# Research Center for Medical Sciences Institute of Clinical Medicine and Research

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## **General Summary**

In addition to performing our own research activities, in 2015 we started an educational laboratory course program with the assignment of third-year students from the School of Medicine. We also fulfilled research support duties for registered researchers from Kashiwa University Hospital (Departments of Gastroenterology; Laboratory Medicine; Neurosurgery; Diabetes, Metabolism and Endocrinology; and Obstetrics and Gynecology) so that physician-researchers could work freely. Their research work has progressed efficiently.

### **Research Activities**

Mechanism of islet injury and beta cell regeneration in diabetes mellitus

Although most cells in the pancreatic islets of Langerhans (pancreatic islets) are derived from endodermal endocrine cells, the islet structure also includes peripheral nerve fibers that are non-endocrine cells, capillaries, and ectoderm oriented, such as neural crestderived peri-islet Schwann cells. The Schwann cell might have the same functions as allogeneic astrocytes and Schwann cells in other tissues of the nervous system. These functions might include the supplementation of nutrients to the blood vessels and endocrine cells and shielding cells from exogenous stress, but the functions remain unclear. Helpful research might be to elucidate the structure-function relationship of the islet compartment structure and to understand the origins of pancreatic islet failure in diabetes. Under this concept of "self-organization of the islet" in 2014, we started a study of "beta cell protection from metabolic stress." Experiments showed that, in the co-culture conditions of MIN6, a murine beta cell line, and IMS32, a murine Schwann cell line, glucosestimulated insulin secretion or insulin secretory capacity was significantly higher than in MIN6 of a single culture system. These phenomena were considered protective effects from Schwann cells. We are planning to identify the mechanism of the increased capacity of glucose-stimulated insulin secretion.

Study of glucose and lipid metabolism through novel technology of biological gas measurements

Continuing from the previous fiscal year, we searched for a method of detection with skin-derived gas-by-gas chromatography.

Study of the change of body components during treatment of diabetes mellitus by sodium-dependent glucose co-transporter inhibitor

In the treatment of type 2 diabetes with dietary restrictions and medication, changes of

body composition associated, in particular, with the possibility of muscle loss and body fat increase, have become a problem. Treatment with sodium-dependent glucose cotransporter (SGLT2) inhibitor, a novel oral antidiabetic agent, is expected to cause body weight loss due to fat reduction, but details of the body-composition change are not known. Furthermore, concerns have been raised about a possible worsening prognosis because of a decrease in skeletal muscle mass (sarcopenia). To clarify these issues, we have started a multicenter, open-label follow-up study of an SGLT2 inhibitor in Japanese patients with type 2 diabetes. So far 11 medical facilities are involved in this prospective study. In the preliminary analysis, body fat mass was found with dual-energy X-ray absorptiometry to have continued to decrease efficiently for as long as 24 weeks. Skeletal muscle mass decreased slightly during the initial 12 weeks yet showed no further decrease after 12 weeks. We plan to extend the study to evaluate several variables after 1 year.

#### **Publications**

Sasaki T, Seino Y¹, Fukatsu A², Ubukata M³, Sakai S³, Samukawa Y³ (¹Kansai Electric Power Hosp, ²Yachiyo Hosp, ³Taisho Pharml. Pharmacokinetics, pharmacodynamics, and safety of luseogliflozin in Japanese patients with type 2 diabetes mellitus: a randomized, single-blind, placebo-controlled trial. Adv Ther. 2015; 32: 319-40. Koido S, Homma S, Kan S, Takakura K, Namiki Y, Kobayashi H, Ito Z, Uchiyama K, Kajihara M, Arihiro S, Arakawa H, Okamoto M, Ohkusa T, Gong J, Tajiri H. Induction of antigenspecific cytotoxic T lymphocytes by fusion cellis generated from allogeneic plasmacytoid dendritic and tumor cells. Int J Oncol. 2014; 45: 470-8.

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Haneda M¹, Seino Y², Inagaki N³, Kaku K⁴, Sasaki T, Fukatsu A⁵, Kakiuchi H⁶, Sato Y⁶, Sakai S⁶, Samukawa Y⁶ (¹Asahikawa Med Univ, ²Kansai Electric Power Hosp, ³Kyoto Univ Grad Sch Med, ⁴Kawasaki Med Sch, ⁵Yachiyo Hosp, ⁰Taisho Pharm). Influence of renal function on the 52-Week efficacy and safety of the sodium glucose cotransporter 2 inhibitor luseogliflozin in Japanese patients with type 2 diabetes mellitus. Clin Ther. 2016; 38: 66-88.

## **Reviews and Books**

**Nemoto M, Sasaki T.** High-throughput screening of small interfering ribonucleic acid identifies important modulators in islet dysfunction and apoptosis. *J Diabetes Investig.* 2015; **6:** 390-2.