kenya Project Manager
Professor, School of Medicine, Keio University

After graduating from Kobe University School of Medicine in 1994, Honda took up a post in the Department of Radiology of Kobe University School of Medicine until 1997. From then until 2001 he worked as a doctor in the Department of Gastroenterology of Kyoto University School of Medicine while researching the origin of gastrointestinal immune tissue as a graduate student in the Department of Molecular Genetics in the Graduate School of Medicine of that university. Between 2001 and 2007 he was an adjunct in the Department of Immunology of Tokyo University Graduate School of Medicine, and from 2007 to 2009 he was Assistant Professor in the Department of Immune Regulation of Osaka University Graduate School of Medicine. Between 2009 and 2013 he was Associate Professor in the Department of Immunology of Tokyo University Graduate School of Medicine. In 2013 he became Team Leader of the RIKEN IMS Laboratory for Gut Homeostasis, a position he still holds, and since 2014 he has been Professor in the Department of Microbiology and Immunology of Keio University School of Medicine. He has been conducting research on the gut microbiome since 2007.

A world of zero cancer risk created by rejuvenation using cell lineage conversion

Making cancer a thing of the past

Today's reality

- Cells keep on getting older
- Cancerous cells continue to proliferate with the help of their surrounding cells

DREAMING POWER

Use the positive aspect of chronic inflammation to try and return tissue to its original state

Our dream

- Senescent cells are rejuvenated
- The cells surrounding cancerous cells recover their ability to inhibit cancer growth

RIKEN Yokohama Campus

Cell lineage conversion

Cells continually change their state in response to environmental stimuli and changes within the body. The alteration of the functions and roles already possessed by cells and the acquisition of new properties and characteristics is called "cell lineage conversion", and we are engaged in research to do this artificially so that cells will be helpful in suppressing cellular aging. The well known iPS cell research also utilized cell lineage conversion.

FOR THE FUTURE

Bring the risk of cancer down to zero, to create a society in which cancer is no longer something to be feared

Chronic inflammation was formerly thought of as a state in which the body's action to return changes to their original state (homeostasis) had broken down, but it is now known that it also acts to push back the state of weakened homeostasis to the surrounding area, evening out the level of cell aging and rejuvenating (reprogramming) cells. If this reprogramming mechanism could be used to induce cell lineage conversion, this might enable tissues to be controlled, and we are conducting research on treatment methods to suppress the growth of cancer by returning cancer cells and the cells surrounding them that assist in cancer growth to their normal state.

- Develop technologies that intervene in cancer cells and their surrounding networks via cell lineage conversion
- Act preventively on precancerous cells to reduce the risk of cancer to zero
- Global extension of medical and preventive technologies

- Unravel the mechanism by which senescent cells and chronic inflammation induce cell lineage conversion
- Understand how cell lineage conversion changes cancer cells and their surrounding networks

TODAY

2030
TARGET

2040
BREAKTHROUGH

KOSEKI Haruhiko Project Manager
Deputy Director, RIKEN Center for Integrative Medical Sciences

After obtaining a Ph.D. at Chiba University Graduate School of Medicine in 1990, Koseki spent time as a postdoctoral researcher at the Max Planck Institute of Immunology and was Associate Professor in the Chiba University School of Medicine before being appointed Professor in the Graduate School of Medicine in 1998. He has been working at RIKEN since 2004. His research focuses on developmental genetics, in particular understanding epigenetic regulation in morphogenesis and cell differentiation in mammals. He is also involved in joint research on human diseases bringing together researchers from different fields, and is running investigator-initiated clinical trials in partnership with Chiba University and other centers toward the development of new cancer immunotherapies using NKT cells derived from iPS cells.

