

Report for Joint/Usage Research Program for Endocrine/Metabolism (Fiscal Year 2019)

Date: (2020)/(04)/(10)

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

Principal Applicant	
Institution	College of Biology, Hunan University
Position	Associate Professor
Name	Hong-Hui Wang

We report on the results of joint research in fiscal 2019 as below.

(Program No. 17007)

1. Research Title	The role of guanine exchange factor (GEF) domain of Girdin in pancreatic islets to control insulin secretion.				
2. Purpose and Significance of the research project	Study mechanistic role of GEF function of Girdin in high glucose-induced insulin secretion in beta-cells. The expecting results may provide a novel pharmacological modulation of GEF function of to fine-tune the pancreatic beta cell function.				
3. Period of The Program	April 1, 2019 ~ March 31, 2020				
4. Project Members					
Name	Age	Gender	Institution/Department	Position	Role
(Principal Applicant) Hong-hui Wang	40	M	Hunan University, College of Biology	Associate Professor	Project director
(Research Collaborators) Cong Chang	27	F	College of Biology, Hunan University	Graduate Student	Cell experiment
Kunli Zhao	27	F	Institute for Molecular and Cellular Regulation, Gunma University	Graduate student	Animal Experiments
Hao Wang	38	M	Institute for Molecular and Cellular Regulation, Gunma University	Assistant Professor	Project guidance
※If additional space is required, attach a separate sheet.					
5. Collaborative Researcher of IMCR	Name of the Laboratory	Molecular Endocrinology and Metabolism	Name	Tetsuro Izumi	



6. Research Plans

- 1) To study the role of the GEF function of Girdin in insulin secretion of primary pancreatic islet and animal.
- 2) Test potential application of TAT-Girdin peptide in the activation of the nephrin phosphorylation and endocytosis for GSIS.
- 3) To treat obesity db/db mouse with TAT-Girdin peptide to test the modulation of insulin level and glucose in the blood.

7. Research results:

We have validated the hypothesis that Girdin mediated the nephrin phosphorylation through the GEF domain, which may contribute to GLUT2 activity in Glucose-sensing for the insulin secretion.

- 1) The GTPase activity of Galphi3 correlating the insulin secretion in db/m mouse and is significantly inhibited in db/db mouse;
- 2) We overexpressed Girdin WT or Girdin FA mutant using adenovirus in MIN6 cells and found that FA mutant fails to activate the GTPase activity of Galphi3 upon high glucose stimulation;
- 3) The TIRF microscopic analysis reveals that the exocytosis of insulin granules MIN6 cells is significantly inhibited in Girdin FA mutant-expression;
- 4) The MIN6 cells overexpressing FA mutant show downregulated nephrin-phosphorylation and decreased nephrin endocytosis after high glucose stimulation;
- 5) The GEF function of Girdin is essential in Akt activation and GLUT2 membrane translocation in GSIS.

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.

The GEF function of Girdin mediates the Glucose-stimulated insulin secretion (GSIS) via the Akt-mediated Glut2 activation. Cong Chang, Kunli Zhao, Hao Wang, Hong-Hui Wang, Tetsuro Izumi. 2020, Manuscript in preparation.

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 yet.

③Enter the name of the conference, the date of the conference, and the title of the presentation of the conference.(up to 3 cases)

The 9th International Symposium on Bioanalysis, Biomedical Engineering and Nanotechnology (ISBBN) will be held at Changsha, Hunan, China, May 28-31, 2020.

Abstract title: The role of guanine exchange factor (GEF) domain of Girdin in pancreatic islets to control insulin secretion.

Authors: Hong-hui Wang, Cong Chang, Kunli Zhao, Hao Wang, Tetsuro Izumi

④Implementation status of information exchange with faculty members in charge of joint research.

I often discussed with Dr. Wang and Professor. Izumi about our collaborative research.