Integrated Understanding of Multi-Sensing Networks and Elucidation of Their Control Mechanisms Leading to the Innovation of Medical Technologies

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Research and Development Objective

Integrated understanding of human multi-sensing networks and elucidation of their control mechanisms

Targets

This Objective aims to develop an integrated understanding of multi-sensory systems, including sensory systems and peripheral nerve networks, and to develop methods to visualize and control these systems. Specifically, this Objective aims to achieve the following:

(1) Understand peripheral neural circuit mechanisms and clarify disease pathology to help overcome disease
(2) Develop methods to visualize and control peripheral nerve activity and new treatment methods
(3) Clarify and apply the mechanisms involved when sensory systems receive, process, and act on signals
(4) Develop technology platforms for methods to visualize and control sensory systems

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Program Supervisor (PS)

Ryozo Nagai, M.D., Ph.D.
President, Jichi Medical University

Profile

Dr. Ryozo Nagai graduated from the School of Medicine, Faculty of Medicine at the University of Tokyo in 1974, and after working at the University of Tokyo Hospital and the Heart Institute of Japan at Tokyo Womens' Medical University he received his Ph.D. in Medical Science from the University of Tokyo in 1982. From 1983 he was Visiting Assistant Professor at the University of Vermont. He was a lecturer in the Department of Clinical Laboratory at the University of Tokyo Hospital from 1988, an associate professor in the 3rd Department of Internal Medicine at the University of Tokyo from 1993, professor in the 2nd Department of Internal Medicine at the University of Gunma from 1995, and a professor in the Department of Cardiovascular Medicine, Graduate School of Medicine at the University of Tokyo from 1999. Dr. Nagai became Director of the University of Tokyo Hospital in 2003, Head of the Translational Research (TR) Initiative at The University of Tokyo in 2009, and has held his present post since April 2012. He has also served as a member of both the MHLW Social Security Council and the Expert Study Panel on Promotion of Healthcare Policy of the Cabinet Secretariat, and in various other capacities.

Recent Research Direction

Dr. Nagai has been working to clarify the homeostatic and pathophysiological significance in the body of the transcription factor KLF5 and progress the development of KLF5 inhibitors. At the same time, he has been integrating different electronic medical records, developing a structure for internal medicine case reports and creating a glossary of terms, and developing diagnostic support systems.

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Program Officer (PO)

Kohji Nishida, M.D., Ph.D.
Professor, Ophthalmology, Department of Ophthalmology,
Graduate School of Medicine, Osaka University

Profile

Dr. Kohji Nishida graduated from the Medical School, Faculty of Medicine at Osaka University in 1988, and after spells in the Department of Ophthalmology in the Faculty of Medicine at Osaka University, and Osaka University Hospital, he became an assistant professor at Kyoto Prefectural University of Medicine in 1992, and acquired his Ph.D. in Medicine from Osaka University in 1997. From 1998 he was a research associate at the Salk Institute for Biological Studies, San Diego, in the US. Dr. Nishida became an assistant professor in Ophthalmology in the Graduate School of Medicine at Osaka University in 2000, subsequently becoming a lecturer then associate professor there in 2004. He was made a professor at the Graduate School of Medicine, Tohoku University in 2006, and has held his present post since April 2010. He was recipient of the Japanese Ophthalmological Society (JOS) Young Investigator Award in 1998, the MEXT Award for Science and Technology (Research Category) in 2009, the JOS Council Award in 2015, and the Japanese Society for Regenerative Medicine (JSRM) Award in 2017. He has served in roles including reviewer for the JSPS Scientific Research Grant Committee, as a member of the Science Council of Japan, and as an AMED Project Evaluation Panel member.

Recent Research Direction

Dr. Nishida works on the clarification of the mechanisms of ocular tissue ontogeny, regeneration, and differentiation using iPS cells etc. and development of new regenerative medicine techniques; relationship between sight and brain/whole body functions; development of artificial retinas; and medical applications of AI.