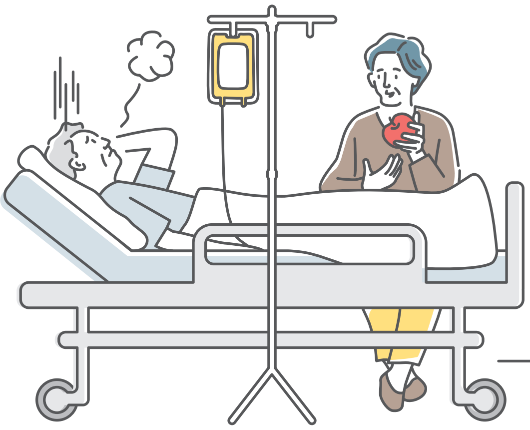
Actualization of a cancer-free society

Bringing the cancer rate down to zero

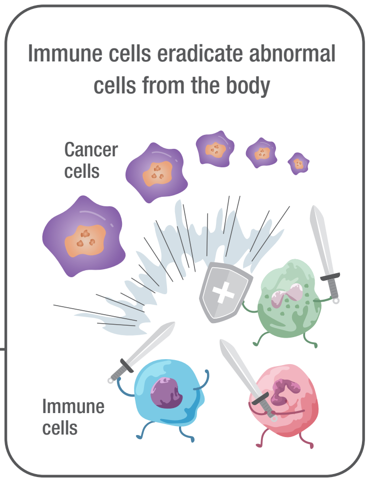
Today's reality

Cancer treatment starts after its diagnosis

- The mechanism that determines whether abnormal cells that have developed within the body will become a cancer or be elminated from the body by the immune system is still poorly understood
- Cancer is the top cause of death among Japanese people, and its rate is increasing every year



Inside the body...

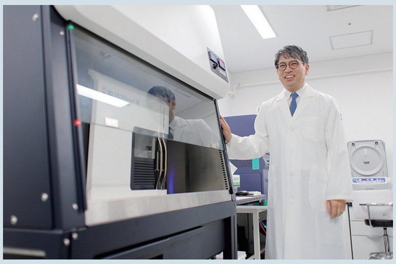


DREAMING POWER

Ability to accurately predict the behavior of abnormal cells within the body

Our dream

Understand the risk of cancer before it develops, and be able to treat it with lifestyle improvements and simple treatment



Equipment for visualizing interactions between immune cells and other immune cells or target cells

Discover cancer and its origins at a very early stage

The abnormal cells that are the origin of cancer are generated in the body by chronic inflammation, and we are working to identify the mechanism that determines whether or not they turn into clinical cancer, thereby this can be predicted accurately. The establishment of technologies to monitor abnormal cells in the body through the highly sensitive detection of immune responses and genetic alterations in these abnormal cells can accurately predict the risk to become clinical cancer. This means that cancer and precancerous abnormal cells will be detected at a very early stage. Considering the diversity of the immune responses, we collect the overseas data to identify a universtal biomarker(s) that can precisely predict cancer risk and are applicable for a wide range of peple.

FOR THE FUTURE

Detect precancerous chronic inflammation and achieve a cancer-free society through very early treatment

Treatment for advanced cancer often takes a long time and imposes a heavy physical and mental stress. If the abnormal cells generated by chronic inflammation and the immune responses to these cells could be detected with high sensitivity, and then, the risk of cancer development could be accurately predicted, their very early detection and treatment before they became cancer can be achieved. If they could be cured by simple treatment (in comparison with that required for advanced cancer), it reliefs the burden on the patient. Developing mathematical models for accurately recapitulating the changes in the body and conducting large-scale cohort studies will further increase this accuracy of the biomarker(s) identified in our study. Our goal is to achieve a cancer-free society by developing a universal model to predict the risk that abnormal cells will become cancer in the body.

TODAY

2030
TARGET

- Construct mathematical models predicting the transformation from chronic inflammation to cancer
- Develop highly sensitive devices to detect the causes of inflammation and precancerous cells at a very early stage
- Develop very early-stage cancer treatments, including cancer immunotherapy, targeting precancerous cells

2040
BREAKTHROUGH

- Predict the cancer risk from the development of abnormal cells generated by chronic inflammation, and provide appropriate preventive treatment
- Build a system to detect the minute changes in cells caused by chronic inflammation before they become cancer
- Provide cancer treatment at a very early stage, rather than an advanced stage

NISHIKAWA Hiroyoshi Project Manager
Professor, Graduate School of Medicine, Kyoto University

