Life Course Research Consortium Secretariat

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TMDU
東京医科歯科大学

TMDU Medical Innovation Consortium

Pioneering the Future of Medicine

国立大学法人
東京医科歯科大学
TOKYO MEDICAL AND DENTAL UNIVERSITY

Medical Innovation Consortium Unit and Unit Leaders

1	Genomics Innovation Unit	Department of Epigenetics, Medical Research Institute	Ishino Fumitoshi
2	Cellular and Structural Physiology Unit	TMDU Advanced Research Institute	Fujiyoshi Yoshinori
3	Genomics Technology Unit	Department of Molecular Neuroscience, Medical Research Institute	Tanaka Kohichi
4	Advanced Technology Unit	Department of Neurology and Neurological Science, Graduate School of Medical and Dental Sciences	Yokota Takanori
5	AI Hospital Unit	Department of Biomedical Information, Institute of Biomaterials and Bioengineering	Nakajima Yoshikazu
6	Bioinformatics Unit	Department of Medical Science Mathematics, Medical Research Institute	Tsunoda Tatsuhiko
7	Platform for Medical Innovation (Biobank)	Bioresource Research Center, Institute of Research / Department of Molecular Cytogenetics, Medical Research Institute	Inazawa Johji
8	Inflammatory Bowel Disease Unit	TMDU Advanced Research Institute	Watanabe Mamoru
9	Immune Disorder Unit	Department of Pediatrics and Development Biology, Graduate School of Medical and Dental Sciences	Morio Tomohiro
10	Maxillofacial Development Disorder Unit	Graduate School of Medical and Dental Sciences Department of Maxillofacial Orthognathics	Moriyama Keiji
11	Rare Tumor Unit	Department of Oral and Maxillofacial Surgery, Graduate School of Medical and Dental Sciences	Harada Hiroyuki
12	Cancer Therapeutics Unit	Precision Cancer Medicine, Medical Hospital	Ikeda Sadakatsu
13	Cardiovascular Disease Unit	Bioresource Research Center, Institute of Research	Tanaka Toshihiro
14	Healthy Aging Unit	Center for Personalized Medicine for Healthy Aging, Medical Hospital	Ishikawa Kinya

Tokyo Medical and Dental University
Director of the Medical Innovation Consortium
Tanaka Toshihiro

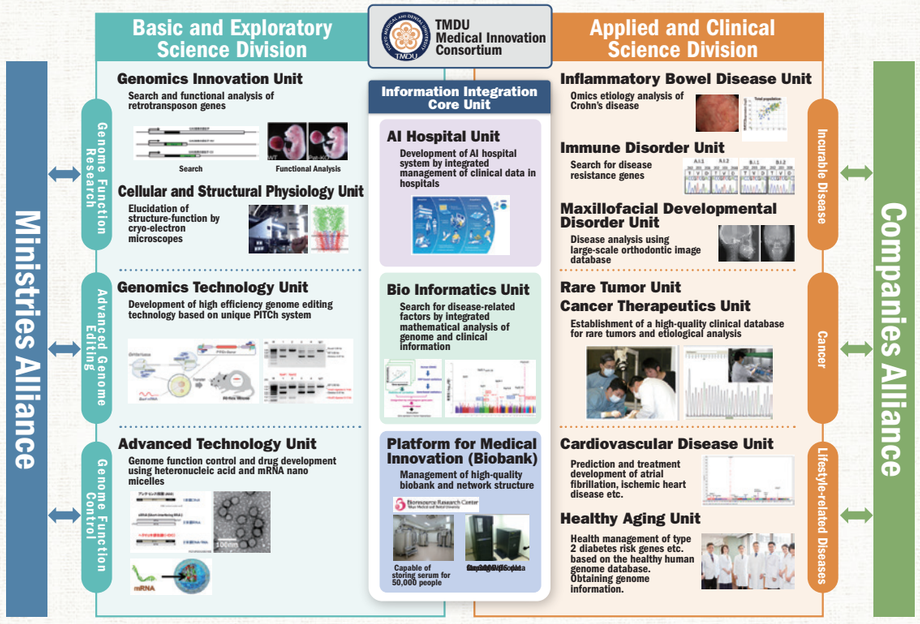
Message from the Director of Medical Innovation Consortium

Striving to realize future medical care with the cooperation of entire university from basic research to clinical practice

