# Osaka Metropolitan University Graduate School of Veterinary Science, Department of Veterinary Science, in Rinku Campus (2024-2025)





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Directory Page 33-34 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

### Welcome

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. Norio Yamagishi The Dean of the Graduate School of Veterinary Science



Dr. Mitsuaki Moriyama 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

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 education system, Naniwa-Daigaku new 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 products, (3) the improvement 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 for Animals			
Integrated Structural Biosciences			
Integrated Functional Biosciences			
Veterinary Environmental Sciences			
<b>Bioenvironmental Sciences</b>			
Infectious Diseases Control			
Veterinary Clinical Sciences			
Advanced Pathobiology			
Advanced Clinical Medicine			

### Laboratory of Veterinary Anatomy

#### Research Interest (T. Nakajima):

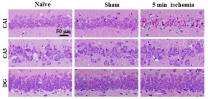
T. Nakajima studies the molecular and biochemical mechanisms in the ischemic brain using a rat model of global cerebral ischemia, induced by occlusion of the common carotid and vertebral arteries. The rat model of global cerebral ischemia has been widely used for studying the pathophysiology of the hypoxic-ischemic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

- Inoue M, Tanida T, Kondo T, Takenaka S, Nakajima T. Oxygen-glucose deprivation-induced glial cell reactivity in the rat primary neuron-glia co-culture. J Vet Med Sci. 2023 Aug 1;85(8):799-808. doi: 10.1292/jyms.23-0175. Epub 2023 Jul 6.
- Nakajima T, Tanaka Y, Takahashi Y, Kondo T, Takenaka S. The expression and phosphorylation of SMAD3 protein in microglia and astrocytes of the rat hippocampus after transient global cerebral ischemia. J Chem Neuroanat. 2022 Nov;125:102146. doi: 10.1016/j.jchemneu.2022.102146. Epub 2022 Aug 25.
- 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. 2021. Apr;113:101941. doi: 10. 1016/j.jchemneu. 2021. 101941. Epub 2021 Mar 9.
- 4. Nakajima T, Hata R, Kunieda Y, Kondo T. Distribution of Smad mRNA and proteins in the rat brain. J Chem Neuroanat. 2018. 90:11-39.
- Nakajima T, Hata R, Kondo T, Takenaka S. Proteomic analysis of the hippocampus in naïve and ischemicpreconditioned rat. J. Neurol. Sci. 2015. 358:158-1716.
   Nakajima T, Yanagihara M, Nishii H.Temporal and regional patterns of Smad activation in the rat hippocampus following global ischemia. J. Neurol. Sci., 2014. 337:25-37.
- Nakajima T, Ochi S, Oda C, Ishii M, Ogawa K. Ischemic preconditioning attenuates of ischemiainduced degradation of spectrin and tau: implications for ischemic tolerance. Neurol. Sci. 2011. 32:229-239.



Histology of the rat hippocampal CA1 region after global cerebral ischemia (J. Neurol. Sci., 2014. ).

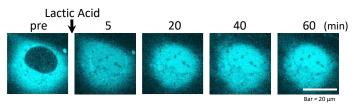
Associate Professor Lecturer Takayuki Nakajima Takashi Tanida

#### 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 and SAFB1. 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, neuroendocrinology, live-cell imaging, metabolism, transcription

Publications:

- 1. Tanida T. 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
- Tanida T, Matsuda KI, Uemura T, Yamaguchi T, Hashimoto T, Kawata M, Tanaka M. Subcellular dynamics of estrogen-related receptors involved in transrepression through interactions with scaffold attachment factor B1. Histochem Cell Biol. 156(3):239–251, 2021
- Tanida T, Matsuda KI, Tanaka M. Novel metabolic system for lactic acid via LRPGC1/ERRγ signaling pathway. FASEB J. 34(10):13239–13256, 2020
- 4. Tanida T, Matsuda KI, Yamada S, Kawata M, Tanaka M. 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. Tanida T, Matsuda KI, Yamada S, Hashimoto T, Kawata M. Estrogen-related receptor  $\beta$  reduces the subnuclear mobility of estrogen receptor  $\alpha$  and suppresses estrogen-dependent cellular function. J Biol Chem. 290(19):12332–12345, 2015



Confocal living-cell imaging showing nuclear translocation of LRPGC1, a lactic acid-responsive protein, following stimulation with lactic acid (Tanida et al., FASEB J. 2020).

#### **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.

#### **Publications:**

- **Izawa T**, Travlos GS, Cortes RA, Clayton NP, Sills RC, Pandiri AR. Absence of increased susceptibility to 1. acetaminophen-induced liver injury in a diet induced NAFLD
- mouse model. Toxicol Pathol 51(3):112–125, 2023. **Tanaka M**, Fujikawa R, Sekiguchi T, Hernandez J, Johnson 2 OT, Tanaka D, Kumafuji K, Serikawa T, Trung HH, Hattori K, Mashimo T, **Kuwamura M**, Gestwicki JE, Kuramoto T. A missense mutation in the Hspa8 gene encoding heat shock cognate protein 70 causes neuroaxonal dystrophy in rats. Front Neurosci. 2023.(in press) Hasan MM, Konishi S, **Tanaka M**, **Izawa** T, Yamate J,
- 3 Kuwamura M. Disrupted neurogenesis, gliogenesis and ependymogenesis in the *Ccdc85c* knockout hydrocephalus model. Cells Dev. 175: 203858, 2023 knockout rat for
- Takami Y, **Tanaka** M, Morita M, Maruno T, Anai N, Sudo T, Kezuka C, **Izawa T**, Yamate J, **Kuwamura M**. Pleural mesothelioma in a California sea lion (*Zalophus californianus*). 4 J Vet Med Sci. 85:1030–1033, 2023.
- Fujiwara S, Izawa T, Mori M, Atarashi M, Yamate J, Kuwamura M. Dietary iron overload enhances Western diet 5. induced hepatic inflammation and alters lipid metabolism in rats sharing similarity with human DIOS. Sci Rep 12:21414, 2022.
- Hassan MM, Konishi S, Tanaka M, Izawa T, Yamate J. Kuwamura M. Expression o CCDC85C, a causative protein 6. for hydrocephalus, and intermediate filament proteins during
- ventricle development in rats. Exp Anim 71(1):100–108, 2022. 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. 7.
- 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. Kuwamura M, Tanimura S, Hasegawa Y, Hoshiai R,
- 9. Moriyama Y, Tanaka M, Takenaka S, Nagayoshi H, Izawa T,

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

Mitsuru Kuwamura Takeshi Izawa

Miyuu Tanaka

#### **Keywords:**

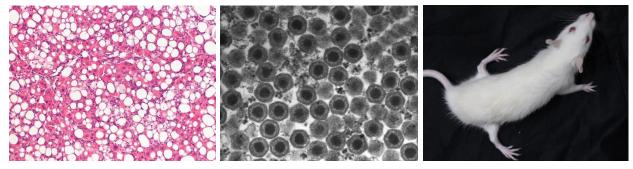
Professor

Associate Professor Associate Professor

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

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 10. 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, 11. 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.
- 12. 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.
- 13. 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. 14.
- Rahman N, Pervin M, Kuramochi M, Karim MR, Izawa T, Kuwamura M, Yamate J. M1-/M2-macrophage polarization-15. based 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,
- 16. Kuwamura M. Expression of Ccdc85C, a causative protein for murine hydrocephalus, in the mammary gland tumors of dogs. Histol Histopathol 32:397–403, 2017.
- 17. 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.



#### Laboratory of Laboratory Animal Science

Professor Lecturer

Tomohiro Kondo

#### **Research Interest:**

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, Preterm infant, Renal Development

#### **Publications:**

- 1. Inoue M, Tanida T, Kondo T, Takenaka S, Nakajima T. Oxygen-glucose deprivation-induced glial cell reactivity in the rat primary neuron-glia co-culture. J Vet Med Sci., 85(8): 799-808, 2023.
- 2. Ogawa S, Yana T, Kondo T, Okada T. Novel intrauterine growth retardation model: effects of maternal subtotal nephrectomy on neonates. J Vet Med Sci., 84(9): 1261-1264, 2022.
- 3. Nakajima T, Tanaka Y, Takahashi Y, Kondo T, Takenaka S. The expression and phosphorylation of SMAD3 protein in microglia and astrocytes of the rat hippocampus after transient global cerebral ischemia. J Chem Neuroanat., 125: 10214, 2022.
- 4. 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.

- T. Kondo research work focuses on the development, 5. 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.
  - 6. 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.
  - 7. 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.
  - 8. 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.
  - 9. 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.
  - 10. 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.

