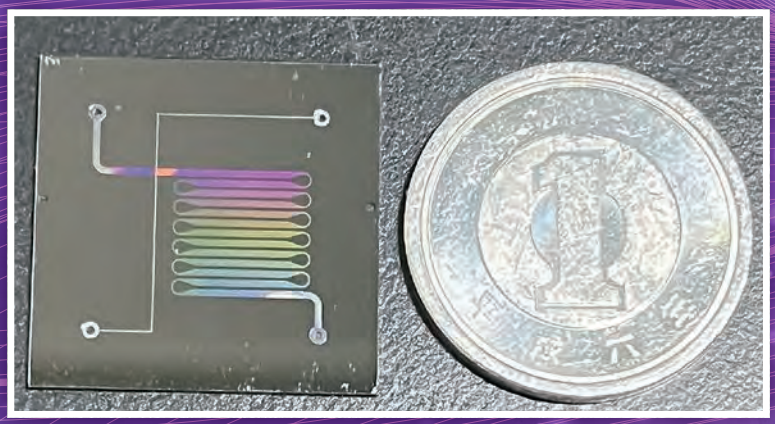
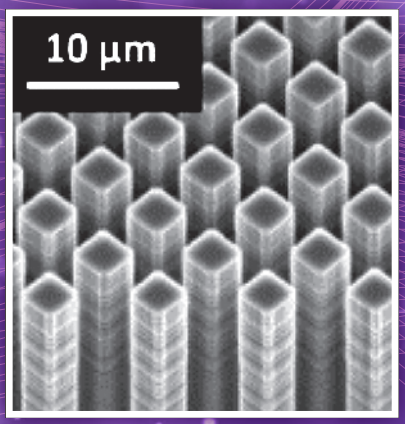
The University of Tokyo

Graduate School of Pharmaceutical Sciences
Faculty of Pharmaceutical Sciences





2025

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Message from the Dean

The University of Tokyo's Faculty of Pharmaceutical Sciences celebrated its 150th anniversary last year in 2023, having its origins in 1873 with the five-year pharmaceutical program in the First University District Medical School, the precursor of the University of Tokyo Faculty of Medicine. In 1958, the Faculty of Pharmaceutical Sciences of the University of Tokyo became independent from the Faculty of Medicine and took a new step forward. In 2006, the Faculty took its current form with Department of Pharmaceutical Sciences (4-year program) and Department of Pharmacy (6-year program).

The Graduate School of Pharmaceutical Sciences conducts state-of-the-art research and education, and has been operating as an organization consisting of the Doctor of Pharmacy program for graduates of 6-year universities such as the Department of Pharmacy, and the Master's and Doctoral programs for graduates of 4-year universities such as the Department of Pharmaceutical Sciences, with many students from other universities and other departments.

The Faculty and Graduate School of Pharmaceutical Sciences is one of the smallest departments in the University of Tokyo, consisting of about 800 members. I am one of the graduates of this department, and I remember particularly fondly the words I heard in many of my undergraduate classes: "Now that you have entered the Faculty of Pharmaceutical Sciences, you should always think about serving the health of the people". I heard this phrase from so many professors that it rubbed this idea into my core. As a result, it has become a compass-like teaching that appears many times when I am unsure of the direction to take in my research as a researcher.

In order to overcome diseases, it is necessary to combine research in a wide range of fields, including not only basic research to clarify the causes of the disease, and to design and develop corresponding drugs, but also applied research in clinical and social pharmacy to ensure that the developed drugs can be used safely by patients and to create a highly sustainable system for the nation. In recent years, many "drugs" based on new principles have emerged; small organic molecules which has a history of over 100 years, biologics based on antibodies, nucleic acid drugs such as mRNA vaccines, and very recent cell-based medicine using genome editing technology. There is an increasing need to seamlessly advance research across multiple fields. Since its opening, our department has had a wide variety of laboratories conducting cutting-edge research in biological, chemical, physical, and clinical sciences, and our greatest strength is the ability to conduct cross-disciplinary research closely within a single department. As an important department that enhances the value of the university "serving the health of the nation," we will continue to strongly promote our unique research and education.

URANO Yasuteru
Dean
Graduate School of Pharmaceutical Sciences
Faculty of Pharmaceutical Sciences

History

1873 ► Department of Pharmaceutical Manufacturing was established in Daiichi-Daigaku-Ku Igakko (The First University District Medical School) in Kanda Izumicho,Tokyo.

1874 ► Daiichi-Daigaku-Ku Igakko was renamed as Tokyo-Igakko (Tokyo Medical School).

1876 ► Tokyo-Igakko was moved to Hongo, Tokyo.

1877 ► Tokyo Daigaku,
The University of Tokyo was established.
Tokyo-Igakko was renamed as the University of Tokyo Faculty of Medicine.
The organization of pharmaceutical education began with the establishment of Pharmaceutical Institute (later Department of Pharmaceutical Manufacturing in the Faculty of Medicine). For the first 10 years, instruction was given by foreigners and in particular a Dutch chemist Dr. J. E. Eijkman. He left a large amount of fine work in the study of components of various domestic medicinal plants.

1886 ► The University of Tokyo was renamed as Imperial University and the name of the Department of Pharmaceutical Manufacturing in the Faculty of Medicine was changed to the Department of Pharmacy in the Imperial University Medical College.
Japanese who had returned from studies in Germany took over the education of students, carried out valuable investigations of their own, and also established the ground for pharmaceutical organic chemistry in Japan.

1897 ► The Imperial University was renamed as Tokyo Imperial University.

1919 ► A faculty system was introduced and renaming the Department of Pharmacy in the Medical College as the Department of Pharmacy in the Faculty of Medicine, Tokyo Imperial University.

1947 ► Tokyo Imperial University was renamed as The University of Tokyo.

1949 ► The University of Tokyo was established under the new system (Junior division for the first two years and Senior Division for the 3rd and the 4th years).

1953 ► The Graduate School of Chemistry-related was established (Master's Program in the field of Pharmaceutical Sciences).

1955 ► Doctoral Program in the field of Pharmaceutical Sciences was added.

1958 ► The Department of Pharmacy separated from the Faculty of Medicine and became an independent faculty as the Department of Pharmaceutical Sciences, the Faculty of Pharmaceutical Sciences.

1960 ► The Department of Pharmaceutical Technochemistry was established.

1965 ► The Graduate School of Pharmaceutical Sciences, The University of Tokyo was established.
(Department of Pharmaceutical Sciences and Department of Pharmaceutical Technochemistry)

1966 ► The Research Institute for Chemical Hazards was established.

1973 ► The Experimental Station for Medicinal Plant Studies was established.

1976 ► The Research Institute for Chemical Hazards was abolished, and instead the Department of Pharmaceutical Life-Science was established.

1991 ► Two departments were unified into the Department of Pharmaceutical Sciences.

1997 ► The graduate school was reorganized along with the new system, "Graduate School Priority System" and reformed into three Departments, that is Pharmaceutical Chemistry, Pharmaceutical Biology, and Pharmaceutical Technology.
Although the Faculty's emphasis of education is shifted from the Undergraduate Program to the Graduate Program, most of the faculty members also continue undergraduate education.

2000 ► Clinical Pharmacy Course was established in the Master's Program.

2004 ► Pharmaceutical Sciences Research Building was constructed.

2006 ► Following the revision of the School Education Act, the Faculty of Pharmaceutical Sciences started a new program with Department of Pharmaceutical Sciences (4-year program) and Department of Pharmacy (6-year program).

2008 ► Department of Integrated Pharmaceutical Sciences was added to the Graduate School, which consists of total 4 departments.

2010 ► The former 4 departments in the Master's Program were abolished and the Department of Pharmaceutical Sciences was established.
Clinical Pharmacy Course was abolished.

2012 ► The former 4 departments in the Doctoral Program were abolished.
Department of Pharmaceutical Sciences and Department of Pharmacy were established in the Doctoral Program.
Dual Speciality Course on Pharmacist Education was established.

Facts & Figures

Number of Academic and Administrative Staff

As of July 1, 2024

Academic Staff									Researcher	Administrative Staff			Total
Professors	Associate professors	Lecturers	Assistant professors	Spec. appt. professors	Spec. appt. assoc. prof.	Spec. appt. lecturers	Spec. appt. assist.prof.	Subtotal		Office	Technical	Subtotal	
17	15	5	27	3	7	5	7	86	24	21	1	22	132

Number of Students

As of May 1, 2024

	Undergraduates					Graduates												
						Master's Program			Doctoral Program (Pharmaceutical Sciences)				Doctoral Program (Pharmacy)					
	3rd year	4th year	5th year	6th year	Total	1st year	2nd year	Subtotal	1st year	2nd year	3rd year	Subtotal	1st year	2nd year	3rd year	4th year	Subtotal	Total
Numbers	84 (21)	88 (31)	8 (2)	9 (4)	189 (58)	81 (23)	91 (21)	172 (44)	42 (17)	36 (12)	64 (22)	142 (51)	5 (3)	8 (1)	8 (5)	9 (5)	30 (14)	344 (109)

( ) Female students

Number of Research Students, etc.

Year	2020	2021	2022	2023	2024
Undergraduate-level			1	1	1
Graduate-level	14	6	4	6	4
Undergraduate auditor	2	1	1	2	0
Subtotal	16	7	6	9	5
Commissioned researcher	4	3	1	0	0
Total	20	10	7	9	5

As of May 1

Number of International Students

As of May 1, 2024

Countries and Regions	Undergraduate		Graduate School			Total
	Undergraduate	Research Student	Master's	Doctoral	Research Student	
Syria				1		1
China	6	1	16	24(1)	3	50(1)
Taiwan			1	1		2
Canada				1(1)		1(1)
United States				1		1
Total	6	1	17	28(2)	3	55(2)

( ) Numbers indicate MEXT Scholarship Students

Number of Doctoral Degree Holders

Year	2019	2020	2021	2022	2023	Cumulative Total
Program Doctorate	52	45	41	48	41	2,099
Thesis Doctorate	16	13	8	3	3	1,578

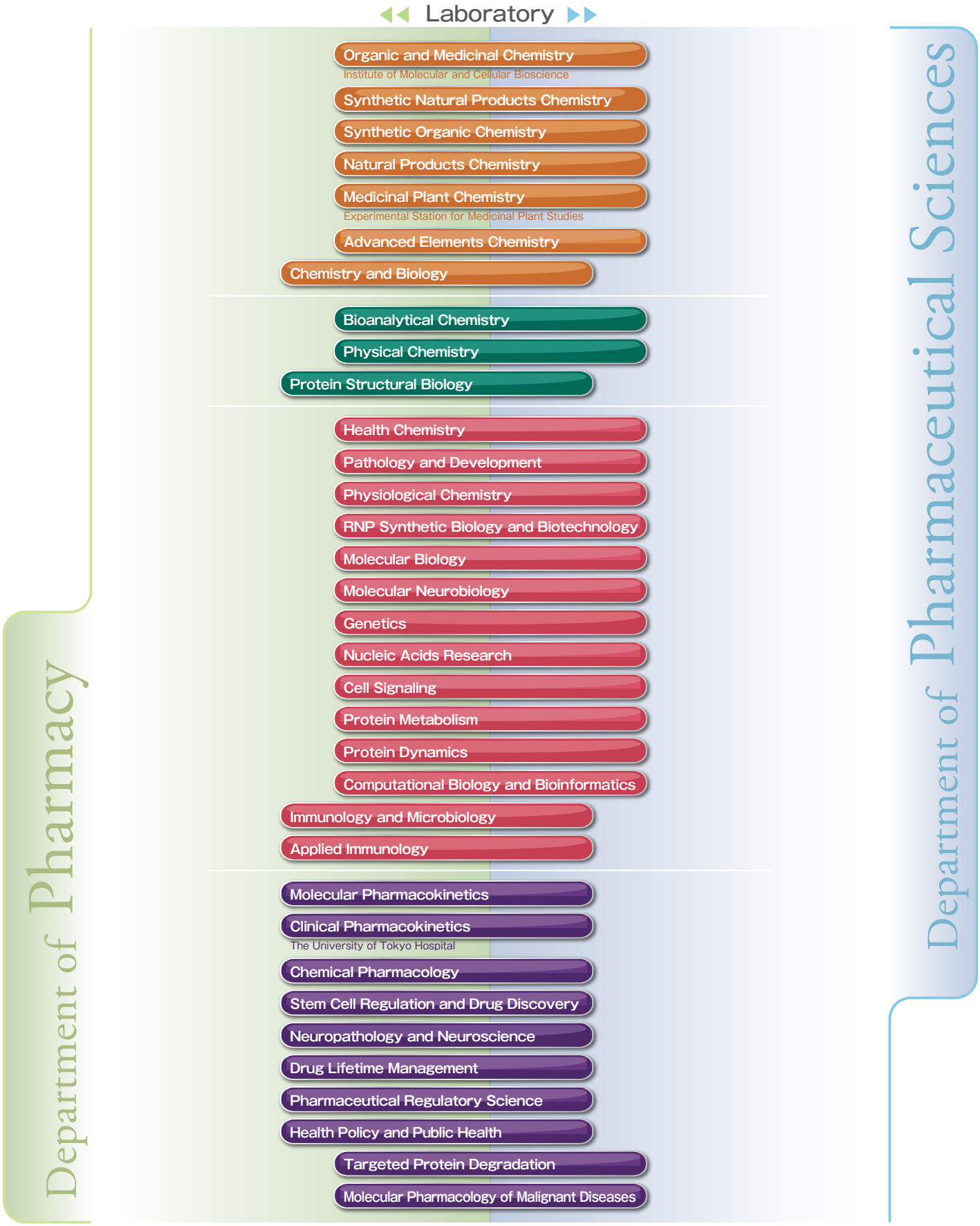
Thesis Doctorate (Old System) : 571

Current Status of Graduates

	Undergraduate-level Graduates										Graduate School Graduates									
											Master's program					Doctoral program				
Academic Year	2019		2020		2021		2022		2023		2019	2020	2021	2022	2023	2019	2020	2021	2022	2023
	◎	△	◎	△	◎	△	◎	△	◎	△										
Pharmaceutical Company	1	4		3		3		3		2	13	12	16	17	15	21	22	19	29	14
Chemical industry companies		1				1					10	5	2	3	3	1	3	1		2
Financial, insurance, & trading companies		2	2				1		1	1	3	3	5	4	2					
Education, government, research institutes, etc.				1	1	2	2		1	2	3	6	6	1	1	15	14	11	12	12
Others	1	1	3	3	2		1	2	2	3	13	16	12	16	5	3	2	4	5	9
Subtotal (Number employed)	2	8	5	7	3	6	4	5	4	8	42	42	41	41	42	40	41	35	46	37
Seeking for further education (Graduate school)	66		70	2	71	3	72	1	70	2	44	36	40	36	35					
Research student, other undergraduate course, etc.	1		2		4	1			2		1	2	3	2	3					
Study abroad											2			1						
JSPS special researcher, etc.																8	2	4	1	
Others		1	3				1	2	4		2	3	2	3	2	4			1	2
Subtotal	67	1	75	2	75	4	73	3	76	2	49	41	45	42	40	12	2	4	2	2
Total (Number graduating/completing program)	69	9	80	9	78	10	77	8	80	10	91	83	86	83	82	52	43	39	48	39

◎ Pharmaceutical Sciences
△ Pharmacy

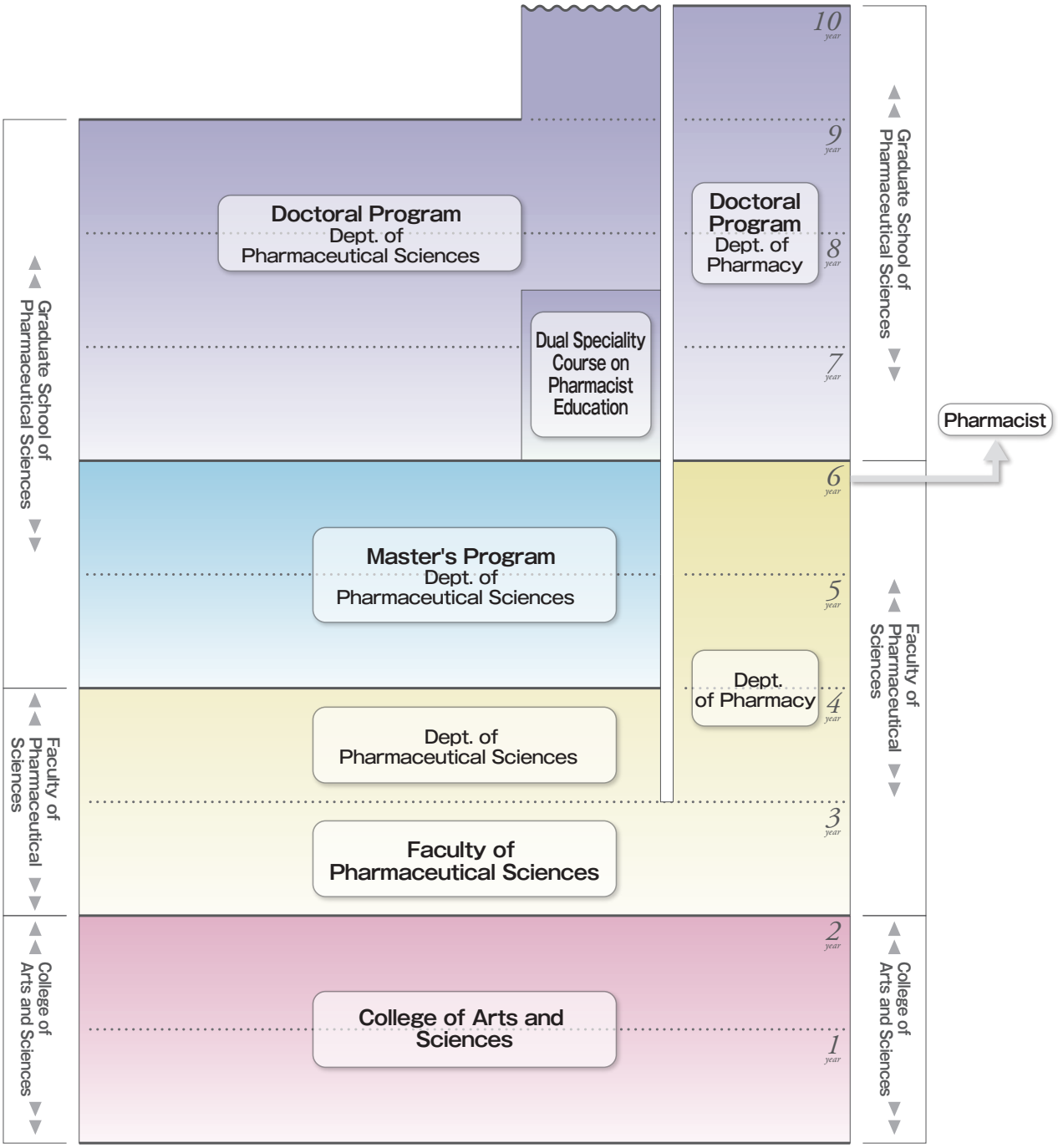
Organization Chart



Pharmaceutical Sciences Education Program

Pharmaceutical sciences is an academic field that covers development of pharmaceuticals and their applications. The field encompasses fundamental, life-related substances and their interactions with life; using organic chemistry, physical chemistry, and biochemistry as a base, upon which is built a wide range of research fields, including interdisciplinary areas. With these parallel 6-year and 4-year programs, the Faculty of Pharmaceutical Sciences not only provides traditional training in basic research for drug discovery but also offers some courses in advanced training for pharmacists. (Graduates of the Department of Pharmacy are qualified for the national examination for pharmacists.) No differentiation is made between the Departments of Pharmacy and Pharmaceutical Sciences from the College of Arts and Sciences until entering higher education, allowing students to gain an ample understanding of research content before deciding between the two departments in their fourth year.

Our doctoral program in the Department of Pharmaceutical Sciences, established in 2012, also provides a Dual Specialty Course on Pharmacist Education allowing students to be qualified for the national examination for pharmacists. (This is provided for students who enter the University of Tokyo by the 2017 school year and graduate from the Department of Pharmaceutical Sciences, Faculty of Pharmaceutical Scineces.)



Syllabus | Faculty of Pharmaceutical Sciences

Department of Pharmaceutical Sciences

Four-year program

Taking on the goal of the previous Department of Pharmacy curriculum, the Department aims to educate high-quality researchers, focusing on developing personnel in the fields of drug discovery and basic life-science research.
With a capacity of 90 percent of all students, the Department offers graduates a two-year master's program, then to a three-year doctoral program. The curriculum is nearly identical to the Department of Pharmacy until the third year, allowing students to experience on-the-ground medical treatment even if they intend to pursue research.

Department of Pharmacy

Six-year program

In response to the advancement of medical care, the purpose of the establishment of this department is to train and develop high-quality pharmacists.
One large difference from the Department of Pharmaceutical Sciences is that the program includes six-month practical hospital/pharmacy training. The Department's capacity is 10 percent of all students, providing high-quality pharmacy education to a small number of students, aiming to create personnel who will be able to lead this field. Six-year pharmacy departments are well over capacity across all of Japan; to avoid disruption, the University of Tokyo's Faculty of Pharmacy will collaborate with the University of Tokyo Hospital and local pharmacies in order to provide smooth, uninterrupted practical training.

Faculty Curriculum

Lectures and practicums lie in the center of the education at the Faculty of Pharmaceutical Sciences. They are provided to students in order for them to acquire the broad knowledge and the perspectives of pharmacists, as well as to have a clear view when they decide which field of pharmacy they should enter as specialists. One can say that lectures provided to faculty students are the essence of pharmaceutical sciences. Furthermore, reflecting the diversity in research areas in the Faculty of Pharmaceutical Sciences, the pharmacy practicums encompass a wide range of training areas. It is efficiently designed in a way that students will be able to put organic chemistry, physical chemistry, biochemistry and clinical pharmacy into practice. When students enter into their fourth year, each student will be allocated to a class of his/her own choice and will have opportunities to get hands-on experience in the cutting-edge pharmacy through the participation in research projects.

Department of Pharmaceutical Sciences 80 credits
(Compulsory: 62 credits, Elective: 18 credits or more)

Department of Pharmacy 120 credits
(Compulsory: 109 credits, Elective: 11 credits or more)

④ = Compulsory 4 = Elective for Department of Pharmaceutical Sciences
⑥ = Compulsory 6 =Elective for Department of Pharmacy

2nd year: Autumn 1

*not included as the number of credits for graduation requirements

Course Title	Credits	Course Outline	
Analytical Chemistry I	1	This course covers chemical equilibrium, qualitative and quantitative chemical analysis, and instrumental analysis.	④⑥
Organic Chemistry II	1	Fundamental organic chemistry which contains Acid and Base, Nucleophilic Substitution and Elimination Reactions.	④⑥
Molecular Biology	1	Students will lean the fundamentals of molecular biology to understand the life sciences.	④⑥
Cell Biology	1	Students will learn the fundamentals of cell biology to understand the life sciences.	④⑥
Radiation Chemistry	1	Lectures pertaining to the fundamentals, applications and biological effects of isotopes and radiation (which are indispensable for the fields of medicine and pharmaceutical sciences) will be given.	④⑥

Organic Chemistry Ⅰ	1	Students will learn the fundamentals such as stereochemistry, structural chemistry, reduction and oxidation.	④⑥
Physical Chemistry Ⅱ	1	Lectures are aimed to allow students to understand important concept of thermodynamics, acquire the physicochemical perspectives and learn methods that are important in pharmaceutical sciences.	④⑥
Physiological Anatomy of Human Body	1	Students will learn the structures and functions of each organ (i.e., anatomy and physiology) as the basic knowledge for them to understand pharmacotherapy and pathophysiology.	④⑥
Physical Chemistry Ⅰ	1	Students will aim to acquire the physiochemical concept by understanding quantum chemistry and spectroscopy.	④⑥
Introduction to Pharmaceutical Sciences	1	The outline, history and the future vision of pharmaceutical sciences will be explained in an easy to understand manner, allowing students to think about the relationship between pharmaceutical sciences and society in terms of industry and medical care. Moreover, students will learn some of the latest studies in the field of pharmaceutical sciences.	④⑥
Biostatistics	1	Students will receive lectures and practicums regarding statistical methods and experimental methods used for drug evaluations.	４６

2nd year: Autumn 2

Course Title	Credits	Course Outline	
Organic Chemistry Ⅳ	1	Students will learn the typical reaction of carbonyl compounds.	④⑥
Analytical Chemistry Ⅱ	1	This course covers qualitative chemical analysis, instrumental analysis, separation sciences, and analytical methods in clinical chemistry.	④⑥
Physical Chemistry Ⅲ	1	Students will learn the hierarchy of protein structure, various intermolecular interactions, enzyme structures and the theory of enzyme reaction.	④⑥
Microbiology and Chemotherapy	1	The basic biochemical and genetic methods will be outlined using microorganisms such as E-coli as materials. Students will also learn the mechanisms of action of antibiotics.	４⑥
Molecular Embryology	1	Developmental genetics will be outlined, and their application to drug discovery science will be explained.	４６
Pharmacology Ⅰ	1	Students will learn the fundamentals of pharmacology in order to understand actions of drugs that affect the autonomic nervous system and the circulatory system.	④⑥
Functional Biology	1	Students will learn the fundamental of higher-order function cell to understand life sciences.	④⑥
Pathology	1	Pathological changes of cells and tissues, classification and treatment of diseases will be explained.	④⑥
Pharmacokinetics	1	To achieve proper use of the pharmaceutical products, and contribute to the drug development, the lecture explains the pharmacokinetics, a theoretical scheme for quantitatively understanding the disposition of drugs in the body, and describes the factors that cause inter-individual variation in drug disposition and response.	④⑥
Organic Chemistry Ⅲ	1	Students will learn chemical reaction theories such as substitution reaction, radical reaction, reduction/oxidation reaction and addition reaction, as well as the organic electron theory which is important for understanding chemical reaction.	④⑥
Drug Discovery and Development	1	Researchers who have succeeded in pharmaceutical companies will be invited to the class to talk about the current situation and future perspectives of drug discovery.	④*

3rd year: Spring 1

Course Title	Credits	Course Outline	
Interactive Organic Chemistry	1	The fundamentals of organic chemistry by practicum and group discussion will be outlined and reviewed.	4 6
Molecular Structural Bio-Sciences	1	The fundamentals and actual examples of structural analysis of biomaterials will be explained using the nuclear magnetic resonance method or the X-ray crystal structure analysis method.	4 *
Pharmacology Ⅱ	1	Students will understand drug actions that affect the central nervous system, endocrine system and immune system by learning the physical function and mental function.	④⑥
Immunology	1	Students will understand the immune system and the immune response to infections and allergies in the level of dynamic behaviors of tissues, cells and molecules.	4 6
Laboratory Works of Pharmaceutical Sciences Ⅰ	5	To aquire fundamental experimental operations, and experience basic organic reactions and some practical synthesis of organic compounds.	④⑥
Laboratory Works of Pharmaceutical Sciences Ⅱ	3	Basic experiments in bio-organic chemistry (extraction, isolation, identification and biosynthesis of natural organic compounds; the fundamentals and applications of the extinction method and the fluorescence method; learning high-speed liquid chromatography; drug metabolism reaction experiments; enzyme kinetics; visits to the Experimental Station for Medicinal Plant Studies)	④⑥

3rd year: Spring 2

Course Title	Credits	Course Outline	
Organic Chemistry Ⅴ	1	Students will learn the chemistry of natural organic compounds having biological activity, as well as the fundamentals of biosynthesis.	④⑥
Organic Chemistry Ⅵ	1	This is a class for learning metabolism of medical drugs, fundamentals of drug development, chemistry of carbohydrates and synthetic polymers. Enzyme induction, polymorphism, metabolic reactions, enzymes, reaction mechanisms of P-450 will be explained in molecular level. The fundamentals of drug development such as molecular design, chemical libraries and lead compounds, and polymers such as carbohydrates and synthetic polymers will be also explained.	④⑥
Health Chemistry	1	The impact of environmental materials toward organisms will be explained.	4 ⑥
Cancer Biology and Biopharmaceutical	1	Lectures pertaining to biology of cancer, clinic and treatment of cancer especially pharmacotherapy will be given.	4 6
Drug Informatics	1	Methods for constructing novel drug information effective in real-life medical care situations will be explained. These methods include methodology to standardize drug information and quantify drug reactions.	4 ⑥
Laboratory Works of Pharmaceutical Sciences Ⅲ	3	Basic experiments in physico-chemistry (acquisition and analysis of drug disposition kinetic data, physicochemical analyses of proteins and structural biological analyses of protein interactions, analyses of molecular structures and understanding of the 3D structure using the X-ray diffration)	④⑥

