



Faculty of Veterinary Medicine  
Graduate School of Veterinary Medicine  
School of Veterinary Medicine  
Hokkaido University

# THE FACULTY OF VETERINARY MEDICINE



HOKKAIDO  
UNIVERSITY





## History of Veterinary Education in Hokkaido University



Dr. Cutter

The history of veterinary education in Hokkaido University can be traced back to the founding of the Sapporo Agricultural College. The Sapporo Agricultural College was founded for education in liberal arts and various agricultural subjects in addition to veterinary medicine. Professional education in veterinary medicine at Sapporo Agricultural College was initiated by Dr. Cutter, who came to Japan in 1878 (Meiji 11) and started the professional education in veterinary medicine from 1880. It should be noted that Dr. Cutter taught medicine and fisheries science, he was also a multifaceted individual who was in charge of the study of English language and literature. Department of Veterinary medicine was

established in 1910; in 1913, the Second Section of the Department of Animal Science was established, the predecessor of current School of Veterinary Medicine. Later, Dr. Koichi Ichikawa graduated, who created the world's first experimental cancer in rabbit ears. In 1952 Department of Veterinary Medicine from the School of Agriculture became independent as the School of Veterinary Medicine.

## Dr. Koichi Ichikawa and Tar Cancer



Dr. Koichi Ichikawa

As an imperishable achievement in the history of cancer, tar cancer was a result of patience and effort from an alumnus of this School, Dr. Koichi Ichikawa, who also became a candidate for the Nobel Prize at the time. Dr. Ichikawa from Ibaraki Prefecture graduated from the School of Agriculture, Tohoku Imperial University (the precursor to the current Graduate School of Veterinary Medicine, Hokkaido University) and then immediately went to study as a special researcher under Dr. Katsusaburo Yamagiwa at Tokyo Imperial University in 1913. He had firmly believed in the theory of carcinogenesis (first proposed by Dr. Virchow in German) and went on to patiently tar on rabbit ears day after day. After testing 101 rabbits over periods lasting 70–450 days, cancer could be found in 31 rabbits. At that time, three years had passed since coming to the University of Tokyo. They were listed as candidates for the Nobel Prize in 1926, but it was awarded to a Danish researcher, Professor Fibiger, who produced cancer in the stomach of rats with a special parasite using cockroaches as the intermediate host. Today, the name of Professor Fibiger does not appear in Western textbooks about cancer, but the tar cancer of Yamagiwa and Ichikawa invariably does. The two won the Japan Academy Prize in 1919 for their work. When Koichi Ichikawa was 31 years old, he returned to the School of Veterinary Science of Hokkaido University and established the Department of

Comparative Pathology. Calligraphy by Dr. Ichikawa for the characters of "effort" and "patience" still decorate the Dean's room.



# History and Outline of the School / Faculty of Veterinary Medicine

Sapporo Agricultural College		1876 Aug. 14	Sapporo School opens.	
Agricultural College, Tohoku Imperial University	Department of Animal Science	1876 Sep. 8	Sapporo School is renamed Sapporo Agricultural College.	
		1907 Sep. 1	Sapporo Agricultural College is renamed Agricultural College, Tohoku Imperial University.	
		Jun. 24	The Department of Animal Science is established.	
		1910 Mar. 26	The Department of Veterinary Medicine is established.	
		1911 May 2	The Second Department of Veterinary Medicine is established.	
		1912 Jun. 25	Regulations on animal hospitals are enacted.	
Agricultural College, Hokkaido Imperial University	Second Section of the Department of Animal Science	1913 Jun. 30	The Department of Animal Science is divided into the first and second sections.	
Faculty of Agriculture, Hokkaido Imperial University		1918 Apr. 1	Hokkaido Imperial University is established. The Agricultural College, Tohoku Imperial University is renamed the Agricultural College, Hokkaido Imperial University.	
		1919 Apr. 1	The Agricultural College, Hokkaido Imperial University is renamed the Faculty of Agriculture, Hokkaido Imperial University.	
		1920 Sep. 14	The Department of Livestock Hygiene is established.	
		1922 May 15	The Department of Comparative Pathology is established.	
		1944 Dec. 19	The Department of Anatomy is established.	
	Faculty of Agriculture, Hokkaido University	Department of Animal Science	1946 Apr. 1	The first and second sections of the Department of Animal Science are renamed the Department of Animal Science.
1947 Oct. 1			Hokkaido Imperial University is renamed Hokkaido University.	
Department of Veterinary Medicine			1949 Apr. 1	The Department of Veterinary Medicine is established.
			May 31	Hokkaido University is established under Japan’s new educational system. (The National School Establishment Law is enacted.)
			1950 Apr. 1	The Department of Physiology is established.
School of Veterinary Medicine, Hokkaido University			School of Veterinary Medicine	1952 Apr. 1
	1953 Apr. 1	The Graduate School of Veterinary Medicine, Hokkaido University is established. The Departments of Biochemistry and Epizootiology are established.		
	May 13	The Departments of Preventive Therapeutics and Biomedical Sciences are established in the Graduate School.		
	Aug. 1	The Livestock Hospital is established. (The National School Establishment Law is partially revised.)		
	1954 Apr. 1	The Departments of Pharmacology and Theriogenology are established.		
	1955 Jul. 1	The Department of Parasitology is established.		
	1964 Apr. 1	Ministerial Ordinance on Courses and Subjects (Order No. 3 of the Ministry of Education for 1964) (12 courses)		
	1969 May 21	The Department of Radiation Biology is established.		
	1984 Apr. 1	The minimum duration of studies in the School of Veterinary Medicine becomes six years due to the partial revision of the School Education Act.		
	1986 Apr. 1	The Department of Laboratory Animal Science and Medicine is established.		
	1990 Apr. 1	The master’s course of the Graduate School of Veterinary Medicine is abolished and the minimum duration of studies in the doctor’s course becomes four years due to the partial revision of the School Education Act.		
	Jun. 8	The Department of Toxicology is established.		
	School of Veterinary Medicine / Graduate School of Veterinary Medicine, Hokkaido University	1995 Apr. 1		Reorganization is made based on a policy of emphasizing the graduate school. • School of Veterinary Medicine (Department of Veterinary Medicine: 4 subjects): Biomedical Science, Etiological Pathology, Applied Veterinary Sciences and Veterinary Clinical Sciences • Graduate School of Veterinary Medicine (Department of Veterinary Medicine: 4 major courses): Biomedical Sciences, Disease Control, Veterinary Clinical Sciences and Environmental Veterinary Sciences, The Laboratory of Molecular Medicine and the Laboratory of Ecology are established. The Livestock Hospital becomes a facility associated with the Graduate School of Veterinary Medicine.
				The Department of Prion Disease is established in the Graduate School of Veterinary Medicine.
2001 Apr. 1				
2003 Apr. 1		The Zoonosis Course (a cooperating course) is established in the Graduate School of Veterinary Medicine.		
2006 Apr. 1				
2007 Apr. 1		The Livestock Hospital becomes the Animal Hospital, which is directly managed by the Graduate School of Veterinary Medicine.		
		The Laboratory of Advanced Veterinary Science is established.		
2008 Apr. 1		The Veterinary Educational Innovation Office is established.		
2009 May 1		The Department of Prion Disease is renamed the Laboratory of Veterinary Hygiene, the Department of Applied Veterinary Science.		
2010 Apr. 1				
		The Laboratory of Ecology is renamed the Laboratory of Wildlife Biology and Medicine.		
2010 Jul. 1		The cooperative veterinary education program of Hokkaido University and Obihiro University of Agriculture and Veterinary Medicine starts.		
2012 Apr. 1				
School of Veterinary Medicine / Graduate School of Veterinary Medicine / Faculty of Veterinary Medicine, Hokkaido University		2017 Apr. 1	The Graduate School of Veterinary Medicine is due to be reorganized as the Faculty of Veterinary Medicine, Graduate School of Veterinary Medicine and Graduate School of Infectious Diseases. • Faculty of Veterinary Medicine (Veterinary Science section: 6 disciplines) [Faculty organization] Basic Veterinary Sciences, Applied Veterinary Sciences, Environmental Veterinary Sciences, Clinical Veterinary Sciences, Disease Control and Preentive Veterinary Medicine • Graduate School of Veterinary Medicine (Division of Veterinary Medicine: 4 courses) [Student organization] Basic Veterinary Sciences, Applied Veterinary Sciences, Environmental Veterinary Sciences, and Clinical Veterinary Sciences • Graduate School of Infectious Diseases (Division of Infectious Diseases [Student organization]	



# Philosophy for Veterinary Education

The Hokkaido University School of Veterinary Medicine aims to foster veterinarians who can meet the diverse social needs for veterinary medicine--needs that go beyond the diagnosis, treatment and prevention of animal diseases to the safe supply of animal products, contributions to drug development and biochemistry, the protection and management of wild animals, and the control of zoonotic disease--based on veterinary medicine as a natural science that is responsible for all animal life on the earth.

However, understanding the diverse social roles played by veterinary medicine requires comprehensive knowledge of cultural and social sciences, as well as of natural science. Additionally, scientific thinking and judgement, along with an international perspective, must be cultivated towards resolving various global issues related to veterinary medicine. Furthermore, students are encouraged to foster the rich humanity and high moral values that are required for veterinarians and researchers, who will play a central role in promoting harmonious relationships between animals and humans.

## Educational Objectives

The School of Veterinary Medicine provides students with specialized knowledge and skills in veterinary medicine to develop new generations of veterinarians equipped with a well-rounded character, a strong sense of ethics and international perspectives, as well as researchers who can take a pioneering approach to veterinary medicine. Graduates are expected to contribute to the maintenance and improvement of animal health, the improvement of public health, food safety and

the development of life sciences. Specifically, the School of Veterinary Medicine helps students:

- to learn standards of conduct that are based on the logic and ethics needed for veterinarians in their duties;
- to acquire proficient knowledge and skills on the prevention, diagnosis and treatment of animal diseases, as well as on the maintenance and improvement of animal health and public health;
- to gain the international perspectives, expertise and specialized skills necessary to contribute to the solving of global issues such as food supply stability, the safety of livestock animals and their products, and the control of zoonoses; and
- to develop, through research experience on leading-edge life sciences, problem-solving abilities based on veterinary medicine and the ability to conduct international activities for new discoveries related to life phenomena and drug development.

