

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

Date : 2022/4/3

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

Principal Applicant	
Institution	Faculty of Medicine Siriraj Hospital, Mahidol University
Position	Instructor-Head of Cellular and Molecular Diabetes Research Group
Name	Prapaporn Thamtarana

We report on the results of joint research in fiscal 2021 as below.

(Program No.)

1. Research Title	Characterization of candidate genes for autosomal dominant diabetes				
2. Purpose and Significance of the research project	Functional characterization of novel autosomal dominant diabetes associated gene ZYG11A in human pancreatic alpha cells and beta cells.				
3. Period of The Program	April 1, 2021 ~ March 31, 2022				
4. Project Members					
Name	Age	Gender	Institution/Department	Position	Role
(Principal Applicant) Prapaporn Thamtarana	40	F	Mahidol University/ Faculty of Medicine Siriraj Hospital	Instructor	Project director
(Research Collaborators) Pa-thai Yenchitsomanus	68	M	Mahidol University	Professor	Consultant
Nattachet Plengvidhya	57	M	Mahidol University	Associate Professor	Clinician/Subject recruitment
Chutima Chanprasert	40	F	Mahidol University	Research Assistant	Genetic and Genomic analyses
Siriporn Riyajan	30	F	Mahidol University	Research Assistant	Cell analysis
※If additional space is required, attach a separate sheet.					
5. Collaborative Researcher of IMCR	Name of the Laboratory	Diabetes and Metabolic Disorders	Name	Jun Shirakawa	



6. Research Plans

We identified a missense mutation (c.T1424C:p.L475P) in ZYG11A identified by exome sequencing as segregating with hyperglycemia in a Thai family with autosomal dominant diabetes. ZYG11A functions as a target recruitment subunit of an E3 ubiquitin ligase complex that plays an important role in the regulation of cell cycle. We assessed the role of ZYG11a in beta cells.

7. Research results:

We demonstrate an increase in cells arrested at G2/mitotic phase among beta-cells deficient for ZYG11A or overexpressing L475P-ZYG11A, which is associated with a decreased growth rate. This is the first evidence linking a ZYG11A mutation to hyperglycemia, and suggesting ZYG11A as a cell cycle regulator required for beta-cell growth. Since most family members were either overweight or obese, but only mutation carriers developed hyperglycemia, our data also suggests the ZYG11A mutation as a genetic factor predisposing obese individuals to beta-cell failure in maintenance of glucose homeostasis.

8. Publications and/or Presentations resulting from Joint Research Program with IMCR. Exchange of information on joint research with faculty members.

① Please 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.

Charoensuk C, **Thamtarana PJ***, Chanprasert C, Tangjittipokin W, **Shirakawa J**, Togashi Y, Orime K, Songprakhon P, Chaichana C, Abubakar Z, Ouying P, Sujjitjooon J, Doria A, Plengvidhya N, *Yenchitsomanus PT. Autosomal Dominant Diabetes Associated with a Novel ZYG11A Mutation Resulting in Cell Cycle Arrest in Beta-Cells. *Mol Cell Endocrinol.* 522:111126, 2021.

② Please 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.

Charoensuk C, **Thamtarana PJ***, Chanprasert C, Tangjittipokin W, **Shirakawa J**, Togashi Y, Orime K, Songprakhon P, Chaichana C, Abubakar Z, Ouying P, Sujjitjooon J, Doria A, Plengvidhya N, *Yenchitsomanus PT. Autosomal Dominant Diabetes Associated with a Novel ZYG11A Mutation Resulting in Cell Cycle Arrest in Beta-Cells. *Mol Cell Endocrinol.* 522:111126, 2021.

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

N/A

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

We usually have web meetings monthly to share the experimental results.