The rapid progress of technology in the field of molecular biology including genomics is changing the nature of medicine. The Human Genome Project, launched in 1990, took more than ten years and 10 billion yen to clarify the entire genome sequence of one person. Now it is possible to obtain whole genomic information in a few days for less than 100,000 yen. Groundbreaking nucleotide sequencing technology has led us to the new era where genomic information is utilized in clinical practice. For example, “Cancer Gene Panel Test” to search for appropriate drug based on altered genome information of cancer cells, has already been covered by insurance. Another good example is preventive mastectomy on patients with abnormalities in the BRCA1/2 gene, genes responsible for familial breast cancer, to take surgical treatment before suffering from cancer. In addition, new genome editing technologies such as CRISPR-Cas9 are expected to be applied to gene therapy. The ultimate goal of this consortium, where the development of "innovative medicine" is the main theme, is the social implementation of cutting-edge technology.

This consortium is made up of three divisions. The “Basic and Exploratory Science Division” aims to search for new knowledge and technologies in the following areas such as: unknown genome function research, cell structure analysis with the aid of cryo-electron microscopy, genome editing, nucleic acid medicine, and mRNA medicine. The "Applied and Clinical Science Division" develops treatments for refractory diseases, cancer and lifestyle related diseases. The “Data Integration Core Unit” integrates multi-level information for future medicine, bridges the two units with the support of big data analysis technology, manages and provides high-quality biological samples and clinical information recruited by the university Biobank, and makes suggestions from the bioethical viewpoint.

We sincerely hope for your generous support to our consortium for the innovative future medicine.



1

Genomics Innovation Unit

Department of Epigenetics, Medical Research Institute
Professor Ishino Fumitoshi

Contributing to AI medical care by understanding human genome functions and identifying disease-related genes

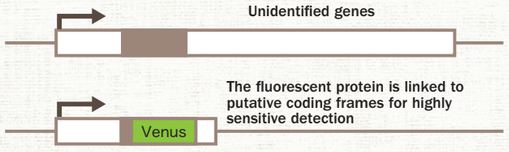
Message from the Unit Leader

The purpose of the Medical Innovation Consortium is to diagnose and treat patients based on individual genome information. Therefore, identification of a specific gene that causes disease is the key. To achieve this goal, the role of this unit is to estimate the exact number of genes in the human genome by finding novel disease-related genes that are not identified yet. Since AI is going to play a crucial role in genomic medicine, what scientists are supposed to do is to lay the groundwork for AI so that it can analyze a complete dataset. There are still many questions about how the human genome works, thus, to what extent this can be solved depends entirely on us, scientists.

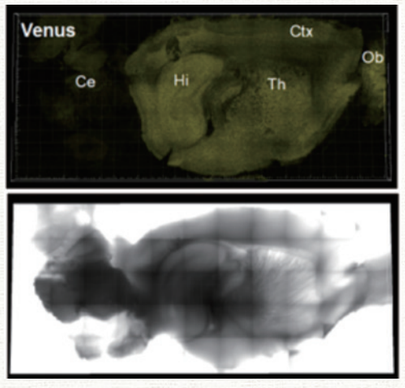
Our Research

It is said that the human genome contains about 20,000 genes. This, however, accounts only for 1.5 % of the whole genome, and the remaining parts may contain many unidentified genes. The main objective of this unit is to find novel protein coding genes that potentially have novel functions, and to understand the genomic function of human genome.

(diagram 1a) The technology to detect unidentified genes in the genome with fluorescence / Unidentified genes



(diagram 2) Example of detected unidentified proteins by fluorescence with high sensitivity in the brain of genome-edited mice



Ob: Olfactory bulb
tx: Cerebral cortex
Th: Thalamus
Hl: Hippocampus
e: Cerebellum

2

Cellular and Structural Physiology Unit

TMDU Advanced Research Institute
Distinguished Professor Fujiyoshi Yoshinori

Providing structural and physiological information useful for future medical technology using cryo-electron microscopes

Message from the Unit Leader

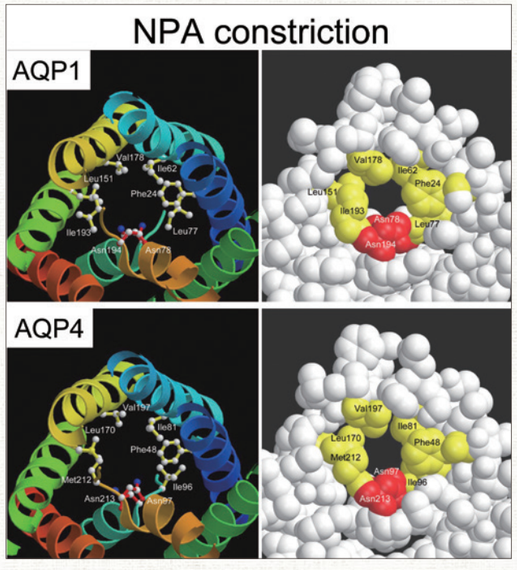
The Cellular and Structural Physiology Unit analyzes the structures of proteins and their conjugated proteins as desired for the Medical Innovation Consortium using cryo-electron microscopes. The unit then provides structural and physiological information for future medicine. We will try to do our best to contribute to future medicine by presenting useful information to the consortium in a timely manner.