## Ideal Students

- Students who love animals and are capable of observing animals from objective, scientific perspectives
- Students who have a sense of awe toward and are scientifically inquisitive about life phenomena
- Students with the desire to make social and international contribution through veterinary medicine



## ■ Career Options of Undergraduate Students

Job Category	2012	2013	2014	2015	2016
Local Official	11	5	9	7	3
National Official	3	1	3	1	0
Company	7	8	5	6	9
Clinic for Domestic Animals	4	5	4	5	3
Clinic for Companion Animals	10	12	7	9	9
Graduate School	5	8	3	7	10
Study or Training Abroad	0	1	2	1	1
etc.	2	1	5	5	4
Total	42	41	38	41	39

# What Can You Learn in the Cooperative Veterinary Education Program in the School of Veterinary Medicine?



Since 2012, Hokkaido University and the Obihiro University of Agriculture and Veterinary Medicine have offered the Cooperative Veterinary Education Program in order to provide international-level veterinary education, and have provided practical and advanced veterinary education leveraging the research field of Hokkaido. The Hokkaido University School of Veterinary Medicine has been engaged in a major way in research on

zoonotic diseases, life science research, preservation of ecosystem and clinical experiments on small animals, while Obihiro University of Agriculture and Veterinary Medicine has focused on medical care for farm animals, production medicine and education on public hygiene, all of which are necessary for veterinarians. Veterinary medicine is facing increasingly diverse social needs. These include the risk management of food safety, the prevention of animal-borne diseases including zoonoses, the appropriate treatment of diverse diseases of domestic animals, the responses to advanced technologies for disease diagnosis, prevention and treatment, animal welfare and wildlife conservation. To effectively address these issues, the two universities have pooled their outstanding educational resources in order to develop a curriculum that the universities individually would not have been able to formulate. Under this new curriculum, teaching staff of Hokkaido University instruct students in some subjects at Obihiro University of Agriculture and Veterinary Medicine, and vice versa. This program also allows students of both institutions to participate in seminars and practical training offered on a different campus and to participate in interactive remote classes using IT.

We firmly believe these educational reforms play a vital role in fostering veterinarians and researchers who not only gain an in-depth understanding of diverse social demands for veterinary medicine, but also develop scientific thinking and judgement, an international perspective, creativity and rich humanity.

The outlines of the Cooperative Veterinary Education Program aimed to encourage students to acquire the abilities stated above are as follows.

**1<sup>st</sup> year:** Enrolled students study in the First-Year Education Division, which offers various lectures as general education, including courses in Humanities and Social/Natural Sciences. Students are recommended to actively attend these

lectures in order to become well refined. During the summer holidays, the Seminar in Agriculture and Food Animal Science and the Elementary Seminar in Veterinary Science at Obihiro are intensively offered as introductory veterinary medicine education at Obihiro University of Agriculture and Veterinary Medicine.

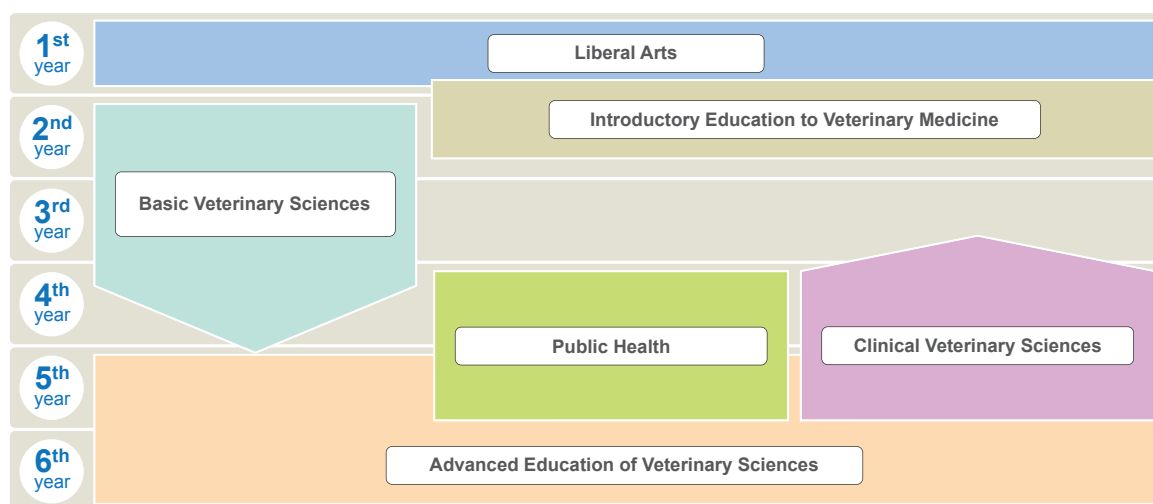
**2<sup>nd</sup> year:** The Introduction to Veterinary Medicine and the Elementary Seminar in Veterinary Science at Sapporo are intensively offered as introductory education at Hokkaido University during the summer holidays. Professional education in the Cooperative Veterinary Education Program starts from the first semester. In this period, students take lectures and conduct practical training in a range of basic veterinary sciences, such as anatomy, physiology, biochemistry, pharmacology, genetics, immunology, radiobiology, microbiology and laboratory animal science, in order to gain knowledge on the structures, functions of the parts, and responses in animal bodies and basis on animal diseases.

**3<sup>rd</sup> year:** Students learn pathogens that cause animal diseases and basis on diagnosis and prevention/treatment of the infectious diseases through lectures and practical training on virology, bacteriology, parasitology, epidemiology, pathology, and wildlife zoology.

**4<sup>th</sup> year:** Students enroll in lectures and practical training on environmental and applied veterinary sciences, such as public health, toxicology, food hygiene, epidemiology and zoonoses, as well as in animal husbandry-related subjects, such as food nutrition, grassland science and animal feeding, and farm animal management. In addition, students are required to take subjects related to clinical veterinary medicine, such as surgery, internal medicine and theriogenology.

**5<sup>th</sup> and 6<sup>th</sup> years:** In addition to lectures and practical training on clinical veterinary medicine, introductory education for veterinarians is offered, including animal welfare, ethics and regulations. From the 5<sup>th</sup> year, students are required to attend clinical rotations, in which students can experience the treatment of animals at the university teaching hospitals (Sapporo and Obihiro), after passing the common national achievement examination in veterinary medicine (since 2016). Students also choose and join one of the research laboratories, where they take advanced courses and seminars and conduct tutorial research, based on their interests and/or plans for future job. Furthermore, students prepare themselves for the entrance examination of a doctoral course or engage in job hunting, cultivating their sense of responsibility as veterinarians or researchers in the future. The National Examination for Veterinarians is given in mid-February, and the results are announced in mid-March.

■ The Course Flow Chart



# Faculty of Veterinary Medicine

Today, as academic research and graduate school education advance further, our efforts must be more interdisciplinary and concerted than ever, in order to facilitate research and education towards the creation and maintenance of a sound, healthy circle of humans, animals and the environment, under a concept referred to as “One Health.” We need to create flexible new concepts according to social needs, thereby providing fascinating, essential scientific research and education, as well as continuing to foster superior doctors and other human resources.

To promote such academic, interdisciplinary graduate school education, it is important to appropriately position teaching staff according to educational intent and content, as well as to make effective, purposeful use of them. Based on this principal concept, we decided to reorganize the Graduate School of Veterinary Medicine as a faculty (a faculty and research organization) and a graduate school (a graduate school education organization) in April 2017. As a new graduate school, the Graduate School of Infectious Diseases plays a leading role in providing comprehensive, interdisciplinary higher education on infectious diseases, as well as in practically cultivating international experts to address infectious diseases. Teaching staff from disciplines related to infectious diseases in

the Faculty of Veterinary Medicine, the Research Center for Zoonosis Control and relevant medical faculties are collectively responsible for this education. In addition, the Graduate School of Veterinary Medicine, where teaching staff members who specialize in disciplines other than infectious diseases in the Faculty provide higher education on veterinary sciences and advanced veterinary medicine based on individual, basic, applied, environmental and clinical research activities, aims to implement educational activities that include unconventional approaches, such as by setting an advanced veterinary healthcare.

Students of the Graduate School of Veterinary Medicine acquire extensive expertise and undergo research instruction. Their research base is naturally the Faculty of Veterinary Medicine, as it was before. The most important roles and responsibilities required of universities are research and the practice of education based on that research. The Faculty serves as a basic organization for supporting educational practice. Individual teaching staff, who also play roles as researchers, and students collaborate to globally disseminate diverse, fascinating, essential scientific research on veterinary sciences and advanced veterinary medicine.

## Undergraduate School

Educational organization (for students)

### School of Veterinary Medicine

Dean of the School

#### Cooperative Veterinary Education Program

[6-Year Undergraduate Program 40 Students Each Year]

●Departments

●Basic Veterinary Sciences

●Pathobiological Veterinary Sciences

●Applied Veterinary Sciences

●Veterinary Clinical Medicine

## Graduate Schools

Research organization (for faculty members)

### Faculty of Veterinary Medicine

Dean of the Faculty

Vice-Dean of the Faculty

#### Division of Veterinary Medicine

●Departments

●Basic Veterinary Sciences

Anatomy Physiology Biochemistry Pharmacology

●Applied Veterinary Sciences

Radiation Biology Laboratory Animal Science and Medicine

●Environmental Veterinary Sciences

Toxicology Wildlife Biology and Medicine

●Clinical Sciences

Internal Medicine Veterinary Surgery  
Comparative Pathology Theriogenology  
Molecular Medicine Advanced Veterinary Medicine

●Disease Control

Microbiology Infectious Diseases Parasitology

●Preventive Veterinary Medicine

Public Health Veterinary Hygiene

#### Veterinary Teaching Hospital

Hospital Director

●Clinical Division

Internal Medicine Surgery Theriogenology Clinical Laboratory

#### Shared Use Facility

Animal Facility Shared Use Equipment Facility  
Veterinary Specimens Facility

Educational organization (for students)

### Graduate School of Veterinary Medicine

Dean of the Graduate School

Vice-Dean of the Graduate School

#### Division of Veterinary Medicine

[ 4-Year PhD Program 16 Students Each Year ]

●Departments

●Basic Veterinary Sciences

●Applied Veterinary Sciences

●Environmental Veterinary Sciences

●Clinical Sciences

### Graduate School of Infectious Diseases

Dean of the Graduate School

Vice-Dean of the Graduate School

#### Division of Infectious Diseases

[ 4-Year PhD Program 12 Students Each Year ]

Research organization (for faculty members)

#### Research Center for Zoonosis Control

Global Epidemiology  
Molecular Pathobiology  
Bioresources  
Collaboration and Education  
Bioinformatics  
Infection and Immunity  
Risk Analysis and Management  
Biologics Development

#### Faculty of Medicine

Microbiology  
and Infectious Diseases

## Administration Office for Veterinary Medicine

General Secretary

General Affairs Section

Academic Affairs Section

Accounting Section

Research Support Section

Library Section





## Graduate School of Veterinary Medicine

Public expectations for multidisciplinary education have been on the rise in recent years, and it has been considered as a top priority for society to educate advanced and flexible knowledge professionals armed with multidisciplinary knowledge based on their expertise. The same is true of veterinary medicine. Hokkaido University has opened the Graduate School of Infectious Diseases because it is imperative that researchers in different fields come together from around the world to educate new generations of professionals capable of combating infectious diseases, most notably emerging and reemerging infectious diseases. The University has also established the new Graduate School of Veterinary Medicine to meet the social needs of educating professionals in veterinary science, advanced veterinary healthcare and global environmental conservation.

The advancement and specialization of veterinary medicine, veterinary healthcare and veterinary science are under way worldwide based on the One Health concept that we cannot maintain a sound ecosystem for the earth unless we can ensure the health of both humans and animals. Against this background, the new Graduate School of Veterinary Medicine offers rigorous curricula built on those of the ongoing Program for Leading Graduate Schools, which focus on the cultivation of global perspectives and expertise in veterinary science. The mission of the Graduate School of Veterinary Medicine is to educate new generations of leaders who have broad, philosophical perspectives, a flexible imagination and comprehensive decision-making abilities as well as the practical competence and leadership skills needed to contribute to the development of veterinary science in Japan and around the world. The Graduate School aims to fulfill this mission with a focus on veterinary science and veterinary healthcare based on the three pillars of animal life science, clinical veterinary medicine and environmental veterinary science.