#### 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**

Professor

Associate Professor

#### Laboratory of Integrative Physiology

#### **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, all-trans retinoic acid, lysophospholipid, amyloid  $\beta$ , 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. Takano-Kawabe K, Matoba K, Nakamura N, Moriyama M. Low density lipoprotein receptor-related protein 2 expression and function in cultured astrocytes and microglia. *Neurochem. Res.*, 49: 199-211 (2024)
- **2. Takano-Kawabe K,** Izumo T, Minamihata T, **Moriyama M.** All-trans retinoic acid increased transglutaminase 2 expressions in BV-2 cells and cultured astrocytes. *Curr. Mol. Pharmacol.*, in press.
- 3. Minamihata T, **Takano K**, Nakamura Y, Seto R, **Moriyama M**. Increase in cellular lysophosphatidylserine content exacerbates inflammatory responses in LPS-activated microglia. *Neurochem*. *Res.*,47: 2602-2616 (2022)
- **4. 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)

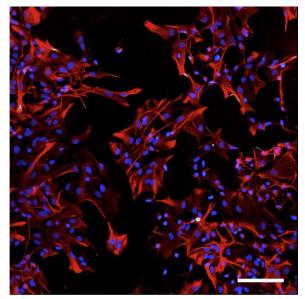
5. Saheki T. Moriyama M, Funahashi A, Kuroda E. AGC2 (Citrin) deficiency-From recognition of the disease till construction of therapeutic procedures. *Biomolecules*. 10 (8) E1100. (2020)

Mitsuaki Moriyama

Katsura Takano

- 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)
- 7. 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)
- 8. 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)
- **9. 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)
- 10.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)
- 11. 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 lipopolysaccharide-stimulated rat astrocytes partially via the GPR30-mediated pathway. *Int. J. Inflam*, 8496973 (2018)

Our cultured astrocytes: GFAP immunostaining with DAPI



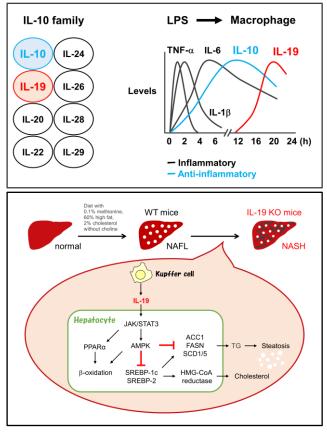
### Laboratory of Prophylactic Pharmacology

Professor Associate Professor

Yasu-Taka Azuma Kazuhiro Nishiyama

#### Azuma Y.T.

I am working to elucidate anti-inflammatory mechanisms using inflammation models in various organs. I apply research methods using pharmacological, pathological, immunological, and genetic approaches. In particular, I am focusing on studies of organ linkage.

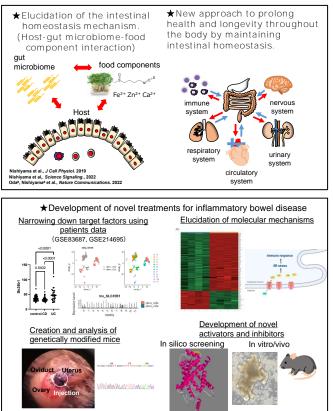


For more information:

- IL-19 gene-deficient mice promote liver fibrosis via enhanced TGF-β signaling, and the interleukin-19-CCL2 axis is important in the direction of liver fibrosis. Biomedicines. 2023;11(7):2064.
- IL-19 contributes to the development of nonalcoholic steatohepatitis by altering lipid metabolism. Cells. 2021;10(12):3513.
- The role of IL-19 in contact hypersensitivity. Biol. Pharma. Bull. 2018; 41(2):182-9.
- IL-19 contributes as a protective factor in experimental Th2-mediated colitis. Naunyn Schmiedebergs Arch. Pharmacol. 2017;390(3):261-8.
- IL-19 reduces inflammation in chemically induced experimental colitis. Int. Immunopharmacol. 2015;29(2):468-75.
- IL-19 protects mice from innate-mediated colonic inflammation. Inflamm. Bowel Dis. 2010;16(6):1017-28.

Nishiyama K.

My research goals are to elucidate the intestinal homeostasis mechanism from the perspective of interactions between the host, gut microbiome, and food components. I am aiming for a new approach to maintain health and longevity throughout the body by maintaining intestinal homeostasis.



For more information:

- Knockout of Purinergic P2Y<sub>6</sub> Receptor Fails to Improve Liver Injury and Inflammation in Non-Alcoholic Steatohepatitis. International Journal of Molecular Sciences 24, 3800. (2023)
- Myocardial TRPC6-mediated Zn<sup>2+</sup> influx induces beneficial positive inotropy through β-adrenoceptors. Nature Communications. 13, 6374. (2022).
- Redox-dependent internalization of purinergic P2Y<sub>6</sub> receptor limits colitis progression. Science Signaling. 15(716):eabj0644 (2022)
- Ibudilast attenuates doxorubicin-induced cytotoxicity by suppressing formation of TRPC3-Nox2 protein complex.
   British Journal of Pharmacology.176(18):3723-3738.
   (2019)
- Chronic kidney disease after 5/6 nephrectomy disturbs the intestinal microbiota and alters intestinal motility. Journal of Cellular Physiology. 234(5):6667-78. (2019)

### Laboratory of Animal Behavioral Sciences

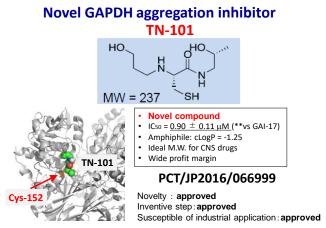
Associate Professor Hidemitsu Nakajima

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 <u>a novel inhibitor of GAPDH aggregation with some PCT-patents</u> as described in the right panel. These projects are going up with techniques of molecular biology, cell biology and GAPDH-mutant-geneticallymodified animals established by our labs using cuttingedge genome edition procedures. Additionally, we aim to develop novel animal-models of Brain Amyloidosis using a wide variety of animal behavioral tests.

#### **Selected Publications:**

\* Itakura M, <u>Nakajima H\*</u>, et al. (2023) Glyceraldehyde-3-phosphate dehydrogenase regulates activation of c-Jun N-terminal kinase under oxidative stress. **BBRC.** 657, 1-7

\* Nakajima H\*,. et al. (2017) GAPDH aggregation causes mitochondrial dysfunction during oxidative stress-induced cell death. JBC. 292(11), 4727-42
\* Kubo T, Nakajima H\*, 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 aggregates accelerate amyloid- $\beta$  amyloidogenesis in Alzheimer disease. **JBC**. 290(43), 26072-87.

\* <u>Nakajima H</u>\*, et al. (2015) Nuclear-translocated glyceraldehyde-3-phosphate dehydrogenase promotes poly(ADP-ribose) polymerase-1 activation during oxidative/nitrosative stress in stroke. **JBC**. 290(23), 14493-503.

\* <u>Nakajima H</u>\*, et al. (2007) The active site cysteine of the proapoptotic protein glyceraldehyde-3phosphate dehydrogenase is essential in oxidative stress-induced aggregation and cell death. **JBC**. 282(36), 26562-74. **The most cited paper.** 

#### **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 implications of its impairment for various diseases. To achieve these goals, various modern molecular biological technologies, including 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.
- Satomi, E., Ueda, M., Katahira, J., Hieda, M. The SUN1 splicing variants SUN1\_888 and SUN1\_916 differentially regulate nucleolar structure. *Genes to Cells*, 25: 730-740, 2020.
- Katahira, J., Ohmae, T., Yasugi, M., Sasaki, R., Itoh, Y., Kohda, T., Hieda, M., Yokota-Hirai, M., Okamoto, T., Miyamoto, Y. Nsp14 of SARS-CoV-2 inhibits mRNA processing and nuclear export by targeting the nuclear cap-binding complex. Nucleic Acids Research, 51: 7602-7618, 2023

Associate Professor Jun Katahira Associate Professor 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 implicated in the progression of fibrosis, threatening quality of life. the patients' То elucidate the pathophysiology of liver fibrosis, my research focuses on the following areas: 1) Understanding the mechanism of structural and functional interactions between hepatocytes and those non-parenchymal cells, and 2) Establishing new anti-fibrosis therapies by targeting key molecules involved in chronic liver failure.

#### **Keywords:**

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

#### **Publications:**

- 1. Okina Y, **Sato-Matsubara M**, Kido Y, Urushima H, *et al.* Nitric oxide derived from cytoglobin-deficient hepatic stellate cells causes suppression of cytochrome c oxidase activity in hepatocytes. *Antioxid Redox Signal.* 2023;38:463-479.
- 2. Hoang TH, **Sato-Matsubara M**, Yuasa H, Matsubara T, *et al.* Cancer cells produce liver metastasis via gap formation in sinusoidal endothelial cells through proinflammatory paracrine mechanisms. *Sci Adv.* 2022;8:eabo5525.
- Dong MP, Thuy LTT, Hoang DV, Sato-Matsubara M, et al. Soluble immune checkpoint protein CD27 is a novel prognostic biomarker of HCC development in HCV-SVR patients. Am J Pathol. 2022;192:1379-1396.
- Okina Y, Sato-Matsubara M, Matsubara T, Daikoku A, *et al.* TGF-β1-driven reduction of cytoglobin leads to oxidative DNA damage in stellate cells during nonalcoholic steatohepatitis. *J Hepatol.* 73:882-895, 2020.

### **Bioenvironmental Sciences**

#### Laboratory of Toxicology

Associate Professor Assistant Professor Kazuhiko Nishimura Hiroshi Nakagawa

#### **Research Interest:**

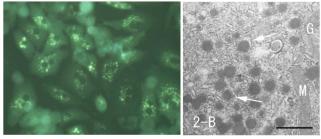
**K. Nishimura:** Erythropoiesis is indispensable to recovery of the anemia. However, the mechanism of erythropoiesis has many questions. I study the mechanism of erythropoietin production and the search of the substance which promotes erythropoietin production.

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

#### **Publications:**

**1.** K. Nishimura, S. Iitaka, T. Sakaki, K. Tsuji, A. Yoshimoto, M. A. Haque, **H. Nakagawa**. Effect of long-term treatment with trivalent chromium on erythropoietin production in HepG2 cells. Arch Biochem Biophys, 752, 109872, 2023.

**2. K. Nishimura**, N. Kiriyama, K. Ogawa, R. Inoue, M. A. Haque, **H. Nakagawa**. Effect of pentavalent inorganic arsenic salt on erythropoietin production and autophagy induction. **Arch Biochem Biophys**, 734, 109487, 2023

**3. K. Nishimura,** S. Iitaka, **H. Nakagawa. Arch Biochem Biophys,** Effect of trivalent chromium on erythropoietin production and the prevention of insulin resistance in HepG2 cells. 708, 108960, 2021.

