

National Center for Geriatrics and Gerontology



Overview
2020



The mission of our center is “We will contribute to establish health and longevity society by promoting mental and physical independence.



**National Center for
Geriatrics and Gerontology**

Greetings from the President



Thank you for visiting the National Center for Geriatrics and Gerontology website. My name is Hidenori Arai, and I have been the Board President of this center since April 1, 2019. The National Center for Geriatrics and Gerontology (NCGG) was established in 2004 as one of six national centers and became an independent administrative agency in 2010. Since this conversion, the NCGG has been arranged into several smaller sub-centers including the following: Center for Comprehensive Care and Research on Memory Disorders, Center for Development of Advanced Medicine for Dental Diseases, Center for Gerontology and Social Science, Center for Information on Geriatric Medicine, Innovation Center for Clinical Research (ICCR), Center for Training in Geriatric Medicine, Center of Assistive Robotics and Rehabilitation for Longevity and Good Health, Center for Development of Advanced Medicine for Dementia, and the Medical Genome Center, and has continued to develop activities in line with their mission. In 2015, the NCGG became the National Research and Development Agency and began to operate with further emphasis on R & D.

During this time, under the excellent leadership of President Emeritus Shinichi Oshima and former president Kenji Toba, the center has been developing human resources to take on the medical, nursing, and welfare needs of a super-aged society while providing medical care, which has become the standard for older adults and which includes advanced care for geriatric syndromes in Japan, such as dementia and frailty. Further, the NCGG has endeavored to develop the necessary public education activities while acting as a think tank for policies in several countries regarding the medical, nursing, and welfare needs of older adults. As a research center, the NCGG has striven to undertake various foundational studies on aging, clinical research, and epidemiological studies which aim for the realization of a society of longevity and good health. As the third board president, I intend to steadfastly continue with the roles the center has fulfilled thus far, and further, to strive for the center staff to work together, allowing us to become an international center on geriatrics and gerontology, open to the world. I would like to request guidance from all of you in this pursuit.

utilize the registry.

In response to the national project of "ORANGE Registry", we have reformed the organization of NCGG. We have the largest memory clinic in Japan, working on the Comprehensive Care and Research on Memory Disorders. We also have the Medical Genome Center, in which the data of clinical information, imaging, blood and genomic information were accumulated. Comprehensive Care and Research on Memory Disorders collaborates tightly with basic dementia science (Center for Development of Advanced Medicine for Dementia) to find new seeds for dementia treatment.

Our mission is to "promote the physical and mental health of older adults in order to build a society of healthy longevity." Behind this mission is the fact that globally, Japan ranks first in longevity, with over 28% of the current population consisting of those aged 65 or above. In a super-aged society in which the only increase in numbers is that of older adults aged 75 or above, there needs to be a paradigm shift from the conventional "cure-seeking medical care" to "cure- and support-seeking medical care." Within this treatment paradigm, the most important task is to handle dementia, which has become the main reason for requiring long-term care. Several organizations within the NCGG, including the centers for Development of Advanced Medicine for Dementia, Comprehensive Care and Research on Memory Disorders, Assistive Robotics and Rehabilitation for Longevity and Good Health, and the Medical Genome Center, have been mobilized for the prevention, diagnosis, treatment, and care of dementia and have experienced some success in their results. Further, to contribute to community development, we have started collaborating with Aichi Prefecture on the Orange Town Plan.

Together, we have a vision for rebuilding the old ward, after 50 years, into the Orange Hospital, a core facility for “building a dementia-friendly community,” to integrate research and medical care, which will be the symbol of Orange Town. We will strive to practice appropriate care, dementia rehabilitation, and family classes promoted by the NCGG and return the results to the community and the public.

Frailty refers to a state in which, although able to lead an independent life, one is vulnerable to various stresses, due to changes in organ functions which accompany aging. This condition is a major obstacle to realizing a society of healthy longevity. With the Locomo-Frailty Center at the core, we hope to elucidate pathologies and establish treatment strategies for related conditions, such as sarcopenia and locomotive syndrome. Further, the active use of robots is imperative, and I plan to emphasize the role of the Center of Assistive Robotics and Rehabilitation for Longevity and Good Health. Through these research activities, I hope to participate in the development of new industries and contribute even a small amount to the longevity of our nation. Beyond these research and development pursuits, the NCGG will continue to improve our meticulous consultation and medical services for older adults more than ever. In these pursuits, I humbly request your continued advice and encouragement.

Hidehiko Arai, MD. PhD.

President, the National Center for Geriatrics and Gerontology



Outline of activities



The purpose of geriatrics and gerontology is to help patients maintain healthy and active lives as long as possible by providing medical treatments that prevent the deterioration of physical and mental independence in the elderly, using experience, knowledge, and technology backed up by science. To achieve that, we first provide the basic medical treatments that improve all patients' lives regardless of age to a standard level or higher evaluating and treating organ specific or systemic conditions. At the same time, we diagnose the cause and determine the severity of symptoms peculiar to the elderly, and provide appropriate preventative, beneficial, or palliative care based on our evaluations. By doing so, we

are helping to preserve the health and longevity of patients.

Yukihiro Washimi M.D. Ph.D.
NCGG Hospital Director

Departments (24 total)

Geriatrics, Endocrinology & Metabolism, Hematology, Psychiatry, Neurology, Respiratory Medicine, Gastroenterology, Cardiology, Surgery, Gastroenterological Surgery, Orthopedics, Neurosurgery, Thoracic Surgery, Dermatology, Vascular Surgery, Urology, Gynecology, Ophthalmology, Otorhinolaryngology, Rehabilitation Medicine, Radiology, Dentistry & Dental/Oral Surgery, Pathology, Anesthesiology (total 24 departments).

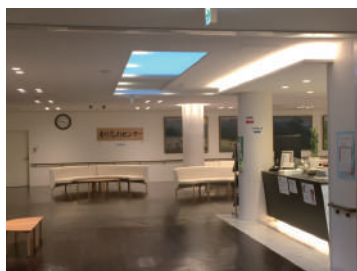
Specific Outpatient Services

Memory Clinic, Osteoporosis Clinic, Hearing Aid Clinic, Total Denture Clinic, Oral Care Clinic, Mammary Gland & Proctology Clinic, Anal Disorder Clinic, Sleep Apnea Clinic, Normal Pressure Hydrocephalus Clinic, Mental Vitality Clinic, Palliative Care Clinic, Arteriosclerosis Clinic, Frailty & Locomotive Syndrome Clinic, Foot Edema Clinic, Rheumatoid Arthritis Clinic.

Number of Beds

Medical Law Approval, General Beds: 383

Number of Inpatient Beds: 321 (8 nursing units)



Topics

A newly constructed outpatient building will be completed in February 2018.

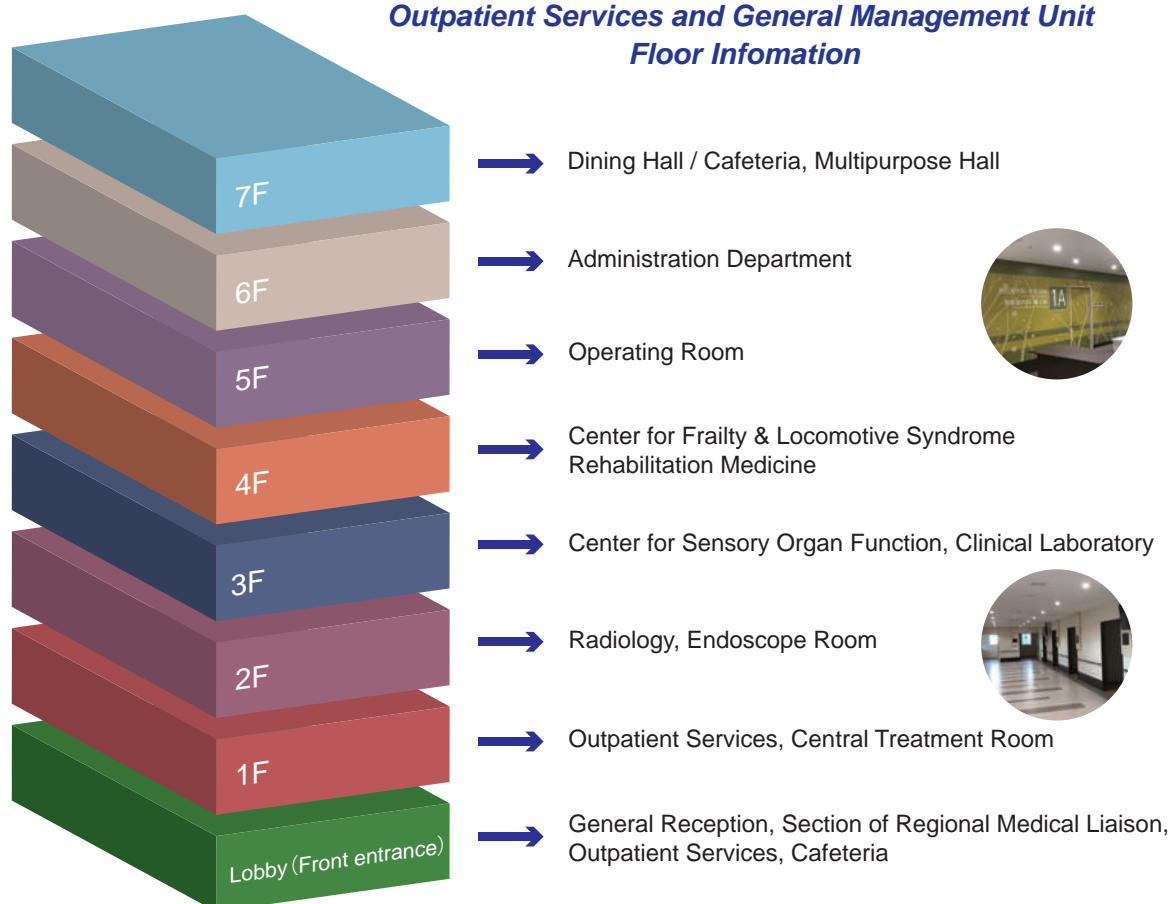
The new building will maintain and develop all current medical department functions, and will include two new cross - departmental centers: the Center for Frailty & Locomotive Syndrome and the Center for Sensory Organs. It is clear that dementia and frailty are the most important pathological conditions affecting the super-aged members of our society. By enhancing our outpatient functions, we can better focus our efforts on these conditions and make maximum efforts to raise independence and living functions of the elderly. In addition to each outpatient clinic and central treatment room, we also have or are developing areas for operating, rehabilitation medicine, a clinical laboratory, radiology, endoscopy and other specialized function provide comprehensive medical treatment.