To achieve these goals, the Graduate School opens its doors to undergraduate students from within and outside the University who are eager to earn a degree in

veterinary medicine and to graduates who are seeking to earn a Ph.D. while playing an active role in society. As a graduate institution open to the world, the school also accepts international students. It offers courses provided in the Program for Leading Graduate Schools: Subjects on Fundamental Veterinary Science, Academic English, Subjects on Advanced Veterinary Science, Advanced and Comprehensive Studies on Chemical Hazard Control, Research on Veterinary Science, Advanced Seminar on Veterinary Science, and internships at home and abroad. New courses include the Research Ethics Seminar and Clinical Medicine Emphasizing Program, which is aimed at educating future experts in clinical veterinary science.

We are confident that the curricula will produce Ph.D. holders in veterinary medicine who are equipped with broad perspectives, an academic foundation and highly specialized expertise in veterinary and related sciences. They will also have the ability to see issues from broad, multidisciplinary perspectives, the insight and flexible imagination necessary to solve challenging issues, and the leadership skills needed to help achieve the One Health concept in the international arena. As I am determined to make every possible effort to fulfill our mission, I would very much appreciate the continued support and encouragement of everyone involved.



## Graduate School of Infectious Diseases

Emerging and re-emerging infectious diseases such as Ebola virus disease, Zika virus disease, and pandemic influenza have recently been occurring worldwide, posing a threat to humanity. In Japan, the occurrence of severe fever with thrombocytopenia syndrome has recently become a major social issue. All of the above diseases arise from zoonotic pathogens, which are transmitted from wild animals and elicit virulent infections in livestock, poultry, and humans. The entry and spread of diseases from outside Japan, such as highly pathogenic avian influenza and foot-and-mouth disease, also result in extensive economic damage in Japan due to their effects on key farm animals in food production. Measures for combatting these zoonoses and transboundary animal diseases require international cooperation that extends beyond the scope of any single individual country. Overcoming these infectious diseases calls for not only basic research on pathogens, but also research on the biology of pathogens in nature, immune response to pathogens by the host, diagnosis, prevention, and therapeutic agents, as well as broad knowledge and advanced specialization regarding occurrence prediction, risk assessment, management, and international health policies for infectious diseases. In Japan and other countries around the globe, demand is heightened for research on infectious diseases and the development of experts who can enact measures to combat those diseases.

The “One Health” concept, which has been gaining prominence worldwide, holds that in order to maintain the health of individuals and societies, the health of animals and conservation of the environment must be considered as a single entity. Many infectious diseases can only be overcome by promoting One Health and fostering interdisciplinary cooperation between academia and research. To that end, the 21<sup>st</sup> Century Center of Excellence Program and the Global Centers of Excellence Program have constructed a base for joint education and research on

zoonotic diseases at Hokkaido University. In order to develop veterinary medicine experts who can contribute on an international stage, a doctoral and education leadership program called Fostering Global Leaders in Veterinary Science for Contributing to One Health has been promoting graduate school education that incorporates enhanced screening and practical international activity to foster a multidisciplinary outlook.

The Hokkaido University Graduate School of Infectious Diseases has been developing and reinforcing the measures described above with an eye to more internationalized, multidisciplinary graduate school education in infectious diseases and veterinary science. With the participation of instructors from the Research Center for Zoonosis Control, Graduate School of Veterinary Medicine, and Graduate School of Medicine, the Graduate School of Infectious Diseases strives to develop “infectious disease professionals” by constructing a cross-disciplinary educational system that takes advantage of its component areas of expertise and utilizing a joint research network consisting of more than 30 countries. The ultimate goal of these efforts is to develop personnel who can lead the way in controlling infectious diseases that pose social problems.



### ■ Career options of graduate students

Job category	2012	2013	2014	2015	2016
Local or National Official	1	2	0	7	2
Researcher or Faculty in Japan	6	9	5	11	6
Company	3	3	5	1	3
Animal Clinic	0	1	0	0	2
Outside Japan	2	8	6	3	6
etc.	5	0	2	1	1
Total	17	23	18	23	20

## International Academic Exchange

At Graduate School/Faculty of Veterinary Medicine, educational and research exchanges with overseas universities, as well as a wide range of contributions to society through veterinary research are being conducted. Through our exchange programs with universities in Europe and the United States, Asia and Africa, extramural study experience is provided for undergraduate students. Since academic year 2013/2014, the Re-Inventing Japan Project has been implemented as an international program, students participating this program can acquire part of their credits (Year 5) at Kasetsart University in Thailand. In academic exchange schemes, graduate students themselves can carry out practical research projects on infectious diseases and environmental science with specimens collected from foreign countries. Certain opportunities for international experience, such as participation to International conferences or academic interns, are provided for all graduate students in all fields of interests on veterinary science.

Our Graduate School has been contributing to one health through international organizations, such as the WHO and OIE, and also technical cooperation to establish veterinary education and human resource development of many foreign universities. Support to establish veterinary education program in Republic of Zambia is its most prominent case. This technical cooperation in University of Zambia began in the early 1980s until 1990s and then extended several research corroborations and bilateral student exchange. This long-lasting relationship results installation of Research Station and Regional Information Center in

University of Zambia. Currently, as part of development of graduate program, educational and research exchange programs with foreign institutions are being expanded, while providing more overseas internship programs for graduate students.

### International Programs

- The International Priority Graduate Programs (PGP) (2007~2020)
- Global Institution for Collaborative Research and Education (GI-CoRE) Global Station for Zoonosis Control (GSZ) (2014~)
- Japan International Cooperation Agency (JICA) Mongolia「Project for Strengthening the Capacity for Human Resource Development in the Field of Veterinary and Animal Husbandry」(2014~2019)
- Japan Science & Technology Agency(JST) Science and Technology Research Partnership for Sustainable Development (SATREPS)「Visualization of Impact of Chronic/Latent Chemical Hazard and Geo-Ecological Remediation」(2015~2019)
- Veterinary academic exchanges with the University of Edinburgh (UK) (alternate student dispatch and acceptance each year)
- Joint symposium with Seoul National University (Korea) (Held alternately every year)



### ■ Inter-University Exchange Agreements (as responsible department)

Partner country	Institution name	Concluded
Sri Lanka	University of Peradeniya	2006/11
Mongolia	Mongolian University of Life Sciences	2009/1
Indonesia	Gadjah Mada University	2010/7
U.K.	University of Edinburgh	2011/2
Zambia	University of Zambia	2011/3
South Africa	University of Pretoria	2016/8
U.S.A.	Colorado State University	2017/3

### ■ Inter-Departmental Agreements

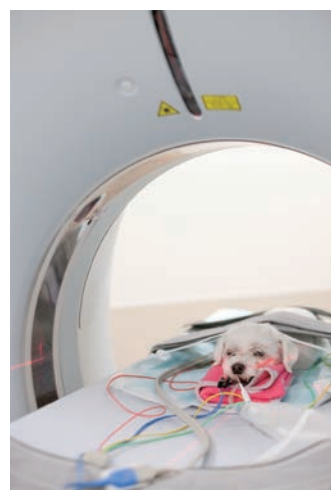
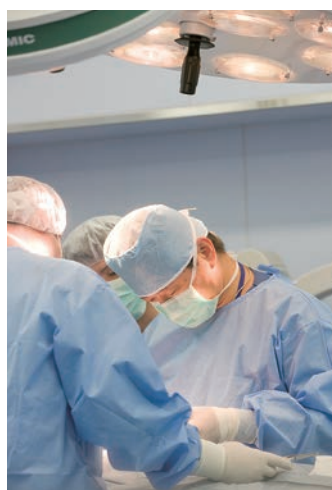
Partner country	Institution name	Concluded
Indonesia	Department of Veterinary Science, Gadjah Mada University	2008/8
Taiwan	College of Veterinary Medicine, National Chung Hsing University	2008/12
U.K.	Royal (Dick) School of Veterinary Studies, University of Edinburgh	2009/7
Germany	Faculty of Veterinary Medicine, Ludwig-Maximilians-Universität München	2011/1
Egypt	Faculty of Veterinary Medicine, Zagazig University	2012/3
Germany	Faculty of Veterinary Medicine, University of Berlin	2012/7
U.S.A.	College of Veterinary Medicine, Cornell University	2013/3
Mongolia	National Center for Zoonotic Diseases, Ministry of Health	2013/5
Ghana	College of Science, Kwame Nkrumah University of Science and Technology	2013/7
Myanmar	University of Veterinary Science	2013/10
Mongolia	Institute of Veterinary Medicine, Mongolian University of Life Sciences	2014/1
Philippines	Philippine Carabao Center	2015/9
Nepal	National Trust for Nature Conservation Nepal Anti-Tuberculosis Association/ German—Nepal Anti-Tuberculosis Project	2016/4
Spain	Faculty of Veterinary Medicine, University of Murcia	2016/5
Vietnam	Vietnam National University of Agriculture	2017/2



## History and Overview of the Veterinary Teaching Hospital

The Veterinary Teaching Hospital was established as the Livestock Hospital in 1912, and has ever since played a leading role in dairy cattle husbandry and livestock medical treatment in Japan. In 1964, it was newly built at the current location as the number one Livestock Hospital in Asia; as time passed, a large renovation was conducted in 1994. In 2002, it changed from an affiliated facility with the Faculty of Veterinary Medicine to become an affiliated facility for Graduate School of Veterinary Medicine; in 2006, its name was changed from the Livestock Hospital to the Veterinary Teaching Hospital. Further, in 2013 it moved from the old facility to the new Veterinary Teaching Hospital facility. The new facility is fully equipped with 12 examination rooms, a counselling room, 5 operating rooms, a dental care unit, 3 ultrasound examination rooms, 2 X-ray examination rooms, a CT laboratory, a MRI laboratory, a low-energy radiation therapy room, a high-energy radiation therapy room, a chemotherapy room, an endoscopy room, an intensive care unit (ICU), and more. As the core hospital for the region, the veterinary teaching hospital has been developed to meet its needs.

Reflecting the fact that dogs and cats have become companion animals with long longevity, medical care for aging-associated diseases (chronic heart disease, digestive disorders, tumors, endocrine diseases, chronic skin disease, etc.) is plentiful. Diseases that require advanced surgical treatment have also been increasing, and so the Veterinary Teaching Hospital plays a role as a secondary medical care facility in the region. Besides, as a teaching hospital, it is not only used for the clinical education of students, but as a place of postgraduate education for clinical veterinarians as well as training veterinarians from overseas. Furthermore, the Hospital has also been utilized in veterinary clinical research in many domains, such as the development of diagnostic techniques with higher imaging modalities, genetic analysis for disease genes and their detection methods, elucidating disease pathogenesis and developing novel therapies based on it, anti-tumor therapeutic methods that put less burden on the animal, establishing guidance and counter-measures to prevent the outbreak of disease, and more.



