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 2017, 747 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. Each lifecycle stage development, involving cell differentiation is essential biological process for the parasite to be cyclically transmitted, and thus could be promising targets of trypanosomiasis controlling measures. However, molecular mechanisms underlying them are yet to be elucidated. We are trying to identify parasite molecules involved in its cell differentiation through proteome analyses on the *Trypanosoma congolense* whose lifecycle developments are reproducible in vitro.

Development of a novel immunological method of fecal occult blood testing for dogs and fecal occult blood tendency in gastrointestinal parasitic infections
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. For the better understanding of host-*Plasmodium* interactions, we focused on amino acids and performed "aminogram", which is a multivariate index analysis using statistical modeling of free amino acid composition of the bloods. In a murine model of cerebral malaria is one of the most severe clinical manifestations of malaria, we have shown that aminogram modification by adjusting amino acid intake with isoleucine deficient diet prolonged survival without inhibiting parasite proliferation (= cerebral malaria tolerance). Interestingly, live imaging indicated no difference in brain parasite burden between control and the deficient diet fed mice. These results indicate the possibility that amino acid-related host-parasites interactions are involved in cerebral malaria. Currently, in an *in vivo* murine model, we are studying the presence or absence of the association between plasma aminogram and cerebral malaria tolerance.

Publications

Kurihara S, Fujioka M[1], Yoshida T, Koizumi M, Ogawa K[1], Kojima H, Okano JH ([1]Keio Univ). A Surgical Procedure for the Administration of Drugs to the Inner Ear in a Non-Human Primate Common Marmoset (Callithrix jacchus). *J Vis Exp.* 2018; **132:** e56374. Epub 2018 Feb 28.