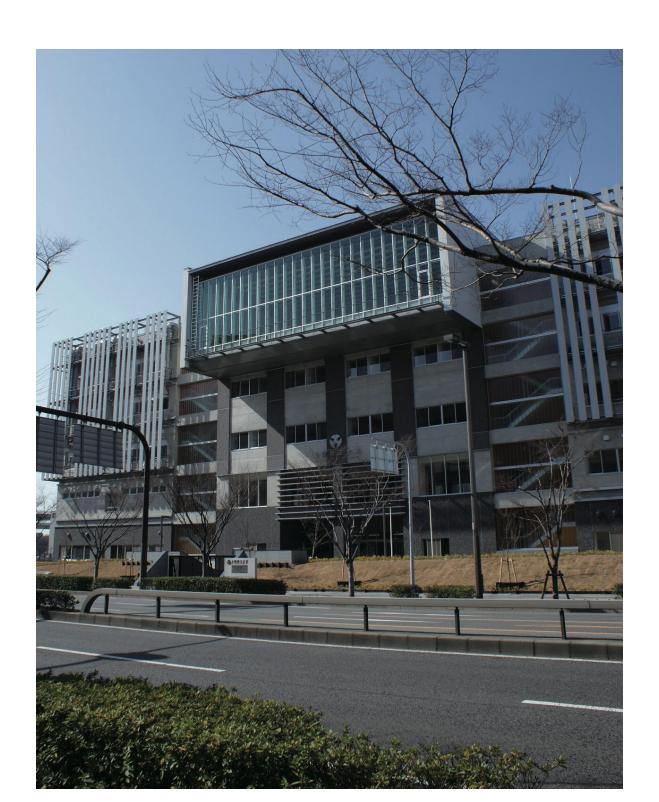
Osaka Metropolitan University Graduate School of Veterinary Science, Department of Veterinary Science, in Rinku Campus (2022-2023)



Welcome

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Osaka Metropolitan University (OMU), the largest public universities in Japan, is a leading advanced research university. Located in southern Osaka. OMU consists of 12 undergraduate schools and 15 graduate schools, distributed across five conveniently-located modern and campuses: Nakamozu, Sugimoto, Abeno, Habikino, and Rinku. OMU also has satellite campuses in the central region of Osaka. At each campus, you can find around ca. 16,000 undergraduate and ca. 3,500 graduate students pursing their academic interests with advanced, cuttingedge facilities under the supervision of ca. 1,400 assigned faculty members.

OMU has been expanding its overseas network, especially in Southeast Asia. As of June, 2020, OPU has relationships with over 300 partner institutions in 64 countries and regions. OMU conducts pioneering research in collaboration with these institutions and promotes student exchange.

OMU actively accepts international students from around the world to promote the internationalization of its education and research. Currently, about 500 international students (not including exchange students) from 37 countries and regions are studying at OMU. More than 100 international exchange students from our overseas partner institutions visit our campus every year.

In April 2009, the OMU School of Veterinary Science (formally Osaka Prefecture University, Division of Veterinary Science) has relocated to our new Rinku Campus on the shore area near the Kansai International Airport. On this new campus, the Veterinary Medical Center and Education and Research Center for Experimental Animal Science have been housed in an education/research building.

With this relocation, undergraduate students in the first year of their veterinary science training who have completed their general subject courses and core courses for their major at the Nakamozu Campus will take their major courses from the second year onwards at the Rinku Campus.

Leading the world in conducting cuttingedge research at the Rinku Campus that is equipped with state-of-the-art facilities, our courses aim to cultivate the next generation of leaders in various areas such as an advanced medical treatment for animals, food safety, communicable diseases between humans and animals, and life science and animal biotechnology research. This is an opportunity to provide an overview of the scientific activities of our departments by this pamphlet.

As you will discover, our research activities span many different disciplines including clinical sciences veterinary medicine and basic sciences, resulting in an impressive number of original publications, which oftentimes stem form our students' doctoral theses (please refer to the list at end of the document).

We are looking forward to your continued support and cooperation.



Dr. Toshiya Okada The Dean of the Graduate School of Veterinary Science



Dr. Masami Miyake The Vice Dean of the Graduate School of Veterinary Science

History

The Osaka Metropolitan University School of Veterinary Science has one of the richest traditions of any veterinary school in Japan, dating back to its inception as a training school for veterinary science (Jyuigaku-Kosyujo) in 1883 in Kita-ku, Osaka city.

In 1888, Osaka-Furitsu-Nogakko was founded and comprised of the Department of Veterinary Science and Department of Agriculture in Sakai-ku, Sakai city. The campus outgrew its space due to facility improvements, and moved to Ikuno-ku, Osaka city in 1890. The new location of the school is commonly known as Katsuyama, which

is a hill known to be one of the historical sites



associated with the Osaka Campaign ("Osaka-no-jin") in the 17th century. The school was named after the hill, as Kachiyama Nogakko.

Kachiyama Nogakko from 1890 to 1925

In 1926, the area around Osaka-Furitsu-Nogakko underwent urbanization and the campus of the school was relocated again to Daisen-cho in Sakai



city. Taking advantage of the relocation to the Daisen school building, a campaign to upgrade the school to a higher education institution was initiated.

Daisen School from 1926 to 1968

In 1949, when universities were established under the new education system, Naniwa-Daigaku was established by the merger of seven technical schools in Osaka, each of which had a different campus. It placed a strong emphasis on "practical learning," thus offering courses in the areas of engineering, agriculture, economics, integrated arts and sciences and social welfare. In 1955, Naniwa Daigaku was renamed as Osaka Prefecture University (OPU). In the 1960s, departments which were dispersed on different campuses were unified to the Nakamozu Campus and thus, formed the basic system on which the current Nakamozu Campus developed.

Meanwhile, the master's course in Veterinary Science at the Graduate School of Agriculture, Osaka Prefecture University, was established in 1955, and the doctoral course was established in 1964, further developing the department into a well-developed veterinary school. In 1977, the Veterinary Medical Act was amended to make it possible to qualify for the National Veterinary Medical Examination after six years of study and a new four-year doctoral course was opened.



Nakamozu Campus (the main campus) from 1969

In 2009, the Department and Division of Veterinary Science, and the Veterinary Medical Center relocated to our new Rinku Campus near the Kansai International Airport.

In 2022, OPU has been integrated with another public university, "Osaka City University" to form the Osaka Metropolitan University, OMU. This unite led the Department to be reorganized as the "School of Veterinary Science".



Rinku Campus from 2009

Organization

Veterinary science, a comprehensive science focused on animal treatment, tackles various issues deeply related to the health and safety of animals and humans and the welfare of the local society: (1) the enhancement of animal treatment, (2) the threat of zoonoses due to the increase in the international movement of people and animals and also distribution of livestock products, (3) the improvement of livestock production efficiency using biotechnology, (4) the development of new medicine, and (5) the safety evaluation of foods and pharmaceuticals.

The School of Veterinary Science aims to develop (1) specialists in veterinary learning, view, and technique who are capable of integrating specialized knowledge and technique in the domain of applied animal science, (2) specialists capable of contributing to the diagnosis and treatment of animals and public hygiene, and (3) international specialists capable of exhibiting innovative leadership in biomedical fields related to both animals and humans.

Since April 2009, the former "Division of Veterinary Science" has moved to our new Rinku Campus located on the shore area near Kansai International Airport. On this new campus, the

Veterinary Medical Center and Education and Research Center for Experimental Animal Science have been housed in an education/research building under the department.

Even after the reorganization as the "School of Veterinary Science", the school is carrying out improved faculty development programs at the new facilities, which are equipped with the latest educational and research equipment.

In 2022, Osaka Prefecture University and Osaka City University was integrated, and the "Division of Veterinary Science" and the "Graduate School of Life and Environmental Sciences" now became the "Department of Veterinary Science" and the "Graduate School of Veterinary Science". Since the integrated university has increased numbers of Graduate Schools such as Graduate School of Medicine and others, our educational environments are very comprehensive, and you may interact with scientists with diverse academic background. We hope this environment will bring you active research motivation and fruitful research outcome, looking forward to sharing scientific joys and growth through the campus life.

Organization Chart of Graduate School of Veterinary Science

Department of Veterinary Science

Structural and Functional Biosciences

Integrated Structural Biosciences
Integrated Functional Biosciences

Veterinary Environmental Sciences

Bioenvironmental Sciences Infectious Diseases Control

Veterinary Clinical Sciences

Advanced Pathobiology
Advanced Clinical Medicine

Integrated Structural Biosciences

Laboratory of Veterinary Anatomy

Research Interest (K. Ogawa):

One major research interest of **K. Ogawa** is properties of macrophages regulated by their niche. Macrophages derived from embryonic precursors can proliferate under a suitable niche and organ-specific niches characterize properties of tissue-resident macrophages. Recently **K. Ogawa** developed a simple propagation method for tissue-resident macrophages by mixed culture with niche-forming cells, and has examined organ-specific niche dependent properties in several tissue-resident macrophages. Another research interest of **K. Ogawa** is regulations of tissue organization by Eph receptors and ephrin ligands in adult organs. Various biological functions have been attributed to these proteins in various tissues/organs during development but largely not in the adult.

Keywords: macrophage, niche, Eph, tissue organization

Publications:

- 1. J. Alam, **K. Ogawa** Expression and localisation of ephrin-B1 and EphB4 in steroidogenic cells in the naturally cycling mouse ovary. *Reprod Biol*, 20:100511, 2021 doi:10.1016/j.repbio.2021.100511
- M. Tsurutani, H. Horie, K. Ogawa Cell properties of lung tissue-resident macrophages propagated by coculture with lung fibroblastic cells from C57BL/6 and BALB/c mice. *Biomedicines*, 9(9):1241, 2021 doi: 10.3390/biomedicines9091241
- **3. K. Ogawa**, M. Tsurutani, A. Hashimoto, M. Soeda Simple propagation method for resident macrophages by co-culture and subculture, and their isolation form various organs. *BMC Immunol*, 20(1):34, 2019 doi: 10.1186/s12865-019-0314-z.

Research Interest (T. Nakajima):

T. Nakajima studies the molecular and biochemical mechanisms in the ischemic brain using a rat model of global cerebral ischemia, induced by occlusion of the common carotid and vertebral arteries. The rat model of global cerebral ischemia has been widely used for studying the pathophysiology of the hypoxic-ischemic encephalopathy induced by circulatory arrest. At present, there is no useful pharmacological therapy for hypoxic-ischemic encephalopathy. Our research is a fundamental study for exploring a novel therapy for attenuating the post-cardiac arrest brain injury.

Keywords:

Brain ischemia, Neuronal cell death

Publications:

1. **T. Nakajima**, Y. Kunieda, Y. Takahashi, Y. Tanaka, T. Kondo, S. Takenaka. Changes in Smad1/5/9 expression and phosphorylation in astrocytes of the rat hippocampus after transient global cerebral ischemia. **J Chem Neuroanat.** 2021. Apr;113:101941. doi: 10.

Professor Kazu Associate Professor Takas Lecturer Takas

Kazushige Ogawa Takayuki Nakajima Takashi Tanida

1016 /j.jchemneu. 2021. 101941. Epub 2021 Mar 9.

- 2. **T. Nakajima**, R. Hata, Y. Kunieda, T. Kondo. Distribution of Smad mRNA and proteins in the rat brain. **J Chem Neuroanat**. 2018. 90:11-39.
- 3. **T. Nakajima**, R. Hata, T. Kondo, S. Takenaka. Proteomic analysis of the hippocampus in naïve and ischemic-preconditioned rat. **J. Neurol. Sci.**, 358: 158-171, 2015.
- 4. **T. Nakajima**, M. Yanagihara and H. Nishii. Temporal and regional patterns of Smad activation in the rat hippocampus following global ischemia. **J. Neurol. Sci.**, 337: 25-37, 2014.
- T. Nakajima, S. Ochi, C. Oda, M. Ishii and K. Ogawa. Ischemic preconditioning attenuates of ischemiainduced degradation of spectrin and tau: implications for ischemic tolerance. Neurol. Sci., 32:229-239, 2011.

Research Interest (T. Tanida):

Nuclear receptors (NRs) play key roles in endocrine and metabolic systems to maintain homeostasis. **T. Tanida** investigates the transcriptional control through estrogen-related receptors (ERRs), the first orphan NRs to be identified, and their coregulators including LRPGC1. Visualization of these factors with fluorescent protein labelling revealed their unique transregulation mechanisms in association with their subcellular/subnuclear dynamics within living cells. This research will also provide new insights into pathophysiology of various endocrine and metabolic disorders including hormone-related cancers and obesity.