## Animal Facility and Ethics Education in Animal Experimentation

The 3Rs principles for animal experimentation (refinement of methods to minimize animal suffering, replacement with alternative methods, and reduction of the number of animals used) were specified under the Law for the Humane Treatment and Management of Animals in 2005. Degree holders from the Graduate School of Veterinary Medicine must be qualified to provide guidance and advice regarding animal testing as well as to manage laboratory animal facilities while considering these principles at all times. In consideration of this background, the Graduate School drafted and adopted the "Training program for the next-generation veterinary research scientist – Towards an international ethics education for animal experimentation", which was adopted and used to apply for a "Initiatives for Attractive Education in Graduate Schools" grant from the Ministry of Education, Culture, Sports, Science and Technology in Japan. New campus regulations were created based on international standards of ethics in animal experimentations: Animal Care and Use Committee that includes members from the general public was founded, and various improvements were carried out. These included: guidelines and strict screening for proper experimental design; improving rearing environment and environmental enrichment; setting appropriate qualities and quantities of animals; elimination or mitigation of animal discomfort, distress, and pain; prescription of appropriate sedatives, analgesics, and anesthetic agents; setting of humane endpoints; and 365 days a year, 24 hours a day management, among others. In order to appraise our implementation of a world-class animal research program with the consideration of animal welfare, our program received review and evaluation from the USA-based AAALAC

International, the most prestigious such NPO accreditation body, and in 2007 was the first university in Japan to obtain full accreditation, which continues to this day. Only a few universities in Japan have an animal research program that conforms to these international standards, and our program uniquely has the internationality and wide-ranging knowledge to train leaders who can lead animal research with consideration of animal welfare.



### Facility for Farm Animal

Facility for Farm Animal was newly built in the financial year 2017 for the main purpose of student practices for treatment of cows and horses. In the loose barn, where 10 cows can be reared concurrently, the cows can move freely without restraints. Additionally, in the summer, cows are free to enter and leave the outdoor paddock, and can live without stress. Although the number of horse stalls is the same as that in the former facility (2 rooms), there is a newly built treatment area for students to practice horse treatment more safely. The new facility also has a horse paddock. In addition, we established a hospitalization stall that can be used to isolate sick animals; therefore, students can practice treatment of hospitalized animals. In addition, we built a small livestock pen whose area can be increased or decreased by moving partitions according to the size of the small ruminants and calves. The passage width in the center of the facility is approximately 5 m; therefore, animals can be moved safely, while simultaneously ensuring that the students can safely practice treatment of the animals.

### Facility for Infection and Hazardous Substance Pathology

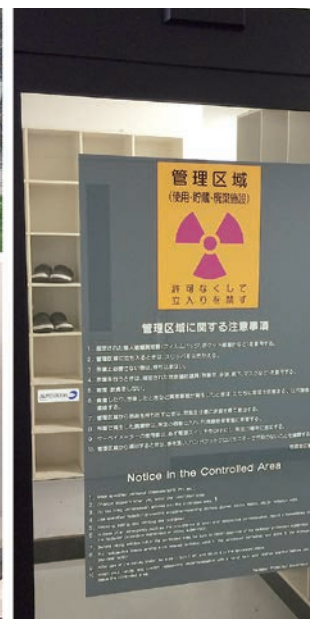
The facility was newly built in 2017 for the purpose of improving and advancing practical training in the field of infectious diseases and environmental toxicity. This facility has a biosafety level-2 (BSL-2) animal room—that can keep farm animals, such as cattle—on the first floor. In addition, the facility has a necropsy room for pathological analyses of animals used in infection experiments and for examination of field materials. There is also a BSL-2 laboratory room for processing materials sampled during necropsy. In addition, 2F has a new chemical exposure laboratory, which is a facility for carrying out enhanced toxicological practices, task research, and advanced exercises in the cooperative curriculum.





## Radiation Experimental Facility

This research facility was set up in a corner of the southeast of the main building in July 1969; the old facility became obsolete in April 1999, when a new RI laboratory facility was established to the east of S facility (site area of ~700m<sup>2</sup>; controlled area of ~350m<sup>2</sup>). Primary RI measurement equipment currently possessed by the facility include various survey meters for radiation protection and personal dosimeters for monitoring, including liquid scintillation counters, Geiger counters, bio-imaging analyzers, auto-gamma counters, X-ray generators, etc. The main unsealed RI nuclides available are <sup>3</sup>H, <sup>14</sup>C, <sup>32</sup>P, <sup>45</sup>Ca, <sup>36</sup>Cl, <sup>125</sup>I, <sup>35</sup>S, <sup>59</sup>Fe, <sup>55</sup>Fe, <sup>42</sup>K, and <sup>51</sup>Cr. The RI management system and the drainage and disposal systems in the new building have been redesigned. There are RI laboratory rooms for contamination examination, small animal testing, student experiments, animal breeding, environmental radioactivity measurements, RI storage, and culturing, as well as a radiation measurement chamber, a irradiation management chamber, a waste storage warehouse, and waste water treatment as well as RI storage and treatment facilities. These facilities are in compliance to the recent Laws Concerning the *Prevention from Radiation Hazards* due to Radioisotopes and Others. Currently, the facility is widely used within the Faculty and Graduate school for RI and radiation use



## Veterinary Specimen Room

Specimens with precious academic values that have been collected for veterinary research and education are kept on display in the specimen exhibition room of the Faculty of Veterinary Medicine, Hokkaido University. Inside this specimen exhibition room, samples are mainly displayed related to research and education of anatomy, pathology, wildlife science, and parasitology.

It is a glorious past research achievement that has been submitted as a candidate for the Nobel Prize in Physiology or Medicine four times since 1925. It is an artificial experimental carcinogenesis specimen of rabbit ear created by Dr. Koichi Ichikawa, a veterinary pathology professor at Hokkaido Imperial University. The artificial cancer (skin cancer) was the world's first to be proven experimentally, by applying coal tar onto the ears of rabbit along with his mentor

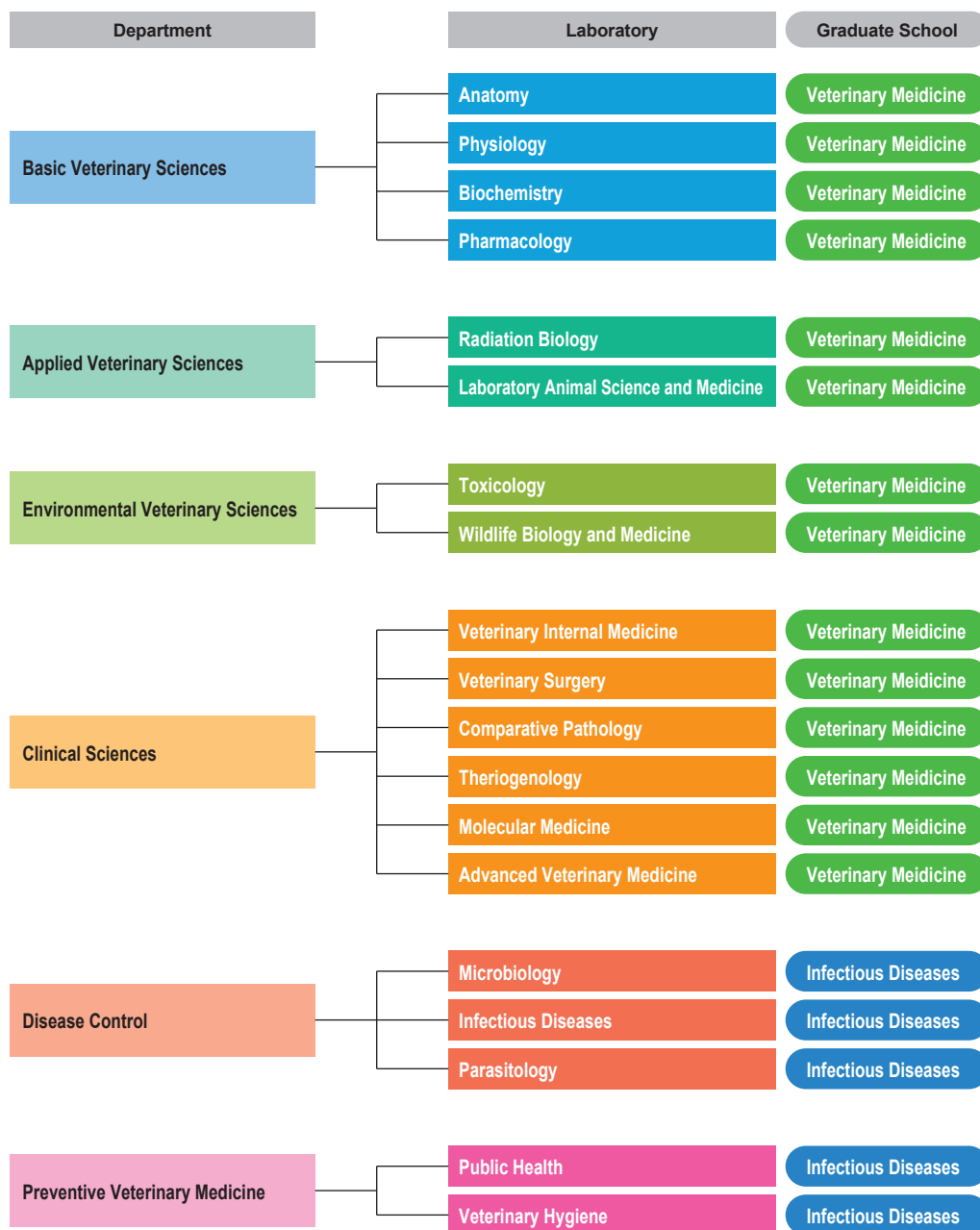
Professor Katsusaburo Yamagiwa (Tokyo Imperial University). Next to it are displayed the German-made (and very expensive) microscope used in the experiment and research papers on artificial carcinogenesis published in German.

Within the research and education of veterinary medicine today, practical education to understand the real thing by seeing it directly is very important. Among the display specimens, besides the glass bottle specimens submerged in liquid, the skeletal preparations and plastination specimens with that feel natural to the touch as described above, cast specimens and detailed anatomical drawings depicting the blood vessels and joint cavities are also included. If you would visit us at the specimen exhibition room, you will be fascinated by the many animal specimens on display.

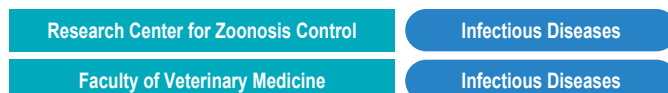




## Departments and Laboratories



Five laboratories in the Faculty of Veterinary Medicine (Microbiology, Infectious Diseases, Parasitology, Public Health, Veterinary Hygiene) as well as the staffs in Research Center for Zoonosis Control and Faculty of Medicine participate in the Graduate School of Infectious Diseases.