Our Research

We will analyze membrane proteins which are considered to be an important element in both the medical and pharmaceutical fields, to get a structural and physiological understanding of the cell by using mainly the cryo-electron microscopes.

Please consult us if 3D structure analysis or an electron microscopy might be useful to your research.

The filter structure of a water channel that shows a highly water selective tendency



3

Genomics Technology Unit

Department of Molecular Neuroscience, Medical Research Institute
Professor Tanaka Kohichi

Promoting the development of genome editing technology that aids in understanding diseases and leads to drug discoveries.

Message from the Unit Leader

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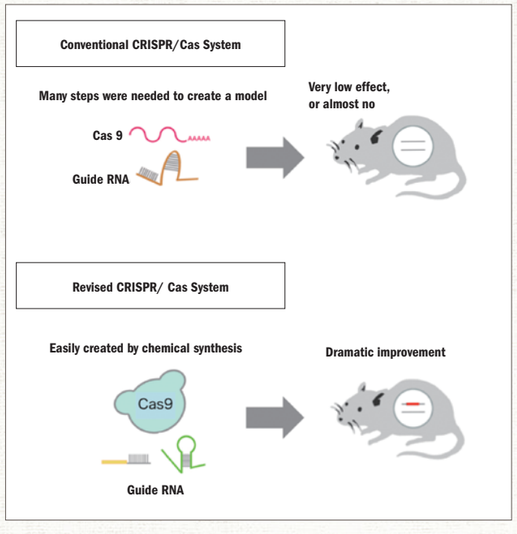
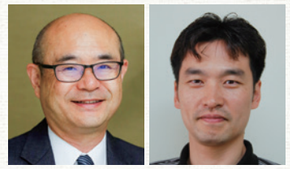




Left : Yokota Takanori
Right: Itaka Keiji

4

Advanced Technology Unit

Department of Neurology and Neurological Science, Graduate School of Medical and Dental Sciences
Yokota Takanori

Department of Biofunction Research, Institute of Biomaterials and Bioengineering
Itaka Keiji

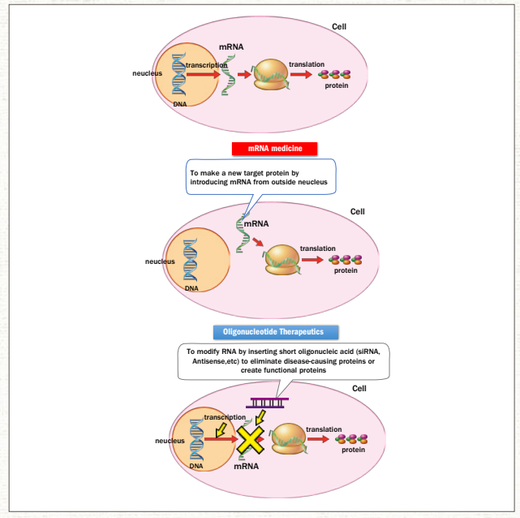
Developing highly efficient and safe molecular targeting drugs with the technology of DNA/RNA heteroduplex oligonucleotide (HDO) and mRNA medicines

Message from the Unit Leader

Nucleic acid medicines are next-generation technologies of molecular target therapy, which are attracting much attention because they have high specificity and broad utility to regulate the target genes. Recent progress in the development of therapeutic oligonucleotides has led to some novel drugs, such as nusinersen for spinal muscular atrophy or patisiran for hereditary polyamyloidosis. The Advanced Technology Unit is working on the development of TMDU original oligonucleotide therapeutics: Heteroduplex oligonucleotides and mRNA medicines. These new technologies are expected to come into practical use for patients in the future in a wide range of medical fields from general disease treatment to preemptive medicines such as the medicine to prevent aging.