**4.** 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.

**5. 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, 54-59, 2020.

**6. K. Nishimura,** K. Goto, **H. Nakagawa.** Effect of erythropoietin production induced by hypoxia on autophagy in HepG2 cells. Biochem Biophys Res Commun, 495, 1317-1321, 2018

**7. 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

**8.** 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, 895-900, 2017

**9.** 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. **PLoS Negl.** Novel Characteristics of Trypanosoma brucei Guanosine 5'-monophosphate Reductase Distinct from Host Animals. **Trop. Dis.**, 10, e0004339.

**10.** 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, 435-441, 2015

**11.** 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, 1300-1309, 2015

**12.** 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

**13. 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

#### **Research Interest:**

**M. Miyake**'s research focus is to clarify the mechanism how the pathogenic bacteria respond to the environmental changes and exert their virulence during infection, and how I could prevent the infectious disease by disturbing the molecular interaction between the bacteria and environments. For this end, I am looking into the pathogens' biology using microbiological, biochemical, immunological, and genetic procedures.

#### **Keywords:**

*Escherichia coli, Clostridia*, sporulation, germination, virulence factors, toxins.

#### **Publications:**

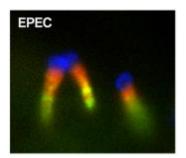
- Yasugi M, Nakagama U, Kaku N, Nitahara Y, Hatanaka N, Yamasaki S, Kido Y. Characteristics of epitope dominance pattern and cross-variant neutralization in 16 SARS-CoV-2 mRNA vaccine sera. 5. Vaccine 41:6248-54, 2023.
- Yasugi M, Hatoya S, Motooka D, Kondo D, Akiyoshi H, Horie M, Nakamura S, Shimada T. Genetic and phenotypic analyses of *mcr*-harboring extended-spectrum beeta-lactamase-producing *Escherichia coli* isolates from companion dogs and cats in Japan. Vet. 6. Microbiol. 280:109695, 2023.
- 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. 7. 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. High-

**M. Yasugi**'s research interest is One Health and the research goal is to control pet and wildlife zoonoses. For this end, I conduct studies on (1) the role of companion animals on cross-species transmission of antimicrobial-resistant bacteria and (2) development of countermeasures involving vaccine and therapeutics against emerging, re-emerging, and neglected viral zoonoses.

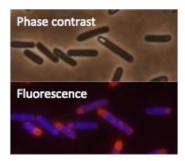
**Keywords:** One Health, zoonosis, antimicrobialresistant bacteria, rabies, SARS-CoV-2, Mpox, companion animal, wildlife, transmission, vaccine

resolution linear epitope mapping of the receptor binding domain of SARS-CoV-2 spike protein in COVID-19 mRNA vaccine recipients. **Microbiol. Spectr.**, 9:e00965-21, 2021.

- 5. 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.
- 6. 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.



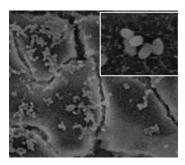
Immunohistochemistry of Zonula occludens-1 (ZO-1) recruitment at the sites of infection by enteropathogenic *E. coli* (EPEC) in HeLa cells. Green, ZO-1; blue, bacterial DNA; red, F-actin. For detail, refer to **Infect. Immun**. 75: 565-573, 2007.



Professor

Associate Professor

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.

Masami Miyake Mayo Yasugi

### 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 7. companion animals, genetical surveys are conducted. From the viewpoints, my interests include development of molecular tools (using chemical biology, or genome or 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 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 utilizing it to develop tolerance inducible methods for allergens to treat allergic patients.

#### **Keywords:**

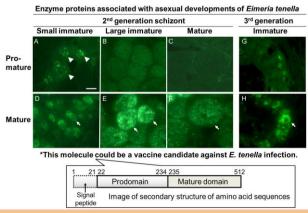
Allergy, *Cryptosporidium*, *Eimeria*, Mucosal immunity, 9. Liposome, Parasite, Pathogenicity, Tolerance, Vaccine

#### **Publications:**

- 1. **M Matsubayashi**\*, M Kinoshita, S Tsuchida, A Kobayashi, N Tamura, T Shibahara, Y Kido, A Kaneko, K Sasai, K Ushida. Experimental evaluation of pathogenicity and acquired immunity of *Eimeria* species, *E. uekii* and *E. raichoi*, infecting Japanese rock ptarmigans in a subspecies of the birds. **Int J Parasitol Parasites Wildl**. 2023. 22:167-174.
- 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. 86:102478.
- 3. M Matsubayashi\*, I Teramoto, I Urakami, J Naohara, K Sasai, Y Kido, A Kaneko. Evaluation of *Cryptosporidium parvum* oocyst inactivation following exposure to ultraviolet light-emitting diodes by in vitro excystation and dye staining assays. **Parasitol Int.** 2022. 88:102557.
- 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. Sato, E.D. Hartuti, D.K. Inaoka, T. Sakura, E. Amalia, M. Nagahama, Y. Yoshioka, N. Tsuji, T. Nozaki, K. Kita, S. Harada, M. Matsubayashi, T. Shiba. Structural and biochemical features of *Eimeria tenella* dihydroorotate dehydrogenase, a potential drug target. Genes (Basel), 11(12): 1468. 2020.

Professor Assistant Professor Makoto Matsubayashi Tadashi Iwasaki

- 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.
- 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.
- 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: 174-179. 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: 1639-1642, 2020.
- **11. 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.
- 12. 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), 10:29. 2019.



### Laboratory of Veterinary Epidemiology

#### **Research Interest:**

Botulism is caused by botulinum neurotoxins (BoNTs) 7. produced by *Clostridium botulinum* and is the most potent toxins to humans and animals. BoNTs are divided antigenically distinct types (BoNT/A-G) but cause a common and characteristic flaccid paralysis. BoNTs are also 8. being used for clinical applications and as drug delivery vehicles. We are trying to elucidate the mechanism of BoNT, including translocation and enzymatic activity to broaden the clinical applications of BoNT. We are also developing human antibody products, not only for BoNT, but also 9. diphtheria toxin. In addition, we focuses on causative Clostridium botulinum and toxin of botulism in livestock.

#### **Keywords:**

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

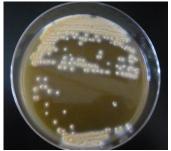
#### **Publications:**

- 1. R. Kaji, A. Miyashiro, N. Seto, T. Furumoto, T. Takeuchi, R. Miyamoto, T. Kohda, Y. Izumi, S. Kozaki. A Pilot Study of A2NTX, a Novel Low-Molecular-Weight Neurotoxin Derived from Subtype A2 for Post-Stroke Lower Limb Spasticity: Comparison with OnabotulinumtoxinA. Toxins. 14, 739. 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-molecularsubtype A2, in comparison with subtype A1 toxins. Toxins. 13, 824, 2021
- AKM A. Islam, M. Nakatani, T. Nakajima, T. Kohda, 3. 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.
- T. Kohda, K. Tsukamoto, Y. Torii, S. Kozaki, M. 5. Mukamoto. Translocation domain of botulinum neurotoxin A subtype 2 potently induces entry into neuronal cells. Microbiol. Immunol., 64: 502-511, 2020.
- T. Kohda, Y. Torii, H. Nakajima. Experimental 6. 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.

Lecturer

Tomoko Kohda

- T. Kohda, K. Nakamura, K. Hosomi, S. Kozaki and M. Mukamoto. Characterization of the functional activity of botulinum neurotoxin subtype B6. Microbiol. Immunol., 61: 482-489, 2017.
- 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.
- 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.
- weight neurotoxin derived from botulinum neurotoxin 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.

#### **Research Interest:**

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

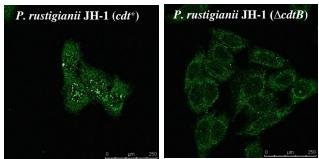
Keywords: food safety, rapid diagnosis, antimicrobial resistance, zoonosis, molecular epidemiology, bacterial protein toxin, pathogenic *E. coli, E. albertii*, STEC/EHEC, cytolethal distending toxin, *Campylobacter*, pathogenesis
toxigenic *Vibrio cholerae* strains and other bacterial pathogens. *Let. Appl. Microbiol.*, 74: 472-281, 2022.
N. Hatanaka, B. Xu, Y. Yamashita, H. Kawakami, M. Yasugi and S. Yamasaki<sup>\*</sup>. ShellCoat, a calcinated