We start a full-scale construction of the new ward for next 20 years, which is going to be completed in 2021.

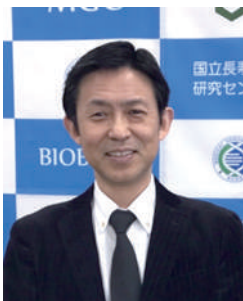
Furthermore, please expect it in the developing hospital.



Outpatient Services and General Management Unit Floor Information



1. Summary



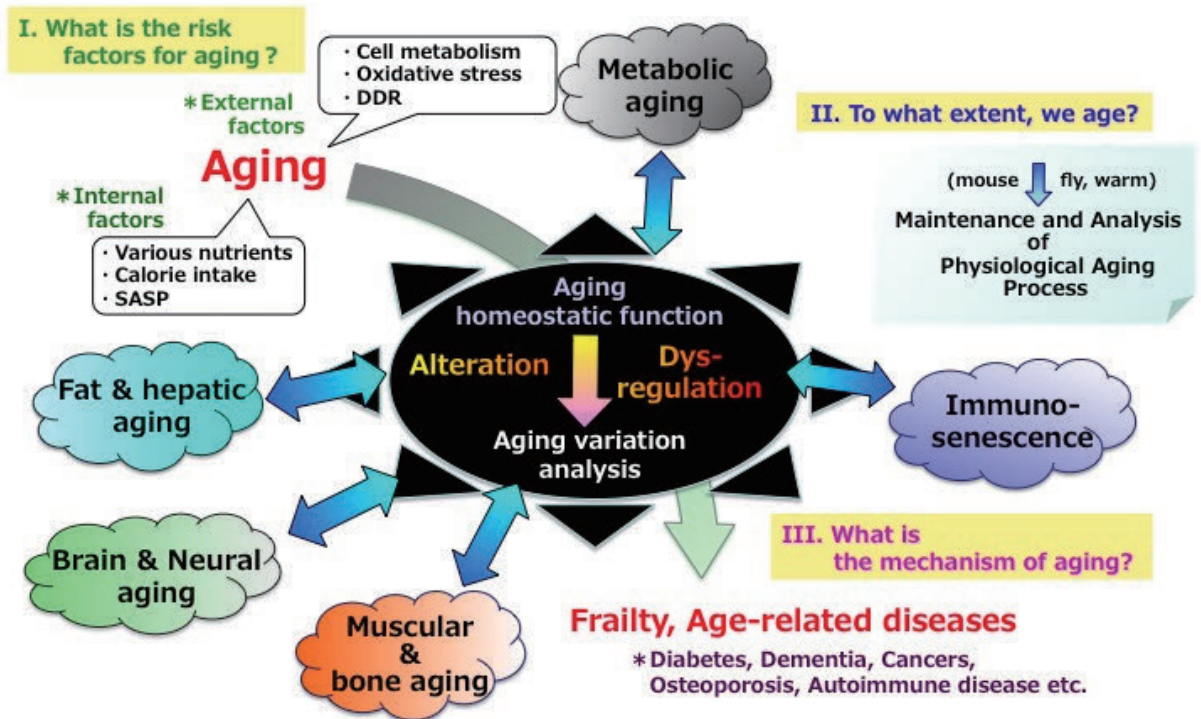
Our institute was originally established in 1995 as a National Institute for Longevity Science (NILS) in the Chubu National Hospital. In 2004, our institute developed into the Research Institute of National Center for Geriatrics and Gerontology (NCGG, one of the six national centers for advanced and specialized medicine in Japan). In association with the reorganization of NCGG as an Independent Administrative Agency in 2010, our institute further developed and expanded. Now NCGG together with other national centers has shifted to the National Research and Development Agency since 2015. Currently, our institute

will be expected to substantially contribute to production of practical applications in the research field of geriatrics and gerontology. Given that we are confronted with unprecedented super-ageing society, now is the time to take action to innovate our ideas and technology to cope with various medical affairs in such a society. Our mission, that has been rather unchanged from the original establishment, is to promote physical and mental health of the elderly through various research activities.

Shumpei Niida
Director-General, Research Institute

Especially here in research institute, as our current research focus area, we have established our "Biomedical Molecular Aging" study that orchestrates the following triangle elements, basic research on molecular level, validation with animal model system and application to clinical research for the elderly. We realize that 'Aging' is the result of alteration or dysregulation of homeostatic function strongly linked to aging variation and at first, try to find what is the risk factors for aging not only internally (various trophic control, calorie intake, inflammatory cytokines as well as senescence associated secretory phenotype; SASP) but also externally (cell metabolism and stress control such as oxidative stress or DNA damage response; DDR). On the other hand, we evaluate to what extent we age referred to by the level of reduced physiological function as well as homeostatic persistence. To do this end, we are interested in finding novel seeds and strategies such as immune- or metabolic- modulators, removal of oxidative stress or specific protein interaction, senolysis or cell competition for clinical application against age-related diseases in addition to biomarkers for frailty, infection and physiological aging. Especially, we focus on brain or neural aging and immune-senescence as well as muscular or bone aging and fat or hepatic aging on the basis of general metabolic aging. One of our practical goals is to reveal how can cellular senescence contribute to a physiological aging in various tissues or organs or even our body itself. In other words, what mechanism or molecules would be involved in not only infection control but also inflammation control broadly linked the frailty to control of age-related decline of physiological function. Consequently, we aim for a life and society with healthy longevity to address the study of molecular mechanism of aging and frailty to control of age-related diseases like dementia or sarcopenia.

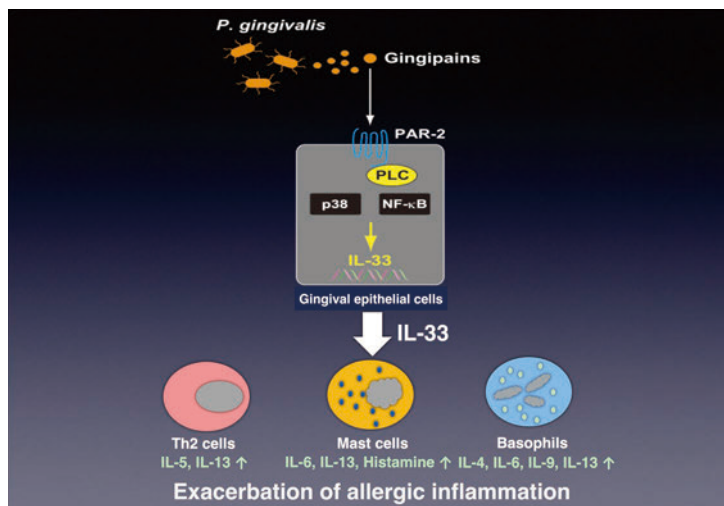
Stronghold of Molecular Aging Research



2. Research topics

1) Possible role of periodontal disease-associated bacteria *Porphyromonas gingivalis* in allergic inflammation.

Epithelial cells work not only as a physical barrier to pathogens, but also play a pivotal role in initiating innate immune responses to microbes. Interleukin (IL)-33, a member of the IL-1 family, is constitutively expressed in epithelial cells and is influentially associated to the pathophysiology of allergic diseases and inflammation. We demonstrated the involvement of a periodontal pathogen, *Porphyromonas gingivalis*, in the enhanced expression of IL-33 in human gingival epithelial cells. Gingipains, cysteine proteases produced by *P. gingivalis*, induced the production of IL-33 via the activation of protease-activated receptor-2. These results indicate that increased expression of IL-33 in gingival epithelial cells induces allergic inflammation and may be involved in the pathogenesis of periodontal disease and systemic allergic disorders.