Our Research

Heteroduplex oligonucleotide (HDO) is a revolutionary technology because it has a different molecular structure from the conventional nucleic acid medicines. HDO technology exerts high efficacy to reach target tissues in vivo and regulate target gene expression with less side effects. mRNA medicine is an artificially synthesized RNA-drug which is administered to the patients with drug delivering systems (DDS). The therapeutic proteins which are produced by the administered mRNA medicines will help to treat the patients. We aim to develop treatments for the patients with intractable diseases, such as disease modified therapy of refractory neuromuscular diseases and regenerative therapy for cartilage and disc diseases.




Left: Nakajima Yoshikazu
Right: Ai Masumi

5

AI Hospital Unit

Department of Biomedical Information, Institute of Biomaterials and Bioengineering
Nakajima Yoshikazu

Department of Insured Medical Care Management, Medical Hospital
Masumi Ai Masumi

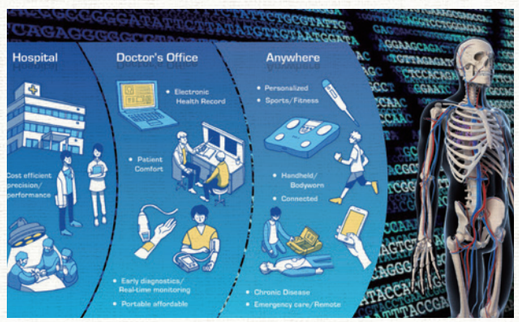
Achieving unexplored levels of an advanced and reliable management system for medical data

Message from the Unit Leader

Data science, such as artificial intelligence analysis, is becoming a major trend in the medical field because it can ensure objectivity and visualize hidden data relationships. However, current computer analysis requires a great deal of effort to convert and normalize the data. The AI Hospital Unit solves these problems and achieves high-level, multidimensional integrated data analysis by introducing automatic digital recording of medical data, efficient management, and the introduction of an autonomous network-type AI analysis algorithm that supports complex systems. Specifically, in addition to digitizing and automating the various sensors and medical data records in hospitals, we will construct an advanced computer network that integrally manages and processes past medical data and knowledge. We will then perform advanced analysis of the high-level and multi-dimensional dataset, and design and propose next-generation electronic medical records utilizing these technologies.

Our Research

We have been steadily studying clinical data measurement, especially high-level and multi-dimensional intra-operative measurements, data integration and analysis mainly using artificial intelligence, efficient integration with medical data and medical knowledge collected in the past and seamless integration of real and cyber data. We will continue our efforts to realize an advanced and reliable processing system for medical care and to raise the potential of the system to the unexplored level.



6

Bioinformatics Unit

Department of Medical Science Mathematics, Medical Research Institute
Professor Tsunoda Tatsuhiko

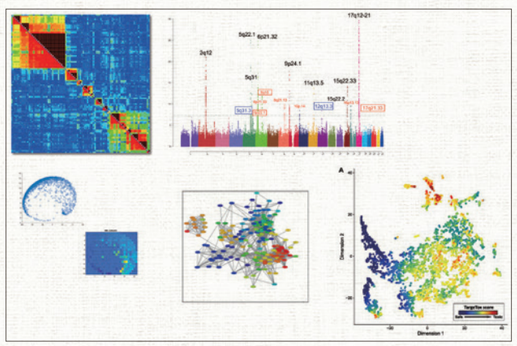
Contributing to future medicine through exploration of disease-related genes and building prediction algorithms for precision medicine

Message form the Unit Leader

The Bioinformatics Unit promotes medical and clinical big data analysis and disease-related gene identification by applying artificial intelligence (AI) and the construction of prediction algorithms for precision medicine. The Medical Innovation Consortium integrates and analyzes biomedical, molecular, and clinical data obtained from the Biobank through various innovative observation techniques developed in the Basic and Exploratory Science Division. Utilizing AI, we will also explore disease-related genes and build prediction algorithms for precision medicine. While supporting the construction of AI hospitals, we will collaborate with the Applied and Clinical Science Division in identifying the causes and therapeutic mechanisms of cancer, refractory and common diseases.

Our Research

We will propose methodologies based on mathematical models, which incorporate biostatistical analysis of data from clinical specimens, as well as molecular and cellular interactions of diseases and individuals' constitutions in order to precisely predict treatment response for each patient. With the dramatic development of experimental techniques and the collection of medical and clinical big data from the clinical specimen data collected in the Biobank, complex relationship among diseases has been considerably clarified. Optimum therapy selection and disease prevention with more precise mechanistic views for each patient will be expected. Our unit will lead the way to integrate and leverage AI such as deep learning, data science, systems medicine and mathematical simulation.