## For 100 years from now... Approach from molecular morphology

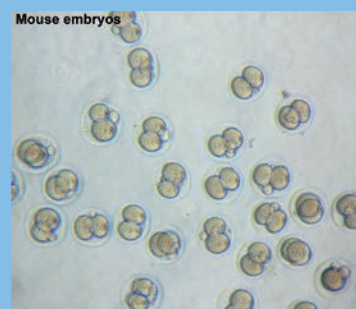
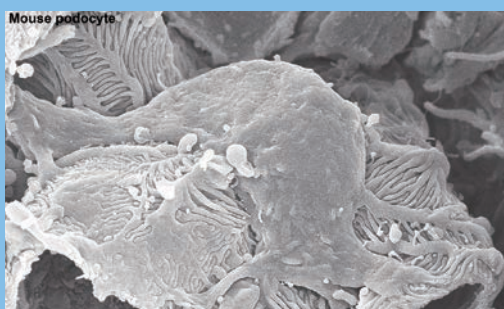
The Laboratory of Anatomy offers subjects of anatomy, histology, and embryology, studying the form and function of cells and organs of animals. Examination of the bodies of animals and observation of the cells by microscope are important techniques for veterinary medicine, therefore anatomy provides fundamental knowledge that is essential to other basic, applied, or clinical subjects.

Using the molecular morphological approach, we are studying dynamic changes in the morphology as well as function and gene expression of cells. Particularly, during the embryonic period, cells form and combine into organs through rapid changes, such as proliferation, apoptosis, and transformation. Currently, we are studying the molecular signals associated with the development of muscle, kidney, and intestine to generate recipes for cells to develop themselves into organs, and seeking applications to regenerative medicine.

Developmental abnormalities are directly linked to organ dysfunction in individual animals, but abnormalities of gametes (sperm and eggs) affect the next generation. We are studying the mechanisms regulating gametogenesis. By exploring

the mechanisms of gametogenesis and how ovarian or testicular environments nurse their gametes, we are beginning to elucidate the sex determination mechanisms and the causes of infertility in animals.

What are the causes of these abnormalities? Essentially, we are focusing on the "disruption of autoimmune system". We are developing autoimmune animal models and carrying out pathological analysis of autoimmune nephritis and exocrinopathy (dacryoadenitis and pancreatitis). In addition, we are trying to identify the causative genes of these diseases to establish diagnostic markers and methods useful in clinical practice. Importantly, autoimmune animal models show morphological and functional abnormalities of the gonads. In short, infertility and autoimmune diseases are threats to animals of the next generation. Basic research to counter these threats is needed now more than ever. Why not join us and make your mark in molecular morphological research?



## From the micro to the macro

Physiology is a discipline that studies the mechanisms of life. In veterinary physiology, focusing on mammals and birds, while keeping in mind the animal species we encounter in veterinary medicine, we aim to understand the functions individual organisms are endowed with to survive.

Currently, our research primarily focuses on cell physiology, but it also involves physiology at the organismal level. Specifically, we have conducted research on the physiology of the intracellular signal transduction system and the olfactory and visual senses; we are moving forward on research on an image analysis method that visualizes changes of calcium ion and nitric oxide in cells by applying fluorescence microscopy image analysis and digital cameras. Moreover, for the last few years, we have been performing other organism-focused studies intermittently, including research related to the brains of ruminants as well as the diving physiology of the emperor penguin.

In order to know the whole picture of the mechanisms at play in life, a broad view of knowledge and fields is essential: from micro to macro levels, at the

subcellular, cellular, tissue, organ, and organismal levels. In our day-to-day research, we are inclined to be devoted to the research challenges at hand and can tend to forget these broader perspectives; we would like to advance research while being careful to avoid this pattern.



## Bioche-mystery of energy metabolism

All the living organisms have very precise systems that maintain homeostasis of their body function and energy storage. This homeostatic control is critical for our health. Deterioration of this function makes diseases and aging. However, the regulatory mechanisms of this system in a healthy state and in a development of diseases are not fully understood. Biochemistry is a way to clarify and explain mysteries of life at the molecular level by elucidating the structure and function of genes, proteins and metabolites. We are investigating the mechanism how our body achieves homeostatic control of energy metabolism, and what is the cause of obesity, diabetes, lactation failure and complications of these diseases. Followings are the main topics of our research.

**Proinsulin C-peptide (Cp):** We have demonstrated that Cp is a biological active peptide to improve abnormalities found in diabetic kidney and that candidate of the Cp receptor is  $\alpha$ -enolase found on the cell membrane. We are currently investigating the receptor-related issues to attempt to apply Cp as a treatment for diabetes.

**Brown fat:** Brown fat, a tissue specified for non-shivering thermogenesis, plays an

important role in body temperature control under cold circumstances and during arousal from hibernation. We have shown that the activation of brown fat increases whole body energy expenditure and thereby reduces body fat amounts. To combat obesity and related metabolic disorders, we are trying to find ways to utilize brown fat and enhance its function.

**Obesity and mammary gland (MG):** It is known that obesity has negative effects on lactation. This might be due to abnormalities of post-natal MG development such as incompleteness of ductal formation and delay of acinar formation in enlarged subcutaneous fat tissue. We are currently investigating effects of obesity on the ability of MG stem cells.

**Glucose sensing by the brain:** Brain can monitor fluctuations of blood glucose levels by glucose sensing neurons. We investigate the neuronal circuit of glucose sensing neurons to control glucose metabolism in peripheral tissues and the role of glucose sensing neurons in a development of diabetes.



## Toward revealing unknown biological functions: Approach from dynamism of drugs!

Pharmacology not only unravels the action exerted by drugs inside the living body and their mechanisms, it is also conversely a discipline that investigates the mechanism of biological phenomena by using the action of drugs. The central research topic of our laboratory is to determine the mechanisms of action of transmitters that are responsible for the transmissions of various kinds of signals. Transmitters and the molecules that respond to them are the targets of many therapeutic agents. We are working on research with the awareness that our own research outcomes form the cornerstone of new drug developments.

### 1. Elucidation of the mechanisms of pain signal transduction

Pain stimuli to sensory nerves such as those in the skin are recognized as pain after transmission to the brain via the spinal cord. In our laboratory, from exploring the mechanisms of pain control by means of transmitters in the spinal cord in particular, we are studying the actions of various drugs and possibilities of new analgesic agents. Moreover, from the perspective of animal ethics, we uphold the

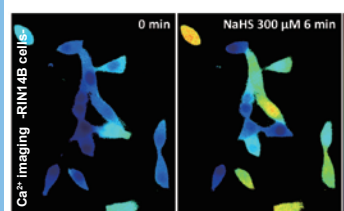
great proposition of analysing pain quantitatively without causing pain to animals, for example by using isolated spinal cord preparations.

### 2. Action of glial transmitters

It has been revealed that glial cells such as astrocytes release transmitters in the same way as neurons. We are continuing to perform research of the production, release, and mechanism of action of adenosine and hydrogen sulfide as the glial transmitters. In addition, we note that astrocytes are activated by a variety of stimuli, and study the role of reactive astrocytes and glial transmitters in pathogenesis from circulatory disorders of the central nervous system.

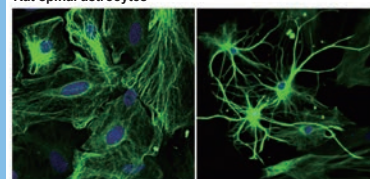
### 3. Functional analysis of chemoreceptor cells

The partial pressure of oxygen in the blood and various substances in the lumen of the gastrointestinal tract are monitored by a group of cells called chemoreceptor cells. In our laboratory, we are conducting research to reveal the response mechanisms to a variety of chemicals, including gaseous substances in enterochromaffin cells and chicken aortic bodies.



Ca<sup>2+</sup> imaging of RIN14B cells line derived from rat pancreatic islet  $\delta$  cells. NaHS (300  $\mu$ M), a hydrogen sulfide (H<sub>2</sub>S) donor, increases intracellular Ca<sup>2+</sup> concentration in RIN14B cells, which express a H<sub>2</sub>S-response protein, TRPA1 channels.

Rat spinal astrocytes



Immunostaining images of cultured normal (left) and reactive (right) astrocytes isolated from rat spinal cord.

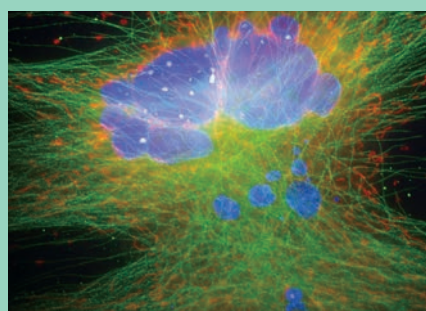


## The Invisible Science of Radiation

In the present day, as the age of companion animals increases, the number of animals suffering from the age-related disease of cancer (malignant tumors) is increasing. Surgery, chemotherapy, and radiation therapy are the treatments mainly adopted. As suggested by its name, radiation therapy is a method that leverages the cytotoxic and cytostatic effects of radiation. While there are advantages to this kind of therapy—its burden to the whole body is small, since it is possible to suppress the cancer without surgery, and it is able to treat cancer sites where surgery would not be possible, there are also disadvantages, such as the facts that normal tissue at the site is damaged by radiation and that there is sometimes cancer that is highly resistant to radiation. Aiming for more effective and efficient radiation therapy for cancer, our laboratory is conducting research on the relationship of radiation and cancer by using a variety of techniques. For example, cell death is triggered when cells are exposed to radiation, but the radiation sensitivity of cancer cells not only varies depending on the type and malignancy of the cancer, it also depends on the cells' location and the state of the intracellular environment. As long as cancer cells are more sensitive to the radiation

than healthy cells, it is possible to enhance the therapeutic effects of radiotherapy. We are conducting research to clarify the mechanisms behind the radiation sensitivity of cancer cells and explore the factors that affect it, focusing specifically on DNA repair mechanisms, energy metabolism, response to oxygen environments, and mitochondrial function of cancer cells.

Moreover, recent developments in molecular imaging are remarkable. Evaluating the effectiveness of radiation therapy and assessing the nature of cancer in the living animal has become more and more important. In our laboratory, we analyze the in vivo environment of complex cancers by using PET for nuclear medicine imaging as well as MRI for functional imaging.



## Analyzing mouse and rat genomes in order to study the functions of genes

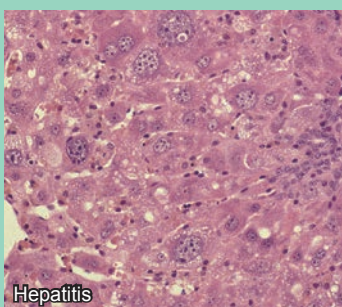
Laboratory animal science is a comprehensive science related to animals used in experiments. The animal species of interest are almost all mammals, such as mice, rats, other rodents, rabbits, dogs, cats, pigs and monkeys, and the field handles the anatomy, physiology, genetics, thremmatology, theriogenology, and pathology of these animals. In other words, it is not an exaggeration to say that the discipline is a miniature of veterinary medicine. From within the wide territory of laboratory animal science, in the Laboratory of Laboratory Animal Science and Medicine, we are conducting infectious disease research and genome analyses of mice and rats utilized in experiments, as well as activities to improve the welfare of all laboratory animals used in the Veterinary School.