#### **Publications:**

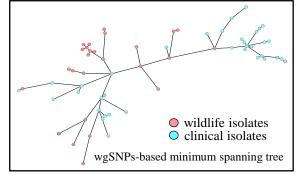
- B. Xu, N. Hatanaka, S. P. Awasthi, A. Hinenoya and S. Yamasaki<sup>\*</sup>. Seasonality of detection rate of *Escherichia albertii* in wild raccoons (*Procyon lotor*) in Osaka, Japan. J. Vet. Med. Sci., in press.
- B. Xu, N. Hatanaka, S. P. Awasthi, K. Takehira, A. Hinenoya and S. Yamasaki<sup>\*</sup>. Cefixime-tellurite-deoxycholate tryptic soy broth (CTD-TSB), a selective enrichment medium, for enhancing isolation of *Escherichia albertii* from wild raccoon fecal samples. J. Appl. Microbiol., 134: 1xad123, 2023.
- J. Hassan<sup>#</sup>, S.P. Awasthi<sup>#</sup>, N. Hatanaka, P.H. Hoang, A. Nagita, A. Hinenoya, S.M. Faruque and S. Yamasaki<sup>\*</sup>. Presence of functionally active cytolethal distending toxin genes on a conjugative plasmid in a clinical isolate of *Providencia rustigianii*. Infect. Immun., 91(6): 1-13, 2023. (#equally contributed.)
- X. Zeng<sup>#</sup>, A. Hinenoya<sup>#</sup>, Z. Guan, F. Xu, J. Lin<sup>\*</sup>. Critical role of the RpoE stress response pathway in polymyxin resistance of *Escherichia coli*. J Antimicrob Chemother., 78(3):732-746, 2023. (<sup>#</sup>equally contributed).
- A. Naka<sup>#</sup>, A. Hinenoya<sup>#</sup>, S.P. Awasthi and S. Yamasaki<sup>\*</sup>. Isolation and characterization of *Escherichia albertii* from wild and safeguarded animals in Okayama prefecture and its prefectural borders, Japan. J. Vet. Med. Sci., 84(9): 1299-1306, 2022. (#equally contributed.)
- A. Hinenoya, H. Wang, E. M. Patrick, X. Zeng, L. Cao, X.-P. Li, R. L. Lindsey, B. Gillespie, Q. He, S. Yamasaki\* and Jun Lin\*. Longitudinal surveillance and comparative characterization of *Escherichia albertii* in wild raccoons in the United States. Microbiol. Res., 262: 127109, 2022.
- 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<sup>\*</sup>. Detection, isolation, and molecular characterization of *Escherichia albertii* from wild birds in west Japan. Jpn. J. Infect. Dis., 75: 156-163, 2022.

Professor Associate Professor Associate Professor Specially Appointed Associate Professor Shinji Yamasaki Atsushi Hinenoya Noritoshi Hatanaka Sharda Prasad Awasthi

- N. Hatanaka, S.P. Awasthi, B. Xu, H. Goda, H. Kawata, I. Horiuchi, M. Yasugi and S. Yamasaki<sup>\*</sup>. Comparative evaluation of chlorous acid and sodium hypochlorite activity against SARS-CoV-2. Access Microbiol., 4: 000354, 2022.
- G. B. Manjunath, S. P. Awasthi, M. S. H. Zahid, N. Hatanaka, A. Hinenoya, E. Iwaoka, S. Aoki, T. Ramamurthy and S. Yamasaki<sup>\*</sup>. Piperine, an active ingredient of white pepper suppresses growth of toxigenic *Vibrio cholerae* strains and other bacterial pathogens. *Let. Appl. Microbiol.*, 74: 472-281, 2022.
- N. Hatanaka, B. Xu, Y. Yamashita, H. Kawakami, M. Yasugi and S. Yamasaki<sup>\*</sup>. ShellCoat, a calcinated calcium solution, effectively inactivate SARS-CoV-2. *Biocont. Sci.*, 27(1): 54-56, 2022.
- N. Hatanaka, M. Yasugi, T. Sato M. Mukamoto and S. Yamasaki<sup>\*</sup>. Hypochlorous acid solution is a potent antiviral agent against SARS-CoV-2. *J. Appl. Microbiol.*, 132: 1496-1502, 2022.
- K. Ishimoto<sup>#</sup>, N. Hatanaka<sup>#</sup>, S. Otani<sup>#</sup>, S. Maeda, B. Xu, M. Yasugi, M. Suzuki, S. Nakagawa<sup>\*</sup> and S. Yamasaki<sup>\*</sup>. Tea crude extracts effectively inactivate severe acute respiratory syndrome coronavirus 2. *Let. Appl. Microbiol.*, 74: 2-7, 2022. (#equally contributed.)
- N. Hatanaka, B. Xu, M. Yasugi, H. Morino, H. Tagishi, T. Miura, T. Shibata and S. Yamasaki<sup>\*</sup>. Chlorine dioxide is a more potent antiviral agent against SARS-CoV-2 than sodium hypochlorite. *J. Hosp. Infect.*, 118: 20-26, 2021



**DNA damage induced by PrCDT on CHO cells.** (Hassan *et al.*, Infect. Immun., 91: 1-13, 2023)



Phylogenetic analysis of Escherichia albertii isolates.

### Laboratory of Veterinary Microbiology

Professor Assistant Professor Masayuki Horie Mai Kishimoto

#### **Research Interest**

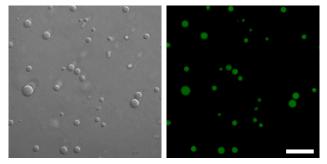
M. Horie is interested in a wide range of virology, from basic research to applied research. For basic research, we are focusing on 1) diversity and evolution of modern and ancient RNA viruses, 2) coevolution of RNA viruses and their hosts, and 3) replication mechanisms of RNA viruses that replicate in the nucleus. M. Kishimoto is interested in 1) detection and characterization of potential zoonotic viruses and 2) their transmission mechanisms. We are researching the above topics by combining wet experiments and dry analyses. 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.

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

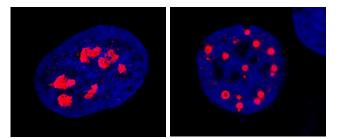
#### Selected publications

- 1. Garcia BCB, Mukai Y, Tomonaga K, **Horie M**. The hidden diversity of ancient bornaviral sequences from X and P genes in vertebrate genomes. Virus Evol. 9: vead038. 2023.
- Hirai Y, Horie M. Nyamanini Virus Nucleoprotein and Phosphoprotein Organize Viral Inclusion Bodies That Associate with Host Biomolecular Condensates in the Nucleus. Int J Mol Sci. 24: 6550. 2023.
- 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.
- Horie, M. Identification of a novel filovirus in a common lancehead (Bothrops atrox (Linnaeus, 1758)). J Vet Med Sci. 2021.
- 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.
- 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.
- Kawasaki, J., Kojima, S., Mukai, Y., Tomonaga, K. and Horie, M. 100-My history of bornavirus infections hidden in vertebrate genomes. Proc Natl Acad Sci U S A 118. 2021.

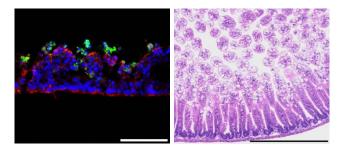
- **8. Kishimoto M**, Kajihara M, and Tabata K et al. Isolation and characterization of distinct rotavirus A in bat and rodent hosts. J Virol. 97(1): e0145522. 2023.
- **9. Kishimoto M**, Hang'ombe BM, and Hall WW et al. *Mastomys natalensis* is a possible natural rodent reservoir for encephalomyocarditis virus. J Gen Virol. 102(3): 001564. 2021.



*In vitro* liquid droplets formed by recombinant Borna disease virus (BoDV) P protein and GFP-tagged BoDV P protein. Scale bar, 10  $\mu$ m. (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)



**Intestinal epithelium** infected with bat rotavirus A (left, immunostaining of human small intestinal epithelial model; right, H&E staining of small intestine of suckling mice). Green, rotavirus antigens; Blue, DAPI; Red . Scale bar, 100 μm and 500 μm. (Kishimoto et al., J Virol. 2023)

### Laboratory of Cell Pathobiology

Professor Lecturer Shingo Hatoya

#### **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) generation of canine and feline induced pluripotent stem cells (iPS cells) from adult cells for regenerative veterinary medicine, 2) establishment of canine and feline embryonic stem cells (ES cells) from blastocyst, 3) development of canine and feline in vitro fertilization techniques, and 4) dendritic cell based tumor immunotherapy.

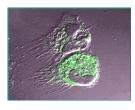
#### **Keywords:**

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

#### **Publications**

- Tsukamoto M, Kimura K, Yoshida T, Tanaka M, Kuwamura M, Ayabe T, Ishihara G, Watanabe K, Okada M, Iijima M, Nakanishi M, Akutsu H, Sugiura K, Hatoya S. Generation of canine induced pluripotent stem cells under feeder-free conditions using Sendai virus vector encoding six canine reprogramming factors. Stem Cell Reports. 19(1):141-157, 2024.
- 2. Kanegi R, **Hatoya S**, Kimura K, Yodoe K, Nishimura T, Sugiura K, Kawate N, Inaba T. Generation, characterization, and differentiation of induced pluripotent stem-like cells in the domestic cat. **J Reprod Dev.** 69(6):317-327, 2023
- Watanabe S, Takagi A, Yuba E, Kojima C, Dei N, Matsumoto A, Tanikawa J, Kawamura T, De Silva NH, Izawa T, Akazawa T, Kanegi R, Hatoya S, Inaba T, Sugiura K. In vivo transfection of cytokine genes into tumor cells using a synthetic vehicle promotes antitumor immune responses in a visceral tumor model. FASEB J. 37(11):e23228, 2023.

- Tsukamoto M, Kimura K, Yoshida T, Sugiura K, Hatoya S. Canine induced pluripotent stem cells efficiently differentiate into definitive endoderm in 3D cell culture conditions using high-dose activin A. Regen Ther. 21:502-510, 2022.
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- Watanabe S, Yuba E, Akazawa T, Wijewardana V, Kakihara Y, Azuma A, Hagimori K, Kanegi R, Hatoya S, Inoue N, Inaba T, Sugiura K. Potent adjuvant effect elicited for tumor immunotherapy by a liposome conjugated pH-sensitive polymer and dendritic celltargeting Toll-like-receptor ligand. Vaccine. 40(10):1448-1457, 2022.
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- 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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- Kimura K, Tsukamoto M, Tanaka M, Kuwamura M, Ohtaka M, Nishimura K, Nakanishi M, Sugiura K, Hatoya S. Efficient reprogramming of canine peripheral blood mononuclear cells into induced pluripotent stem cells. Stem Cells Dev 30(2):79-90, 2021



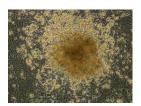
Canine Dendritic cells, generated from monocytes



Canine ES cells isolated in our labs



Canine iPS cells isolated in our labs



Feline iPS cells isolated in our labs

#### **Research Interest:**

1) In our laboratory, we are researching the causes and testing methods for tumors in companion animals, especially breast cancer in cats, with a focus on the following two genes. We also aim to apply the obtained results to clinical practice.