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Program Officer (PO)

Shoji Takeuchi, Ph.D.
Professor, Graduate School of Information Science and Technology, the University of Tokyo

Profile

Dr. Shoji Takeuchi graduated from the Department of Industrial Mechanical Engineering, Faculty of Engineering at the University of Tokyo in 1995, completed the Doctoral Program of the Graduate School of Engineering at The University of Tokyo in 2000 and obtained his Ph.D. in Engineering the same year. From 2001 he was a lecturer at the Institute of Industrial Science at the University of Tokyo, where in 2003 he became an associate professor and later jointly held the post of visiting scholar in the Department of Chemistry and Chemical Biology at Harvard University. In 2014 he took up the post of professor at the Institute of Industrial Science. Dr. Takeuchi has held his present post since April 2019 . He has been a member of the IEEE MEMS Steering Committee since 2017, a board member of the Society for Chemistry and Micro-Nano Systems since 2018, and a Chemical and Biological Microsystems Society (CBMS) board member since 2021. Amongst other honors, he was a recipient of the MEXT Young Scientists' Award in 2008, the 6th Japan Society for the Promotion of Science (JSPS) Prize in 2010, and the American Chemical Society's Analytical Chemistry Young Innovator Award in October 2015.

Recent Research Direction

Dr. Takeuchi is engaged in research into bio-hybrid systems that combine living bodies and machines. He works on developing microcapsules for cell therapy or implantable sensors for continuous blood glucose monitoring, organ chips built from 3D tissues, cultured meat, and odor sensors using olfactory receptors.

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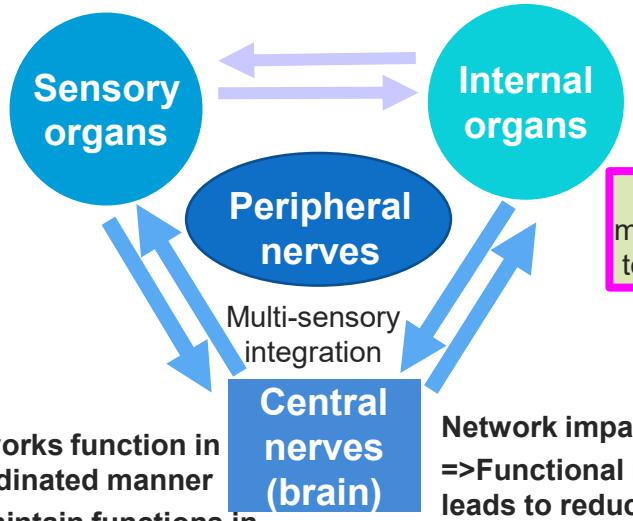
Image of the R&D Area

The target is to develop an integrated understanding of multi-sensory systems that includes sensory systems and peripheral nerve networks, and create innovative seeds for medical technologies based on an understanding of control mechanisms.

Multi-sensing networks

The sensory organs and central nerves (brain), the internal organs, and the peripheral nerves that are widely distributed throughout these areas are anatomically and functionally related.

