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 2019, 868 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.). Because the parasites evade host immunity by continuous antigenic variation of their surface coats, all attempts to develop vaccines against the parasites have been hampered. The parasites undergo lifecycle development involving cell differentiation, which is believed to be a promising target for developing novel control measures of the disease. However, the molecular mechanisms underlying cell differentiation are unknown.
We are studying the molecular mechanisms of differentiation from the tsetse fly stage to the mammalian stage in *Trypanosoma congolense,* the lifecycle development of which is reproducible *in vitro*. To investigate the dynamics of parasite infection of the host body, we generated a parasite that overexpressed a reporter gene (luciferase gene fused with enhanced green fluorescent protein gene. Using this genetically modified parasite, we plan to conduct *in vivo* imaging research for analyzing infection dynamics of the parasite and for evaluating the efficacies of vaccine candidates against it.

Study of postoperative nausea and vomiting in common marmosets
Common marmosets (*Callithrix jacchus*) are small primates with a high degree of sociability and genetic homology to humans. marmosets often vomit as a complication of anesthetic during induction and awakening. We have previously searched for risk factors for postoperative nausea and vomiting in marmosets by multivariate analysis and found that inhalation anesthesia and prolonged general anesthesia were associated with a significant increase in vomiting. In addition, an anesthesia protocol with the addition of malopitant citrate, a neurokinin-1 receptor antagonist, was investigated to control vomiting. The results showed that preoperative administration of malopitant significantly inhibited vomiting under both injection and inhalation anesthesia (poster presentation at the 66th annual meeting of the Japanese Association for Laboratory Animal Science). We continue to

investigate the effective prevention of postoperative nausea and vomiting in marmosets through the use of several antiemetic agents with mechanisms that differ from those of malopitant.

Preventing malaria by adjusting amino acid intake

Novel 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* parasites, and these parasites are incapable of most types of amino acid biosynthesis, depending on a part of the amino acid source on free amino acids in plasma. For better understanding of host-*Plasmodium* interactions, we focused on plasma amino acids and performed "aminogram analysis," which is the multivariate index analysis using statistical modeling of the free amino acid composition of blood. In a murine model of cerebral malaria, which is a severe clinical manifestation 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, the observation with optical microscopy of a Giemsa-stained thin blood smear demonstrated that erythrocytes are smaller in mice fed an isoleucine-deficient diet. However, in the case of *Plasmodium falciparum*, erythrocyte did not differ between a control medium and an isoleucine-free medium. These results indicate the possibility that the size of erythrocyte is involved in the progression of cerebral malaria. We are now studying the effect of isoleucine deficiency on erythrocyte size and the severity of cerebral malaria in a murine model.

Publications

Kawahata K, Cordeiro IR, Ueda S, Sheng G, Moriyama Y, Nishimori C, Yu R, Koizumi M, Okabe M, Tanaka M. Evolution of the avian digital pattern. *Sci Rep*. 2019 Jun 12; **9**(1): 8560. doi: 10.1038/s41598-019-44913-w. PubMed PMID: 31189916; PubMed Central PMCID: PMC6561939.