3rd year: Autumn 1

Course Title	Credits	Course Outline	
Molecular Physiological Chemistry	1	The latest knowledge regarding acceptance and transduction of extracellular signaling molecules such as hormones will be explained.	4 6
Clinical Pharmacy	1	Aiming for understanding pharmaceutical sciences in medical care, the following subjects will be outlined: the medical system; drug development, and its efficacy and safety; diseases and their therapeutic agents; medical care and pharmacists; fundamentals of drug compounding/formulation; drug administration guidance and drug history management; and clinical pharmacokinetics.	④⑥
Medicinal Chemistry Ⅱ	1	Students will learn organic chemistry of biologically active substances and pharmaceutical molecules, as well as that of molecular design.	④ 6
Metabolism and Disease	1	Metabolism and various diseases caused by metabolic failure will be explained.	4 ⑥
Medicinal Chemistry Ⅰ	1	Lectures pertaining to advanced level of organic synthetic chemistry, transition metal chemistry, heterocyclic ring and natural product synthetic chemistry will be given.	④ 6

Special Lectures on Pharmaceutical Sciences Ⅰ	1	Students will learn the ethics, communication skills, etc. necessary for life-related professionals.	4 ⑥
Special Laboratory Works of Pharmaceutical Sciences Ⅰ	1	Through the determination of genetic polymorphism of drug metabolizing enzymes, students will learn the significance and interpretation method of genetic polymorphism in consideration of future medical care. Furthermore, they will learn the appropriate process of research on human genome and genes, as well as the importance of compliance of ethical guidelines.	④⑥
Laboratory Works of Pharmaceutical Sciences Ⅳ	5	(1) Experiments in physiological chemistry: Regulation of blood sugar levels (physiological/metabolic experiments); proliferative response of culture cells (isotope experiments) (2) Experiments in molecular biology: Basic experiments in molecular biology using culture cells (3) Experiments in genetics: Basic experiments in molecular genetics using animal models (4) Experiments with microorganisms: Basic experiments with microorganisms and antibiotics; basic experiments on gene manipulation	④⑥

3rd year: Autumn 2

Course Title	Credits	Course Outline	
Medicinal Chemistry Ⅲ	1	In lectures on organic chemistry (which is essential for drug development), the fundamentals of organic reaction chemistry, and chemistry of bio-related reaction and physiologically active substances will be explained. The fundamentals of chemical biology especially about photo-functional molecules will be explained.	④ *
Natural Product Chemistry	1	Students will learn the origins, ingredients, evaluations and applications of natural drugs (primarily those described in the Pharmacopoeia of Japan) as well as plant biotechnology.	4 ⑥
Pharmaceutics	1	In addition to drug delivery system, students will learn dosage forms, design/manufacturing methods and usability evaluation methods.	4 ⑥
Biophysics	1	Students will learn about the hierarchic structure of an organism (from molecules to an individual) as well as each level of the hierarchy.	4 6
Toxicological Pharmacology	1	Scientific proof of drug safety will be explained from the molecular biological, cell biological, pathophysiological and sociological perspectives, mainly focusing on the stress response of organisms.	4 ⑥
Laboratory Works of Pharmaceutical Sciences Ⅴ	3	Basic experiments in pharmacology using whole animals and organs, observation of pathology specimens, histochemistry, analysis of the mechanism of cell signaling, genetic experiments using budding yeast	④⑥
Special Lectures on Pharmaceutical Sciences Ⅱ	1	Students will learn the ethics, communication skills, etc. necessary for life-related professionals.	4 ⑥

4th year: Spring 1

Course Title	Credits	Course Outline	
Public Health	1	Students will learn the fundamentals of the general idea of health, epidemiology, pharmacoepidemiology and pharmacoeconomics.	4 ⑥
Clinical Pharmacology	1	Students will learn the fundamentals of pharmacotherapy and clinical development with the clinical perspectives from pathophysiology through pharmacokinetics, clinical pharmacology to clinical testing. Students will also learn diagnoses, treatment and clinical trials in real-life situations from experts in the departments of clinicopathology, internal medicine, surgery and radiology to understand the disease “cancer.”	*⑥
Pharmaceutical Affairs Law and Patent Law	1	Students will learn the basics of the Patent Act and pharmacy-related laws and regulations.	4 ⑥
Pharmaceutical Regulatory Science	1	Drug development and efficacy evaluation methods, domestic and overseas drug development environment and guidelines will be explained using specific examples.	4 ⑥

4th year (Department of Pharmaceutical Sciences)

Course Title	Credits	Course Outline	
Special Laboratory Works of Pharmaceutical Sciences	20	Students will be allocated to a laboratory in the Faculty of Pharmaceutical Sciences (including the Dept. of Pharmacy, the Univ. of Tokyo Hospital), and participate in frontline pharmaceutical research.	④

4th～6th year (Department of Pharmacy)

Course Title	Credits	Course Outline	
Laboratory Works of Pharmaceutical Sciences Ⅵ	20	Students will be assigned to a laboratory in the Faculty of Pharmaceutical Sciences and participate in frontline pharmaceutical research. They will also independently conduct research and study for practical hospital/pharmacy training.	⑥
Practice for Clinical Pharmacy Ⅱ	4	To work as a pharmacist in the clinical practice of hospital and pharmacy, students will acquire basic requirements for drug treatment and team approach medical care/regional medical care from perspective of patients and living people. For Practice for Clinical Pharmacy Ⅲ・Ⅳ, students will acquire basic knowledge, skills and attitude required for fulfilling pharmacists' duties within the University, such as preparation and formulation of drugs and drug administration guidance.	⑥
Practice for Clinical Pharmacy Ⅲ	10	In order to understand duties and responsibilities of hospital pharmacists and be able to participate in team approach to medical care, students will acquire basic knowledge, skills and attitude required for fulfilling pharmacists' duties, such as preparation and formulation of drugs and drug administration guidance.	⑥
Practice for Clinical Pharmacy Ⅳ	10	In order to understand social roles and responsibilities of pharmacies and be able to participate in medical care in their local communities, students will acquire basic knowledge and skills regarding, and attitude toward, pharmacy services under health insurance, drug supply and management, information provision, health examinations and relationship with medical institutes and local communities.	⑥
Special Laboratory Works of Pharmaceutical Sciences	20	Students will be allocated to a laboratory in the Faculty of Pharmaceutical Sciences (incl. Dept. of Pharmacy, the Univ. of Tokyo Hospital) and participate in frontline pharmaceutical research.	⑥

Syllabus | Graduate School of Pharmaceutical Sciences

Graduate School of Pharmaceutical Sciences

Pharmaceutical education experienced major changes beginning with students entering in the 2006 school year. As a result, the University of Tokyo's Faculty of Pharmaceutical Sciences established two new departments: The Department of Pharmaceutical Sciences, a four-year program designed to train researchers in basic drug discovery, and the Department of Pharmacy, a six-year program that qualifies graduates for the national examination for pharmacists. New graduate schools were also established based on student progression through their programs.
In April of 2010, we established a master's program in pharmaceutical sciences for graduates of the four-year Department of Pharmaceutical Sciences program. This research program unites the four departments that previously existed, creating a single department instead.
In April of 2012, we established a doctoral program in pharmaceutical sciences for graduates of the master's program (duration of program: three years), along with a doctoral program in pharmacy for graduates of the six-year Department of Pharmacy program (duration of program: four years). The doctoral program in pharmaceutical sciences also offers a Dual Specialty Course on Pharmacist Education to qualify four-year doctoral graduates for the national examination for pharmacists (Only applied to those students enrolled at the University of Tokyo in April, 2017 and graduated from the Department of Pharmaceutical Sciences, Faculty of Pharmaceutical Sciences).

Graduate School Curriculum

The main part of graduate school curriculum is "special research" through participations in research conducted in each laboratory. At the Graduate School lectures are targeted at students in master's program/doctoral program(Department of Pharmacy). Those lectures are highly specialized, covering the latest information in the field, thus allowing them to be the world's top class.

Master's Program (two-year program)

Department of Pharmaceutical Sciences

30 credits or more including 20 credits of special research in pharmaceutical sciences must be completed.

Doctoral program

Department of Pharmaceutical Sciences (three-year program)

20 credits or more including 20 credits of special research in pharmaceutical sciences must be completed.

Department of Pharmacy (four-year program)

30 credits or more including 20 credits of special research in pharmaceutical sciences must be completed.

＊Courses are open every other year

Course Title	Credits	Course Outline	
Special Lecture Basic Pharmaceutical Science Ⅰ	2	To understand basic and advanced chemical principles and concepts that is important for pharmaceutical sciences	
Special Lecture Basic Pharmaceutical Science Ⅱ	2	To understand X-ray crystallography, structural analysis by NMR, sensitive analysis by fluorometric and mass spectrometric method, biosynthesis of natural products, and chemical biology for drug development	
Special Lecture Basic Pharmaceutical Science Ⅲ	2	To learn the fundamentals of biopharmaceutical sciences, including biochemistry, molecular biology, cell biology, molecular genetics, and pathology	
Special Lecture Basic Pharmaceutical Science Ⅳ	2	To learn the fundamental knowledge in the fields of pharmacokinetics, pharmacology, pathology, drug informatics, regulatory science, pharmacobusiness, and pharmacoeconomy among clinical pharmaceutical sciences	
Special Lecture Chemical Biology	2	To learn the chemistry that are essential for carrying out cutting-edge pharmaceutical research related to the life sciences	
Special Lecture Biomolecular Analysis	2	Explains the principles of X-ray crystallography, nuclear magnetic resonance imaging, single-molecule fluorescence imaging, and methods for high sensitivity analysis of biomolecules, and introduces methods for analyzing the structure and function of biomolecules and applications of those methods	＊
Special Lecture Cell Biology	2	Introduces the latest research trends in biopharmaceutical sciences from the perspective of cell biology	＊
Special Lecture Molecular Biology	2	To understand living organisms according to the functions of genes and proteins and to learn the current molecular biology, including disease pathophysiology, while also learning the latest methods in genetics and biochemistry	＊
Special Lecture Disease Biology	2	From a biological perspective, outlines the academic disciplines and the mechanisms leading to disease onset while focusing primarily on infection and immunity	＊
Special Lecture Clinical Pharmaceutical Science	2	To learn cutting-edge medical and pharmaceutical research in an omnibus format	＊
Special Lecture Social Pharmaceutical Science	2	To gain a deeper understanding of the relationship between pharmaceutics and society from a variety of different angles, including information, statistics, government policy, business management, the pharmaceutical industry, etc	＊
Special Lecture English for Science	2	To train in both listening and speaking by learning topics related to pharmaceutical sciences in English	
Special Lecture Pharmaceutical Regulatory Science	2	To learn regulatory frameworks and practical methodology for evaluating the effectiveness, safety, risks, and benefits of new pharmaceuticals	
Special Lecture Clinical Science	2	This course aims on the systematic comprehension of pharmacotherapy and clinical development of drugs on the basis of pathophysiology of diseases; students will learn pharmacokinetics, clinical pharmacology and regulatory and ethical issues of clinical trials. This course also aims on the comprehension of the cancer as a disease; students will learn practical aspects of diagnosis, treatment and clinical trial from medical professionals in clinical pathology, internal medicines, surgical therapy, radiation therapy and others.	

Department of Pharmaceutical Sciences

Course Title	Credits	Course Outline
Special Studies for Pharmaceutical Science Ⅰ	20	(Master's course) To gain a foothold toward specialization; learn pharmaceutical modes of thought and logical, cutting-edge methodology; and develop advanced analytical skills through practice, seminars, and individualized laboratory research activities
Special Studies for Pharmaceutical Science Ⅱ	20	(Doctoral course) To establish deep roots in a specialization; learn pharmaceutical modes of thought and logical, cutting-edge methodology; and develop advanced analytical skills through individualized laboratory research activities

Department of Pharmacy

Course Title	Credits	Course Outline
Practical Studies for Clinical Pharmacy	4	To acquire the practical methodology, awareness of the issues, and independence to respond to the needs of society in sophisticated medical environments
Practical Studies for Social Pharmacy	4	To acquire the practical methodology, awareness of the issues, and independence to respond to the needs of society in medical administration environments
Practical Studies for Drug Discovery	4	To acquire the practical methodology, awareness of the issues, and independence to respond to the needs of society in drug discovery environments
Special Studies for Pharmacy	20	To learn—through practice, seminars, and individualized laboratory research activities—comprehensive methodology pertaining to the interaction of molecules and organisms for the purpose of discovering and appropriately using pharmaceuticals

Laboratory of
Organic and Medicinal Chemistry

Synthesis of novel intelligent molecules which link chemical structures to biological functions in organic and medicinal chemistry

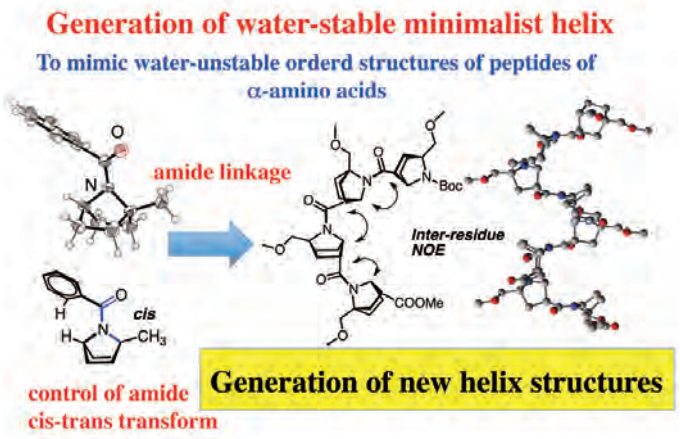
Assoc. Prof. **Y. Otani**

http://www.f.u-tokyo.ac.jp/~yakka/english.html

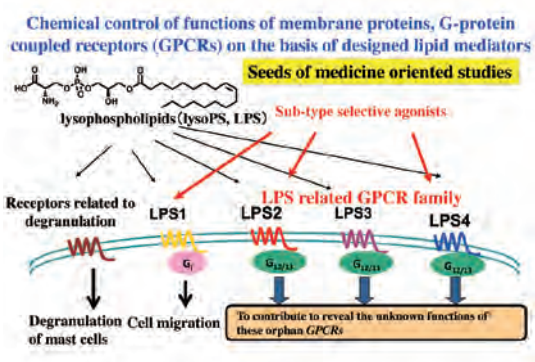
Research Topics

1. Synthesis of new compounds exhibiting characteristic structural features and properties, finally relevant to biological functions
2. New reactions to functionalize aromatic compounds based on designed superelectrophiles
3. Design and synthesis of intelligent molecules, which will have impacts on functions of membrane proteins
4. Computational modeling and simulations of organic and macromolecular systems

Our aims of researches emphasize on design and synthesis of structurally novel organic molecules, which are characteristic in terms of structural (bonding) features and intrinsic functions such as chemical reactivities and biological functions. Designs of such novel molecules are based on our finding new chemistry including **ground-state stable non-planar amide peptides and nitrosamines**, and structures of multiply positively charged molecules. We study nitrogen-pyramidal amides and related nitrosamines, i.e., molecules that take nonplanar structures, different from the common planar amides. We apply this chemistry to construction of molecules of highly ordered structures such as **helix peptide mimetics** stable in water. We also develop new chemistry involving dication or trication molecules and apply them as **superelectrophiles** to synthesize a variety of novel multi-functionalized aromatic compounds, which are pharmaceutically relevant. We are also creating chemical molecules, which will be useful to **controlling biological events of membrane proteins** such as ion channels, neurotransporters and G-protein-coupled receptors. These molecules also contribute to understanding the phyisiological functions of these membrane proteins. We combine all the experimental projects with computational chemistry, which will lead to deep understanding of the underling chemistry.



Helical structure of artificial amino acid peptide stable in water



Chemical modulation of functions of membrane proteins

Otani, Y.; Ichinose, A.; Wang, X.; Huang, Z.; Kasahara, A.; Ishii, M.; Watanabe, E.; Kanamitsu, K.; Tai, K.; Kusuhara, H.; Ueda, T.; Takeuchi, K.; Ohwada, T. An N-ortho-nitrobenzylated benzanilide amino acid enables control of the conformation and membrane permeability of cyclic peptides Chemical Communications, 2024, 60, 9242.

Huang, Z.; Ishii, M.; Watanabe, E.; Kanamitsu, K.; Tai, K.; Kusuhara, H.; Ohwada, T.; Otani, Y. Effect of N-o-nitrobenzylation on conformation and membrane permeability of linear peptides Bioorganic Chemistry, 2024, 145, 107220.

Cheng, Y.; Hyodo, T.; Yamaguchi, K.; Ohwada, T.; Otani, Y. Complete amide cis–trans switching synchronized with disulfide bond formation and cleavage in a proline-mimicking system Chemical Communications, 2024, 60, 6158.

Su, A.; Tabata, Y.; Aoki K.; Sada, A.; Ohki, R.; Nagatoishi, S.; Tsumoto, K.; Wang, S.; Otani, Y.; Ohwada, T. Elaboration of non-naturally occurring helical tripeptides as p53-MDM2/MDMX interaction inhibitor Chemical & Pharmaceutical Bulletin, 2021, 69, 7, 681.

Otani, Y.; Liu, X.; Ohno, H.; Wang, S.; Zhai L.; Su, A.; Kawahata, M.; Yamaguchi, K.; Ohwada, T. Amide nitrogen pyramidalization changes lactam amide spinning Nature Communications, 2019, 10, Article number: 461.

Prof. M. Inoue

Assoc. Prof.
H. Itoh
Assist. Prof.
K. Hagiwara
Project Assist. Prof.
H. Fujino

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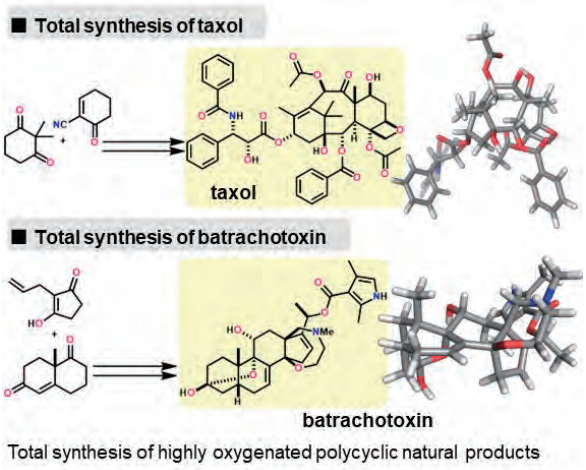
Laboratory of
Synthetic Natural Products Chemistry

Total synthesis and functional analysis of biologically active natural products

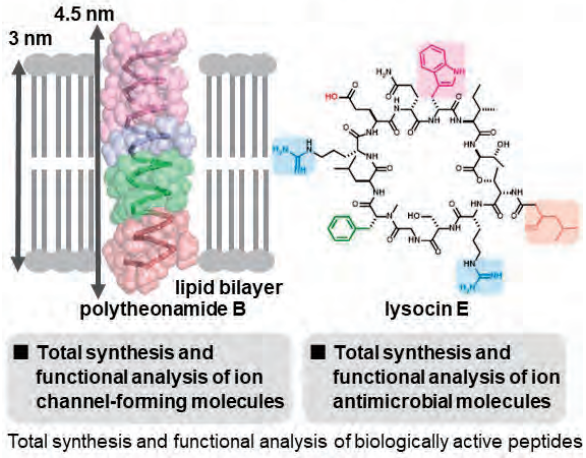
Research Topics

1. Development of new synthetic methodologies for total synthesis
2. Total synthesis of highly oxygenated polycyclic natural products
3. Total synthesis and functional analysis of ion channel-forming molecules
4. Total synthesis and functional analysis of antimicrobial molecules
5. Synthesis of new artificial molecules by modification of natural products templates

Natural products have been tremendously important in biology and human medicine because of their power to modulate signal transductions of biological system. Since the removal of sub-structures of the natural products often leads to significant losses of their activity, total chemical syntheses of their entire structures with a precision at an atomic level are necessary to provide sufficient amounts of material required for biological and medical applications. Architecturally complex natural products with molecular weight over 1000 are capable of highly specific interactions with their target proteins. Therefore, they are powerful agents for selectively controlling intricate biological systems. The goal of our research program is efficient, practical and flexible syntheses of gigantic natural molecules, which include highly oxygenated polycyclic natural products as well as ion channel-forming peptides. At the core of this research program is the development of new strategies for assembling architecturally complex natural products in a concise fashion. These synthetic developments would enable unified synthesis of new artificial analogs by modification of natural products templates. The new synthetic methods for the natural products and the synthetic analogs will allow us to tailor and enhance their drug like properties, to gain control over diverse signal transductions thereby offering new research methods for the study of life science.



Total synthesis of highly oxygenated polycyclic natural products



Total synthesis and functional analysis of biologically active peptides

Taguchi, J., Fukaya, S., Fujino, H., Inoue, M. Total Synthesis of Euphorbialoid A. *J. Am. Chem. Soc.* 146: 34221-34230 (2024)

Lin, Y., Itoh, H., Dan, S., Inoue, M. Methyl Scanning Approach for Enhancing the Biological Activity of the Linear Peptidic Natural Product, Efrapeptin C. *Chem. Sci.* 15: 19390-19399 (2024)

Watanabe, A., Nagatomo, M., Hirose, A., Hikone, Y., Kishimoto, N., Miura, S., Yasutake, T., Abe, T., Misumi, S., Inoue, M. Total Syntheses of Phorbol and 11 Tigliane Diterpenoids and Their Evaluation as HIV Latency-Reversing Agents. *J. Am. Chem. Soc.* 146: 8746-8756 (2024)

Watanabe, T., Oga, K., Matoba, H., Nagatomo, M., Inoue, M. Total Synthesis of Taxol Enabled by Intermolecular Radical Coupling and Pd-Catalyzed Cyclization. *J. Am. Chem. Soc.* 145: 25894-25902 (2023)

Watanabe, Y., Morozumi, H., Mutoh, H., Hagiwara, K., Inoue, M. Total Synthesis of (–)-Batrachotoxin Enabled by a Pd/Ag-Promoted Suzuki–Miyaura Coupling Reaction. *Angew. Chem. Int. Ed.* 62: e202309688 (2023)

Shimakawa, T., Nakamura, S., Asai, H., Hagiwara, K., Inoue, M. Total Synthesis of Puberuline C. *J. Am. Chem. Soc.* 145: 600-609 (2023)

Prof. M. Kanai

Assoc. Prof.
S. Kawashima
Assist. Prof.
H. Mitsunuma
Assist. Prof.
Y. Yamanashi
Assist. Prof.
M. Yamane

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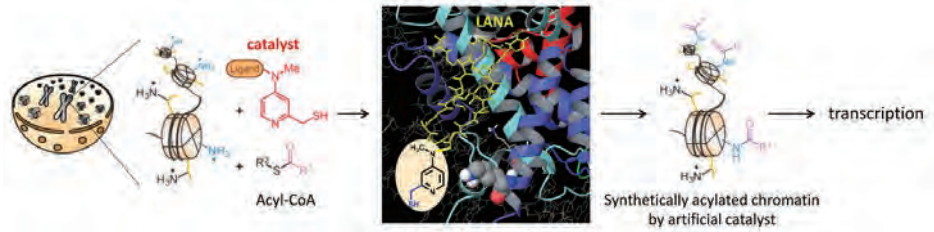
Laboratory of
Synthetic Organic Chemistry

Catalysis for clean, robust, and concise complex molecule synthesis and new modal medicine

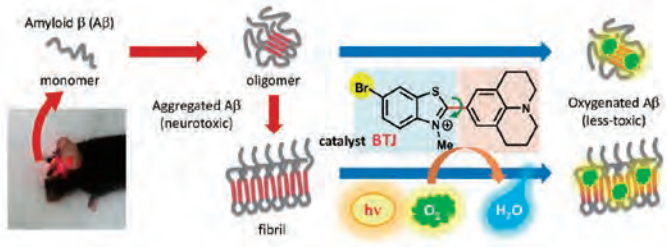
Research Topics

1. Development of new catalysis to facilitate complex molecule synthesis
2. Clean, robust, and concise synthesis of pharmaceuticals and their leads
3. Catalytic H_2 and O_2 activation
4. Conceptually new approach to promote human health

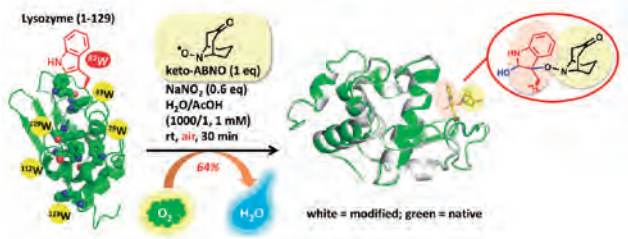
The main theme of our research is the development of revolutionary catalyses facilitating new drug design and synthesis. In this direction, we would like to promote human health based on the catalysis development. Chemical synthesis in 21st century should be clean, robust, and concise, no matter how complex the target molecules are. The "ideal synthesis" will be only possible by new catalytic methodologies. Moreover, new catalyses will expand the diversity of readily available building blocks, leading to structurally novel artificial drug design. Sustainability based on new catalysis is another direction of our research. Specifically, we are interested in catalytic activations of small molecules such as H_2 and O_2.



Artificial Catalysis in Cells for Synthetic Epigenetics



Catalytic Oxygenation of Aβ as a Potential Therapeutic Chemical Reaction



Biomacromolecules as Substrates for Chemical Catalysis

Jagtap, R. A., Nishioka, Y., Geddis, S. M., Irie, Y., Takanashi, T., Adachi, R., Yamakata, A., Fuki, M., Kobori, Y., Mitsunuma, H., Kanai, M.,Catalytic acceptorless complete dehydrogenation of cycloalkanes Nat. Commun. 2025, 16, 428.

Umeda, H., Suda, K., Yokogawa, D., Azumaya, Y., Kitada, N., Maki, S. A., Kawashima, S. A., Mitsunuma, H., Yamanashi, Y., Kanai, M., Unimolecular chemiexcited oxygenation of pathogenic amyloids. Angew. Chem. Int. Ed. 2024, 63, e202405605.

Habazaki, M., Mizumoto, S., Kajino, H., Kujirai, T., Kurumizaka, H., Kawashima, S. A., Yamatsugu, K., Kanai, M. A chemical catalyst enabling histone acylation with endogenous acyl-CoA. Nat. Commun. 2023, 14, 5790.

