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실험적 반월상 사구체 신염에서 IL-17 signaling의 역할

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Role of IL-17 Signaling in the Experimental Crescentic Glomerulonephritis

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T cells play a major role in the pathogenesis of crescentic glomerulonephritis (GN), which is the most severe form of GN and progresses to end-stage renal disease unless treated adequately. Th17 cells have been reported to contribute to renal injury in crescentic GN. In the present study, we examined the notion that the modulation of Th17 response could reduce the renal injury utilizing a murine cresentic GN model. IL-17 deficient and STAT-3β deficient mice were used because IL-17 is the major cytokine of Th17 cells and STAT-3 is the essential transcriptional factor of Th17 cell differentiation.

Experimental crescentic GN was induced by the injection of anti-glomerular basement membrane (GBM) antibodies into Balb/c, C57BL/6, IL-17 deficient Balb/c, and STAT-3β deficient C57BL/6 mice. After 7 days of disease induction, the elevated BUN and urine protein/creatinine ratio in wild type mice were significantly reduced in IL-17 deficient (BUN 55$\pm$22.7 vs 154$\pm$17.5 mg/dL, $p<0.01$; U prot/cr 114$\pm$10.6 vs 143$\pm$16.6 mg/mg, $p<0.05$) and STAT-3β deficient mice (BUN 116$\pm$25.0 vs 156$\pm$8.0 mg/dL, $p<0.05$; U prot/cr 53$\pm$6.8 vs 99$\pm$6.8, $p<0.05$). In addition, the glomerular injury and crescent formation by anti-GBM antibody were attenuated in IL-17 deficient and STAT-3β deficient mice compared to those of wild type mice. Accordingly, intrarenal mRNA expression of IL-1β, TGF-β, MCP-1, IL-12p19 and STAT-3 were elevated in wild type mice, but these changes were attenuated in IL-17 and STAT-3β deficient mice. Treatment of CD3 in co-cultured mesanigal cells and NKT cells induced mRNA expression of IL-17 receptor and secretion of IL-17 and IL-12p70 as well as inflammatory cytokines such as IL-2, TNF-α and IL-6. Blocking of IL-17 receptor reduced these inflammatory reactions.

Taken together, these data suggest that Th17 cells play an important role in the pathogenesis of experimental cresecentic GN. IL-17 and STAT-3 might be a feasible target in protecting renal injury in the disease.

Key Words: 인터류킨-17, 사구체 신염, STAT-3
IL-17 signaling, Glomerulonephritis, STAT-3