The veterinary medicine is supposed to protect the lives of animal; why do we study using mice and rats in experiments? This is because mice and rats also are breeding animals to a human end; they have becoming a kind of livestock as subjects of interest for veterinary medicine. Some laboratory mice and rats spontaneously develop the same diseases as humans and animals. By studying the causes of disease in these model animals, we can apply the results to medicine and veterinary medicine. The photograph is of a rat that spontaneously develops

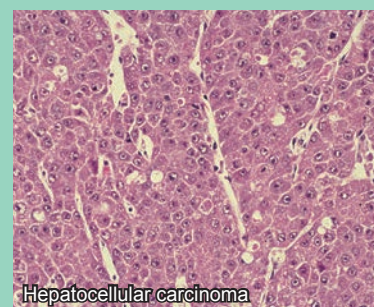
hepatitis and liver cancer called LEC discovered at Hokkaido University. The other photographs contain the histology of liver cancer and hepatitis of this rat. Other genome research studies include the identification of the causative genes for quantitative traits (e.g. resistance to infection or susceptibility) that occur in various inbred strains, and developmental engineering (production of transgenic and knockout animals) to verify these causative genes.

Regarding activities related to welfare improvement of laboratory animals, faculty members and postgraduate students, as laboratory animal medical specialists or resident physicians under the Laboratory of Laboratory Animal Science and Medicine, have been contributing to the prevention and treatment of diseases for laboratory animals, the elimination of suffering during animal experimentation, and the improvement of breeding environments. All members report research outcomes in a research meeting held once every two months with the aim of improving their respective research studies. In addition, we conduct literature seminars introducing articles from Nature, Science, and Cell and group readings of "Molecular Biology of the Cell", by which each member strives to acquire the latest knowledge. "Enjoy Science" is the motto of our laboratory, and we conduct first-class research while enjoying each other's company.

LEC and LEA rats



Hepatitis



Hepatocellular carcinoma

## Exploring Species Differences in Biological Defense Mechanisms to Combat Xenobiotics

In addition to various chemicals like pharmaceuticals, environmental chemicals and food additives, even components of natural origin included in food become a “foreign substance” to an organism, when it is taken into its body. Ingestion of excessive foreign substances is known to be toxic to a living organism. Before the foreign substances (i.e., xenobiotics) become toxic to a living organism, including us, the organism uses a mechanism to excrete these chemicals from the body as soon as possible.

Cytochrome P450 is a group of enzymes that works on the front lines for the detoxification of xenobiotics. Focusing on the cytochrome P450 family, we investigate the detoxification mechanism of xenobiotics possessed by organism, aiming to elucidate animal species differences in terms of their biological defense mechanisms to combat foreign matter in humans and animals.

Among the xenobiotics, there are a number of known environmental contaminants spreading on a global scale that can accumulate in humans and wildlife. Yet, the enzymes that metabolize these foreign substances, as the cytochrome P450

family does for the detoxification and metabolism of xenobiotics, are relatively unknown for most wildlife, comparing to humans and laboratory animals. We seek to clarify what environmental pollutants may accumulate in wildlife, what kind of toxic effects may result, and whether the wildlife have detoxification or biological defense mechanism to counter them. To this end, we are conducting a comprehensive analysis of xenobiotic metabolic enzymes including the cytochrome P450 family, impact analysis on genetic and epigenetic changes, and chemical analysis of the accumulation profile of pollutants. Furthermore, through our active efforts in conducting outdoor toxicological experiments (field toxicology) for the environmental pollution that is rapidly progressing in Africa, we are carrying out impact assessments of toxins on humans, livestock, and wildlife.



## We strive to be professionals in wildlife biology and medicine

With conservation of bio-diversity as the final goal, we practice wildlife/conservation medicine education and research to contribute to the conservation and management of wildlife. We primarily target large mammals such as deer and bears to shed light on their physiology and ecology, while keeping in mind applications of conservation and management. Moreover, we clarify the actual nature of infections mediated by wildlife in order to elucidate their modes of infection and routes of transmission between wildlife and humans & livestock. Furthermore, we are also studying issues brought about by invasive species including raccoons, in particular their effects on humans and native organisms as well as problem-solving measures.

Our research themes include, for example: the relationship of reproduction and nutrition for bear species during winter hibernation as well as the relevant physiological and metabolic machinery; the ecology, behavior, and genetic structure of the brown bear population in eastern Hokkaido; the mode of infection of tick-borne diseases found in the wildlife of Hokkaido; infectious disease control and biodiversity conservation in Nepal; and the reproduction, infectious diseases, and

genetic structure of raccoon.

In particular, the research on the physiology and ecology of bear species is now the pillar of the current research in our laboratory. The bear is an animal that acquires unique physiological mechanisms when it undergoes pregnancy, parturition, and lactation under the severe conditions of low metabolism and fasting that occur during hibernation. In additions, while it belongs to the order Carnivora, it depends on plants as the majority of its food, and uses food resources efficiently, varying season-to-season and year-to-year. In short, its ecology is very interesting.

Reducing these research findings to the level of education of wildlife and conservation medicine, we hope that students will gain some knowledge of wildlife before graduating. Moreover, we provide post-graduate students with the education improve their expertise even more, and foster them to become the wildlife professionals in their future. Furthermore, we practice a wide range of outreach activities, for groups from the general public to researchers.





## Our research themes are in veterinary medical care

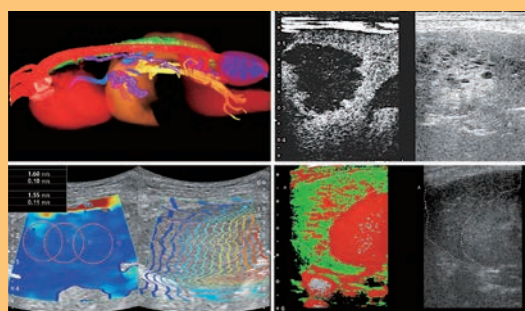
The missions of our laboratory are both to reveal the pathogenesis of various diseases of companion animals, and to establish novel diagnosis and treatment methods. Members of our laboratory provide Internal Medicine service for companion animals at Veterinary Teaching Hospital of Hokkaido University. The Internal Medicine service diagnoses and provides treatment for a wide range of life-threatening health conditions including gastrointestinal, hematologic, immune-mediated, endocrine, respiratory, and liver disorders. Our research focus on naturally occurring disease in companion animals, especially focus on gastrointestinal diseases, immune-mediated disease, and hematologic diseases. We aim to overcome diseases of companion animals with a wide variety of approaches, such as diagnostic imaging, molecular biology, and others. The main research themes of our laboratory are as shown below.

1) Establishment of the procedures for contrast-enhanced ultrasonography by using second-generation ultrasound contrast agent on small animals clinically and their diagnostic significance.

2) Development of new diagnostic and therapeutic strategy for chronic inflammatory disorders in dogs and cats.  
3) Development of novel strategy for non-invasive ultrasound therapy.

Focused on finding the root cause of disease, we are seriously committed to providing medical care for companion animals. By conducting research based on clinical experience, we work day and night to give feedback on research results to clinical care and to establish crosstalk between clinical care and research.

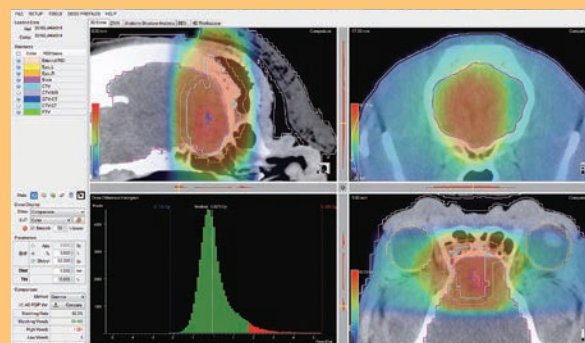
Nowadays, the diagnostic techniques in veterinary practice are increasingly improving, and as a result, emerging diseases will be discovered in near future. By elucidating the cause of these novel diseases, new therapies will be developed. It will not only lead to improvement of clinical care in veterinary practice, but also contribute significantly to the development of the life sciences. Why don't you come together with us to advance our research and help sick animals?



## Towards world-leading treatment technology

The Laboratory of Veterinary Surgery is specialized for research and education in the area of surgery. Clinical activity of our laboratory in the veterinary teaching hospital includes small animal orthopedics, soft tissue surgery, and comprehensive oncology services, managing a high number of referral cases from the area as a regional center of secondary/tertiary practice. Age-related diseases of companion animals, such as arthritis and cancers, are becoming more and more common, requiring advanced practice in small animal medicine. To meet the social expectations for specialized clinical services, our orthopedic team has been investigating diagnostic and treatment technologies of fracture repair, joint diseases, and neurological disorders. Our oncology research team has been working on comprehensive cancer management, integrating advanced surgical, medical, and radiation therapy techniques. Through our daily clinical experiences and observation of animals with generally ill-prognosis recovering successfully with proper treatment, we strongly believe further advancement will be achievable with continued effort and sophistication of clinical technologies. Our laboratory is also conducting a number of research projects to give

solutions to clinical problems we encounter daily in the practice. The orthopedic team has been researching pathological mechanisms of cartilage damage with arthritis and its treatment methodology, including novel medications and cartilage-regeneration technology. The oncology team has been focusing on treatment of refractory cancers using bone marrow transplant technique, allogeneic cell-based immunotherapy, and state-of-art high accuracy radiotherapy. The cross-talk of clinical experiences and basic research activity has been providing us an ideal environment for practical research projects aiming at world-leading novel treatment strategies. With an increasing number of international graduate students we are accepting, the Laboratory of Veterinary Surgery also places emphasis on the globalization of the veterinary medicine.





## Unveiling the mechanisms of disease

Pathology is the study of the cause of disease and the mechanisms of disease development (pathogenesis). Moreover, necropsy and histological analysis of surgical specimens also play a major role in pathology to diagnose the illnesses of individual animals.

Our laboratory was established in 1922. At that time, since veterinary pathology is an academic field that contributes also to basic medical sciences, it was given the name the Laboratory of Comparative Pathology, and has been kept alive in this spirit even today.

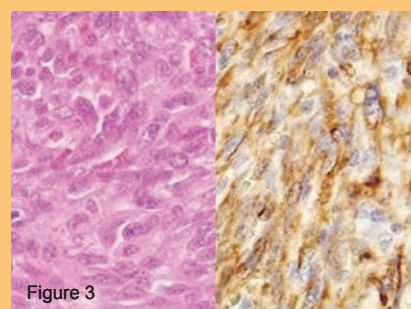
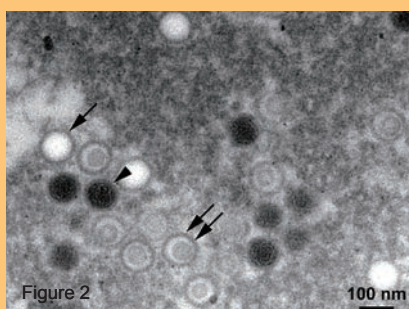
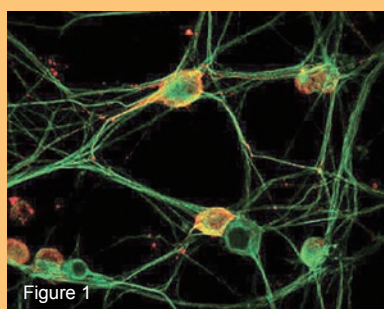
The research work in our laboratory is divided into two major categories. One is pathological diagnosis of naturally occurring diseases. By pathologically diagnosing the diseases of companion animals, livestock, poultry, and zoo animals, and then providing clinical feedback, work in this category contributes to disease prevention and treatment. The other is the experimental study of animal diseases, setting our focus on the elucidation of the pathogenesis of various diseases. Being able to deeply and widely learn about disease through these two research activities is a major

characteristic of our laboratory. An essential part of our research relies on morphological analyses using microscopes (anatomic pathology); however, we actively incorporate them with in vitro research using the methods of cellular and molecular biology. Our current major research interests are (1) infectious diseases in animals such as equine herpes virus infection, flavivirus encephalitis, and (2) canine hemangiosarcoma.