Prof. I. Abe

Assoc. Prof. **T. Mori**
Assist. Prof. **R.Ushimaru**

http://www.f.u-tokyo.ac.jp/~tennen/index-e.html

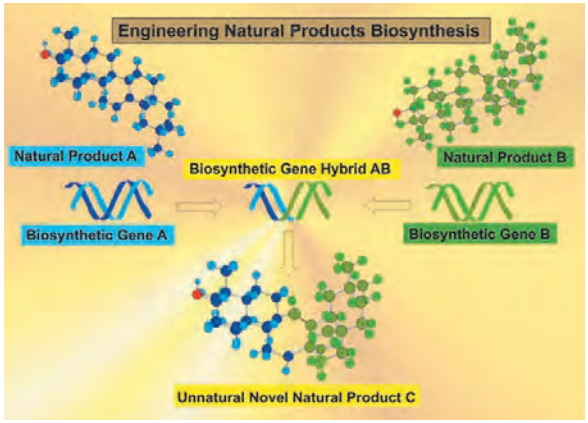
Laboratory of
Natural Products Chemistry

We establish the mechanisms of natural product biosynthesis as a science in their own right, to construct a rational system for the production of new and useful substances

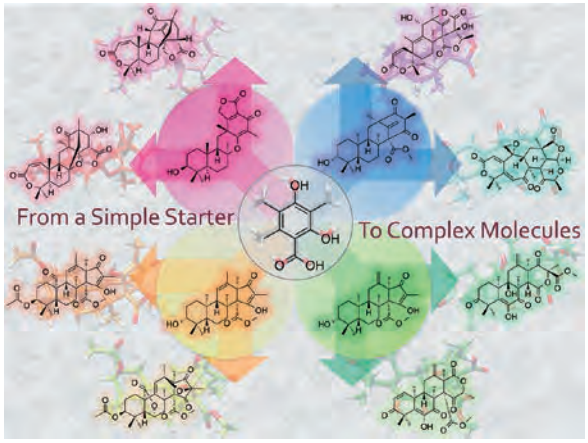
Research Topics

1. The biosynthesis and bioengineering of medicinal natural products (genome mining, engineered biosynthesis)
2. The enzyme biocatalysts (structure-function analysis, enzyme engineering, mechanistic studies)
3. The search for bioactive substances and isolation/structure determination

Natural organic compounds, prominent among which are antibiotics such as penicillin, are gifts from nature, and the benefits they have bestowed upon humankind as sources for the pharmaceuticals, etc., that maintain health is inestimable. In our laboratory, we study the process of biosynthesis of natural organic compounds produced by plants and microorganisms, using not only the foundation discipline of organic chemistry, but also incorporating the methods of biochemistry and molecular biology in an effort to understand the enzymes that catalyze each biosynthesis reaction and the functions and control mechanisms of the genes that govern their expression at the molecular level. In addition, we are expanding our research into "biosynthesis engineering," by which rational systems for the biological production of new and useful substances can be designed and constructed, based on the mechanisms of biosynthesis that have been brought to light. We also are carrying out research on the mechanisms by which the bioactivity of natural products is expressed, while at the same time searching for natural products that are active in intracellular signaling.



Concept of "biosynthesis engineering," by which non-natural compounds are generated



Synthetic biology of complex natural products

Tao, H., Lauterbach, L., Bian, G., Chen, R., Hou, A., Mori, T., Cheng, S., Hu, B., Lu, L., Mu, X., Li, M., Adachi, N., Kawasaki, M., Moriya, T., Senda, T., Wang, X., Deng, Z., Abe, I., Dickschat, J. S., Liu, T. Discovery of non-squalene triterpenes. Nature 606: 414-419 (2022)

Tao, H., Ushimaru, R., Awakawa, T., Mori, T., Uchiyama, M., Abe, I. Stereoselectivity and substrate specificity of the Fe(II)/α-ketoglutarate-dependent oxygenase TqaL. J. Am. Chem. Soc. 144: 21512-21520 (2022)

Tao, H., Mori, T., Chen, H., Lyu, S., Nonoyama, A., Lee, S., Abe, I. Molecular insights into the unusually promiscuous and catalytically versatile Fe(II)/α-ketoglutarate-dependent oxygenase SptF. Nat. Commun. 13: 95 (2022)

Barra, L., Awakawa, T., Shirai, K., Hu, Z., Bashiri, G., Abe, I. β-NAD as a building block in natural product biosynthesis. Nature 600: 754-758 (2021)

Mori, T., Zhai, R., Ushimaru, R., Matsuda, Y., Abe, I. Molecular insights into the endoperoxide formation by Fe(II)/α-KG-dependent oxygenase NvfI. Nat. Commun. 12: 4417 (2021)

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Lecturer **N. Toriumi**
Assist. Prof.
Y. Nagashima
Project Assist. Prof.
T. Matsuyama

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Koyamada, K., Miyamoto, K., Uchiyama, M.
Room-temperature Synthesis of m-Benzyne
Nature Synthesis, 2024, 3: 1083–1090.

Watanabe, Y., Hashishin T., Sato, H., Matsuyama, T., Nakajima, M., Haruta, J., Uchiyama, M.
DFT Study on Retigerane-Type Sesterterpenoid Biosynthesis: Initial Conformation of GFPP Regulates Biosynthetic Pathway, Ring-Construction Order and Stereochemistry
JACS Au, 2024, 4: 3484–3491.

Shimose, A., Ishigaki, S., Sato, Y., Nogami, J., Toriumi, N., Uchiyama, M., Tanaka, K., Nagashima, Y.
Dearomative Construction of 2D/3D Frameworks from Quinolines via Nucleophilic Addition/Borate-Mediated Photocycloaddition
Angew. Chem. Int. Ed., 2024, 63: e202403461.

Yanagi, S., Matsumoto, A., Toriumi, N., Tanaka, Y., Miyamoto, K., Muranaka, A., Uchiyama, M.
A Switchable Near-Infrared-Absorbing Dye Based on Redox-Bistable Benzitetraazaporphyrin
Angew. Chem. Int. Ed., 2023, 62: e202218358.

Iida, T., Kanazawa, J., Matsunaga, T., Miyamoto, K., Hirano, K., Uchiyama, M.
Practical and Facile Access to Bicyclo[3.1.1]heptanes: Potent Bioisosteres of meta-Substituted Benzenes
J. Am. Chem. Soc., 2022, 144: 21848–21852.

Laboratory of

Advanced Elements Chemistry

Understanding of chemical phenomena at the atomic and electron levels and creation of a new science of materials through flexible construction of molecules

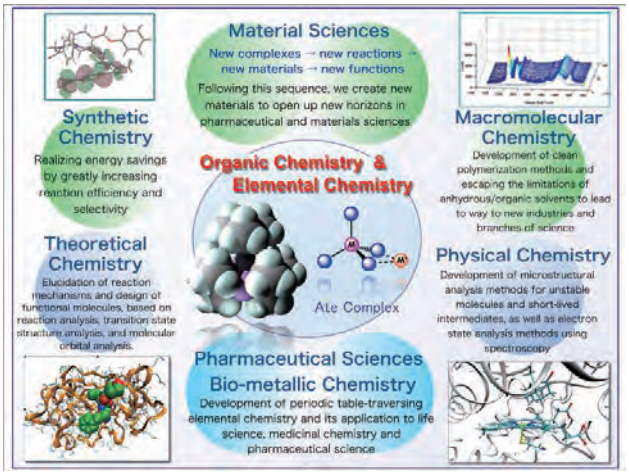
Research Topics

1. Research on structure, bonding, aromaticity, and movement of molecules
2. Development of new reactions to freely manipulate chemical bonds
3. Theoretical and synthetic chemistry for manipulating light
4. Research on the origin of life and the evolution of matter

Our laboratory focuses on understanding the properties and phenomena of substances by “language of chemistry” such as molecules, atoms, and electrons (**Seeing /Knowing**); on developing reactions that manipulate the bonds between atoms completely in control (**Designing**); and on producing functional materials (**Producing**).

In our laboratory, we strive to develop technologies for the precise chemical conversion of tiny, tiny molecules less than 1 billionth of a meter in size (nanometer scale; nm). Thanks to recent advances in spectroscopy and theoretical calculation, it is getting possible to accurately predict and reproduce snapshots of the state of the electrons that form materials, as well as of reactions between molecules. With the 3 methods, namely, synthetic chemistry, spectroscopy, and theoretical calculation as the pillars of our science, we expand upon elements chemistry in an interdisciplinary manner as we meet the challenges of elucidating life phenomena and creating a new materials science.

Developing new reactions and designing/producing new materials based on computational chemistry and theoretical chemistry (Adopted for the cover of Chemistry: A European Journal)



Life sciences and materials science that open new frontiers in basic organic chemistry and elemental chemistry

Prof. Y. Urano

Assist. Prof. **T. Ueno**
Assist. Prof.
T. Komatsu
Assist. Prof.
R. Tachibana

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Laboratory of
Chemistry and Biology

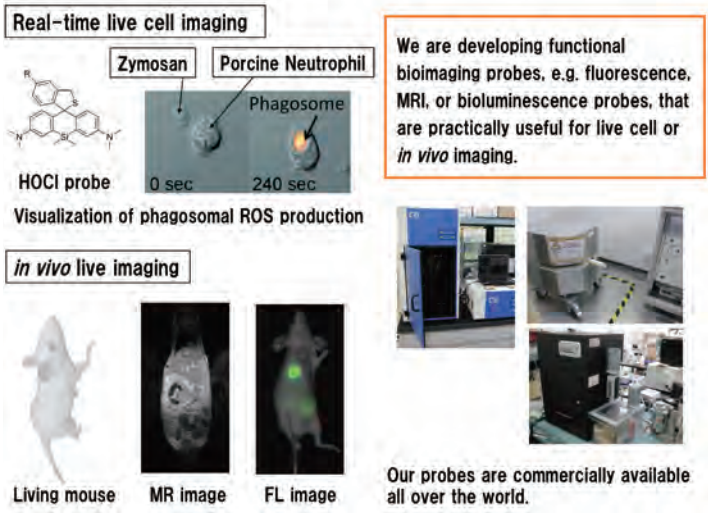
"Chemical Biology" and "Chemical Medicine" in order to promote life science research and to develop novel medical tools

Research Topics

1. Fundamental photophysical and photochemical research to establish rational design principle for novel chemical tools
2. Theoretical design, synthesis and biological application of novel chemical tools, including sensor molecules and signal perturbation techniques for cellular signaling molecules, such as Ca^{2+} ion, reactive oxygen species, or various enzymes
3. Development of chemical tools, e.g, MRI probe and fluorescent probe, for diagnostic imaging and their *in vivo* application
4. Clinical use of our newly developed fluorescence probes for rapid imaging of tumor with human clinical fresh specimens
5. Research on drug discovery: Searching for novel lead compounds that control disease-related proteins, and development of high-quality screening systems

Our laboratory conducts research on the analysis and perturbation of dynamic living systems, using chemistry as a powerful tool. One of the important goals in modern life sciences is to elucidate the dynamic behaviors of biomolecules *in situ* in the living cells/organisms. So far, our laboratory has succeeded in developing bioimaging probes/other chemical tools including signal perturbation methodology and high quality screening systems by applying the probe design strategies that we established. Likewise, we utilize our probe design principle to establish chemical tools for clinical use, including a tumor-specific intraoperative fluorescence imaging methodology. On top of that, we are now conducting dozens of pilot clinical trial projects by utilizing above mentioned chemical tools with external collaborators in domestic hospital and abroad.

The above-described areas of research have attracted enormous attention in recent years under the name of" Chemical Biology", and we believe that they will open up new horizons in life sciences.



Development of bioimaging probes

Kuriki Y, Kamiya M, Kubo H, Komatsu T, Ueno T, Tachibana R, Hayashi K, Hanaoka K, Yamashita S, Ishizawa T, Kokudo N, Urano Y: Establishment of Molecular Design Strategy To Obtain Activatable Fluorescent Probes for Carboxypeptidases. J. Am. Chem. Soc., 140: 1767-1773, 2018.

Umezawa K, Yoshida M, Kamiya M, Yamasoba T, Urano Y: Rational design of reversible fluorescent probes for live-cell imaging and quantification of fast glutathione dynamics. Nat. Chem., 9: 279-286, 2017.

Uno SN, Kamiya M, Yoshihara T, Sugawara K, Okabe K, Tarhan MC, Fujita H, Funatsu T, Okada Y, Tobita S, Urano Y: A spontaneously blinking fluorophore based on intramolecular spirocyclization for live-cell super-resolution imaging. Nat. Chem., 6: 681-689, 2014.

Laboratory of
Bioanalytical Chemistry

We measure the functions of biomolecules at the level of a single molecule to elucidate vital functions

Assoc. Prof.
M. Tsunoda

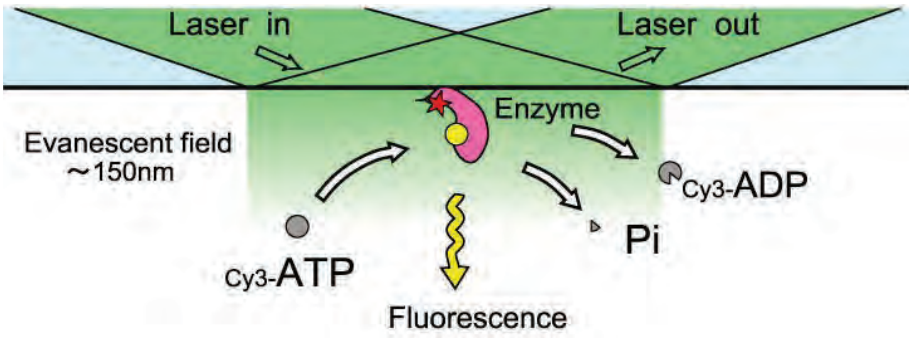
https://bunseki.f.u-tokyo.ac.jp/index_e.html

Research Topics

1. Research on the principles of action by which biomolecular machines such as molecular chaperonin and ribosomes operate
2. Single-molecule fluorescence imaging of intracellular mRNA processing and transport
3. Development of micro nanodevices for analyzing the functions and interactions of biomolecules

Fluorescence microscope system for imaging single molecules within living cells

In order to understand living organisms, it is necessary to conduct research at a variety of different levels. The lowest level is that at which biomolecules such as proteins and DNA work. When these come together, biological supramolecules, cells, organs, and the like are created, while at the higher end, individual organisms, societies, and ecosystems are constituted. We focus on the level of the smallest unit, the "biomolecule," together with the level of the "cell," at which life functions are first expressed, to find answers to questions like "By what mechanisms do biomolecules function?" and "When they aggregate, what kinds of systems do they construct?" Concretely speaking, we bind a fluorescent dye to a single biomolecule and observe it with a sensitive fluorescence microscope. Some biomolecules can exhibit their functions even at the level of the single molecule. For example, the motor protein known as kinesin moves on rail proteins called microtubules. Humankind does not at this point in time possess the technology for creating this kind of molecular machine, but we believe that humankind will be able to make this kind of molecular machine in the near future through research on the motor protein. On the other hand, self-assembly of a variety of different biomolecules creates complex systems which differ greatly from manmade ones. By researching such biological systems, we close in on the mysteries of life.



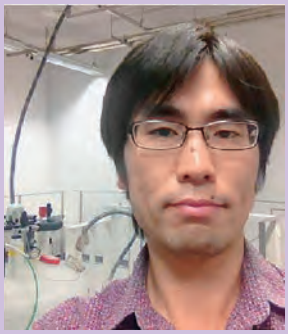
The principle of single-molecule imaging of enzyme reaction (ATPase) using evanescent illumination

M. Isokawa, K. Nakanishi, T. Kanamori, T. Sekiguchi, T. Funatsu, S. Shoji, M. Tsunoda, Pillar Array Mixer for Postcolumn Derivatization Integrated into Liquid Chromatography-Based Microfluidic Device. *Anal. Chem.* 96: 11002-11008 (2024)

M. Tsunoda, T. Tsuda, Quantification of amino acids in small volumes of palm sweat samples. *Heliyon* 10: e36286 (2024)

T. Ohtawa, A. Hattori, M. Isokawa, M. Harada, T. Funatsu, T. Ito, M. Tsunoda, Determination of intracellular 2-hydroxyglutarate enantiomers using two dimensional liquid chromatography. *J. Chromatogr. Open* 1: 100005 (2021)

A. Hattori, M. Tsunoda, T. Konuma, M. Kobayashi, T. Nagy, J. Glushka, F. Tayyari, D. McSkimming, N. Kannan, A. Tojo, A. Edison, T. Ito, Cancer progression by reprogrammed BCAA metabolism in myeloid leukaemia. *Nature* 545:500-504 (2017)



Laboratory of
Physical Chemistry

Prof.
K. Takeuchi

Assist. Prof. **Y. Kofuku**
Assist. Prof.
Y. Tokunaga
Assist. Prof. **Y. Toyama**

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Approaching life from dynamic structural information obtained by original NMR strategies.

Research Topics

1. Functional mechanism of biologically and pharmacologically important proteins based on dynamic structural information.
2. Functional mechanism of biomolecules that regulate signal transduction and energy metabolism based on interaction analysis.
3. Development of nuclear magnetic resonance (NMR) techniques to analyze the structure and dynamics of high-molecular-weight proteins.
4. Sample preparation strategies to reproduce the functional environment of biomolecules and sophisticated stable isotope labeling methods.
5. In-cell NMR and its application to intracellular drug discovery.

The structural information of proteins plays a vital role in elucidating biological functions and their applications to drug discovery. In addition, it has become clear that proteins do not adopt only a single conformation but also an equilibrium among multiple functional conformations.
These dynamic properties are directly related to the expression and regulation of protein functions. In our lab, we analyze the structure and dynamics of proteins mainly by using NMR to understand biological phenomena through elucidating the functional mechanisms of biomolecules.

We focus on membrane proteins, such as G-proteincoupled receptors (GPCRs) and transporters, as well as macromolecules that regulate intracellular signal transduction and energy metabolism, which are important in biological and pharmaceutical sciences. By developing original NMR methods, we have obtained structure and dynamics information of the macromolecules of interest that were previously difficult to analyze. In addition, we are developing an in-cell NMR strategy to analyze the structure and dynamics of proteins in the actual cellular environment and extending these strategies to establish intracellular drug discovery.

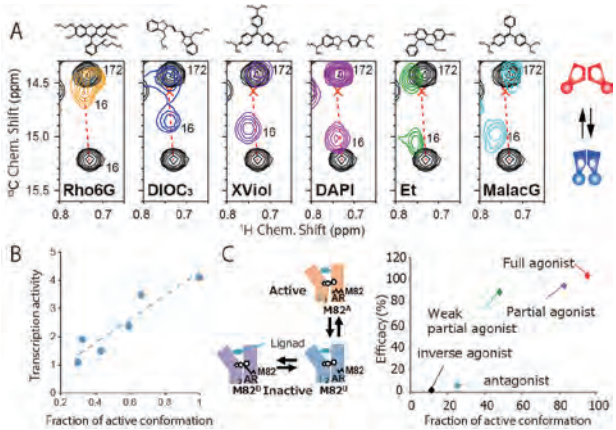

Fig.1: Biological phenomena elucidated by dynamic structural analysis using NMR in our laboratory. (A) Structural equilibrium determines (B) transcriptional activity of multidrug-resistant transcription factors (*Proc Natl Acad Sci* (2019) 116, 19963. (C) Drug efficacy of each ligand of GPCR (*β2* adrenergic receptor) (*Nat Commun* (2012) 3, 1045; *Angew Chem Intl Ed* (2014), 53, 13376)

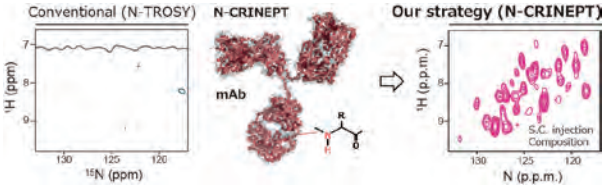

Fig2: Novel NMR experiments developed in our laboratory and their application to mAb (*J Med Chem* (2020) 63, 5360; *Nat Methods* (2019) 16, 333).

Takeuchi K, Ueda T, Imai M, Fujisaki M, Shimura M, Tokunaga Y, Kofuku Y, Shimada I.
Affinity-directed substrate/H^{+}-antiport by a MATE transporter. Structure. 32. 1150-1164.e3. (2024) .

Mizukoshi, Y., Takeuchi ,K., Tokunaga, Y., Matsuo, H., Imai, M., Fujisaki, M., Kamoshida, H., Takizawa, T., Hanzawa, H., Shimada, I., Targeting the cryptic sites: NMR-based strategy to improve protein druggability by controlling the conformational equilibrium. *Sci Adv.* 6, eabd0480 (2020).

Tokunaga, Y., Takeuchi, K., Okude, J., Ori, K., Torizawa, T., Shimada, I., Structural Fingerprints of an Intact Monoclonal Antibody Acquired under Formulated Storage Conditions via ^{15}N Direct Detection Nuclear Magnetic Resonance. *J Med Chem*. 63, 5360-5366 (2020).

Takeuchi, K., Imai, M., Shimada, I., Conformational equilibrium defines the variable induction of the multidrug-binding transcriptional repressor QacR. *Proc Natl Acad Sci U S A*. 116, 19963-19972 (2019).

Boeszoermenyi, A., Chhabra, S., Dubey, A., Radeva, D.L., Burdzhiev, N.T., Chanev, C.D., Petrov, O.I., Gelev, V.M., Zhang, M., Anklin, C., Kovacs, H., Wagner, G., Kuprov, I., Takeuchi, K., Arthanari, H. Aromatic ^{19}F- ^{13}C TROSY: a background-free approach to probe biomolecular structure, function, and dynamics. *Nat Methods*. 16, 333-340 (2019).

Prof. T. Shimizu

Assoc. Prof. **U. Ohto**
Assist. Prof. **Y. Hirano**
Assist. Prof. **Z. Zhang**

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Architecture of the high-affinity immunoglobulin E receptor (2024)
Zhang Z, Yui M, Ohto U, Shimizu T.
Science signaling **17**, eadn 1303

Structural basis for thioredoxin-mediated suppression of NLRP1 inflammasome. (2023)
Zhang Z, Shibata T, Fujimura A, Kitaura J, Miyake K, Ohto U, Shimizu T.
Nature **622**(7981), 188-194

TLR3 forms a laterally aligned multimeric complex along double-stranded RNA for efficient signal transduction. (2023)
Sakaniwa K, Fujimura A, Shibata T, Shigematsu H, Ekimoto T, Yamamoto M, Ikeguchi M, Miyake K, Ohto U, Shimizu T.
Nature Commun. **14**(1):164

Structural insight into the activation of an Arabidopsis organellar C-to-U RNA editing enzyme by active site complementation (2023)
Toma-Fukai S, SawadaY , Maeda A, Shimizu H, Shikanai T, Takenaka M, Shimizu T *The Plant Cell* **35**, 1888-1900

Structure of SARS-CoV-2 membrane protein essential for virus assembly (2022)
Zhang Z, Nomura N, Muramoto Y, Ekimoto T, Uemura T, Liu K, Yui M, Kono N, Aoki J, Ikeguchi M, Noda T, Iwata S, Ohto U & Shimizu T
Nature Commun. **13**: 4399

Cryo-EM structures of Toll-like receptors in complex with UNC93B1 (2021)
Ishida H, Asami J, Zhang Z, Nishizawa T, Shigematsu H, Ohto U, Shimizu T
Nature Struc Mol Biol. **28**, 173-180

Ohto U, Shibata T, Tanji H, Ishida H, Krayukhina E, Uchiyama S, Miyake K, Shimizu T (2015)
Structural basis of CpG and inhibitory DNA recognition by Toll-like receptor 9
Nature **520**, 702-705

Tanji H, Ohto U, Shibata T, Miyake K, Shimizu T (2013)
Structural reorganization of the Toll-like receptor 8 dimer induced by agonistic ligands
Science **339**, 1426-1429

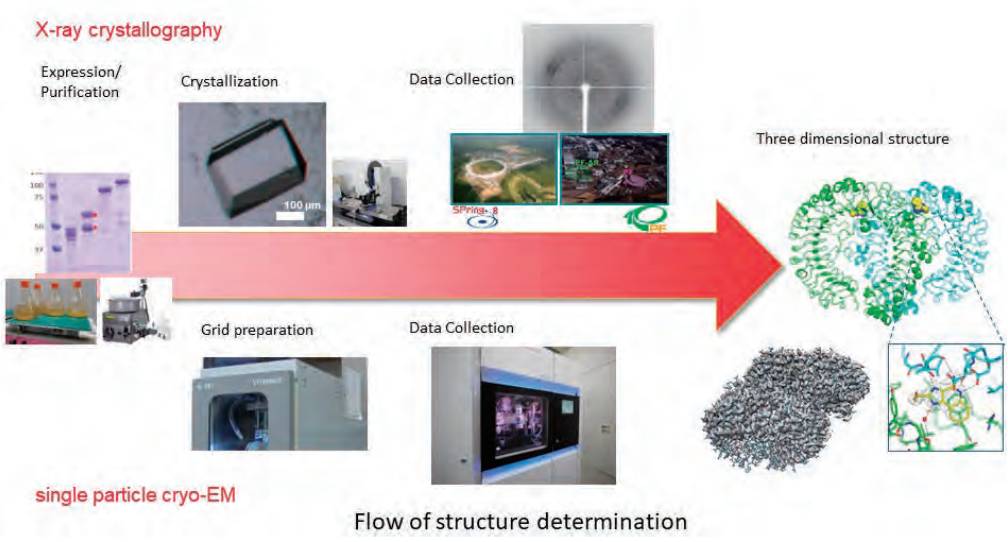
Protein Structural Biology

Determining three-dimensional structures of proteins and nucleic acids, and elucidating their functions in living cells

Research Topics

1. Structural analyses of proteins and nucleic acids using X-ray crystallography and small angle X-ray scattering
2. Structures of immune-system proteins and their complexes
3. Structures of proteins in signal transduction and their complexes
4. Single particle analysis by cryo-electron microscopy

Structural biology seeks to provide a complete and coherent picture of biological phenomena at the molecular and atomic level. The three-dimensional structure of macromolecules at an atomic level can create an actual picture of how they work. These days, structural biology is also called structural cell biology and/or structural life science, and is changing into the research field toward life science. Our laboratory aims at achieving a comprehensive understanding of structure/function relationships of key cellular components and processes, and roles in living cells. In the elucidation of three-dimensional structures, X-ray crystallography is extensively used since this method provides us with detailed structural information on the biological functions and roles. We also take an interdisciplinary approach, combined with methods of biophysics, biochemistry, molecular biology, genetic and protein engineering. Moreover, we take small angle X-ray scattering (SAXS) and cryo-electron microscopy (cryo-EM). SAXS can provide a wealth of structural information on biomolecules in solution and is compatible with a wide range of experimental conditions. Cryo-EM has triggered a revolution in structural biology and has become a newly dominant discipline. Especially, single particle cryo-EM has become a powerful method for atomic structure determination. With these structural biological approaches, we can obtain the information on three dimensional structures that are required for drug design and discovery.
We are now carrying out structural biological researches into immune-system proteins, nuclear proteins and proteins in signal transduction.



Flow of structure determination

Prof. J. Aoki

Assoc. Prof. **N. Kono**
Assist. Prof. **K. Kano**
Assist. Prof. **Y. Shimanaka**
Assist. Prof. **J. Omi**

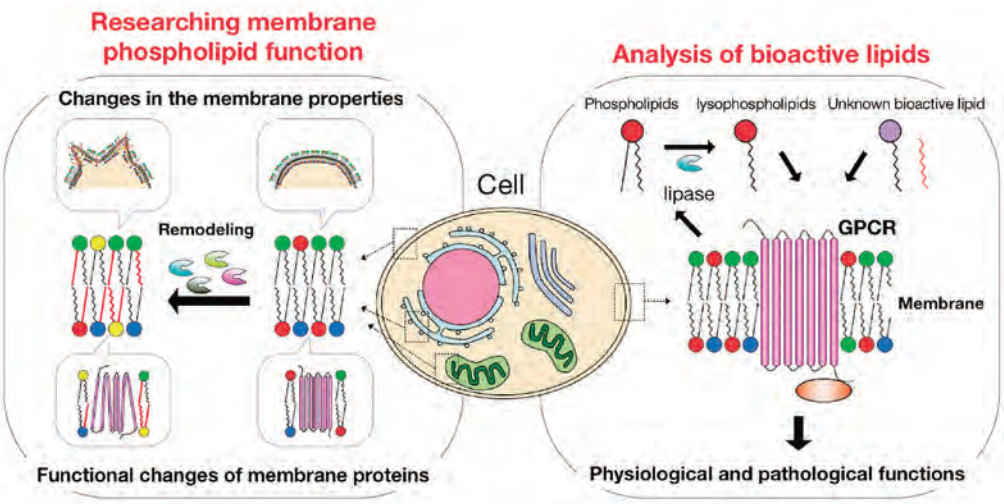
https://sites.google.com/view/eiseikagaku-en/

Laboratory of
Health Chemistry

Exploration of new functions for biomembranes and their constituent lipids

Research Topics

1. Reveal the physiological and pathological functions of lysophospholipids that work via GPCR
2. Discover new bioactive lipids and their receptors
3. Identify novel molecules involved in phospholipid biosynthesis and homeostasis, and elucidating their functions.



