

Progress report 2022

Project Associate Professor: Miki Okada-Iwabu, Ph.D

■ Introduction and Organization

Laboratory for Advanced Research on Pathophysiology of Metabolic Diseases was launched in 2017 to promote cutting-edge research aimed at unraveling the underlying pathophysiology of diabetes and related metabolic diseases thereby contributing to the development of effective preventive measures against these diseases.

“Individuals at risk of diabetes”, i.e., those strongly suspected of having diabetes and those in whom the possibility of diabetes cannot be denied, are currently estimated to account for 28.5% of males and 21.4% of females in Japan, thus making it an urgent task not only for metabolic science but for society at large to fully elucidate the underlying pathophysiology of diabetes. Diabetes is defined as a hyperglycemic condition resulting from decreased secretion and/or action of insulin from the pancreas and encompasses a wide disease spectrum from such rare conditions as mitochondrial diabetes and lipotrophic diabetes to diabetes mellitus as a common disease. Diabetes occurs not only through genetic susceptibility to the disease but due to disorderly living habits, such as overeating, lack of physical activity and obesity. Therefore, the Laboratory is intended to promote wide-ranging research into human tissues from patients with diabetes mellitus as a common disease but from those with rare forms of diabetes by drawing on state-of-the-art genomic, epigenomic, metabolomic, metagenomic and iPS-cell technologies and to bring resulting research insights to bear on the development of

innovative diagnostic, preventive and therapeutic modalities for diabetes.

■ Research activities

Diabetes occurs due not only to genetic factors but to the influence of environmental factors, such as overeating, lack of physical activity, and obesity. Therefore, while diabetes represents a disease condition with a wide spectrum from inherited rare forms of diabetes to diabetes as a common disease, its pathophysiology remains yet to be fully elucidated.

The Laboratory thus focuses on the analysis of the physiological functions of organs and systems that play a key role in the onset of diabetes, i.e., pancreatic endocrine cells, liver, adipose tissue, skeletal muscle, nervous system, immune system and intestinal tract, as well as diseases resulting from disruption of their functions by drawing fully on state-of-the-art omic (genomic, epigenomic, metabolomic, and metagenomic) and iPS-cell technologies and genetic cell and animal engineering.

Research themes also being pursued at the Laboratory include the onset/progression of chronic diseases associated with aging and rare diseases, such as mitochondrial diabetes and lipotrophic diabetes, to facilitate the development of innovative diagnostic, preventive and therapeutic modalities for these diseases, based on resulting research findings and insights.

■ Future perspectives

Within the research milieu that the Laboratory offers, therefore, the research currently being promoted is expected to lead to the elucidation of the pathophysiology of diabetes and related metabolic diseases, where rare disease-derived tissue- and iPSC cell-based investigations are expected to provide invaluable insights into the pathophysiology of diabetes as a common disease.

Thus, the Laboratory is devoted to promoting relevant research leading to the development of innovative diagnostic, preventive and therapeutic modalities, thereby contributing to the effective prevention and treatment of diabetes.

■ References

- Iwabu M, Okada-Iwabu M, Kadowaki T, Yamauchi T. Elucidating exercise-induced skeletal muscle signaling pathways and applying relevant findings to preemptive therapy for lifestyle-related diseases. *Endocr J.* 69, 1-8, 2022