Keywords: estrogen-related receptors (ERRs), endocrinology, live-cell imaging, metabolism, transcription

- 1. **T. Tanida**. Molecular dynamics of estrogen-related receptors and their regulatory proteins: roles in transcriptional control for endocrine and metabolic signaling. *Anat Sci Int*. 97(1):15–29, 2022
- 2. **T. Tanida**, *et al.* Subcellular dynamics of estrogenrelated receptors involved in transrepression through interactions with scaffold attachment factor B1. *Histochem Cell Biol.* 156(3):239–251, 2021
- 3. **T. Tanida**, *et al.* Novel metabolic system for lactic acid via LRPGC1/ERRγ signaling pathway. *FASEB J*. 34(10):13239–13256, 2020
- 4. **T. Tanida,** *et al.* Immunohistochemical profiling of estrogen-related receptor gamma in rat brain and colocalization with estrogen receptor alpha in the preoptic area. *Brain Res.* 1659:71–80, 2017
- 5. **T. Tanida**, *et al*. Estrogen-related receptor β reduces the subnuclear mobility of estrogen receptor α and suppresses estrogen-dependent cellular function. *J Biol Chem*. 290(19):12332–12345, 2015

Laboratory of Veterinary Pathology

Professor Associate Professor Assistant Professor Mitsuru Kuwamura Takeshi Izawa Miyuu Tanaka

Research Interest

Common project: Diagnostic pathology for companion, zoo and laboratory animals.

M. Kuwamura studies rat and mouse mutants with neurological disorders pathologically. He is also interested in comparative pathological aspects of diseases in companion, domestic and laboratory animals.

T. Izawa studies on the pathogenesis of liver diseases such as nonalcoholic fatty liver disease (NAFLD), drug-induced liver injury (DILI), and liver cirrhosis and cancer, by molecular pathological approaches (i.e. laser microdissection, microarray, RNA-seq) using rodent models.

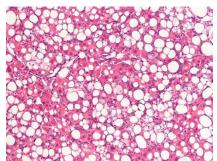
M. Tanaka studies on the pathomechanism of neurodegenerative diseases such as neuroaxonal dystrophy and myelin diseases using animal disease models by neuropathological and genetic analyses.

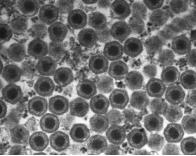
Keywords:

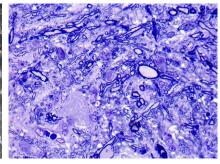
Animal models, Hepatotoxicity, Immune reaction, Iron disorder, Liver cirrhosis, Metabolic syndrome, Myelinogenesis, Neurodegenerative disease, Transcriptome

- Hassan MM, Konishi S, Tanaka M, Izawa T, Yamate J. Kuwamura M. Expression o CCDC85C, a causative protein for hydrocephalus, and intermediate filament proteins during ventricle development in rats. Exp Anim (in prerss)
- Inai Y, Izawa T, Mori M, Atarashi M, Tsuchiya S, Kuwamura M, Yamate J. Analyses of hemorrhagic diathesis in high-iron diet-fed rats. J Toxicol Pathol 34:33–41, 2021.
- 3. Konishi S, Tanaka N, Mashimo T, Yamamoto T, Sakuma T, Kaneko T, **Tanaka M**, **Izawa T**, Yamate J, **Kuwamura M**. Pathological characteristics of Ccdc85c knockout rats: a rat model of genetic hydrocephalus. Exp Anim 69:26-33, 2020.
- 4. Kuwamura M, Tanimura S, Hasegawa Y, Hoshiai R, Moriyama Y, Tanaka M, Takenaka S, Nagayoshi H, Izawa T, Yamate J, Kuramoto T, Serikawa T. Downregulation of aspartoacylase during the progression of myelin breakdown in the dmy mutant rat with mitochondrial magnesium channel MRS2 defect. Brain Res 1718:169-175, 2019.
- Ioannidis M*, Tanaka M*, Yasui S, Kezuka C, Oyamada M, Hasegawa T, Izawa T, Yamate J, Kuwamura M. Late onset of cerebellar cortical degeneration in a Magellanic penguin (Spheniscus magellanicus). J Vet Med Sci. 81:750-752, 2019. (*equally contributed)
- Mori M, Izawa T, Sasaki H, Sonoyama J, Nishimura S, Shimamura S, Shimada T, Hasegawa T, Kuwamura M, Yamate J. A case of feline T-cell lymphoma with tropism for striated muscle and peripheral nerve. J Comp Pathol 168:8-12, 2019.
- 7. Tanaka M, Kuramochi M, Nakanishi S, Kuwamura M,

- Kuramoto T. 2018. Rat polyomavirus 2 infection in a colony of X-linked severe combined immunodeficiency rats in Japan. J Vet Med Sci. 80:1400-1406, 2018.
- Atarashi M, Izawa T, Mori M, Inai Y, Kuwamura M, Yamate J. Dietary iron overload abrogates chemically-induced liver cirrhosis in rats. Nutrients 10:1400, 2018.
- Atarashi M, Izawa T, Miyagi R, Ohji S, Hashimoto A, Kuwamura M, Yamate J. Dietary iron supplementation alters hepatic inflammation in a rat model of nonalcoholic steatohepatitis. Nutrients 10:175, 2018.
- Rahman N, Pervin M, Kuramochi M, Karim MR, Izawa T, Kuwamura M, Yamate J. M1-/M2-macrophage polarizationbased hepatotoxicity in D-galactosamine-induced acute liver injury in rats. Toxicol Pathol 46:764-776, 2018.
- Tanaka N, Izawa T, Takenaka S, Akiyoshi H, Yamate J, Kuwamura M. Expression of Ccdc85C, a causative protein for murine hydrocephalus, in the mammary gland tumors of dogs. Histol Histopathol 32:397-403, 2017.
- Tanaka M, Yamaguchi S, Akiyoshi H, Tsuboi M, Uchida K, Izawa T, Yamate J, Kuwamura M. Ultrastructural features of canine neuroaxonal dystrophy in a Papillon dog. J Vet Med Sci. 9:1927-1930, 2017.
- Shimotsuma Y, Tanaka M, Izawa T, Yamate J, Kuwamura M. Enhanced expression of Trib3 during the development of myelin breakdown in dmy myelin mutant rats. PLoS One 11: e0168250, 2016.







Professor Lecturer Toshiya Okada Tomohiro Kondo

Research Interest:

- **T. Okada** and **T. Kondo** research work focuses on the development, improvement and biological differences of laboratory animals. The present major studies are:
- (1) Developmental studies of laboratory animals during perinatal period.
- (2) Effects of environmental factors on the development of laboratory animals.
- (3) Development and improvement of animal models for human diseases.
- (4) Studies on the species and strain differences in laboratory animals.
- (5) Genetic analysis in laboratory animals.

Keywords:

Behavioral Analysis, Cataract, Cerebral Ischemia, Environmental Enrichment, Fetal Growth Restriction, Genetic Analysis, Intrauterine Growth Retardation, Renal Development

Publications:

- Nakajima T, Kunieda Y, Takahashi Y, Tanaka Y, Kondo T, Takenaka S. Changes in Smad1/5/9 expression and phosphorylation in astrocytes of the rat hippocampus after transient global cerebral ischemia. J. Chem. Neuroanat., 113:101941, 2021.
- Nishiyama K, Aono K, Fujimoto Y, Kuwamura M, Okada T, Tokumoto H, Izawa T, Okano R, Nakajima H, Takeuchi T, Azuma YT. Chronic kidney disease after 5/6 nephrectomy disturbs the intestinal microbiota and alters intestinal motility. J Cell Physiol., 234(5): 6667-6678, 2019.
- 3. **Kondo T**, Yoshida S, Nagai H, Takeshita A, Mino M, Morioka H, Nakajima T, Kusakabe KT, **Okada T**. Transient forebrain ischemia induces impairment in cognitive performance prior to extensive neuronal cell death in Mongolian gerbil (Meriones unguiculatus). J Vet Sci., 19(4): 505-511, 2018.

- 4. Kuniyoshi N, Yoshida Y, Itoh Y, Yokota SI, Kuraishi T, Hattori S, **Kondo T**, Yoshizawa M, Kai C, Kiso Y, Kusakabe KT. Morphological analyses of the retinal photoreceptor cells in the nocturnally adapted owl monkeys. J Vet Med Sci., 72(2): 203-9, 2018.
- 5. Nakajima T, Hata R, Kunieda Y, **Kondo T**. Distribution of Smad mRNA and proteins in the rat brain. J Chem Neuroanat., 90: 11-39, 2018.
- Nakamura J, Shimomoto T, Collins LB, Holley DW, Zhang Z, Barbee JM, Sharma V, Tian X, Kondo T, Uchida K, Yi X, Perkins DO, Willis MS, Gold A, Bultman SJ. Evidence that endogenous formaldehyde produces immunogenic and atherogenic adduct epitopes. Sci Rep., 7(1):10787, 2017.
- Kondo T, Nakamori T, Nagai H, Takeshita A, Kusakabe KT, and Okada T. A novel spontaneous mutation of BCAR3 results in extrusion cataracts in CF#1 mous strain. Mamm Genome, 27(9-10): 451-459, 2016.
- 8. Yuasa K, **Kondo T**, Nagai H, Mino M, Takeshita A, **Okada T**. Maternal protein restriction that does not have an influence on the birth weight of the offspring induces morphological changes in kidneys reminiscent of phenotypes exhibited by intrauterine growth retardation rats. Congenit Anom., 56(2): 79-85, 2016.
- Kondo T, Kitano-Amahori Y, Nagai H, Mino M, Takeshita A, Kusakabe KT, Okada T. Effects of maternal subtotal nephrectomy on the development of the fetal kidney: A morphometric study. Congenit Anom., 55(4): 178-182, 2015.
- Nakajima T, Hata R, Kondo T, Takenaka S. Proteomic analysis of the hippocampus in naïve and ischemicpreconditioned rat. J Neurol Sci., 358(1-2):158-171, 2015.
- 11. **Kondo T**, Nagai N, Kawashima T, Taniguchi Y, Koyabu N, Takeshita A, Kusakabe KT, **Okada T**. Hereditary and histological characteristics of a new cataract mouse model originating from CF#1 strain (CF#1/b cac). Comp Med., 64(5): 360-368, 2014.

Morioka cataract (MCT) mouse



a new cataract mouse model originated in the ddY strain

Enrichment material





left: plastic igloo and plastic crawl ball, right: paper house

Integrated Functional Biosciences

Laboratory of Integrative Physiology

Professor Associate Professor Mitsuaki Moriyama Katsura Takano

Research Interest:

In the central nervous system, there are three kinds of glial cells other than neurons: astrocytes, oligodendrocytes, and microglia. They play various important roles in both pathological and physiological conditions. Goal of our research is to elucidate the glial regulation mechanism of inter- and intra-cellular signaling using cultured cells as basic experimental systems, with biochemical, immunological, morphological techniques, and so on.

Various glial functions; eg. the productions of NO, cytokines and neurotrophic factors and phagocytosing activity, are closely related on the pathomechanisms of neurodegeneration; such as, Alzheimer disease, Parkinson disease, prion disease, traumatic brain injury, and brain ischemia. We have examined the effects of many substances on the glial function and found various interesting results; recent outcomes are; the effects of zinc, insulin, amphotericin B, amyloid β , acetate, and so on (see publication list).

We have also focused on the glial enzymatic activities such as type 2 transglutaminase and superoxide dismutase of extracellular type.

We believe that the elucidation of the mechanism of glial regulation shall lead a basic construction of therapeutics of various neurodegenerative diseases above mentioned.

Keywords:

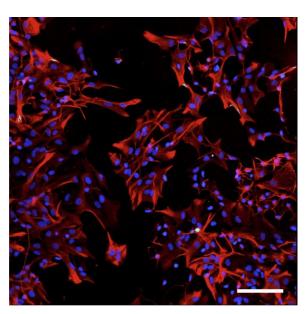
Astrocytes, Microglia, Neurodegenerative diseases, Saturated fatty acid, Traumatic brain injury, Transglutaminase, Extracellular superoxide dismutase, Phagocytosis

Publications:

- 1. Minamihata T, **Takano K**, Nakamura Y, Seto R, **Moriyama M.** Increase in cellular lysophosphatidylserine content exacerbates inflammatory responses in LPS-activated microglia. *Neurochem. Res.*, in press.
- 2. Moriyama M, Nishimura Y, Kurebayashi R, Minamihata T, Kawabe K, Takano K, Nakamura Y. Acetate suppresses lipopolysaccharide-stimulated nitric oxide production in primary rat microglia but not in BV-2 microglia cells. *Curr. Mol. Pharmacol.*, 14: 253-260 (2021)
- Saheki T. Moriyama M, Funahashi A, Kuroda E. AGC2 (Citrin) deficiency-From recognition of the disease till construction of therapeutic procedures. *Biomolecules*. 10 (8) E1100. (2020)
- Minamihata T, Moriyama M, Takano K, Nakamura Y. Lysophosphatidylinositol, an endogenous ligand for G proteincoupled receptor 55, has anti-inflammatory effects in cultured microglia. *Inflammation* 43: 1971-1987 (2020)
- Saheki T, Moriyama M, Kuroda E, Funahashi A, Yasuda I, Setogawa Y, Gao Q, Ushikai M, Furuie S, Yamamura KI, Takano K, Nakamura Y, Eto K, Kadowaki T, Sinasac DS,