Left: Inazawa Johji
Right: Yoshida Masayuki

7

Platform for Medical Innovation (Biobank)

Bioresource Research Center, Institute of Research
Department of Cytogenetics, Medical Research Institute
Inazawa Johji

Life Science and Bioethics Research Center, Institute of Research
Yoshida Masayuki

Seeking to contribute to future medical research through the construction of the TMDU biobank infrastructure.

Message from the Unit Leader

Each of the TMDU Medical and Dental University Hospitals is a large-scale hospital with a cumulative total of approximately 500,000 patients visiting each year. The Tokyo Medical and Dental University's Bioresource Research Center (TMDU BRC) has been working on the Biobank Project with the cooperation of the entire university, providing electronic medical records to outpatients and inpatients at both hospitals since November, 2013. As of March 31, 2020, we have obtained comprehensive consent from 7,000 patients and have collected and stored 17,000 high-quality biological samples such as DNA derived from peripheral blood, saliva, serum, plasma, surgical specimen frozen samples and FFPE tissue microarrays. The Platform for Medical Innovation has the role of supplying bioresources, which is essential for promoting advanced research and integrated information analysis for the realization of AI hospitals that are being worked on by each research unit of the Medical Innovation Consortium.

Our research

At TMDU BRC, a cross-disciplinary biobank of medical and dental hospitals has been established, such as lifestyle-related diseases and various types of cancer, autoimmune diseases that are our specialty, dental pathology such as periodontal disease, oral psychosomatic disorders, oral cancer and rare diseases in the dental field. At the same time, utilizing the expertise of clinical departments, high-quality samples with highly accurate clinical data have been collected. We provide the infrastructure that is the basis for research using ICT technology such as medical big data and AI, and support research results that contribute to future medicine. In addition, AMED R&D projects centered on three major biobanks in Japan (there are 6 National Centers, Biobank Japan and the Tohoku Medical Megabank) and 4 university bioresource centers (Tokyo Medical and Dental University, Kyoto University, Tsukuba University, Okayama University) contributed to the release of the first search database for locating specimens within our biobank network in October 2019. Furthermore, at the Tokyo Medical and Dental University Life Science and Bioethics Research Center (TMDU BERC) created a "Biobank User Handbook" to promote the use of biobank samples and information. We also provide a service to help biobank users to solve ELSI- and MTA-related issues.

8

Inflammatory Bowel Disease Unit

TMDU Advanced Research Institute
Distinguished Professor Watanabe Mamoru

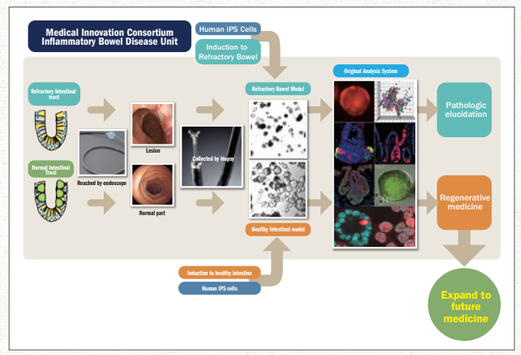
Aiming for clinical application of innovative treatments for refractory inflammatory bowel disease by development of an ex vivo intestinal model representing disease and health

Message from the Unit Leader

In the Inflammatory Bowel Disease Unit, we aim to elucidate the pathogenesis of inflammatory bowel disease and develop new drugs by establishing an ex vivo model of the inflamed human intestine, resembling actual human disease. We will also aim to establish an ex vivo model of the normal human intestine, which will not only help to overcome intestinal diseases, but will pioneer a completely novel form of medicine which seeks to control systemic homeostasis from the intestine. Our unit will work in collaboration with other units in the Medical Innovation Consortium. We will provide our ex vivo bowel models to the Information Integration Unit. We can then analyze the functions of key molecules obtained back from the Information Integration Unit, and with technological cooperation from the Basic and Exploratory Science Division, we aim for clinical application of innovative treatment for refractory inflammatory bowel disease by targeting these key molecules.

Our Research

An increasing number of patients suffer from idiopathic, chronic, and relapsing intestinal diseases, including inflammatory bowel disease. We will develop innovative treatments of the future by combining research into the pathogenesis of intractable intestinal disorders with regenerative medicine. Ultimately, our aim is to treat not only intractable intestinal diseases but also other intractable diseases, by taking control of systemic homeostasis from the intestine.




