Form 3

Report for Joint/Usage Research Program for Endocrine/Metabolism (Fiscal Year 2020)

Date：2021/06/07

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

Principal Applicant	
Institution	Nagoya University/ UT Southwestern Medical Center
Position	Designated Professor/ Assistant Professor
Name	YOUNGJAI YOU

We report on the results of joint research in fiscal 2020 as below.

（Program No.　19007　　）

1．Research Title	The role of nuclear receptors in epigenetic regulation of feeding
2．Purpose and Significance of the research project	Based on our discovery that certain nuclear receptors (NRs) control feeding and fat storage in *C. elegans*, and that our results from last year's study that starvation increases the expression of an NR and also a histone marker, this study aims to continue to investigate the roles of NRs in epigenetic regulation of feeding and metabolism. Combining the genetic and biochemical approaches, this study will reveal new mechanisms by which NRs contribute to misregulation of feeding and obesity. In addition, because the NRs we found are mostly expressed in the neurons or in the intestine, this study will also provide the novel link between two organs mediated by transcriptional and epigenetic regulations.
3．Period of The Program	April 1, 2020 ～ March 31, 2021

4．Project Members

Name	Age	Gender	Institution/Department	Position	Role
（Principal Applicant） Youngjai You	54	F	Nagoya University/ Graduate School of Science/ Division of Biological Science	Designated Professor	Project director
（Research Collaborators） Binta Aleogho	28	F	Nagoya University/ Graduate School of Science/ Division of Biological Science	Graduate student	Analysis of the mutants' phenotypes

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

5．Collaborative Researcher of IMCR	Name of the Laboratory	Epigenetics and metabolism	Name	Takeshi Inagaki

6． Research Plans

We continue to investigate how NRs regulate metabolism via epigenetic regulation, in collaboration with the Dr. Inagaki group. Three aims are

- To determine where H3K4me3 level is increased by starvation by an immunohistochemistry method: this is to determine the action site of epigenetic regulation.
- To examine whether the available mutants of NRs are sensitive to starvation.
- As a long-term goal: To examine the detail of histone modifications by extending to determine H3K27Ac (active enhance mark) by ChIP and chromatin openness by performing ATAC-seq, because the combination of H3K27Ac ChIP and ATAC-seq is a promising approach to determine consensus sequences of NHR biding sites.

7． Research results:

- For the first aim: We found that although we previously succeeded to detect changes in H3K4 tri-methylation by Western blot method, an immunohistochemistry approach to detect H3K4 tri-methylation did not yield informative results. From the results, we learned we have to take a different approach to locate the action site of epigenetic regulation.
- For the second aim: There are several NRs important for metabolism and feeding. We tested NHR-64, an ortholog of mammalian HNF4 family that we have previously reported to regulate fat storage and feeding. The two available strains of NHR-64 showed intact starvation survival, however, suggesting either NHR-64 does not play a role in starvation or there are other NRs that function redundantly to NHR-64. Considering the many *C. elegans* NRs that belong to HNF4 family, we consider the latter is the best explanation of our result.
- For the third aim: Due to my move to the US, unfortunately this aim was not able to be pursued.

8． Publications and/or Presentations resulting from Joint Research Program with IMCR.
Exchange of information on joint research with faculty members.

①Please describe a list of publications in which the name of the collaborative researcher of IMCR appears and send one paper reprints of each publication to IMCR.
Not applicable
②Please describe a list of publications which include the description that the research is supported by Joint Research Program with IMCR and send one copy of each publication to IMCR.
Not applicable
③Enter the name of the conference, the date of the conference, and the title of the presentation of the conference.(up to 3 cases)
Not applicable
④Implementation status of information exchange with faculty members in charge of joint research.
Dr. Inagaki and I have continuously discussed the project over e-mails and Skype communication. In addition, we visited IMCR on Jan 28-29th, 2020 and discussed the detailed plan with Dr. Inagaki.