- Furukawa T, Horiuchi M, Tai YH. Pivotal role of inter-organ aspartate metabolism for the treatment of citrin deficiency, based on the mouse model. *Sci. Rep.*, 9: 4179 (2019)
- 6. Takano K, Koarashi K, Kawabe K, Itakura M, Nakajima H, Moriyama M, Nakamura Y. Insulin expression in cultured astrocytes and the decrease by amyloid β. *Neurochem. Int.*, 119: 171-177 (2018)
- **7. Takano K,** Ishida N, Kawabe K, **Moriyama M,** Hibino S, Choshi T, Hori O, Nakamura Y. A dibenzoylmethane derivative inhibits lipopolysaccharide-induced NO production in mouse microglial cell line BV-2. *Neurochem. Int.*, 119: 126-131 (2018)
- Nishimura Y, Moriyama M, Kawabe K, Satoh H, Takano K, Nakamura Y. Lauric acid alleviates neuroinflammatory responses by activated microglia: involvement of the GPR40dependent pathway. *Neurochem. Res.*, 43: 1723-1735 (2018)
- **9. Moriyama M,** Hashimoto A, Satoh H, Kawabe K, Ogawa M, **Takano K,** Nakamura Y. *S*-Equol, a major isoflavone from soybean, inhibits nitric oxide production in lipopolysaccharidestimulated rat astrocytes partially via the GPR30-mediated pathway. *Int. J. Inflam.*, 8496973 (2018)
- **10. Moriyama M,** Fujitsuka S, Kawabe K, **Takano K,** Nakamura Y. Zinc potentiates lipopolysaccharide-induced nitric oxide production in cultured primary rat astrocytes. *Neurochem. Res.*, 43: 363-374 (2018).
- 11. Takano K, Ogawa M, Kawabe K, Moriyama M, Nakamura Y. Inhibition of gap junction elevates glutamate uptake in cultured astrocytes. *Neurochem. Res.*, 43: 50-56 (2018).
- 12. Kawabe K, **Takano K, Moriyama M,** Nakamura Y. Microglia endocytose amyloid β through the binding of transglutaminase 2 and milk fat globule EGF Factor 8 protein. *Neurochem. Res.*, 43: 32-40 (2018).

Our cultured astrocytes: GFAP immunostaining with DAPI

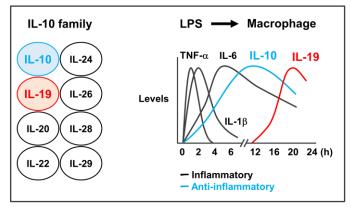


Professor Yasu-Taka Azuma

Associate Professor Hidemitsu Nakajima Office@Nakamozu C.

Azuma Y.T.

I am particularly interested in understanding the function of interleukin-19 (see Figure) on inflammatory bowel disease, mucosal immunology, inflammation (skin, lung, liver, pancreas, colon, kidney), and fibrosis, and systems-level regulatory networks in basic T cell and macrophage biology. I apply interdisciplinary strategies by integrating pharmacological, pathological, immunological and genetic approaches.



Please see the following articles published over the past ten years for additional information:

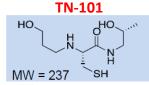
- ➤ <u>Azuma YT</u>, et al. (2021) IL-19 contributes to the development of nonalcoholic steatohepatitis by altering lipid metabolism. **Cells.** 10(12), 3513.
- ➤ Fujimoto Y, Kuwamura M, <u>Azuma YT</u>. (2020) Deficiency of interleukin-19 exacerbates lipopolysaccharide/D-galactosamine-induced acute liver failure. **J. Vet. Med. Sci.** 82(10):1450-1455.
- ➤ Azuma YT, Nishiyama K. (2020) Interleukin-19 enhances cytokine production induced by lipopolysaccharide and inhibits cytokine production induced by polyI:C in BALB/c mice. J. Vet. Med. Sci. 82(7):891-896.
- Fujimoto Y, <u>Azuma YT</u>, et al. (2018) The Role of Interleukin-19 in contact hypersensitivity. **Biol.** Pharma. Bull. 41(2), 182-189.
- Fujimoto Y, Azuma YT, et al. (2017) Exacerbated experimental pancreatitis in interleukin-19 knockout mice. Glob. Drugs Therap. 2(5), 1-5.
- ➤ Fujimoto Y, <u>Azuma YT</u>, et al. (2017) Interleukin-19 contributes as a protective factor in experimental Th2-mediated colitis. **Naunyn Schmiedebergs Arch. Pharmacol.** 390(3), 261-268.
- Matsuo Y, Azuma YT, et al. (2015) Interleukin 19 reduces inflammation in chemically induced experimental colitis. **Int. Immunopharmacol.** 29(2), 468-475.

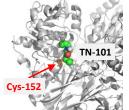
➤ <u>Azuma YT</u>, et al. (2011) IL-19 as a potential therapeutic in autoimmune and inflammatory diseases. **Curr. Pharm. Des.** 17(34), 3776-3780.

Nakajima H.

Major goal is to elucidate molecular mechanisms underlying neuronal dysfunction elicited by a multifunctional protein GAPDH, which has been first identified in brain disorders. **H. Nakajima** has discovered a novel inhibitor of GAPDH aggregation with some PCT-patents as described below. These projects are going up with techniques of molecular biology, cell biology and GAPDH-mutant-genetically-modified animals established by our labs using cutting-edge genome edition procedures.

Novel GAPDH aggregation inhibitor





- Novel compound
- IC50 = $0.90 \pm 0.11 \,\mu\text{M}$ (**vs GAI-17)
- Amphiphile: cLogP = -1.25
- Ideal M.W. for CNS drugs
 Wide profit margin

PCT/JP2016/066999

Novelty: approved Inventive step:approved Susceptible of industrial application:approved

Selected Publications:

- * Nakajima H,. et al. (2017) GAPDH aggregation causes mitochondrial dysfunction during oxidative stress-induced cell death. J. Biol. Chem. 292(11), 4727-4742
- * Kubo T, <u>Nakajima H</u>, et al. (2016) Active site cysteine-null GAPDH rescues nitric oxide-induced cell death. **Nitric Oxide**. 53, 13-21.
- * Itakura M, <u>Nakajima H</u>, et al. (2015) GAPDH aggregation inhibitor peptide: A potential therapeutic strategy against oxidative stress-induced cell death. **Biochem Biophys Res Commun.** 467(2):373-376
- * Itakura M, Nakajima H, et al. (2015) GAPDH aggregates accelerate amyloid- β amyloidogenesis in Alzheimer disease. **J. Biol. Chem**. 290(43), 26072-26087.
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Laboratory of Cellular and Molecular Biology

Research Interest:

Katahira: Transport of macromolecules, such as RNAs and proteins, between the nucleus and the cytoplasm is fundamental for eukaryotic gene expression. Different classes of the "cargo" molecules are transported by dedicated "transport receptors" through the nuclear pore complexes. I am currently interested in elucidating the molecular mechanism of mRNA nuclear export in mammals, with special emphasis on 1) the link between nuclear export and transcription/processing of mRNA, 2) the functions of tissue specific mRNA transport receptors. To achieve these goals, various modern molecular technologies, including biological next-generation sequencing and CRISPR/Cas9-mediated genome editing etc., are employed.

Keywords:

nucleo-cytoplasmic transport, Tap/NXF family proteins, TRanscription-EXport (TREX) complex

Publications:

- **1. Katahira, J.**, Ishikawa, H., Tsujimura, K., Kurono, S., Hieda, M. Human THO coordinates transcription termination and subsequent transcript release from the HSP70 locus. *Genes to Cells*, 24: 272-283, 2019.
- **2. Katahira, J.,** Senokuchi, K., Hieda, M. Human THO maintains stability of repetitive DNA. *Genes to Cells*, 25: 334-342, 2020.
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Associate Professor
Associate Professor

Jun Katahira Misako Matsubara

Matsubara: Liver is a large vital organ involved in metabolism, immunity and detoxification in mammals. Disruption of cell-cell interactions between parenchymal hepatocytes and non-parenchymal cells (hepatic stellate cells, liver sinusoidal endothelial cells and Kupffer cells, etc.) is involved in the progression of fibrosis that threatens the patients' quality of life. In order to clarify the pathophysiology of liver fibrosis, my research subjects are as follows. 1) Understand the mechanism of structural and functional interaction between hepatocytes and those non-parenchymal cells, 2) Establish new anti-fibrosis therapies by targeting key molecules involved in chronic liver failure.

Keywords:

Fibrosis, liver cells, cell-cell interaction, metabolism, antifibrotic therapy

- 1. Dat, NQ., Thuy, LTT., **Misako, Sato-Matsubara.**, *et al.* 6His-tagged Recombinant human cytoglobin deactivates hepatic stellate cells and inhibits liver fibrosis by scavenging reactive oxygen species. *Hepatology*, 73:2527-2545, 2021.
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Bioenvironmental Sciences

Laboratory of Toxicology

Associate Professor Kazuhiko Nishimura Assistant Professor Hiroshi Nakagawa

Research Interest:

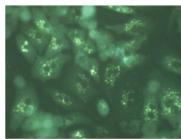
K. Nishimura: Erythropoiesis is indispensable to recovery of the anemia. However, the mechanism of erythropoiesis has many questions. I study the mechanism of erythropoietin production and the search of the substance which promotes erythropoietin production.

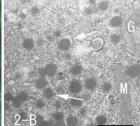
It is reported that the erythropoietin participates in mechanism of cell protection. I study the interaction of erythropoietin production and autophagy induction as the cell protective function.

H. Nakagawa: Newly synthesized proteins are transported from ER to Golgi apparatus through the COPII transport vesicles. The failure of COPII vesicle formation causes the ER stress and then leads to ER stress-induced apoptosis. I study the mechanism of the COPII vesicle transport.

Keywords:

Autophagy, Endoplasmic reticulum stress, Vesicular transport, Programmed cell death, G protein, Apoptosis, Microflora, Anemia and Erythropoiesis





Autophagy

- 1. K. Nishimura, S. Iitaka, H. Nakagawa. Effect of trivalent chromium on erythropoietin production and the prevention of insulin resistance in HepG2 cells. Arch Biochem Biophys, 708, 108960, 2021.
- **2. H. Nakagawa,** M. Komori, **K. Nishimura**. Carbon tetrachloride suppresses ER-Golgi transport by inhibiting COPII vesicle formation on the ER membrane in the RLC-16 hepatocyte cell line. **Cell Biol Int**, 45(3), 633-641, 2020.
- 3. K. Nishimura, H. Katsuyama, M. Ohishi, A. Hirabayashi, K. Matsuda, H. Nakagawa. Effects of sorbitol and lactate on erythropoietin production in HepG2 cells. Effects of sorbitol and lactate on erythropoietin production in HepG2 cells. Biochem Biophys Res Commun, 523(1), 54-59, 2020.
- **4. K. Nishimura**, K. Goto, **H. Nakagawa**. Effect of erythropoietin production induced by hypoxia on autophagy in HepG2 cells. **Biochem Biophys Res**Commun. 495(1) 1317-1321 2018

- K. Nishimura, R. Matsumoto, Y. Yonezawa, H. Nakagawa. Effect of quercetin on cell protection via erythropoietin and cell injury of HepG2 cells. Arch Biochem Biophys, 636, 11-16, 2017
- 6. H. Nakagawa, K. Hazama, K. Ishida, M. Komori, K. Nishimura, S. Matsuo. Inhibition of PLD1 activity causes ER stress via regulation of COPII vesicle formation. Biochem Biophys Res Commun. 490(3), 895-900, 2017
- T. Bessho, T. Okada, C. Kimura, T. Shinohara, A. Tomiyama, A. Imamura, M. Kuwamura, K. Nishimura, K. Fujimori, S. Shuto, O. Ishibashi, BK. Kubata, T. Inui. Novel Characteristics of Trypanosoma brucei Guanosine 5'-monophosphate Reductase Distinct from Host Animals. PLoS Negl. Trop. Dis., 10, e0004339. doi: 10.1371/journal.pntd.0004339, 2016
- 8. K. Murakami, **H. Nakagawa**, **K. Nishimura**, Matsuo S. Changes in peptidergic fiber density in the synovium of mice with collagenase-induced acute arthritis. **Can J Physiol Pharmacol**, 93(6), 435-441, 2015
- N. Iwasaki, Y. Sugiyama, S. Miyazaki, H. Nakagawa, K. Nishimura, S. Matsuo. An ATF4-Signal-Modulating Machine Other Than GADD34 Acts in ATF4-to-CHOP Signaling to Block CHOP Expression in ER-Stress-Related Autophagy. J Cell Biochem, 116(7), 1300-1309, 2015
- A. Hinenoya, K. Shima, M. Asakura, K. Nishimura, T. Tsukamoto, T. Ooka, T. Hayashi, T. Ramamurthy, SM Faruque, S. Yamasaki. Molecular characterization of cytolethal distending toxin gene-positive *Escherichia coli* from healthy cattle and swine in Nara, Japan. BMC Microbiol, 14:97 doi: 10.1186/1471-2180-14-97, 2014
- **11. K. Nishimura**, K. Tokida, H. Katsuyama **H. Nakagawa**, S. Matsuo. The effect of hemin-induced oxidative stress on erythropoietin production in HepG2 cells. **Cell Biol Int**, 38, 1321-1329, 2014
- **12. K. Nishimura**, H. Katsuyama, **H. Nakagawa**, S. Matsuo. Stimulating Effect of Ethanol on Erythropoietin Production in the Liver Cells. **J. Metab Synd**, 3, 164 doi: 10.4172/2167-0943.1000164, 2014

Laboratory of Veterinary Public Health

Professor Associate Professor Associate Professor Masami Miyake Takeshi Matsuzawa Mayo Yasugi

Research Interest:

The research projects in the laboratory deal with the pathogenic bacteria and viruses, such as diarrhogenic *Escherichia coli*, *Clostridium perfringens*, *Salmonella*, *Listeria*, rabies virus, and SARS-CoV-2 that cause foodborne diseases and zoonoses. The projects are directed toward understanding the molecular mechanism and epidemiology of 1) how these pathogens respond to the surroundings to exert their virulence, 2) how they induce pathological alterations in host cells, 3) how the host cells respond at molecular and cellular levels defending themselves against the pathogens' attack, and 4) how the pathogenic and potentially life-threatening pathogens

disseminate among environments and human society. Microbiological, biochemical, immunological, and genetic procedures, as well as cell biology techniques, are employed to visualize the molecular events in the course of host-parasite interactions.

