Laboratory Animal Facilities

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General Summary

The purpose of the Laboratory Animal Facilities (LAF) is to support *in-vivo* research and to contribute to the development of basic and clinical medicine. In 2012, 179 researchers used the LAF. 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

Establishment and characterization of model animal for cancer research derived from Phodopus hamster

Our inbred strains derived from *Phodopus* hamsters are maintained in this laboratory. The *Phodopus* hamster is a small rodent that differs taxonomically from the Syrian hamster, which is the major laboratory hamster. We recently determined that this hamster is a good candidate for a new laboratory animal and have established an inbred strain named PMI. A PMI hamster with a morphologically abnormal stomach was found on anatomical screening in May 2010. Pathological observation suggested this abnormality represented a well-differentiated adenocarcinoma. By successive anatomical screening of 41 PMI hamsters, we confirmed the occurrence of morphologically abnormal stomachs in 39 of 41 hamsters (95.12%) at a mean age of 309 days (range, 196 to 515 days). On the other hand, all 12 hamsters of the inbred TAK strain, which was established from *Phodopus campbelli* in 2009, showed normal stomachs at a mean age of 256 days (range, 236 to 293 days). The high incidence of morphologically abnormal stomachs was thought to be a special feature of the PMI inbred strain.

Filarial nematode diverts thermoregulation to developmental transition following transmission by Aedes mosquito

Parasitic nematodes of humans, livestock, and other animals cause diseases of major socioeconomic significance globally. The parasitic nematode employing obligate diapause arrests development at this particular stage in each generation. Recovery to the progressive stage from diapause is induced upon host infection by both intrinsic and extrinsic (environmental) elements of the host. *Dirofilaria immitis*, a filarial nematode, develops through a series of 4 molts during the transmission cycle between mammalian hosts and mosquito vectors. The L1 and L2 larvae mature in the mosquito's body before reaching the infective larval stage (L3), and further developmental transition (re-initiation) occurs just after transmission to the host. We found that the combination of proper temperature (37°C) and nutrition supply is required for the filarial L3 to resume development with acute expression of stress marker *hsp70*, which was rapidly decreased in *D.*

immitis but showed sustained expression in *Caenorhabditis elegans*. Unordinary duplication of a part of the kinase domain ensured the poor activation of the stress kinase c-Jun N-terminal kinase in response to 37ºC. Both *cuticlin-1* and *cathepsin-L*, identified as thermoregulated genes, were required for adequate L3 molting. Taken together, our findings suggest that thermoregulation for adapting to environmental change also exerts control over the developmental transition in filarial parasites.