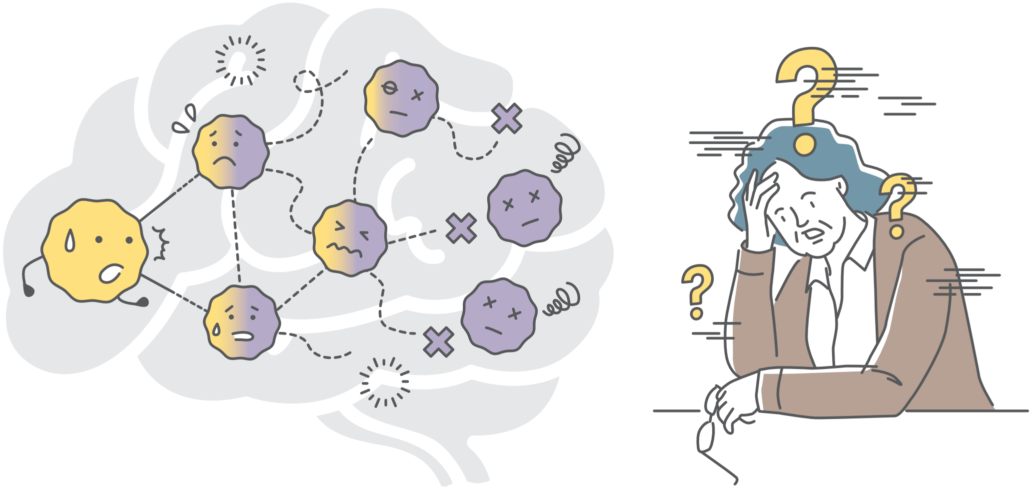
Nishikawa decided to study tumor immunology in graduate school for developing new cancer therapies considering the poor effectiveness of chemotherapy for patients with advanced cancer when he was a medical resident. He obtained his Ph.D. degree by the identificaiton of the regulatory mechanism of the immune response to cancer, and went on to study at the Memorial Sloan Kettering Cancer Center, the world’s main center of cancer immunology research. He took up appointments at the National Cancer Center Research Institute in 2015, simultaneously at Nagoya University in 2016, and from 2024, he also holds an appointment at Kyoto University, where he is engaged in research for studying the mechanisms that regulate “immune tolerance” and “immunosurveillance” against self and non-self, respectively, via deeply considering the diversity of cancer, paticularly in humans. He is a world leader in studying the mechanism by which the genetic alterations in cancer cells directly modulate the immune system to form an immunosuppressed tumor environment, thereby establishing innovative concepts and strategies for cancer treatment.

Study of reservoir functions that support resilience of the brain and its enhancement to overcome dementia

Maintaining brain health and eliminating dementia

Today’s reality

- Cognitive function declines with age
- Methods to slow the progression of dementia are beginning to be developed

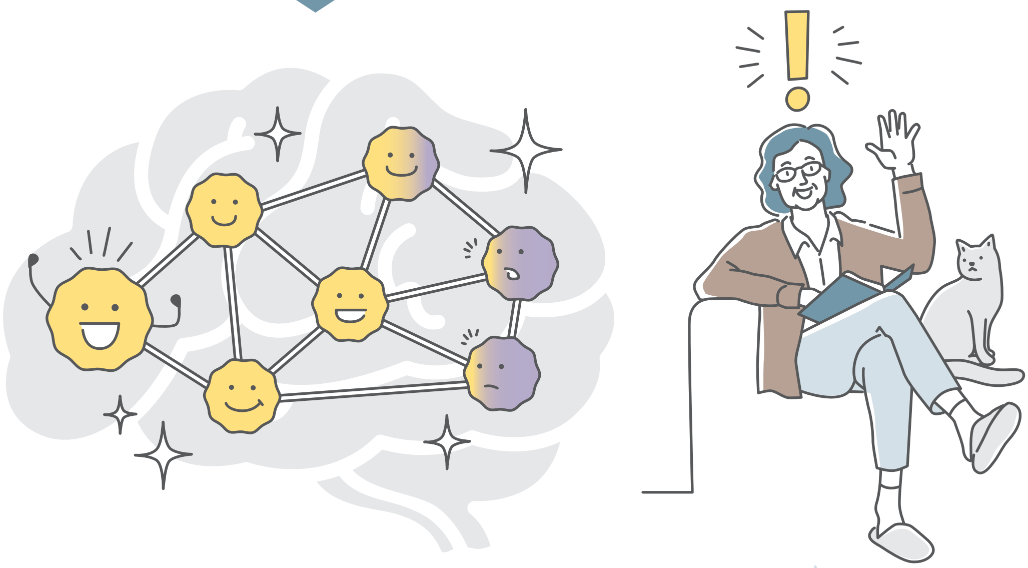


DREAMING POWER

Enhance neuronal reservoir function

Our dream

- Achieve prevention and treatment of dementia using the brain reservoir function
- Healthy brains can be maintained until 100 years old



Fundamental Medicine Memorial Hall in Kyoto University School of Medicine

Research life in Kyoto

The Fundamental Medicine Memorial Hall in Kyoto University School of Medicine was completed in 1902 as an auditorium for the Department of Anatomy at Kyoto Imperial University. It was unused for many years but was renovated in 2014 and is now used for basic medicine lectures. The maple tree in front of it bears bright red leaves every year at the end of autumn. It is my favorite “fall foliage” tree in Kyoto. I look at this view from my laboratory window every day and feel a little happiness.