【Related link】

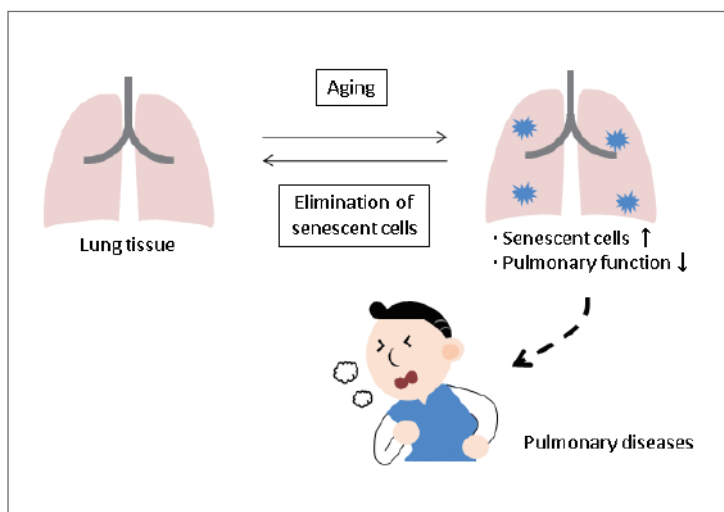
<http://biomedfrontiers.org/ep-2016-8/>

【Original Article】

Tada H, Matsuyama T, Nishioka T, Hagiwara M, Kiyoura Y, Shimauchi H, Matsushita K. Porphyromonas gingivalis gingipain-dependently enhances IL-33 production in human gingival epithelial cells. PLOS ONE 11(4):e0152794, 2016.

2) Pathophysiological roles of cellular senescence in pulmonary aging

Senescent cells accumulate in tissues as animals age, but little is known about its consequence. Our laboratory established a new genetically modified mouse of which senescent cells can be eliminated by sensitizing them to a specific drug. Using this system, we discovered senescent cells that accumulate in lung tissue during aging contribute to pulmonary aging. Removal of senescent cells from lung tissue of aged animals restored pulmonary functions which progressively decline during aging. Since aging of the lung tissue increases a risk for pulmonary diseases such as COPD (chronic obstructive pulmonary disease), our findings suggest that senescent cells are potential therapeutic and preventive targets for pulmonary diseases.



【Related links】

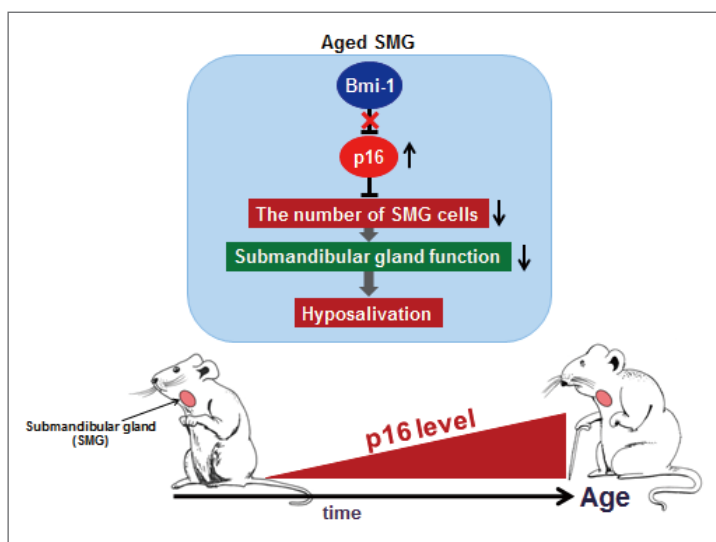
https://www.eurekalert.org/pub_releases/2016-08/jj-eos080216.php

【Original Article】

Hashimoto M., Asai A., Kawagishi H., Mikawa R., Iwashita Y., Kanayama K., Sugimoto K., Sato T., Maruyama M., and Sugimoto M. Elimination of p19^{ARF}-expressing cells enhances pulmonary function in mice. JCI Insight 1(12). e88057. 2016.

3) The mechanism of aging-associated decline in submandibular gland function

Xerostomia (the feeling of dry mouth) is a common problem that is particularly prevalent among the aged. Advances in research on the mechanism of xerostomia are desired. Using real-time *in vivo* imaging of the cyclin-dependent kinase inhibitor p16 expression in mice lacking Bmi1 which prevents stem cell aging by blocking expression of p16, we uncovered a novel function of the Bmi1/p16 pathway in controlling homeostasis of the submandibular glands (SMGs). This pathway is dysregulated during aging process, leading to the induction of p16 expression and subsequent decline in SMG function. These findings extend the current understanding of the molecular mechanisms underlying the aging-related decline of SMG function and associated degenerative diseases and will open up new possibilities for its control.



【Related link】

<http://jcb.rupress.org/content/186/3/393.long>

【Original Article】

Yamakoshi, K., Katano, S., Iida, M., Kimura, H., Okuma, A., Ikemoto-Uezumi, M., Ohtani, N., Hara, E., Maruyama, M. Dysregulation of the Bmi-1/p16^{ink4a} pathway provokes an aging-associated decline of submandibular gland function. Aging Cell, 14(4), 616-624, 2015.



The Center for Gerontology and Social Science (CGSS) was founded in April, 2012 to promote empirical research in the field of gerontology and social sciences in the National Center for Geriatrics and Gerontology. The concept of the center is to promote the independence of older people's mind and body, contributing to the development of a vigorous society and longevity.

CGSS consists of 6 divisions and 10 subdivisions and is inviting more than 20 researchers from outside. We are conducting empirical research on sociogerontological issues to develop a society where older people can live safely and independently in the community. The research key words in CGSS are social participation, independence support, social support, social welfare, home care, and regional comprehensive care. We are also taking the problem solution approach for the laws and measures related to older people along with health economics. Based on these research activities, CGSS is trying to promote the independence of older people, to improve the QOL, and to contribute to the end-of-life with dignity and thereby committing to the development of a vigorous society with longevity.

Hiroyuki Shimada, Dr.

Director of CGSS

【Department of Preventive Gerontology】

This department conducts surveys on community-dwelling older people and builds the system for early detection of dementia and geriatric syndromes. Addressing whether non-pharmacological treatments such as exercise, nutritional supplementation, and intellectual activity are effective for preventing dementia and physical frailty, and developing programs for disability prevention and to extend the period during which people can safely drive a car.

【Department of Gerontological Policy】

Research on caregiver burden and issues related to driving of older people with dementia.

【Department of Frailty Research】

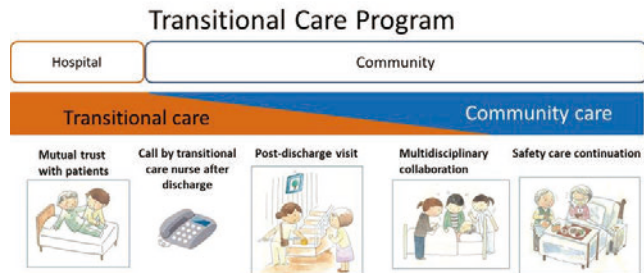
Verifying the usefulness of frailty concept and facilitating its introduction in health care service and geriatric medicine. Examining how we can utilize the assessment of frailty and effectively intervene for frail seniors in daily practice to minimize dependency and disability in older adults.



Sarcopenia and frailty research

[Department of Homecare Medicine]

Research on factors related to continuation of home care for the elderly and development of indicators to evaluate home care and effective home care. Investigating the way to promote home care collaboration based on the actual situation of each community. In the local setting, investigating the effect of home care support ward and transitional care with enhancement of collaboration between hospitals and local outpatient clinics and interdisciplinary team approach



[Department of Social Science]

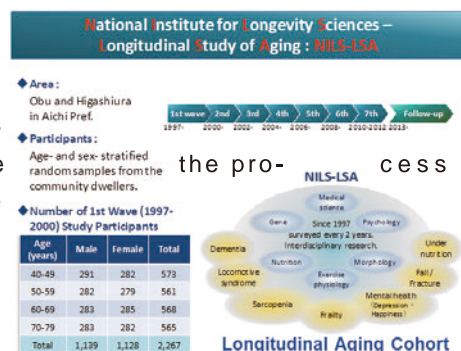
Studies on the effect of environmental factors such as community level social capital or medical care system on the health of older adults and on social activities or social relationships among the older population using a longitudinal data, evaluation of mental health intervention programs for older adults, studies on the association between individual- and community-level social factors and health in older adults using a large-scale community sample, evaluation of community-based health promotion programs targeted at older adults, studies to develop support programs for family caregivers, and evaluation of quality of home-based medical care programs

[Department of Gerontological Evaluation]

Central office of JAGES (Japan Gerontological Evaluation Study) project which aims to create a scientific foundation for the healthy ageing policy. Conducting surveys on 200,000 older people and develop JAGES HEART (Health Equity Assessment and Response Tool) and implementing and evaluating policy.

[Section of NILS-LSA]

NILS-LSA, "National Institute for Longevity Sciences – Longitudinal Study of Aging" is a long-term, epidemiological study on aging conducted by the NCGG. Utilizing the NILS-LSA data among interdisciplinary researchers for the study of aging to elucidate of aging and identify factors that contribute to the onset of geriatric diseases including dementia, osteoporosis, and frailty.