Left: Morio Tomohiro
Right: Kochi Yuta

9

Immune disorder unit

Department of Pediatrics and Developmental Biology, Graduate School of Medical and Dental Sciences
Morio Tomohiro

Department of Genomic Function and Diversity, Medical Research Institute
Kochi Yuta

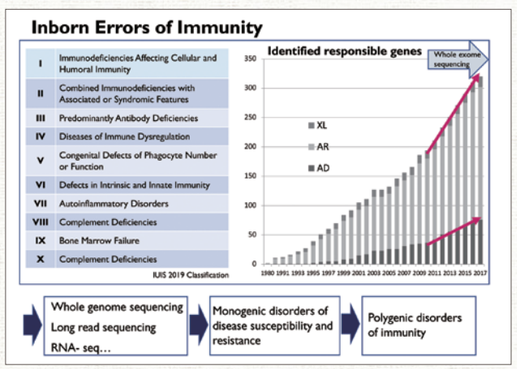
Pioneering advanced research and personalized medicine for immune diseases with big data analysis and establishment of disease models.

Message from the Unit Leader

Abnormalities in the immune system can cause a variety of disorders, including immunodeficiency, collagen and autoimmune diseases and allergic disorders. This unit aims to realize personalized genomic medicine by analyzing the etiology and pathology of a wide range of immune diseases, from children to adults, and by analyzing big data such as genomes and transcriptomes. We will establish and analyze disease models and will endeavor to establish novel measures to cure the disorders. We hope to pursue research in close collaboration with other units in this consortium, since abnormalities in the immune related molecules often lead to disorders in a wide variety of tissues and organs. We are committed to carry out cutting-edge research and to develop novel medical treatment. We are hoping to attract and work with enthusiastic students, doctors and companies, with whom we try to pioneer personalized medicine in the field of immunological diseases.

Our Research

Approximately 400 responsible genes have been identified in primary immunodeficiency diseases (PID), and this provides a good model for in-depth analysis of pathogenesis of single-gene disorder. We continue to search for disease susceptibility and also disease resistance genes in PID. In parallel, we will endeavor to decode molecular basis of polygenic immunological diseases, more complex diseases. Using “immunity” as a common language and multi-level omics analysis as an analytical tool, we hope to elucidate the pathogenesis of various diseases from the perspective of genetic background and epigenetic changes, which will eventually lead to innovative “gene therapy”. Furthermore, as a study in the post-GWAS and whole genome sequencing era, we are in a process of conducting analysis that introduced the latest statistical theories, such as deep learning. We are committed to nurture talents who can utilize multi-layered information obtained from clinical data, pathology data, genomic data, and so on for in-depth research and drug discovery.




Left: Moriyama Keiji
Right: Nakashima Tomoki

10

Maxillofacial Development Disorder Unit

Department of Maxillofacial Orthognathics, Graduate School of Medical and Dental Sciences
Moriyama Keiji

Department of Cell Signaling, Graduate School of Medical and Dental Sciences
Nakashima Tomoki

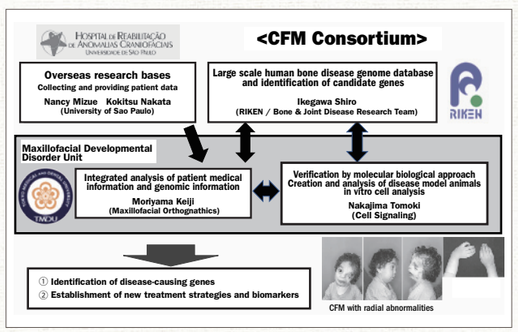
Analyzing genetic information of rare diseases that occur in the oral cavity and maxillofacial region to elucidate the pathology and develop new treatments.

Message from the Unit Leader

The oral and maxillofacial areas play an important role in communication, in addition to functions that are fundamental to human life activities such as eating, swallowing, pronunciation and respiration. The Maxillofacial Development Disorder Unit analyzes genes from various congenital disease patients with phenotypes in the oral and maxillofacial regions, identifies mutant genes and analyzes functions in vitro and in vivo. We elucidate the pathology of congenital diseases that present morphological abnormalities in the skull and maxillofacial skeleton and teeth and attempt to develop new treatments. While establishing a collaborative research platform with each unit in the Medical Innovation Consortium, we analyze genetic information on rare diseases that occur in the oral and maxillofacial regions and create model animals reflecting the genetic information of human disease by applying genome editing technology. Thus, we will promote translational research for clinical applications.