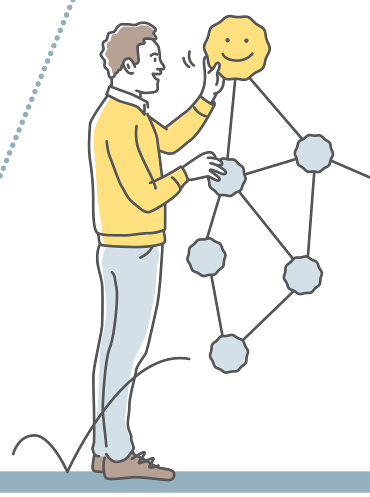
FOR THE FUTURE

Our goal is to create a society that can maintain healthy brains by increasing the brain's reserve capacity to overcome difficulties.

This study explores the possibility of enhancing the vitality of damaged nerve cells, strengthening reservoir functions through stimulation to the brain's neural networks or behavioral therapy, and maintaining a brain with high resilience (the ability to overcome and recover from difficulties). By elucidating the mechanism of reservoir function and how to strengthen it, and by applying a combination of various coping methods, we aim to build a society in which people can prevent and treat dementia and live to 100 in good health.

- Develop a method to strengthen reservoir function
- Prevent and treat dementia by enhancing and utilizing the brain's reservoir function for each stage of dementia symptoms

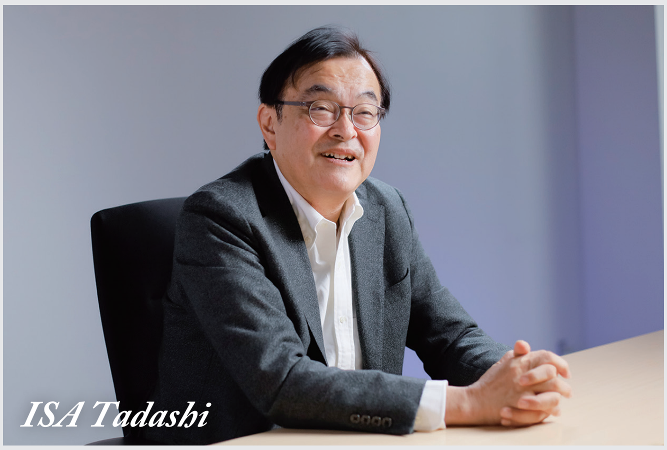
- Establish a model for symptom improvement in animals with dementia
- Identify reservoir function to help treat dementia



TODAY

2030
TARGET

2040
BREAKTHROUGH



ISA Tadashi Project Manager
Professor, Graduate School of Medicine, Kyoto University

In 1985 he graduated from the University of Tokyo School of Medicine. He further graduated from the Department of Research, Graduate School of Medicine, the University of Tokyo in 1989, becoming a Doctor of Medicine. After serving as a visiting scientist at Göteborgs Universitet, Sweden, from 1988-90, he joined the Brain Research Institute at the University of Tokyo School of Medicine as an assistant professor. He became a lecturer at Gunma University School of Medicine in 1993, and a professor at the National Institute for Physiological Sciences, Okazaki, in 1996 (at the National Institute for Physiological Sciences, he also became a professor at the National Institutes of Natural Sciences through a reorganization). He joined Kyoto University Graduate School of Medicine as a professor of neuroscience in 2015, then took the position of Vice Director of the Institute for the Advanced Study of Human Biology (WPI-ASHBi) there in 2018, and becoming the same university's Dean of the Graduate School of Medicine and Faculty of Medicine, which is his current position.

