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실험적 사구체신염에서 NKT 세포의 역할

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The Cross-Talk between NKT Cell and Th17 Response in the Experimental Autoimmune Glomerulonephritis

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Th17 cells are emerging as a major player in several autoimmune diseases such as multiple sclerosis and rheumatoid arthritis which was known as a Th1 mediated disease previously. NKT cells, which have a role of linkage between the innate and adaptive immune response, are also associated with the development of autoimmune disease. But the cross-talk between NKT cell and Th17 has not been evaluated simultaneously in the context of autoimmune disease. In present study, we examined the role of NKT cell/Th17 response in autoimmune glomerulonephritis (AGN) utilizing a murine model of chronic graft-versus-host disease.

AGN was induced by the adoptive transfer of lymphocytes from (C57BL/6 x DBA/2J) F1 hybrids into wild C57BL/6, type I/II NKT cell deficient, and type I NKT cell deficient mice. The transferred lymphocytes infiltrated into the glomeruli inducing cellular proliferation. The severity of AGN, confirmed by deterioration of kidney function, proteinuria, and renal pathology, was attenuated with the absence of NKT cells compared to wild type mice. Complement 3 deposition and T cell infiltration were consistent with the severity of AGN. NKT cells were recruited into glomerulus with the induction of AGN. The systemic immune responses as measured by splenic T cell activation, intracellular IL-17, and inflammatory cytokines, are enhanced with the induction of AGN. But the absence of NKT cells, especially both of type I and II NKT cells, reduced the systemic immune responses. The intrarenal immune response induced by AGN was paralleled with systemic responses. Moreover, intrarenal STAT3 phosphorylation, which is the major transcription factor for Th17 response, was significantly attenuated in NKT cell deficient hosts. NKT cells secreted IL-17 as well as inflammatory cytokines (TNF-α, IL-6, IL-12, IFN-g) when activated. Blocking of IL-17signaling reduced the mesangial cell responses against the stimuli induced by the nephritogenic lymphocytes.

Taken together, the cross-talk between NKT cell and Th17 response might be a pivotal linkage for the development of AGN.

Key Words: NKT 세포, Th17, 사구체신염
NKT cell, Th17, Glomerulonephritis