

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 goal, 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 using continuous glucose monitoring are being performed.

Molecular diabetology and islet medicine

Injuries to islet cells and the reduced regenerative capacity are novel therapeutic targets in the pathophysiology of diabetes. Our study group has succeeded in direct *in vivo* transfer of genes, including cell-cycle regulators. We confirmed that regulated proliferation of mature beta cells restored glucose metabolism in diabetic mice. This year, we have also begun to focus on peri-islet Schwann cells to investigate their critical role in the protection of islet endocrine cells. We found by a developmental engineering technique in mice that peri-islet Schwann cells are derived from the neural crest.

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 a new oral hypoglycemic agent (dipeptidyl peptidase IV inhibitor) on insulin resistance were investigated.

Dietary therapy

A highly monounsaturated enteral formula suppressed postprandial hyperglycemia,

without exaggerated insulin secretion, to a greater extent than did a high-carbohydrate enteral formula in patients with type 2 diabetes mellitus and in healthy subjects. Continuous glucose monitoring showed that a highly monounsaturated enteral formula significantly suppressed postprandial hyperglycemia and markedly reduced the 24-hour glycemic variations in tube-fed patients with type 2 diabetes to a greater extent than did a high-carbohydrate enteral formula, even if carbohydrate nutrients were adjusted to have a low glycemic index.

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 endothelial cells, mesangial cells, neural cells, and retinal pericytes have investigated the role of Kruppel-like factor 2, Rho/Rho-kinase, and the peroxisomal proliferator-activated receptor α -mediated signaling pathway in the pathogenesis of diabetic vascular complications. These studies have provided evidence that these molecules are potential pharmacological targets in the treatment of diabetic vascular injury.

Endocrinology

To identify and separate stem-like cells in human pituitary adenomas, we focused on the expression of CD133, a tumor stem-cell marker in brain tumors, and examined the differences indicating stem properties between CD133(+) cells and CD133(-) cells.

The effects of Ca-channel antagonists on the expression of steroidogenic enzymes were evaluated with a human adrenocortical carcinoma cell line, NCI-H295R.

The 12-lipoxygenase (12-LO) pathway may be involved in the pathogenesis of diabetic cardiomyopathy. Therefore, the role of 12-LO in cardiomyopathy was studied in vivo in a rat model of diabetic cardiomyopathy and in vitro with a primary cardiomyocyte culture system.

The possible direct effect of endotoxin on human stellate cells, which play a critical role in the progression of nonalcoholic steatohepatitis, was studied using LX-2 human stellate cells.

Previous studies have shown that the cardiac secretion of ACTH is increased in patients with hypertension, indicating that ACTH may be involved in the pathophysiology of cardiovascular diseases. Recently, it has been shown that pro-opiomelanocortin messenger RNA is expressed in the murine heart. Therefore, we designed a study to clarify the pathophysiological role of pro-opiomelanocortin using HL-1 cardiomyocytes.

Publications

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