

Department of Internal Medicine

Division of Diabetes, Metabolism and Endocrinology

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General Summary

Physicians should practice patient-oriented medicine based on the concept of evidence-based medicine, which consists of research evidence, clinical expertise, and patients' preferences. To accomplish this, we encourage the members of our staff to do basic and clinical research. Areas of research include diabetes, metabolism, and endocrinology.

Research Activities

Epidemiology and evidence-based medicine

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. A population-based interventional study of childhood obesity and glucose intolerance has also continued. Several clinical trials of the treatment of type 2 diabetes are being performed.

Genetic epidemiology of diabetes mellitus

To study the molecular mechanisms of the development of macrovascular complications, we have analyzed sets of human single nucleotide polymorphisms and have found that one antioxidant enzyme has a genetic association with increased coronary calcification. We will extend the analysis to other antioxidant enzymes.

Gene- and cell-based therapy for diabetes mellitus

For *in vivo* gene therapy to promote proliferation of pancreatic beta cells by activating the G1/S cell-cycle transition, we have developed an efficient gene-transfer method, direct injection of an adeno-associated virus vector expressing the CDK4R24C gene. We will present our results at the upcoming annual scientific session of the American Diabetes Association.

Diabetic vascular complications

Research has focused on the pathogenesis and treatment of diabetic vascular complications. Clinical studies have examined dietary therapy for type 2 diabetes. Experimental studies using vascular smooth muscle cells, mesangial cells, and retinal pericytes have investigated the role of the Rho/Rho-kinase-mediated signaling pathway in the path-

ogenesis of diabetic vascular complications and have provided evidence that these molecules are potential pharmacological targets in the treatment of diabetic vascular injury.

Insulin resistance and obesity

A series of basic research studies of insulin resistance were performed in Otsuka Long-Evans Tokushima Fatty rats. The effects of new oral hypoglycemic agents on insulin resistance were investigated.

Endocrinology

The possible relationship between tumor necrosis factor α and urocortin II was examined in HL1 cardiomyocytes, a cardiac cell line derived from mouse atrial cardiomyocytes. Clinical and pathological characteristics of preclinical Cushing's disease due to ACTH-precursor-producing pituitary macroadenoma were studied.

The effect of ghrelin, a stomach-derived hormone, on the generation of pancreatic beta cells was studied in streptozotocin-treated rats, an animal model of diabetes mellitus.

The cardioprotective role of heat shock transcription factor-1(HSF-1) were studied using HSF-1 transgenic and knockout mice.

Functional analysis of the novel S179R *POU1F1* mutation associated with combined pituitary hormone deficiency was performed.

A retrospective cohort analysis of patients with Grave's disease was performed to compare the efficacy and safety of antithyroid drugs.

Changes in levels of anti-thyrotropin receptor antibody after radioiodine therapy were evaluated in patients of childbearing age with Grave's disease.

Dietary therapy in patients with diabetes mellitus

The effects of pregerminated brown rice on postprandial blood glucose and insulin concentrations were compared with those of white rice in subjects with hyperglycemia. Postprandial blood glucose levels were lower with brown rice than with white rice. The incremental area under the curve of blood concentrations for 180 minutes after ingestion was significantly lower with brown rice than with white rice. The postprandial blood insulin concentration was slightly but not significantly lower with brown rice than with white rice.

Publications

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