Figure 1 shows an image of primary-cultured neurons infected with influenza virus. Viral antigens (labeled as red) were overlaid on neuron-specific  $\beta$ III tubulin (labeled as green). The co-localization of viral antigens with tubulin is shown in yellow.

Figure 2 is a transmission electron microscope image showing viral capsids (the protein shells that enclose viral genomes; arrows and arrowheads), in the nucleus of a cell infected with a newly isolated virus from a wild flying fox.

Figure 3 is an image when we see canine hemangiosarcoma with microscope. The left panel shows the morphology of neoplastic cells. In the right panel, expression levels of a differentiation-related protein (labeled as brown) are investigated.



## Elucidating the Mysteries of Reproduction and Applying Reproductive Technology in the Field

If animals did not give birth to offspring, there would be no caring for pets such as cats and dogs, no production of livestock products from farm animals such as pigs and cattle, and the wildlife would not exist as part of the ecosystem in a natural environment. Because of this, theriogenology is the most important field of study within veterinary medicine. Every student who aims to be a veterinarian learns through lectures and practices about reproductive mechanisms of normal animals and the problems those obstruct the breeding and about the technologies to promote breeding effectively.

In recent years, our laboratory has been investigating various phenomena related to animal reproduction, focusing especially on the reproductive technologies involved for various species. In these days, we are investigating the most suitable culture systems for effective use of ova derived from bovine ovaries which disappear during follicular development. Also, we are studying the cryopreservation of mammalian embryos and germ cells, and establishing methods that evaluate quality of germ cells before and after freezing objectively. Thus, we are conducting researches and

contributing to the improvement of technology in the livestock industry, efficient in vivo production of livestock embryos, and the elucidation of the physiological mechanisms of reproduction. Moreover, for the conservation and management of wild species, we are working on research on the development and application of artificial reproductive technologies those developed for livestock.

Other than research, we are managing reproduction of dairy cows and pigs in the experimental farm in Hokkaido University, by artificial insemination and assisting labor of dairy cows, so that students who belong to our laboratory will understand the reproductive physiology of the animals and the reproductive technologies. Moreover, we are responsible for general medical care in the farm. At the Veterinary Teaching Hospital of Faculty of Veterinary Medicine, we are responsible for embryo transfer and embryo recovery of cattle. Thus, our laboratory can provide many opportunities to learn about farm animals.



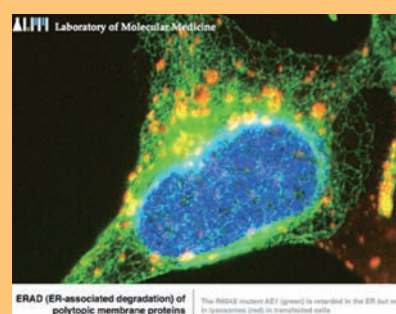
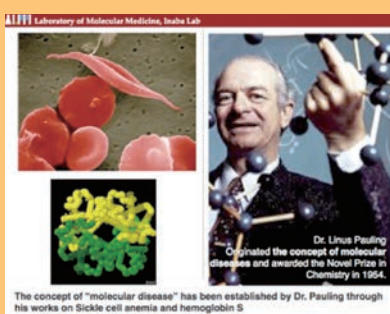
## Life and death depend on the membrane: Exploring the life of membrane proteins in the pathology of red blood cell membrane disorders

The biological membrane is a basic cell structure of cells. Cells engage in their living activities based on its structure and function, and their various functions and characteristics of the membrane are generated based on the distribution of various membrane proteins while they maintain dynamic equilibrium states and on membrane structures while they interact with one another. The life of red blood cells with typical membrane structures, from creation as precursor cells until collapse in due course of aging, is an excellent model to understand the functional construction and control of biological membranes. In our laboratory, based on pathological ideas primarily in hereditary diseases of red blood cells (erythroid cells), we are pursuing the mechanisms of production, transport, function, and destruction of membrane proteins in the cell by using biochemistry and cell biology methods.

One of our main themes is (1) the quality control mechanism for integral membrane proteins: i.e. the mechanistic elucidation of endoplasmic reticulum-associated degradation (ERAD) based on band 3 deficiency (hereditary spherocytosis) in cows. We are tackling the elucidation of the unknown molecular

mechanisms of degradation by the proteasome when proteins are recognized by the ER as abnormal membrane proteins. Another hot topic is (2) the illumination by genome analysis of the functions of gene that controls the HK/LK type of canine red blood cells, aiming to reveal a completely new universal mechanism of still-mysterious erythroid maturation.

Additionally, we aim to elucidate: (3) structural and functional abnormalities due to genetic abnormalities and post-translational modification of the membrane skeleton protein; (4) the mechanisms of intracellular vesicle trafficking of membrane proteins; and (5) the cell-specific gene transcription control mechanisms of an erythroid, consisting primarily of globin switching. Furthermore, in the clinical regard, we work on genetic predisposition for diseases and epigenetic analysis on hematopoietic cell tumors with the motto of "Life and death depend on the (genetics of the) membrane" in the hopes of fostering essential research for acceptance in medical science world-wide.



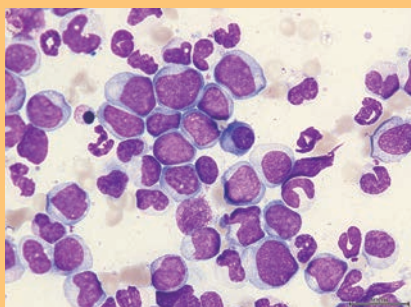
## Opening up New Approaches in the Development of Veterinary Clinical Sciences

Everyone associates the word "veterinarian" with the so-called clinical veterinarian, a figure who diagnoses diseases by performing various tests on animals and treat them with medication or surgery. The Laboratory of Advanced Veterinary Medicine, which emphasizes clinical practice and is affiliated with the Veterinary Teaching Hospital, comprises faculty members who are responsible for anesthesia, surgery, and medical care.

Our aim is to enhance the development of veterinary medicine, and we work daily on medical care, education, and research so that we can contribute to the society by improving animal welfare. The main feature of this laboratory is that it blurs the boundaries between internal medicine and veterinary surgery; this enables a new approach that involves an unprecedented collaboration between internal medicine and surgery. Even though the laboratory has a relatively short history since its inception, its staffs work smoothly together as a team. We have also developed light extracurricular activities in various situations other than the medical and research activities of the hospital.

We are currently working on research topics that include the elucidation and clinical application of tumor microenvironment in dogs and cats, the study of the pathogenesis of non-regenerative immune-mediated anemia in dogs, and the development of non-invasive diagnostic imaging modalities for canine hepatic disease. The biggest attraction of our research is that our results could potentially be readily implemented or evaluated in a clinical setting owing to our regular management of clinical cases. Currently, we are earnestly working towards resolving various questions and difficulties encountered in veterinary medicine, as well as to identify valuable clues that cannot be simply identified in a clinical setting.

We sincerely hope that by conveying to younger generations about the fun involved in clinical care, their interest in pursuing a future in veterinary clinical science will also significantly increase. Why not immerse yourself in the deep and tempting riddles of veterinary clinical science and find out for yourself?





## Protecting animals and humans from infectious diseases

The microbiology laboratory's goal is to prevent and control infections by revealing the biological character of pathogenic microorganisms at the levels of host animal groups, individuals, their organs, cells and molecules. Focusing on the study of the molecular basis for the ecology and pathogenicity of influenza, pestiviruses, and phleboviruses, in which our laboratory has played the leading role, faculty members and graduate and undergraduate students are constantly working in collaboration with researchers in Japan and overseas. Designated by the World Organization for Animal Health (OIE) as a reference laboratory for avian influenza, supporting diagnoses of avian influenza in countries around the world.

### 1. What is "infectious disease"?

The 1st focus of our research is the pathogenicity of a virus. Molecular mechanism of a fatal disease in animals caused by a highly pathogenic virus infection is studied by comparing the highly pathogenic virus and non-pathogenic virus.

### 2. Species barrier

The 2nd topic of our research is a species barrier for a virus between humans and animals and also between animals and another animals. The host factor(s) which can be the species barrier and the virus factor(s) which is responsible to spill over the species are studied.

### 3. Ecology of viruses

"A life of the virus" is the 3rd topic of our research. Behind the emergences of highly pathogenic viruses, there are several non-pathogenic or less pathogenic viruses in their natural host. We have performed surveillances every year since decades ago.

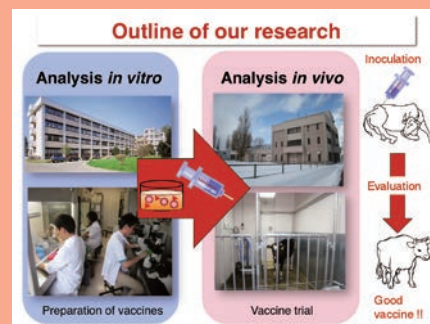
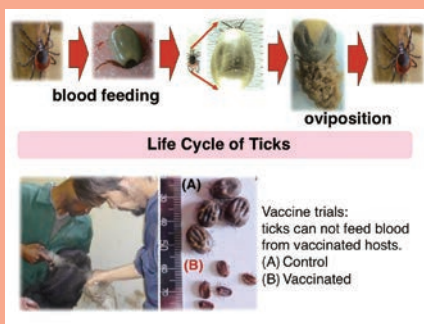


## Survival strategy of pathogens ~ interplay between the pathogens and the hosts ~

Invention of more effective antibiotics and vaccines, and dramatic improvements in sanitation and public health have accelerated the downward trends of many infectious diseases, such as dysentery and cholera, promising that infectious agents can be totally eradicated from the earth. However, many infectious diseases remain among the greatest health problems in the world as microorganisms have developed several strategies to escape from host immune forces and to strike back (i.e. acquired resistance to antibiotics, new virulent factors, and active antigenic shift or mutation). In the veterinary field, although major bacteria and virus infections have been brought under control by effective vaccines and antibiotics, many infectious diseases, which are not successfully controlled, are still present. Since enormous economic losses are caused by those infections on the global scale, establishment of effective preventive measures to control these infections is the most important subject to maintain maximum food production in the restricted spaces we have on the earth.

For these reasons, our research activities are concentrated on systematic analysis of the pathogenesis of infectious agents (including vectors that transmit pathogens) in

domestic animals, and the interplay between the pathogens and the hosts, such as the host immune responses and the immune evasion of the pathogens. Our current research activities are as follows: 1) development of anti-tick vaccine that inhibits blood feeding of tick to prevent tick transmitted diseases, 2) molecular cloning and characterization of bovine and avian immunoinhibitory molecules for future clinical application for the control of chronic infections and tumors.