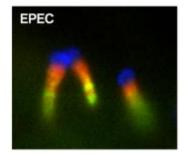
Keywords:

Escherichia coli, Clostridia, Salmonella, Listeria, stress response, inflammation, autophagy, zenophagy, sporulation, germination, virulence factors, toxins, high through-put screen, antimicrobial resistance, rabies, COVID-19

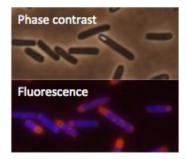
Publications:

- Wakabayashi Y, Takemoto K, Iwasaki S, Yajima T, Kido A, Yamauchi A, Kuroiwa K, Kumai Y, Yoshihara S, Tokumoto H, Kawatsu K, Yasugi M, Miyake M. Isolation and characterization of *Staphylococcus* argenteus strains from retail foods and slaughterhouses in Japan. Int J Food Microbiol. 363:109503, 2022.
- Nitahara Y, Nakagama Y, Kaku N, Candray K, Michimuko Y, Tshibangu E, Kaneko A, Yamamoto H, Mizobata Y, Kakeya H, Yasugi M, Kido Y. Highresolution linear epitope mapping of the receptor 6. binding domain of SARS-CoV-2 spike protein in COVID-19 mRNA vaccine recipients. Microbiol. Spectr., 9:e00965-21, 2021.
- 3. Yasugi M, Hatoya S, Motooka D, Matusmoto Y, Shimamura S, Tani H, Furuya M, Mie K, Miyake M, Nakamura S, Shimada T. Whole-genome analyses of extended-spectrum or AmpC β-lactamase-producing *Escherichia coli* isolates from companion dogs in Japan. PLoS One, 16:e0246482, 2021.

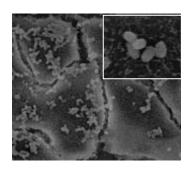
- **4. Yasugi M**, Motooka D, Nakamura S, **Miyake M**. Phosphorothioation of foreign DNA influences the transformation efficiency in *Clostridium perfringens* NCTC8239. **Anaerobe**, 61:102085, 2020.
- Wakabayashi Y, Nariya H, Yasugi M, Kuwahara T, Sarker MR, Miyake M. An enhanced green fluorescence protein (EGFP)-based reporter assay for quantitative detection of sporulation in *Clostridium* perfringens SM101. Int. J. Food Microbiol. 291: 144-150, 2018.
- 6. Sakanoue H, Yasugi M, Miyake M. Effect of sublethal heat treatment on the later stage of germination-to-outgrowth of *Clostridium perfringens* spores. Microbiol. Immunol., 62: 418-424, 2018.



Immunohistochemistry of Zonula occludens-1 (ZO-1) recruitment at the sites of infection by enteropathogenic *E. coli* (EPEC) in HeLa cells. Green, ZO-1; blue, bacterial DNA; red, F-actin. For detail, refer to **Infect. Immun**. 75: 565-573, 2007.



Phase contrast (Upper) and fluorescence (lower) micrographs of *Clostridium* perfringens cells in the process of sporulation. Bacterial cells at different sporulation stages can be observed. Blue, DNA; red, membrane structure.



Scanning electron micrograph of cultured intestinal epithelial cells Caco-2 treated with *Clostridium perfringens* spores. It is notable the numerous spores attached to the surface of the cells. The inlet features the higher magnification.

Laboratory of Veterinary Immunology

Research Interest:

Matsubayashi's research work focuses on immunological strategies against protozoan infections, host-parasite interactions, and mechanism of pathogenicity induced by the parasites. Additionally, to understand the distribution of intestinal protozoans (*Cryptosporidium*, *Giardia*, *Eimeria*, and *Entamoeba* etc.) in human, livestock, and wild and companion animals, genetical surveys are conducted. From the viewpoints, my interests include development of molecular tools (using chemical biology, or genome or 7. transcriptome analyses), producing vaccines and anti-drugs, and host-parasite adaptations using mouse or chick models.

T. Iwasaki is focusing on the potential usefulness of 8. liposomes as carriers and adjuvants for modulating immunological reaction. He is interested in applying the liposomes to establish effective vaccines to induce protective immunity against mucosal and skin challenging pathogens, and on the contrary, utilizing it to develop tolerance inducible methods for allergens to treat allergic patients.

9.

Keywords:

Allergy, *Cryptosporidium*, *Eimeria*, Mucosal immunity, Liposome, Parasite, Pathogenicity, Tolerance, Vaccine

Publications:

- P. Hastutiek, N.D.R. Lastuti, L.T. Suwanti, A. Sunarso, E. Suprihati, D.A. Kurniawati, M. Matsubayashi M*. Coproparasitological examinations and molecular determination of *Eimeria* species in Madura cattle reared on Madura Island, Indonesia. Parasitol. Int., 2022. In press.
- 2. M. Matsubayashi*, A. Kobayashi, M. Kaneko, M. Kinoshita, S. Tsuchida, T. Shibahara, M. Hasegawa, H. Nakamura, K. Sasai, K. Ushida. Distribution of *Eimeria uekii* and *Eimeria raichoi* in cage protection environments for the conservation of Japanese rock ptarmigans (*Lagopus muta japonica*) in the Japanese Alps. Int. J. Parasitol. Parasites Wildl., 15: 225-230. 2021.
- D.T. Ho, H.H.S. Pham, W. Aota, M. Matsubayashi, N. Tsuji, T. Hatabu*. Reduction of macrophages by carrageenan decreases oocyst output and modifies local immune reaction in chick cecum with *Eimeria tenella*. Res. Vet. Sci., 139: 59-66. 2021.
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- A.H. Wardhana, D.H. Sawitri, F. Ekawasti, E. Martindah, D. Apritadewi, T. Shibahara, M. Kusumoto, M. Tokoro, K. Sasai, M. Matsubayashi*. Occurrence and genetic identifications of porcine *Entamoeba*, *E. suis* and *E. polecki*, at Tangerang in West Java, Indonesia. Parasitol. Res., 119(9): 2983-2990. 2020.

Professor Assistant Professor Makoto Matsubayashi Tadashi Iwasaki

- 6. M. Matsubayashi*, M. Kinoshita, A. Kobayashi, S. Tsuchida, T. Shibahara, M. Hasegawa, H. Nakamura, K. Sasai, K. Ushida. Parasitic development in intestines and oocyst shedding patterns for infection by *Eimeria uekii* and *Eimeria raichoi* in Japanese rock ptarmigans, *Lagopus muta japonica*, protected by cages in the Southern Japanese Alps. Int. J. Parasitol. Parasites Wildl., 12: 19-24. 2020.
- T. Iwasaki*, S. Watarai. Oral λ-carrageenan intake alleviates skin symptoms in a hapten induced atopic dermatitis-like model J. Vet. Med. Sci., 82 (11): 1639-1642, 2020.
- K. Takahashi, M. Matsubayashi*, Y. Ohashi, J. Naohara, I. Urakami, K. Sasai, Y. Kido, A. Kaneko, I. Teramoto. Efficacy of ultraviolet light-emitting diodes (UV-LED) at four different peak wavelengths against *Cryptosporidium parvum* oocysts by inactivation assay using immunodeficient mice. Parasitol. Int., 77: 102108. 2020.
- D.H. Sawitri, A.H. Wardhana, E. Martindah, F. Ekawasti, D.A. Dewi, B.N. Utomo, T. Shibahara, M. Kusumoto, M. Tokoro, K. Sasai, M. Matsubayashi*. Detections of gastrointestinal parasites, including *Giardia intestinalis* and *Cryptosporidium* spp., in cattle of Banten province, Indonesia. J. Parasit. Dis., 44(1): 174-179. 2020.
- 10. M. Matsubayashi*, H. Yamaguchi, T. Hatta, F. Kawahara, T. Hatabu, H. Iseki, J. Yamagishi, T. Isobe, I. Teramoto, A. Kaneko, K. Kita, N. Tsuji, K. Sasai. Transitions in morphological forms and rapid development of the asexual schizonts of *Eimeria tenella* through serial passaging in chicks. Infect. Genet. Evol., 75: 103993. 2019.
- 11. M. Matsubayashi*, D.K. Inaoka, K. Komatsuya, T. Hatta, F. Kawahara, K. Sakamoto, K. Hikosaka, J. Yamagishi, K. Sasai, T. Shiba, S. Harada, N. Tsuji, K. Kita. Novel characteristics of mitochondrial electron transport chain from *Eimeria tenella*. Genes (Basel), 10(1):29, 2019.
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Enzyme proteins associated with asexual developments of Eimeria tenella

2nd generation schizont

Small immature

A

Promature

D

E

F

H

Mature

*This molecule could be a vaccine candidate against *E. tenella* infection.

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Infectious Diseases Control

Laboratory of Veterinary Epidemiology

Research Interest:

M. Mukamoto's research work focuses on clarification of molecular mechanisms on the infection of pathogenic microorganisms to elicit infectious diseases in domestic animals. **M. Mukamoto** attempts to analyze functional mechanisms of pathogenic factors and host factors for pathogens by use of various molecular biological, biochemical and immunological techniques. The present main research is analysis of molecular structures and biological activities in toxins from *Clostridium perfringens*, *C. septicum* and *C. chauvoei*.

T. Kohda focuses on the areas of research closely related to current knowledge on the structure and function of botulinum neurotoxins. The main task of the present research is the mechanism of receptor recognition and the different affections of host animals.

Keywords:

Pathogenic microorganisms, Diagnosis, Infectious diseases control, Pathogenic factor, Clostridia, toxin

Publications:

1. N. Hatanaka, M. Yasugi, T. Sato, **M. Mukamoto**, S. Yamasaki. Hypochlorous acid solution is a potent antiviral agent against SARS-CoV-2. **J. Appl. Microbiol.**, 132, 1496. 2022.

2. T. Takeuchi, T. Okuno, A. Miyashiro, **T. Kohda**, R. Miyamoto, Y. Izumi, S Kozaki, R. Kaji. Clinical safety and tolerability of A2NTX, a novel low-molecular-weight neurotoxin derived from botulinum neurotoxin subtype A2, in comparison with subtype A1 toxins. **Toxins.** 13, 824. 2021

3. AKM A. Islam, M. Nakatani, T. Nakajima, T. Kohda, M. Mukamoto. The cytotoxicity and molecular mechanisms of the *Clostridium perfringens* NetB toxin. J. Vet. Med. Sci., 83, 187. 2021.

4.Y. Sakaguchi, J. Uchiyama, A. Take, K. Gotoh, M. Sakaguchi, T. Suziki, Y. Yamamoto, K. Hosomi, **T. Kohda, M. Mukamoto**, S. Kozaki, S. Hayashi, K. Oguma. Analysis of a plasmid encoding botulinum neurotoxin type G gene in *Clostridium argentinense*. **Anaerobe**. 66, 102281, 2020.

5. **T. Kohda**, K. Tsukamoto, Y. Torii, S. Kozaki, **M. Mukamoto.** Translocation domain of botulinum neurotoxin A subtype 2 potently induces entry into neuronal cells. **Microbiol. Immunol.**, 64: 502-511, 2020.

6. **T. Kohda**, Y. Torii, H. Nakajima. Experimental comparative effects of botulinum toxin A between subtypes A1 and A2 in movement disorders in rats. **IntechOpen. Botulinum Toxin.** DOI: 10.5772/intechopen.80886, 2018.
7. **T. Kohda**, K. Nakamura, K. Hosomi, S. Kozaki and **M. Mukamoto**. Characterization of the functional activity of

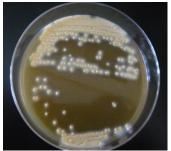
Professor Masafumi Mukamoto Lecturer Tomoko Kohda

botulinum neurotoxin subtype B6. **Microbiol. Immunol.**, 61: 482-489, 2017.