(1) Expression of Special AT-rich sequence Binding Protein 1, SATB1 using cultured feline breast cancer cell lines, functional analysis using RNA interference, and trial of molecular target therapy

(2) Functional analysis of the tumor suppressor gene BH3like Motif Containing, Cell Death Inducer, BLID using cultured feline breast cancer cell lines and trial of molecular complementary therapy

#### **Publications:**

1. S. Noguchi, A. Hattori, N. Tanimoto, R. Nishida, K. Hirano, Y. Wada, **S. Matsuyama**, T. Shimada, and H. Akiyoshi. Establishing cell lines for canine tonsillar and non-tonsullae oral squamous cell carcinoma and identifying characteristics associated with malignancy. **Tissue Cell.**, 67:101408, 2020.

2. S. Noguchi, R. Ogusu, Y. Wada, **S. Matsuyama**, and T. Mori. PTEN, A Target of Microrna-374b, Contributes to the Radiosensitivity of Canine Oral Melanoma Cells. **Int. J. Mol. Sci.**, 20: 4631, 2019.

3. Y. Wada, S. Noguchi, Y. Nishiyama, **S. Matsuyama**, T. Mori, M. Igase, T. Mizuno, S. Shimamura, and T. Shimada. MicroRNA-205 enhances the radiosensitivity of canine oral melanoma cells by inhibiting E2F1. **Jap. J. Vet. Res.**, 67: 151-161, 2019.

4. H. Tamada, K. Takemoto, M. Tominaga, N. Kawate, M. Takahashi, S. Hatoya, **S. Matsuyama**, T. Inaba, and T.

Associate Professor Associate Professor Satoshi Matsuyama

2) 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 tumorrelated gene expression in various companion animal tumors.

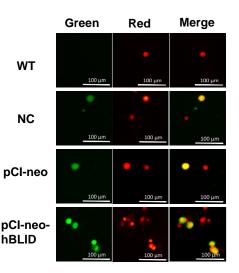
#### **Keywords:**

Oncogene, Tumor suppressor gene, DNA repair, oxydative damages, tumorigenesis, adaptive response, Companion Animals.

Sawada. Expression and localization of epidermal growth factor, transforming growth factor- $\alpha$  and epidermal growth factor receptor in the canine testis. J. Reprod. Dev., 62: 59, 2016

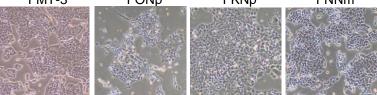
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Matsuyama, and K. Kubo. Abundance of BER-related proteins depends on cell proliferation status and the presence of DNA polymerase β. J. Radiat. Res., 56: 607, 2015.
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Transfection of expression vector containing human cell death inducer, BLID to feline mammary tumor cell line (FMT-3). Green; Early Apoptotic cells, Red; Late Apoptotic cells or Necrotic cells.

# Feline mammary tumor cell lines FMT-3 FONp FKNp FNNm



Professor Associate Professor Noritoshi Kawate Keisuke Koyama

#### **Research Interest:**

We are studying on reproductive phenomena and their 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 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:**

- Age–related changes in circulating INSL3 concentrations and their associations with ovarian conditions in Japanese Black beef cattle. Wimalarathne HDA, Nakamura Y, Ishizaka K, Silva BDK, Sasakura K, Shimada M, Kibushi M, Sakase M, Kawate N\*. Theriogenology. 211:97–104. 2023.
- Predicting nuclear maturation speed of oocytes from Japanese Black beef heifers through non-invasive observations during IVM: An attempt using machine learning algorithms. Ho TC, Kawate N, Koyama K\*. Theriogenology. 209:235–242. 2023.
- Parity affects the relationship between the insemination–ovulation interval and the conception rate in lactating dairy cows. Koyama K\*, Kubo T, Koyama T, Takahashi Y. Reprod Domest Anim. 58:895–902 2023.
- Insulin–like peptide 3 in domestic animals with normal and abnormal reproductive functions, in comparison to rodents and humans. Kawate N. Reprod Med Biol. 21:e12485. 2022.
- Quantitative analyses of insulin–like peptide 3 and sex steroid hormones in dominant follicles and corpora lutea during the estrus cycle and in follicular cysts in beef heifers. Wimalarathne HAD, Wako H, Kawate N\*. J Reprod Dev. 68:324–329. 2022.

- 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. 68:30–37. 2021.
- 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.
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- Hirayama H, Sakumoto R, Koyama K, Yasuhara T, Hasegawa T, Inaba R, et al. Expression of C-C motif chemokines and their receptors in bovine placentomes at spontaneous and induced parturition. J Reprod Dev. 66: 49–55. 2020.
- Hannan MA, Murase H, Sato F, Tsogtgerel M, Kawate N, Nambo Y. Age related and seasonal changes of plasma concentrations of insulin–like peptide 3 and testosterone from birth to early–puberty in Thoroughbred male horses. Theriogenology. 132: 212–217. 2019.
- 15. Yasuhara T, Koyama K, Sakumoto R, Fujii T, Naito A, Moriyasu S, et al. Enhanced glucocorticoid exposure facilitates the expression of genes involved in prostaglandin and estrogen syntheses in bovine placentomes at induced parturition. Theriogenology. 139: 1–7. 2019.

# Advanced Clinical Medicine

### Laboratory of Veterinary Internal Medicine

Professor Associate Professor Associate Professor Kazumi Sasai Hiroyuki Tani Masaru Furuya

#### **Research Interest:**

common research theme include 1) Our development of novel detection and prevention tools infectious disease, especially for zoonosis in 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 and for epidemiological studies of zoonosis in wild animals. Moreover, he is involved in the study of host defense mechanism against chicken coccidiosis using 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

#### **Publications:**

- M. Matsubayashi\*, M. Kinoshita, S. Tsuchida, A. Kobayashi, N. Tamura, T. Shibahara, Y. Kido, A. Kaneko, K. Sasai, K. Ushida. Experimental evaluation of pathogenicity and acquired immunity of *Eimeria* species, *E. uekii* and *E. raichoi*, infecting Japanese rock ptarmigans in a subspecies of the birds. Int J Parasitol Parasites Wildl. 22:167-174. 2023.
- M. Matsubayashi\*, S. Tsuchida, A. Kobayashi, T. Shibahara, I. Teramoto, Y. Kido, A. Kaneko, H. Nakamura, M. Hasegawa, **K. Sasai**, K. Ushida. Evaluation of the host specificity of *Eimeria uekii* and Eimeria raichoi for Japanese rock ptarmigans by oocyst transfer to taxonomically related birds. Parasitol Res. 122(8):1795-1800. 2023.
- S. Takami, T. Shibahara, K. Sasai, M. Matsubayashi\*. Occurrence, Histopathological Findings, and Molecular Identification of Pathogenic *Eimeria* Infections in Rabbits (*Mammalia*: Lagomorpha) in Japan. Acta Parasitol. 68(2):453-457. 2023.

- T. Ito, T. Tanaka, I. Kiyatake, T. Izawa, M. Furuya\*, K. Sasai. Contrast-enhanced computed tomography and cross-sectional anatomy of the trunk in the brownbanded bamboo shark (*Chiloscyllium punctatum*). Anat Histol Embryol. 52(3):437-447. 2023.
- K. Katsui, S. Takami, K. Ohashi, H. Otsuka, S. Uni, T. Shibahara, K. Sasai, M. Matsubayashi\*. Molecular identification of Eimeria species in liver and feces of naturally infected rabbits in Japan. Parasitol Res. 121(9):2733-2738. 2022.
- 6. M. Matsubayashi\*, I. Teramoto, I. Urakami, J. Naohara, **K. Sasai**, Y. Kido, A. Kaneko.
- 7. Evaluation of *Cryptosporidium parvum* oocyst inactivation following exposure to ultraviolet light-emitting diodes by in vitro excystation and dye staining assays. **Parasitol Int**. 88:102557. 2022.
- 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.
- 10. F. Ekawasti, K. Kitagawa, H. Domae, AH. Wardhana, J. Nagasawa, T. Shibahara, M, Tokoro, K. Sasai, M. Matsubayashi\*. Phylogenetic characterization of *Isospora jaracimrmani* oocysts from a veiled chameleon (family *Chamaeleonidae; Chamaeleo calyptratus*) reared at a zoo in Ishikawa, Japan. J Vet Med Sci. 83(8):1240-1243. 2021.
- 11. DV. Fletcher\*, SI. Camba, DV. Umali, K. Sasai, K. Shirota, H. Katoh. Biochemical Properties and Cell Culture Affinity of Fowl Adenovirus Serotype-4 Strains Isolated from the Oviducts of Layer Hens in East Japan. JWPR. 11(2) 241 251. 2021.
- 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.
- 13. H. Kanai, M. Furuya\*, K. Yoneji, K. Hagiwara, A. Nukaya, M. Kondo, T. Aso, A. Fujii, K. Sasai. Canine idiopathic chylothorax: Anatomic characterization of the pre- and postoperative thoracic duct using computed tomography lymphography. Vet Radiol Ultrasound. 62(4):429-436. 2021.
- 14. 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.

