Form 3

Report for Joint/Usage Research Program for Endocrine/Metabolism (Fiscal Year 2022)

Date：2023/5/15

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

Principal Applicant	
Institution	Beijing Tongren Hospital, Capital Medical University
Position	Professor
Name	Jinkui Yang

We report on the results of joint research in fiscal 2022 as below.

（Program No.　　）

1． Research Title	Berberine promotes GLP-1 secretion through hERG potassium channel in en-teroendocrine L-cells.
2． Purpose and Significance of the research project	Berberine (BBR), one kind of Chinese traditional medicine, has applications as a drug in treating type 2 diabetes mellitus and hyperlipidemia for hundreds of years. However, the mechanism is still unknown. This study is to explore the function of BBR on GLP-1 exocytosis and clarify the molecular mechanism of BBR in enteroendocrine L-cells.
3． Period of The Program	April 1, 2022 ～ March 31, 2023

4． Project Members

Name	Age	Sex	Affiliation	Position	Role
(Principal Applicant) Jinkui Yang	60	M	Endocrinology department, Beijing Tongren Hospital, Capital Medical University	Position：Professor Degree：MD, PhD Acquisition date：2003.10	Project director
(Research Collaborators) Hao Wang	41	M	Endocrinology lab, Beijing Tongren Hospital, Capital Medical University	Associate professor	Experimental executor
Yingchao Yuan	29	F	Endocrinology department, Beijing Tongren Hospital, Capital Medical University	Graduate student	Experimental executor

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

5． Collaborating Researcher of IMCR	Name of Laboratory	IMCR	Name	Tetsuro Izumi

6． Research Plans

1. Generation of hERG intestinal epithelial cell specific null mice (hERG pVillin-cre).
2. Check blood glucose and serum insulin, GLP-1, GIP concentrations in control and hERG pVillin-cre mice that underwent an oral glucose tolerance test after treatment with NS or BBR.
3. Detect GLP-1 secretion ability of NS or BBR treated intestinal epithelial cells that were stimulated with glucose plus forskolin and IBMX.
4. Detect GLP-1 secretion ability of NS or BBR treated Glutag cells (L cell line) that were stimulated with glucose plus forskolin and IBMX.

7． Research results:

1. Finishing generation of hERG-pVillin-cre mice.
2. BBR treated control mice showed relieved glucose tolerance and increased serum GLP-1 level compared with those of NS treated control mice.
3. BBR treated hERG pVillin-cre mice showed no effect on glucose tolerance and serum GLP-1 level compared with those of NS treated control mice.
4. BBR promoted GLP-1 secretion in intestinal epithelial cells.
5. BBR promoted GLP-1 secretion in L cells.

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.

(a) Zhao MM, Lu J, Li S, Wang H, Cao X, Li Q, Shi TT, Matsunaga K, Chen C, Huang H, Izumi T, Yang JK. Berberine is an insulin secretagogue targeting the KCNH6 potassium channel. Nat Commun. 2021 Sep 23;12(1):5616.
(b) Wang Hao*, Yuan Ying-Chao, Chang Cong, Izumi Tetsuro, Wang Hong-Hui*, Yang Jin-Kui*. The Signaling Protein GIV/Girdin Mediates the Nephrin-dependent Insulin Secretion of Pancreatic Islet β Cells in Response to High Glucose. Journal of Biological Chemistry, 2023, doi: 10.1016/j.jbc.2023.103045.

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.

a) Zhao MM, Lu J, Li S, Wang H, Cao X, Li Q, Shi TT, Matsunaga K, Chen C, Huang H, Izumi T, Yang JK. Berberine is an insulin secretagogue targeting the KCNH6 potassium channel. Nat Commun. 2021 Sep 23;12(1):5616.

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

The 4th international symposium of endocrinology and metabolism, 12th Nov, 2022, Berberine is an insulin secretagogue targeting the KCNH6 potassium channel.

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

The institutional collaboration agreement between IMCR and Beijing Tongren Hospital was established in

April, 2016. Applicant and Dr. Hao Wang at Prof. Izumi's laboratory have started this project and obtained promising results to support future collaboration.