Our Research

Future research includes organizing an international research network to analyze and integrate medical information and DNA samples from patients with craniofacial microsomia (CFM) accompanied with radial abnormalities, and to identify disease candidate genes through comprehensive genomic analysis. We aim to create drug seeds by identifying disease onset signals by analyzing model mice. Furthermore, we will contribute to improve the quality of medical care by establishing biomarkers for this disease and laying the foundation for new diagnosis, prevention and treatment strategies.




Left: Harada Hiroyuki
Right: Asakage Takahiro

11

Rare Tumor Unit

Department of Oral and Maxillofacial Surgery, Graduate School of Medical and Dental Sciences
Harada Hiroyuki

Department of Head and Neck Surgery, Graduate School of Medical and Dental Sciences
Asakage Takahiro

Aiming to prevent head and neck cancer and develop new treatments based on our extensive medical and dental experience

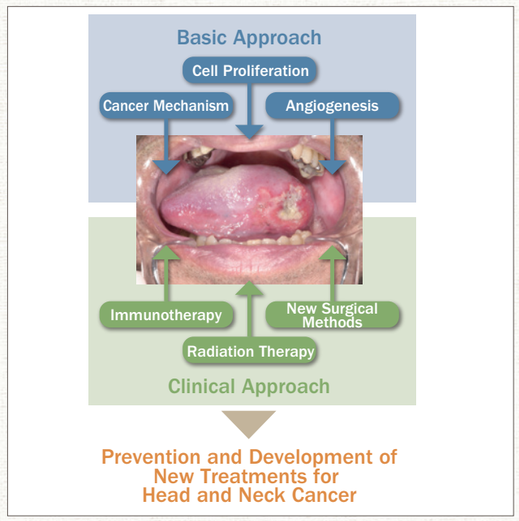
Message from the Unit Leader

Head and neck cancer is a refractory disease for which no causative gene or malignant factor has yet been identified. In addition, the number of cases is low, and according to statistics in Japan in 2014, there were approximately 24,000 patients with oral, pharyngeal and laryngeal cancers.
The Rare Tumor Unit aims at prevention and the development of new treatments for head and neck cancer.
Our medical hospital and dental hospital were established side by side with the number of outpatients who visit totaling 500,000. Utilizing these abundant cases we aim to create a large patient database and develop diversified new therapies that simultaneously target the cancer cells and tumor blood vessels.
Moreover, we will investigate various types of treatment combining these new therapies with immunotherapy and radiation therapy. We also aim to develop new treatments, in clinical settings, and minimally invasive surgical methods.

Our Research

In recent years, morbidity and mortality rates of head and neck cancer have been increasing year by year in Japan due to the aging population. We would like to take a new strategy for head and neck cancer, from basic research to elucidate the mechanisms of growth, invasion, and metastasis of cancer, and from clinical aspects such as the development of new treatments.

Rare Tumor Unit




Left: Ikeda Sadakatsu
Right: Tateishi Ukihide

12

Cancer Therapeutic Unit

Precision Cancer Medicine, Medical Hospital
Ikeda Sadakatsu

Department of Diagnostic Radiology and Nuclear Medicine, Graduate School of Medical and Dental Sciences
Tateishi Ukihide

Developing a foundation for creating real world evidence, and contributing to the development of data science

Message from the Unit Leader

The aim of the Cancer Therapeutic Unit is to build real world evidence in the oncology area. Real-world evidence is evidence generated based on databases obtained from real clinical patient groups, not from patient groups selected in clinical trials. For rare cancers, regulatory approval is granted only with real-world evidence, and this is receiving a great deal of attention now.

The Medical Innovation Consortium set up by Tokyo Medical and Dental University aims to develop genomic medicine and AI systems that utilize big data, and to implement them in society. As a member of this consortium, our unit seeks to develop the necessary foundation for creating real world evidence and contribute to the development of data science fields such as precision medicine and AI systems.

Our Research

Real-world evidence is expected to be used in a variety of ways, including the development of new diagnostic and therapeutic methods, the creation of guidelines, and with an application to clinical trials.
In the future of medical treatment, where the aging of society is expected to accelerate and the patient background in actual clinical practice is expected to become more and more diversified, the construction of real-world evidence is indispensable. This research aims to be the world’s leading model case.
The real-world database built by this unit is supposed to be used by research institutions, pharmaceutical companies, and also diagnostic drug manufacturers to be utilized as effectively as possible.