#### **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

#### **Publications**

- Nishida H, Kakimoto R, Noguchi S, Kanegi R, 1. Shimamura S, Tanaka T, Fumimoto T, Nishibata K, Fujiwara H, Akiyoshi H. A feline spinal dermoid cyst treated with surgical intervention. J Vet Med Sci. 2024 Jan 26;86(1):116-119.
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- 5. Yasugi M, Hatoya S, Motooka D, Kondo D, Akiyoshi H, Horie M, Nakamura S, Shimada T. Genetic and phenotypic analyses of mcr-harboring extendedspectrum β-lactamase-producing Escherichia coli isolates from companion dogs and cats in Japan.Vet Microbiol. 2023 May;280:109695.
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Professor

- Yoshizaki K, Nishida H, Tabata Y, Jo JI, Nakase I, 7. Akiyoshi H. Controlled release of canine MSCderived extracellular vesicles by cationized gelatin hydrogels. Regen Ther. 2022 Dec 10;22:1-6.
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- 9. Tanaka T, Wada Y, Noguchi S, Nishida H, Akiyoshi H\*. Contrast-enhanced CT features of pyloric lesions in 17 dogs: Case series. Vet Radiol Ultrasound. 2023 Mar;64(2):262-270.
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- 11. Yamazaki H, Tanaka T, Nishida H, Hatoya S, Akiyoshi H. Hypoxia-targeting therapy for intestinal T-cell lymphoma in dogs: Preclinical study using 3D in vitro models. Vet Comp Oncol. 2023 Mar:21(1):12-19.
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- Akiyoshi H. SLUG is upregulated and induces epithelial mesenchymal transition in canine oral squamous cell carcinoma. Vet Comp Oncol. 2022 Mar;20(1):134-141.
- 15. Kurokawa S, Tanaka T, Yamazaki H, Noguchi S, Wada Y, Nishida H, Akiyoshi H. Comparing the CT and MRI findings for canine primary hepatocellular lesions. Vet Rec. 2022 Jun;190(11).
- 16. Tanaka T, Noguchi S, Wada Y, Nishida H, Akiyoshi H\*. Preliminary study of CT features of intermediateand high-grade alimentary lymphoma and adenocarcinoma in cats. J Feline Med Surg. 2022 Oct;24(10):1065-1071.
- 17. Tanaka T, Yamazaki H, Ashida K, Iimori Y, Mie K, Nishida H, Akiyoshi H\*. Computed tomography may detect liver infiltration of canine diffuse hepatic lymphoma. Vet Med Sci. 2021 Nov;7(6):2172-2177.
- 18. Wada Y, Yamazaki H, Tanaka M, Kaneguchi A, Tanaka T, Akiyoshi H, Noguchi S. Radiotherapyinduced tumor lysis syndrome in a dog with thymoma. J Vet Med Sci. 2021 Aug 26;83(8):1290-1294.

### Laboratory of Veterinary Advanced Diagnosis and Treatment

Professor	Takashi Hasegawa
Associate Professor	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

**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 swimmerpuppy 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**:

- 1. **Hasegawa, T.**, Amako, H., Hagi. K., **Tomihari, M.** and Sawa, S. Effective emulsification formulation dodecahydrosqualene (squalene) by adding polyvinyl alcohol in a tear substitute containing sodium hyaluronate and squalene. **Anim. Eye Res.** 41: 15-21, 2022.
- Hagi, K., Hasegawa, T., Yamamoto, T., Tomihari, M., Fujimoto, Y., Sakamoto, Y. and Sawa, S. Corneal protective effects of novel tear substitutes containing sodium hyaluronate and dodecahydrosqualene, squalane, on a porcine dry eye model. J. Vet. Med. Sci. 84(1): 94-101, 2022.
- 3. **Tomihari, M**, Nobutoki Y, Nakajima N, Yanagawa M, Tagawa M, Hagiya K, Nomura T, Suwa Y, Suzuki H. Factors contributing to the swimmer puppy syndrome found in Labrador retrievers. **BMC Vet Res.** 18(1):120., 2022.

#### **Publications**:

- 4. Worden, N. J., Ash, K. J., Ordway, N. R., Miller, M., Mann, K. A., VanDeventer, G. M., Valenzano, D. M., Kayano, M., **Tomihari, M.** and Hayashi, K. Effect of stem positioning on biomechanical performance of a novel cementless short-stem canine total hip implant. **Vet. Comp. Orthop. Traumatol.** online ahead of print, 2021.
- 5. Liu, M., Ji, S., Kondoh, D., Galon, E. M., Li, J., Tomihari, M., Yanagawa, M., Tagawa, M., Adachi, M., Asada, M., Igarashi, I., Iguchi, A. and Xuan, X. Tafenoquine is a promising drug candidate for the treatment of babesiosis. Antimicrob. Agents Chemother. 65(7): e0020421, 2021.
- Tagawa, M., Shimbo, G., Tomihari, M., Yanagawa, M., Watanabe, K. I., Horiuchi, N., Kobayashi, Y. and Miyahara, K. Intramedullary spinal nephroblastoma in a mixed breed dog. J.Vet. Med. Sci. 82(7): 917-921, 2020.
- Tagawa, M., Tambo, N., Maezawa, M., Tomihari, M., Watanabe, K. I., Inokuma, H. and Miyahara, K. Quantitative analysis of the BRAF V595E mutation in plasma cell-free DNA from dogs with urothelial carcinoma. PLoS One. 15(4): e0232365, 2020.
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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.
- Yukawa, S., Uchida, I., Tamura, Y., Ohshima, S. and Hasegawa, T. Characterization of antibiotic resistance of Salmonella isolated from dog treats in Japan. Epidemiol. Infect. 147: e102, 2019.
- 11. **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.

#### **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 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.

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.

S. Kim has focused on research on analyzing breathing pattern in cow, using infrared camera and artificial intelligence. In particular, we are planning to evaluate respiratory disease and stress through the breathing pattern.

Keywords: artificial intelligence, breathing pattern, circulating biomarker, clinical biochemistry, infrared camera, innate immunity, mucosal vaccine, stem cell, stress

#### **Publications:**

- Sato R, Kim S., Okada S, (...), Steiner A. Case report: Abdominal hernia repair using a surgical wire and an autologous omental graft in a Japanese Black calf. Frontiers Vet. Sci. 10: 1119034, 2023 Inoue Y, Mogi W, Naik MV, **Kim S**, (...), Sato R.
- 2. Repair of a calcaneal fracture with a combination of internal and external fixation in a calf. J. Vet. Med. Sci. 85: 739-742, 2023 **Kim S**, Naik MV, Kirino Y, (...), Hidaka, Y. A
- 3. retrospective analysis for criteria of surgical intervention in Japanese Black calves with respiratory
- Hintervention in Japanese Black carves with respiratory signs caused by perinatal rib fracture. J. Vet. Med. Sci. 85: 40-43, 2023 Hamano T, Jibiki Y, **Ishikawa S**, Hobo S. An evolutionary medicine perspective on the cetacean pulmonary immune system The first identification of SD and LDD in the better and on the cetacean 4 of SP-D and LBP in the bottlenose dolphin (Tursiops truncatus). Resp. Physiol. Neurobiol. 312: 104038, 2023
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- Ijiri M, Ishikawa S, Hobo S. Distribution of 6. enrofloxacin within the bronchoalveolar region of healthy pigs. J. Vet. Med. Sci. 85: 296-300, 2023 Takehana K, Adachi M, Ishikawa S, Yamagishi N.
- 7 The serum activities of alkaline phosphatase isoenzymes measured using two approved methods in zoo-managed Asian elephants (*Elephas maximus*). J. Vet. Med. Sci. 85: 232-235, 2023
- Takehana K, Adachi M, Ishikawa S, Yamagishi N. Case report: Measuring the circulating bone metabolic 8. markers of two Asian elephant (*Elephas maximus*) Calves Around Weaning. Jpn. J. Zoo Wildlife Med. 28: 115-120, 2023
- 9. Takehana K, Adachi M, Ishikawa S, Yamagishi N.

Professor	Norio Yamagishi
Associate Professor	Shingo Ishikawa
Assistant Professor	Sueun Kim

Agarose gel electrophoresis pattern of serum creatine kinase and lactate dehydrogenase isoenzymes in zoomanaged Asian elephants (Elephas maximus). J. Vet.

