# Department of Internal Medicine
# Division of Kidney and Hypertension

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## General Summary

Major fields of research are 1) nephrology, 2) hypertension, and 3) uric acid metabolism. Published achievements and recent reports are summarized here.

## Research Activities

*Nephrology*

1. Glomerulonephritis

The serum level of granulocyte-colony stimulating factor (G-CSF) might be a useful biomarker for predicting the course of diabetic nephropathy, and G-CSF might show antiapoptotic effects on renal vascular cells through the G-CSF receptor.

Glomerular density in renal biopsy specimens might be used as a long-term prognostic indicator in of IgA nephropathy. We reported the generation of a stem-cell-derived organoid that could produce erythropoietin and was sensitive to regulation by anemia, indicating a function in erythropoiesis. Podocyte-derived bone morphogenic protein 4 might act as a paracrine factor on the precursor cells of the glomerular capillary tuft, thereby regulating morphogenesis of the glomerulus.

2. Dialysis

We compared clinical features in the management of renal osteodystrophy between Japan and the United States. The clinical effectiveness of percutaneous injection therapy with ethanol and active vitamin D was verified for secondary hyperparathyroidism. We revealed that the function of L-type $Ca^{2+}$ channels of cultured parathyroid cells depends on the extracellular $Ca^{2+}$ concentration. We assessed the clinical value of combined therapy with peritoneal dialysis and hemodialysis; we found that combined therapy is a useful way to control body fluids and, moreover, that peritoneal function may be maintained long term. We studied the safety and efficacy of combination therapy with diltiazem and tacrorimus-based immunosuppressive treatment to maintain optimal serum tacrorimus concentrations in patients with poor bioavailability after renal transplantation. In transplant glomerulopathy, glomerular expression of plasmalemmal vesicle-associated protein-1 is positively correlated with the severity of transplant glomerulopathy and proteinuria. We are investigating the mechanism of cyst formation in polycystic kidney disease by using cells derived from the PKD knockout mouse.

*Hypertension*

The T-type $Ca^{2+}$ channel blocker is a promising agent for the treatment of hypertension in chronic kidney disease. Candesartan is specifically indicated for patients with chronic kidney disease who require a more intensive treatment to prevent cardiovascular complications. Carotid-femoral pulse wave velocity, urinary albumin excretion, and brain natriuretic peptide were related to each other as predictors of and risk factors for cardiovascular diseases in patients with hypertension.

*Uric acid metabolism*

Renal function deteriorates more quickly in patients with gouty kidney than in patients with nongouty kidney. Allopurinol was mainly used to treat hyperuricemia in airline cockpit crew; however, the control of hyperuricemia was not sufficient, due, in part, to the complex procedure for changing prescriptions. The high incidence of renal hypouricemia in Japanese reflects the high incidence of the G774A mutation of URAT1 genes.

**Publications**

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