**Neuro-immune systems-mediated renal protection mechanism**

The nervous system and immune systems have been studied independently as they were thought to be autonomous parallel systems. However, recent advances have shown that these two systems interact in complex ways to maintain homeostasis and respond to stress or injury. Some immune cells have receptors for neurotransmitters and the existence of immune cells that produce neurotransmitters such as acetylcholine has been clarified, and the mechanism of immune system regulation via the nervous system is being elucidated. The cholinergic anti-inflammatory pathway is a well-studied neuroimmune interaction involving the vagus nerve. In fact, electrical vagus nerve stimulation (VNS) has been shown in animal experiments to ameliorate various diseases such as myocardial infarction, pancreatitis, and sepsis. In addition, the effectiveness of the implantable vagus nerve stimulator has been confirmed in Crohn’s disease and rheumatoid arthritis patients in pilot studies.

We have so far showed the following: 1) VNS protected the kidney from acute kidney injury. 2) α7 nicotinic acetylcholine receptor (α7nAChR) positive macrophages and β2 adrenergic receptor positive CD4 T cells play an important role in exerting the renal protective effect by VNS. 3) We newly identified Hes1 (hairy and enhancer of split-1) as downstream gene of α7nAChR by RNA-seq and functional analysis of genes. 4) It was discovered that C1 neuron stimulation in the medulla by optogenetics had a renoprotective effect. Thus, as the elucidation of the renal protective effect through the neuro-immune system is gradually progressing, the development of further research on the neuro-immune-renal linkage is expected to lead to a new therapeutic option for inflammation-related disorders including kidney diseases.