Life course approaches through sleep to protect, nurture, and activate the brain

Aspiring to overcome dementia by improving sleep quality

Today's reality

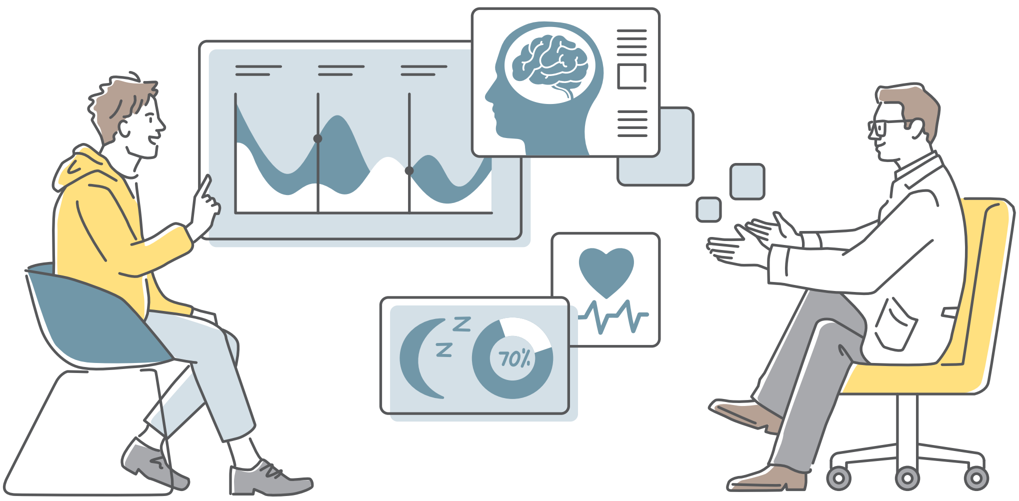
- Many dementia patients have sleep disorders
- Caring for patients with sleep disorders is a great burden on their families

DREAMING POWER

Elucidate the relationship between sleep and the brain

Our dream

- Use the mechanisms of sleep to prevent and treat dementia
- Lighten the load on patients and their families



Sleep is the best medicine

Many eminent people assert the importance of sleep in achieving peak performance. For example, the manga artist MIZUKI Shigeru lived and worked to the age of 93 and credited sufficient sleep as the key to sustaining his vitality throughout his life. Our dream is to scientifically elucidate the power of sleep and create a future where everyone can sleep well and lead healthy, happy lives.

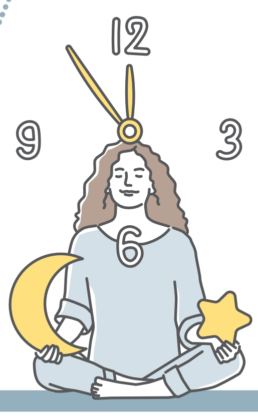
FOR THE FUTURE

Elucidate the influence of sleep on the brain and use it to prevent and treat dementia.

We now know that some dementia patients develop sleep disorders due to defects in the neurons that control sleep. Sleep is thought to be deeply involved in the development and maintenance of brain functions. Our research particularly focuses on optimizing sleep pattern and identifying risk factors for dementia, and our goal is to make sleep research serve to prevent and treat dementia. By measuring and improving the quality of sleep, we aim to prevent and treat dementia naturally in ways that suit each person in their daily lives, and so create a society that lightens loads on patients and their carers.

- Prevent and overcome dementia by improving sleep quality
- Prevent and overcome dementia by complementing the inherent role of sleep
- Develop technology that enables anyone to easily measure the quality of their sleep, and achieve personal sleep therapy with benefits such as early discovery and treatment of dementia risks

- Elucidate the inherent role of sleep and the overall effects of sleep on the brain
- Establish technology to deliver the same benefits as sleep
- Development of a device to measure sleep quality that can be used without discomfort



TODAY

2030
TARGET

2040
BREAKTHROUGH

HAYASHI Yu Project Manager
Professor, Graduate School of Science, The University of Tokyo

