KSN 2016 Abstract Submission

Clinical & Experimental Pathology & Cell Biology

KSN2016ABS-1551

Mitochondrial dysfunction aggravate high glucose induced podocyte injury.

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Background: Podocyte injury plays a major role in diabetic glomerulosclerosis. High glucose induces oxidative stress, the changes of actin dynamics, and apoptosis in podocyte. Our previous report showed mitochondrial injury of podocyte induces massive albuminuria, glomerular sclerosis. Using crif1 deletion in podocyte, we evaluated that mitochondrial injury aggravate high glucose induced podocyte injury
Methods: We used a conditionally immortalized mouse podocyte cell line and podocyte specific crif1 half deletion mouse (crif1 (△/+)). Crif1 siRNA in podocyte was used for inducing mitochondrial injury. We compared high glucose (25mmol/L) to low glucose (5.5mmol/L) in Crif1 siRNA treated podocyte. We make the phenotype of crif1 (△/+) in streptozotocin (75mg/kg, i.p., 3 days) induced diabetes mice. Using confocal microscopy, we observed actin and mitochondria in immortalized podocyte. In mice, we evaluated renal histology and metabolic finding including blood glucose, urine albumin and creatinine.
Results: High glucose with Crif1 siRNA treated podocyte showed decrease of actin to cell ratio comparing to low glucose with Crif1 siRNA and high glucose with wild type podocytes. In mice, it showed normal range of albuminuria, normal renal histologic finding and normal mitochondria morphology in both control mice and podocin specific half deletion of crif1 (crif1 (△/+)). After 10 weeks STX treatment, podocin specific heterozygous deletion of crif1 (crif1 (△/+)) showed massive albuminuria. However, Control mice showed normal range of albuminuria.
Conclusion: Damage and instability of mitochondria induced by podocyte crif1 deletion aggravate high glucose induced podocyte injury.

Keywords: diabetes mellitus, mitochondria, Podocyte injury