Objective: The expression of vitamin D receptor (VDR) was decreased in diabetic patients. Our primary results found that the expression of VDR was decreased in mouse podocytes induced by high glucose, accompanied by the epithelial-mesenchymal transition of podocytes. This experiment was designed to investigate the mechanism that VDR take part in the epithelial-mesenchymal transition of podocytes.

Methods: Conditionally immortalized mouse podocytes cell line in vitro were adopted. Podocytes incubated in RPMI-1640 medium with high glucose (25 mmol/L) or normal glucose (5.6 mmol/L). And normal glucose were divided into the following three groups according to the experiment's design: (1) normal glucose group (5.6 mmol/L); (2) scramble-siRNA group: normal glucose + 100 pmol/L scramble-siRNA; (3) VDR-siRNA group: normal glucose + 100 pmol/L VDR-siRNA. After 36 hours, cells were harvested for protein. The protein expressions were detected by both western-blot and qRT-PCR. Meanwhile, the change of monolayer barrier function is tested by using the detection of the albumin influx. The co-localization of VDR and β-catenin was detected by immunofluorescence.

Results: (1) After high glucose treatment, the protein and gene expressions of VDR, nephrin and podocin were down-regulated (P < 0.05) while β-catenin, α-SMA and MMP9 was up-regulated (P < 0.05). The albumin flow was increased. Additionally, more VDR transferred to the nuclear and increased the co-localization of β-catenin in podocytes under high glucose. (2) Compared with normal glucose and scrambled-siRNA group, the the protein and gene expressions of VDR nephrin and podocin was down-regulated (P < 0.05), and α-SMA, MMP9 and β-catenin was up-regulated (P < 0.05). The albumin flow of podocytes was increased (P < 0.05).

Conclusion: Vitamin D receptor may participate in the epithelial-mesenchymal transition of mouse podocytes induced by high glucose through wt/β-catenin.

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Objective: Tristetraprolin (TTP) is a well-characterized, zinc finger-containing, RNA-binding protein, which plays a role in the regulation of inflammatory factor expression by targeting the 3' untranslated region (3'UTR). In the current study, we investigate whether TTP modulates inflammation in high glucose induced-podocytes and in db/db mice kidneys.

Methods: Differentiated mouse podocytes were treated by high glucose, and TTP expression and inflammatory factors was measured by quantitative real-time PCR or ELISA. TTP siRNA or lentiviral vectors containing TTP sequences were transfected into podocytes to down-regulate or up-regulate TTP expression. Db/db mice were used as the diabetic model in in vivo experiment. At the age of 10 weeks, db/db mice were injected via tail vein with lentiviral vectors containing TTP sequences. At the age of 14 weeks, the lentivirus injection was repeated. Mices were sacrificed at the age of 24 weeks. Inflammatory factors (IL-6, IL-18, TNF-α), fibrosis markers (fibronectin, MMP-9) and podocyte markers (nephrin, podocin) in mice kidneys were examined by western blot and immunohistochemistry. Urine albumin to creatinine ratio and serum creatinine was also detected.

Results: (1) After high glucose treatment, the protein and gene expressions of sirt1and TTP, and increased the IL-6 and IL-18 expressions. (2) Sirt1 might modulate the expressions of TTP through MAPK P38 and TNF-α.

Conclusion: These results verify that VDR may play a role of renal protection in diabetic nephropathy.

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Objective: Sirt1 (silent information regulator 1), a type III protein deacetylase, is considered as a novel anti-aging protein involved in regulation of inflammation in diabetic nephropathy. The objective of this study was to observe the expressions of sirt1, TTP and inflammatory factors in high glucose-induced mouse podocytes, and initially explore its regulatory mechanism.

Methods: (1) Differentiated podocytes were divided into: the normal glucose group (NG: glucose 5.6 mM), the HG groups (HG: 25 mM of glucose), and the NG groups as compared with NG group (plasma VD 0.78 ± 0.24 and 0.88 ± 0.29 vs. 3.23 ± 1.33 ng/ml, P < 0.05, VDR 157.52 ± 98.36 and 164.20 ± 64.50 vs. 325.33 ± 194.68 ng/ml, P < 0.05). Urinary VD and VDR levels were significantly lower in DN2 and DN3 groups as compared with NC group (urinary VD 1.34 ± 0.58 and 1.42 ± 0.44 vs. 1.18 ± 0.65 ng/ml, P < 0.05, VDR 83.60 ± 31.78 and 88.40 ± 28.10 vs. 60.93 ± 12.03 ng/ml, P < 0.05). Urinary VD and VDR levels were significantly elevated in DN2 and DN3 groups as compared with NC group (urinary VD 1.34 ± 0.58 and 1.42 ± 0.44 vs. 1.18 ± 0.65 ng/ml, P < 0.05, VDR 83.60 ± 31.78 and 88.40 ± 28.10 vs. 60.93 ± 12.03 ng/ml, P < 0.05).

Conclusion: Sirt1 might modulate the expressions of TTP and inflammatory factors.