Biological membranes are composed of more than 1,000 lipid molecular species, and each of them is thought to have a specific function. Recently, some functions of lipids have been elucidated, and it is becoming clear that lipid molecules play essential roles in physiological situations such as reproduction, development, angiogenesis, and cell proliferation, and in pathological processes such as cancer and fibrosis development. On the other hand, the recent progress of mass spectrometry has revealed that there are more lipid molecules with unknown functions in the body. Unlike proteins, lipid molecules are not encoded by genes and lipid synthesis usually involves multiple proteins. Therefore, investigating the function of lipids is much more complicated than that of proteins. We are tackling to clarify the functions of various phospholipids by using the latest technologies including mass spectrometry and mass spectrometry imaging.

Our research results are promising to be applied to drug discovery and biomarker discovery.

Iwama T, Kano K, Kawana H, Shindou H, Shimizu T, Kono K, Aoki J. Visualization of Phospholipid Synthesis on Tissue Sections Using Functional Mass Spectrometry Imaging. Anal Chem 96: 11771-11779 (2024)

Izume T, Kawahara R, Uwamizu A, Chen L, Yaginuma Shun, Omi J, Kawana H, Hou F, Sano FK, Tanaka T, Kobayashi K, Okamoto HH, Kise Y, Ohwada T, Aoki J, Shihoya W, Nureki O. Structural basis for lysophosphatidylserine recognition by GPR34. Nat Commun. 15:902 (2024).

Omi J, Kato T, Yoshihama Y, Sawada K, Kono N, Aoki J. Phosphatidylserine synthesis controls oncogenic B cell receptor signaling in B cell lymphoma. J Cell Biol. 223:e202212074 (2024)

Sugahara S, Ishino Y, Sawada K, Iwata T, Shimanaka Y, Aoki J, Arai H, Kono N. Diseaserelated PSS1 mutant impedes the formation and function of osteoclasts. J Lipid Res. 64:100443 (2023).

Kawana H, Ozawa M, Shibata T, Onishi H, Sato Y, Kano K, Shindou H, Shimizu T, Kono N, Aoki J. Identification and characterization of LPLAT7 as an sn-1-specific lysophospholipid acyltransferase. J Lipid Res. 63:100271 (2022).

Prof. D. Kitagawa

Lecturer **M. Fukuyama**
Project Lecturer **S. Hata**
Assist. Prof. **T. Chinen**
Assist. Prof. **S. Yamamoto**

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Takeda, Y., Chinen, T., Honda, S., Takatori, S., Okuda, S., Yamamoto, S., Fukuyama, M., Takeuchi, K., Tomita, T., Hata, S., Kitagawa, D. Molecular basis promoting centriole triplet microtubule assembly. Nature Communications, 2024 Mar 22;15(1):2216. doi: 10.1038/s41467-024-46454-x.(2024)

Ito K.K., Watanabe K., Ishida H., Matsuhashi K., Chinen T., Hata S., Kitagawa D. Cep57 and Cep57L1 maintain centriole engagement in interphase to ensure centriole duplication cycle. Journal of Cell Biology, 220, e202005153 (2021)

Chinen T., Yamamoto S., Takeda Y., Watanabe K., Kuroki K., Hashimoto K., Takao D., Kitagawa D. NuMA assemblies organize microtubule asters to establish spindle bipolarity in acentrosomal human cells. EMBO journal, doi: 10.15252/embj.2019102378. (2020)

Yamamoto S., Kitagawa D. Self-organization of Plk4 regulates symmetry breaking in centriole duplication. Nature Communications, doi: 10.1038/s41467-019-09847-x.(2019)

Watanabe K., Takao D., Ito K.K., Takahashi M., Kitagawa D. The Cep57-pericentrin module organizes PCM expansion and centriole engagement. Nature Communications,doi: 10.1038/s41467-019-08862-2.(2019)

Laboratory of
Physiological Chemistry

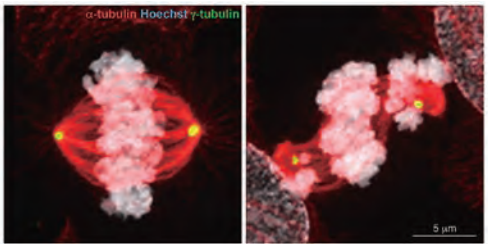
Mechanisms of cell division and their application to drug development

Research Topics

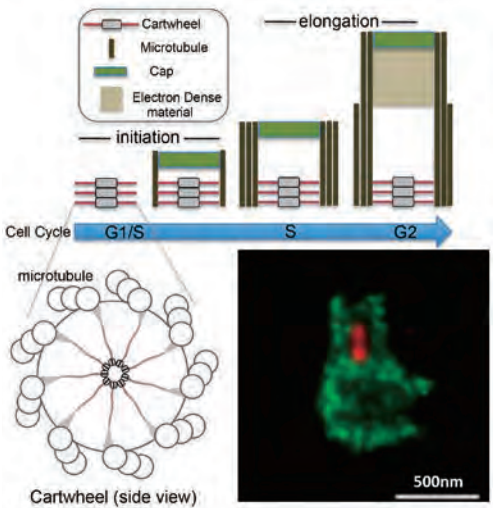
1. Mechanisms of centrosome duplication and its theoretical model
2. Mechanisms of cell division regulated by divergent molecular machineries
3. Identification and characterization of non-coding RNAs that regulate cell division
4. Comparative cancer cell biology and its application to anticancer drug development
5. Forward genetic analysis of cell-cell communication with human cells

Our laboratory mainly focuses on understanding the mechanisms of cell division, with a particular emphasis on the molecular basis and theoretical model of centrosome duplication. We are also interested in elucidating how divergent molecular machineries, including a protein complex and protein-lncRNA complex, regulate somatic and meiotic cell division. Based on these studies, we then explore a new approach to develop a novel anti-cancer therapy. To this end, we currently use the combination of innovative and multi-disciplinary methods including molecular biology, biochemistry, biophysics, structural biology, genetics, computer simulation and cell biology.

Furthermore, to understand molecular mechanisms and basic principles underlying a wider range of biological phenomena *in vivo*, we are also trying to establish a forward genetic approach with *in vitro* reconstitution of human cell-cell communication.



Bipolar spindle formation in mitotic HeLa cells. Control (left panel) and a cell defective in forming a proper mitotic spindle and chromosome segregation (right panel).



Centriole duplication and structure. An image obtained by super-resolution microscopy: centriole wall in green, cartwheel structures in red.

Prof. Y. Gotoh

Assoc. Prof. **D. Kawaguchi**
Project Assoc. Prof. **K. Oishi**
Assist. Prof. **T. Kuniya**
Project Assist. Prof. **H. Sugishita**

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Kuwayama N, Kujirai T, Kishi Y, Hirano R, Echigoya K, Fang L, Watanabe S, Nakao M, Suzuki Y, Ishiguro KI, Kurumizaka H, Gotoh, Y. HMGA2 directly mediates chromatin condensation in association with neuronal fate regulation. Nat. Comm. 14, 3420 (2023)

Harada, Y., Yamada, M., Imayoshi, I., Kageyama, R., Suzuki, Y., Kuniya, T., Furutachi, S., Kawaguchi, D. and Gotoh, Y. Cell cycle arrest determines adult neural stem cell ontogeny by an embryonic Notch- nonoscillatory Hey1 module. Nat. Comm. 12, 6562 (2021).

Eto, H., Kishi, Y., Yakushiji-Kaminatsu, N., Sugishita, H., Utsunomiya, S., Koseki, H. and Gotoh, Y. The Polycomb group protein Ring1 regulates dorsoventral patterning of the mouse telencephalon. *Nat. Comm.* 11, 5709 (2020).

Tsuboi, M., Kishi, Y., Kyozuka, W., Koseki, H., Hirabayashi, Y., and Gotoh, Y. Ubiquitination independent repression of PRC1 targets during neuronal fate restriction in the developing mouse neocortex. *Dev. Cell* 47, 758-772 (2018).

Lanjakornsiripan, D., Pior, B. J., Kawaguchi, D., Furutachi, S., Tahara, T., Katsuyama, Y., Suzuki, Y., Fukazawa, F., and Gotoh, Y. Layer-specific heterogeneity of astrocytes and its dependence on neuronal layers. *Nat.Commun.* 9, 1623 (2018).

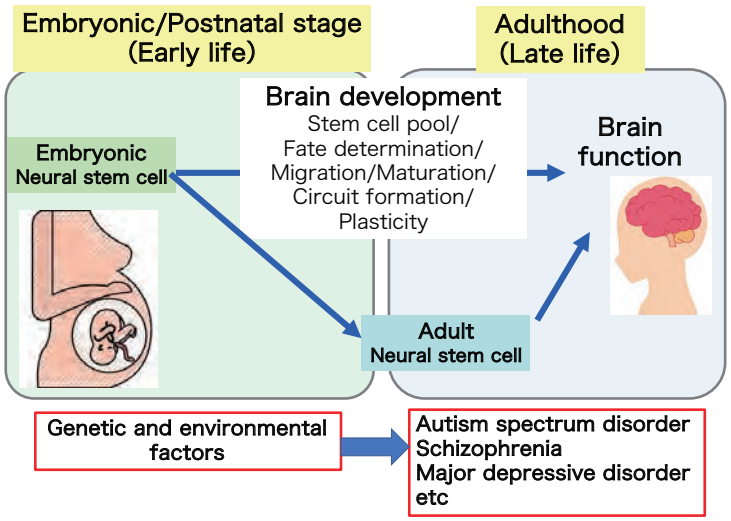
Laboratory of
Molecular Biology

Molecular studies of brain development, homeostasis and disease

Research Topics

1. Molecular mechanisms responsible for the regulation of neural stem-progenitor cell fate during development and adulthood
2. Epigenetic regulation of cell fate determination
3. Dysregulation of neural development associated with neurodevelopmental disorders

How does a cell determine its fate? This is a fundamental question in understanding multicellular organisms. Our laboratory aims to understand development of the mammalian brain from the viewpoint of cell fate determination at the molecular level. The brain, the organ responsible for our thoughts and actions, processes sophisticated information through extremely complex neural circuits. The mammalian brain is formed during development by the repeated proliferation and differentiation of neural stem-progenitor cells (NSCs), which give rise to various types of neurons and glial cells, and by the proper positioning of these progeny cells and circuit maturation. The brain contains many regions that perform different functions, and NSCs are responsible for the generation and construction of functional elements specific to each region. In addition, a specific subset of NSCs persists in the adult mouse brain and continues to produce neurons throughout life, with these neurons being thought to play essential roles in learning, memory, recovery from stress, and innate behaviors. We are particularly interested in temporal and spatial cues as well as epigenetic regulation of gene expression and nuclear chromatin architecture that underlie proper brain development and function. For example, we are currently investigating the contribution of chromatin and epigenome regulation to the developmental stage–dependent control of NSC fate as well as to the history-dependent plasticity of neural circuits. We are also investigating the molecular basis of neurodevelopmental disorders with the use of mouse models. We hope to contribute to a better understanding of the principles of normal brain development and of the pathogenesis of developmental brain abnormalities.



Laboratory of

Genetics

Molecular logic underlying the formation and maintenance of cell society in the body

Assoc. Prof. **Y. Nakajima**
Assist. Prof. **N. Shinoda**

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Research Topics

1. Regulatory mechanisms of non-apoptotic caspase
2. Metabolic regulation of development, regeneration, growth and aging
3. Molecular mechanisms of phenotype expressivity
4. Mechanisms of tissue size control during development
5. Cellular plasticity in tissue homeostasis and environmental responses

Programmed cell death functions in dynamic tissue formation and remodeling. We have revealed that in the embryonic development, or aging process, caspases are activated by physiological stresses and exert not only apoptosis but also regulatory functions. We aim to reveal how caspase and metabolisms are involved in the determination of phenotype expressivity during development, growth, regeneration and aging. We also study the mechanisms of tissue size control during development and cellular plasticity in tissue homeostasis and environmental responses. We believe that our research would stimulate and encourage students and researchers to have the breadth of vision for life science research and provide new insights into the molecular logic underlying the formation and maintenance of cell society in the body.

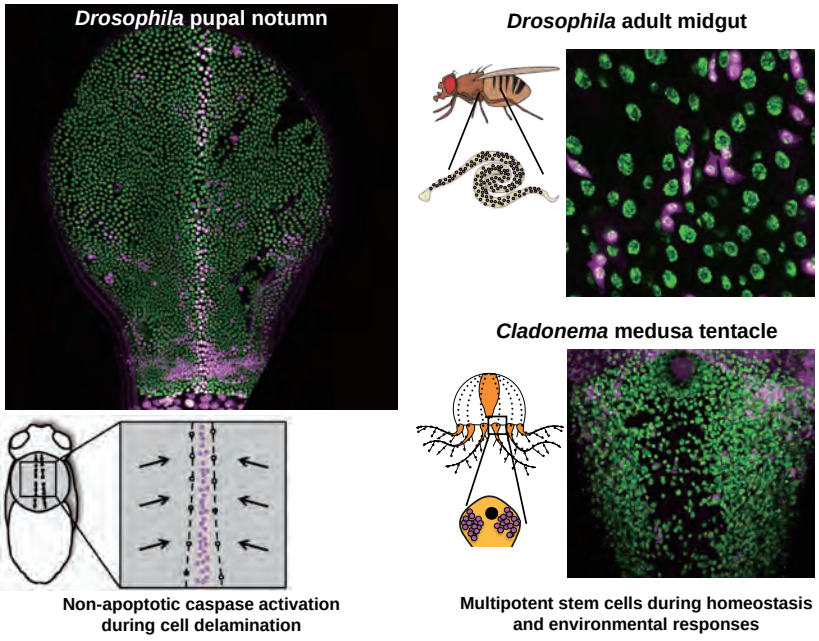

Figure
Confocal stack image of the *Drosophila* pupal notumn. In this picture, caspase-3 activated cells (magenta) are observed in the midline (left picture). Visualization of tissue stem cells in *Drosophila* adult midgut and *Cladonema* medusa tentacle. Multipotent stem cells contribute to tissue homeostasis and environmental responses (right picture).

Obata, F., and Miura, M.: Regulatory mechanisms of aging through the nutritional and metabolic control of amino acid signaling in model organisms. Ann Rev Genetics 58, 19-41 (2024)

Shinoda, N., and Miura, M.: Exploring caspase-dependent non-lethal cellular processes using *Drosophila*. *Front. Cell. Death* 3, 1472108 (2024)

Nagai, H., Adachi, Y., Nakasugi, T., Takigawa, E., Ui, J., Makino, T., Miura, M., and Nakajima, Y.: Highly regenerative species-specific genes improve age-associated features in the adult Drosophila midgut. *BMC Biol.* 22, 157 (2024)

Muramoto, M., Hanawa, N., Okumura, M., Chihara, T., Miura, M., and Shinoda, N.: Executioner caspase is proximal to Fasciclin 3 which facilitates non-lethal activation in *Drosophila* olfactory receptor neurons. *eLife* (Reviewed Preprint)

Hikawa, N., Kashio, S., and Miura, M.: Mating-induced increase of kynurenine in *Drosophila* ovary enhances starvation resistance of progeny. *J. Biol. Chem.* 300, 105663 (2024)

Fujita, S., Takahashi, M., Kumano, G., Kuranaga, E., Miura, M., and Nakajima, Y.: Distinct stem-like cell populations facilitate functional regeneration of the *Cladonema* medusa tentacle. *PLOS Biol.* 21: e3002435 (2023)

Nagai, H., Nagai, LAE., Tasaki, S., Nakato, R., Umetsu, D., Kuranaga, E., Miura, M., and Nakajima, Y.: Nutrient-driven dedifferentiation of enteroendocrine cells promotes adaptive intestinal growth in *Drosophila*. *Dev. Cell* 58: 1764-1781(2023)

Laboratory of
Cell Signaling

From signal transduction to drug discovery

Assist. Prof. **T. Fujisawa**

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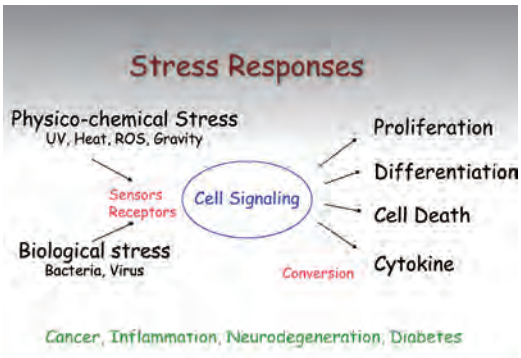
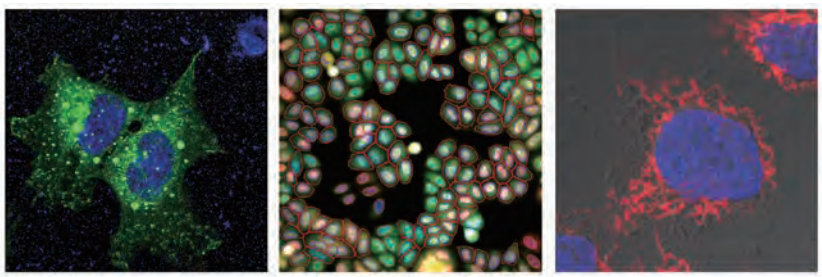
Research Topics

1. Exploration of novel signaling molecules involved in cell death and stress responses
2. Molecular mechanisms of pathogenesis induced by dysfunction of stress signaling

The Laboratory of Cell Signaling has been focusing on analyses of the intracellular signal transduction, through which we seek to elucidate molecular basis of human diseases and identify novel drug targets. Our current research mainly focuses on the pathophysiological roles of stress responsive signals in various diseases such as cancers, immune disorders, cardiovascular diseases and neurodegenerative diseases. In addition to molecular genetic tools such as mice, flies and worms as well as basic experimental techniques from molecular cloning to protein biochemistry, we always incorporate novel analytic technologies such as mass spectrometry-based proteomic analysis and genome-wide RNAi screening systems into our research exploring “target molecules and molecular mechanisms”. By taking advantage of such experimental approaches, we aim to open up new fields in pharmaceutical sciences with paying attention to whole body physiology, diseases and drug discovery.





Stress-induced formation of P-body.
green: Venus-Dcp1a, blue: Nuclei

Image analysis using a high-content image analyzer.
red: NFAT5, green: GFP, blue: Nuclei

Visualized Mitochondria by DsRed-Mito.
blue: Nuclei

Morishita, K., Watanabe, K., Naguro I. and Ichijo H. Sodium ion influx regulates liquidity of biomolecular condensates in hyperosmotic stress response. Cell Rep. 42,112315 (2023).

Watanabe, K., Morishita, K., Zhou, X., Shiizaki, S., Uchiyma, Y., Koike, M., Naguro, I. and Ichijo, H. Cells recognize osmotic stress through liquid–liquid phase separation lubricated with poly(ADP-ribose). Nat. Commun., 12,1353 (2021).

Ogawa, M., Kawarazaki, Y., Fujita, Y., Naguro, I. and Ichijo, H. FGF21 induced by the ASK1-p38 pathway promotes mechanical cell competition by attracting cells. Curr. Biol., 31, 1-10 (2021).

Nakamura, T., Ogawa, M., Kojima, K., Takayanagi, S., Ishihara, S., Hattori, K., Naguro, I. and Ichijo, H. The mitochondrial Ca2+ uptake regulator, MICU1 is involved in cold stress-induced ferroptosis. EMBO Rep., 22, e51532 (2021).

Watanabe, K., Umeda, T., Niwa, K., Naguro, I. and Ichijo, H. A PP6-ASK3 module coordinates the bidirectional cell volume regulation under osmotic stress. Cell Rep., 22, 2809-2817 (2018).

Prof. S. Murata

Lecturer. **J. Hamazaki**
Assist. Prof. **Y. Shibata**

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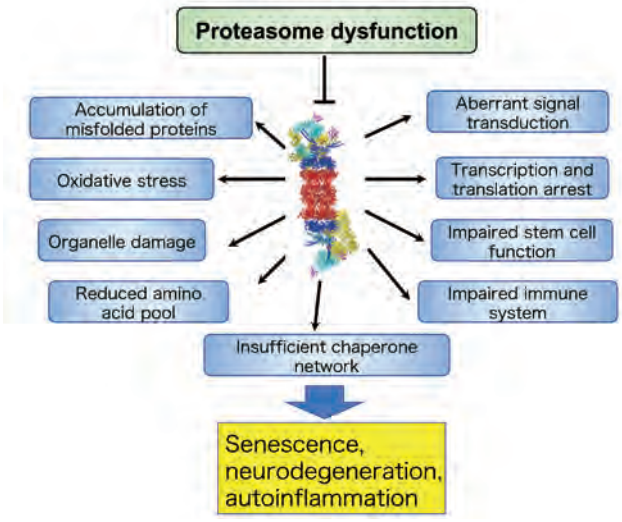
Laboratory of
Protein Metabolism

Elucidating various biological phenomena controlled by proteolysis

Research Topics

1. The action mechanisms of the proteasome, a multisubunit macromolecular complex responsible for regulated protein degradation in eukaryotic cells
2. Proteasome dysfunction in human diseases (senescence, malignant tumors, inflammation, neurodegeneration)
3. The mechanism of maintenance of protein homeostasis by the ubiquitin-proteasome system

The proteasome is a supramolecular proteolytic apparatus that exists in all eukaryotic cells. The proteasome plays pivotal roles in various cellular functions by selectively degrading ubiquitinated proteins. It is also central to the maintenance of protein homeostasis (proteostasis). In recent years, it has become evident that the impairment of proteostasis is a hallmark of senescence, and the decline of proteasome function is drawing attention as one of the primary factors. Indeed, it has been shown that age-associated diseases develop as proteasome function declines with age, and that artificial increase in proteasome activity prolongs the healthy lifespan in nematodes and Drosophila. However, in mammals, means to enhance proteasome function has not been established at present. This is because in mammals the proteasome is controlled more complicatedly and because the mechanisms by which the proteasome function decreases with aging and by which a decrease in proteasome function causes senescence are not understood. On the other hand, it has become clear that inhibition of proteasome function is an important therapeutic strategy in malignant tumors where proteasome hyperactivity is observed.
The ultimate goal of Laboratory of Protein Metabolism is to create a method of intervention in pathologies involving proteasome dysfunction. To this end, we are researching detailed mechanisms of action and regulation of the proteasome by using techniques such as molecular and cell biology, comprehensive gene screening, proteomics, and mouse genetics.



Iriki T, Iio H, Yasuda S, Masuta S, Kato M, Kosako H, Hirayama S, Endo A, Ohtake F, Kamiya M, Urano Y, Saeki Y, Hamazaki J, Murata S. Senescent cells form nuclear foci that contain the 26S proteasome. Cell Rep. 112880. (2023)

Takehara Y, Yashiroda H, Matsuo Y, Zhao X, Kamigaki A, Matsuzaki T, Kosako H, Inada T, Murata S, The ubiquitination-deubiquitination cycle on the ribosomal protein eS7A is crucial for efficient translation., .iScience. 102145. (2021)

Hashimoto E, Okuno S, Hirayama S, Arata Y, Goto T, Kosako H, Hamazaki J, Murata S. Enhanced O-GlcNAcylation Mediates Cytoprotection under Proteasome Impairment by Promoting Proteasome Turnover in Cancer Cells. iScience. 101299 (2020)

Murata S, Takahama Y, Kasahara M, Tanaka K. The immunoproteasome and thymoproteasome: functions, evolution and human disease. Nat Immunol. 923-931. (2018)

Hirayama S, Sugihara M, Morito D, Iemura SI, Natsume T, Murata S, Nagata K. Nuclear export of ubiquitinated proteins via the UBIN-POST system. Proc Natl Acad Sci U S A. E4199-E4208. (2018)

Koizumi S, Irie T, Hirayama S, Sakurai Y, Yashiroda H, Naguro I, Ichijo H, Hamazaki J, Murata S. The aspartyl protease DDI2 activates Nrf1 to compensate for proteasome dysfunction. Elife. 5, e18357. (2016)

Assoc. Prof.
R. K. Kawaguchi

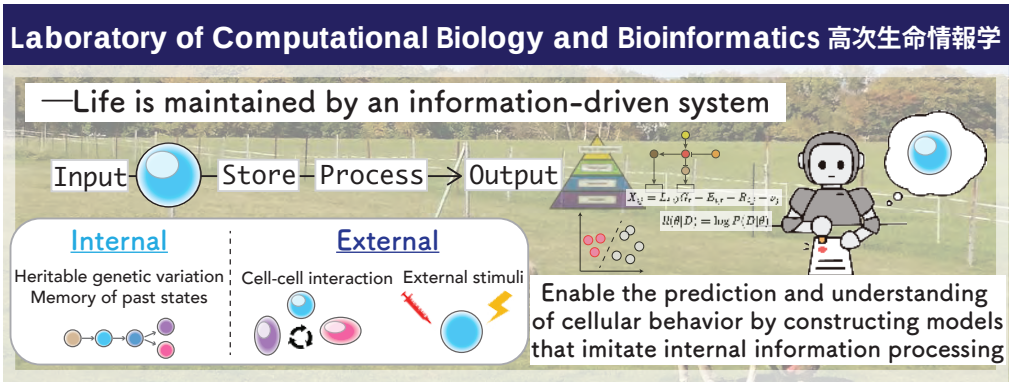
https://carushi.github.io/cb_lab/index_en.html

Laboratory of Computational Biology and Bioinformatics

Decoding how living organisms shape their future behaviors by orchestrating body cells through the dynamic processing of external and internal information signals

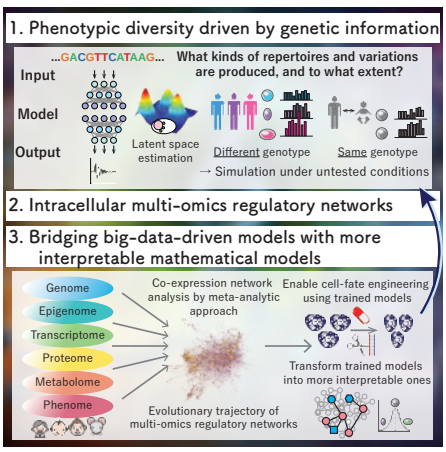
Research Topics

1. Understanding the diversity of cellular and organismal phenotypic variations arising from discrete genetic information
2. Elucidating the evolutionary trajectory of intracellular multi-omics regulatory networks
3. Bridging the gap between biological big data and mathematical models using cutting-edge techniques of information science



We, the Laboratory of Computational Biology and Bioinformatics, conduct research in life and pharmaceutical sciences from the perspective of how biological systems store, receive, and transmit information. The advancement of experimental techniques in recent years has enabled the acquisition of large-scale, high-dimensional biological data, necessitating new computational approaches to reveal the underlying regulatory mechanisms behind data. Our goal is to develop innovative data analysis methods based on information science, statistics, and mathematical sciences, ultimately leading to the discovery of complex biological systems and the development of drugs to manipulate them.

Our research focuses on understanding cellular and organismal phenotypic diversity originated from both heritable and non-heritable information. Using computational methods based on statistics and machine learning, we aim to construct gene and molecular interaction networks from multi-omics data, and predict cellular responses to external stimuli or drug treatments under untested environmental conditions. Additionally, we work on bridging big-data-driven models with interpretable mathematical models to enhance human comprehension and facilitate intuitive visualization.



1 Miyake H, Kawaguchi RK, Kiryu H. RNAelem: an algorithm for discovering sequence-structure motifs in RNA bound by RNA-binding proteins . Bioinfo. Adv., vbae144 (2024).

