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 2018, 806 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*. Using this system, the variation of the parasite's protein expression level during the differentiation from metacyclic forms (tsetse fly stage) to bloodstream forms (mammalian stage) was investigated with liquid chromatography/tandem mass spectrometry analyses. The results show that the expression levels of several proteins thought to be involved in important biological processes, such as iron uptake and mitochondrial electron transport chain, are changed. In addition, the expression levels of several unknown proteins were shown to be altered. Through the functional analyses of these unknown proteins, we are attempting to identify parasite molecules involved in its cell differentiation.

Study on postoperative nausea and vomiting in common marmosets
Common marmosets (*Callithrix jacchus*) are unique laboratory animals. They are primates but are small and have high sociality and good reproductive efficiency. Marmosets often vomit as a complication of anesthesia during induction or awakening. Because vomiting when a patient is half-awake triggers fatal conditions, such as aspiration pneumonia, a reliable method of control is needed. Therefore, we searched for risk factors for postoperative nausea and vomiting (PONV) in marmosets by multivariate analysis. We

found that the incidence of PONV significantly was greater if the patient was young or female or had received general anesthesia, isoflurane, or long-term anesthesia. The presence of multiple factors further increased the incidence of PONV. We are now considering methods to control vomiting through the use of several antiemetic agents with different mechanisms.

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 the better understanding of host-*Plasmodium* interactions, we focused on the amino acids of host plasma and performed "amniography," 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 the malaria, we have shown that aminogram modification, by adjusting amino acid intake with an isoleucine-deficient diet, prolonged survival in the mice without inhibiting parasite proliferation (cerebral malaria tolerance). Interestingly, analysis with Evans blue of the permeability of the blood-brain barrier of mice indicated no significant difference in the severity of cerebral malaria between control mice and mice fed a isoleucine-deficient diet. However, with magnetic resonance imaging, no inflammatory lesion in olfactory bulb was observed in mice fed an isoleucine-deficient diet. These results indicated the possibility that novel amino acid-mediated mechanisms are involved in the progression of cerebral malaria. Currently, in an *in-vivo* murine model, we are studying the effect of isoleucine deficiency on blood cell morphology and the severity of cerebral malaria.

Publications

Sombié A*[1]*, Saiki E, Yaméogo F*[1]*, Sakurai T, Shirozu T*[2]*, Fukumoto S*[2]*, Sanon A*[1]*, Weetman D*[3]*, McCall PJ*[3]*, Kanuka H, Badolo A*[1] *([1]Université Ouaga 1 JKZ, [2]Obihiro University of Agriculture and Veterinary Medicine, [3]Liverpool School of Tropical Medicine). High frequencies of F1534C and V1016I kdr mutations and association with pyrethroid resistance in Aedes aegypti from Somgandé (Ouagadougou), Burkina Faso. *Trop Med Health.* 2019; **47.** doi: 10.1186/s41182-018-0134-5.