## FP258 VNN1 MEDIATES RENAL MALADAPTIVE REPAIR AFTER AKI BY INDUCING PREMATURE SENESCENCE OF RENAL TUBULAR CELLS

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**INTRODUCTION:** Renal maladaptive repair after acute kidney injury (AKI) can easily progress to chronic kidney disease. Sustained renal interstitial damage caused by accelerated senescence of renal tubular cells leads to renal fibrosis. Vanin-1 (VNN1) is an extracellular enzyme with panthenylmethylaminease activity that indirectly reduces the synthesis of glutathione, causing oxidative stress. The purpose of this study was to investigate the expression and of VNN1 in renal tissue and to study its role in senescence of renal tubular cells after ischemia reperfusion (I/R).

**METHODS:** Thirty male wild BALB/c mice were randomly divided into control group, sham group and I/R group. In the I/R group, the bilateral renal pedicle was ligatured for 35 min followed by reperfusion. The expression of VNN1 and aging markers (P16, P21, SA-b-gal) were detected. Furthermore, wild type mice and VNN1 knockout mice were used to compare the degree of renal tissue and functional damage and the senescence of renal tubular cells after I/R injury.

**RESULTS:** Compared with sham group, Scr, BUN and renal injury score increased significantly in I/R group at the early stage (3d) of renal injury. Renal fibrosis was observed in the later stage (28-42d). The expression of VNN1 in renal tubular cells of I/R group increased after I/R injury. VNN1 was coexpressed with P16, suggesting that VNN1 might be related to cellular stress senescence. The SCr, BUN of VNN1 KO mice was significantly lower than that of wild type mice at 7-28 d after renal reperfusion. The renal interstitial injury score of VNN1 KO mice was significantly lower than that of wild type mice, and the renal interstitial fibrosis level was significantly higher than that of wild type mice at 42d after reperfusion. The results suggest that VNN1 KO promotes renal repair of AKI. The ratio of P16 positive tubule cells in VNN1 KO mice was significantly higher than that in wild-type mice at 7d after renal reperfusion, suggesting that VNN1 could promote the senescence of renal tubule cells during AKI repair.

**CONCLUSIONS:** VNN1 mediates renal maladaptive repair after AKI by inducing premature senescence of renal tubular cells.