Goal2 Realization of ultra-early disease prediction and intervention by 2050.
Challenge for Eradication of Diabetes and Comorbidities through Understanding and Manipulating Homeostatic Systems

Here begins our new MIRAI
**MOONSHOT** RESEARCH & DEVELOPMENT PROGRAM

R&D item

1. Elucidation of homeostatic mechanisms by inter-organ communication and development of therapeutic and diagnostic methods

## Progress until FY2023

1. Outline of the project

This R&D item is responsible for the project's themes of (i) elucidating the inter-organ network mechanisms (See figure below) that maintain metabolic and circulatory homeostasis, and (ii) developing new prevention, diagnosis, and treatment methods for diabetes and its co-morbidities based on these mechanisms.

To achieve this goal, we are tackling this challenging theme by conducting detailed analyses to elucidate the molecules involved in the signaling of afferent, central, and efferent nerves connecting organs and their regulatory mechanisms. With the idea of developing preventive, diagnostic, and therapeutic methods for diabetes using inter-organ networks through the nervous system, which is completely different from conventional methods, we are working on this project using single cell RNA sequencing, optogenetics, fMRI, artificial nerve connections, plasma lipidomics, and other techniques.
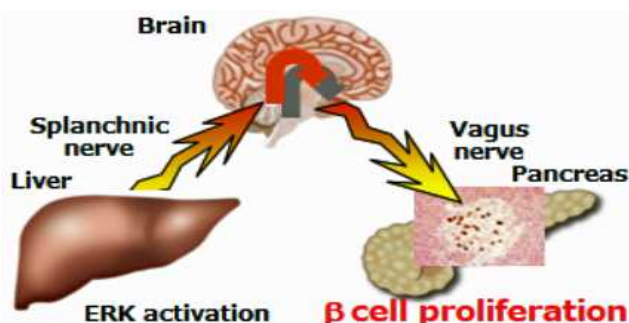

2. Outcome so far

(1) Nerve stimulation of the pancreas increases insulin-producing cells
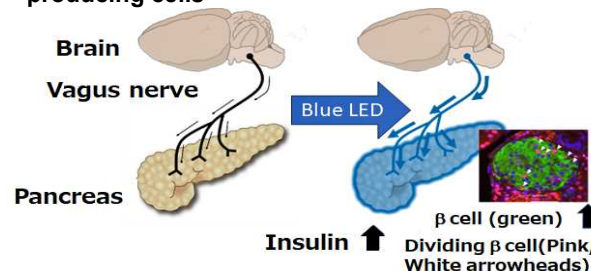
Press Release with Tohoku University and JST (2023.11.10)

This is an important achievement that demonstrates POC for the regulation of inter-organ networks and vagus nerve stimulation to the pancreas as a method of diabetes prevention and treatment.

**(2) Elucidating the mechanism of middle-aged obesity**
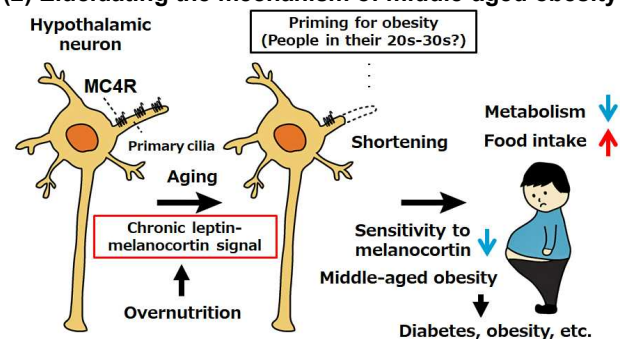
Press Release with Nagoya University and JST (2024.3.7)

The results show that the length of primary cilia in the brain's neurons determines the susceptibility to obesity and that their shortening due to aging and overnutrition is the cause of middle-aged obesity. It is expected to lead to the development of preventive methods and treatments for lifestyle-related diseases at a pre-symptomatic stage.

(3) Development of mice in which cell proliferation can be observed in a living state
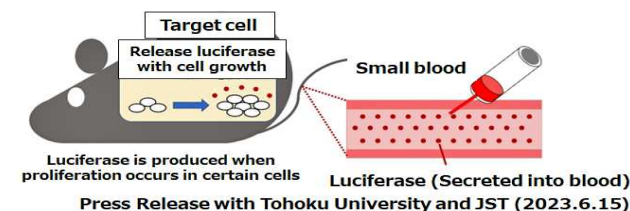
Press Release with Tohoku University and JST (2023.6.15)

This is the result of the development of mice in which proliferating cells can be observed alive by simply drawing a very small amount of blood when necessary. It is expected to be applied to research on treatments in various diseases, such as regenerative therapy for diabetes that increases insulin-producing cells and drug development that suppresses the growth of cancer cells.

3. Future plans

In the future, we will try to analyze glucose metabolism in epilepsy patients with implanted vagus nerve stimulator in order to validate the results of vagus nerve stimulation obtained in mice in humans. This will lead to the development of methods to prevent and treat diabetes using vagus nerve stimulation.

In addition, to elucidate the molecular mechanism of afferent activation and to control it by compounds, we will try to screen for molecules that activate afferent nerves and regulate pancreatic β cell proliferation, basal metabolic increase, and blood pressure fluctuations. This will lead to the development of methods to prevent and treat diabetes and its co-morbidities with the compounds.