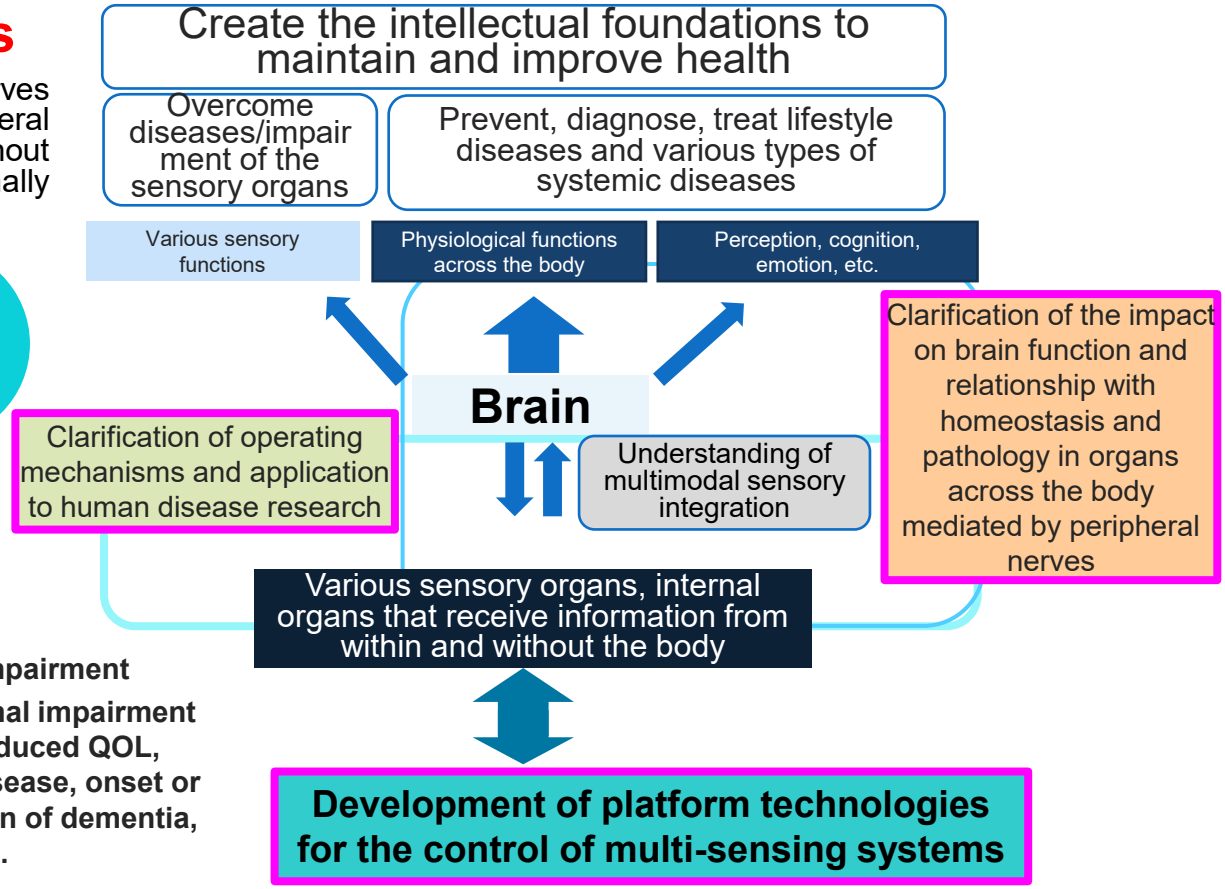


Networks function in coordinated manner

=>Maintain functions in the body

Network impairment

=>Functional impairment leads to reduced QOL, chronic disease, onset or progression of dementia, cancer, etc.



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Direction and Collaboration by JST and AMED

Acquire new functions
Expand sensing functions

- Develop biomeasurement devices, sensory sensors
- Develop platform technologies for sensory sharing, sensory substitution
- Clarify multimodal networks
- Develop a completely new understanding of life
- Collaboration between medicine and engineering

Recover, maintain lost functions
Restore, preserve sensing functions and prevent impairment/loss

- Clarify disease mechanisms as they relate to sensory organs and peripheral nerves such as autonomic nerves and develop therapeutic methods
- Understand multi-sensing networks and their systemic nature
- Conduct R&D to overcome/prevent disease (metabolism, immune system, circulatory organs, etc.) and contribute to greater wellbeing
- Biological applications of technologies to measure and control biosignals
- Develop bioelectronic therapeutic agents and minimally invasive devices
- Develop devices aimed at application

Not limited to model organisms for humans

Mainly humans and animal models for humans

Clarify basic principles
Develop platform and applied technologies

From basic research to medical applications with a view on healthcare and medical applications

JST — **AMED**

Multidisciplinary approach

Including medical science, biology, mathematical analysis, information science, robotics, electronics, materials science, and psychology

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Outline of the Research and Development Area

An integrated understanding of multi-sensory physiological mechanisms comprising the sensory systems and peripheral nerve networks could lead to the development of new treatment methods resulting in improved Quality of Life (QOL) and longer healthy life expectancies. Furthermore, the origination of innovative medical technologies to control multi-sensory systems and their real-world application is expected to contribute significantly to achieving a healthy and long-lived society.

The R&D area will promote and foster **the coming together and participation of researchers in a wide range of fields**, including medical science and biology, engineering, materials science, and informatics, and coordinated collaboration with research institutions and companies in Japan and overseas to investigate the items listed below. There will be a particular emphasis on pursuing **research that will lead to the creation of seeds for innovative healthcare** (note that this aspect will be run by AMED).