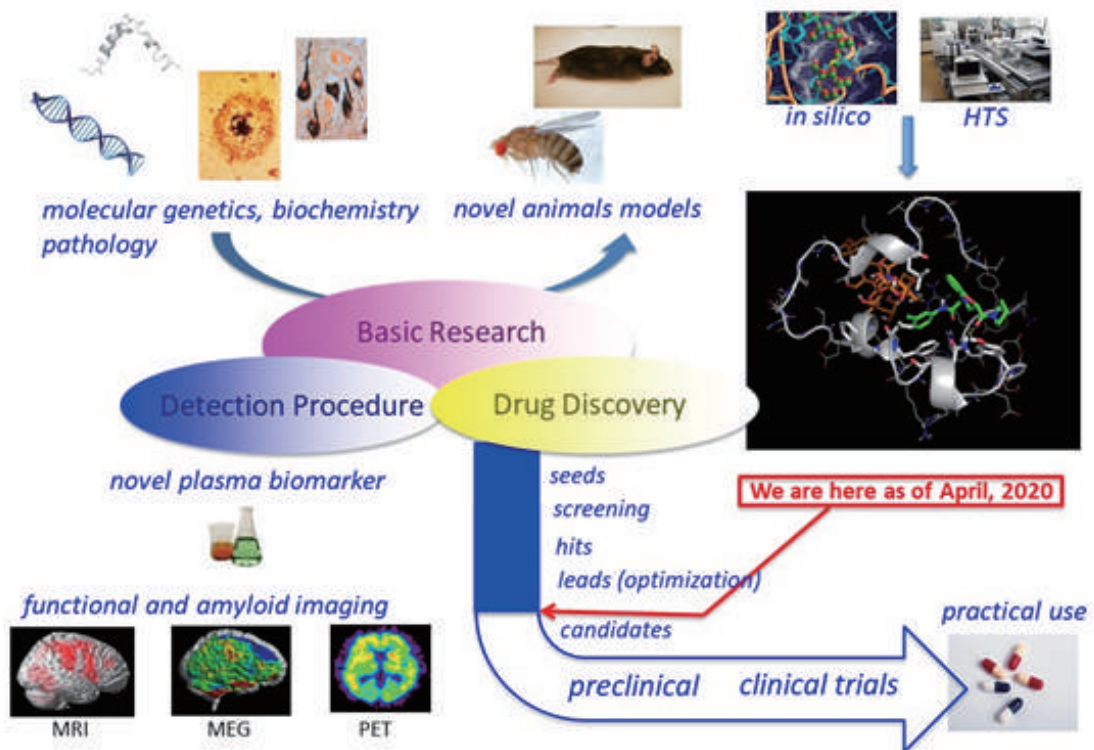
Center for Development of Advanced Medicine for Dementia (CAMD) was established in 2010 in National Center for Gerontology and Geriatrics (NCGG) to accelerate basic and applied researches for dementia, especially focusing on Alzheimer's disease. As of April 2020, through partial restructuring, our center consists of departments and laboratories indicated as follows; Department of Clinical and Experimental Neuroimaging, Department of Alzheimer's Disease Research, Department of Aging Neurobiology, Department of Drug Discovery, Department of biomarker research, Laboratory of Animal Models of Aging, and Laboratory for Liaison.

Our mission is to control and prevent dementia, mainly Alzheimer's disease. To this end, the research activity of our center is mainly divided into three areas, including the elucidation of molecular and cellular mechanisms underlying development of Alzheimer's disease, the development of procedures for detecting early or even preclinical stages of Alzheimer's disease, and the drug discovery for preemptive therapy of Alzheimer's disease. We believe that combining these three areas of research in one center provides a credible achievement to overcome this intractable disease.

Kengo Ito, MD, PhD,
Director
Center for Development of Advanced Medicine for Dementia

Recent scientific achievements of our center are as follows. First, novel imaging biomarkers to detect preclinical and prodromal stages of Alzheimer's disease has been developed, employing positron emission tomography (PET), magnetic resonance imaging (MRI) and magnetoencephalography (MEG). Second, basic neuropathological mechanisms underlying Alzheimer's disease have been elucidated from viewpoints of intraneuronal traffic impairment including endocytic impairment, genetic network disorders which are likely responsible for neuronal death in the disease and synaptic dysfunctions which are related to the pathological accumulation of amyloid and tau. Third, pathological significance of genetic and environmental risk factors for development of Alzheimer's disease such as apolipoprotein E and diabetes mellitus has been investigated. Fourth, novel animal models for Alzheimer's disease have been developed using drosophila and mice, which enable us to monitor neurotoxicities of amyloid and tau in the brain. Fifth, novel small compounds, which specifically binds an endogenous seed for Alzheimer amyloid (ganglioside-bound amyloid β -protein; GA β) and inhibits amyloid fibril formation in the brain, have been explored through refined medicinal chemistry. Sixth, a novel blood biomarker has been developed for the early diagnosis of Alzheimer's disease. Seventh, information on prevention, diagnosis, treatment and long-term care of dementia have been collected, analyzed and disseminated to improve the situation surrounding the dementia.

Unfortunately, trials to develop therapy that prevents or slows Alzheimer's disease has not succeeded so far. One of possible reasons for the failures is that intervention in the clinical trials until now were too late since the emergence of neuropathological changes of Alzheimer's disease precedes the onset of cognitive decline by more than 20 years. To overcome this problem, detection method to identify individuals at risk of developing Alzheimer's disease is urgently needed. In addition, development of effective measures for secondary prevention of Alzheimer's disease are keenly awaited. We strongly hope to contribute to this field in near future.





The basic mission of the National Center for Geriatrics and Gerontology (NCGG) is to contribute to society through the results of advanced clinical research on diseases such as dementia and osteoporosis that require a rapid response in a super-aging society. In order to establish a support system for conducting a greater number high-quality clinical trials and clinical studies, the Innovation Center for Clinical Research (ICCR) was founded on April 1, 2014.



Kengo Ito, MD, PhD,
Director of ICCR

Outline of ICCR

With the aim of facilitating and supporting high-quality clinical trials and clinical studies at NCGG, ICCR is composed of the Clinical Research Promotion Division, the Clinical Research Support Division, the Data Center, and the Development and Affiliate Promotion Division (Figure 1).

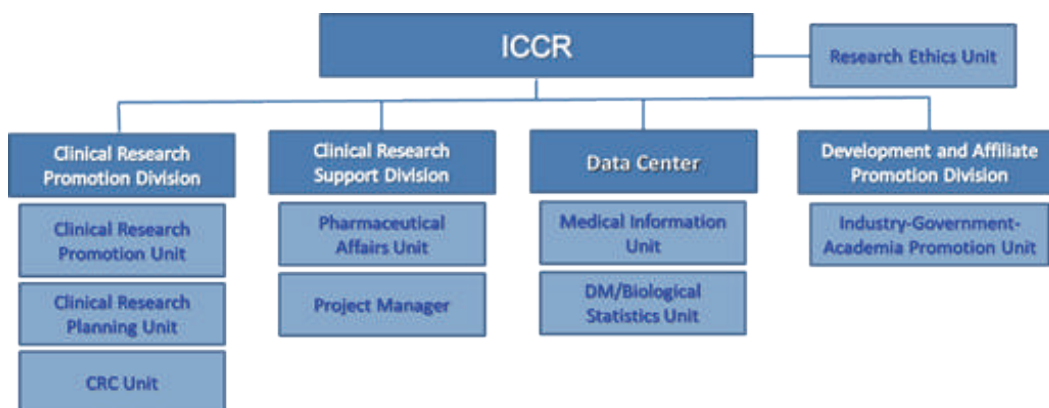


Figure 1 The Organization of ICCR (as of April 1, 2020)

• **The Clinical Research Promotion Division** has three units, the Clinical Research Promotion Unit, the Clinical Research Planning Unit, and the CRC Unit. In addition to clinical research coordinators (CRCs), clinical psychologists, three medical doctors, one pharmacist, and one nurse are also members of the Clinical Research Promotion Division and play a role as the driving force behind the clinical trials and clinical studies conducted at NCGG. The clinical trial secretariat that provides administration support for the Institutional Review Board belongs to the Clinical Research Promotion Division. In addition to the seven CRCs who are professionals that support the progress of clinical trials and clinical studies, the unit has two clinical psychologists who evaluate cognitive

functions that are indispensable for dementia research. Amyloid imaging, which is the latest diagnostic method for the selection of patients in dementia trials, is used at NCGG, and the Clinical Research Promotion Division is actively applying this technology (Figure 2).

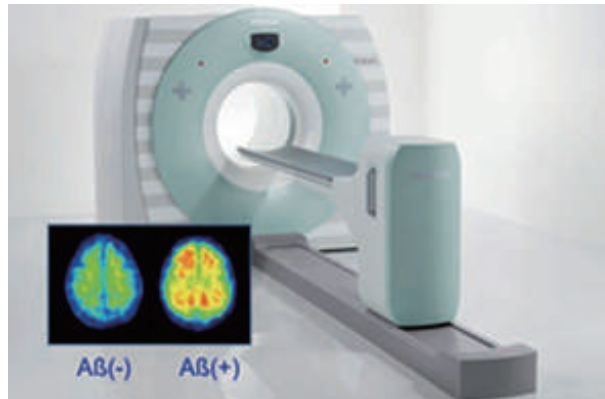


Figure 2 The Amyloid imaging in clinical trials for Alzheimer's disease

- **The Clinical Research Support Division** conducts various support activities related to clinical trials and clinical studies, including intellectual property management, monitoring, and regulatory assurance performed by two project managers. The division also provides consultation services for researchers. Clinical research consultation includes biostatistics, research ethics, protocol planning, monitoring, auditing, and data management. The division also conducts education and training on clinical research in collaboration with the Clinical Research Planning Unit of the Clinical Research Promotion Division. The workshop on planning high-quality clinical studies have been held since 2017 for clinical researchers in NCGG and provided attendees with practical examples.
- **The Data Center** performs quality control of clinical research by appropriately collecting, managing, and analyzing clinical research data from an independent standpoint to ensure the reliability of the results. The medical doctor who belongs to the Medical Information Unit of the Data Center is promoting the digitization of data to improve the efficiency of the above work. In addition, one biostatistician belongs to the DM-Biological Statistics Unit of the Data Center. Together with the Clinical Research Support Department, the Data Center responds flexibly to various questions from researchers, such as selection of appropriate statistical methods, calculation of sample sizes, selection of test designs, and biostatistics counseling.
- **The Development and Affiliate Promotion Division** and its Industry-Government-Academia Promotion Unit was established with the aims of discovering the seeds of future research, not only in NCGG but also in the academic and corporate sectors, and providing a seamless bridge to clinical research. To realize a healthy and long-living society, it is extremely important to develop innovative new drugs, promising diagnostic devices, effective rehabilitation equipment, and nursing robots for elderly medical care. Therefore, it is necessary to discover promising seeds at the basic research stage, nurture the seeds until they proceed to clinical studies or clinical trials, and confirm their usefulness.