2 Ballouz S†, Kawaguchi RK†, Pena MT, Fischer S, Crow M, French L, Knight FM, Adams LB, Gillis J. The transcriptional legacy of developmental stochasticity. Nat. Comm., 14:7226 (2023) † contributed equally

3 Kawaguchi RK, Tang Z, Fischer S, Rajesh C, Tripathy R, Koo PK, Gillis J. Learning single-cell chromatin accessibility profiles using meta-analytic marker genes. Brief. in Bioinfo., bbac541 (2022)

4 Sheu YJ, Kawaguchi RK, Gillis J, Stillman B. Prevalent and dynamic binding of the cell cycle checkpoint kinase Rad53 to gene promoters. eLife, 11:e84320 (2022)

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Laboratory of
Immunology and Microbiology

Understanding the principles of immunological tolerance and homeostasis

Research Topics

1. Mechanisms of immunological tolerance and homeostasis
2. Mechanisms of regulatory T cell development and function
3. Mechanisms of memory CD8 T cell maintenance

The immune system has evolved the ability to distinguish "self" from "non-self" to maintain homeostasis of the body. The immunological "self" is established in an adaptive and acquired manner through continuous interactions with changing internal as well as external environments. The ultimate goal of this laboratory is to elucidate, throughout multiple layers, from molecules, cells, cell populations, tissues, to individuals, the principles that govern the development of such immunological "self" and its transformation during diseases. Towards this end, we focus on a cell-extrinsic, dominant control mechanism of the immune system that depends on a subpopulation of T lymphocytes called regulatory T (Treg) cells. As one approach, we elucidate how mutations in the *Foxp3* gene, encoding a transcription factor critical for Treg cell development and function, lead to a breakdown of immunological tolerance and homeostasis.

Fig. 1

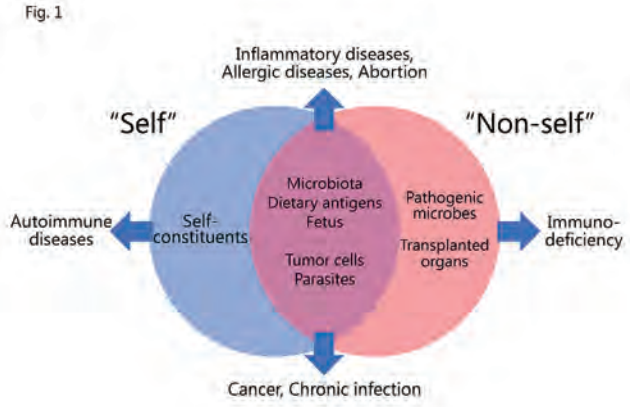

Fig. 1: Disintegration of immunological "self" underlies a variety of diseases

Fig. 2

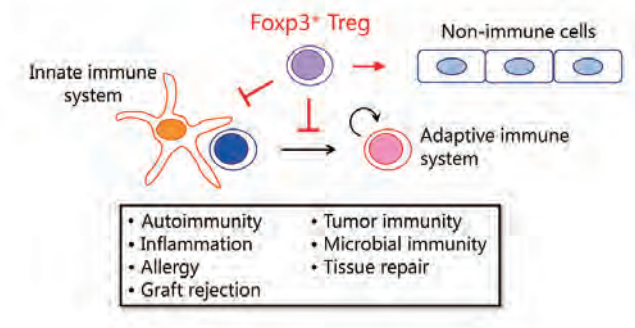

Fig. 2: Foxp3-expressing regulatory T (Treg) cells are indispensable for immunological tolerance and homeostasis

Setoguchi, R., Sengiku, T., Kono, H., Kawakami, E., Kubo, M., Yamamoto, T., Hori, S. 2024. Memory CD8 T cells are vulnerable to chronic IFN-γ signals but not to CD4 T cell deficiency in MHCII-deficient mice. Nature Communications 15(1):4418

Nakajima, A., R. Murakami, and S. Hori. 2023. Functional Analysis of Foxp3 and Its Mutants by Retroviral Transduction of Murine Primary CD4(+) T Cells. *Methods Mol Biol* 2559:79-94.

Hori, S. 2021. FOXP3 as a master regulator of Treg cells. *Nat Rev Immunol* 21:618-619.

Hori, S., and R. Murakami. 2021. The adaptability of regulatory T cells and Foxp3. *International Immunology* 33:803-807.

Hayatsu, N., T. Miyao, M. Tachibana, R. Murakami, A. Kimura, T. Kato, E. Kawakami, T.A. Endo, R. Setoguchi, H. Watarai, T. Nishikawa, T. Yasuda, H. Yoshida, and S. Hori. 2017. Analyses of a Mutant Foxp3 Allele Reveal BATF as a Critical Transcription Factor in the Differentiation and Accumulation of Tissue Regulatory T Cells. *Immunity* 47:268-283 e269.

Prof.
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Maedera S, Mizuno T, Kusuhara H. Investigation of latent representation of toxicopathological images extracted by CNN model for understanding compound properties in vivo. Comput Biol Med. 168:107748 (2024).

H ashimoto Y, et al. Evaluation of the risk of diarrhea induced by epidermal growth factor receptor tyrosine kinase inhibitors with cultured intestinal stem cells originated from crypts in humans and monkeys. Toxicol In Vitro. 93:105691 (2023).

Tamura R, et al. Intestinal Atp8b1 dysfunction causes hepatic choline deficiency and steatohepatitis. Nat Commun. 14(1):6763 (2023).

Michiba K, et al. Usefulness of Human Jejunal Spheroid-Derived Differentiated Intestinal Epithelial Cells for the Prediction of Intestinal Drug Absorption in Humans. Drug Metab Dispos. 50(3):204-213 (2022).

Mochizuki T, et al. Effect of Cyclosporin A and Impact of Dose Staggering on OATP1B1/1B3 Endogenous Substrates and Drug Probes for Assessing Clinical Drug Interactions. Clin Pharmacol Ther. 111(6):1315-1323 (2022).

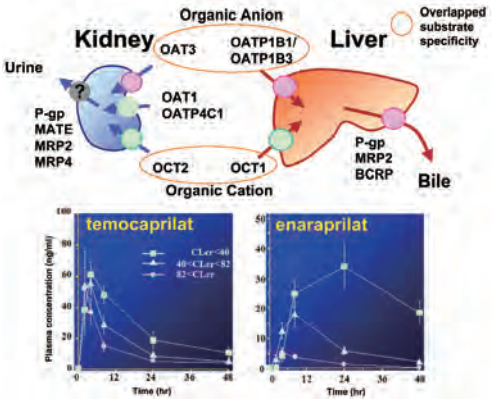
Laboratory of
Molecular Pharmacokinetics

Elucidation of the mechanisms determining pharmacokinetic properties of drugs that contributes to drug design, and safe and effective utilization of drugs

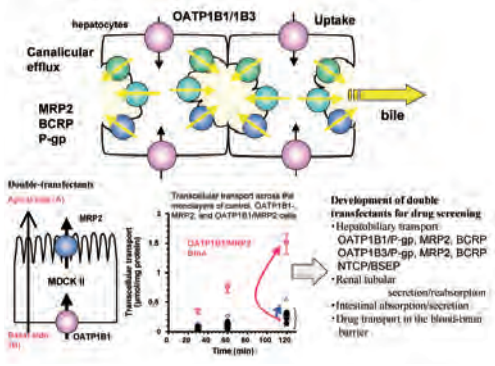
Research Topics

1. Establishment of the methodologies for in vitro-in vivo extrapolation of drug pharmacokinetics and pharmacological effect
2. Elucidation of molecular mechanisms determining the intestinal absorption of drugs, clearance of drugs from liver/kidney and drug transport at the barrier organs such as blood-brain barrier
3. Prediction of the effect of genetic polymorphisms of metabolic enzymes/transporters on the inter-individual variations of drug pharmacokinetics
4. Establishment of the methodologies for the quantitative prediction of drug-drug interaction risks
5. Elucidation of mechanisms for the membrane trafficking of transporters
6. Development of qualitative and quantitative prediction methods by in silico analysis for pharmacokinetic properties of drugs
7. Understanding of drug effects by data-driven analysis

Pharmacological and adverse effects of drugs depend on their pharmacokinetic properties, which determine their exposure to the targets. Our laboratory aims to establish methods for quantitative and theoretical prediction of pharmacokinetic properties of new chemical entities in humans based on the molecular mechanisms. In particular, we investigate the impact of transporters on the elimination of drugs from the liver and kidney, the distribution of drugs into their target organs *e.g.*, the brain, and drug absorption in the small intestine, in order to develop drug screening systems and to elucidate the mechanisms of drug-drug interaction, and interindividual variation in pharmacokinetics of drugs. We have also started research on the regulation of membrane trafficking of the transporters using low molecular weight compounds to cure transporter related-diseases. Research achievements in this laboratory contribute to predicting and evaluating rational pharmacokinetic properties in drug development, drug review and regulation, and in clinical use, and to developing medical therapy for transporter related-diseases.



An example of a drug successfully designed to minimize interindividual variation in pharmacokinetics by considering transporter characteristics.



As a high-throughput screening system for hepatobiliary transport, uptake and efflux transporters are simultaneously expressed in a single polarized cell (double transfectant).

Prof. Y. Ikegaya

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Assist. Prof.
N. Matsumoto
Project Assist. Prof.
T. Kashima

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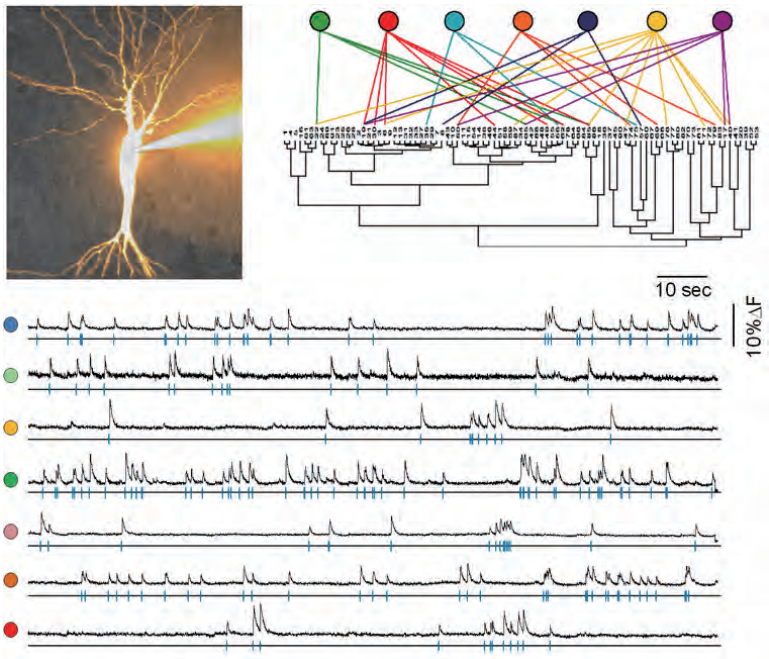
Laboratory of
Chemical Pharmacology

Pharmacological approach toward the brain: from molecule to animal

Research Topics

1. Exploring a new dimension of brain function via Brain-AI hybrid
2. Studying brain network operation using multicellular activity recording
3. Studying neuronal network formation during development

Pharmacology includes two aspects: 1) to analyze the biological action of drugs and 2) to search the strategies for developing treatments for diseases. We conduct our pharmacological research by taking advantage of state-of-the-art technologies and a wide range of knowledge from molecule to animal.
We focus on the roles of the cerebral limbic system and cerebral cortex, in particular, the hippocampus and amygdala, which are involved in learning, memory, and emotion.
Our experimental techniques cover from genetics, biochemistry, and cell biology to electrophysiology, histochemistry, and behavioral pharmacology. Recent technical advances have allowed us to investigate the neuronal network dynamics on far larger scales than hitherto. Functional multineuron calcium imaging reveals the dynamics of network activity with single cell/synapse resolution (Upper Figure), through which we elucidate the structural and functional relationship that generates spatiotemporally organized spike patterns. We also address the mechanisms of learning and memory using in situ mapping learning-relevant neuronal circuits with immediate early genes with cellular and temporal resolution (Lower Figure). We believe that these novel approaches open up a new avenue for our mesoscopic understandings of network function and malfunction associated with depression, stress-relevant disease, and epilepsy.



Functional multineuron calcium imaging from neuron populations

Yoshimoto, A., Morikawa, S., Kato-Ishikura, E., Takeuchi, H., and Ikegaya, Y. Top-down brain circuits for operant bradycardia. Science, 384:eadl3353, 2024.

Ikegaya, Y., Matsumoto, N. Spikes in the sleeping brain. Science,366:306-307 (2019)

Nakashima, A., Ihara, N., Shigeta, M., Kiyonari, H., Ikegaya, Y., Takeuchi, H. Structured spike series specify gene expression patterns for olfactory circuit formation. Science, 365:eaaw5030 (2019)

Norimoto, H., Makino, K., Gao, M., Shikano, Y., Okamoto, K., Ishikawa, T., Sasaki, T., Hioki, H., Fujisawa, S., Ikegaya, Y. Hippocampal ripples down-regulate synapses. Science, 359:1524-1527 (2018)

Takahashi, N., Kitamura, K., Matsuo, N., Mayford, M., Kano, M., Matsuki, N., Ikegaya, Y. Locally synchronized synaptic inputs. *Science* 335: 353-356 (2012)

Sasaki, T., Matsuki, N., Ikegaya, Y. Action-potential modulation during axonal conduction. *Science* 311: 599-601 (2011)

Prof. T. Tomita

Visiting. Prof. **S. Torii**
Assoc. Prof. **Y. Hori**
Assist. Prof. **S. Takatori**
Assist. Prof. **T. Kimura**

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Nakamura R, Tomizawa I, et al. Photo-oxygenation of histidine residue inhibits α-synuclein aggregation. *FASEB J.* 37(12):e23311 (2023)

Matsuzaki, M., Yokoyama, M., et al. ADAMTS4 is involved in the production of the Alzheimer disease amyloid biomarker APP669-711. *Mol. Psychiatry* 28(4):1802-1812 (2023)

Ozawa, S., Hori, Y., et al. Photo-oxygenation by a biocompatible catalyst reduces Aβ levels in the brains of Alzheimer disease model mice. *Brain* 144(6):1884-1897 (2021)

Nagashima, N., Ozawa, S., et al. Catalytic photooxygenation reduces brain Aβ *in vivo*. *Sci Adv* 7(13): eabc9750, (2021)

Schweighauser, M., Shi, Y., Tarutani, A., et al. Structures of α-synuclein filaments from multiple system atrophy. *Nature* 585(7825):464-469 (2020)

Nakamura, A., Kaneko, N., et al. High performance plasma Aβ-amyloid biomarkers for Alzheimer's disease. *Nature* 554(7691):249-254 (2018)

Kidana, K., Tatebe, T., Ito, K., et al. Loss of astrocyte-derived kallikrein 7 exacerbates amyloid pathology in Alzheimer disease model mouse. *EMBO Mol Med*. e8184 (2018)

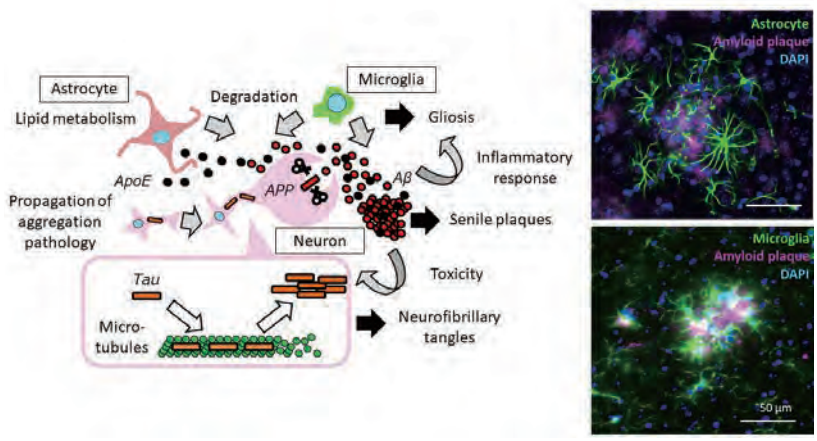
Laboratory of
Neuropathology and Neuroscience

From understanding the molecular pathogenesis of neurodegenerative and psychiatric diseases to development of therapeutics and novel basic science

Research Topics

1. Research on Aβ metabolism (production, secretion and clearance) and its regulatory mechanisms
2. Understanding the cellular pathology after Aβ deposition towards the development of diagnostics
3. Elucidation of mechanism of amyloid formation deposited in the brains of patients
4. Investigation of the pathological function of microglia in Alzheimer disease
5. Understanding the molecular pathomechanisms of Parkinson disease
6. Elucidation of molecular mechanism of propagation of α-synuclein pathology
7. Biological and pathological roles of synaptic adhesion molecules in psychiatric disorders
8. Development of exercise program for dementia prevention

Aim of our laboratory is that understanding the molecular pathogenesis of neurodegenerative and psychiatric diseases to develop novel approaches to therapeutic, prevention and diagnosis. Also, we are pursuing novel basic science by understanding the molecular basis of diseases. Especially, we are studying Alzheimer disease, autism spectrum disorder and schizophrenia to identify the pathological mechanisms and therapeutic targets of these diseases at molecular levels. To understand the disease condition, we have to realize the basic mechanisms of cells and living organisms, and vice versa. We believe that this disorder-to-normal cycle in research is a basis of modern disease and basic biology, and bolsters both scientific areas by novel knowledge and technology. From this standpoint, we proceed disease-oriented molecular and cellular research in a multidisciplinary manner by mutual collaborations with organic chemists, structural biologists, physicians and pharmaceutical companies.



Molecular and cellular pathologies in Alzheimer disease

Visiting Prof. Y. Sawada

Project Assoc. Prof.
H. Satoh
Project Assist. Prof.
N. Yanagi

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Tanaka, S., Kanagawa, T., Momma, K., Hori, S., Satoh, H., Nagamatsu, T., Fujii, T., Kimura, T., Sawada, Y. Prediction of sustained fetal toxicity induced by ketoprofen based on PK/PD analysis using human placental perfusion and rat toxicity data. *Br J Clin Pharmacol*. 83(11): 2503-2516 (2017)

Park, H., Miki, A., Satoh, H., Sawada, Y. Survey on the attitudes and concerns of fee-based elderly nursing homes staff regarding medication assistance in Japan: a questionnaire survey. *Jpn J Drug Inform*. 19(3): 133-141 (2017)

Miyazaki, S., Satoh, H., Ikenishi, M., Sakurai, M., Ueda, M., Kawahara, K., Ueda, R., Ohtori, T., Matsuyama, K., Miki, A., Hori, S., Fukui, E., Nakatsuka, E., Sawada, Y. Pharmacokinetic model analysis of interaction between phenytoin and capecitabine. *Int J Clin Pharmacol Ther*. 54(9): 657-665 (2016)

Matsuo, N., Hori, S., Suehira, M., Satoh, H., Miki, A., Sawada, Y. Sisters who developed piloerection after administration of milnacipran. *Int J Clin Pharmacol Ther.* 54(3): 208-211 (2016)

Park, H., Satoh, H., Miki, A., Urushihara, H., Sawada, Y. Medications associated with falls in older people: systematic review of publications from a recent 5-year period. *Eur J Clin Pharmacol*. 71(12): 1429-1440 (2015)

Endowed Laboratory of
Drug Lifetime Management

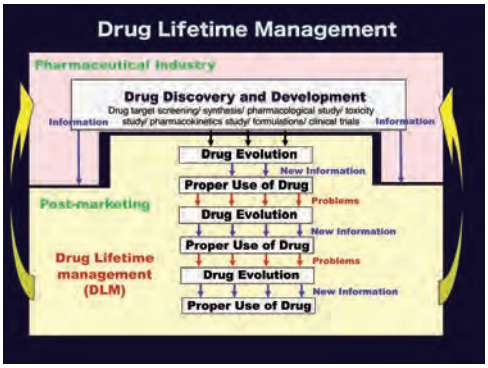
Drug lifetime management for development of excellent drugs, proper use of drugs, and evolution of drugs

Research Topics

1. Development and practice of methodologies for the collection, evaluation, analysis, and distribution of drug post-marketing information
2. Creation of programs for promoting proper use and evolution of drugs in community healthcare
3. Development of new features in the community pharmacy to practice the above-mentioned 2
4. Specification, standardization, and digitization of drug information, and their clinical applications
5. Quantitative prediction of the effects of biodisturbance factors on pharmacokinetics and drug effects

Our university's Faculty of Pharmaceutical Sciences bears the social mission of promoting drug discovery and the proper use and evolution of drugs while improving the quality of drug therapies. To these ends, this course in Drug lifetime management pursues various research to ensure that the developed drugs can amply exhibit their effects and lead a substantial "drug life."

The research topics of this course are that (1) the proper collection of drug information (DI), (2) evaluation/analysis of DI based on pharmacokinetics and pharmacodynamics and quantitative prediction of changes in pharmacokinetics and drug effect due to various risk factors, (3) Qualitative evaluation and analysis of the individual cases, (4) Creation of archive based on the optimal specification/standardization/digitization of DI, and (5) their proper provision to the clinical field. Concretely speaking, the content of our research is to seize drug post-marketing problems (including trouble and needs related with drugs), to make a proposal, to the pharmaceutical field, for evolving drugs and their information in order to solve the problems, and to feedback them to the clinical field.



The central dogma of pharmaceutical development consists of the cycle of drug discovery → proper use of drugs → post-marketing drug development → drug discovery and so on

Collection of drug post-marketing information with appropriate method (from whom? from where? How?).

Assoc. Prof.
S. Ono

Visiting Prof.
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https://yakuhyou.f.u-tokyo.ac.jp/study/eindex.html

Laboratory of
Pharmaceutical Regulatory Science

Establishing scientific drug evaluation

Research Topics

1. Advancing methods for rational drug evaluation
2. Analyzing drug development behaviors and policies
3. Evaluating drug regulation and guidelines
4. Developing systems to implement the above policies and guidelines

The goal of our research is to establish scientific principles and methods in drug evaluation with societal perspectives in mind. Pharmaceutical research and development (R&D), clinical development in particular, regulatory review and approval of new drugs, and post marketing activities are our research interests. We provide evidence on R&D efficiency, performance and outcomes of regulations, and public health impact through rigorous analysis based on economic models. Conflicts in global pharmaceutical R&D, including recent launch delay of new drugs in Japan and so-called ethnic differences, are always high on our agenda. Aside from the research activities, we also make efforts to develop human resources in both private and public sectors with up-to-date knowledge, ethics, and philosophy, and rationale in drug evaluation. We offer lectures for graduate and undergraduate students, and a half-year training course for industry and regulatory professionals. We aim to secure transparency and social responsibility on drug regulation through our research and educational programs.

Ishizuka, K., Ono, S. The impact of survival benefit and study design on FDA approval for anticancer drugs. Journal of Clinical Pharmacology (2024)

Sato, Y., Ono, S. Regulatory Environment and Approvals in Cell and Gene Therapy Products between Japan, the USA, and the EU. Therapeutic Innovation & Regulatory Science (2022)

Sugitani, Y., Ito, K., Ono, S. Patient Preferences for Attributes of Chemotherapy for Lung Cancer. Frontiers in Pharmacology DOI: 10.3389/fphar.2021.697711 (2021)

Harada, K., Toriyabe, K., Ono, S. Survey of Japanese orphan drug program: factors related to successful marketing approval. Journal of Clinical Pharmacology DOI: 10.1002/jcph.1501 (2020)

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Laboratory of
Medicinal Plant Chemistry

(Experimental Station for Medicinal Plant Studies)

An overall analysis is made of the old-yet-new drugs known as “medicinal plants” (crude drugs) to develop new ways of using them (utilizing the resources in the Experimental Station for Medicinal Plant Studies)

Research Topics

1. The cultivation of medicinal plants and tissue cultures
2. The production of useful secondary metabolites, using plant tissue culture technology
3. Chemistry and biosynthesis of plant-derived biologically active substances

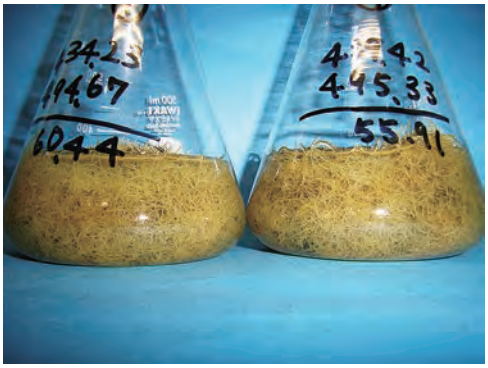
Since prehistoric times, plants have been the principal material used as drugs by humankind. Many have fallen by the wayside through a long process of trial and error (human experiments), and the ones that remain can be considered the crude drugs of the present day. In recent years, the percentage of all drugs accounted for by antibiotics and biologics has increased, but the importance of plant-derived pharmaceuticals is by no means diminished and has led to the discovery of new drugs such as Taxol and vinblastine. Thus, the study of medicinal plants is by no means completed, and is continuing to evolve.
The Experimental Station for Medicinal Plant Studies, formally established in 1973, is located adjacent to the Kemigawa Athletic Ground. The saplings transplanted there back then have grown large and now form a dense enclosure of trees around the garden.
At the research lab in Hongo, we conduct research on the production of useful secondary metabolites using plant tissue culture technologies (from the induction of culture cells to the production of substances). Some of the research topics we are currently pursuing are the biosynthesis of diterpene constituents from Gymnosperm plant cultured cells, the production and biosynthesis of diterpene alkaloids using cultured tissue of monkshood, the production and biosynthesis of phenylethanoids using cultured cells of olive, and the production of biologically active constituents of Egyptian medicinal plants by means of plant tissue culture technologies.

Fukuyama, N., Shibuya, M., Orihara, Y. Antimicrobial polyacetylenes from Panax ginseng hairy root. *Chem. Pharm. Bull.* 60(3): 377-380 (2012)

Fukuyama, N., Ino, C., Suzuki, Y., Kobayashi, N., Hamamoto, H., Sekimizu, K., Orihara, Y. Antimicrobial sesquiterpenoids from *Laurus nobilis* L. *Natural Product Research* 25(14): 1295-1303 (2011)

Saimaru, H., Orihara, Y. Biosynthesis of acteoside in cultured cells of *Olea europaea*. *J. Nat. Med.* 64: 139–145 (2010)

Orihara, Y., Hamamoto, H., Kasuga, H., Shimada, T., Kawaguchi, Y., Sekimizu, K. Evaluation of therapeutic effects of antiviral agents using a silkworm baculovirus infection model. *Journal of General Virology* 89: 188-194 (2008)



Aconitum japonicum cultured root

The sweetener glycyrrhizin is contained in the roots and stolons of *Glycyrrhiza uralensis* Fisher

Prof.
R. Shinkura

Assist. Prof. **N. Morita**
Assist. Prof. **P. Gao**
Assist. Prof. **G. Furuya**

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Laboratory of
Applied Immunology
(IQB Laboratory of Immunology and Infection Control)

Research on immunoglobulin diversification and gut microbial regulation by intestinal IgA

Research Topics

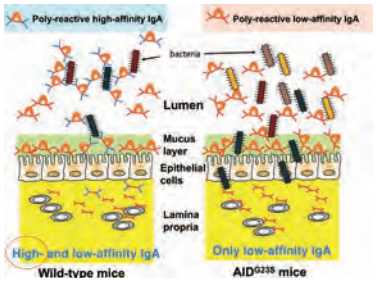
1. Mechanism of gut microbial regulation by intestinal IgA
2. Molecular mechanism of somatic hypermutation of immunoglobulin genes
3. Search for IgA class switch inducer

The immune response has evolved to protect us from pathogenic infectious agents and toxic foreign substances. In acquired immune response, antigen stimulation of B cells induces two distinct genetic alterations in the immunoglobulin (Ig) loci: somatic hypermutation (SHM) and class switch recombination (CSR), both of which require an enzyme, activation-induced cytidine deaminase (AID). After these processes, among diversified Ig repertoire, selected high-affinity Igs efficiently defend host. AID plays a crucial role in host defense but it introduces DNA cleavage into Ig loci and aberrantly into non-Ig loci causing lymphoma. Our aim is to answer 'how AID's activity targets Ig loci specifically' using AID mutant protein and mutant knock-in mice and to understand the precise molecular mechanism of SHM and CSR. Recently dysbiosis (gut commensal microbial imbalance) is frequently reported to be associated with illnesses such as inflammatory bowel disease (IBD), obesity, cancer, etc. We found that the high-affinity intestinal IgA produced by SHM is important to control non-pathogenic gut bacteria as well as pathogens. Our main question is how intestinal IgA recognizes and targets a huge variety of gut bacteria. We have isolated a useful monoclonal IgA to modulate gut microbiota leading to symbiosis (balanced host-microbial relationship in gut). We aim at applying the findings of our basic research to practical medicine.

