Form 3

Report for Joint/Usage Research Program for Endocrine/Metabolism (Fiscal Year 2023)

Date：(2024)/(6)/(19)

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

Principal Applicant	
Institution	Shanghai Institute for Endocrine and Metabolism diseases
Position	Professor
Name	Yanyun Gu

We report on the results of joint research in fiscal year 2023 as below.

（Program No. 23005）

1． Research Title	The role of Fxr in pancreatic islet PP cells during postnatal endocrine pancreas maturation
2． Purpose and Significance of the research project	Our previous studies have given implication that bile acid signaling in pancreatic β cells plays a role in compensatory β cell proliferation in adult. There has been well studied how intra β cell signaling is involved in postnatal β cell maturation, First purpose of this study is to examine the role of bile acid receptor, Fxr in pancreatic PP cells for endocrine pancreas maturation. however, whether and how other intraislet endocrine cells contribute to this process has not yet been fully characterized. Second purpose of the study is to use PPYcre knockin mice to do lineage tracing experiment if PP cell could transdifferentiation to other pancreas endocrine cells in conditions that bile acid signaling is activated or inactivated.
3． Period of The Program	April 1, 2023 ～ March 31, 2024

4． Project Members

Name	Age	Sex	Affiliation	Position	Role
(Principal Applicant) Yanyun Gu	46	F	Shanghai Institute for Endocrine and Metabolism diseases	Professor	Project director
(Research Collaborators)					

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

5． Collaborating Researcher of IMCR	Name of Laboratory	Lab of Developmental Biology & Metabolism	Name	Yoshio Fujitani

6． Research Plans

2023.Jan-Jun： To obtain the PP cell specific knockout and knock in mice, and mating with R26GFP mice
22023.July-Dec: Metabolic phenotyping of mice during weaning and after nutrient stress in different genotype mice with or without Fxr agonist antagonist treatments
2024 Jan-Jun: Lineage tracing to examine whether PP cells with activated or blunted Fxr signaling could endure dysplasia, apoptosis or transdifferentiation to β cells.
2024 July-Dec: RNA seq with isolated islets to get different expression genes profile, select candidate genes that might mediate the function of Fxr and confirm in both mRNA and protein level.
2025 Jan-Jun:： manipulate confirmed genes with knockdown or overexpressing with lentivirus or AAV transduction in primary islets ex vivo to further confirm their role in regulating cell proliferation and apoptosis or identity transdifferentiation.
2025 July-Dec:： Manuscript preparation.

7． Research results:

Please describe the details of the contribution of the joint research with IMCR in obtaining the results.

1, confirm the role of BA signaling in β cell maturation as well as dedifferentiation
2. elaborate the role of Fxr in PP cells to regulate pancreatic β cell maturation as well as dedifferentiation
3. explore the new markers in the BA signaling pathway to predict or evaluate the status of β cell identity or functionality after birth
4 explore the potential druggable targets to promote β cell maturation and prevent cell dedifferentiation.

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@ml.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.

n/a

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.

n/a

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

n/a

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

We have successfully obtained the PPYcre mice from Prof. Fujitani with MTA prepared and succeed in backcross the mice with B6N.