The medical genome center (MGC) was launched in 2016 as a research infrastructure to promote genomic medicine for more accurate diagnosis and more appropriate treatment using personal genomics. The implementation of genomic medicine in geriatric syndromes, including dementia and sarcopenia, requires further research.

Our MGC is organized in three divisions: biobank, the division of genomic medicine, and the information management division. Biobank extensively collects and stores patient samples. The division of genomic medicine comprehensively analyzes the omics data, including genomic information obtained from the samples. The information management division ensures the sample clinical information is handled with a high level of security. The development of genomic medicine is facilitated through the collaboration of these three divisions. Moreover, our MGC provides the biobank samples and analyzed outcomes to outside researchers, which positively supports genomic medical research.

Shumpei Niida
Director
Medical Genome Center

Division of Biobank (NCGG Biobank)

Recent data-driven medical research requires a large number of patient samples. Our NCGG biobank collects and stores blood samples (serum, plasma), cerebrospinal fluid (CSF), urine, tissue, feces, DNA, and associated data from patients, which are mainly affected with geriatric syndromes, including dementia and joint disease. As of Sep. 2017, there are approximately 7,000 enrolled from our hospital and approximately 13,000 from a cohort study of recruited local residents. More than 10,000 samples have been distributed to many medical researchers and has contributed to development of medical science.

NCGG biobank is a member of the National Center Biobank Network (NCBN), a collaboration of six national centers. The sample information collected in our biobank is enrolled in a catalogue database of NCBN central biobank and available for inspection by anyone via <http://ncbiobank.org/>.

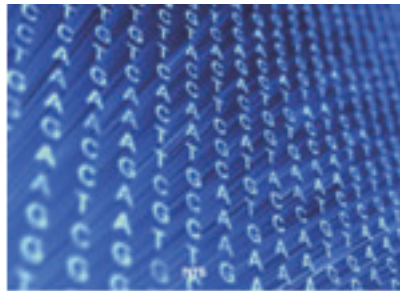


Biobank Building

バイオリソース保管設備	
液体窒素タンク 容量450ℓ	ディープフリーザー 容量500ℓ
気相5台・液相1台	横型20台・縦型4台 (-80℃)
	
	
16,000検体/台 × 6台 = 96,000検体収容	横型: 26,730検体/台 × 20台 = 534,600検体収容
	縦型: 計4台 = 132,192検体収容

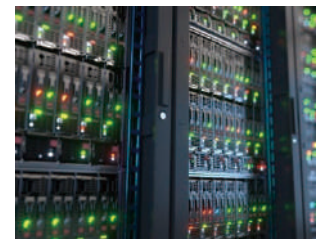
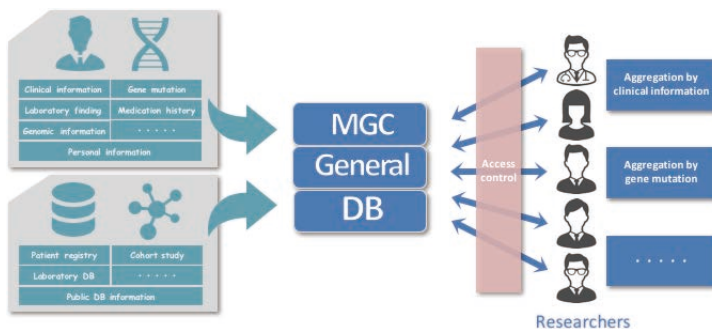
Division of Genomic Medicine

To promote genomic medicine for the Japanese population, the accumulation of a large number of Japanese personal genomes is important. The division of genomic medicine analyzes data in collaboration with our biobank. Currently, genomic analysis of dementia has been performed using 10,000 samples. This is expected to identify risk factors and genes associated with complicated multifactorial disorders such as late onset Alzheimer disease. We are further engaged in the construction of disease risk prediction models and discovery of drug repositioning using artificial intelligence (AI) techniques. These data resources accumulated in MGC is available to outside researchers through approval by our ethic committee.



Data and Information Management Division (DIM)

The information management division (IMD) has centralized control over all information that our MGC handles: biobank enrollment information, diagnostic information, and the other omics information. Moreover, the IMD develops its own integrated data anonymization system which allows for the use of the omics data and clinical information in a safe and effective manner. Currently, the IMD is developing a general database system that enables effective use for medical scientists in NCGG. This system converts the personal information written in the electronic health record into completely anonymized information. Furthermore, this system enables integrated analysis by linking omics data, including genomic information, to the clinical information. This will be a model of AI research in medical field.



Center of Advanced Medicine for Dental and Oral Diseases



Recent studies revealed that the elderly's oral conditions are closely associated with their systemic health. For example, there are associations between oral bacteria and systemic diseases and between the oral function and ADL/dementia in elderly people. Plaque as a hotbed for oral bacteria is a direct risk factor of caries and periodontal disease, and it may provide a reservoir for major causative bacteria of aspiration pneumonia and systemic infections represented by infective endocarditis, which can be lethal for the elderly. As periodontal disease also leads to the development of systemic diseases, such as diabetes, ischemic heart disease, cancer, cerebrovascular disease, arteriosclerosis, premature delivery, and Buerger disease, 'oral health' is being increasingly focused on in geriatric care.

The Center of Advanced Medicine for Dental and Oral Diseases was founded to promote surveillance and research for the development and improvement of preventive, diagnostic, and treatment methods used in dental and oral care. Our center consists of 3 research departments: 1) Department of Dental and Oral Infrastructure Development, 2) Department of Dental Regenerative Medicine, and 3) Department for Advanced Dental Research, to each of which specialized researchers are assigned. The center conducts research and development to support the elderly's mental and physical independence by promoting their oral health, with the goal of contributing to the realization of a society with healthy longevity.

Yasunori Sumi, D.D.S., Ph.D
Director

Department of Dental and Oral Infrastructure Development

We are conducting a study to clarify the causal relationship between periodontal disease and geriatric diseases and to determine whether we clarify that periodontal disease can become an exacerbating factor of Alzheimer's disease (Figures 1 and 2). We will also attempt to clarify the molecular mechanism of oral senescence by analyzing age-related changes in the oral mucosa. We have also established collaborative programs at the dental departments of six universities in Japan, and we are aiming at promotion of basic dentistry for elderly and making people aware of the idea of extending a healthy life span by maintenance of a healthy oral cavity.

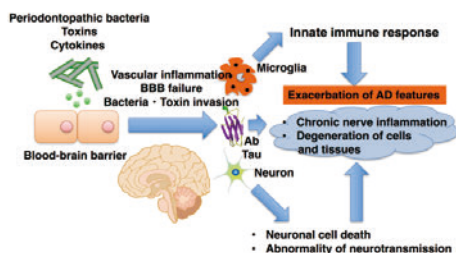
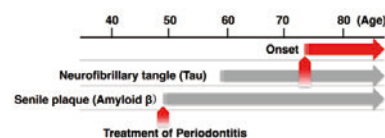


Figure 1. Possible mechanisms by which periodontitis induced by bacterial infection exacerbates features of Alzheimer's disease

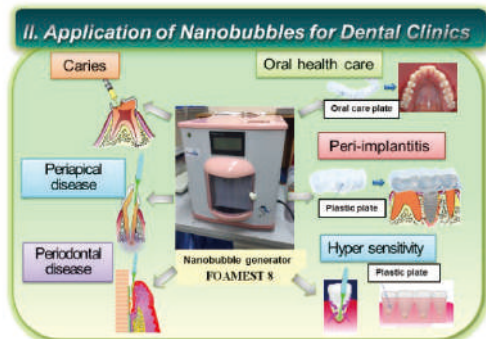
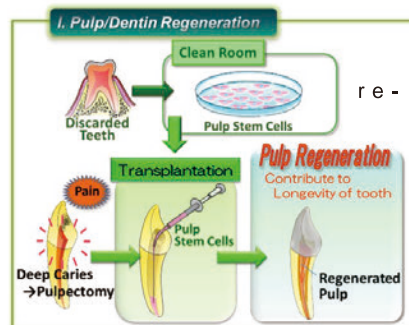


Providing an effective means for prevention and treatment of Alzheimer's disease by the prevention and treatment of periodontal disease may contribute to improvement of national welfare and to reduction of national medical expenses.

Figure 2. Prevention and treatment of periodontal disease for prevention of AD

Department of Dental Regenerative Medicine

I) Pulp Regeneration Therapy: Dental pulp stem cells are transplanted into mature pulpectomized teeth for pulp regeneration. The generative therapy may contribute to the functional survival and endurance of the tooth, leading to good health and longevity.



II) Application of Nanobubbles for Dental Clinics: Nanobubbles can enhance delivery of medicament to complex tooth structure and irrigate to remove smeared layer, biofilm and bacterial plaque for Caries, Periapical disease and Periodontal disease.