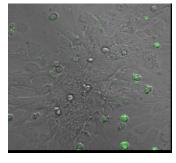
8. M. Nishiike, M. Haoka, T. Doi, **T. Kohda** and **M. Mukamoto**. Development of a preliminary diagnostic measure for bovine leukosis in dairy cows using peripheral white blood cell and lymphocyte counts. **J. Vet. Med. Sci.**, 78: 1145-1151, 2016.

9. H.Teramoto, Y. Kumeda, K. Yokoigawa, K. Hosomi, S. Kozaki, M. Mukamoto, and T. Kohda. Genotyping and characterization of the secretory lipolytic enzymes of *Malassezia pachydermatis* isolates collected from dogs. Vet. Rec. Open, 2: e000124, 2015.

10. K. Hosomi, R. Kuwana, H. Takamatsu, T. Kohda, S. Kozaki, and M. Mukamoto. Morphological and genetic characterization of group I Clostridium botulinum type B strain 111 and the transcriptional regulator spoIIID gene knockout mutant in sporulation. **Anaerobe**, 33: 55-63, 2015. 11. K. Hosomi, Y. Sakaguchi, T. Kohda, K. Gotoh, D. Motooka, S. Nakamura, K. Umeda, T. Iida, S. Kozaki, and **M. Mukamoto**. Complet nucleotide sequence of a plasmid containing the botulinum neurotoxin gene in Clostridium botulinum type B strain 111 isolated from an infant patient in Japan. **Mol. Genet. Genomics**, 289: 1267-1274, 2014. 12. Y. Sakaguchi, K. Hosomi, J. Uchiyama, Y. Ogura, K. Umeda, M. Sakaguchi, T. Kohda, M. Mukamoto, N. Misawa, S. Matsuzaki, T. Hayashi, and S. Kozaki. Draft Genome Sequence of Clostridium botulinum Type B Strain Osaka05, Isolated from an Infant Patient with Botulism in Japan. **Genome Announc.**, 2: e01010, 2014.



Colonies of *C. botulinum* isolated from a botulism cow on GAM agar plate with egg yolk.



Rounding cell death of rat cardiac cells by alpha-toxin from *C. septicum*.

Laboratory of International Prevention of Epidemics

Professor Associate Professor Specially Appointed Lecturer Specially Appointed Lecturer Assistant Professor Shinji Yamasaki Atsushi Hinenoya Sharda Prasad Awasthi Norihisa Yamamoto Noritoshi Hatanaka

Research Interest:

S. Yamasaki, A. Hinenoya, SP Awasthi and N. Hatanaka have mostly focused on enteric bacteria such as enterohemorrhagic *E. coli*, other diarrheagenic *E. coli*, *E. albertii*, *Campylobacter* and *Vibrio* in terms of molecular epidemiology, development of diagnostic method, virulence mechanism and antimicrobial resistances. Our goal is to develop rapid and simple diagnostic, therapeutic and preventive methods against these microbial infections.

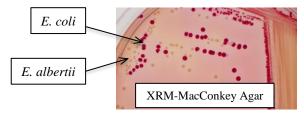
N. Yamamoto is interested in molecular epidemiology of antimicrobial resistance bacteria.

Keywords: food safety, rapid diagnosis, antimicrobial resistance, zoonosis, molecular epidemiology, bacterial protein toxin, pathogenic *E. coli, E. albertii*, STEC/EHEC, cytolethal distending toxin, *Campylobacter*, pathogenesis

Publications:

- G. B. Manjunath, S. P. Awasthi, M. S. H. Zahid, N. Hatanaka, A. Hinenoya, E. Iwaoka, S. Aoki, T. Ramamurthy and S. Yamasaki*. Piperine, an active ingredient of white pepper suppresses growth of toxigenic *Vibrio cholerae* strains and other bacterial pathogens. *Let. Appl. Microbiol.*, in press.
- N. Hatanaka, B. Xu, Y. Yamashita, H. Kawakami, M. Yasugi and S. Yamasaki*. ShellCoat, a calcinated calcium solution, effectively inactivate SARS-CoV-2. *Biocont. Sci.*, in press.
- A. Hinenoya, S.P. Awasthi, N. Yasuda, K. Nagano, J. Hassan, K. Takehira, N. Hatanaka, S. Saito, T. Watabe, M. Yoshizawa, H. Inoue and S. Yamasaki*. Detection and molecular characterization of *Escherichia albertii* in wild birds in Japan. *Jpn. J. Infect. Dis.*, in press.
- N. Hatanaka, M. Yasugi, T. Sato M. Mukamoto and S. Yamasaki*. Hypochlorous acid solution is a potent antiviral agent against SARS-CoV-2. *J. Appl. Microbiol.*, 132: 1496-1502, 2022.
- K. Ishimoto[#], N. Hatanaka[#], S. Otani[#], S. Maeda, B. Xu, M. Yasugi, M. Suzuki, S. Nakagawa^{*} and S. Yamasaki^{*}. Tea crude extracts effectively inactivate severe acute respiratory syndrome coronavirus 2. *Let. Appl. Microbiol.*, 74: 2-7, 2022. (#equally contributed.)
- 6. N. Hatanaka, B. Xu, M. Yasugi, H. Morino, H. Tagishi, T. Miura, T. Shibata and S. Yamasaki*. Chlorine dioxide is a more potent antiviral agent against SARS-CoV-2 than sodium hypochlorite. *J. Hosp. Infect.*, 118: 20-26, 2021
- 7. X. Fuzhou*, **A. Hinenoya***, X. Zeng*, X.-P. Li, Z. Guan and J. Lin*. Critical role of 3'-downstream region of *pmrB* in polymyxin resistance in *Escherichia coli* BL21(DE3). **Microorganisms.**, 9:655, 2021. (*equally contributed)

- P. Q. Le, S. P. Awasthi, N. Hatanaka, A. Hinenoya, J. Hassan, R. A. Ombarak, A. Iguchi, N. T. T. Tran, K. V. T. Dao., M. Q. Vien, H. X. Le., H. T. Do, Y. Yamamoto and S. Yamasaki*. Prevalence of mobile colistin resistance (mcr) genes in extended- spectrum β-lactamase-producing Escherichia coli isolated from retail raw foods in Nha Trang, Vietnam. Int. J. Food Microbiol., 346: 109164, 2021.
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- 10. D.T.A. Nguyen, S.P. Awasthi, P.H. Hoang, P.D. Nguyen, N. Hatanaka, A. Hinenoya, C.V. Dang, S.M. Faruque and S. Yamasaki*. Prevalence, serotype and antimicrobial resistance of non-typhoidal *Salmonella* in vegetable, fruit and water samples in Ho Chi Minh City, Vietnam. *Foodborne Pathog. Dis.*, 18:354-363, 2021.
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 Prevalence, O-genotype and Shiga toxin (Stx) 2 subtype of Stx-producing *Escherichia coli* strains isolated from Argentinean cattle. *J. Vet. Med. Sci.*, 83:630-636, 2021.
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Hinenoya et al., Diagn. Microbiol. Infect. Dis., 97: 115006, 2020.

Professor Associate Professor Masayuki Horie Yoshiyuki Seto

Research Interest

M. Horie is interested in a wide range of virology, from basic research to applied research. For basic research, we are focusing on 1) diversity and evolution of RNA viruses, 2) coevolution of RNA viruses and their hosts, and 3) replication mechanisms of RNA viruses that replicate in the nucleus. We are researching the above topics by combining wet experiments and dry analysis. For applied virology, we are trying to develop rapid and simple virus diagnostic methods. We are also developing viral vectors for basic research and, potentially, for future gene therapy and vaccine use. By combining these studies, we aim to gain a deeper understanding of viruses, to control viral diseases and to utilize viruses in our lives.

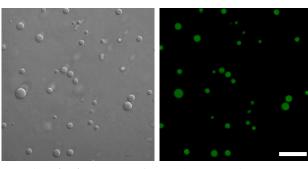
Y. Seto is interested in the infectious diseases, and developing the laboratory diagnostic methods using the various molecular approaches to control the infectious diseases.

Key words: Viruses, infectious diseases, viral evolution, viral diversity, paleovirology, bioinformatics, diagnosis

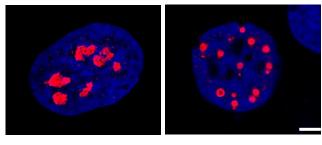
Selected publications

- 1. Hirai, Y., Tomonaga, K. and **Horie, M**. Borna disease virus phosphoprotein triggers the organization of viral inclusion bodies by liquid-liquid phase separation. Int J Biol Macromol 192: 55-63. 2021.
- 2. **Horie, M**. Identification of a novel filovirus in a common lancehead (Bothrops atrox (Linnaeus, 1758)). J Vet Med Sci. 2021.
- 3. Iwamoto, M., Shibata, Y., Kawasaki, J., Kojima, S., Li, Y. T., Iwami, S., Muramatsu, M., Wu, H. L., Wada, K., Tomonaga, K., Watashi, K. and **Horie, M**. Identification of novel avian and mammalian deltaviruses provides new insights into deltavirus evolution. Virus Evol 7: veab003. 2021.
- 4. Kawasaki, J., Kojima, S., Tomonaga, K. and **Horie, M**. Hidden Viral Sequences in Public Sequencing Data and Warning for Future Emerging Diseases. mBio 12: e0163821. 2021.
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- 7. Mukai, Y., **Horie, M.**, Kojima, S., Kawasaki, J., Maeda, K. and Tomonaga, K. An endogenous bornavirus-like nucleoprotein in miniopterid bats retains the RNA-binding properties of the original viral protein. FEBS letters. 2022

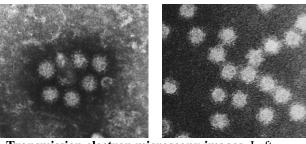
- 8. Rubbenstroth, D., Briese, T., Durrwald, R., **Horie, M.**, Hyndman, T. H., Kuhn, J. H., Nowotny, N., Payne, S., Stenglein, M. D., Tomonaga, K. and Ictv Report, C. ICTV Virus Taxonomy Profile: Bornaviridae. J Gen Virol 102. 2021
- 9. **Horie, M.**, Akashi, H., Kawata, M. and Tomonaga, K. Identification of a reptile lyssavirus in Anolis allogus provided novel insights into lyssavirus evolution. Virus genes. 2020.



In vitro liquid droplets formed by recombinant Borna disease virus (BoDV) P protein and GFP-tagged BoDV P protein. Scale bar, 10 µm. (refer to Hirai et al., Int J Biol Macromol. 2021)



Intranuclear viral inclusion bodies formed by deltaviruses (left, deltavirus detected from passerine birds; right, deltavirus detected from woodchuck) which we discovered using publicly available RNA-seq data. Red, deltavirus antigens; Blue, DAPI. Scale bar, 50 μm. (Iwamoto et al., Virus Evol. 2021)



Transmission electron microscopy images. Left, Norovirus detected in fecal specimen; right, Norovirus-like particle expressed by Baculovirus expressing system.

Advanced Pathobiology

Laboratory of Cell Pathobiology

Professor Kikuya Sugiura
Associate Professor Shingo Hatoya
Visiting Professor Toshio Inaba
Visiting Professor Takashi Akazawa

Research Interest:

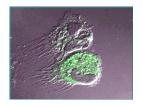
Our research work focuses on the cellular mechanisms of blood, incretion and metabolism taking place in the control of homeostasis in animals, the pathophysiology of disorders caused by the structural or functional abnormalities in the cells, and diagnosis and therapy in those disorders. Projects under investigation include; 1) dendritic cell based tumor immunotherapy, 2) establishment of canine and feline embryonic stem cells (ES cells) from blastocyst, 3) generation of canine and feline induced pluripotent stem cells (iPS cells) from adult cells for regenerative veterinary medicine, and 4) development of canine and feline in vitro fertilization techniques.

