Research Center for Medical Sciences Laboratory Animal Facilities

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General Summary

The purpose of the Laboratory Animal Facilities is to support *in vivo* research and to contribute to the development of basic and clinical medicine. In 2015, 657 researchers were registered as users of the Laboratory Animal Facilities. We undertake breeding of experimental animals and provide technical guidance to researchers in animal experimentation. In addition, we performed the following studies to develop basic medical sciences, including laboratory animal science.

Research Activities

Studies of parasite-vector and parasite-host interactions of African trypanosomes
African trypanosomiasis is a deadly protozoan disease of humans and animals. The disease is caused by African trypanosomes, which are transmitted by tsetse flies (*Glossina* spp.). To adjust to the mammalian host and insect vector environments, the parasite has a complicated lifecycle involving developmental stages. The bloodstream forms are parasitized in the bloodstream of the vertebrate hosts. During blood feeding of tsetse, the bloodstream form is taken up and differentiates to the procyclic form in the midgut. Subsequently, procyclic forms migrates to the tsetse salivary gland or proboscis where they differentiate to epimastigote forms. Then, at the end of tsetse infection, the epimastigote form differentiates into the animal infective metacyclic form, which differentiates to the bloodstream form after being injected into vertebrate hosts. Although the cell differentiations between each lifecycle stage are considered promising targets for developing novel control measures against the disease, their molecular mechanisms have not been elucidated. Previously, protein tyrosine phosphatase 1 (PTP1) has been reported to be involved in the cell differentiation regulations of trypanosomatid parasites *Trypanosoma brucei* (bloodstream form to procyclic form) and *Trypanosoma cruzi* (epimastigote form to metacyclic form). Currently, we focus on the PTP1 of *Trypanosoma congolense,* the cause of animal African trypanosomiasis. Because all lifecycle-stage developments of *T. congolense* are reproducible *in vitro*, with the use of the parasite, more detailed biological functions of the protein could be studied. So far, the *T. congolense* PTP1 has been cloned, and its expression pattern and phosphatase activity were investigated with biochemical analyses. We are now studying the biological functions of the *T. congolense* PTP1, especially its roles in the regulation of cell differentiation.

Development of a novel immunological method of fecal occult blood testing for dogs and fecal occult blood trend in digestive diseases
With advances in veterinary medicine, the lives of companion animals, such as dogs and

cats, have been extended. On the other hand, neoplastic diseases have also been increasing, and the development of screening methods has become an urgent task. The fecal occult blood test (FOBT) is a method for detecting in feces a small amount of blood that is undetectable with the naked eye or under a microscope. The FOBT was originally developed as a screening test for alimentary canal tumors in human patients. However, the FOBT remains rarely used in veterinary medicine. In addition, little is known about its clinical significance, because the chemical FOBT is based on the peroxidase activity of hemoglobin. Thus, this chemical test had low sensitivity and specificity and was not suitable for dogs, which live in various environments today. We developed a novel FOBT test using laser nephelometric immunoassay for dogs and investigated its performance. We demonstrated that our immunological FOBT method is independent of a dog's diet. We also demonstrated that infection with a specific type of gastrointestinal parasite causes a significant increase of FOBT values in dogs and that this increase was significantly decreased with anthelmintic treatment. We are now evaluating cases of gastrointestinal cancer in dogs over time and investigating the diagnostic value of our FOBT method.

Preventing malaria by adjusting amino-acid intake

Preventive and therapeutic methods against malaria, a major parasitic disease, need to be established because of the emergences of multiple drug-resistant *Plasmodium* strains. Malaria is caused by the *Plasmodium* parasite, and this parasite is incapable of most types of amino acid biosynthesis, depending on a part of the amino acid source on free amino acids in plasma. Thus, we are searching for a method of malaria control based on nutritional knowledge by performing the global analysis of amino acid composition in plasma (plasma aminogram analysis). With an *in vivo* murine model, we have shown that *Plasmodium* infection causes drastic alteration of plasma aminograms and that the treatment of mice with food in which the amino acid composition has been modified significantly inhibits parasitemia. Furthermore, a combination study with artificial food and artesunate, which is the first-line drug against malaria, indicated that this food has a synergistic effect with antimalarial agents. Currently, in an *in vivo* murine model, we are studying the presence or absence of the association between plasma aminograms and cerebral malaria, which is one of the most severe clinical manifestations of malaria.

Publications

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