Department for Advanced Dental Research

Our department conducts the following activities to realize healthy longevity in aged society.

- (1) Research for development of advanced medical equipment and drugs
 - (2) Dissemination activity for oral care
 - (3) Dental treatment for elderly patients
 - (4) Post graduate training and human resource development of dentists and dental hygienist
- Part of our activity will be introduced below.

Development of the gel for oral care to prevent aspiration pneumonia

The oral care is very important for prevention of aspiration pneumonia. In our department, a gel for oral care to prevent aspiration pneumonia was developed and related researches are being conducted. By using the developed viscous gel without water, it is possible to reduce aspiration risk during oral care and to effectively remove contaminants. We also conduct researches and dissemination activities on oral care systems including this oral care gel.



Oral gel for professional oral care



Before oral care



After oral care using our new gel

Welcome to our memory center in NCGG!



The number of demented patients in Japan is increasing. The Ministry of Health, Labor and Welfare is planning to establish 500 medical centers for dementia all over Japan. In 2010, we established the Center for Comprehensive Care and Research on Memory Disorders (3CRMD) in the National Center for Geriatrics and Gerontology (NCGG), as an ideal model of medical center for dementia. Geriatricians, neurologists, psychiatrists, radiologists and neurosurgeons are cooperatively working together in the 3CRMD. The 3CRMD offers a series of services for the demented, from the

latent stage to the terminal-care by providing precise diagnosis with the most advanced clinical instruments, implementing “interdisciplinary and comprehensive medical care” through cooperation of healthcare professionals and families of patients, thereby developing medico-social network.

The 3CRMD also creates prospective and longitudinal database on demented patients, and offers information based on the clinical and translational researches in cooperation with researchers all over Japan and abroad. Here, the fully equipped and functional 3CRMD, a new model of medical center for dementia, is briefly introduced.

Takashi Sakurai, MD., PhD
Director

3CRMD's Mission

We attend to requests and hopes of demented patients and their families so that they can lead peaceful lives at home as long as possible.

To achieve the mission, we:

1. Provide care and services required to maintain the cognitive function
2. Promote rapid improvement of behavioral and psychological symptoms of dementia (BPSD)
3. Improve patients' ability to perform activities of daily living
4. Prevent patients from developing geriatric syndrome including fall, aspiration, and incontinence
5. Ease the care burden on patients' families or carers
6. Provide information on readily accessible dementia care services
7. Maintain readiness for urgent hospitalization

Clinical activities in 3CRMD

Staff: Physicians and Surgeon (19), Nurses (8), Psychologists (9), Psychiatric social worker (1) and Reception Clerk (1)

Establishing an ideal model of medical care for dementia: ① Providing medical care to more than 1,000 new patients per year, ② Treatment of BPSD by cognitive rehabilitation, ③ Treatment of geriatric syndromes associated with dementia by board-certified geriatricians, ④ Interdisciplinary care in cooperation with patients and their families by offering classes for families (figure 1), and ⑤ cognitive rehabilitation aiming to improve daily life function from prodromal stage (figure 2).

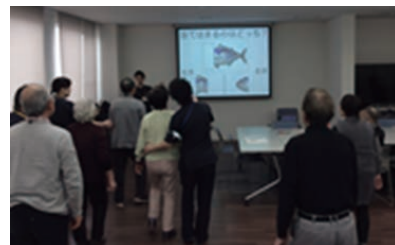
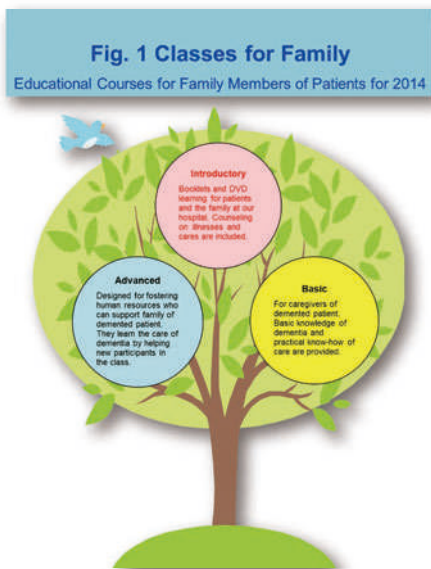


Fig. 2 Cognitive rehabilitation (Dual task exercise and Botanical therapy)

Accumulation of database for clinical researches and trials (Orange registry): including comprehensive geriatric assessment, neuropsychiatric battery, frailty measurement (Body composition analyzer, Hand grip meter, gait speed), advanced neuroimaging [3.0T MRI, SPECT, PET-CT (FDG, Amyloid & Tau imaging), NIRS] and Lumbar puncture.

Education for medical and care staff in Japan and Asian countries

Breakthrough in 3CRMD

Clinical and translational researches are intensively conducted for dementia prevention and care in 3CRMD, such as development of blood biomarker for early dementia detection, preventive activities for dementia, robotics to help carers, and establishment of a new socio-medical network (Orange town).

We are very looking forward to seeing you and collaborating with you in 3CRMD.



The Education and Innovation Center was founded on April 1, 2014, with the mission of fostering human resources that will contribute to the development of a healthy longevity society. In April 2015, we built an education and training facility with the main seminar hall for 200 people and accommodations for 30 attendees.

We aim to share the expertise and experience accumulated through our clinical and research activities with medical, nursing, administrative and other professionals and the general public, in order to contribute to better improve medical and long-term care for the elderly in the entire country and to their

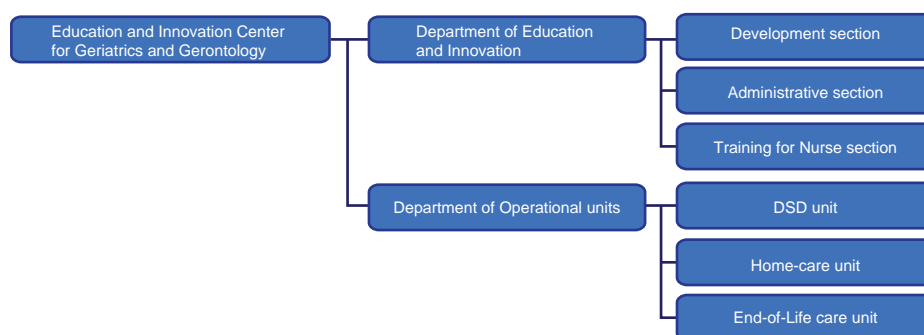
spiritual, physical independence.

To be more specific, we plan and manage education programmes commissioned by the national and local governments, such as training for the "Dementia Support Doctors (DSDs)" and the "Initial-Phase Intensive Support Team for dementia (IPIST)" members, as well as "Comprehensive educational programme for nurses on Elderly Health Care and Home Care" and "Cognicise" training programme for dementia prevention.

We also offer workshops and lectures for the broader range of people all year round, so we hope you will take your time to check our website for the latest information and join us.

Akinori Takeda MD, PhD
Director, Education and Innovation Center
for Geriatrics and Gerontology

Organization



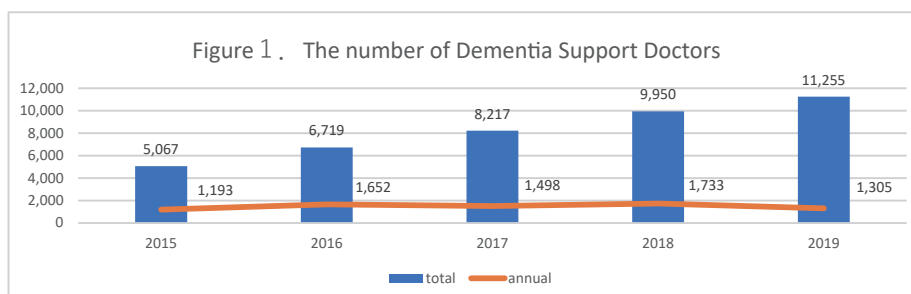
Key Programmes

① Education Programme for "Dementia Support Doctors (DSDs)"

DSD Education Programme was launched in 2005, and a total number of over 11,000 doctors had been certified as DSD by the end of JFY 2019 (Figure 1). DSDs are expected to play a crucial role in facilitating the development of a regional dementia network, such as serving as lecturers for the "Educational Programme for Family Doctors to Upskill Dementia Practice" and participating as team members of the "Initial-Phase Intensive Support Team for dementia (IPIST)".

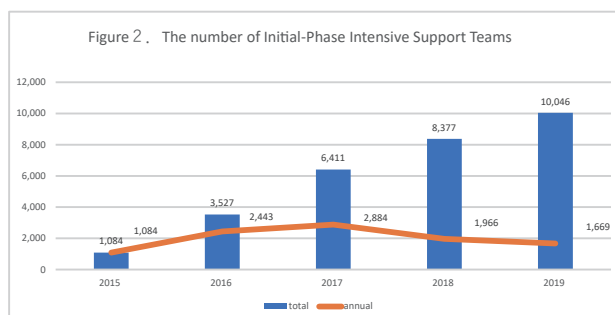
Also, DSDs are one of the staffing requirements for the additional fee for dementia care in acute care hospitals, and many doctors are actively involved in a wide range of fields.

The Government aims to increase the number of DSD to 16,000 by JFY 2025.