## Playing with worms and solving riddles

Parasites are organisms that live inside the body or on the body surface of other creatures (also known as hosts) that survive by depriving their hosts of their nutrition. Parasites are found in all animals. There are many types of parasites, and their forms and life cycles remain mysterious. How do parasites infect humans and animals? Which animal species are infected? Which insects and ticks act as parasite vectors? What are the survival mechanisms of parasites inside the host? Why do parasites cause diseases? Are there better ways of detecting parasites? What weaknesses in the parasites can we develop therapeutic agents against? How do parasites evolve? We conduct state-of-the-art research in cooperation with local and international research institutes to investigate these mysteries of parasites.

### Field Parasitology

There are many parasites in the world that differ in every aspect, including shape, habitat, host animal, genetic background. We believe that understanding the differences between parasites is one of the ways to control the parasitic diseases. We

have visited domestic and overseas fields in both Southeast Asia and Africa in our search for diverse parasites. In particular, we have a long-time collaboration with researchers from Myanmar and Zambia.

### Parasite Genomics

Recent progress in genome sequencing technologies has enabled genomic analysis of parasites with large genome sizes. In addition to the analysis of parasites genomes, we conduct genetic analyses of diverse microbes, including viruses and bacteria infecting parasites. We believe that the microbes can provide a key to understanding the survival strategies and evolutionary processes of parasites. This effort can lead to the development of therapeutic and diagnostic tools for parasitic diseases in humans and animals.



## Solving the Riddles of Virus Survival in the Natural World

In recent years, zoonoses have broken out as emerging and re-emerging infectious diseases in many parts of the world. These epidemics are considered to be due to changes in the global environment, such as deforestation and land reclamation, by which the opportunities for humans to encounter pathogen carriers like wildlife and arthropod vectors have increased dramatically.

With the aim of eradication zoonotic viral diseases, we are conducting important research focusing on flavivirus infection and Bunyavirus infection, zoonotic viral diseases that are highly pathogenic to humans.

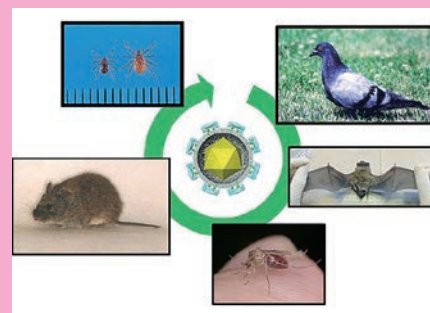
The flaviviruses includes pathogens of many zoonotic diseases, such as Japanese encephalitis, West Nile fever, dengue fever, yellow fever, tick-borne encephalitis, and others, and it causes severe symptoms, such as encephalitis and hemorrhagic fever in humans. One of the main features of flaviviruses is that arthropods such as mosquitoes and ticks play key roles in the transmission of the virus in nature; people and animals become infected with the viruses via the blood-sucking activities of virus-carrying arthropods.

Hantaviruses in the family Bunyaviridae cause hemorrhagic fever with renal syndrome and Hantavirus pulmonary syndrome in humans. Multiple rodent species carry the Hantavirus.

Even in Japan, there is a risk of infection with such viruses, and once infected, it causes severe symptoms and possibly leads to death. Thus, infectious disease control is an important public health challenge.

For the control of zoonotic viral diseases, we have been conducting research related to the following:

1. Elucidation of their ecology and transmission in the nature;
2. Elucidation of the molecular basis of their pathogenicity;
3. Development of diagnosis and prophylaxis methods for them.

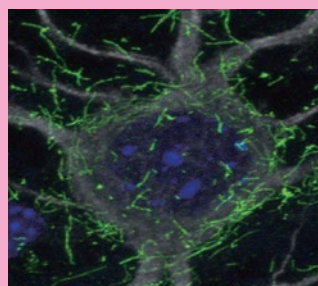
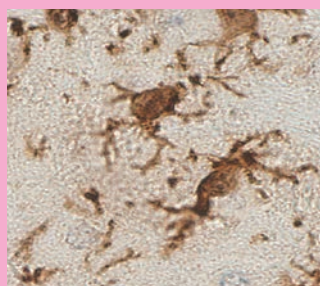
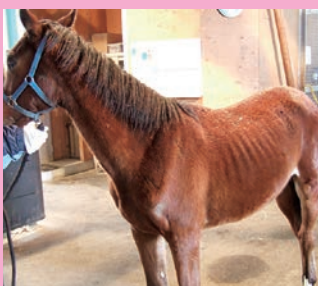


## Control of Infectious Diseases and Exploring the Unknown

One of the missions of veterinary science is to play an important role in countermeasures against continuously emerging infectious diseases. Intrinsic knowledge of characteristics of pathogens, mechanisms of their propagation and transmission, host defence and pathogenesis, are required to overcome problems on infectious diseases. Based on advanced knowledge on infectious diseases, multidirectional activities, such as planning and implementation of countermeasures to prevent further spread and to minimize the damage caused by infection, to develop preventions and treatments and so on, are required to tackle infectious diseases. In the Laboratory of Veterinary Hygiene, we are focusing on elucidation of the neurodegenerative mechanism of prion diseases, which are fatal, intractable neurodegenerative disorders and also known as a zoonosis. To understand a process of neuropathological conditions, including neuronal stress caused by prion propagation, abnormalities of innate immune responses in the brains, and clinical manifestation caused by neurodegeneration, we are conducting diversified researches from the molecular level to animal studies, such as comprehensive gene expression

analysis, primary-cultured system of neurons and glial cells and neuropathological analysis. Moreover, to develop treatments for neurodegenerative disorders including prion diseases, we are attempting to apply regenerative medicine using mesenchymal stem cells and also searching for anti-prion compounds. Furthermore, we are studying epidemiology and transmission mode of food-borne pathogens in humans and neglected infectious diseases in animals, and also attempting to develop diagnostic method. Target animals are broad, ranging from domestic animals to wildlife.

We believe that universities have two missions regarding research, one is promotion of basic research to reveal novel principles by exploring phenomena, and the other is practical research to apply research findings to the development of society. Being aware of this, we consider the balance of the in-depth exploratory research driven by intellectual curiosity and applied research aiming at contribution to society. We are always promoting education and research using both cutting-edge technologies and common techniques, depending on appropriate problem-solving solutions.



## Graduate School of Infectious Diseases

**Graduate School of Infectious Diseases pursues the mission to develop the human resources who has the wide knowledge of infectious diseases, flexible imagination and comprehensive decision making ability to contribute the development of the infectious disease research and education field as well as infectious disease control around the world with practical ability and leadership.**

Researchers who specialize in veterinary medicine, medicine, pharmacy, science, agriculture, information science, belonging to the Faculty of Veterinary Medicine, Research Center for Zoonosis Control, and Faculty of Medicine have a responsible for the research advising to the students in the Graduate School of Infectious Diseases.

### ■ Faculty of Veterinary Medicine

Laboratory of Microbiology  
Laboratory of Infectious Diseases  
Laboratory of Parasitology  
Laboratory of Public Health  
Laboratory of Veterinary Hygiene

### ■ Research Center for Zoonosis Control

Division of Global Epidemiology  
Division of Molecular Pathobiology  
Division of Bioresources  
Division of Collaboration and Education  
Division of Bioinformatics  
Division of Infection and Immunity  
Unit of Risk Analysis and Management  
Laboratory for Biologics Development

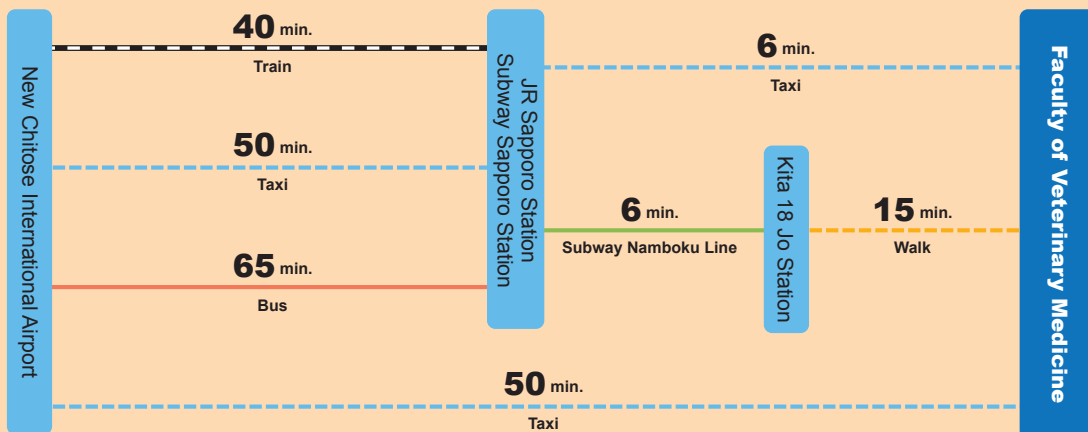
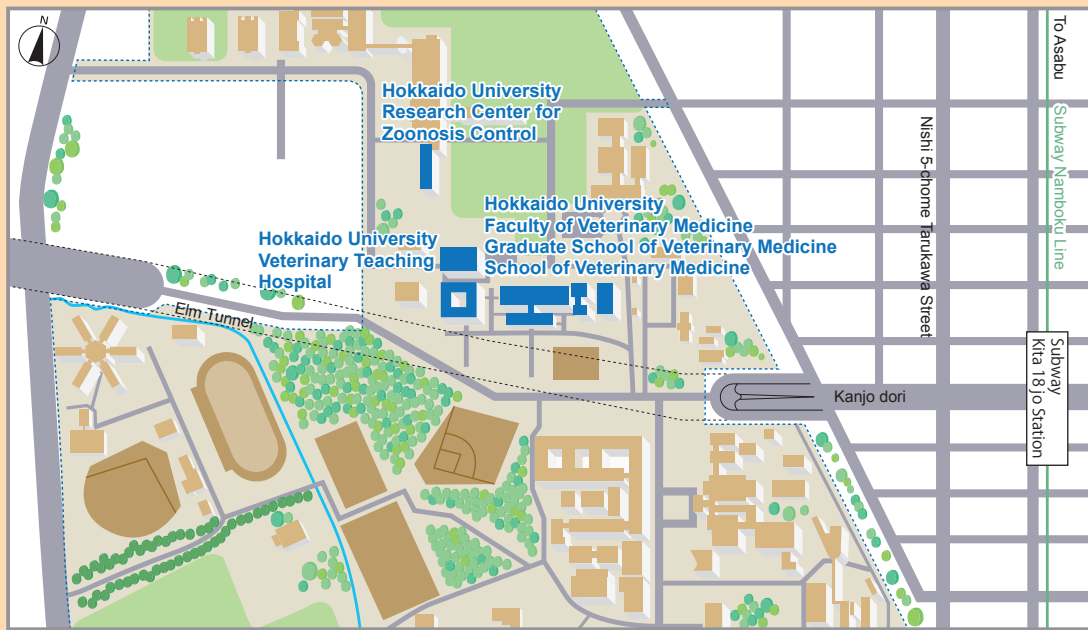
### ■ Faculty of Medicine

Laboratory of Microbiology and  
Infectious Diseases





## Traffic Guide



Sapporo Campus



Faculty of Veterinary Medicine



HOKKAIDO  
UNIVERSITY

**Faculty of Veterinary Medicine,  
Hokkaido University**

Kita 18, Nishi 9, Kita-ku, Sapporo 060-0818 Hokkaido, Japan  
<http://www.vetmed.hokudai.ac.jp/en/>