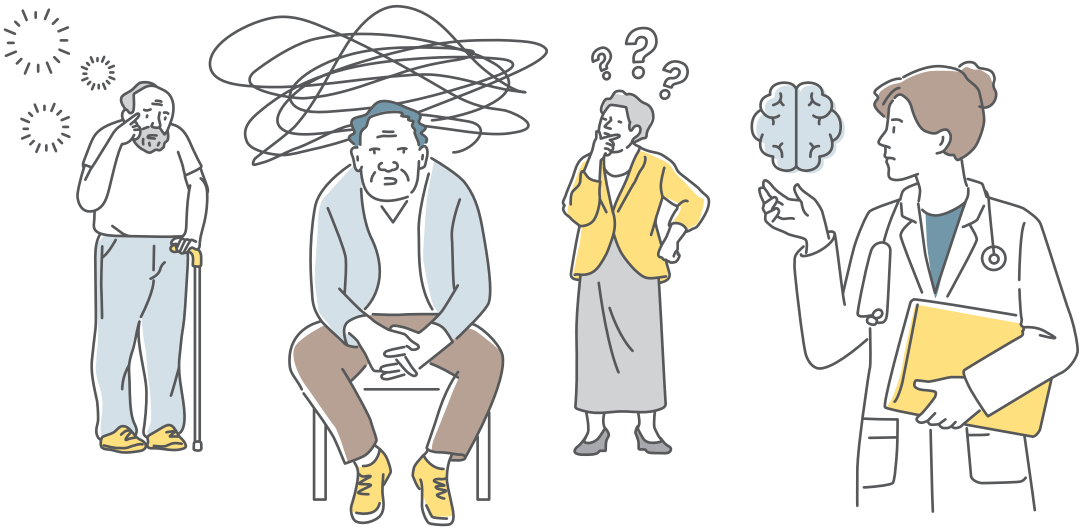
Graduated from the Department of Biology, Faculty of Science, the University of Tokyo in 2003. From 2008, he served as a Special Postdoctoral Researcher at the RIKEN Brain Science Institute. In 2013, he became a Principal Investigator and Assistant Professor at the International Institute for Integrative Sleep Medicine (WPI-IIIS) at the University of Tsukuba, later becoming an Associate Professor. Since 2020, he has been a Professor at the Graduate School of Medicine, Kyoto University, and concurrently a Visiting Professor at the International Institute for Integrative Sleep Medicine (WPI-IIIS) at the University of Tsukuba. Since 2022, he has held his current position. He is engaged in elucidating the role of sleep and the bidirectional relationship between sleep, aging, and diseases through a multifaceted approach using various organisms.

Early detection and modulation of the dementia pathogenesis based on the concept evolving from glial pathology to senoinflammation

Making Dementia Prevention and Treatment More Accessible

Today's reality

- Dementia progresses as the brain ages
- No method has been established for the early detection and treatment of dementia



DREAMING POWER

Targeting substances that play a key role in brain aging

Our dream

- Early detection of dementia is possible through simple tests
- The symptoms of dementia can be suppressed

This is my personal "moonshot", showing a total lunar eclipse and eclipse of Uranus, taken in 2022. My childhood fascination with astronomy gradually transformed into an interest in observing people.

Senoinflammation

Cells in the body stop dividing, due to age or stress, and transform into "senescent cells." Aged cells actively release inflammatory substances and other factors. As a result, surrounding cells are exposed to stress and age, leading to a cycle of aging (senescence) and inflammation (inflammation) termed "senoinflammation," which fundamentally contributes to the onset of dementia.

FOR THE FUTURE

Identifying substances that are key to brain aging to enable early detection and treatment of dementia

Dementia is conceived to be caused by three detrimental processes occurring in the brain: the accumulation of protein waste, the aging of brain cells leading to inflammation, and the transformation of glial cells from homeostatic to deleterious modes. This study aims to identify key substances that trigger the cycle of aging and inflammation (senoinflammation). By focusing on key substances, we aim to make it possible to downsize blood tests and imaging tests and develop new drugs, in order to build a healthy and long-lived society that overcomes dementia.

TODAY

2030 TARGET

- Identifying the most effective key substance among the multiple candidates for overcoming dementia
- Establish a system to evaluate dementia symptoms based on the results of blood tests and imaging studies
- Advance human trials of dementia treatments and "next-generation supplements" that have proven safety and efficacy

2040 BREAKTHROUGH

- Practically apply next-generation supplements developed on the basis of scientific evidence
- Realize medical care that integrates diagnosis and treatment through interactive imaging and manipulation of key substances
- Develop a method to quickly and easily detect key substances from small amounts of blood, etc.

HIGUCHI Makoto Project Manager
Director, Advanced Neuroimaging Center,
National Institutes for Quantum Science and Technology

After graduating from Tohoku University in 1993, he worked as a gerontologist, focusing on the diagnosis and treatment of dementia. He became fascinated by the microscopic images of protein aggregates that accumulate in the brains of dementia cases and went to the US for advanced molecular pathology studies, where he worked on generating animal models of these protein lesions. After returning to Japan in 2003, he worked at RIKEN and then at the National Institute of Radiological Sciences (currently National Institutes for Quantum Science and Technology), where he developed imaging technologies to visualize the protein depositions using model animals as evaluation systems. Since the 2010s, he has progressively applied these techniques to humans. Meanwhile, realizing that protein aggregates alone are not essential culprits of dementia, he launched the "Brain Senoinflammation" project.

MOONSHOT
RESEARCH & DEVELOPMENT PROGRAM

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