Major Research Topics

1. Mechanism of gut microbial regulation by intestinal IgA

We generated hybridomas from IgA producing cells in small intestine of wild type mice. We selected W27 monoclonal IgA as a best gut microbial modulator because of its strong binding ability specifically against colitogenic bacteria. We are analyzing the bacterial target molecule for W27 to control microbial community, and will elucidate the reason why IgA selects that target in the point of physiological view. We aim at the development of therapeutic W27 IgA antibody.

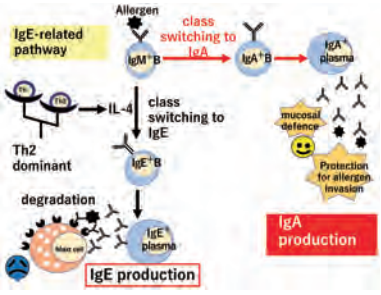


2. Molecular mechanism of SHM

We have found that a N-terminal mutant AID (G23S; glycine to serine mutation at the 23rd AA) showed defective SHM but relatively intact CSR both in vitro and in vivo, suggesting the N-terminus of AID may be the domain responsible for SHM-specific co-factor binding. Through the search of SHM-specific co-factor, we will understand how AID distinguishes SHM from CSR.

3. Search for IgA CSR inducer

Upon antigen stimulation B cells can undergo CSR to IgG, IgE or IgA isotype. However, what induces B cells to each isotype specifically is not completely understood. We focus on searching a novel IgA CSR inducer, which may drive IgA CSR instead of IgE CSR at mucosal surface, helping prevent allergy, as well as enhance the mucosal immunity.



Intestinal IgA as a modulator of the gut microbiota. Okai S, Usui F, Ohta M, Mori H, Kurokawa K, Matsumoto S, Kato T, Miyauchi E, Ohno H, Shinkura R. Gut Microbes 2017 Sep 3;8(5):486-492. doi: 10.1080/19490976.2017.1310357. Epub 2017 Apr 6.

High-affinity monoclonal IgA regulates gut microbiota and prevents colitis in mice. Okai S, Usui F, Yokota S, Hori-I Y, Hasegawa M, Nakamura T, Kurosawa M, Okada S, Yamamoto K, Nishiyama E, Mori H, Yamada T, Kurokawa K, Matsumoto S, Nanno M, Naito T, Watanabe Y, Kato T, Miyauchi E, Ohno H, Shinkura R. Nat Microbiol. 2016 Jul 4; 1(9):16103. doi: 10.1038/nmicrobiol.2016.103.

Mice carrying a knock-in mutation of Aicda resulting in a defect in somatic hypermutationhave impaired gut homeostasis and compromised mucosal defense. Wei M, Shinkura R, Doi Y, Maruya M, Fagarasan S, Honjo T. Nat Immunol. 12(3), 264-270, 2011

Prof. Y. Okada

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Assist. Prof. **M. Hada**

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Laboratory of
Pathology and Development
(Institute for Quantitative Biosciences)

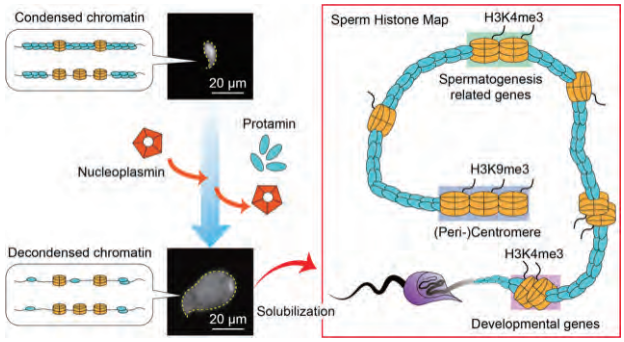
Investigation of chromatin dynamics in germ cells

Research Topics

1. Profiling sperm-retained histones
2. Elucidating the sperm chromatin structure
3. Investigation of the machamism of histone retentaion in sperm during histone-protamine exhange

"Neuronal cells are who you are, while germ cells are where you came from."— This is the word by a leading scientist in the field of germ cell research. Somatic cells including neuronal cells compose ourselves, while germ cells play transgenerational roles. Recently, scientists demonstrated that not only DNAs but also certain non-DNA factors can be transgenerationally transferred from ancestors to progenies. The substance of this is non-DNA material is supposed to "epigenome" such as chromatin and small RNAs, although the real entity hasn't been determined. For now, the most possible idea is that the parental epigenetic information in their germ cells is altered upon stress responses and transferred to the progeny by fertilization.

In our laboratory, we are investigating how epigenetic information is established in germ cells (especially in male germ cells) and altered upon various stress responses using biochemical, molecular biological, and genomic approaches. In addition, we are trying to utilize our research outcome for sperm quality control in Assisted Reproductive Technologies (ART).



An example of our research achievement. Mammalian sperm nuclei are tightly condensed due to the highly basic proteins called protamines. This unique chromatin structure prevents us from performing various kinds of biochemical approaches to investigate the characteristics of sperm chromatin. In order to overcome this problem, we developed a new method to artificially remove protamines from sperm chromatin by treating them with nucleoplamin (left figure). This treatment enabled us to extract histone-DNA complex from sperm chromatin, then we performed Chromatin Immunoprecipitation-Sequencing (ChIP-seq) to determine where histones are retained in sperm genome. The result tells us that histones are scattered across the genome and exhibit modest enrichment in repeat regions. Interestingly, post-translationally modified histones are retained in specific genome elements depending on the patterns of their modifications (right figure). Recently, paternal lifestyle and habits are supposed to be transferred to their children through sperm. This phenomenon is called "epigenetic inheritance", and our research outcome is expected to provide a useful knowledge for understanding its molecular mechanisms.

Fujiwara Y, Hada M, Fukuda Y, Koga C, Inoue E, *Okada Y. Isolation of stage-specific spermatogenic cells by dynamic histone incorporation and removal in spermatogenesis. Cytometry A. 2023 Dec 12. doi: 10.1002/cyto.a.24812. Epub ahead of print. PMID: 38087848.

*Okada Y. "Sperm chromatin structure: Insights from in vitro to in situ experiments". Curr Opin Cell Biol. 2022 Apr;75:102075. doi: 10.1016/j.ceb.2022.102075. Epub 2022 Mar 25. PMID: 35344802.

Fukuda Y, Shintomi K, Yamaguchi K, Fujiwara Y, *Okada Y. "Solubilization of Mouse Sperm Chromatin for Sequencing Analyses Using a Chaperon Protein". Methods Mol Biol. 2023;2577:161-173. doi: 10.1007/978-1-0716-2724-2_11. PMID: 36173572

Fujiwara Y, Horisawa-Takada Y, Inoue E, Tani N, Shibuya H, Fujimura S, Kariyazono R, Sakata T, Ohta K, Araki K, Okada Y, *Ishiguro KI. "Meiotic cohesins mediate initial loading of HORMAD1 to the chromosomes and coordinate SC formation during meiotic prophase". PLoS Genet.2020 Sep 15;16(9):e1009048. doi:10.1371/journal.pgen.1009048. PMID: 32931493; PMCID: PMC7518614..

Kim CR, Noda T, Kim H, Kim G, Park S, Na Y, Oura S, Shimada K, Bang I, Ahn JY, Kim YR, Oh SK, Choi HJ, Kim JS, Jung I, Lee H, Okada Y, *Ikawa M, *Baek SH. "PHF7 Modulates BRDT Stability and Histone-to-Protamine Exchange during Spermiogenesis".Cell Rep. 2020 Jul 28;32(4):107950. doi:10.1016/ j.celrep.2020.107950. PMID: 32726616.

Makino Y, Jensen NH, Yokota N, Rossner MJ, Akiyama H, Shirahige K, *Okada Y. "Single cell RNA-sequencing identified Dec2 as a suppressive factor for spermatogonial differentiation by inhibiting Sohlh1 expression". Sci Rep. 2019 Apr 15;9(1):6063. doi: 10.1038/s41598-019-42578-z. PMID: 30988352; PMCID: PMC6465314.

Yamaguchi K, Hada M, Fukuda Y, Inoue E, Katou Y, Shirahige K, *Okada Y. "Re-evaluating the localization of sperm-retained histones revealed the modification-dependent accumulation in specific genome regions". Cell Rep. 2018Jun 26;23(13):3920-3932. doi: 10.1016/j.celrep.2018.05.094. PMID: 29949774.

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Laboratory of Molecular Neurobiology

Understanding how the brain functions through epigenetic analysis

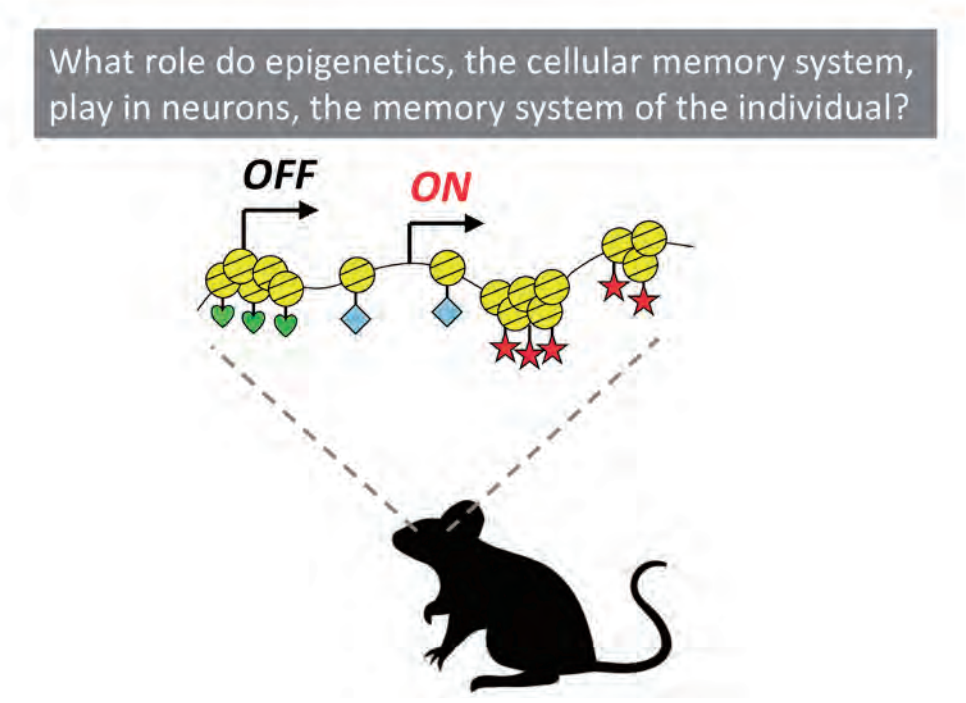
Research Topics

1. Epigenetics analysis of brain cells to understand alterations in brain function under aging, stress, and psychiatric disorder conditions
2. Epigenome editing of neurons to improve brain function

Our genetic information is encoded in our genomic DNA. Several mechanisms are used to properly identify and access the necessary genetic information contained within our three billion base pairs of DNA. One of these mechanisms is epigenetic regulation. Through epigenetic regulation, chemical modifications on DNA and histones—such as methylation and acetylation—function as "bookmarks," resulting in the expression of only the necessary genes.

These epigenetic "bookmarks" are modified in response to the cell's previous exposures to stimuli and experiences. In other words, epigenetic regulation functions as the memory system of cells. The question then becomes, what role does epigenetics play in the brain, which is the memory system of individuals?

In our laboratory, we are working to understand the mysteries of the brain through epigenetic analysis by combining the biochemical, molecular biological, and bioinformatics technologies needed to carry out the latest genomic analysis with the genetic and neuroscience technologies necessary to analyze brain function. Through this research, we aim to understand the basis of changes in brain function caused by aging, stress, and psychiatric disorders.



A simple method for gene expression in endo- and ectodermal cells in mouse embryos before neural tube closure
Yurie Maeda, Jingwen Ding, Mai Saeki, Naohiro Kuwayama, and Yusuke Kishi, *Developmental Biology*, 516:114-121, 2024

Tanita Frey, Tomonari Murakami, Koichiro Maki, Takumi Kawaue, Ayaka Sugai, Naotaka Nakazawa, Taiji Adachi, Mineko Kengaku, Kenichi Ohki, Yukiko Gotoh, and Yusuke Kishi. Age-associated reduction of nuclear shape dynamics in excitatory neurons of the visual cortex. *Aging Cell*, e13925, 2023

Miho Koizumi, Hikaru Eto, Mai Saeki, Masahide Seki, Tsuyoshi, Fukushima, Shoichiro Mukai, Hisamitsu Ide, Yasuyuki Sera, Masayuki, Iwasaki, Yutaka Suzuki, Atsushi Tohei, Yusuke Kishi, and Hiroaki Honda. UTX deficiency in neural stem/progenitor cells results in impaired neural development, fetal ventriculomegaly, and postnatal death. *FASEB Journal*, 36(12):e22662, 2022

Prof. H. Saito

Lecturer **T. Yoshii**
Assist. Prof. **H. Ono**
Assist. Prof. **S. Hirano**
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Laboratory of
RNP Synthetic Biology and Biotechnology
(Institute for Quantitative Biosciences)

Empowering new life systems through synthetic biology and bioengineering

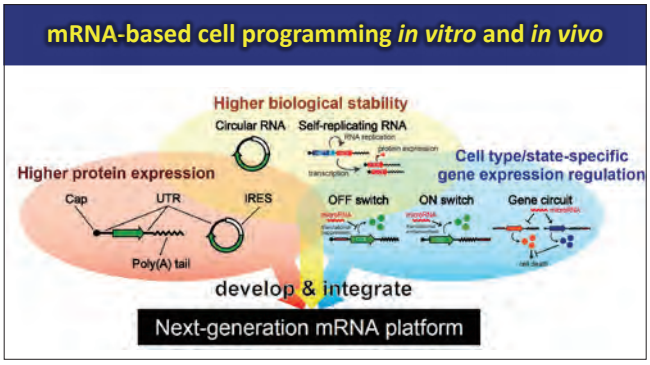
Research Topics

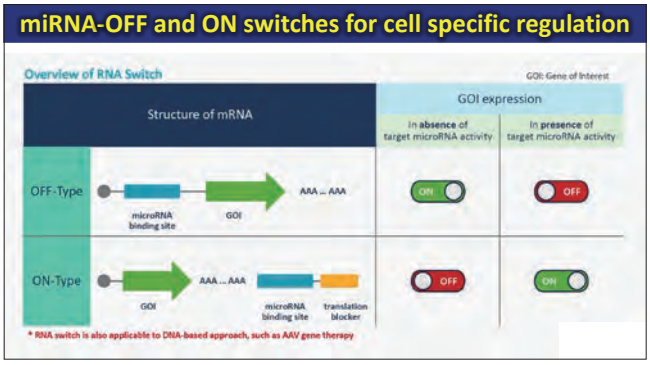
1. Basic biology and drug discovery based on RNA and RNP
2. Synthetic biology and bioengineering for gene expression and cell-fate control
3. Creation of artificial biomolecules and living matters for medical applications

In our laboratory, we delve into the fascinating world of RNA and RNA-Protein complexes (RNPs), pivotal elements in myriad life processes. Our research is dedicated to unraveling the mysteries of RNA and RNP interactions, aiming to deepen our understanding of life systems, discover new biological phenomena, and pioneer groundbreaking technologies.

RNPs, formed through the recognition of RNA sequences and structures by proteins, are central to the cellular mechanisms controlling gene expression and intracellular localization. By elucidating the sequences and structures involved in RNP interactions, along with their molecular mechanisms, we unlock the potential to artificially modify the functions and formations of RNA and RNP complexes. This capability opens up exciting possibilities for manipulating cellular functions at will, creating artificial RNAs and RNPs with novel functions, and exploring the interactions between RNA and various molecules “X” (RNX) as a foundation for understanding and creating new biomolecules and life systems (RNX Synthetic Biology).

We believe in the importance of integrating interdisciplinary technologies and developing new ones to forge new research fields. By merging techniques and knowledge from synthetic biology, evolutionary engineering, informatics, and biophysical chemistry, we aim to develop new technologies for understanding and controlling life systems. Leveraging our unique technologies, we strive to elucidate the mechanisms behind RNA-based life systems, contributing to the life sciences and paving the way for new pharmaceutical developments. Our lab is not just a place of research but a crucible of innovation, where we challenge the boundaries of science to create a future where the mysteries of life are not just understood but harnessed.





1. Sumi S, Hamada M*, and **Saito H***: Deep generative design of RNA family sequences. ***Nature Methods*** ,2024 Mar;21(3):435-443. doi: 10.1038/s41592-023-02148-8. Epub 2024 Jan 18.
2. Kawasaki S*, Ono H, Hirosawa M, Kuwabara T., Sumi S., Lee S, Woltjen K., and **Saito H***: Programmable mammalian translational modulators by CRISPR-associated proteins. ***Nature Commun***, 2023;2243.
3. Fujita Y*, Hirosawa M, Hayashi K, Hatani T, Yoshida Y, Yamamoto T, **Saito H***: A versatile and robust cell purification system with an RNA-only circuit composed of microRNA-responsive ON and OFF switches. ***Science Adv.***, 2022 Jan 7;8(1):eabj1793.
4. Wroblewska L, Kitada T, Endo K, Siciliano V, Stillo B, **Saito H***, Weiss R*: Mammalian synthetic circuits with RNA binding proteins for RNA-only delivery. ***Nature Biotechnol***, 2015;33(8):839-41.

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Yang J H*, Hayano M, Griffin P T, Amorim J A, Bonkowski M S, Apostolides J K, Salfati E L, Blanchette M, Munding E, Bhakta M, Chew Y, Blanchette M, Munding E M, Bhakta M, Chew Y C, Guo W, Yang X, Maybury-Lewis S, Tian X, Ross J M, Coppotelli G, Meer M V, Rogers-Hammond R, Vera D L, Lu Y R, Pippin J W, Creswell M L, Dou Z, Xu C, Mitchell S J, Das A, O'Connel B L, Thakur S, Kane A E, Su Q, Mohri Y, Nishimura EK, Schaevitz L, Garg N, Balta A-M, Rego M A, Gregory-Ksander M, Jakobs T C, Zhong L, Wakimoto H, Andari J E, Grimm D, Mostoslavsky R, Wagers A J, Tsubota K, Bonasera S J, Palmeira C M, Seidman J G, Seidman C E, Wolf N S, Kreiling J A, Sedivy J M, Murphy G, Green R E, Garcia B A, Berger S L, Oberdoerffer P, Shankland S J, Gladyshev V N, Ksander B R, Pfenning A R, Rajman L A, Sinclair D A*.
Loss of epigenetic information as a cause of mammalian aging.
Cell, 186(2):305-326, 2023

Karigane D, Haraguchi M, Toyama-Sorimachi N, Nishimura EK, Takubo K.
Mitf is required for T cell maturation by regulating dendritic cell homing to the thymus.
Biochem Biophys Res Commun., 596: 29-35, 2022

Nanba D, Toki F, Asakawa K, Matsumura H, Shiraishi K, Sayama K, Matsuzaki K, Toki H, Nishimura EK.
EGFR-mediated epidermal stem cell motility drives skin regeneration through COL17A1 proteolysis.
J Cell Biol., 220(11): e202012073, 2021

Eshiba S, Namiki T, Mohri Y, Aida T, Serizawa N, Shibata T, Morinaga H, Nanba D, Hiraoka Y, Tanaka K, Miura K, Tanaka M, Uhara H, Yokozeki H, Saida T, Nishimura EK*.
Stem cell spreading dynamics intrinsically differentiate acral melanomas from nevi.
Cell Reports, 36(5):109492, 2021

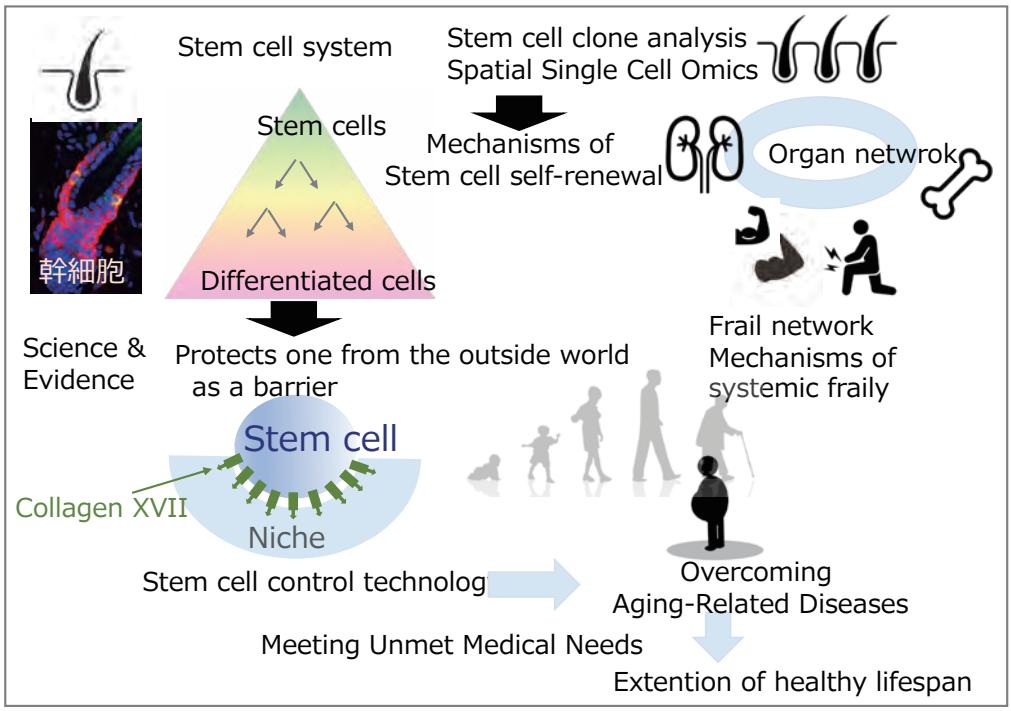
Laboratory of
Stem Cell Regulation and Drug Discovery
(Institute of Medical Science)

Study of skin stem cell dynamics and aging as a clue for the serach of therapeutic drugs for age-associated diseases

Research Topics

1. Elucidation of the mechanism of self-renewal of tissue stem cells and their quality control
2. Elucidation of the mechanism of tissue aging, diseases and systemic frailty
3. Development of therapeutic drugs using stem cell technology.

Many of the tissues and organs that make up our bodies form a tissue stem cell system, maintaining their homeostasis. Tissue stem cells are the backbone cell population for maintaining homeostasis, such as tissue regeneration, but they gradually undergo changes due to aging and various environmental stresses, leading to the onset of many age-related diseases, including cancer. We believe that in treating age-related diseases, it is essential to clarify the aging processes and mechanisms leading to their onset, explore the key cell populations and molecules to be targeted, which can contribute to new drug development. Based on this approach, we are developing stem cell control technology targeting stem cells, searching for substances that enable tissue regeneration and control tissue aging and diseases.
https://www.ims.u-tokyo.ac.jp/aging-regeneration/



In our laboratory, we focus on elucidating the mechanism of stem cell self-renewal and quality control, utilizing techniques such as single-cell omics analysis of skin, tracking the fate of stem cells in epithelial organoids and in vivo, and analyzing interactions with surrounding cells and other organs to elucidate the breakdown mechanism and the diseases.

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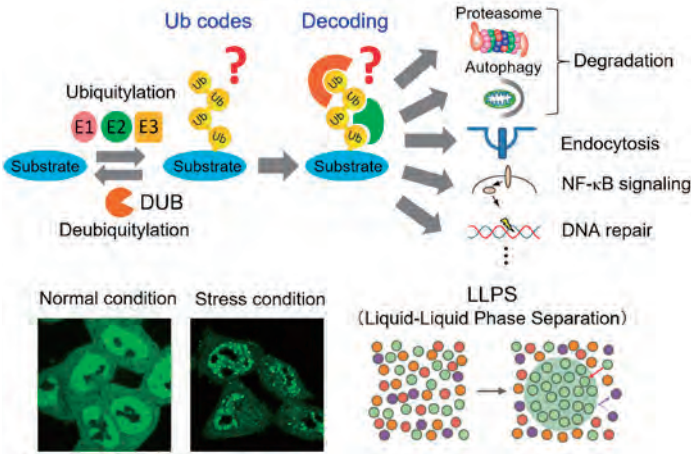
Laboratory of
Protein Dynamics

(Division of Protein Metabolism, The Institute of Medical Science)

Understanding diverse cellular functions through protein dynamics

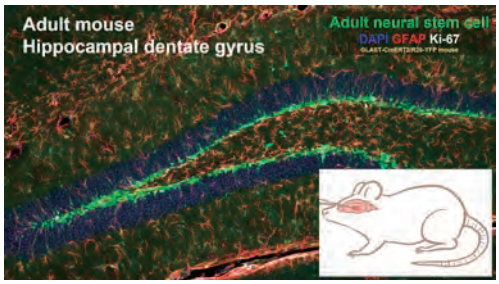
Research Topics

1. Regulation of Cellular Functions by the Ubiquitin Code
2. Stress adapation mechanisms by liquid-liquid phase separation
3. Proteostasis of adult neural stem cells



Regulation of Cellular Functions by the Ubiquitin Code

The Laboratory of Protein Dynamics studies how the cellular proteome is shaped and maintained in response to changes in the cellular environment. It has become clear that dysregulation of proteostasis has emerged as a key factor contributing to a range of pathologies, including neurodegenerative diseases. The ubiquitin system plays a pivotal role in proteostasis and proteome remodeling by spatiotemporally regulating diverse biological phenomena such as protein degradation, cellular localization, and protein-protein interactions. Behind the diverse functions of ubiquitin modifications, we have shown that higher-order structures of ubiquitin chains act as “ubiquitin code”. More recently, we have also discovered a ubiquitin code drives liquid-liquid phase separation with specific ubiquitin decoders. Additionally, our laboratory focuses on neural stem cell proteostasis, in which protein degradation plays a crucial role in reactivating neural stem cells from dormancy to proliferation. Thus, our goal is to uncover the impact of proteome remodeling and proteostasis on disease pathogenesis and contribute to drug discovery.



Proteostasis of adult neural stem cells

Yasuda, S., Tsuchiya, H., Kaiho, A., Guo, Q., Ikeuchi, K., Endo, A., Arai, N., Ohtake, F., Murata, S., Inada, T., Baumeister, W., Fernandez-Busnadiego, R., Tanaka, K., Saeki Y. Stress- and ubiquitylation-dependent phase separation of the proteasome. *Nature*, 578, 296-300 (2020)

Kobayashi, T., Piao, W., Takamura T., Kori, H., Miyachi, H., Kitano, S., Iwamoto, Y., Yamada, M., Imayoshi, I., Shioda, S., Ballabio, A., Kageyama, R. Enhanced lysosomal degradation maintains the quiescent state of neural stem cells. *Nat. Commun.*, 10, 5446 (2019)

Tsuchiya, H., Burana, D., Ohtake, F., Arai, N., Kaiho, A., Komada, M., Tanaka, K., Saeki Y. Ub-ProT reveals global length and composition of protein ubiquitylation in cells. *Nat. Commun.*, 9, 524 (2018)

Prof.
N. Akimitsu

Project Assoc. Prof.
K. Taniue
Assist. Prof. **K. Tao**
Project Assist. Prof.
R. Onoguchi-Mizutani
Project Assist. Prof.
R. Matsubara
Project Assist. Prof.
S. Miyao

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1. Taniue K, Sugawara A, Zeng C, Han H, Gao X, Shimoura Y, Nakanishi-Ozeki A, Onoguchi-Mizutani R, Seki M, Suzuki Y, Hamada M and Akimitsu N. (2024) The MTR4/hnRNPK complex surveils aberrant polyadenylated RNAs with multiple exons, Nature Comm. 15, 8684.

2. Kurosaki T, Mitsutomi S, Hewko A, Akimitsu N. and Maquat LE. (2022) Integrative omics indicate FMRP sequesters mRNA from translation and deadenylation in human neuronal cells. Mol. Cell, 23, 4564-4581.

3. Kurosaki T., Imamachi N., röschel C., Nagao R., Mitsutomi S., Akimitsu N. and Maquat LE. (2020) Loss of the fragile X syndrome protein FMRP results in misregulation of nonsense-mediated mRNA decay. Nature Cell Biol. 23, 40-48.

