Form 3

Report for Joint/Usage Research Program for Endocrine/Metabolism (Fiscal Year 2024)

Date：2024/4/22

To Director of Institute for Molecular and Cellular Regulation, Gunma University

Principal Applicant	
Institution	The Hong Kong University of Science and Technology
Position	Assistant Professor
Name	Yukinori Hirano

We report on the results of joint research in fiscal year 2024 as below.

（Program No. 22003）

1． Research Title	Study of the link between metabolome and age-related sleep dysfunction in Drosophila
2． Purpose and Significance of the research project	Aging process can be variable between individuals, although underlying mechanisms are unknown. In the previous year, we investigated how the transcriptome and metabolome are variable in aged individuals using flies, that could be linked to specific aging phenotypes.
3． Period of The Program	April 1, 2023 ～ March 31, 2024

4． Project Members

Name	Age	Sex	Affiliation	Position	Role
（Principal Applicant） Yukinori Hirano	44	M	The Hong Kong University of Science and Technology, Division of Life Science	Position：Assistant professor Degree：PhD Acquisition date：2008.3.31	Project director
（Research Collaborators） Priyanshu Bhargava	33	M	The Hong Kong University of Science and Technology, Division of Life Science	Position：Postdoc Degree：PhD Acquisition date：2018.9.30	Researcher

※If additional space is required, please attach a separate sheet.

5． Collaborating Researcher of IMCR	Name of Laboratory	Metabolic Regulation and Genetics	Name	Takashi Nishimura

6. Research Plans

1) Metabolic analysis in flies showing sleep fragmentation

Metabolome will be investigated using aged flies showing sleep fragmentation, by comparing to aged flies with normal sleep cycle, or young flies. A widely targeted metabolome analysis will be conducted by Dr. Nishimura lab at IMCR, Gunma University.

2) Causal relationship of metabolome to sleep fragmentation

The obtained metabolic compounds will be tested by either feeding method or genetic manipulations, to see if sleep fragmentation is induced or suppressed. Firstly, aged flies will be fed the compounds. Secondly, the genes involved in the metabolic process will be knocked down. Thirdly, if the compounds are derived from bacteria, genes in the synthesis pathway of the compounds will be mutated in bacteria. These will directly demonstrate the causal relationship of the metabolome to sleep fragmentation.

3) Identification of causal tissues for sexual dimorphism in sleep phenotype

Drosophila sex is determined by the expression level of *Tra*. Ectopic *Tra*-expression in male can induce sex reversal, which can be done in a cell-type specific manner using the GAL4/UAS system. To elucidate the mechanism by which male and female show different aging phenotype in sleep cycle, we will express *Tra* in specific cell type, and test sleep fragmentation and metabolome in the brain.

7. Research results:

1) Metabolic analysis in flies showing sleep fragmentation

We have separately sampled the aged flies with or without sleep fragmentation, and conducted the metabolome analysis from head, thorax, and abdomen. We have determined the change in monoamine in sleep fragmentated flies.

2) Causal relationship of metabolome to sleep fragmentation

We tested the causal roles of monoamine in sleep fragmentation using inhibitors and mutant flies, and found that one of monoamine has a causal role, while another has a protective role in sleep fragmentation.

3) Identification of causal tissues for sexual dimorphism in sleep phenotype

Overexpression of TRA induces sex reversal, which allows us to test the causal cell type in sexually dimorphic sleep phenotype. We overexpressed TRA in the intestine stem cells as in the previous report, showing the change in gut homeostasis, but found that sleep fragmentation is not affected. We are currently testing other cell types to determine the causal relationship in sexual dimorphism.

８．Present status of academic conference presentations and research papers associated with the results of the joint research, and exchange of information on the joint research with the collaborating researcher at IMCR.
(As much as possible, please state papers that include the names of the collaborating researcher at IMCR or papers stating that the research was supported by the Joint Research Program with IMCR.
Regarding papers, please send a PDF file together with the report to the email address of the general affairs section of the Institute.) Office of General Affairs: kk-msomu4@jimu.gunma-u.ac.jp

① Please list the publications that include the name of the collaborating researcher from IMCR and send a reprint of each publication to IMCR.

No paper is published yet.

② Please list the publications that include a description that the research was supported by the Joint Research Program with IMCR and send a reprint of each publication to IMCR.

No paper is published yet.

③ List up to 3 conferences (name of conference, date of conference, and title of the presentation).

The Asia Pacific Drosophila Research Conference 6, 2023/7/23-27, Leveraging Drosophila melanogaster as an aging model to dissect the mechanism behind aging individuality.

④ Exchange of information exchange with collaborating researcher from IMCR (please list main points of communication).

Expertise regarding the sample preparation, and data analyses