Left: Tanaka Toshihiro
Middle: Furukawa Tetsushi
Right: Sasano Tetsuo

13

Cardiovascular Disease Unit

ioresource Research Center, Institute of Research
Tanaka Toshihiro

Department of Bio-information Pharmacology, Medical Research Institute
Furukawa Tetsushi

Department of Cardiovascular Medicine, Graduate School of Medical and Dental Sciences
Sasano Tetsuo

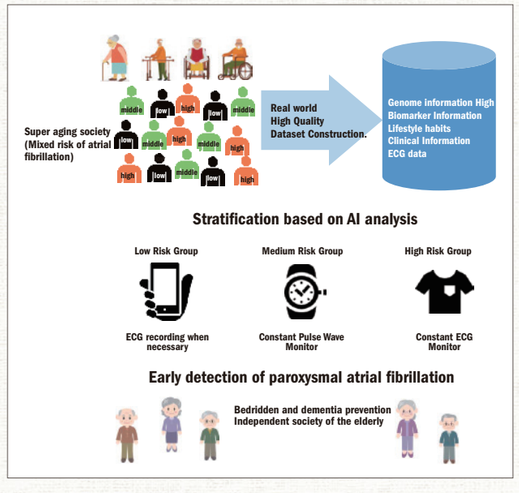
New light for the super-aged society through the development of future medicine in the cardiovascular field.

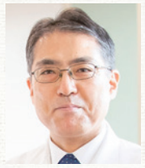
Message from the Unit Leader

Ultimate goal of our Cardiovascular Disease Unit is to realize preemptive medicine for cardiovascular diseases by comprehensively analyzing multi-dimensional information consisting of genomic information, gene expression information, and clinical information including ECG data. With the precious supports from the Platform for Medical Innovation in Medical Innovation Consortium, all the three members of our unit, who have a common footing in cardiovascular diseases, will utilize their respective strengths sharing their roles and by working closely together on their clinical and research projects.

Our Research

The principle focus of our research at present is to develop an early detection system for paroxysmal atrial fibrillation (paf) as the main target cardiovascular disease. One of the most serious problems in the super-aged society is the increasing number of bedridden elderly people and 20% of them are thought to be basically suffering from atrial fibrillation. By our early detection system for paf, we can identify high-risk group and through preemptive therapy, we can significantly improve their QOL and also reduce the number of bedridden patients.






Above left: Ishikawa Kinya
Upper right: Takahashi Hiromitsu
Lower left: Minakuchi Shunsuke
Lower right: Tohara Haruka

14

Healthy Aging Unit

Center for Personalized Medicine for Healthy Aging, Medical Hospital
Ishikawa Kinya

Pharmacy, Medical Hospital
Takahashi Hiromitsu

Department of Gerodontology and Oral Rehabilitation, Graduate School of Medical and Dental Sciences
Minakuchi Shunsuke

Department of Dysphagia Rehabilitation, Graduate School of Medical and Dental Sciences
Tohara Haruka

Offering total medical care that contributes to the realization of a long-lived and healthy society by analyzing genomes, lifestyles and environmental factors etc.

Message from the Unit Leader

The Healthy Aging Unit aims to implement new medical practice to realize a society that can maintain total health based on personal genomic information, age and environmental factors. Specifically, we will work to realize new medical treatments, developed through joint research with other organizations inside and outside of our university to find better coping strategies to prevent common conditions in diseases such as cancer, diabetes, sarcopenia caused by aging, oral and cognitive decline.

Our Research

Our unit consists of 4 specialists from medicine, dentistry and pharmacy. As one of the Units in the Applied and Clinical Science Division, our study aims to develop a total medical care to attain healthy aging and longevity. For example, we will use genetic testing developed in the Center for Personalized Medicine for Healthy Aging to assess genetic risk factors for common diseases. We need to update disease risk information by incorporating newly identified genetic markers and identify risk assessment methods every year. These will be done in cooperation with the Bio Informatics Unit in the Information Integration Core Unit. Using individual genetic risks, life style and clinical data, we seek to propose new prevention methods for diabetes, and then, the themes would be expanded. We will also start a special program to evaluate oral and swallowing functions, and study how maintaining these would improve people's cognitive functions and social activities. Expecting our future medical advance, one of our goals is developing an efficient tool using artificial intelligence for instructing patients for their better understanding of their health status, nutritional management and exercise.

TMDU 東京医科歯科大学

Life Course Research Consortium Secretariat

Administrative Office, Institute of Research, Tokyo Medical and Dental University (TMDU)
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URL:http://www.tmd.ac.jp/labs/research