4. Yamada T., Imamachi N., Imamura K., Taniue K., Kawamura T., Suzuki Y., Nagahama M., Akimitsu N. (2020) Systematic Analysis of Targets of Pumilio-mediated mRNA Decay Reveals that PUM1 Repression by DNA Damage Activates Translesion Synthesis, Cell Rep.31, 107542.

5. Imamura K., Takaya A., Ishida Y., Fukuoka Y., Taya T., Nakaki R., Kakeda M., Imamachi N., Sato A., Yamada T., Onoguchi-Mizutani R., Akizuki G., Tanu T.,Tao K., Miyao S., Suzuki Y., Nagahama M., Yamamoto T., Jensen TH. and Akimitsu N., (2018) Diminished nuclear RNA decay upon Salmonella infection upregulates antibacterial noncoding RNAs, EMBO J. 37, e97723

Laboratory of

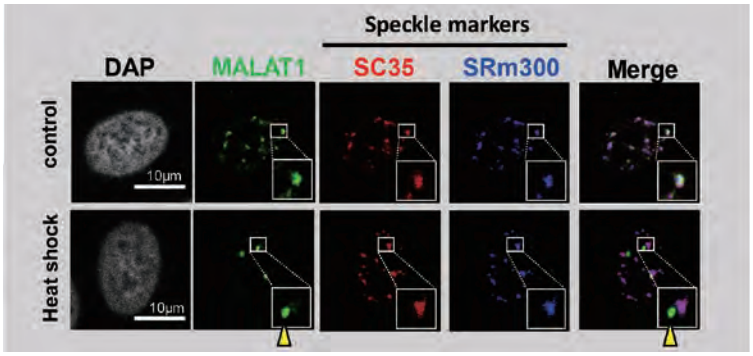
Nucleic Acids Research

Investigation of the molecular functions of nucleic acids (especially, RNA), and development of nucleic acid therapeutics

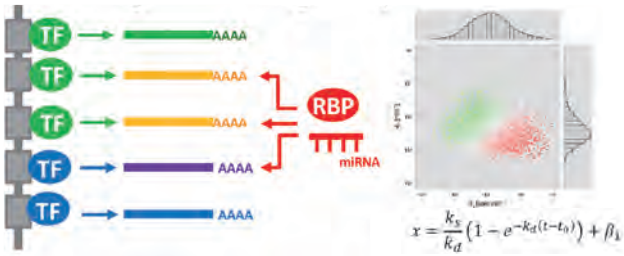
Research Topics

1. Investigation of molecular mechanisms of noncoding RNAs for the gene regulation.
2. Investigation of physiological and pathological roles of membrane-less organelle.
3. Development of basic technology to control nucleic acid medicine.
4. Integrative research on radiopharmaceutical and nucleic acid drug

Nucleic acids such as DNA and RNA play a central role in gene expression flow. This laboratory has been focusing on investigation of roles of nucleic acids. We have revealed that long noncoding RNAs regulate the cellular responses against stresses such as pathogenic infection, heat shock, and DNA damage. We also investigate physiological and pathological roles of membrane-less organelle formed by nucleic acids and RNA binding proteins. In addition, we have revealed the biological significances of RNA turnover regulated by RNA binding proteins through omics-based approaches. Based on these achievement, we also develop technologies for nucleic acid therapeutics. To develop the designer RNAs, we are also working on radiation theranostics using nucleic acid aptamers, integrating radiopharmaceutical and nucleic acid drug discovery.



Discovery of novel nuclear body involved in heat shock response.
HiNoCo-body, a novel nuclear body containing long noncoding RNA, is formed in response to heat shock through liquid-liquid phase separation. HiNoCo-body controls heat-induced 4D-genome organization and gene expression.



Network-based study of gene expression.
Gene expression is precisely regulated by many steps, such as transcription, RNA processing, and RNA decay. We study the regulatory network of gene expression flow based on molecular biology, biochemistry, genomics, and multi-omics. In addition, we develop novel technologies contributing on development of nucleic acids therapies.

Prof.
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Lecturer **Y. Yamanashi**
Lecturer **Y. Ikebuchi**

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Laboratory of
Clinical Pharmacokinetics

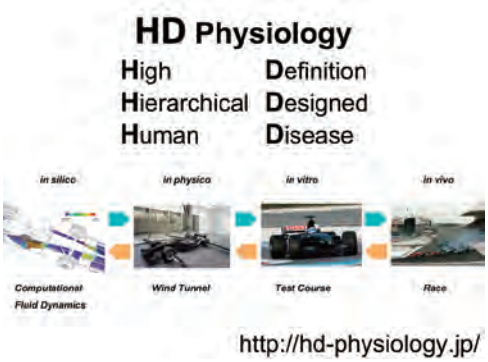
(The University of Tokyo Hospital)

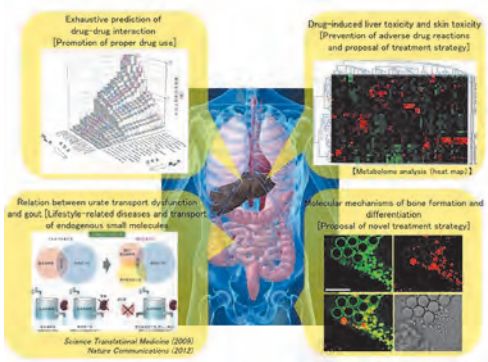
Systems-pharmacological studies for drug development in the next-generation

Research Topics

1. Therapies for lifestyle-related diseases based on the comprehensive understanding of molecular mechanisms that control the transport of endogenous small molecules
2. Therapies for bone metabolism diseases based on the comprehensive understanding of the dynamic control mechanisms of signal molecules involved in bone resorption and formation
3. Quantitative understanding of the pharmacological and toxicological effects of molecular targeted anti-cancer drugs to establish clinical applications and new drug discovery techniques
4. Large-scale omics analysis to establish methods of preventing and treating adverse drug reactions based on the quantitative understanding of underlying molecular mechanisms
5. Clinical pharmacokinetics based on detailed quantification of related molecular functions

It has been recognized very well that we need to describe / predict the functions of cells, tissues and organisms from the function of each constituent molecule in a quantitative manner in order to understand the life activities. Although we have used such approach in analyzing and predicting the drug disposition in humans, it is quite important for us to expand the concept to the analysis of pharmacological / toxicological actions of drugs in humans. We are using such "systems-pharmacological" methods to solve many kinds of problems that remain great challenges in drug discovery, such as how to identify the most effective target molecules among numerous candidates, and how to comprehensively predict the adverse drug reactions in humans.





Miyata, H., Toyoda, Y., Takada, T., Hiragi. T., Kubota. Y., Shigesawa. R., Koyama. R., Ikegaya. Y., Suzuki, H. Identification of an exporter that regulates vitamin C supply from blood to the brain. *iScience.* 25(1): 103642 (2022)

Toyoda, Y., Takada, T., Miyata, H., Matsuo, H., Kassai, H., Nakao, K., Nakatochi,M., Kawamura, Y., Shimizu, S., Shinomiya, N., Ichida, K., Hosoyamada, M., Aiba, A., Suzuki, H. Identification of GLUT12/SLC2A12 as a urate transporter that regulates the blood urate level in hyperuricemia model mice. *Proc Natl Acad Sci USA.* 117(31):18175-18177 (2020)

Ikebuchi, Y., Aoki, S., Honma, M., Hayashi, M., Sugamori, Y., Khan, M., Kariya, Y., Kato, G., Tabata, Y., Penninger, J.M., Udagawa, N., Aoki, K., Suzuki, H. Coupling of bone resorption and formation by RANKL reverse signalling. *Nature.* 561(7722):195-200 (2018)

Takada, T., Yamanashi, Y., Konishi, K., Yamamoto, T., Toyoda, Y., Masuo, Y., Yamamoto, H., Suzuki H. NPC1L1 is a key regulator of intestinal vitamin K absorption and a modulator of warfarin therapy. *Sci Transl Med.* 7(275):275ra23 (2015)

Project Prof. M. Naito

Prof. **S. Murata**

Social Cooperation Program of
Targeted Protein Degradation

Inducing targeted protein degradation by chemical compounds

Research Topics

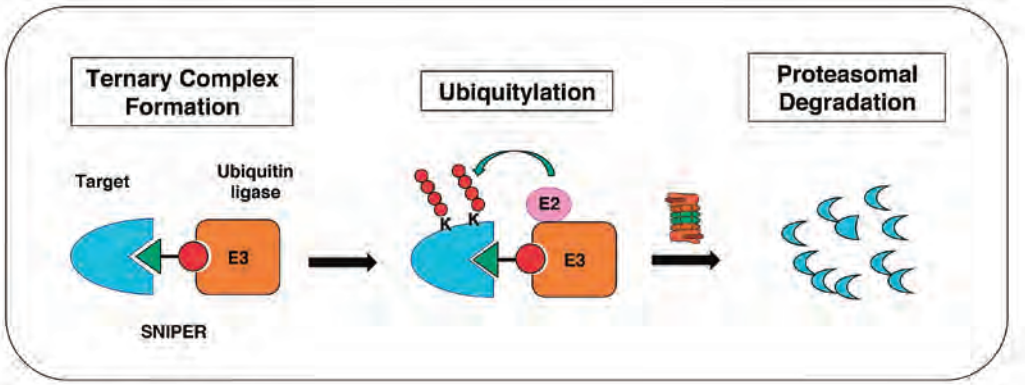
1. Development of new technologies to induce protein degradation

2. Development of SNIPER compounds that degrade disease causative proteins

As the mechanisms of various diseases are better understood at the molecular level, it will become possible to develop molecular target drugs that specifically inhibit pathogenic proteins. With the current drug discovery technologies, however, it is not possible to develop such drugs against all pathogenic proteins. Especially, most of the intracellular proteins without enzymatic activity have been considered undruggable.

Targeted protein degradation is a promising approach for suppressing such undruggable targets. Chimeric compounds such as PROTACs and SNIPERs are attracting attention because they allow us to develop novel drugs that degrade proteins of your interest.

In our laboratory, we have developed a series of SNIPER compounds that degrade various target proteins. SNIPERs recruit IAP ubiquitin ligases to target proteins for ubiquitylation and proteasomal degradation. We are currently developing new technologies to induce protein degradation, which include cancer-specific or tissue-specific degradation of target proteins. We are also developing new compounds that degrade disease causative proteins.



SNIPER compounds induce ubiquitylation and proteasomal degradation of target proteins.

Akizuki Y, Morita M, Mori Y, Kaiho-Soma A, Dixit S, Endo A, Shimogawa M, Hayashi G, Naito M, Okamoto A, Tanaka K, Saeki Y, and Ohtake F: cIAP1-based degraders induce degradation via branched ubiquitin architectures. Nat Chem Biol 19, 311-322 (2023)

Naito M: Targeted protein degradation and drug discovery. J Biochem 172, 61-69 (2022)

Kaiho-Soma A, Akizuki Y, Igarashi K, Endo A, Shoda T, Kawase Y, Demizu Y, Naito M, Saeki Y, Tanaka K, and Ohtake F: TRIP12 promotes small-molecule-induced degradation through K29/K48-branched ubiquitin chains. Mol Cell 81, 1411-1424 e1417 (2021)

Naito M, and Murata S: Gluing Proteins for Targeted Degradation. Cancer Cell 39, 19-21 (2021)

Shibata N, Ohoka N, Tsuji G, Demizu Y, Miyawaza K, Ui-Tei K, Akiyama T, and Naito M: Deubiquitylase USP25 prevents degradation of BCR-ABL protein and ensures proliferation of Ph-positive leukemia cells. Oncogene 39, 3867-3878 (2020)

Prof. S. Hori

Project Assoc. Prof.
Y. Enomoto
Researcher
T. Kitamura

Social Cooperation Program of

Molecular Pharmacology of Malignant Diseases

Research on hematopoietic stem cells and hematopoietic malignancies toward the development of new therapeutic approaches

Research Topics

1. Elucidation of the mechanism of drug resistance
2. Development of drug combination therapies
3. Therapy with immune activation in the treatment of hematopoietic malignancies
4. Elucidation of T cell function in clonal hematopoiesis

We aim to elucidate the mechanisms of drug resistance and to develop combination therapies in order to overcome drug resistance of hematopoietic malignant cells. To determine which genes contribute to becoming drug resistance, we utilize genome-wide libraries for Crispr-A system and culture cells transduced with each sgRNA in the presence of drugs. In addition, pathway analysis of the gene groups identified by this method will reveal the mechanism of drug resistance and the mechanism of action.

We will then devise drug combination therapies by revealing the mechanisms of drug resistance. We have obtained interesting research results on HDAC inhibitors and DNA methyltransferase inhibitors. In the future, we will also investigate other drugs and expand the scope of our research. Immune checkpoint inhibitors have attracted attention for their efficacy in the treatment of malignant tumors. By using G0 marker mice, our group has reported that 1) leukemic stem cells of chronic myeloid leukemia (CML) after the treatment are in G0 phase and express PD-L1, 2) IRAK inhibitors suppress PD-L1 expression and augment the therapeutic effect of tyrosine kinase inhibitors (TKIs), and 3) the combination therapy with TKIs and anti-PD-L1 antibody has a dramatic synergistic effect on murine CML models. Immune activation is a crucial strategy for the treatment of malignant tumors, and we aim to develop new effective therapies, including drug combination therapies.

On the other hand, it has received attention that approximately 10% of healthy elderly people have clonal hematopoiesis (CH) with one leukemia-related gene mutation. People with CH have a 10-fold higher incidence rate of hematopoietic malignancies than healthy people without CH. Therefore, CH can be assumed to be a preleukemic state. Interestingly, the incidence rate of atherosclerotic disease is about twice as high in people with CH, one in four cancer patients has CH, and cancer patients with CH have significantly worse prognosis. We assume that those high incidence rate and worse prognosis can be caused by abnormal function of T cells with CH.

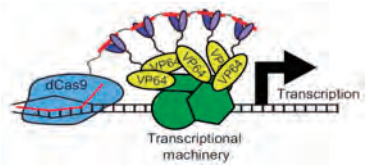


Fig. 1 Principle of the SunTag method, a type of Crispr-A.
Cells expressing 1) complex of dCAS9, which lacks its DNA cleavage activity, and peptides containing multiple repetitive sequences (red part), and 2) a fusion of a single chain antibody that recognizes the repetitive sequences and a tetramer of the transcriptional activator VP16 (VP64) can artificially overexpress any gene with a single-guide RNA that recognizes the promoter region (Marvin et al. Cell 2014).

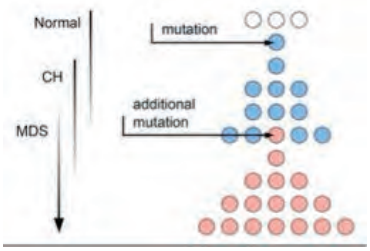


Fig. 2 Clonal hematopoiesis: CH
The incidence rate of hematopoietic malignancies is about 10 times higher and the incidence rate of myocardial infarction and cerebral infarction is about twice as high. The latter diseases are the reason why people with CH have worse prognosis.

Yabushita T, Chinen T, Nishiyama A, Asada S, Shimura R, Isobe T, Yamamoto K, Sato N, Enomoto Y, Tanaka Y, Fukuyama T, Satoh H, Kato K, Saitoh K, Ishikawa T, Soga T, Nannya Y, Fukagawa T, Nakanishi M, Kitagawa D, Kitamura T, Goyama S. : Mitotic perturbation is a key mechanism of action of decitabine in myeloid tumor treatment. Cell Reports 42(9):113098 (2023)

Project Assoc. Prof. A. Igarashi

Project Assist. Prof.
A. Shoji

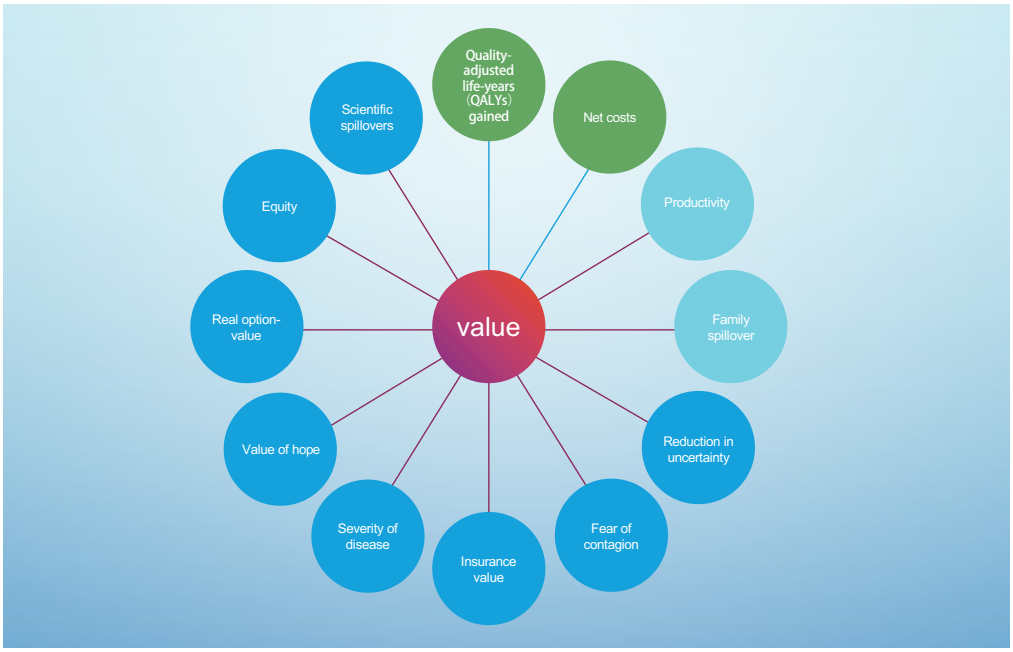
Social Cooperation Program of
Health Policy and Public Health

The generation and application of evidence tailored to clinical needs, and the proposal of value-based health policies.

Research Topics

1. Building an evidence foundation in the field of infectious diseases that can respond to both normal and emergency situations
2. Proposal for a sustainable Value-Based Healthcare System from the perspectives of both innovation and social security systems

Following the pandemic and the increasing medical and pharmaceutical expenses, “optimal allocation of medical resources based on evidence” has become an important issue to maintain the sustainability of both the public healthcare system and innovation.
We aim to contribute to the promotion of researchers and the improvement of policy-making / public health by simultaneously: i) creating a system for evaluating therapeutic and preventive interventions from multiple perspectives in various disease areas, ii) building a composite database capable of generating evidence over time in response to environmental changes , and iii) developing frameworks for the social implementation of the evidence obtained through SIB/PFS and proposals for healthcare policies.



The concept of the Value Flower developed by the ISPOR (International Society for Pharmacoeconomics and Outcomes Research) Task force

Igarashi A, Nakano Y, Yoneyama-Hirozane M. Public preferences and willingness to accept a hypothetical vaccine to prevent a pandemic in Japan: a conjoint analysis. Expert Rev Vaccines. 2022:1-8.

Sekiguchi M, Igarashi A, Mizuguchi Y, et al. Cost-effectiveness analysis of endoscopic resection for colorectal laterally spreading tumors: Endoscopic submucosal dissection versus piecemeal endoscopic mucosal resection. Dig Endosc. 2021.

Ashizawa T, Igarashi A, Sakata Y, et al. Impact of the Severity of Alzheimer's Disease on the Quality of Life, Activities of Daily Living, and Caregiving Costs for Institutionalized Patients on Anti-Alzheimer Medications in Japan. J Alzheimers Dis. 2021;81(1):367-74.

Ikeda T, Igarashi A, Odani S, et al. Health-Related Quality of Life during COVID-19 Pandemic: Assessing Impacts of Job Loss and Financial Support Programs in Japan. Appl Res Qual Life. 2021 Jan 30:1-17.

Tan RL, Yang Z, Igarashi A, et al. How Do Respondents Interpret and View the EQ-VAS? A Qualitative Study of Three Asian Populations. Patient. 2021 Mar;14(2):283-93.

One-Stop Sharing Facility Center for Future Drug Discoveries

Sharing research facilities to promote research for drug discoveries

https://onestop.f.u-tokyo.ac.jp/

Professor (concurrent) **S. Murata** Project Assoc. Prof. **K. Okabe**

Research Topics

1. Development of methods for quantitative cellular fluorescence imaging
2. Elucidation of the mechanism and significance of intracellular thermal signaling
3. Control of physiological functions by manipulation of intracellular temperature

The One-Stop Drug Discovery Facility Center offers a variety of advanced facilities for mass spectrometry, structural analysis, and biofunctional analysis. These tools allow for detailed investigation of drug candidates and targets, including structure elucidation and assessment of drug effects through precise intracellular imaging. The Center employs mass spectrometers, NMR, confocal microscopes, and cell image analyzers.

This initiative aims to enhance collaboration between industry and academia in drug discovery, promote cross-disciplinary integration, support start-up ventures, and provide a research environment for emerging scientists and students through resource sharing.

Moreover, the Center encourages the communal use of its facilities to foster a collaborative spirit. The Center regularly updates its website with relevant information, presents its capabilities at the Pharmaceutical Sciences Foundation of Japan's FDD Seminar, and collaborates with the WINGS-LST International Graduate Program at the University of Tokyo. A descriptive video about the Center can be found on its website.

Additionally, the Center hosts One-Stop Technology Seminars, which provide hands-on experience with state-of-the-art equipment tailored to meet evolving technological needs.

Drug Discovery Initiative

Support for Drug Discovery

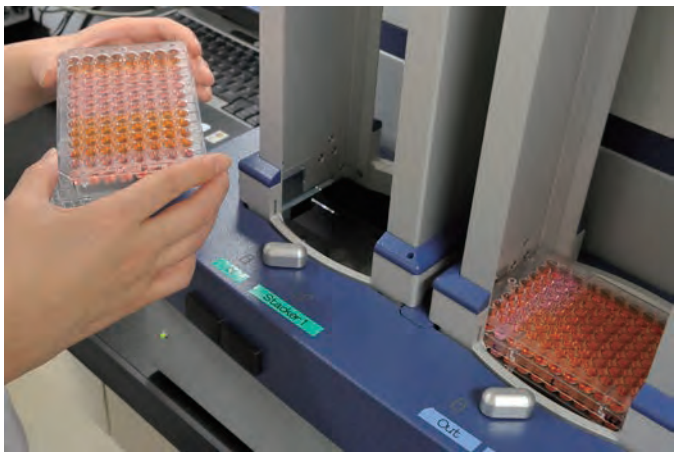
https://www.ddi.f.u-tokyo.ac.jp/en/

Director Prof.	**Y. Urano**	Project Assoc. Prof.	**K. Yasuda**
Duputy Director Project Prof.	**H. Kojima**	Project Lecturer	**R. Imamura**
Project Assoc. Prof.	**T. Iijima**	Project Lecturer	**K. Kanamitsu**
Project Assoc. Prof.	**T. Zenkoh**	Project Lecturer	**M. Takamiya**

Research Topics

1. Comprehensive research support for drug discovery
2. Research on chemical library
3. Research on chemical screening
4. Drug lead discovery and optimization
5. Evaluation of pharmacokinetics and physical properties of candidate compounds

Drug Discovery Initiative, DDI, was established to contribute to our health through the elucidation of life phenomena and the discovery of new drug leads. DDI is a hub of national collaborative research networks for drug discovery based on our public chemical library. DDI promotes open innovation by providing advice, technical support and chemical samples to the researchers who need to screen chemical samples. DDI also provides chemical synthesis and pharmacokinetic research support for lead compound generation.



Education Center for Medical Pharmaceutics

Director
Prof. Y. Urano

Vice Director
Project Prof. **H. Hosono**
Prof. **T. Tomita**
Prof. **T. Takada**
Visiting Prof. **Y. Sawada**
Assoc. Prof. **U. Ohto**
Project Assoc. Prof.
H. Satoh
Lecturer **Y. Kariya**

The center has been established in June, 2012.
The purpose of the establishment is to enhance the educational research structure in those new educational programs, especially 6-year undergraduate program (Department of Pharmacy) and 4-year doctoral program (Department of Pharmacy).

Research Topics

1. Development of educational program for practice for medical pharmaceutics
2. Development of educational program of medical pharmaceutics
3. Development of postgraduate educational program for training leading pharmacists

We are in charge of the preclinical training, the administration of the Pharmaceutical Common Achievement Tests for clinical pharmacy (CBT and OSCE), and the pharmacy practice experiences in hospitals and pharmacies. Additionally, we conduct research aimed at developing educational programs for clinical pharmacy. Pharmacy practice experiences are critical opportunities for students to engage with patients directly, reflecting on how they can contribute as pharmacists within the interprofessional team-based care and what competencies they need to develop to make such contributions. In collaboration with the University of Tokyo Hospital and local pharmacies, our education programs are designed to nurture a “pharmacist mindset” by encouraging students to identify and solve problems with maximum support.

Clinical pharmacy, particularly closely related to the activities of pharmacists, is related to a broad range of research areas: one area includes basic and clinical research to understand how drugs move to their target organs or molecules, exhibit their therapeutic effects, and potentially cause side effects, while another area of focus is social pharmacy, which approaches the sustainable provision of better healthcare through the appropriate use of medications and information. The medical field is inevitably uncertain and involves the responsibility of patient care, making research in all these areas crucial for acquiring the information required by healthcare professionals. By advancing clinical pharmacy research, we aim to equip students with the capability to gather and disseminate information, connect people through effective communication, and solve problems. Our programs also prepare them to become pharmacists with a “research mindset,” capable of adapting to the evolving landscape of healthcare and unprecedented societal changes.

After Graduating from Graduate School of Pharmaceutical Sciences

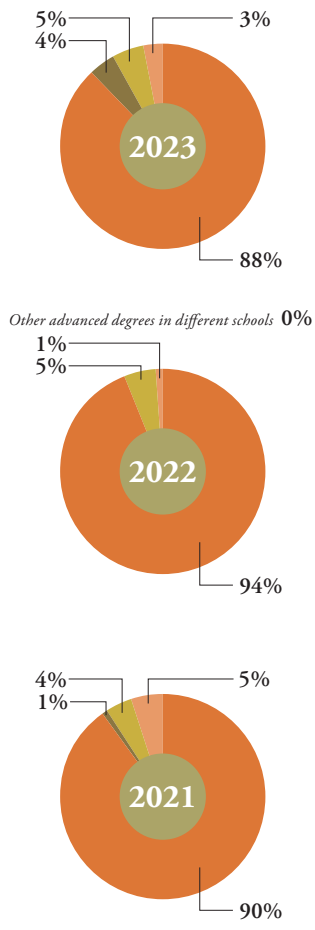
Graduates of Faculty of Pharmaceutical Sciences, who have acquired a comprehensive fundamental understanding and applied knowledge of the field, receive extremely high respect, resulting in relative easiness to find a job. Over 90 percent of graduates choose to move forward to Graduate School of Pharmaceutical Sciences, the University of Tokyo. An increasing number of applications from the University of Tokyo, other universities, and foreign universities take an annual entrance exam in August.

We have seen more and more of a social trend that prefers an individual with a researcher background and research experience higher than a Master's level. Our graduates who completed either undergraduate or graduate courses find positions in a wide array of fields, such as pharmaceuticals, chemical, and food related companies, universities, as well as government agencies.

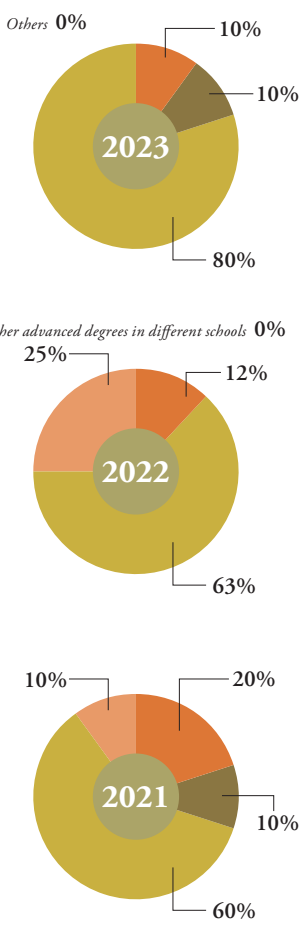
Half of graduate students opt for the doctoral course. After acquiring a PhD., they find vast opportunities not only in the academic field, such as universities and public research agencies, but in researching departments of companies, as leaders of projects.