- Med. Sci. 85: 578-583, 2023 10. Murata D, Ishikawa S, Sunaga T, Saito Y, Sogawa T, Nakayama K, Hobo S, Hatazoe T. Osteochondral regeneration of the femoral medial condyle by using a scaffold-free 3D construct of synovial membrane-derived mesenchymal stem cells in horses. BMC Vet Res. 53: https://doi.org/10.1186/s12917-021-03126-y, 2022
- 11. Yamagishi N, Kawashima C. Prepartum measurement of serum biomarkers reflecting osteoclastic and osteoblastic bone metabolism for predicting the risk of milk fever in dairy cows. J Dairy Res. 89: 44-52, 2022
- 12. Ishikawa S, Miyazawa M, Tanaka C, Uesawa R, Nishizawa J, Uemura R, Kobayashi I, Hobo S. Interferon gamma, lipopolysaccharide, and modified-live viral vaccines stimulation alter the mRNA expression of tumor necrosis factor  $\alpha$ , inducible nitric oxide synthase, and interferon  $\beta$  in bovine alveolar macrophages. Vet Immunol Immunopathol. 4:244:110378 2022
- 13. Kim S, Hidaka Y. Breathing pattern analysis in cattle using infrared thermography and computer vision. Animals 11: 207, pp. 1-11. 2021
- 14. Naik MV, Kirino Y, Uemura R, Kim S, Inoue Y, Hidaka Y. Radiographic diagnosis and surgical management for successful outcomes for osteochondrosis in japanese black calves. J Vet Med Sci. 83:151-157. 2021
- 15. Hatai H, Hatazoe T, Seo H, Tozaki T, Ishikawa S, Miyoshi N, Misumi K, Hobo S. Primary sinonasal malignant melanoma with systemic metastasis in a non-gray horse J Vet Diagn Invest. 33(2):379-383. 2021
- 16. Kawashima C, Kume S, Yamagishi N. Nutritional parameters in the blood of dams during late gestation and immediately after calving, in the umbilical vein at calving, and in the blood of calves immediately following birth in Holstein heifers pregnant with either Holstein or beef breed
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- Kizaki K, Kato-Kageyama T, Toji N, Koshi K, Sasaki K, 20. Yamagishi N, Ishiguro-Oonuma T, Takahashi T, Hashizume K. Gene expression profiles in bovine granulocytes reflect the aberration of liver functions. Anim Sci J. 91: e13324, 2020
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- Chiba A, Hatate K, Onomi R, Moriyama T, Goto A, 22. Yamagishi N. Agarose gel electrophoretic pattern of serum alkaline phosphatase isoenzymes in Holstein cows during lactation. Polish J Vet Sci. 23: 317-319, 2020
- Chiba A, Onomi R, Hatate K, Moriyama T, Goto A, Yamagishi N. Peripartum changes in serum activities of three major alkaline phosphatase isoenzymes in Holstein dairy cows. Polish J Vet Sci. 23: 457-459, 2020

Professor

Terumasa Shimada

#### **Research Interest:**

This laboratory aims to elucidate influence of human behavior and breeding environment to animal (companion animals, zoo animals and. so on) health.

**T. Shimada** has started to focus on the relationship among human behavior, breeding environment and animal health. Evaluation of physical condition of animals under various breeding environment has been started by clinical,

physiological and immunological parameters.

#### Keywords:

human behavior, breeding environment, animal health,

#### **Publications:**

- Sakai K, Kanegi R, Nabetani T, Tanaka T, Shimamura S, Shimada T, Sugiura K, Hatoya S. Mesenteric lymph node abscesses due to Escherichia coli in a cat. Vet Med Sci. 2022 Jul;8(4):1611-1616.
- 2. Sakai K, Hatoya S, Furuya M, Nabetani T, Kanegi R, Shimamura S, Tani H, **Shimada T**. Retrospective evaluation of nimustine use in the treatment of feline lymphoma. Vet Med Sci. 2022 Jan; 8(1): 3–8.
- 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.
- Sakai K, Hatoya S, Furuya M, Shimamura S, Nabetani T, Tani H, Shimada T. Decreased serum zinc concentration in dogs with lymphocytic-plasmacytic enteritis, and its associations with disease severity and prognosis. J Vet Med Sci. 2020 Jun; 82(6): 759–763.
- Kuramochi M, Izawa T, Mori M, Shimamura S, Shimada T, Kuwamura M, Yamate J. Diffuse leiomyomatosis with circumferential thickening of the gastrointestinal wall, resembling human diffuse leiomyomatosis, in a young miniature dachshund. J Vet Med Sci. 82(2):139-142, 2020

#### **Research Theme**

The laboratory is engaged in research aimed at elucidating the pathogenesis of diseases and providing novel diagnostic methods in dogs and cats.

**S. Shimamura** focuses on the following research projects; 1) Development of new diagnostic techniques and treatments for canine and feline cardiac diseases.

2) Development of a stress evaluation method based on analysis of canine heart rate variability

K. Sakai focuses on the following studies;

 Pathological analysis of tumors occurring in dogs and cats
 Development of new diagnostic techniques and therapies for canine and feline tumors

3) Pathological analysis of canine and feline gastrointestinal **9.** diseases

#### **Keywords:**

immune response, intractable disease, cancer, cardiology, oncology, heart rate variability analysis

#### Publications:

- 1. Sakai K, Hatoya S, Furuya M, Nishida H, Kakimoto R, Noguchi S, Kanegi R, Shimamura S, Tanaka T, Fumimoto T, Nishibata K, Fujiwara H, Akiyoshi H. A feline spinal dermoid cyst treated with surgical intervention J Vet Med Sci. 2023
- Maeda S, Sakai K, Kaji K, Iio A, Nakazawa M, Motegi T, Yonezawa T, Momoi Y. Lapatinib as first-line treatment for muscle-invasive urothelial carcinoma in dogs. Sci Rep. 2022 Jan 13;12(1):4.
- Sakai K, Kanegi R, Nabetani T, Tanaka T, Shimamura S, Shimada T, Sugiura K, Hatoya S. Mesenteric lymph node abscesses due to Escherichia coli in a cat. Vet Med Sci. 2022 Jul;8(4):1611-1616.
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- Nabetani T, Kanegi R, Shimamura S, Tani H, Shimada T. Retrospective evaluation of nimustine use in the treatment of feline lymphoma. Vet Med Sci. 2022 Jan; 8(1): 3–8.
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- Morita C, Tanaka M, Noguchi S, Shimamura S, Wada Y, Izawa T, Yamate J, Kuwamura M. An aortic body carcinoma with sarcomatoid morphology and chondroid metaplasia in a French Bulldog. J Vet Med Sci. 2020 May; 82(5): 576–579.
- **9.** Sakai K, Hatoya S, Furuya M, Shimamura S, Nabetani T, Tani H, Shimada T. Decreased serum zinc concentration in dogs with lymphocytic-plasmacytic enteritis, and its associations with disease severity and prognosis. J Vet Med Sci. 2020 Jun; 82(6): 759–763.
- 10. Kuramochi M, Izawa T, Mori M, **Shimamura S**, Shimada T, Kuwamura M, Yamate J. Diffuse leiomyomatosis with circumferential thickening of the gastrointestinal wall, resembling human diffuse leiomyomatosis, in a young miniature dachshund. J Vet Med Sci. 82(2):139-142, 2020
- **11. Sakai K**, Maeda S, Saeki K, Yoshitake R, Goto-Koshino Y, Nakagawa T, Nishimura R, Yonezawa T, Matsuki N. *ErbB2* Copy Number Aberration in Canine Urothelial Carcinoma Detected by a Digital Polymerase Chain Reaction Assay. Vet Pathol. 57(1):56-65, 2020
- 12. Tsuboi M, **Sakai K**, Maeda S, Chambers JK, Yonezawa T, Matsuki N, Uchida K, Nakayama H. Assessment of HER2 Expression in Canine Urothelial Carcinoma of the Urinary Bladder. Vet Pathol. 56(3):369-376, 2019
- Wada Y, Noguchi S, Sasaki H, Taketomi A, Hamakawa M, Shimamura S, Shimada T. Prognostic significance of midline shift of the olfactory or frontal lobes of the brain in canine nasal carcinomas treated by palliative radiotherapy: a pilot study. J Vet Med Sci. 80(11):1724-1727, 2018
- 14. Shimamura S, Shiota Y, Takagi N, Habara T, Hirata S, Komai H, Nishimura S, Tani H, Shimada T. EBSTEIN ANOMALY IN THE TSUSHIMA LEOPARD CAT (PRIONAILURUS BENGALENSIS EUPTILURUS). J Zoo Wildl Med. 48(2):586-589, 2017

# Veterinary Medical Center

#### **Veterinary Medical Center**

Director Takashi Hasegawa

Specially Appointed Professor Gen Kato
Specially Appointed Professor Naoaki Matsuki
Specially Appointed Associate Professor Toshiyuki Tanaka
Specially Appointed Associate Professor Yuya Nakamoto
Specially Appointed Lecturer Tomoyo Nabetani
Specially Appointed Lecturer Shougo Hirata
Specially Appointed Lecturer Ryouji Kanegi
Specially Appointed Lecturer Akifumi Ito
Specially Appointed Lecturer Kakeru Tanaka
Specially Appointed Assistant Professor Kiyomi Hagi
Specially Appointed Assistant Professor Kengo Nagatani
Specially Appointed Assistant Professor Chihiro Ichida
Specially Appointed Assistant Professor Hana Tsuruta
Specially Appointed Assistant Professor Kazuhiro Maeda
Specially Appointed Assistant Professor
Yasunori Tsujimoto

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

Masaru Furuya

#### Soft tissue Surgery Service:

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

Director

Shougo Hirata

### Neurology and Orthopedic Surgery Service:

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

Director

Mizuki Tomihari

#### **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 treatme

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:

Director

Director

Akifumi Ito

**Diagnostic Imaging Service:** 

Toshiyuki Tnaka

#### Gastroenterology Service:



MRI

# Veterinary Medical Center

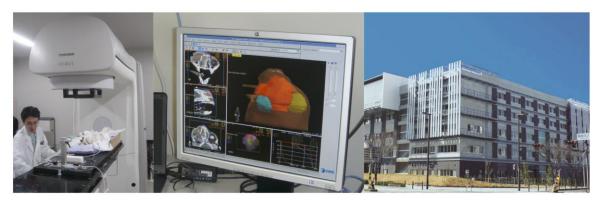
### Veterinary Medical Center

### 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)

## Education and Research Center for Experimental Animal Science

# Learning practical skills in conducting laboratory animal experiments

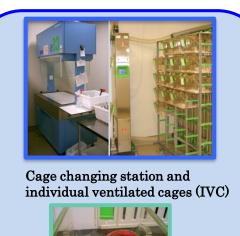
The Education and Research Center for Experimental Animal Science is established on the Rinku Campus as an inter-faculty core facility for conducting experimental animal research in the university.

