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General Summary

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

Research Activities

Nephrology

1. Glomerulonephritis

We have established 4 histological grades corresponding to the percentage of glomeruli exhibiting pathological variables. Our evidence-based histological classification can identify the magnitude of the risk of progression to end-stage kidney disease and is useful for predicting long-term renal outcomes in immunoglobulin A (IgA) neuropathy.

We demonstrated that glomerular density in renal biopsies may be an important determinant of glomerular size variability and can influence the clinical phenotype in adult patients with minimal change nephrotic syndrome.

Dysregulation of vascular endothelial growth factor (VEGF) expression plays an important role in the pathogenesis of certain renal diseases. We generated and analyzed inducible and podocyte-specific VEGF transgenic mice using the Tet-On system. Our results demonstrate that the dysregulation of VEGF expression can alter the characteristics of both endothelial and mesangial cells, thereby leading to the impairment of glomerular capillary formation.

We determined the metabolic function of transplanted metanephroi with particular reference to maintaining blood pressure. We found that transplantation of metanephroi produces plasma rennin activity and contributes to raising blood pressure in a rat model of acute hypotension.

2. Dialysis and kidney transplantation

We investigated the effects of cinacalcet on serum levels of Ca and P in patients undergoing hemodialysis with or without high levels of parathyroid hormone to control serum levels of Ca and P. We concluded that administration of cinacalcet to patients with or without high parathyroid hormone levels facilitates the control of Ca and P levels.

Encapsulating peritoneal sclerosis is a severe complication of long-term peritoneal dialysis (PD) and has a high mortality rate. We used a laparoscopic approach to evaluate peritoneal injury in patients undergoing PD. We found that PD peritonitis is a risk factor

for encapsulating peritoneal sclerosis and hypothesized that the bacterial species causing PD peritonitis changes depending on the neutral-pH PD solution.
We showed an association between peritubular capillary endothelial c-Jun activation and interstitial fibrosis in chronic antibody-mediated rejection.
We investigated the mechanism by which the intracellular Ca^{2+} concentration changes by applying drugs or by changing the extracellular Ca^{2+} concentration. Calcium oscillations may be associated with the function of renal tubular epithelial cells.

Hypertension
The Jikei Optimal Antihypertensive Treatment (JOINT) study is a large-scale prospective interventional observational study that examined the effects of a fixed-dose combination of losartan and hydrochlorothiazide in patients with chronic kidney disease. The study has been finished and recruited a total of 280 participants. The main results have been published in *Clinical and Experimental Nephrology*. Additionally, as a subanalysis of the JOINT study, an extensional observation was performed on the relationship between uric acid and its associates.
A study of the effect of intensive antihypertensive therapy on the increased intrarenal-renin angiotensin system in patients with chronic kidney disease was designed and performed. The main finding was that both urinary protein and angiotensinogen were decreased in response to the intensive treatment.
Change in blood pressure during hemodialysis is not associated with water removal but is correlated with changes in hormones of the renin-angiotensin-aldosterone system (RAAS). Moreover, the response of RAAS hormones to fluid removal is improved in the presence of RAAS inhibitors, suggesting that RAAS blocking modulates the blood pressure-controlling mechanism in patients undergoing hemodialysis. This abnormal blood pressure regulation might be accelerated in the presence of diabetes.

Uric acid metabolism
The urinary excretion of uric acid and sodium was examined in patients with IgA nephropathy. There were two types of patients: in one type urinary excretion of uric acid was significantly correlated with that of sodium (sodium-dependent type), and in the other type the urinary excretion of uric acid was not correlated with that of sodium (sodium-independent type). Renal tubule-interstitial damage was present only in patients with sodium-dependent-type IgA nephropathy.

Publications

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Reviews and Books

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