CD8+NKT Cells and CD4+T Cells Mediate Ischemia Reperfusion Injury at Early Phase in Rat Experimental Model

Introduction and Objective: Renal ischemia-reperfusion (I/R) injury is an unavoidable occurrence in renal transplantation. The suppression of damage to kidney grafts caused by I/R injury could potentially improve the outcome of renal allografts. I/R injury has a complex pathophysiology that involves cellular mediators of immunity and recent studies have identified T cells as important mediators in renal I/R injury. Furthermore, the recruitment of T cells is induced by chemotaxis factors such as CXCR3 and CCR5. We investigated the expression of chemokines and the population of the infiltrating T cells using a rat renal I/R injury model.
Materials and Methods: Sprague–Dawley rats were subjected to left renal occlusion for 45min. After confirming reperfusion, a right nephrectomy was performed. To examine the role of chemokines, these animals were also given an intraperitoneal injection of 10 mg/kg CCR5 and CXCR3 antagonist (TAK) 30 min prior to I/R injury. Kidneys were sampled after being flushed with cold PBS at each time point.
Results: The expression of mRNA of chemokines that bind to CXCR3 and CCR5 in the post-ischemic kidneys was elevated at 1h after reperfusion. CXCL10 level were elevated from 1h after the reperfusion and peaked at 3h, and finally decreased at 6 h in I/R groups. While the phenotype and number of CD8+ NKT cells and CD4+T cells was increased at 3 h in post-ischemic kidney, TAK injection resulted in a reduction in the infiltration of T cells into the post-ischemic kidney. The TAK treatment suppressed the elevation in serum creatinine (sham group 0.40±0.05 mg/dl, I/R group 2.86±0.67 mg/dl, TAK group 1.60±0.73mg/dl), and resulted in less tubular damage compared with the I/R group.
Conclusions: The result of our present study demonstrated that chemokine production in the kidney was upregulated from the early phase after reperfusion and CD4+ Tcells and CD8+NKT cells mediate rat I/R injury.

	sham	control	TAK
KMNCs ($n\times10^6$)	9.6±2.5	19±6.1	9.3±2.3
population of T cells (%)			
CD4 (%)	26.3±1.8	33.0±6.5	27.2±2.8
CD8 (%)	35.8±9.5	25.8±3.2	41.4±7.4
NKT (%)	24.9±2.4	33.9±3.2	25.7±7.2
number of T cells (n)			
CD4 ($n\times10^4$)	14.5±3.4	31.9±17.3	13.4±1.8
CD8 ($n\times10^4$)	20.8±10.4	23.4±7.0	21.0±7.1
NKT ($n\times10^4$)	13.9±3.9	30.8±10.4*	12.6±3.0**