

## 면역글로불린 A 신병증에서 TNFSF13의 메커니즘 규명을 위한 B 세포 연구

서울대학교병원 내과학교실 신장내과<sup>1</sup>, 서울대학교 신장이식면역연구소<sup>2</sup>, 서울대학교 의과대학<sup>3</sup>  
서울대학교 병리과<sup>4</sup>, 서울대학교 해부학과<sup>5</sup>, 연세대학교 의과대학 내과학교실 신장내과<sup>6</sup>

한승석<sup>1</sup>, 양승희<sup>2</sup>, 최무림<sup>3</sup>, 문경철<sup>4</sup>, 김항래<sup>5</sup>, 이하정<sup>1</sup>  
이정표<sup>1</sup>, 주권욱<sup>1</sup>, 임춘수<sup>1</sup>, 강신욱<sup>6</sup>, 김연수<sup>1</sup>, 김동기<sup>1</sup>

### Experimental Approach to Evaluate the Role of TNFSF13 in the Progression of IgA Nephropathy

Seung Seok Han<sup>1</sup>, Seung Hee Yang<sup>2</sup>, Murim Choi<sup>3</sup>, Kyung Chul Moon<sup>4</sup>, Hang-Rae Kim<sup>5</sup>, Hajeong Lee<sup>1</sup>  
Jung Pyo Lee<sup>1</sup>, Kwon Wook Joo<sup>1</sup>, Chun Soo Lim<sup>1</sup>, Shin-Wook Kang<sup>6</sup>, Yon Su Kim<sup>1</sup>, Dong Ki Kim<sup>1</sup>

Department of Internal Medicine<sup>1</sup> Seoul National University College of Medicine  
Kidney Research Institute<sup>2</sup> Seoul National University

Department of Biomedical Sciences<sup>3</sup> Seoul National University College of Medicine  
Department of Pathology<sup>4</sup> Seoul National University College of Medicine  
Department of Anatomy<sup>5</sup> Seoul National University College of Medicine  
Department of Internal Medicine<sup>6</sup> College of Medicine Yonsei University

**Background:** We had previously reported that tumor necrosis factor superfamily 13 (TNFSF13) is associated with both the susceptibility to and progression of IgA nephropathy. In this study, we further evaluated the role of TNFSF13 in the IgA nephropathy as *in vitro* study.

**Methods:** We isolated B cells from IgA nephropathy patients (n=30) and healthy individuals (n=29), and stimulated the cells with/without TNFSF13. We evaluated the production and proportion of IgA and galactose-deficient IgA (GdIgA) by ELISA and flow cytometry. Additionally, we estimated the proportion of viable B cells by annexin V staining and examined whether glycosyltransferase expression is altered with TNFSF13 treatment by the realtime PCR and RNA sequencing. Furthermore, we compared the ectopic expression of TNFSF13 mRNA in renal tissues from healthy individuals with that in IgA nephropathy and lupus nephritis patients.

**Results:** After 4 days of culture, the total IgA level was higher in TNFSF13-treated group than in the control group. IgA levels reduced upon treatment with receptor blockers (TACI-Fc or BCMA-Fc). Similar results were also obtained by flow cytometry and in the healthy individuals. However, unrelated or contrasting results were obtained for the effect of TNFSF13 treatment on GdIgA levels. ELISA revealed that the proportion of GdIgA was reduced in the TNFSF13-treated group; flow cytometry did not reveal any correlation between TNFSF13 and GdIgA+ B cell proportion. Additionally, TNFSF13 treatment did not alter the expression of glycosyltransferase mRNA. Annexin V staining revealed that the viability of B cells was significantly higher in the TNFSF13-treated group than the control group or in the group with receptor blockers. Tubular or glomerular expression of TNFSF13 did not differ between the healthy controls and IgA nephropathy patients; however, tubular expression was higher in lupus patients than in the other groups.

**Conclusions:** TNFSF13 affects the outcome of IgA nephropathy by enhancing the survival of B cells rather than by increasing GdIgA production.

**Key Words:** 면역글로불린 A 신병증, B 림프구, 예후  
IgA nephropathy, B cell, Outcome