Keywords:

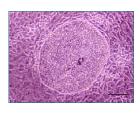
Cancer, Cat, Dendritic cell, Dog, Embryonic stem cell, Induced pluripotent stem cell, *in vitro* fertilization, Regenerative veterinary medicine, Tumor immunotherapy

- Mitani K, Ito Y, Takene Y, Hatoya S, Sugiura K, Inaba T. Quality of life-improving effect of autologous ex vivo expanded cytotoxic and opioid-producing lymphocytes for dogs with cancers. Vet Immunol Immunopathol 238:110292, 2021.
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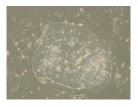
- Ito T, Sugiura K, Hasegawa A, Ouchi W, Yoshimoto T, Mizoguchi I, Inaba T, Hamada K, Eriguchi M, Koyama Y. Microbial antigen-presenting extracellularvesicles derived from genetically modified tumor cells promote antitumor activity of dendritic cells. Pharmaceutics 13(1):57, 2021
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- Ramanayake Mudiyanselage TMR, Michigami M, Ye Z, Uyeda A, Inoue N, Sugiura K, Fujii I, Fujiwara D. An immune-stimulatory helix-loop-helix peptide: selective inhibition of CTLA-4/B7 interaction. ACS Chem Biol 15(2):360-368, 2020.
- Wijesekera DPH, Yuba E, De Silva NH, Watanabe S, Ichida C, Izawa T, Itoh K., Kanegi R, Hatoya S, Yamate J, Inaba T, Sugiura K. Manipulation of the tumor microenvironment by cytokine gene transfection enhances dendritic cell-based immunotherapy. FASEB BioAdov 2(1):5-17, 2020.
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- Tsujimoto Y, Fujiki K, Alam ME, Tsukamoto M, Azuma R, Kanegi R, Anzai M, Inaba T, Sugiura K, Hatoya S. Development of feline embryos produced by Piezo-actuated intracytoplasmic sperm injection of elongated spermatids. J Reprod Dev 65(3):245-250 2019.
- Alam ME, Iwata J, Fujiki K, Tsujimoto Y, Kanegi R, Kawate N, Tamada H, Inaba T, Sugiura K, Hatoya S. Feline embryo development in commercially available human media supplemented with fetal bovine serum. J Vet Med Sci 81(4):629-635, 2019



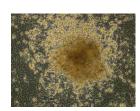
Canine Dendritic cells, generated from monocytes



Canine ES cells isolated in our labs



Canine iPS cells isolated in our labs



Feline iPS cells isolated in our labs

Laboratory of Veterinary Radiology

Associate Professor Associate Professor Shunsuke Noguchi Satoshi Matsuyama

Research Interest of Prof. Noguchi:

MicroRNAs (miRNAs) have been known to contribute to tumor development and progression. Therefore, the tumor-specific miRNAs are considered to be therapeutic targets and biomarkers. The aims of our research are to understand the molecular mechanisms involved in development or progression of canine cancers by elucidating the functions of tumor-specific miRNAs and to develop the novel therapeutic modalities based on the molecular mechanisms. Also, we participate in cancer therapy in veterinary medical center and we attempt to apply the achievements of our study to cancer therapy.

Key words:

Canine cancer, miRNA, biomarker, cancer therapy

Research Interest of Prof. Matsuyama:

DNA damages by environmental and intracellular agents, if left unrepaired, lead to carcinogenesis, aging and other adverse health effects. The major focus of our research is to understand molecular mechanisms of cellular DNA base excision repair that remove DNA lesions and restore genetic information. Another major focus is identification of tumor-related gene expression in various companion animal tumors. **Keywords:**

DNA repair, oxydative damages, tumorigenesis, adaptive response.

Publications (*; corresponding author):

- 1. **S. Noguchi**, N. Tanimoto, R. Nishida, and A. Matsui. Functional analysis of the miR-145/Fascin1 cascade in canine oral squamous cell carcinoma. **Oral Dis.**, 2022 in press.
- H. Yamazaki, Y. Wada, T. Tanaka, and S. Noguchi*. Single-modality palliative radiotherapy versus palliative radiotherapy after chemotherapy failure for cats with nasal lymphoma. Vet. Radiol. Ultrasound., 2021 in press.
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- S. Noguchi, M. Inoue, T. Ichikawa, K. Kurozumi, Y. Matsumoto, Y. Nakamoto, H. Akiyoshi, and H. Kamishina. The NRG3/ERBB4 signaling cascade as a novel therapeutic target for canine glioma. Exp. Cell. Res., 400(2):112504. 2021.
- H. Yamazaki, H. Sasai, M. Tanaka, T. Tanaka T, H. Nishida, S. Noguchi S, M. Kuwamura, and H. Akiyoshi. Assessment of biomarkers influencing treatment success on small intestinal lymphoma in dogs. Vet. Comp. Oncol.,19(1):123-131, 2021.
- Y. Hamamura, T. Nakagawa, M. Okuda, S. Noguchi, M. Igase, and T. Mizuno. The inhibitory effect of canine interferon gamma on the growth of canine tumors. Res. Vet. Sci., 132: 466-473, 2020.
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- 8. M. Igase, Y. Nemoto, K. Itamoto, K. Tani, M. Nakaichi, M. Sakurai, Y. Sakai, S. Noguchi, M. Kato, T. Tsukui, and T. Mizuno. A pilot clinical study of the therapeutic antibody against canine PD-1 for advanced spontaneous cancers in dogs. Sci. Rep., 10(1):18311, 2020.

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- 14. R. Yoshikawa, T. Mori, S. Noguchi, Y. Akao, K. Maruo, and Y. Kitade. Synthetic microRNA-205 exhibited tumour suppression in spontaneous canine malignant melanoma by intratumoral injection. Vet. Comp. Oncol., 17: 407–412, 2019.
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- 80: 1724-1727, 2018.

 19. **S. Noguchi**, S. Shibutani, K. Fukushima, T. Mori, M. Igase, and T. Mizuno. Bosutinib, an SRC inhibitor, induces caspase-independent cell death associated with permeabilization of lysosomal membranes in melanoma cells. **Vet. Comp. Oncol.**, 16: 69-76, 2018.

Professor Lecturer Noritoshi Kawate Keisuke Koyama

Research Interest:

We are studying on reproductive phenomena and their 6. artificial controls in domestic animals, and clarifying causes and developing methods of diagnosis, treatment and prevention of reproductive diseases.

The purposes of our research are clarifying the roles of hormones and factors in animal reproduction, controlling 7. reproductive phenomena and contributing to prevention and treatment for reproductive diseases.

Research themes for each professor:

Dr. Noritoshi Kawate:

- (1) Elucidation of roles of insulin-like peptide 3 (INSL3) in bovine sperm and female reproductive organs
- (2) Application and improvement of INSL3 assay for evaluations of reproductive functions in domestic animals including cattle and horses
- (3) Study on associations of semen characteristics in Japanese Black beef bulls with testicular and metabolic hormones

Dr. Keisuke Koyama

- (1) Establish of optimal individual culture system for bovine oocyte
- (2) Study on the relationship between ovarian reserves of dam and calf in dairy cows
- (3) Prediction of reproductive performance in dairy cows by using the farm-related data

Publications:

- Inaba R, Kawahara-Miki R, Shinozawa A, Yasuhara T, Fujii T, Koyama K, et al. Impaired placentomal interferon signaling as the possible cause of retained fetal membrane in parturition-induced cows. J Reprod Dev. 2021.(in press)
- Balogh O, Somoskői B, Kollár E, Kowalewski MP, Gram A, Reichler IM, Klein R, Kawate N, et al. Anti-Müllerian hormone, testosterone, and insulin-like peptide 3 as biomarkers of Sertoli and Leydig cell function during deslorelin-induced testicular downregulation in the dog. Theriogenology. 175:100-110. 2021.
- Kawate N*, Kanuki R, Hannan MA, Weerakoon WWPN. Inhibitory effects of long-term repeated treatments of a sustainable GnRH antagonist, degarelix acetate, on caprine testicular functions. J Reprod Dev. 66:587-592. 2020.
- 4. Koyama K*, Takahashi T. Relationship between sire predicted transmitting ability for daughter pregnancy rate and daughter's reproductive performance and milk production in Japanese dairy herds. J Reprod Dev. 66: 445-452. 2020.
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Tsogtgerel M, Komyo N, Murase H, Hannan MA, **Kawate N**, et al. Serum concentrations and testicular expressions of insulin-like peptide 3 and anti-Müllerian

hormone in normal and cryptorchid male horses.

machine learning. J Dairy Sci. 103: 8535-8540. 2020.

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Weerakoon WWPN, Sakase M, Kohama N, Kawate N*. Plasma estradiol-17β, cortisol, and insulin concentrations and serum biochemical parameters surrounding puberty in Japanese Black beef bulls with normal and abnormal semen. Theriogenology. 148:18-26. 2020.

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- Sakase M, Weerakoon WWPN, Hannan MA, Kohama N, Tamada H, Kawate N*. LH and testosterone secretions in response to GnRH challenge in pubertal Japanese Black beef bulls with normal and abnormal semen. J Vet Med Sci. 80: 1829-1833. 2018.
- 12. Pathirana IN, Rajapaksa C, **Kawate N**, Wimalarathne A, Fonseka L, Weerakoon PN, Hannan MA, et al. Effects of gonadotropin-releasing hormone antagonist degarelix on musth and serum testosterone concentrations in Asian elephants (*Elephas Maximus*). **J Zoo Wildl Med**. 49: 779-783. 2018.
- 13. Sakase M, Kitagawa K, Kibushi M, Kawate N*, Weerakoon WWPN, Hannan MA, Kohama N, Tamada H. Relationships of plasma insulin-like peptide 3, testosterone, inhibin, and insulin-like growth factor-I concentrations with scrotal circumference and testicular weight in Japanese Black beef bull calves. J Reprod Dev. 64: 401-407. 2018.
- 14. Weerakoon WWPN, Sakase M, Kawate N*, Hannan MA, Kohama N, Tamada H. Plasma IGF-I, INSL3, testosterone, inhibin concentrations and scrotal circumferences surrounding puberty in Japanese Black beef bulls with normal and abnormal semen. Theriogenology. 114: 54-62. 2018.

Advanced Clinical Medicine

Laboratory of Veterinary Internal Medicine

Professor Kazumi Sasai Associate Professor Hiroyuki Tani Associate Professor Masaru Furuya

Research Interest:

common theme include 1) Our research development of novel detection and prevention tools infectious disease, especially zoonosis companion and industrial animals, 2) epidemiological studies of zoonosis in companion, industrial and wild animals, 3) development of diagnostic and therapeutic tools for neoplastic diseases in companion animals using immunological methods, and 4) establishment of novel diagnostic and therapeutic procedures for dermatological and autoimmune diseases in companion animals.

Professor Sasai's interests involve the study of dermatological disorder in small mechanism of animals using immunological technique. He is also interested in establishment of new diagnosis technique zoonosis, especially Cryptosporidium epidemiological studies of zoonosis in wild animals. Moreover, he is involved in the study of host defense against mechanism chicken coccidiosis monoclonal antibodies. Associate Professor H. Tani has focused on the development of detection tools and oral mucosal vaccine for microbial infections due to Staphylococcus and Salmonella spp.. **Associate** Professor M. Furuya has focused on the identification of specific tumor antigen leads to the development of novel diagnostic method and cancer immunotherapy for companion animals. Our research would provide the versatile information and tools for small animal medicine, livestock industry, and wildlife management.

Keywords:

Dermatology, Zoonosis, *Cryptosporidium*, Coccidia, Monoclonal antibody, *Salmonella*, Tumor antigen

- T. Ito, M. Furuya*, K. Sasai. The establishment of an optimal protocol for contrast-enhanced microcomputed tomography in the cloudy catshark (*Scyliorhinus torazame*). J Aquat Anim Health. 33(4):264-276. 2021.
- M. Matsubayashi*, K. Takami, M. Kinoshita, S. Tsuchida, K. Ushida, T. Shibahara, K. Sasai. Morphological and molecular identification of *Eimeria tetartooimia* oocysts from a Japanese green pheasant (*Galliformes*; *Phasianidae*; *Phasianus versicolor*) at a zoo in Japan. Parasitol Res. 120(8):2973-2979. 2021.
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- Strains Isolated from the Oviducts of Layer Hens in East Japan. **JWPR**. 11(2) 241 251. 2021.
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- M. Yasugi*, S. Hatoya, D. Motooka, Y. Matsumoto, S. Shimamura, H. Tani, M. Furuya, K. Mie, M. Miyake, S. Nakamura, T. Shimada. Whole-genome analyses of extended-spectrum or AmpC βlactamase-producing Escherichia coli isolates from companion dogs in Japan. PLoS One. 16(2):e0246482. 2021.
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- K. Sakai*, S. Hatoya, M. Furuya, S. Shimamura, T. Nabetani, H. Tani, T. Shimada. Decreased serum zinc concentration in dogs with lymphocytic-plasmacytic enteritis, and its associations with disease severity and prognosis. J Vet Med Sci. 82(6):759-763, 2020.
- 10. K. Takahashi, M. Matsubayashi, Y*. Ohashi, J. Naohara, I. Urakami, K. Sasai, Y. Kido, A. Kaneko, I. Teramoto. Efficacy of ultraviolet light-emitting diodes (UV-LED) at four different peak wavelengths against *Cryptosporidium parvum* oocysts by inactivation assay using immunodeficient mice. Parasitol Int. 77:102-108. 2020.
- 11. T. Soma*, M. Ogata, K. Ohta, R. Yamashita, K. Sasai. Prevalence of astrovirus and parvovirus in Japanese domestic cats. J Vet Med Sci. 82:1243-1246. 2020.
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- 13. H. Kanai, M. Furuya*, K. Hagiwara, A. Nukaya, M. Kondo, T. Aso, A, Fujii, K. Sasai. Efficacy of enbloc thoracic duct ligation in combination with pericardiectomy by video-assisted thoracoscopic surgery for canine idiopathic chylothorax. Vet Surg. 49:102-111. 2020.

Professor Associate Professor Hideo Akiyoshi Hidetaka Nishida

Research Interest:

This laboratory aims to clarify the pathophysiological mechanisms of intractable diseases in companion animals and to develop the novel surgical therapies for these diseases. The laboratory has studied on: (1) the development of surgical treatment in soft tissue and orthopedic surgery for companion animals, (2) the pathophysiology, diagnosis and therapies in disorders of neurological, urinary and cardiovascular system, (3) the relationship between tumor and inflammatory response, (3) the pathophysiology, diagnosis and therapies in systemic inflammatory response syndrome, especially sepsis, (4) the development of new biomarkers in tumorbearing animals, and (5) interventional radiology for tumor-bearing animals.