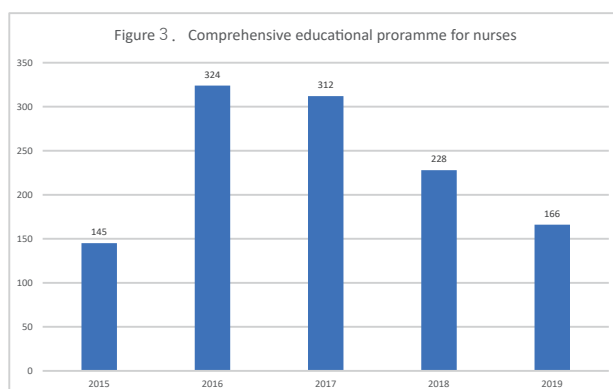
② Education Programme for "Initial-Phase Intensive Support Team for dementia (IPIST)" members

IPIST member Education Programme has already been completed by more than 10,000 people in the past five years, with participants from a variety of prefectures (Figure 2). The IPISTs are playing an active role in providing initial support for the people with dementia and their families in the community, and we are planning to deliver further training sessions in JFY 2020.



③ Comprehensive educational programme for nurses on Elderly Health Care and Home Care

We trained more than 100 nurses every year (Figure 3), and our dementia courses are also designated as a requirement for one of the additional fee for dementia care at hospitals.



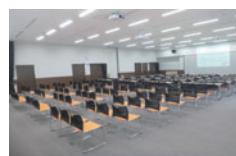
④ Training sessions for Instructors and Practitioners of "Cognicise"

"Cognicise" is a uniquely designed programme aimed at preventing dementia. We host training sessions for its instructors and practitioners twice a year each. Due to the high number of applicants, participants will often be randomly selected by lottery.

Education and Training Facility

A spacious seminar hall is available for large groups. It is used ten occasions per month on average.

Photo Gallery



General outline



In order to support longevity and good health for older adults, it is necessary to equip robots at the place for medical remedy, care and usual life. It means that there are demands of robots for treatment of diseases, recovery, return to life, support for daily life and care. In addition, we have to consider the life place of older adults both at nursery home and usual house.

Izumi Kondo
Director

Topic

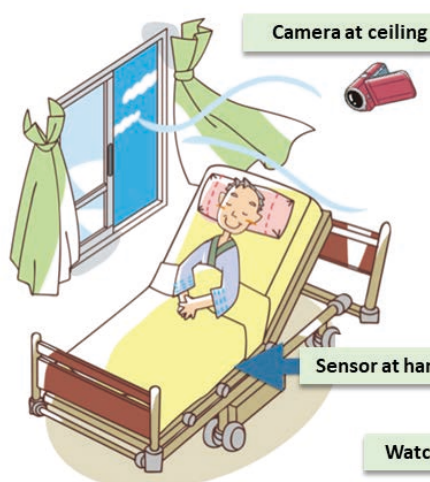
Thinking about the amount of manpower for the management of robot, the largest is the hospital and the smallest is the usual house. The needs of robot at these places are overlapped each other for example the robot used at hospital can be applied to the nursery home and also usual house. Under the situation like this, the way of efficient development will be that for the first instance, the robot developed at hospital where is place of the most proficient manpower should be tried at nursery home in the next phase and a last it would be applied to usual house after the enough refinement at hospital and nursery home. It is dangerous to introduce the newly developed robot to the usual house.

The other problem in the introduction of robot is the "death valley" between the places of development and application. It means that many robots developed at the companies and the Universities would disappear during the process i.e. death valley before the application to actual life. The reasons why many robots have disappeared at death valley are 1) the engineers at the companies and the Universities make robots without the knowledge of reality at hospital, nursery home, and house, 2) especially in the Universities, many professors would like to invent elemental technology in order to acquire academic achievements, 3) the health professions who will make comments and suggestions to development have very narrow views coming from the personal idea for the user's needs, 4) especially clinician cannot discriminate the needs whether it would be suitable for the treatment or for use in usual life. In order to overcome the problem of "death valley" it is necessary to set a point to make a link between developer and user with the proper information about needs from user and to decide the application of already existed or being developed seeds to the user.

Under the consideration for these problems, the mission of this robotic center would be to 1) suggest the needs of older adults to the developers properly, 2) collect the existed or being developed seeds as many as possible, 3) provide the place to validation to applicable seeds, 4) foster the application of seeds in the hospital and home, 5) prepare the framework of rules to apply the robot, i.e. guideline for safety use and make a proposal for legal system, 6) make the system for provision and maintenance with the support of developer, and 7) set the education process for the professional to adjust the use of robot from the expert knowledge.

This center was founded in April 2015 and it had opening ceremony on 17th August 2015. Aichi service robot support center, founded by Aichi regional government was placed at next door and currently both of two centers have established close relationship each other. However, these centers are at the initial phase of essential activities, so we hope to have as many as supports not only from inside of this country but also from abroad.

Application of robots to daily life



Watching robot



Monitoring system of driving



Rehabilitation robots for walking



Walking support robot





Extension of the healthy life expectancy, i.e., elongation of the period when elderly people can live independently to keep mental and physical health, has become a very important social challenge against the rapid graying of the Japanese society. In the Center for Frailty and Locomotive Syndrome we have been engaging in the approach to contribute to the promotion of healthy longevity, by establishing the Integrated Healthy Aging Clinic, the world's first novel diagnostic system that comprehensively evaluates problems among elderly patients through a multidepartmental and multidisciplinary cooperation and assesses their physical frailty status and sarcopenia.

Yasumoto Matsui

Director

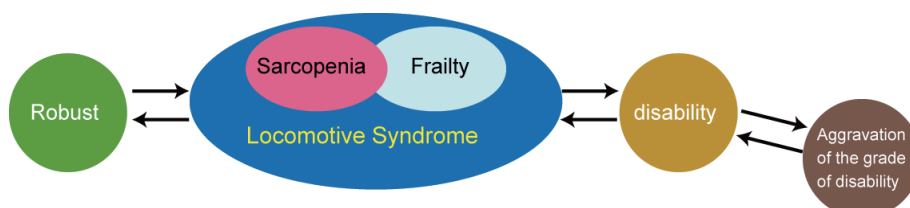
Center for Frailty and Locomotive Syndrome

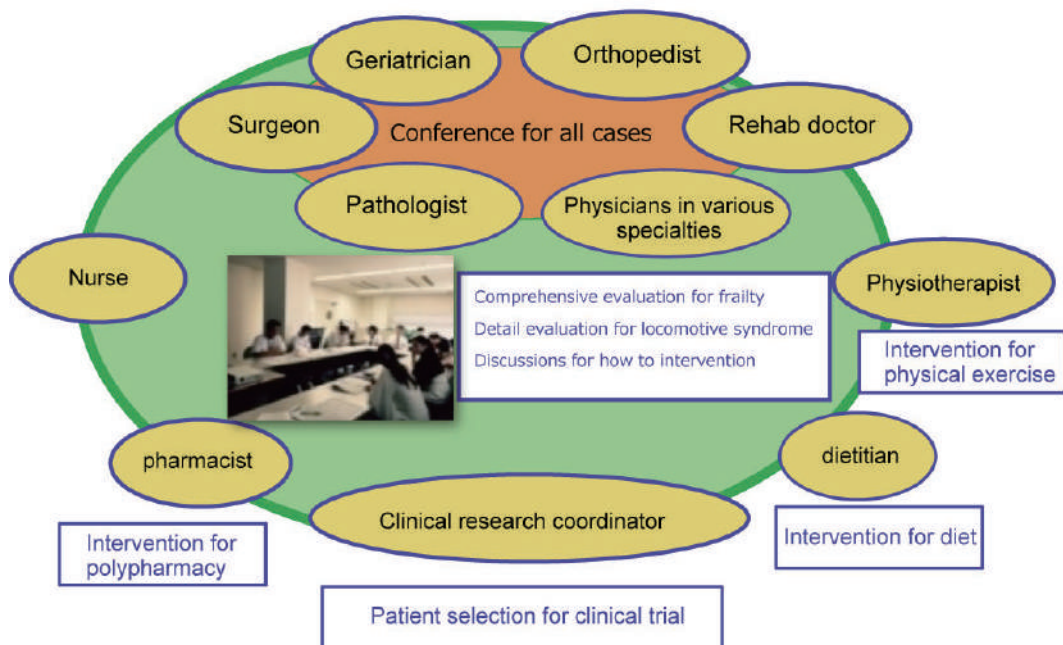
The aims

- Providing medical service to improve and keep physical, life and cognitive capability
- Prevention for disability and its aggravation
- Proper diagnosis, prevention and treatment of locomotive syndrome, frailty and sarcopenia
- Development and research to clarify pathologies and useful interventions for locomotive syndrome, frailty and sarcopenia
- Development of innovative medical and life instruments to prevent these conditions through collaboration with academia and industries
- Enlightenment and permeation of these conditions

The activities

- Comprehensive clinical evaluation of locomotive syndrome, frailty and sarcopenia through multidisciplinary cooperation
- Establishment of the database for clinical research and clinical trial
- Comprehensive evaluation for these conditions and case conference by multidisciplinary specialists
- Interventions for malnutrition and physical impairment
- Activities to promote the public awareness and dissemination of these geriatric conditions
- Development of innovative medical devices for these conditions and evaluation of newly provided various equipment by industries
- Collaboration and association with internal researchers and academic societies
- Holding lectures for general public to prevent and improve these conditions





Medical practice

Staffs : MDs [geriatrics, orthopedics, pulmonary medicine, metabolism, rehabilitation medicine, surgery, pathology] , physical therapist, dietician, pharmacist, nurse, clinical research coordinator, research assistant, medical clerk

clinic : Mon, Tue, Fri (AM/PM) , Thu (AM) (need reservation)

Assessments or tests : Questionnaires regarding basic attributes (e.g. age, sex, educational level, family structure, recognition of need for long-term care), higher cognitive function, sociability, frailty, locomotive syndrome, number of comorbidities, number of medications, nutrition, and anthropometric measurements, spinal radiography, dual-energy x-ray absorptiometry whole-body images, thigh computed tomography scan, body composition, blood biochemical profile (including nutrition, bone metabolism, and endocrinology), and motor function (walking speed; grip strength; timed up and go; SPPB (walking, balance, chair rise, total score); one leg standing time; two locomotive syndrome tests; ankle dorsiflexion angle measurement, etc.)

