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Natural Killer T (NKT)세포가 실험적 항기저막 사구체 신염의 발생과 경과에 미치는 영향

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Effects of NKT Cells on the Development and Progression of Experimental Glomerulonephritis in Mice

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Background and Methods : Natural killer T (NKT) cells expressing semi-invariant CD1d-reactive TCR have been known to exert protective roles in the autoimmune and infectious diseases. Semi-invariant NKT cells produce multiple cytokines and confer protection in immune-mediated disorders upon activation. But the regulatory function of CD1d- dependent NKT cells in glomerulonephritis (GN) has not been investigated thoroughly. Here we have evaluated the immune regulatory capacity of CD1d-dependent NKT cells using a mouse anti-GBM GN model. GN was induced in C57BL/6 (B6) and NKT cell deficient mice (B6.CD1d$^{-/-}$) by the injection of rabbit anti-GBM Ab.

Results : B6.CD1d$^{-/-}$ mice showed a markedly accelerated GN compared to wild type mice (urine protein/cr 177.0±18.10 mg/mg vs. 92.7±11.07, $p<0.004$) by the induction of disease. But the repletion of NKT cells into B6. CD1d$^{-/-}$ mice by adoptive transfer of hepatic NKT cells, lessened the severity of GN similar to wild type mice (urine protein/cr 92.73±11.07 mg/mg vs. 87.18±6.46, p=ns). Adoptive transfer of hepatic NKT cells on B6.CD1d$^{-/-}$ mice was also effective to protect renal function and prevent from crescent formation compared to non-treated deficient mice. Intra-glomerular expression of TGF-β was markedly attenuated in hepatic NKT cell-reconstituted B6.CD1d$^{-/-}$ mice and the expression of nuclear p65, cytosolic iKB and TGF-β decreased by the adoptive transfer of hepatic NKT cells in a dose-dependent manner. After injection of hepatic NKT cell into affected B6.CD1d$^{-/-}$ mice, fluorescent-labeled NKT cells were distributed in 10 to 30% of glomeruli which were damaged by anti-GBM Ab, but the introduced cells were not found in the tubulointerstitial area. D32.D3, a NKT cell line, secreted abundant IL-4 and IFN-γ with the activation by α-galactosyl ceramide, but LPS stimulation on activated NKT cells suppressed TGF-β production. The adoptive transfer of hepatic NKT cells into B6.CD1d$^{-/-}$ mice lessened the severity of GN along with the reduced expression of TGF-β and IFN-γ in glomeruli perse.

Conclusion : These findings highlight the CD1d-dependent NKT cells have the direct regulatory capacity in experimental GN and the regulation may be dependant on, at least in part, NFκB- ikB interaction.