Keywords:

Soft tissue surgery, Urology, Cardiology, Neurology, Oncology, Orthopedics, Inflammatory response, Sepsis, Biomarker, Interventional radiology, Regenerative medicine

- S. Noguchi*, K. Hirano, N. Tanimoto, T. Shimada, H. Akiyoshi. SLUG is upregulated and induces epithelial mesenchymal transition in canine oral squamous cell carcinoma. Vet. Com. Oncol., in press.
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- S. Noguchi, M. Inoue, T. Ichikawa, K. Kurozumi, Y. Matsumoto, Y. Nakamoto, H. Akiyoshi, H. Kamishina. The NRG3/ERBB4 signaling cascade as a

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- T. Tanaka, H. Nishida, K. Mie, H. Yamazaki, L. S. Lin, H. Akiyoshi*. Assessment of hepatitis and fibrosis using Gd-EOB-DTPA MRI in dogs. Vet. Rec. Open, 7: e000371, 2020.
- S. Noguchi, A. Hattori, N. Tanimoto, R. Nishida, K. Hirano, Y. Wada, S. Matsuyama, T. Shimada, H. Akiyoshi. Establishing cell lines for canine tonsillar and non-tonsillar oral squamous cell carcinoma and identifying characteristics associated with malignancy. Tissue Cell, 67: 101408, 2020.
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Laboratory of Veterinary Advanced Diagnosis and Treatment

Professor Associate Professor Takashi Hasegawa Yuka Fujimoto Mizuki Tomihari

Research Interest:

T. Hasegawa's research is the analysis of pathophysiology, and advanced diagnostic and/or therapeutic procedures on intractable disorders in the areas of veterinary ophthalmology, orthopedics, and neurology. In addition, my current major interests are the development of novel diagnostic and therapeutic procedures including regeneration therapy to some diseases including keratoconjuctivitis sicca, corneal disorders, glaucoma, and delayed- and/or non-union bone fractures. My research groups are now investigating the analysis of pathophysiology via ultrasound biomicroscopye on canine glaucoma and developing novel artificial tears containing sodium hyaluronate/dodecahydrosqualene for treatment of keratoconjuctivitis sicca.

Keywords: veterinary, pathophysiology, advanced diagnosis, advanced therapy, ophthalmology, orthopedics, neurology

Y. Fujimoto is interested to study innate immunity in veterinary medicine and has focuses on gastrointestinal immunity and oral immunity in dogs and cats. And, study of anesthesia and pain control for dogs and cats is one of research themes, too.

Keywords: chronic inflammation, inflammatory bowel disease, chronic enteritis, gingivostomatitis, innate immunity, veterinary science, regulatory T cell, anesthesia, pain control

M. Tomiohari's research interst is the study of oncology, surgery, and immunology in veterinary medicine. We are conducting research aimed at establishing new diagnostic criteria and treatment methods based on clinical cases. In particular, our current interests are 1) analysis of immunotolerance-inducing factors in canine malignant melanoma cells, 2) investigating the causes of the swimmer-puppy syndrome in retriever breeds, and 3) research on laparoscopic and minimally invasive surgery.

Keywords: oncology, surgery, immunology, melanoma, mast cell tumor, swimmer puppy syndrome, laparoscopy

Publications:

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- Mori, M., Izawa, T., Sasaki, H., Sonoyama, J, Nishimura, S., Shimamura, S., Shimada, T., Hasegawa, T., Kuwamura, M. and Yamate, J. A feline case of T-cell lymphoma with tropism for the striated muscle and peripheral nerve. J. Comp. Pathol. 168: 8-12, 2019.
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- 12. **Hasegawa, T.,** Tanaka, S. and Sawa, S. A preliminary clinical trial for evaluation of the therapeutic effects of a tear substitute containing 0.1% polyvinyl alcohol, 0.3% sodium hyaluronate, and 5% dodecahydrosqualene in dogs with corneal ulcers. **Vet. Ophthalmol.** 20: E13-E14, 2017.

Laboratory of Large Animal Clinical Medicine

Professor Norio Yamagishi Associate Professor Shingo Ishikawa

Research Interest:

This laboratory aims to elucidate pathophysiological mechanism of large animal diseases and provide novel methods for the diagnosis, prevention and/or treatments.

- N. Yamagishi has focused on circulating biomarkers for prediction of various diseases and decision-making of health management in animals. We have developed sensitive assays for measuring circulating TRAP5b (secreted by osteoclasts) and ALP3 (secreted by osteoblasts), showing the prepartum prediction of milk fever in dairy cows. We have also evaluated the bone metabolism of captative Asian elephants using the circulating biomarkers.
- **S. Ishikawa** has focused on the development of disease prevention and treatment using innate immunity. In particular, we are conducting research on equine locomotor diseases and bovine respiratory diseases using stem cells and mucosal vaccines.

Keywords: circulating biomarker, clinical biochemistry, innate immunity, mucosal vaccine, stem cell

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 Hayashi J, Otomaru K, Hirata M, Ishikawa S, Ikedo T,
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Veterinary Medical Center

Laboratory of Veterinary Clinical Pathology

Professor Terumasa Shimada Associate Professor Shunsuke Shimamura Assistant Professor Kosei Sakai

Research Interest:

This laboratory aims to elucidate pathologic condition of the disease in companion animals and provide novel method for the diagnosis for the disease.

- **T. Shimada** has focused on the relationship between an immune response and an intractable disease such as cancer, IBD and so on. We have analyzed immune cells and immunological products such as cytokines in clinical samples of the disease with doctor course students and exclusive staffs. Our goal of the study is to develop immunological methods of diagnosis and therapy against the intractable disease.
- **S. Shimamura** has focused on the identification of novel biomarkers for cardiorenal syndrome and their utility in prognosis, diagnosis and targeted treatment of heart failure-induced renal disease in companion animals.
- **K. Sakai** has focused on the following research;
- 1) Pathological analysis of tumors occurring in dogs and cats
- 2) Development of new diagnostic techniques and therapies for canine and feline tumors
- 3) Pathological analysis of gastrointestinal diseases occurring in dogs and cats

Keywords:

immune response, intractable disease, cancer, cardiology, oncology

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- Yasugi M, Hatoya S, Motooka D, Matsumoto Y, Shimamura S, Tani H, Furuya M, Mie K, Miyake M, Nakamura S, Shimada T. Whole-genome analyses of extended-spectrum or AmpC β-lactamase-producing Escherichia coli isolates from companion dogs in Japan. PLoS One. 2021; 16(2): e0246482.
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- 12. Mie K, Shimada T, Akiyoshi H, Hayashi A, Ohashi F. Change in peripheral blood lymphocyte count in dogs following adoptive immunotherapy using lymphokine-activated T killer cells combined with palliative tumor resection. Veterinary Immunology and Immunopathology. 177:58–63, 2016

Veterinary Medical Center

Veterinary Medical Center

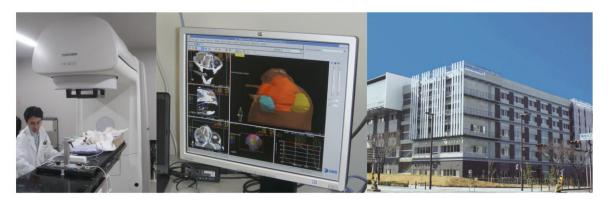
One of the Nation's Leading Center of Veterinary Clinical Care

The Department of Veterinary Science originated as a veterinary clinic back in 1883. Transferred to the Rinku Campus in April 2009, it has added advanced medical facilities to its educational setting. The buildings on the campus are soundproof, odor-controlled, and fully prepared against biohazard and virus attacks.

The Veterinary Medical Center, one of the cutting-edge facilities on the new campus, provides secondary care for animals utilizing high-tech medical devices such as linac radiation therapy machines and MRI. It also responds to specialized care and emergency operations, many of which treat age-related diseases that are increasing in animals similarly to humans.



The contemporary operating room (left) and CT scanner (right)



The high-energy radiation therapy facility (left and middle)

Veterinary Medical Center

Veterinary Medical Center

Director Hideo Akiyoshi

Exclusive staffs

Professor Terumasa Shimada Associate Professor Shunsuke Shimamura

Assistant Professor Kosei Sakai

Specially Appointed Professor Gen Kato
Specially Appointed Professor Naoaki Matsuki
Specially Appointed Lecturer Toshiyuki Tanaka
Specially Appointed Lecturer Yuya Nakamoto
Specially Appointed Assistant Professor Tomoyo Nabetani
Specially Appointed Assistant Professor Shougo Hirata
Specially Appointed Assistant Professor Kiyomi Hagi
Specially Appointed Assistant Professor Yusuke Wada
Specially Appointed Assistant Professor Ryouji Kanegi

The Veterinary Medical Center is a referral and teaching hospital. The aims of the center are to provide a comprehensive and demonstrably excellent clinical service across a range of species and disciplines to clients, to continue to make advances in veterinary knowledge, diagnosis, treatment and patient welfare through clinical research and to provide a wide range of clinical cases and species for teaching students and training postgraduate clinical professionals. The center has clinical services as below.

Oncology Service:

Our staff provides diagnosis and treatment of patients with cancer (including mast cell tumors, soft tissue sarcomas, nasal tumors, brain tumors, spinal tumors, and melanomas).

Director Shunsuke Noguchi

Soft tissue Surgery Service:

Our staff provides diagnosis and surgical treatment of patients with soft tissue diseases.

Director Hideo Akiyoshi



X-RAY FLUOROSCOPY SYSTEM

Neurology and Orthopedic Surgery Service:

Our staff provides diagnosis and treatment of patients with diseases of the nervous system and the musculoskeletal system.

Director Hidetaka Nishida

Ophthalmology Service:

Our staff provides diagnosis and treatment of patients with diseases of the eye.

Director Takashi Hasegawa

Cardiology Service:

Our staff provides diagnosis and treatment of patients with diseases of heart and vascular

Director Shunsuke Shimamura

Internal Medicine Service:

Our staff provides diagnosis and treatment of patient with general internal diseases.

Director Hiroyuki Tani

Large Animal Medicine and Surgery Service:

Our staff provides diagnosis and treatment of large animal patients with various diseases .

Director Norio Yamagishi

Diagnostic and Support Service:

Our staff provides diagnostic supports (clinical pathology laboratory, diagnostic imaging and pathology) and support of transfusion treatment.

Director Terumasa Shimada

Anaesthesia Service and Diagnostic Imaging Service are scheduled to open in April 2022, and Emergency Service will be opened in October 2022.



MRI

Education and Research Center for Experimental Animal Science

Learning practical skills in conducting laboratory animal experiments

The Education and Research Center for Experimental Animal Science is established on the Rinku Campus as an inter-faculty core facility for conducting experimental animal research in the university.

The main feature of the center is an animal farm for breeding small laboratory animals such as specific pathogen-free rodents and genetically modified mice as well as mediumsized animals such as dogs and goats under proper breeding conditions as directed by a central control system. The center is also equipped with laboratory equipment supporting various investigations into the development of novel medical treatments, the clarification of mechanisms of disease onset, prevention of infectious the diseases. particularly zoonotic diseases, and so on. The scientists should consider the welfare of various kinds of animals, including domestic

animals, companion animals, animals for exhibition and laboratory animals, ethical issues surrounding the relationship between humans and animals and promote animal welfare and protection from a practical point of view. The center will also effectively and efficiently provide not only equipment and rooms for animal experiments but also information covering all aspects experimental animal research including genetic features of animals, proper handling, and appropriate experimental protocols. The center will also promote animal welfare and protection from a practical point of view. Through these activities, the center will practically support education and research in animal biology as the core element of its veterinary science program.



A researcher working at procedure room



Cage changing station and individual ventilated cages (IVC)



Environmental enrichment (Rodent Crawl Ball)

Industry-Academia-Government Collaboration Institution

Joint Use Institution

The various results of research in animal life science are accumulated in the "Rinku campus" which is a creation base of "intelligence" of Kansai as intellectual through property scientific research activities and practical veterinarian clinical activity. The "intellectual property" must be returned to society as property common to human beings. From this point, the social role of the "Rinku campus" which serves as a central base of "intelligence" of a south Osaka area is important. Of course we contribute to society through education and research from a long-term viewpoint. **Furthermore** directly return the "intellectual property" accumulating society by practicing densely the constant cooperation with private enterprises, the government and a self-governing body. We think that it is our important mission who is working at the creation base of "intelligence". The "intellectual creation cycle" which we aim at is standing on a global view, performing the advanced and innovative research activities, and using all the created results for society from a public situation.

An industry-academia-government collaboration institution and a joint use institution are the bases of an "intellectual creation cycle". Therefore, our institution comprises the latest facilities and devices.



Live Cell Imaging System

We can analyze a living cell including the time lapse observation using luminescence or fluorescence.

GC/MS

GC/MS is an analytical instrument that combines gas chromatography and mass spectrometry. It is capable of high-speed, highly sensitive analysis of small molecules from minute samples.