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 of 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





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 we "intellectual property" accumulating to 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

The SVSOMU, as one of the 17 schools offering undergraduate veterinary education courses in Japan, provides a six-year educational program to foster students specializing in veterinary medicine and veterinary science. The curriculum of the undergraduate veterinary course consists of 13 liberal arts (26 credits) and 108 specialized subjects relating to veterinary science. 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

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 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 of the 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 products, (3) the improvement of livestock product 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.upcosaka.ac.jp/new-univ/enresearch/admissions/veterinary\_science/>

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# Summary of Employment

# CLASS OF 2021

Number of Respondents 43

### Type of Employment Accepted

Employment	Number of Graduates
Small Animal Practice	22
Large Animal Practice	3
Local Government	8
Federal Government	0
Private Company	5
National Research Center	0
Others	5
Total	43

### Type of Advanced Education Positions Accepted

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

# CLASS OF 2022

Number of Respondents 40

### Type of Employment Accepted

Employment	Number of Graduates
Small Animal Practice	14
Large Animal Practice	2
Local Government	5
Federal Government	1
Private Company	7
National Research Center	0
Others	11
Total	40

### Type of Advanced Education Positions Accepted

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

# Doctoral Theses from 2022 to 2024

Author	Title of the thesis	Supervisor	
2024			
Wimalarathne Hewage Dilhan Anuradha	Secretion of insulin-like peptide 3 in female cattle and expression of its receptor in oocyte and sperm	N. Kawate	
Youhei Fujimoto	Study on cultivation method of feline mesenchymal stem cells for enhancing therapeutic efficacy in inflammatory disorders	K. Sugiura	
Shunich Watanabe	Study of effective therapeutic strategies to enhance tumor specific immunity	K. Sugiura	
Kazuto Kimura	Development of methodology for canine iPSC generation, culture, and differentiation into red blood cells	S. Hatoya	
	2023		
Yasuko Yamazaki	Development and evaluation of simple, rapid, and accurate testing methods for animal infectious diseases	S. Yamasaki	
Bingting XuDevelopment of an Escherichia albertii selective enrichment broth and bacteriological characterization of E. albertii isolated from wild raccoons (Procyon lotor) in Osaka, Japan		S. Yamasaki	
Yohei Inai	Pathological studies on bleeding diathesis and modulation of acute liver injury by dietary iron overload using rat experimental models	M. Kuwamura	
Tomoki Minamihata	Studies in lysophospholipid-mediated regulation of glial inflammatory responses	M. Moriyama	
Eri Hamamura	Study of differential susceptibility to Mas-related G-protein coupled receptor X2-mediated allergy-like reactions	YT. Azuma	
Md. Mehedi Hasan	Pathological studies on the roles of CCDC85C protein in neurogenesis, gliogenesis, and ependymogenesis in the rat model of hydrocephalus	M. Kuwamura	
Shoji Ogawa	Development of newborn pups born from mothers with renal dysfunction: Production of intrauterine growth retardation (IUGR) model.	T. Okada	

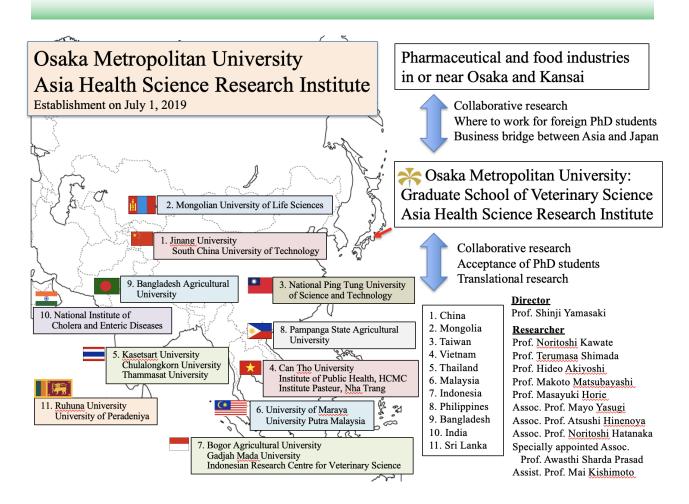
# Doctoral Theses from 2022 to 2024

Author	Title of the thesis	Supervisor
	2022	
Le Quoc Phong	Detection and characterization of extended-spectrum $\beta$ -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
Yasu-Taka Azuma	Studies to elucidate the pathophysiological role of interleukin-19	M. Moriyama

# Current and past PhD student

Name	Grade/ Graduation year	Laboratory	Nationality
WEN WEN	D4	Veterinary International Prevention of Epidemics	China
HSU YUANKAI	D4	Veterinary Surgery	Taiwan
CHANG YANLEI	D4	Veterinary International Prevention of Epidemics	China
WIMALARATHNE H. D. A	D4	Theriogenology	Sri Lanka
HAQUE MD ANAMUL	D4	Toxicology	Bangladesh
ELBASTAWESY ASMAA	D3	Veterinary International Prevention of Epidemics	Egypt
OBI OKECHUKWU	D3	Veterinary International Prevention of Epidemics	Nigeria
ΗΟ CΗΙΑΤΑΝG	D3	Theriogenology	Taiwan
ABOUOUF AHMED MOHA MED	D3	Veterinary International Prevention of Epidemics	Egypt
UNG SIVLIN	D3	Veterinary International Prevention of Epidemics	Cambodia
SANCHEZ JACOB ANDE RSON C	D2	Veterinary Microbiology	Philippines
NURE JANNAT	D2	Veterinary Pathology	Bangladesh
XU BINGTING	2023	Veterinary International Prevention of Epidemics	China
HASAN MD MEHEDI	2022	Veterinary Pathology	Bangladesh
ALAM JAHAGIR	2021	Veterinary Anatomy	Bangladesh
ISLAM AKM AZHARUL	2020	Veterinary Epidemiology	Bangladesh
DEL VALLE FLETCHER	2019	Veterinary Internal Medicine	Philippines
CAMBA SHERWIN	2019	Veterinary Internal Medicine	Philippines
THARANGA MADHUSHAN I RAMANAYAKE	2019	Cell Pathobiology	Sri Lanka
WANNIARACHCHIGE NI LMINI	2019	Theriogenology	Sri Lanka
RAHMAN NAHID	2019	Veterinary Pathology	Bangladesh

### **Collaboration Creation Research Center under Department of Veterinary Science**



Osaka Metropolitan University Research Center for Food Safety



**Food Security** 

#### **Purpose of Establishment**

In this century, concerns regarding the food safety and food security have escalated due to numerous incidents, directly impacting human health. This has led to significant public interest in "food safety."

Hence, in 2009, several investigators in Osaka Metropolitan University and related institutions have responded to this situation and united to establish a new research group. The research group was named "Research Center for Food Safety" (RCFS) and continued to analyze the mechanism of problems regarding food safety and to propose scientific ideas to solve the problems.

#### **Overview of Research Content**

Food Agronomy

The RCFS consists of two divisions focusing on microbiology and chemistry. Each division focuses on developing and improving methods for testing food poisoning causative agents, as well as devising methods for identifying the contamination sources of these agents.

#### **Research members**

Prof. Masami Miyake (Veterinary Science)
Prof. Shinji Yamasaki (Veterinary Science)
Prof. Shu Ihara (Science)
Assoc. Prof. Noritoshi Hatanaka (Veterinary Science)
Assoc. Prof. Hidenobu Hoshi (Sustainable Science)
Visiting Prof. Kazuo Hisa (Risk management)

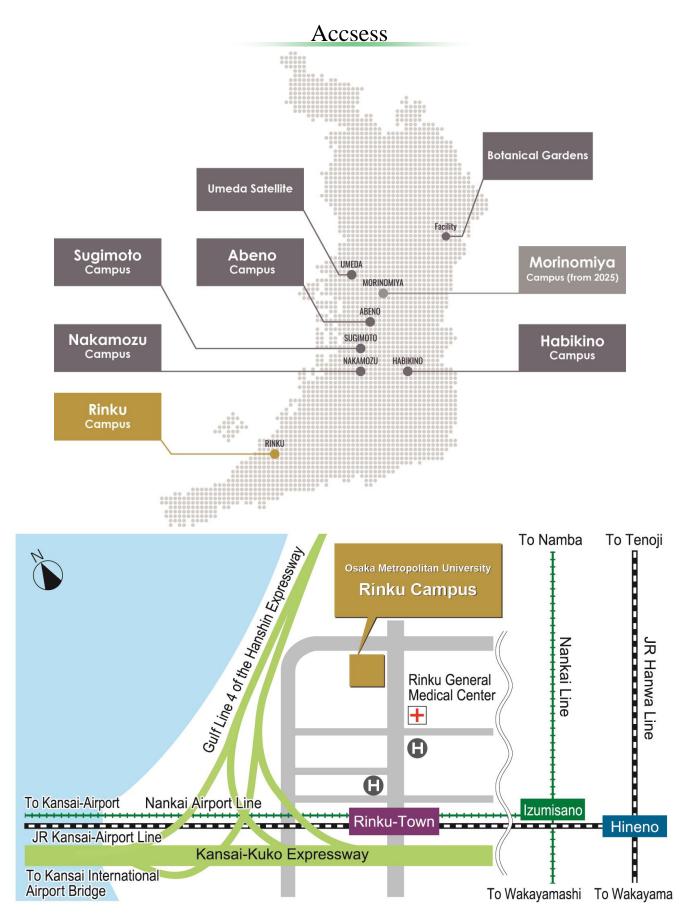
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JR Airport Line or Nankai Airport Line: a 6-minute walk from Rinku-Town Station (Exit 3)

