

Submission No. : KRFP-0005

Session Title : KSN Research Fund Project

Session Topic : -

Date & Time, Place : June 14 (Fri) / 08:30-10:00 / Room 4 (201)

The Effect of HNF4A on Podocytes

Su Woong Jung

Kyung Hee University Hospital at Gangdong, Republic of Korea

HNF4A is a transcriptional factor regulating fatty acid oxidation and solute transport mainly in proximal tubular cells of the kidneys. However, we found that its expression was noted in podocytes as well and increased in diabetic kidneys. Thus, we investigated how HNF4A activity affects podocytes. Using mouse podocytes transduced with either mock vector or lentiviral vector carrying mouse *Hnf4a* cDNA, we performed RT-PCR, chromatin immunoprecipitation-quantitative real-time PCR (ChIP-qPCR), Seahorse XF Cell Mito Stress Test and XF Glycolysis Stress Test. In HNF4A-transfected podocytes, ChIP-qPCR found significant enrichment of HNF4A binding to promoter region of its target genes (*Ldha*, *Ppara*) and RT-PCR also showed increased expressions of several genes implicated in fatty acid oxidation (*Hadh*, *Acs15*, *Acsf2*). Consistent with this finding, HNF4A transfection increased oxygen consumption rate (OCR) and extracellular acidification rate, indicating upregulation of mitochondrial function and glycolytic flux. We found that OCR was markedly higher when we added palmitate to HNF4A-transfected podocytes, indicating that HNF4A helps podocytes efficiently metabolize palmitate. CPT1 inhibitor etomoxir offset an increase in OCR in HNF4A-transfected podocytes, confirming implication of HNF4A in fatty acid oxidation. These findings collectively suggest that HNF4A promotes ATP production in podocytes, which is a source of energy that could be used for its adaptive response in diabetic kidney disease.

Keywords: HNF4A, podocytes, lentiviral transfection