Form 3

# Report for Joint/Usage Research Program for Endocrine/Metabolism (Fiscal Year 2021)

Date：**2022/04/23**

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 2021 as below.

（Program No.　　）

| | |
|---|---|
| 1． Research Title | Development of a Glucose-gated DNA-nanodevice for Glucose Control in Type II Diabetes. |
| 2． Purpose and Significance of the research project | Design a glucose-gated DNA-nanodevice that dynamically responds to diabetic blood glucose levels and automatically promotes glucose uptake by activating the translocation of GLUT4 to the cell membrane in the liver and skeletal muscle. The proposed nanodevice would restore normal blood glucose levels in the diabetic mouse. The expected results may provide an intelligent therapeutic strategy for glucose control during type II diabetes treatment. |
| 3． Period of The Program | April 1, 2021 ～ March 31, 2022 |

4． Project Members

| Name | Age | Gender | Institution/Department | Position | Role |
|---|---|---|---|---|---|
| （Principal Applicant）Hong-Hui Wang | 42 | M | Hunan University, College of Biology | Associate Professor | Project director |
| （Research Collaborators）Kunli Zhao | 27 | F | Institute for Molecular and Cellular Regulation, Gunma University | Graduate student | Animal experiments |
| Fang He | 24 | F | Hunan University, College of Biology | Graduate student | Cell experiment |
| MeiXia Wang | 23 | F | Hunan University, College of Biology | Graduate student | Animal experiments |
| Juan Li | 22 | F | Hunan University, College of Biology | Graduate student | Data analysis |

※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. Investigate the role of glucose-gated nanodevice in regulating the dynamics of c-Met dimerization on membrane and the GLUT4 translocation using TIRF microscope.

②. Study the glucose uptake using skeletal muscle organoids and liver organoids in the presence of the glucose-gated DNA nanodevice.

③. Carry out an intraperitoneal glucose tolerance test (IPGTT) to examine if glucose-gated DNA nanodevice can regulate the hyperglycemia status of Type II diabetic mice.

7． Research results:

We have demonstrated that the glucose-gated DNA-nanodevice in regulating blood glucose levels of skeletal muscle and liver organoids in vitro. We realized smart control of serum glucose using the diabetic mouse models (Type II) and achieved intelligent control of glucose levels in vivo without causing the side effect of hypoglycemia.

①. The glucose-gated DNA nanodevice only function when the glucose level increases to higher than 8 mM, which can effectively switch-on the c-Met/AKT signaling of muscle organoids.

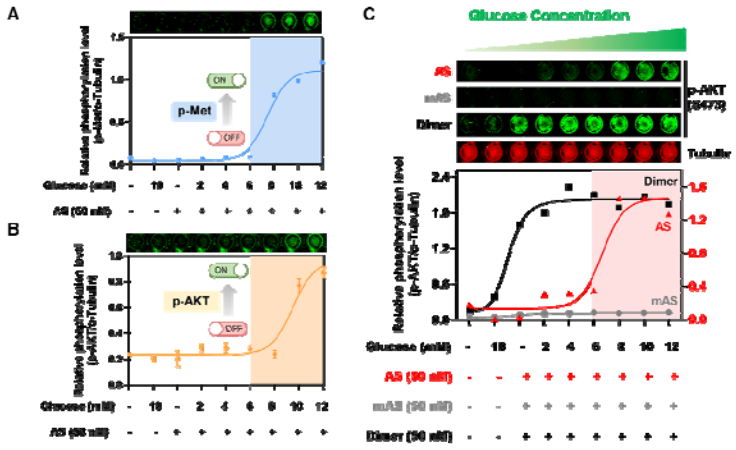


**Fig.1, High glucose-responsive c-Met/AKT signaling of the muscle organoids using the DNA-nanodevices (AS).**

②. The glucose-gated DNA nanodevice autonomously responds to high glucose level (> 7 mM ) and enhance glucose uptake of skeletal muscle organoids.

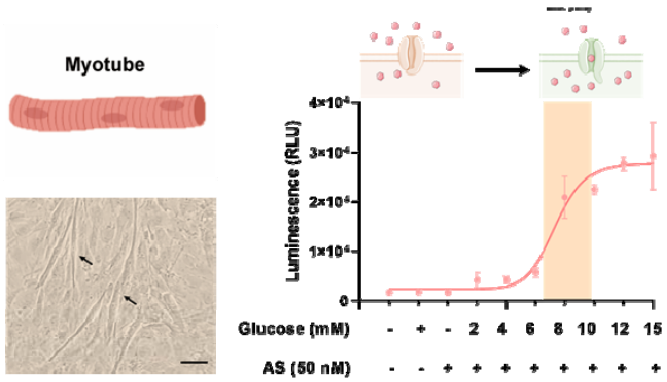


**Fig.2, High glucose-responsive glucose of myotube using the DNA-nanodevices(AS)**



Institute for Molecular and Cellular Regulation IMCR
Gunma University

③. We performed intraperitoneal glucose tolerance test (IPGTT) and the result confirmed the glucose regulation function of DNA-nanodevices in diabetic II mice. We found that the capability of DNA-nanodevices in the improvement of glucose tolerance and the hypoglycemia was greatly avoided.

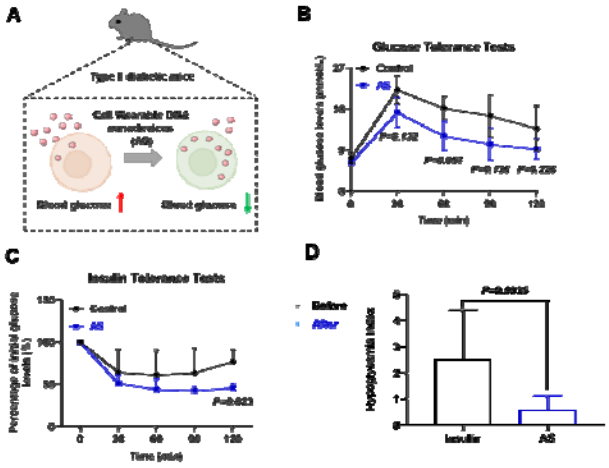


**Fig.3, The IPGTT results in diabetic mice treated with the DNA-nanodevice (AS)**

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.

Girdin mediates phosphorylation and endocytosis of nephrin in glucose-stimulated insulin secretion (GSIS). Cong Chang, Kunli Zhao, Hao Wang, Hong-Hui Wang, Tetsuro Izumi. 2021, Manuscript in submission.

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.

1) Wang Song, Zhang Zhenhua, Wei Shaohua, He Fang, Li Zhu, Wang Hong-Hui*,Huang Yan, Nie Zhou*. Near-infrared light-controllable MXene hydrogel for tunable on-demand release of therapeutic proteins. Acta Biomaterialia, 2021, 130:138-148.
2) Zheng Jihui, Zhu Wenjing, He Fang, Li Zhu, Cai Na*, Wang Hong-Hui*. An Aptamer-Based Antagonist against the Receptor for Advanced Glycation End-Products (RAGE) Blocks Development of Colorectal Cancer. Mediators of Inflammation, 2021, 9958051. doi: 10.1155/2021/9958051. eCollection 2021.

③Enter the name of the conference, the date of the conference, and the title of the presentation of the conference.(up to 3 cases)
None

④Implementation status of information exchange with faculty members in charge of joint research.
The institutional collaboration agreement between IMCR and College of Biology Hunan university was established in April, 2016. Applicant and Dr. Hao Wang at Dr. Izumi's laboratory have started this project and obtained promising results to support future collaboration.