

## 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 glomeruli from patients with obesity-related glomerulopathy showed glomerulomegaly, and the glomerular number and the body-mass index were independent factors correlated with glomerular size. We demonstrated that both the nephron number and glomerular enlargement play a crucial role as compensatory mechanisms against the deterioration of renal function in chronic kidney disease. We have created inducible vascular endothelial growth factor (VEGF) transgenic mice, in which we have found several distinct glomerular phenotypes. It is suggested that Pax2-expressing human mesenchymal stem cells differentiate into the Wolffian duct by the influence of local signals in the chicken ureteric bud progenitor region.

##### 2. Dialysis

We found that changes in bone turnover or osteoprotegerin itself affected the response of urinary phosphate excretion via fibroblast growth factor (FGF)-23 to a high-phosphate diet in osteoprotegerin knockout mice. In cultured parathyroid cells isolated from patients with secondary hyperparathyroidism, we found that L-type  $\text{Ca}^{2+}$  channels play a role in the high extracellular  $\text{Ca}^{2+}$ -activated increase in cytoplasmic  $\text{Ca}^{2+}$  concentration. We found that treatment with both peritoneal dialysis and hemodialysis is a useful way to control body fluids and that peritoneal function may be maintained for a long time. We studied acute humoral rejection and performed ABO-incompatible renal transplantation and husband-to-wife renal transplantation. In transplant glomerulopathy, glomerular expression of plasmalemmal vesicle-associated protein-1 is positively correlated with the severity of transplant glomerulopathy and proteinuria.

#### *Hypertension*

Insulin resistance was a significant risk factor for the deterioration of renal function in patients with hypertension and chronic kidney disease but without diabetes.

Our clinical experiment suggested that in men with untreated essential hypertension, the serum uric acid level is an independent marker of systemic arterial stiffness and microalbuminuria.

#### *Uric acid metabolism*

To clarify the significance of uric acid in toxemia and pregnancy-induced hypertension (PIH), the relationship between uric acid and clinical variables was investigated in patients with toxemia and PIH in our hospital. Levels of uric acid and lactate dehydrogenase (LDH) were inversely correlated with birth weight in both conditions. A significant correlation was seen between the levels of LDH and uric acid. In multiple regression analysis, only LDH was associated with birth weight in both toxemia and PIH. Some common humoral factors, such as soluble fms-like tyrosine kinase 1, might contribute to the correlation between LDH and uric acid through endothelial cell injury. In inflammatory arthritis after parathyroidectomy in patients with secondary hyperparathyroidism, pseudogout must be considered. Uric acid dynamics was investigated after renal transplantation.

#### Publications

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