Form 3

Report for Joint/Usage Research Program for Endocrine/Metabolism (Fiscal Year 2017)

Date: 2018/04/20

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

Principal Applicant	
Institution	University of California San Francisco
Position	Associate Professor
Name	Shingo Kajimura

We report on the results of joint research in fiscal 2017 as below.

(Program No. 17008)

1. Research Title	Histone code analysis of brown and beige adipose cells
2. Purpose and Significance of the research project	Epigenetic regulatory factors are recently reported to regulate brown and beige adipose cell fate and their function. We revealed that EHMT1 which is a H3K9 methyltransfarase regulates biogenesis of brown and beige adipocytes (Ohno et al. *Nature* 2013) and the group of Prof. Inagaki in IMCR, Gunma University revealed that a H3K9 demethylase JMJD1A regulates brown adipocyte function (Abe et al. *Nat. Commun.* 2015). Thus, histone modifications mediate brown and beige adipose cell biogenesis. It is known that histone modifications regulate gene expression either positively or negatively. The bivalent modified histone signature of both positive and negative mark keep active genes poised for future activation. However, the combinations of various histone marks during brown and beige adipose cell biogenesis is mostly unrevealed. In the current study we seek to elucidate the combinations of histone codes in brown and/or beige adipose cells.
3. Period of The Program	April 1, 2017 ～ March 31, 2018

4. Project Members

Name	Age	Gender	Institution/Department	Position	Role
(Principal Applicant) Shingo Kajimura	41	M	UCSF Diabetes Center	Associate Professor	Project leader
(Research Collaborators)					

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

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

6. Research Plans

Pre-adipocytes adipocytes are differentiated into adipocytes using the method which we previously reported. Core histones are isolated from the cell cultures using the histone purification kit (Active motif). Histone H3 tail is digested from the purified histones using restriction enzyme and applied to the mass spectrometry analysis for determining the combinations of multiple histone marks.

7. Research results:

The novel screening technique of bivalent histone modification mark using mass spectrometry analysis was established in consequence of the collaboration in this fiscal year. Briefly, histones purified from pre- and post-differentiated adipocytes were applied into the mass spectrometer and the obtained data was analyzed using JMP software. The data presented an unknown bivalent histone modifications comprised of methylation and acetylation in a single histone. The novel bivalent marks were resolved following adipocyte differentiation, indicating potential role to regulate adipogenic gene expression. We are going to confirm these findings and investigate further roles of the novel histone bivalent modifications.

8. Publications and/or Presentations resulting from Joint Research Program with IMCR.

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.

Fukunaka A., Fukada T, Bhin J.H., Suzuki L., Tsuzuki T., Takamine Y., Bin B.H., Yoshihara T., Ichinoseki-Sekine N., Naito H., Miyatsuka T., Takamiya S., Sasaki T., **Inagaki T.**, Kitamura T., **Kajimura S.**, Watada H., Fujitani Y. (2017). Zinc transporter ZIP13 suppresses beige adipocyte biogenesis and energy expenditure by regulating C/EBP-b expression. *PLoS Genetics* 13(8):e1006950.

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.

N/A