Form 3

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

Date: 2018/04/22

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 2017 as below.

(Program No. 17013)

1. Research Title	The Role of Girdin in Insulin Exocytosis
2. Purpose and Significance of the research project	The activation of Trimeric G protein Galphi3 is abnormal during diabetes progression and Girdin activates Galphi3 through its GEF function. In proposed collaborative research, we will investigate the mechanistic role of Galphi3 activation in the glucose stimulated insulin secretion. The expecting results may provide a novel pharmacological modulation of Girdin/Nephrin to facilitate pancreatic beta cell function.
3. Period of The Program	April 1, 2017 ～ March 31, 2018

4. Project Members

Name	Age	Gender	Institution/Department	Position	Role
(Principal Applicant) Hong-Hui Wang	38	M	Hunan University, College of Biology	Associate Professor	Project director
(Research Collaborators) Cong Chang	25	F	College of Biology, Hunan University	Graduate Student	Experiment executor
Hao Wang	35	M	Institute for Molecular and Cellular Regulation, Gunma University	Assistant Professor	Experimental Investigation, and methodology

※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 check the expression of Girdin and nephrin in Min-6 and INS1 beta cells.
2) To investigate the physical interaction between Gridin and nephrin.
3) To compare the protein level, post-translational modifications and subcellular localization of Girdin in beta cells.
4) To study glucose-stimulated insulin level in Min6 cells transfected with Girdin siRNA and scramble siRNA or infected with adenovirus carrying Girdin WT or Girdin FA mutant (lacking it's GEF function for Galphi3 activation).

7. **Research results:**

1) We identified that Girdin and nephrin were highly expressed in Min-6 and INS1 beta cells.
2) We confirmed that high glucose induced nephrin phosphorylation and endocytosis in Min6 and INS1 beta cells.
3) We confirmed that high glucose quickly increases the protein level of Gridin.
4) We observed Girdin and nephrin co-localized at cell membrane of primary beta cells from mouse by Immunofluorescence and the high glucose treatment caused the decreases of co-localization.
5) We confirmed the physical interaction between Gridin and nephrin using GST-pulldown assay.
6) We constructed lentivirus for shRNA delivery for knocking-down murine Girdin in MIN6 cells to study the insulin secretion.
7) We constructed Adenovirus for Girdin WT and FA mutant for study the role of GEF function of Girdin on insulin secretion.

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.

None

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.

None