

## Th17세포가 실험적루프스신염 발생에 미치는 영향

고려대 구로병원<sup>1</sup>, 서울대학교 신장연구소<sup>2</sup>, 동국대일산병원<sup>3</sup>, 서울대병원<sup>4</sup>

전은실<sup>1</sup> · 양승희<sup>2</sup> · 신성준<sup>3</sup> · 이정표<sup>2</sup> · 차란희<sup>4</sup> · 김연수<sup>4</sup>

### Th17 Cells as the One of the Playmakers in the Pathogenesis of the Experimental Lupus Nephritis

Un Sil Jeon<sup>1</sup>, Seung Hee Yang<sup>2</sup>, Sung Joon Shin<sup>3</sup>, Jung Gil Lee<sup>2</sup>, Ran-hui Cha<sup>4</sup>, Yon Su Kim<sup>4</sup>

Department of Internal Medicine<sup>1</sup> Korea University Guro Hospital Seoul Korea

Seoul National University<sup>2</sup> Kidney Research Institute Seoul Korea

Department of Internal Medicine<sup>3</sup> Dongguk University College of Medicine Ilsan Korea

Department of Internal Medicine<sup>4</sup> Seoul National University College of Medicine Seoul Korea

Th17 cells, secreting potent proinflammatory cytokine IL-17, are emerging as a major player in the autoimmune diseases such as multiple sclerosis, previously known as Th1 mediated disease. Lupus nephritis (LN) is also known as Th1 cell mediated disease, but there were evidences that Th17 cells might be involved in the pathogenesis of LN. We already observed that experimental LN was attenuated in NKT cells-depleted mice. In this study, we examined the role of Th17 cells in the experimental LN mice model, and the effect of NKT cells as a regulator of Th17 cells in this process.

The experimental LN was induced by injection of lymphocytes from (C57BL/6xDBA/2J) F1 hybrids into wild C57BL/6, type I/II NKT cell deficient B6.CD1d<sup>-/-</sup> and type I NKT cell deficient B6.J $\alpha$ 18<sup>-/-</sup> mice. Induction of LN was confirmed by the infiltration of hybrid donor lymphocytes in recipient glomeruli and the development of glomerulonephritis. BUN, serum creatinine and proteinuria increased in the disease-induced mice. There were significant mesangial proliferation and glomerular crescents accompanied with CD3 cell infiltration in LN mice kidney. In the spleen of LN mice, CD69, activated T cell marker, and intracellular IL-17 expression increased. The expression of IL-17, IL-23 and IL-27 mRNA also increased in the spleen. In the kidney, intracellular IL-17 protein increased in the LN mice. The immunohistochemical study showed that IL-17 was observed only in the disease-induced mice kidney. IL-17 receptor (IL-17R), IL-27 and STAT3 mRNA all increased in the diseased kidney. All these findings suggest that Th17 cells play an important role in the experimental LN. When LN was induced in NKT depleted mice, the severity of disease was attenuated as we'd already observed.

In addition, Th17 cellular responses decreased both in the spleen and the kidney of NKT depleted LN mice. Next, we observed Th17 cellular response using co-culture of mesangial and NKT cells. The secretion of IL-17 increased in co-cultured cells after stimulated with CD3. When the NKT cells were stimulated by  $\alpha$ -GalCer, the level of IL-17 secretion was increased by dose-dependent pattern. In addition, IL-17R mRNA also increased in the co-cultured mesangial cells by CD3 stimulation, but not in the NKT cells alone.

Taken all together, Th17-cellular response was activated in the experimental LN. NKT deficiency attenuated the renal injury in experimental LN probably through the modulation of Th17 cellular response.

**Key Words** : Th17세포, 루프스신염, NKT세포

Th17 cells, Lupus nephritis, NKT cells