TEM

Transmission electron microscope (TEM) is used to investigate the fine structure of biological samples including microorganisms and cellular organelle.

Undergraduate Veterinary Course: School of Veterinary Science

The School of Veterinary Science OMU (SVSOMU), originally known as Jyuigaku-Kosyujo, was established in 1883 as a public training and medicare center for animals in Osaka. Since then, over the past 100 years the school has been cultivating many specialists who have become leaders in veterinary medical practice, higher education, public health, research, disease control, food safety, and environmental protection and biotechnology. The mission of this school is

to foster veterinarians, technical experts, and researchers to contribute to social and industrial development and scientific progress. Students gain specialized knowledge on advanced veterinary medical care, problem-solving skills, and creativity together with a deep understanding of bioethics and the coexistence of human beings and animals.

The SVSOMU, as one of the 17 schools offering undergraduate veterinary education courses in Japan, provides six-year educational program to foster students specializing in veterinary medicine veterinary science. The curriculum of the undergraduate veterinary course consists of 13 liberal arts (26 credits) and 108 specialized subjects relating to veterinary Students must earn at least 203 credits in total, including 174 credits for specialized subjects, for their graduation. Graduation requirements include finishing two years of research work and a graduation thesis. Through the program, the graduates will be qualified as an applicant for the Japanese "National License for Veterinarian". Successful applicants who pass

the national exams can hold a Japanese veterinary license and are eligible for veterinary clinic practice, food inspection, and related occupations specified for veterinarians. 40-50 Among the annual graduates, approximately half of them are employed as veterinary clinicians. A quarter of the graduates work as public employees, as experts for infection control in animal diseases and for food safety control. The rest graduate enter pharmaceutical companies, where they work in basic and applied research, or attend graduate school to continue his/her research experiences.



In the "Large Animal Practice A" program, undergraduate students learn basic knowledge on handlings and diagnostic procedures for Large animal practice

Graduate School of Veterinary Science

Veterinary science, a comprehensive science focused on animal treatment, tackles various issues deeply related to the health and safety of animals and humans and the welfare of the local society: (1) the enhancement of animal treatment, (2) the threat of amphixenosis due to the increase in the international movement of people and animals and also distribution of livestock products, (3) the improvement of livestock production efficiency using biotechnology, (4) the development of new medicine, and (5) the safety evaluation of foods and pharmaceuticals.

The Division of Veterinary Science aims to develop (1) specialists in veterinary learning, view, and technique who are capable of integrating specialized knowledge and technique in the domain of applied animal science, (2) specialists capable of contributing to the diagnosis and treatment of animals and public hygiene, and (3) international specialists capable of exhibiting innovative leadership in biomedical fields related to both animals and humans.

Since April 2009, the Division of Veterinary Science has transferred to our new Rinku Campus located on the shore across from Kansai International Airport. On this new campus, the Veterinary Medical Center and Education and Research Center for Experimental Animal Science have been housed in an education/research building under the department. The division is carrying out improved faculty development programs at the new facilities, which are equipped with the latest educational and research equipment.

Course: Structural and Functional Bioscience

Our major objective is to disseminate the latest animal biological information. To achieve this goal, we conduct research; from both morphological and functional view points, into complicated and varied life processes regarding gene, protein, cell organelle, cell, tissue, and organism functions in animals while keeping in mind the differences in biomechanisms among species. We try to provide superior educational opportunities based on

research and integrate this into a comprehensive body of knowledge.

Subcourse: Integrated Structural Biosciences Subcourse: Integrated Functional Biosciences

Course: Veterinary Environmental Sciences

We aim to maintain and improve quality of the life environment and the health of livestock, pets, and human beings from the veterinary science point of view. To achieve this goal, we educate and conduct research into harmful factors in terms of (1) their action mechanisms, influences and controls on the molecular, cellular, organismal, and group levels, (2) their relation to food safety, and (3) their analysis and evaluation using advanced techniques. In this course, all units required for graduation can be taken by English lectures.

Subcourse: Bioenvironmental Sciences Subcourse: Infectious Diseases Control

Course: Veterinary Clinical Sciences

We aim to maintain the highest educational and research standards on the organismal, cellular, and molecular levels regarding (1) the latest diagnosis, treatment and prevention methods for animal diseases and (2) the etiopathogenesis and pathema of animal diseases or production difficulties caused by environmental changes.

Subcourse: Advances Pathobiology Subcourse: Advanced Clinical Medicine

See our webpage for detail https://www.upc-osaka.ac.jp/new-univ/en-

research/admissions/veterinary_science/>



Summary of Employment

CLASS OF 2019

CLASS OF 2020

Number of Respondents 42

Number of Respondents

Type of Employment Accepted

• • • • • • • • • • • • • • • • • • • •	-
Employment	Number of Graduates
Small Animal Practice	20
Large Animal Practice	3
Local Government	5
Federal Government	0
Private Company	8
National Research Center	0
Others	6
Total	42

Type of Employment Accepted

35

• • • • • • • • • • • • • • • • • • • •	•
Employment	Number of Graduates
Small Animal Practice	19
Large Animal Practice	1
Local Government	4
Federal Government	1
Private Company	8
National Research Center	0
Others	2
Total	35

Type of Advanced Education Positions Accepted

Position	Number of graduates
Ph.D. in Osaka Pref.	3
Univ.	
Ph.D. in Other Vet.	1
School	
Ph.D. in Medical	2
School	
Total	6

Type of Advanced Education Positions Accepted

Position	Number of graduates
Ph.D. in Osaka Pref.	2
Univ.	
Ph.D. in Other Vet.	0
School	
Ph.D. in Medical	0
School	
Total	2

Doctoral Theses from 2021 to 2022

Author	Title of the thesis	Supervisor	
2022			
Le Quoc Phong	Detection and characterization of extended-spectrum β-lactamase (ESBL)-producing <i>Escherichia coli</i> isolated from retail raw foods and children with diarrhea in Khanh Hoa province, Vietnam	S. Yamasaki	
Goutham B Manjunath	Effects of piperine, an active ingredient of white pepper, on growth, virulence expression and biofilm formation of <i>Vibrio cholerae</i>	S. Yamasaki	
Alam Jahagir	Ephrin-B1 and EphB4 as novel markers for steroidogenic cells in naturally cycling mouse ovary and adrenal gland	K. Ogawa	
Mayu Tsurutani	Development of a novel propagation method for lung tissue-resident macrophages and analyses on properties of the propagated lung macrophages	K. Ogawa	
Kosuke Mitani	Studies on quality of life-improving as an indicator of therapeutic effect, and isolation of cells with high therapeutic potency in dogs	K. Sugiura	
Masaya Tsukamoto	Studies on generation of footprint-free and high-quality canine induced pluripotent stem cells and differentiation toward definitive endoderm	K. Sugiura	
Yuki Wakabayashi	Isolation and characterization of Staphylococcus argenteus strains from retail foods and slaughterhouses in Japan	M. Miyake	
Yuu Shimizu	Molecular epidemiological survey of intestinal protozoan parasites in cattle and study for prevention of the infectious diseases in the farms	M. Matsubayashi	
Hiroo Kanai	Clinical applications of endoscopic surgery in dogs	K. Sasai	
Shizuka Konishi	Analyses of genetic and retinal lesions in Ccdc85c knockout rats: a rat model of genetic hydrocephalus	M. Kuwamura	
Mari Okamoto	Studies on renal injury caused by cisplatin administration and its prevention in dogs	H. Akiyoshi	
	2021		
Hiroki Matsumoto	Establishment of the experimental infection model for post-weaning diarrhea by Enterotoxigenic Escherichia coli and development of a prevent mixed feed against its desease.	M. Mukamoto	
AKM Azharul Islam	The cytotoxicity and mechanism of Clostridium perfringens NetB toxin.	M. Mukamoto	
Kazuya Takehana	Developmment of bone metabolic evaluation method and convenient detection assay for elephant endotheliotropic herpesvirus viremia in young captive Asian elephants (Elephas maximus)	N. Yamagishi	
Machi Atarashi	Pathological studies on the modulation of chronic liver diseases by dietary iron overload using rat experimental models	J. Yamate	
Miwa Kondo	Study of the hepatocarcinogenic mode of action of the synthetic insecticide permethrin in mice and its extrapolation to humans	T. Okada	
Yasunori Tsujimoto	Study on the application of new technologies in in vitro fertilization for the conservation of felines	K. Sugiura	

Doctoral Theses from 2019 to 2021

Author	Title of the thesis	Supervisor	
	2021		
Shuhei Matsumoto	In vitro and in vivo antimicrobial effects of cefiderocol, a novel siderophore cephalosporin	S. Yamasaki	
Yuta Ukai	Study of antioxidant of mitochondria and antifungal resistance by activation of fungal Yap1 transcription factor	S. Yamasaki	
Dao Nguyen Thi Anh	Studies on prevalence, serotype, antimicrobial resistance and clonal relationship of <i>Salmonella</i> in foods, waters and humans in Ho Chi Minh City, Vietnam	S. Yamasaki	
Kentaro Okuno	Studies on molecular epidemiology of Shiga toxin-producing <i>Escherichia coli</i> (STEC) isolated from Argentina and Thailand, and effect of lactic acid producing bacteria on growth inhibition and bactericidal activity for STEC	S. Yamasaki	
Yasumasa Iimori	Preparation by in-body tissue architecture and application of sheet-like biomaterials in dogs	H. Akiyoshi	
	2020		
Nobuo Arai	Molecular epidemiological study utilizing whole-genome sequence data for <i>Salmonella enterica</i> serovar Typhimurium and its monophasic variant isolated from food animals in Japan	S. Yamasaki	
Shoichiro Yukawa	Survey of Salmonella contamination on canine foods and treats in Japan	T. Hasegawa	
Sherwin I. Camba	Salmonella contamination in layer farm: The consequence of rodent infestation	K. Sasai	
Fletcher Del Valle	Molecular and pathologic characterization of avian adenovirus isolated from the oviducts of laying hens in eastern Japan	K. Sasai	
Mizuki Kuramochi	Pathological studies on characteristics of macrophages and damage- associated molecular patterns (DAMPs) in thioacetamide-induced rat liver injury	J. Yamate	
Tharanga Ramanayake Mudiyanselage	Generation of molecular-targeting peptides for selective inhibition of the interaction between CTLA-4 and B7 in the dog: a new immune checkpoint inhibitor for cancer therapy	K. Sugiura	
2019			
Tatsuhiro Yamaguchi	Generation of visualizing mice of type I collagen-producing cells and application on renal fibrosis	J. Yamate	
Rahman Nahid	Pathogenesis of D-galactosamine-induced rat liver failure with special emphasis on macrophages and myofibroblasts	J. Yamate	
W.W.P.N. Weerakoon	Blood concentrations of testicular and metabolic hormones and biochemical parameters differed in Japanese Black beef bulls with normal versus abnormal semen	N. Kawate	

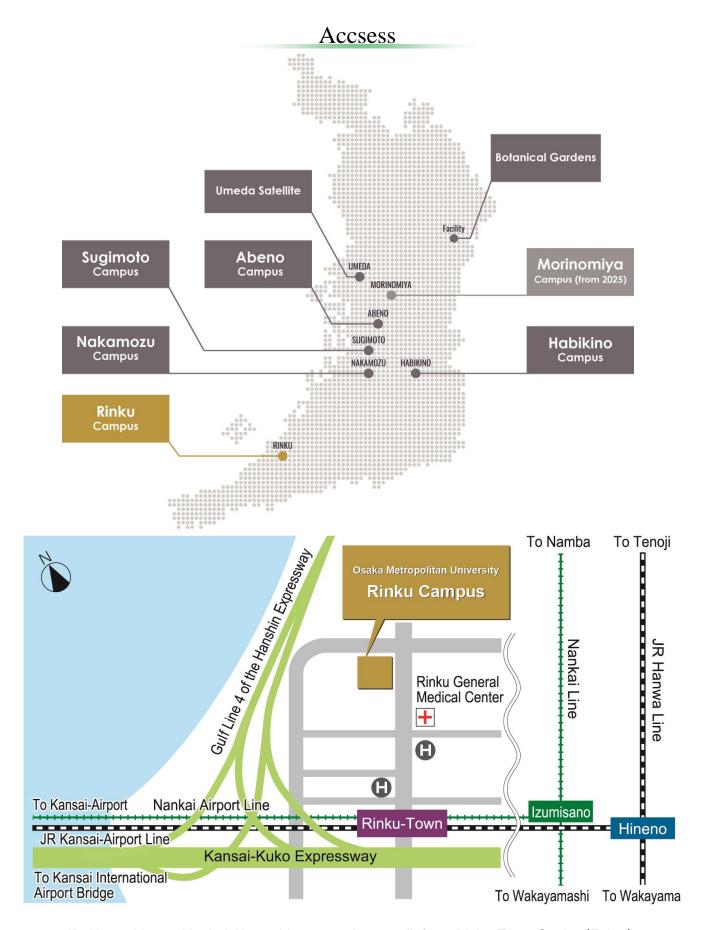
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JR Airport Line or Nankai Airport Line: a 6-minute walk from Rinku-Town Station (Exit 3)

