

KSN-17-O019

### TARGETING HISTONE DEACETYLASE IN RENAL TUBULAR EPITHELIAL CELLS INHIBITS AMPLIFICATION OF TH1 CELL-MEDIATED INFLAMMATION

\*Sunwoo KANG<sup>1</sup>, Yeong-hoon KIM<sup>1</sup>, Tae-hee KIM<sup>1</sup>, Su-kil SEO<sup>2</sup>

<sup>1</sup>Nephrology, Busan Paik Hospital, Inje University, Korea, South, <sup>2</sup>Microbiology, Inje University, Afghanistan

**Objectives :** More studies are focusing on renal tubular epithelial cells (RTECs) as a new target to restore inflammatory environment as clarifying their immune regulatory function. Here, we investigated whether histone deacetylases (HDACs) are activated in RTECs during T cell-mediated inflammation and their blockade is able to reduce the inflammatory responses.

**Methods :** Human renal proximal tubular epithelial cell line HK-2 was cultured in the presence or absence of recombinant interferon gamma (IFN-g) 200 U/ml plus tumor necrosis factor alpha (TNF-a) 5 ng/ml. The HDAC activity was determined on the expression levels of acetylated H3 and  $\alpha$ -tubulin by immune blot assay. To determine the functional activity of HDAC inhibitor SB939, we analyzed the immune stimulatory phenotype of HK-2 cells such as class II MHC molecule, CD80, CD86, and CD40 by flow cytometry. In addition, the culture supernatants were used for measuring cytokines and chemokines by ELISA assay.

**Results :** We found that HDAC activity was markedly increased in HK-2 cells by treatment of IFN-g/TNF-a within 12 hours. Treatment of pan-HDAC inhibitor SB939 in HK-2 cells completely prevented HDAC activity increased by IFN-g treatment. SB939 treatment predominantly inhibited up-regulating CD40 expression but not MHC class II, CD80, and CD86. In addition, MCP-1 was significantly inhibited more than IL-6 and TNF-a by SB939 treatment. We found that HDAC activity was markedly increased in HK-2 cells by treatment of IFN-g/TNF-a within 12 hours. Treatment of pan-HDAC inhibitor SB939 in HK-2 cells completely prevented HDAC activity increased by IFN-g treatment. SB939 treatment predominantly inhibited up-regulating CD40 expression but not MHC class II, CD80, and CD86. In addition, MCP-1 was significantly inhibited more than IL-6 and TNF-a by SB939 treatment.

**Conclusions :** Our results demonstrate that 1) HDAC activity is increased in RTECs in response to IFN-g, 2) which further facilitates T cell-mediated inflammatory responses through CD40 and MCP-1. Therefore, our study suggests that HDAC inhibitor has a therapeutic potential for the treatment of

## **KSN 2017 Abstract**

acute renal inflammatory diseases such as allograft rejection in transplantation.

**Keywords** : HDAC, T-cell mediated, allograft rection, kidney transplantation