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 2016, 698 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, bloodstream forms are taken up and differentiate to procyclic forms which lack host-infectivity in the midgut. Subsequently, procyclic forms migrate to tsetse salivary gland or proboscis where they differentiate to the epimastigote forms. The epimastigote forms strongly adhere to tsetse tissue, proliferate, and differentiate into animal infective metacyclic forms. The differentiation (from the epimastigote form to metacyclic form) is called metacyclogenesis, which is indispensable for the parasite to be cyclically transmitted. The cell adhesion of the epimastigote forms are known to be essential for the metacyclogenesis of *Trypanosoma congolense*, the cause of animal African trypanosomiasis. By using *T. congolense*, we are trying to elucidate the molecular mechanisms underlying metacyclogenesis through transcriptome analyses on the epimastigote forms whose cell adhesion and subsequent metacyclogenesis are inhibited.

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 *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 the treatment of mice with isoleucine deficient diet (Ile-def diet) significantly inhibited parasitemia. A combination studies with Ile-def diet and artesunate, the first-line drug against malaria, indicated that this food has synergistic effect with antimalarial agents. Furthermore, Ile-def diet treatment prolonged the survival of the mice that is experimental model of cerebral malaria. Currently, using an *in vivo* murine model, we are studying the effect of Ile-def diet on liver-stage parasite development.