B.S. Graduates

Department of Pharmaceutical Sciences



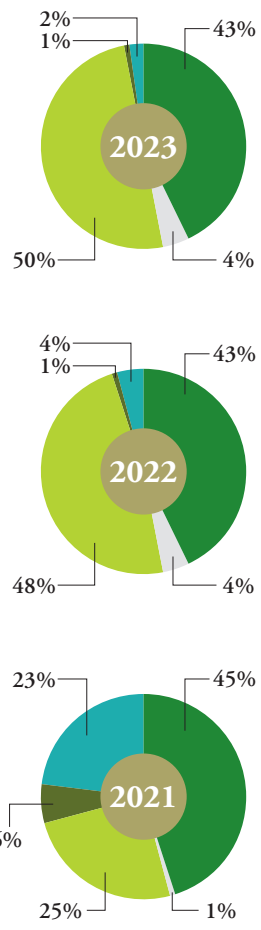
Department of Pharmacy



Graduate School of Pharmaceutical Sciences, The University of Tokyo(Master's Program)
Other advanced degrees in different schools
Government agencies and private enterprises
Others

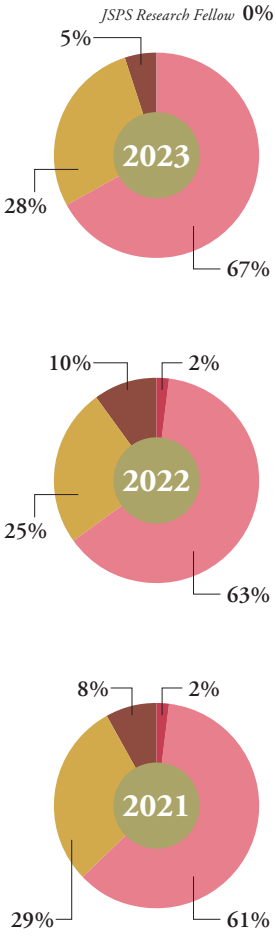
Graduate School of Pharmaceutical Sciences, The University of Tokyo(Doctoral Program)
Other advanced degrees in different schools
Government agencies and private enterprises
Others

M.S. Graduates



Graduate School of Pharmaceutical Sciences, The University of Tokyo (Doctoral Program)
Other advanced degrees in different schools
Research labs of private enterprises
Universities and government agencies
Others

PhD. Graduates



JSPS Research Fellow
Research labs of private enterprises
Universities, government agencies, public research labs, and overseas postdoctral research fellow
Others

Life on Campus

Undergraduate

There are roughly 80 students in each grade at the Faculty of Pharmaceutical Sciences, and this is one of the smallest faculties at the University of Tokyo. New students form close friendships in no time after starting their first year. They attend lectures and engage in pharmaceutical training, all the while maintaining close relationships with faculty members. Lectures encompass a broad range of academic fields closely related to real life medicine. Assistant professors and graduate students as teaching assistants also take part in the pharmaceutical training classes.
Second-year students begin to attend lectures on specialized topics for three days at the Hongo campus in the fall after receiving liberal arts education at the Komaba campus.
In the third year, students sit in on lectures in the morning and engage in pharmaceutical training in the afternoon. Lectures become more specialized, and during training sessions students work in groups of two to four.
Fourth-year students work in the laboratory of their choice, and they begin to focus less on classes and more on their senior research project.

Students must choose either the four-year program of the Department of Pharmaceutical Sciences or the six-year program of the Department of Pharmacy in their fourth year. Students who choose the Department of Pharmaceutical Sciences must complete a year-long senior research project in order to complete their degree. Those who decide on the Department of Pharmacy begin to work in the laboratory while they receive laboratory training for clinical pharmacy. At the end of the fourth year, students are expected to go through the Pharmaceutical Common Achievement Tests for clinical pharmacy. In the fifth year, students receive training for clinical pharmacy, and work in their laboratories. In the sixth year, students dedicate their time to working on their senior research project until graduation.

Postgraduate

Each laboratory and related laboratories (Institutes) of the Graduate School of Pharmaceutical Sciences and the Department of Pharmacy of the University of Tokyo Hospital conducts leading research in their specialized areas of focus. Students at the start of their graduate studies begin their research career by attending seminars and conducting experiments in world-renowned laboratories which are equipped with state-of-the-art facilities.

Campus Social Events

All the members form close-knit friendships, and this is not just because it is a relatively small department. The department hosts a slew of social events that include but are not limited to sports events, and activities with international students and researchers. These events contribute to the growth of friendships and close bonds outside of academic life. The close bonds of the students and researchers in this department foster collaboration, and this leads to a wider spectrum of academic insights and new developments in research.

Message from Student and Graduate

Shiseido global innovation center
Shiseido Company, Limited

Xiaomin Li
M.S. Completed in September 2017
Laboratory of Bioanalytical Chemistry

With the dream of doing cosmetic research in Japan, I decided to take a master's degree in Japan after graduating from Beijing University of Chemical Technology. Fortunately, with the acceptance of Pro. Funatsu, I won the opportunity to join the Laboratory of Bioanalytical Chemistry.

In the first year, as a research student, I started my research while preparing for the entrance exam of the Graduate School of Pharmaceutical Sciences. At first, I was a little uneasy because of the different major and new language environments. However, with the kind help from members of my laboratory, I quickly adapt to life at the University of Tokyo.

In the second year, I passed the entrance exam successfully and became a master student. During my master's degree, I did two research projects, but one of the projects did not go well at first. Even so, my mentors and seniors continued giving me useful guidance, which encouraged me a lot. Then we started to collaborate with the Laboratory of Advanced Elements Chemistry and Ajinomoto. Finally, we completed the research successfully. Though the research experience, I began to realize the importance of cooperation because it allows us to analyze problems from multiple perspectives and find solutions more effectively.

In addition to laboratory life, I had many unforgettable experiences at the University of Tokyo. ISAR organized a variety of activities, such as international student trips, dumpling parties, and various Japanese cultural experience activities, which enabled me to enhance communication and understand different cultures. Also, ISAR provided Japanese classes and helped me to apply for a dormitory and scholarship. I appreciate all members of ISAR, especially, my Japanese teacher Ezure-sensei. She not only taught me Japanese but also gave me much good advice on my life and career plan. Thanks to these supports, I was able to complete my studies and found my ideal job.

After graduation, I entered a cosmetics company as I wish. My main job is to develop new skincare products. I have been working for two years and a half. However, I still miss lovely people, beautiful campus, and delicious Akamon Ramen of the University of Tokyo. I hope you can come here to pursue your dreams, and I believe this university can help you to make your dream come true!

Boston Consulting Group

Luo, Cong
M. S. Completed in March 2017
Laboratory of Chemical Pharmacology

I obtained a bachelor's degree from the Department of Pharmaceutical sciences of the Univ. of Tokyo and a master's degree from the Graduate School later. In these few years, I have not only achieved academic achievements, but also spent a wonderful university life. I sincerely thank all the mentors and classmates for their the great support and generosity. At the same time, as an international student, I must give special thanks to ISAR, who have been so supportive to all international students including myself.

I entered the Univ. of Tokyo in 2011. I chose pharmaceutical science as my major because of my interest in biology and the willing to contribute to medical development that can cure and save people. During in-depth study, I also found my interest in neurology and central nervous disease given that various diseased in this area have not been clearly understood by human-beings ever before. Thus I entered the Chemistry Pharmacology laboratory and researched key topics such as Neurogenesis and Neuron-Glia interaction. With the help of my supervisors, Prof. Koyama, Prof. Ikegaya, and my lab mates, I successfully published my scientific findings in academic societies and international journals. I feel very fortunate for the high academic competencies and the environment that professors and students are so supportive to each other.

In the study and life of the Department of Pharmacy of the University of Tokyo, ISAR teachers have always given us a lot of care and help to the international students. Whether it is consulting and helping with various issues such as studying Japanese, applying for scholarships, or various travel and social activities to enrich our life in Japan. It can be said that ISAR makes us feel like home here.

After graduation, I entered a pharmaceutical company to engage in drug research and development. I sincerely feel that the professional knowledge and general education I learned at the University of Tokyo have benefited me a lot. Now I am in the field of management consulting, I continue to investigate and research the medical and pharmaceutical industry from a business perspective. Life is a journey of continuous learning and growth. I am deeply honoured to be able to study at the University of Tokyo in the early stages of my life.

College of Pharmacy, Kyung Hee University

Dong-Soon Im

Ph.D. Completed in September 1996
Laboratory of Physiological Chemistry

In March of 1993, I came to Japan as a research student in Department of Physiological Chemistry, the University of Tokyo. From October of 1993 to September of 1996, I had worked as a PhD student under supervision of Drs Michio Ui and Toshiaki Katada. It was a huge challenge to study in foreign country. In the years, I have not only achieved scientific achievements but also had a wonderful university life. Honestly, I went out to sightsee the Tokyo after lab meeting on every Saturday for the initial several months. Later, I found other lab members were working hard after the meeting. Given that my experience in the master degree wasn't good enough to do my own research as a PhD student, the first year was a period of learning techniques. In the second year, I had a great chance to meet Dr Fumikazu Okajima at Gunma University. As a mentor, he taught me a lot of things and raise me a scientist. It was fantastic and unforgettable of me to do research under his supervision. I'd like also to express special thanks to the ISAR staff for her full supports. She made me to feel comfortable in the campus and helped me to establish my life in Japan, in addition to advices and helps of many Japanese lab mentors and members. ISAR organized many activities for international students, most memorable of which were the yearly visiting places around Tokyo like hot spring and sumo wrestling.

Right after finishing my PhD, I went to the University of Virginia as a postdoctoral fellow in Pharmacology. At the time, my supervisor wanted me to translate patents applications in Japanese to English. It was my pleasure to translate Japanese to English, and I realized that there are huge differences between Japanese ways of thinking and American ways of strategies in science. In 2002, I moved back to my home country (Korea) as an assistant professor. Since 2020, I have been the Dean, College of Pharmacy, Kyung Hee University (Seoul). I am confident that my experiences in Japan and the ways of thinking during my PhD study at the University of Tokyo made me to grow up and be present myself. In the young ages, you have dreams, face challenges, and make experiences, which make your dreams come true. I strongly recommend you to join this university and pursue your dreams!

Osanni Bio, Inc.

Yung-Wen Chiu

Ph.D. completed in March 2021
Laboratory of Neuropathology and Neuroscience

Studying at the University of Tokyo was undoubtedly the best decision I have ever made. My journey began when I received a response from Prof. Tomita, leading to an amazing six-and-a-half years at the Laboratory of Neuropathology and Neuroscience. Over this time, I progressed from a research student to a master's student, then a Ph.D. candidate, and eventually an assistant professor. After moving to the U.S. for personal reasons, the education and experiences I gained at the University of Tokyo continue to shape my career. I now work as a scientist at a pharmaceutical company, developing novel therapeutics for retinal diseases.

When I first joined Prof. Tomita's lab, I could barely understand half of the conversations, which made following lectures and discussions challenging. However, ISAR was always there to help international students, and my mentors and lab members were patient, guiding me through everything and keeping me on track. Their support helped me settle in quickly and enjoy my research.

My research focus was on Alzheimer's Disease, aiming to identify novel molecules related to its pathology. Despite my limited background, my lab helped me build a solid foundation in scientific knowledge and thinking, project design, presentations, experimental techniques, and troubleshooting. These skills have been invaluable in my career, and I also got the chance to collaborate and form great professional connections along the way.

Studying abroad, for me, was not only about professional growth but also about diving into a new culture. ISAR organized activities to help international students connect with Japanese culture, such as dumpling parties, exploring prefectures, and watching sumo tournaments. I also bonded with my lab mates through annual events like ski trips and group outings, which created lasting memories and strengthened our friendships.

One big concern of studying abroad is managing living expenses. I was fortunate to receive a scholarship from the Japan-Taiwan Exchange Association, except for one year. During that year, Lecturer Gosho and Prof. Tomita were a huge help, guiding me through applying for additional scholarships and navigating financial challenges. Thanks to their support, I could focus on my research without financial worries.

Looking back, I am grateful for the transformative experiences at the University of Tokyo that shaped my professional career and the people who made it possible. I encourage anyone thinking about this path to go for it, and I hope current students continue to enjoy both their research and the rich culture of Japan!

International Student Advising Room

The International Student Advising Room (ISAR), established in 1994, provides a variety of services to support international students and researchers. https://israr.f.u-tokyo.ac.jp/en/isar/index.html

ISAR offers:

- Advisory assistance and a counseling service
- Information for prospective international students
- Event planning
- Inter-university academic exchange program
- Information services

Lecturer **E. Gosho**
International Student Adviser

Academic Exchange Agreements between Universities

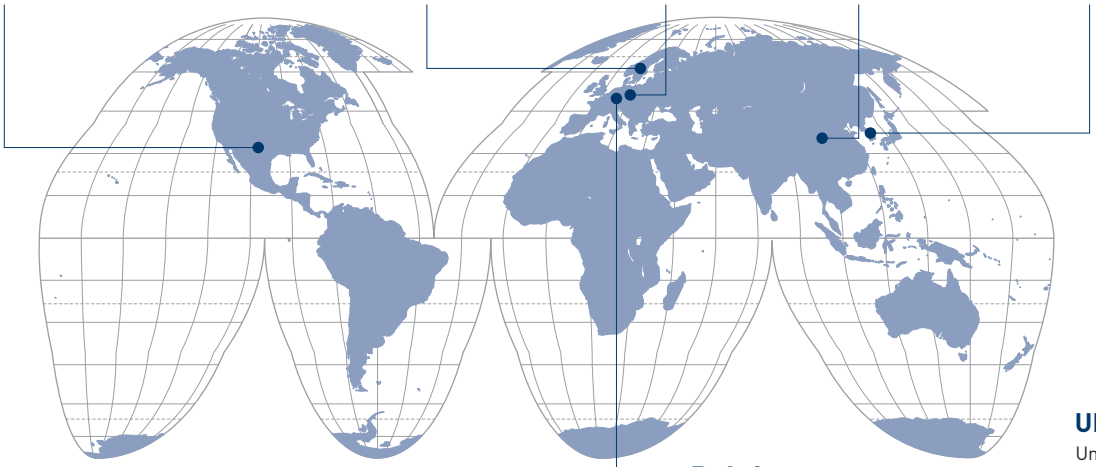
USA
The University of Texas M. D. Anderson Cancer Center

Sweden
The Sahlgrenska Academy, University of Göthenburg

Germany
Research Training Group 1873 The University of Bonn

P.R.China
Shenyang Pharmaceutical University

Republic of Korea
School of Pharmacy, Sungkyunkwan University



Belgium
The Faculty of Science, KU Leuven

UK
University of Cambridge

Experimental Station for Medicinal Plant Studies

Hanamigawa-ku, Chiba-shi, Chiba

The Experimental Station for Medicinal Plant Studies is located about 30 km east of the Hongo Campus. Its 6,123 m^2 plant specimen garden includes the medicinal plants that are considered important for the students' education. This garden serves a variety of purposes, including maintenance of plant lineages; research on plant breeding and cultivation; collection and cultivation of medicinal plants native to Japan as well as introduced from overseas; research on medicinal plant ingredients from the standpoints of chemistry, pharmacology, biosynthesis, plant physiology, and pharmacognosy; and research on the medicinal plant cultivation and maintenance. The grounds of the Experimental Station also encompass a greenhouse, administration building, and laboratory building.

At present, about 250 varieties of plants are under cultivation. Each year, 3rd-year students receive practical training in the plant specimen garden during the summer session. In 1982, the laboratory for medicinal plant studies was set up within the building in Hongo Campus and have continued research until now.

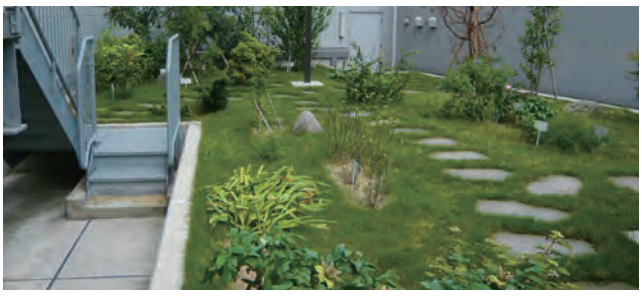
The University Museum, The University of Tokyo (Hongo Campus) houses a Pharmaceutical Sciences Division on its first floor, where a large number of specimens – mainly crude drugs and medicinal plants – are stored and managed.

In October 2004, the first rooftop herb garden, with an area of approximately 100 m^2, was created on the rooftop of the auditorium of Pharmaceutical Sciences Research Building for enabling the students to come into close contact with medicinal plants. Several dozen varieties of medicinal plants are cultivated in light soil with a depth of about 60 cm, equipped with an automatic irrigation system.

Greenhouse

Vanilla planifolia (Andr.) G.Jackson

Magnolia obovata Thunb.



Roof Garden

Pharmaceutical Sciences Library

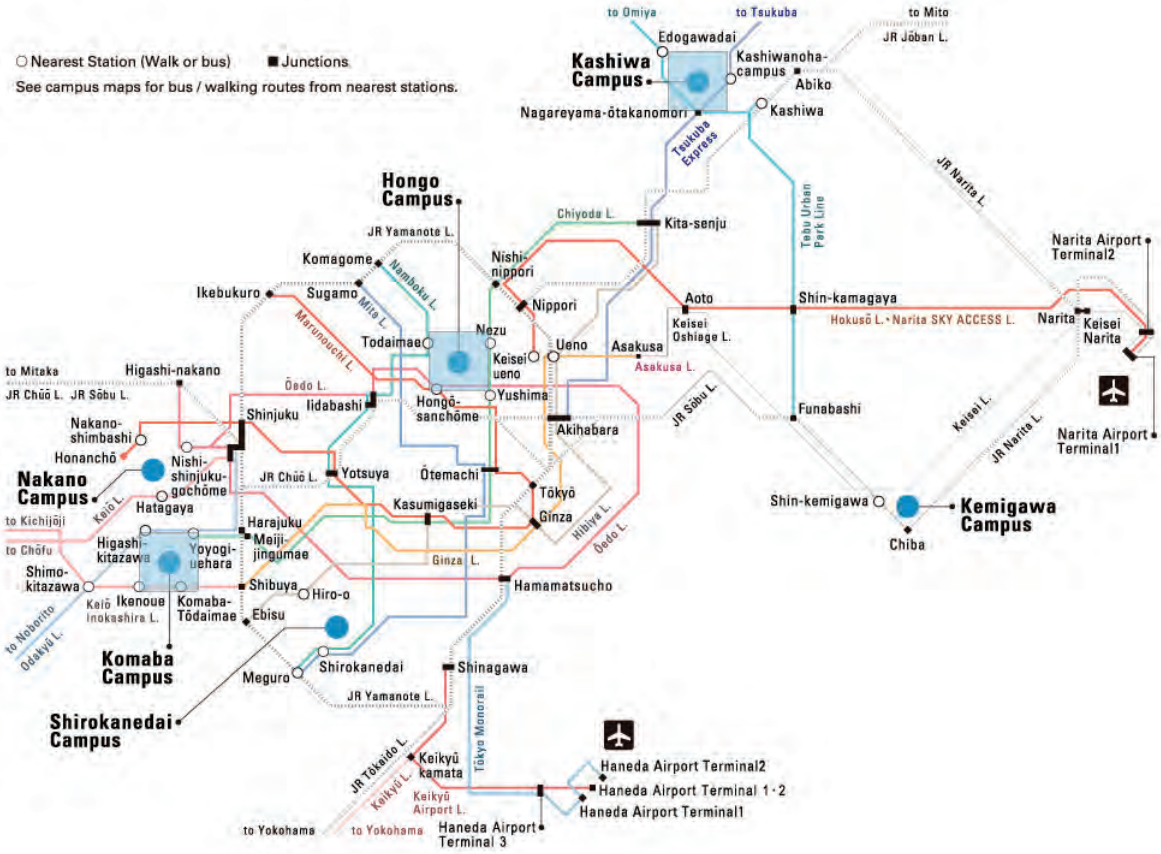
Books	Japanese books	International books	Total
	14,962	37,142	52,104
Academic Journals (titles)	Japanese Journals	International Journals	Total
	414	426	840

(As of March, 2024)

Main Entrance

Reading Room

Access Map



Dr. Leopold Müller

In 1869, Meiji government decided to adopt German medicine and asked the minister of the North German Federation to send 2 instructors. In 1871, Müller (chief Army physician/staff surgeon) and Hoffman (Navy physician/staff internist) arrived in Japan and assumed their duties at the University East Building (Tôkô) in Shitaya Izumibashi (precursor of the Faculty of Medicine, University of Tokyo).

Müller and Hoffman, who were under the direct supervision of the Meiji Minister of Education, had absolute authority over medical education in Japan. A new curriculum was established with 3 preparatory years (changed to 2 the following year) and a 5-year main program.

Müller and Hoffman regarded "pharmaceutical sciences" as an independent branch of the natural sciences that was closely related to medicine, and they proposed the establishment of a pharmaceutical institute. This took shape in 1873 as the Department of Pharmaceutical Manufacturing, established in The First University District Medical School. Müller returned to Germany in 1875. In October of 1895, upon the third anniversary of his death, a bust of Müller was erected to honor him as a benefactor of Japanese medicine and pharmaceutical sciences.

Dr. Leopold Müller (1824 - 1893)

Dr. Junichiro Shimoyama

Dr. Shimoyama was born in Owari Inuyama in 1853. In 1873, after transferring to the Department of Pharmaceutical Manufacturing, The First University District Medical School (the precursor of the Faculty of Pharmaceutical Sciences, University of Tokyo), he graduated in 1878. He gave the "address in reply" at the first degree-conferring ceremony held by the Faculty of Medicine.

In 1886, Dr. Shimoyama received the Doktor der Philosophie degree from Strasburg University in Germany and in 1899, he became the first person in Japan to be awarded a Doctor of Pharmaceutical Sciences degree.

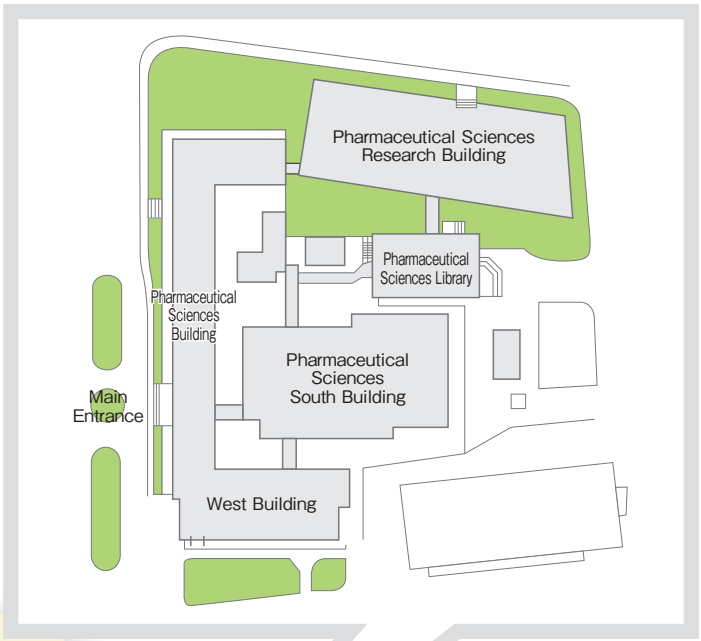
Dr. Shimoyama became a professor of the Department of Pharmacy in the Faculty of Medicine in 1887, and a professor of a laboratory of Pharmacognosy, the Department of Pharmacy in 1893. While devoting great efforts to education and research, he also helped to cultivate successors through the establishment of the Pharmaceutical Society of Tokyo (the present Pharmaceutical Society of Japan) and the creation of a privately funded medicinal herb garden (Zekô Yakuen), etc.

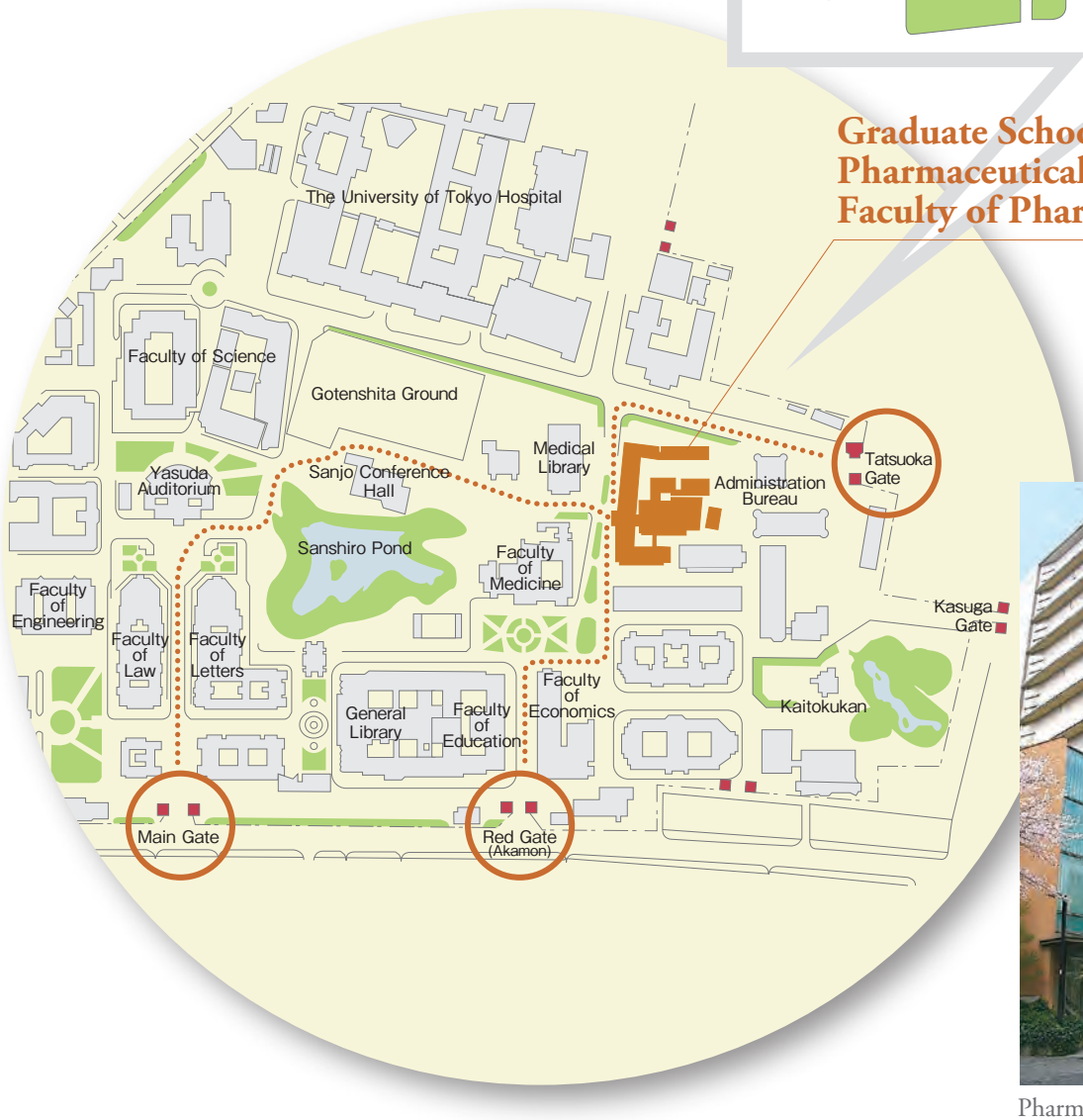
Dr. Shimoyama died suddenly in February of 1912 while still in service as an educator. In remembrance of him, a bronze statue was erected beside the Pharmaceutical Sciences Building in 1913.

Dr. Junichiro Shimoyama (1853 - 1912)

Hongo Campus

Pharmaceutical Sciences Building





Graduate School of Pharmaceutical Sciences
Faculty of Pharmaceutical Sciences

Pharmatical Sciences Research Building

Left :
Photograph of on-chip high-performance separation media (pillar array columns)

Right :
Electron microscope image of its separation channels

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