

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 prognosis of patients with IgA nephropathy and metabolic syndrome may be unfavorable because these patients show resistance to renin-angiotensin system (RAS) inhibitors owing to obesity and insulin resistance. Our data demonstrated that plasmalemmal vesicle-associated protein 1 is expressed in the lesions of polar vasculosis and glomerular capillaries in the early stage of diabetic nephropathy, suggesting that the phenotypic change of endothelial cells forming caveolae may occur in the development of diabetic nephropathy. Vascular endothelial growth factor and bone morphogenetic protein 4 can act on the endothelial precursor cells, as a stimulator and an inhibitor, respectively, thereby orchestrating the morphogenesis of glomerular capillary tufts. We successfully induced kidney regeneration without an adenovirus by using an artificial pathogen-free biomaterial as a tool to diffuse glial-cell—derived neurotrophic factor.

2. Dialysis

We found that the changes in bone turnover or in osteoprotegerin itself influenced the response of urinary phosphate excretion via fibroblast growth factor 23 to a high-phosphate diet in osteoprotegerin knockout mice. We also evaluated the role of collagen enzymatic and glycation-induced cross-links as a determinant of bone quality in patients with secondary hyperparathyroidism.

We found that L-type Ca^{2+} channels play a role in the high extracellular Ca^{2+} -activated increase in cytoplasmic Ca^{2+} concentration.

We evaluated the clinical value of the combination of peritoneal dialysis and hemodialysis and found it is a useful way to control body fluids and may allow peritoneal function to be maintained for a long period of time. In transplant glomerulopathy, the glomerular expression of plasmalemmal vesicle-associated protein 1 was found to be positively correlated with the severity of transplant glomerulopathy and proteinuria.

Hypertension

Blockade of T-type Ca channels constitutes a new therapeutic target for protecting against cardiovascular disease in patients with chronic kidney disease. The levels of 24-hour urinary protein excretion, serum creatinine, global glomerulosclerosis, and interstitial damage before pregnancy may be predictors of the risk of hypertension due to superimposed preeclampsia in patients with IgA nephropathy. In male patients with untreated essential hypertension, the serum level of uric acid is an independent marker of systemic arterial stiffness and microalbuminuria.

Uric acid metabolism

The G774A mutation in the SLC22A12 gene encoding urate transporter 1 is common in Japanese patients with renal hypouricemia. This G774A mutation was likely introduced by immigrants from mainland Asia and thereafter expanded in the Japanese population by founder effects or genetic drift or both. Carotid artery intimal-medial thickness in patients with gout or hyperuricemia was suggested to be increased by decreased renal function.

Publications

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