Department of Internal Medicine
Division of Nephrology and Hypertension

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General Summary

Our department is one of the largest nephrology departments in Japan and includes all subspecialties of nephrology, i.e., from early chronic kidney disease (CKD) with proteinuria to dialysis and kidney transplantation. Therefore, our research groups are investigating diverse subjects and aim to eventually find new therapeutic strategies and mechanisms of disease progression, which may help decrease the number of patients with end-stage renal diseases.

Research Activities

Studies on IgA nephropathy (IgAN)
A multicenter, prospective cohort study (J-IGACS) is currently in progress. By using a national survey database (JRBR), we have conducted a study on regional variations of the clinical features at diagnostic renal biopsy in Japanese patients with IgA nephropathy.

Studies on low glomerular density (GD) in CKD
We have reported on glomerular density and volume in renal biopsies of children with proteinuria relative to preterm birth and gestational age (Koike K et al. Clin J Am Soc Nephrol. 2017). Collaborative research about the estimation of nephron numbers in Japanese is currently in progress.

Impact of hypertension, diabetes and aging on renal damage
Studies on renal alteration caused by hypertension, diabetes and aging using autopsy kidneys are currently in progress.

Studies on podocyte damage
Micro-array analysis of damaged podocytes in in vitro and in vivo revealed that ratios of increase in some 100 transcripts showed quite strong correlation between the two situations. Among these, Egr1 and Maff were included, transcription factors that antagonize Wt1 and Mafb, respectively. Indeed, level of podocin mRNA was dysregulated by a change in Egr1 or Maff expression. The result suggested that these two transcription factors can have an important role for the development of podocyte damage.

Studies of CKD-MBD
We previously reported that the DNA methylation patterns in CaSR and VDR genes were modified in the parathyroid glands (PTGs) of chronic kidney disease-mineral and bone disorder (CKD-MBD) (Uchiyama T et al. Hum Cell 2016). We then analyze the effect of histone modification in the PTGs of CKD-MBD. Furthermore, we are investigating how glial cells missing 2 (Gcm2) in PTGs, which is the essential transcription factor for parathyroid development in terrestrial vertebrates, affects PTGs function.
Magnesium (Mg) concentration is a proven predictor of mortality in hemodialysis patients. Judging from these facts, we showed that proton pump inhibitor use is associated with an increased risk of hypomagnesemia in hemodialysis patients by prospective cohort study (Nakashima A et al. PLOS ONE 2015).

Study of renal transplantation
We participated in Japan Academic Consortium of Kidney Transplantation (JACK) and published the following clinical and pathological analysis focused on; 1. HSPN(Kawabe M et al. CEN case Reports. 2016), 2. The prognostic value of Caveolin-1 in peritubular capillary(Nakada Y et al. Clinical Transplant. 2016) and 3. The significance of medullary ray injury(Niikura T et al. Transplant Proc. 2017).

Studies of peritoneal dialysis
We reported the change in clinical form of PD-associated peritonitis during 36 years and the difference of calcium and PTH levels PD and HD. We conduct clinical research of bicarbonate/lactate-buffered neutral PD solution, diabetic PD patients, and peritoneal membrane pathology.

Studies of anemia in CKD
We reported the association between higher serum ferritin and higher mortality among 191,902 HD patients using Japanese nationwide dialysis registry, We continue the clinical research among hepcidin, an important regulator of iron homeostasis, and clarified the clinical utility among non-dialyzed CKD patients.

Renal protective effects of T-type calcium channel blockade via blood brain barrier in chronic kidney disease model rats
We investigate whether there is different mechanism of renal protective effect via the agent's difference from capacity of penetrating the blood-brain barrier, using the new T-CCB agent, which can or cannot penetrate the blood-brain barrier.

Renal protective effects of azilsartan in adenine-induced renal failure model rats
Although daily urinary sodium excretion is decreased in non-medication group, azilsartan (Azi) suppressed the decreasing sodium excretion, urinary protein excretion and sympathetic nerve activity and upregulated renal ACE2 activity. We will investigate further molecular mechanism of renal protection.

Significance of serum uric acid level in patients receiving dialysis

In hemodialysis patients, lower levels of serum uric acid (SUA) were independently associated with all-cause and cardiovascular mortality among hemodialysis patients. However, in peritoneal dialysis patients, there are no relationship between SUA and mortality. Close monitoring of SUA is thought to be necessary for the management of hemodialysis patients.

Basic study for kidney regeneration

A novel system to regenerate the kidney by replacing nephron progenitor cells in an empty niche.

The kidneys develop through reciprocal and sequential interactions between the ureteric bud (UB) and surrounding cap mesenchyme (CM). The engraftment efficiency of cells transplanted to a nephrogenic niche has been very low, with the underlying cause considered to be the competition with the existing native host cells occupying the niche.

We demonstrated that the transplanted progenitor cells replaced the native progenitor cells in CM using a nephron progenitor eliminate system that used Cre-LoxP technology in combination with diphtheria toxin (DT)-mediated cell elimination.

Using the progenitor eliminate system, it was shown that competing native progenitor cells were completely replaced by transplant cells in CM. Furthermore, the replaced transplant cells displayed reciprocal interactions with the host UB and complete differentiation to nephrons.

Publications

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