

**Abstract Submission No. : 2584**

## **Inhibition of STAT3 signaling mitigates inflammation of experimental proliferative glomerulonephritis**

**Jae Yoon Park**<sup>1</sup>, Kyung Don Yoo<sup>2</sup>, Jangwook Lee<sup>1</sup>, Yong Chul Kim<sup>3</sup>, Sung Joon Shin<sup>1</sup>, Yon Su Kim<sup>3</sup>, Seung Hee Yang<sup>4</sup>

<sup>1</sup>Department of Internal Medicine-Nephrology, Dongguk University Ilsan Hospital, Korea, Republic of

<sup>2</sup>Department of Internal Medicine-Nephrology, Ulsan University Hospital, Korea, Republic of

<sup>3</sup>Department of Internal Medicine-Nephrology, Seoul National University Hospital, Korea, Republic of

<sup>4</sup>Department of Biomedical Research Institute, Seoul National University Hospital, Korea, Republic of

**Objectives:** Signal transducer and activator of transcription 3 (STAT3) is a pivotal mediator of IL-6-type cytokine signaling. However, the role of STAT3 in glomerulonephritis remains elusive. Herein, the role of STAT3 in glomerulonephritis was characterized using an anti-Thy-1.1 glomerulonephritis mouse model and primary cultured human mesangial cells.

**Methods:** Glomerulonephritis in mice was induced by injection of an anti-Thy-1.1 antibody. The antibody was administered to C57BL/6 mice at a dose of 1.2 mg/kg intravenously 5 times at 7-day intervals. The effect of the STAT3 inhibitor, Stattic<sup>®</sup> on human mesangial cells cultured under treatment with serum IgG of focal segmental glomerulosclerosis (FSGS) patients was also evaluated.

**Results:** In the mouse anti-Thy-1.1 glomerulonephritis model, the deposition of pSTAT3 and IL-17 was increased in the glomeruli. Expression of pSTAT3 was also increased in the human glomeruli and tubulointerstitial areas. Deposition of desmin, a mesangial cell marker, and Thy1.1 were merged in the glomeruli and it was accompanied by the increased expression of pSTAT3 in the mesangial area of the glomeruli. After treatment with serum IgG of FSGS patients, the proliferation of mesangial cells was increased about 2 times compared to control group, and it was significantly decreased after Stattic<sup>®</sup> treatment. The expression of IL-6 and IL-17 was increased with administration of serum IgG of FSGS patients and Stattic<sup>®</sup> treatment decreased the expression.

**Conclusions:** Hence, STAT3 may affect inflammation of glomerulonephritis, suggesting a novel strategy for FSGS management with STAT3 inhibitors.