- **Clarification of the operating mechanisms of multi-sensing systems and application to human disease research**
- **Clarification of the relationship between multi-sensing systems and brain function, and maintenance mechanisms of homeostasis and pathology for all organs of the body**
- **Development of platform technologies for the control of multi-sensing systems; artificial sensory organs, development of new therapeutic methods mediated by sensory organs and nerves, and innovative R&D relating to the measurement, control, and utilization of biosignals using new devices that fully apply engineering technologies**

Under the shared Research and Development Objective “Integrated understanding of human multi-sensing networks and elucidation of their control mechanisms” established by the Japan Agency for Medical Research and Development (AMED) and the Japan Science and Technology Agency (JST), this R&D area will initiate four programs simultaneously (the AMED-CREST and PRIME programs run by AMED, and the CREST and PRESTO programs run by the JST) and researchers in these programs will work in collaboration to conduct the research.

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Selection Policy

(1) Innovative research proposals aimed at clarifying and applying to disease research the operating mechanisms of multi-sensing systems—including sensory systems and peripheral nerve networks—and clarifying how these mechanisms are involved in maintaining the function of the brain and all organs of the body and disease pathology.

(2) Innovative research proposals aimed at deepening our understanding of the anatomical structures and physiological functions of sensory receptors and peripheral nerve systems; developing technologies to visualize and quantify the state of activity; originating engineering technology platforms to clarify control mechanisms; and developing therapeutic and preventive methods.

【AMED-CREST】

Original research proposals capable of causing a paradigm shift in the life sciences, medical science, and disease research fields and research aimed at medical applications in line with AMED's mission (**looking to originate evidence demonstrating a pathway to applied research in healthcare fields**). We expect **the formation of units that bring together various different fields of research**, such as neurology, physiology, molecular and cell biology, regenerative medicine, clinical medicine, tissue engineering, materials science, information science, and micro-mechatronics. For research proposals aimed at developing new technologies to visualize and quantify sensory system activity and develop new control technologies, we welcome proposals that pursue the development of bioelectronic medicines and devices, organ chips, or micro-electro mechanism systems (MEMS).

【PRIME】

Challenging proposals that are particularly original and at the early, formative stages that may lead to new breakthroughs. The research does not have to originate evidence demonstrating a pathway to applied research in healthcare fields. We look for research that takes a proactive approach to the creation of networks by interacting with other research groups in the same or different fields, researchers in AMED-CREST research units, and researchers participating in CREST and PRESTO programs run by the JST.

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Examples of R&D Proposals

【Clarification of operating mechanisms and applications to human disease research】

- Clarification of the operating mechanisms in the sensory organs (including the five senses, perception, and sense of position and vibration) and peripheral nerve networks and clarification of the processes by which abnormalities in these operating mechanisms lead to disease
- R&D that will contribute to the creation of various modalities of medical technology to compensate for sensory organ dysfunction

【Clarification of the impact on brain function and relationship with homeostasis and pathology in organs across the body mediated by peripheral nerves】

- Clarification of metabolic, immune, and endocrine mechanisms etc. involved in homeostasis, the mechanisms that maintain brain function, and the mechanisms behind disease onset that involve the multi-sensory network
- Clarification of the mechanisms of sensory organ impairment and neurologic dysfunction accompanying chronic disease, lifestyle disease, stress, and aging, and research that will contribute to methods to prevent these dysfunctions and help to maintain/promote good health.

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Examples of R&D Proposals

【Development of control technology platforms】

- Development of innovative device technologies to measure and control sensory organ and nerve activity in humans or animal models
- Devices targeting the nervous system, medical device development, and technology development for rehabilitative and surgical operative methods
- Development of devices and equipment for the measurement, control, and use of biological signals (does not have to be signals that directly involve the nerves)
- Development of organ chips that recreate sensory organs or nerve systems in vitro
- Development of innovative technologies for measurement, control, and practical application that utilize the operating mechanisms of multi-sensory systems

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Points to Note When Submitting a Proposal (1)

- **Please state the objective in concise and concrete terms. Clearly describe challenges and solutions, as well as the ingenuity and feasibility of the research.**
- **Insert photographs and diagrams as appropriate and ensure that the proposal document is not just text.**
- We encourage **collaborations between different fields** that are logical and challenging.
- Please clearly indicate how the various research projects run by the PI and the Co-Investigators could generate synergistic effects and whether this will contribute to the goals and objectives for the overall research proposal.

