Department of Internal Medicine
Division of Diabetes, Metabolism and Endocrinology

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General Summary

The number of patients we see in our department per month in now 15,000 and is increasing every year. We mainly see patients with diabetes (including 10% of type 1 diabetes) or endocrinological disorders. Clinically, we attempt to provide best healthcare to our patients with research evidence, clinical expertise, and patients' preferences. To accomplish this goal, we encourage the members of our division to perform basic and clinical research of high quality. With respect to education, we accept international students from other institutions. We encourage our trainees to improve their presentation skills. Finally, we strongly encourage our investigators to write manuscripts.

Research Activities

Diabetic complications
1. Molecular mechanisms governing intracellular signal transduction focusing on cell types relevant to the complications of diabetes
2. Roles of small guanosine triphosphate (GTP)-binding protein Rho and Rho-kinase in renal, retinal, neuronal, and endothelial biology
3. Isoform-specific roles of Rho-kinase in pathogenesis of the complications of diabetes
Approaches to this study range from in vitro to in vivo using gene-targeting approaches in mice

Epidemiology
1. Clinical trials of the treatment of patients with diabetes using continuous and flash glucose monitoring
2. A nationwide epidemiologic study of mortality in approximately 3,500 patients with type 1 diabetes was started in 1986 and has continued to provide much information about the prognosis of Japanese children with type 1 diabetes
3. A population-based study of childhood obesity, insulin resistance and diabetes in the elderly, and genetic factors has also continued in Niigata Prefecture
4. Epidemiological study using data from more than 6,000 patients with diabetes from the 4 hospitals affiliated with The Jikei University

Molecular biology for pancreatic islets

Type 2 diabetes is known as a "bi-hormonal disorder" because of the dysregulated insulin and glucagon secretion. Reduced β cell mass is a major cause of dysregulated insulin secretion. Although a combination of elevated levels of glucose and free fatty acids (glucolipotoxicity) strongly induces β cell dysfunction and cell death, the underlying cause remains unclear. Also unclear is the precise molecular mechanism of glucagon in α cells. We found that serine/threonine kinase protein kinase c (Pkc) δ is involved in β cell death and glucagon secretion from α cells. Ongoing projects are as follows.

1. Molecular mechanisms of Pkcδ-dependent β cell mass reduction under conditions of glucolipotoxicity using β-cell-specific Pkcδ knockout mice and the insulin-secreting mouse insulinoma (MIN6) cell line
2. Involvement of the Pkcδ-pancreatic duodenal homeobox 1 (Pdx1) pathway studied with the chemical and genetic inhibition of Pkcδ in the MIN6 cell line
3. Molecular mechanisms of Pkcδ-dependent glucagon secretion under high-glucose conditions in the glucagon-secreting αTC1 cell line
4. The association of Pkcδ and peptide tyrosine tyrosine signals in glucagon secretion using the αTC1 cell line
5. Pkcδ function of insulin resistance in α cells studied with the chemical and genetical inhibition of Pkcδ in αTC1 cell line and islets
6. To elucidate the molecular mechanism of Pkcδ *in vivo*, establishment of α-cell- specific Pkcδ knockout mice
7. Physiological and histological characterization of deficiency of the gene protein kinase C, delta (*Prkcd*), in α cells under the diabetic condition

Endocrinology

1. Basic research

1) The role of 12-lipoxygenase in diabetic cardiomyopathy
2) The role of baroreflex sensibility on diabetic macroangiopathy, especially the effects of glycemic variability and blood pressure variability
3) Effect of a sodium-dependent glucose co-transporter (SGLT) 2 inhibitor in a rat model of diabetes
4) Effect of aldosterone in macula lutea degeneration

2. Clinical research

1) Effect of SGLT-2 inhibitor in patients with diabetes
2) The role of baroreflex sensibility in patients with diabetes
3) The durability of basal insulin affects day-to-day glycemic variability assessed by continuous glucose monitoring in patients with type 2 diabetes
4) Investigation of HbA1c, blood pressure, and body weight variability in patients with type 2 diabetes
5) Achievement of HbA1c and blood pressure and low-density lipoprotein-cholesterol goal of patients with type 2 diabetes (the Japan Diabetes Clinical Data Management Study Group)

Publications

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