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실험적 루프스신염에서의 Th17 반응

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Th17 Responses in the Experimental Lupus Nephritis

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Th17 cells, secreting potent proinflammatory cytokine IL-17, are emerging as a major player in several autoimmune diseases such as multiple sclerosis which was known as a Th1 mediated disease previously. We hypothesized that Th17 immune response might be involved in the pathogenesis of lupus nephritis (LN). In present study, we examined the Th17 response in the experimental LN utilizing a murine model of chronic graft-versus-host disease.

The experimental LN was induced by injection of lymphocytes from (C57BL/6xDBA/2J) F1 hybrids into wild C57BL/6 mice. The transferred donor lymphocytes infiltrated into the recipient glomeruli inducing cellular proliferation. Induction of LN was confirmed by deterioration of kidney function, progressive proteinuria, and renal pathology (mesangial proliferation and glomerular crescents formation accompanied with CD3 cell infiltration in mice kidney). CD69, an activated T cell marker, and intracellular IL-17 expression increased in the spleen of LN mice. Inflammatory cytokine/chemokine (MCP-1, IL-6, INF-γ) mRNA increased in LN mice systemically. Th17 response related cytokines such as IL-17, IL-23 and IL-27 were also increased in the spleen by real-time PCR. In LN kidney, IL-17 receptor (IL-17R), IL-27 and STAT3 mRNA were all increased. The expression of intracellular IL-17 protein also increased in LN kidney. In addition, immunohistochemical study showed that IL-17 and STAT3, the essential transcriptional factor of Th17 cell differentiation, were observed only in the disease-induced kidney. Treatment of CD3 in co-cultured mesanigal cells and NKT cells induced the secretion of inflammatory cytokines like IL-2, TNF-α and IL-6. The expression of IL-17R mRNA and secretion of IL-17 and IL-12p70 also increased in the co-cultured cells. Blocking of IL-17R reduced these inflammatory reactions.

Taken all together, Th17 response was enhanced in the experimental LN. Th17 related molecules might be the novel therapeutic target of LN.

Key Words: 실험적 루프스신염, Th17 반응, 자연살해세포
Experimental Lupus Nephritis, Th17 Response, NKT cell