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STAT3/Th17 신호에 의한 실험적 반월상사구체신염의 기전 연구

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The Role of STAT3/Th17 Axis in the Experimental Crescentic Glomerulonephritis

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Background: Th17 cell has been known to play an important role in the pathogenesis of autoimmune glomerulonephritis (GN). However, definite signaling pathway remained to be determined. IL-17 is the major cytokine of Th17 cells and STAT-3 is the essential transcriptional factor of Th17 cell differentiation. Therefore, we evaluated the role of Th17 pathway focusing IL17, STAT3 and RORγt in the experimental autoimmune GN model.
Method: Experimental crescentic GN animal model was induced by the injection of anti-GBM antibodies into Balb/c, C57BL/6, IL-17 deficient Balb/c, and STAT-3β deficient C57BL/6 mice.
Results: The renal function and proteinuria were significantly improved in IL-17 deficient and STAT-3β deficient mice compared to wild-type mice at day 7. In addition, degree of glomerular proliferation, crescent formation and tubulointerstitial destruction was alleviated in IL-17 deficient and STAT-3β deficient mice. Intrarenal mRNA expressions of IL-6, IL-12p40, IL-23, TGFβ, STAT3, RORγt and IL-17 in the kidney were up-regulated in the mice rendered experimental crescentic GN, whereas the levels of those mRNA were suppressed following the deletion of Th17 cells. Moreover, intracellular production of IFNγ and IL-17 increased in regional renal lymph node of experimental crescentic GN mice. We also found that mRNA expressions of TGFβ and RORγt was mitigated, while Ctr9 mRNA (down-regulation of IL-17) expression was elevated in STAT-3β deficient mice than in wild type mice. In an in-vitro mesangial cell-T cell interaction system, Th17 cells enhanced the secretion of pro-inflammatory cytokines.
Conclusion: We suggest that STAT3 plays an important pro-inflammatory role in anti-GBM antibodies-induced crescentic glomerulonephritis by promoting the activation of Th17 cells, and cytokine secretion, and it leads to severe kidney injury.

Key Words: 반월상사구체신염, IL-17, STAT3
Crescentic glomerulonephritis, IL-17, STAT3