Laboratory Animal Facilities

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General Summary

The purpose of the Laboratory Animal Facilities (LAF) is to support *in vivo* research and to contribute to the development of basic and clinical medicine. In 2010, 173 researchers used the LAF. We undertake breeding of experimental animals and technically guide researchers in animal experimentation. In addition, we performed the following studies to develop basic medical sciences, including laboratory animal science.

Research Activities

Identification of a novel Col2a1 mutant mouse

In the RIKEN N-ethyl-N-nitrosourea (ENU) mutagenesis project, we identified a novel Col2a1 mutant mouse (termed M856). The M856 mouse has a missense mutation, c.4406A>C (p.Asp1469Ala), in the C-propeptide coding region of Col2a1 and in the position corresponding to human COL2A1 mutation (p.Asp1469His) responsible for platyspondylic dysplasia, Torrance type (PLSD-T). The M856 homozygote exhibits lethal skeletal dysplasias, including extremely short limbs, severe spondylar dysplasia, and severe hypoplasia of the pelvis. As expected, these defects were similar to those in patients with PLSD-T. The M856 mutant should serve as a good model to study PLSD-T.

Generation of Cant1 knockout mice

Desbuquois dysplasia is a severe skeletal dysplasia inherited in an autosomal recessive manner, characterized clinically by severe growth retardation, joint laxity, flat midface, and characteristic hand abnormalities. Recently, mutations in the gene that encodes for calcium-activated nucleotidase 1 (CANT1) have been identified in a subset of patients with Desbuquois dysplasia. CANT1 is an extracellular protein that functions as a nucleotide triphosphatase and diphosphatase. It preferentially hydrolyzes uridine diphosphate followed by guanidine diphosphate, uridine triphosphate, and ADP. To investigate the in vivo function of CANT1, we started to generate Cant1 knockout mice. By using the inverse polymerase chain reaction and rapid amplification of 5′-complementary DNA ends, we isolated Cant1 knockout embryonic stem cells from the Gene-Trap ES Library.

Establishment and characterization of strains originated from Japanese wild mice and Phodopus hamster

Our inbred strains derived from Japanese wild mice (*Mus musculus molossinus*) and *Phodopus* hamsters were maintained in this laboratory.

Japanese wild mice are classified as *M. m. molossinus* and originated from a natural intersubspecific hybrid between *Mus musculus castaneus* inhabiting southwest Asia and *Mus*

musculus musculus distributed in north Asia. The *molossinus* subspecies is an excellent source for improving laboratory mice, because it was suspected to be greatly different in gene constitution from common laboratory mice derived from the *Mus musculus domesticus* subspecies. We have established several new inbred strains based on *molossinus* mice captured in Osaka prefecture. These strains are being maintained in our laboratory, and new consomic strains based on these strains are being developed.

In collaboration with the Department of Molecular Biology, we developed 2 new mouse strains using our original *molossinus* inbred strain named MSKR. One is the congenic strain having knockout allele of *Oaz1* derived from the B6.129-*Oaz1*^{tm} to the MSKR background, and the other is a consomic strain that has chromosome 10 derived from the above-mentioned strain to the MSKR background. We have confirmed that these newly established strains are useful for researching genetic modifications in *Oaz1* knockout mice.

The *Phodopus* hamster is a small rodent that differs taxonomically from the Syrian hamster, which is the major laboratory hamster. We recently determined that this hamster is a good candidate for a new laboratory animal and have established an inbred strain. Furthermore, we continue to establish new inbred strains and congenic strains and to develop models of human diseases to research their biomedical characteristics.

The search of the novel atopic dermatitis therapeutic drug using NC/Nga inbred strain

The NC/Nga inbred strain is the current mouse model for atopic dermatitis. However, the onset rates of dermatitis differ among separate lines in each laboratory. The NC/Nga inbred strain maintained in our laboratory has an extremely severe dermatitis diathesis.

In collaboration with the Department of Tropical Medicine, we are using the NC/Nga mice to research new drugs for treating atopic dermatitis.

Publications

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