Case conference : one in 2 weeks. Pathological status or problems are examined for all cases to decide intervention methods (nutritional and exercise interventions, Interventions for polypharmacy, cognitive impairment, and social issues)

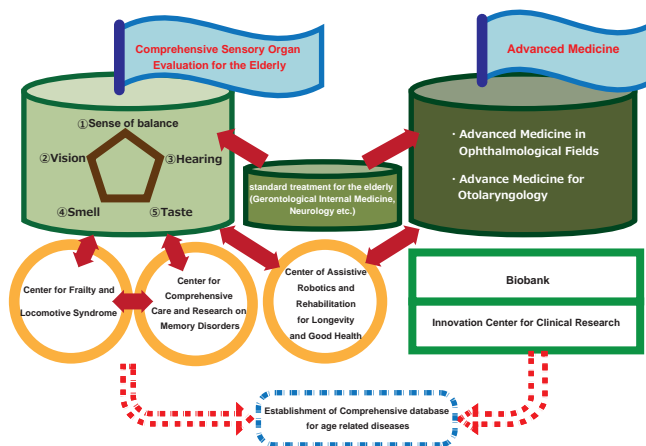


We receive external information through sensory organs. Aging results in sensory impairment, reducing cognitive and vital functions, which in turn reduces the self-reliance of the elderly.

The Sensory Organ Medical Center evaluates the functions of sensory organs and identifies elements that may compromise the independence of the elderly. Clinical treatment is performed in other centers of NCGG to improve vital functions.

Activities of the center, based on regular clinical diagnosis, are composed of “Comprehensive Sensory Organ Evaluation for the Elderly” and “Advanced Medicine”

Tsutomu Inatomi, MD, PhD
Director
Center for Sensory Organ



Comprehensive Sensory Organ Evaluation for the Elderly

Goals:

Producing clinical programs for patients with low “Independence Index” scores, based on comprehensive evaluation of the five senses, and treatment of patients with advanced medicine.

- ① Sense of balance : Using 3T Magnetic Resonance Imaging to evaluate inner-ear pathology, and causes of Meniere’s disease and related diseases; these symptoms are then treated.
- ② Vision : Elucidating the relationship between visual acuity and vital functions of the elderly, using advanced and regenerative medicine to help them become independent.
- ③ Hearing : Early detection of age-related hearing loss or earwax thromboembolism, and using cochlear implants and other new technologies, and hearing aids to prevent impairment of cognitive functions, and depression.

- ④ Smell : Conducting research on the relationship among olfaction, aging, and cognitive function, facilitating early detection of neurodegenerative diseases such as Parkinson's disease and Alzheimer's disease, and mild cognitive impairment (MCI), and olfaction training to maintain the vital functions.
- ⑤ Taste : Conducting research on the relationship between gustation and olfaction, and the early detection of MCI by Tasting test.

Advanced Medicine

① Advanced Medicine in Ophthalmological Fields.

- Innovative Regenerative Medicine, using cultured corneal endothelial cell transplant for bullous keratopathy patients.
- Cultured auto-oral mucosal epithelium sheet transplant for refractory corneo-conjunctival disease.



② Advance Medicine for Otolaryngology

- Cochlear implant
- Pathogenesis of Meniere's disease
- Introducing hearing aids to patients with dementia
- Research on gene polymorphism for treatment of hearing loss



Clinic

Staff : Physician [Ophthalmology、Otolaryngology] , Nurse、Orthoptis, Speech-language hearing therapist, Clerk

Clinic timings : Monday through Friday (am/pm)

Tests :

Balancing tests [Body sway test, Nystagmus test (infrared Charge-coupled Device camera), Thermal Nystagmus test, Vestibular neck muscle reaction]

Visual tests [Converted visual acuity test, Intraocular pressure test, Refraction test, Corneal curvature radius measurement]

Hearing tests [Pure tone audiometry, Speech audiometry, Pitch-matching and loudness-balance test, Evaluation of hearing aid fitting, Auditory brainstem response, Cochlear function test, Tympanometry, Distortion product otoacoustic emission]

Tasting tests [Electrogustometry, Quantitative examination of gustatory function by, Filter-paper disc method for taste assessment]

Smelling tests [T&T olfactometry, Intravenous olfactometry,]

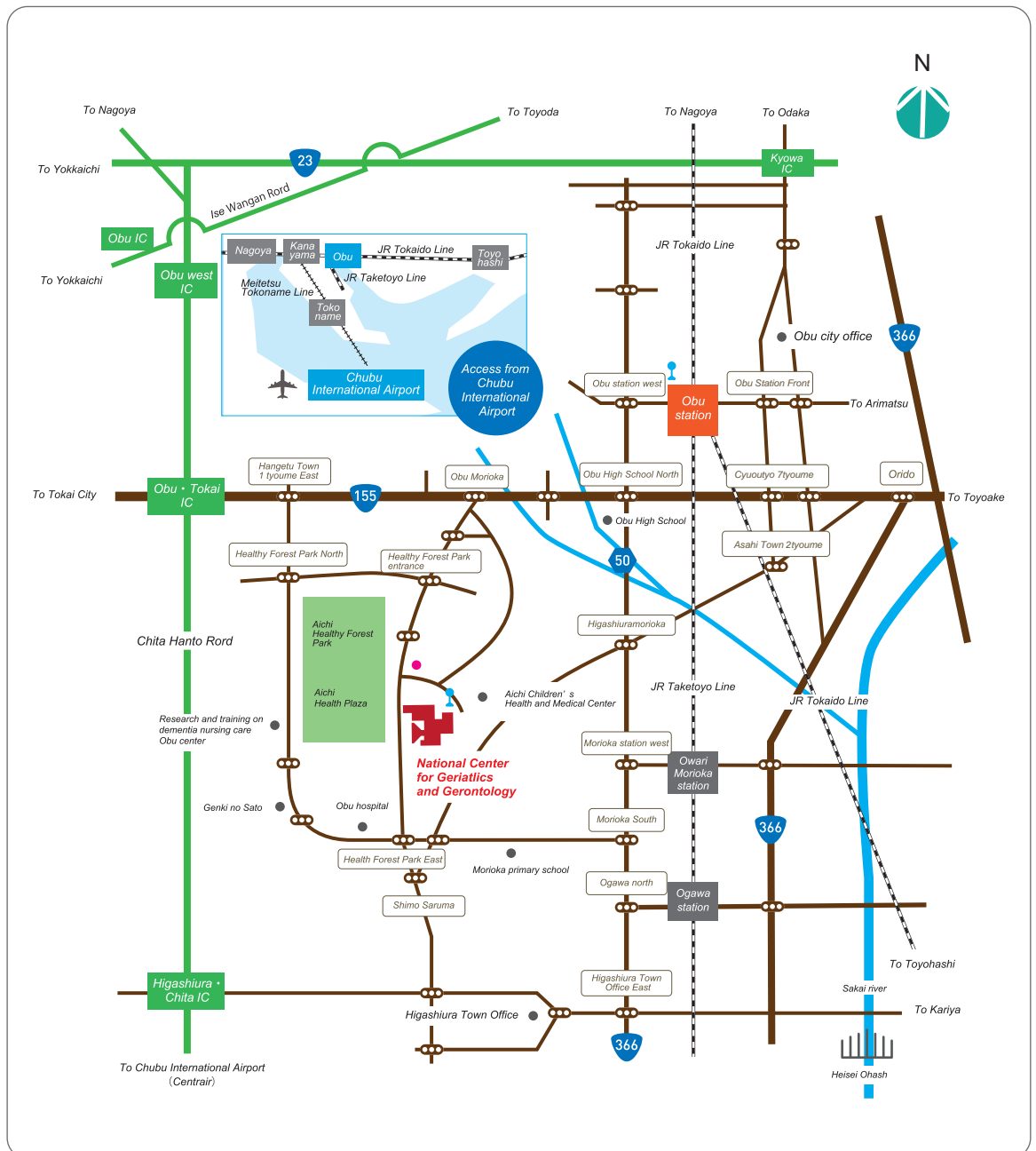


Guide map for National Center for Geriatrics and Gerontology



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|------------------------------|---|----------------------------|---|
| 1 New Outpatient building | 5 Second research building | 9 Middle ward | 13 Energy Center Building |
| 2 First Research Building | 6 Center for Comprehensive Care and Reserch on Memory Disorders | 10 East building | 14 Education and Innovation Center for Geniatrics and Gerontology |
| 3 Genome Center Building | 7 Under construction | 11 Rehabilitation Building | |
| 4 Laboratory Animal Building | 8 Under construction | 12 South ward | |

Access



Address

7-430, Morioka-cho, Obu City, Aichi Prefecture, Japan, 474-8511
 TEL +81-562-46-2311 <http://www.ncgg.go.jp>