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Points to Note When Submitting a Proposal (2)

- For AMED-CREST, the research content does not have to include actual plans for the development of innovative medical technologies, but we are looking for research to generate evidence demonstrating the pathway to applied research in healthcare fields (for example, clarification of human disease states). However, under the PRIME program, researchers are not necessarily expected to produce evidence demonstrating links to the development of healthcare applications.
- This program does not include development phases beyond non-clinical studies, and we recommend out-licensing to other programs according to the status of R&D progress.
- We encourage the participation of medical science researchers engaged in clinical practice in the relevant fields, because the goal is the creation of innovative medical technologies.
- PIs do not necessarily have to be active in the medical field but can also be from engineering and other fields.

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R&D costs and R&D period

In order to select a wide variety of R&D projects related to the integrated understanding of multi-sensing networks and elucidation of their control mechanisms leading to the innovation of medical technologies, AMED is soliciting research proposals according to the following conditions.

Type of proposal	R&D funds	R&D period	No. of projects to be selected
AMED-CREST (unit-type)	300 million yen or less (entire direct costs)	Up to 5.5 years	Around 2-4 projects
PRIME (solo-type)	40 million yen or less (entire direct costs)	Up to 3.5 years	Around 8–12 projects

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Message from the Program Supervisor Ryozo Nagai

- The R&D Objective “Integrated understanding of human multi-sensing networks and elucidation of their control mechanisms” does not only involve sight, hearing, smell, taste, and touch, but is a project that should also encompass signal inputs into the body’s systems or integration by autonomic nerves or humoral factors. In other words, we are looking for broad-ranging, novel proposals that are not limited to the five senses.
- As concepts change in the medical and life sciences, we are interested in research that takes a reductionist approach to understanding systems. In particular, please demonstrate a new spin on medical and life sciences research through the combination of mathematics and information science with engineering.
- Under AMED-CREST and PRIME, we expect research proposals that combine the fields of human medical and life sciences with engineering. For projects only in the medical and life sciences, we look for projects aimed at subsequent therapeutic methods (including device development), while for device development, we look for projects in these R&D areas that have the potential to connect to future developments in health and healthcare.

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Message from the Program Officer Kohji Nishida

- Information inputs from inside and outside the body through the sensory systems (comprising the sensory organs and other organs) are thought to play an important role in maintaining physiological functions across the body and in the brain via the peripheral nerve network. We hope to receive original proposals for research to demonstrate previously unexpected roles played by sensory systems and the relationship with disease in humans.
- In the research proposals on operating mechanisms for individual sensory organs or peripheral nerve networks, we are soliciting research proposals that are at the cutting edge of global research; we also hope that application of these research results will clarify human disease pathology.
- We welcome proposals on new approaches, mediated via multi-sensing systems, to systemic diseases or diseases of the sensory organs or brain that have proved difficult to cure thus far.
- The focus is on basic research, but AMED-CREST projects include an emphasis on research targeted at strategic outcomes, so we are interested in plans that constantly refer to the clinical significance or utility of the research.
- We particularly welcome proposals where young researchers are the R&D applicants.

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Message from Program Officer Shoji Takeuchi

- For AMED-CREST proposals, we are looking for research capable of creating world-first technology seeds through projects that combine work in different fields and based on innovative technologies or devices from the applicant's group.
- We expect the proposal documents to describe, including through the use of diagrams, what types of technology seeds will be created, why these technology seeds are novel, why the research is important, and why the applicant's research group can pursue this project, in a way that researchers from other fields can easily understand.
- For PRIME proposals, we will accept themes specialized in one field, but will prioritize themes that can be developed into research combining different fields if the proposal is selected.
- We hope to receive original research proposals that may generate unexpected results.

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We also hope to receive research proposals capable of causing a paradigm shift in life and medical sciences and in disease research.
We are looking forward to your application.

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