Conclusion: Our data suggested that AngII promoted ROS-dependent autophagy in podocyte, which was involved with AMPK/mTOR signaling. Ginsenoside Rg1 protect podocyte from AngII-induced autophagy may be through reducing phosphorylation of AMPK and preserving mTOR signaling.

Objective: Podocyte injury has been increasingly shown to be involved in the pathogenesis of diabetic nephropathy (DN). The ligand of receptor activator of NF-kappaB (RANKL) and its cognate receptor RANK are upregulated in damaged podocytes. However, little is known about the relation between RANKL-RANK, HG-induced podocyte and DN. The objective of this study is to determine the impact and mechanism of RANKL-RANK on HG-induced podocyte injury.

Methods: Male db/db mice and db/m mice were sacrificed for this experiment. Their kidneys were used for Western blot and immunohistochemical analysis. Mouse podocytes were cultured in normal (5 mM) or high (30 mM) D-glucose respectively for 3, 6, 12, 24 hours or treated with RANK siRNA and HG for 24 hours then examined cell migration and permeability to albumin by Transwell filters, measured MCP-1 by ELISA, detected NF-kB/p65, IKKbeta, MAPKs(p38, ERK1/2, JNK) by Western blot and performed nucleus translocation of p65 by Confocal microscopy.

Results: We found that RANKL-RANK were overexpressed in db/db mice compared to db/m mice (1.42 ± 0.33 vs 0.44 ± 0.13, p = 0.020), mainly locating along the glomerular capillary loop. Moreover, RANKL-RANK was upregulated in HG-induced podocytes in a time-dependent manner. In addition, HG induced cell migration (92.00 ± 7.00 vs 12.00 ± 3.00, p = 0.000), increased permeability to albumin (9.40 ± 1.06 vs 5.90 ± 0.30, p = 0.001), upregulated the expression of MCP-1 (513.82 ± 77.53 vs 85.57 ± 13.81, p = 0.000) and decreased nephrin (0.32 ± 0.10 vs 0.64 ± 0.11, p = 0.004) compared to normal glucose in podocytes. RANK siRNA inhibited remarkably HG-induced migration (18.33 ± 4.16 vs 92.00 ± 6.08, p = 0.000), permeability to albumin (6.73 ± 0.91 vs 9.91 ± 1.44, p = 0.002) and the expression of MCP-1 (186.10 ± 75.60 vs 472.42 ± 84.35, p < 0.001) but slightly increased nephrin (0.42 ± 0.11 vs 0.34 ± 0.14, p = 0.37) compared to si-control + HG. Furthermore, The phosphorylation of NF-κB/p65, IKKbeta, MAPKs and nuclear translocation of p65 were induced by HG in a time-dependent manner and reversed by RANK siRNA.

Concusion: HG induces podocyte injury by regulating RANKL-RANK mediated NF-κB and MAPK signaling pathways.

Figure 1. Sample path of structural equation model coefficients (t value) and explain variance results.

http://dx.doi.org/10.1016/j.hkjn.2015.08.032

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Podocyte SIRT1 Deficiency Contributes to Albuminuria and Renal Fibrosis in Diabetic Kidney Damage in Mice

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Objective: SIRT1 has been shown to play an important role in stress response in metabolic disorder and aging process, and is suggested to be involved in the pathogenesis of diabetic kidney damage. The present study examines whether and how SIRT1 deficiency is involved in diabetic nephropathy.

Methods: HFD plus five-day-low-dose STZ was used to model type 2 diabetes. The role of SIRT1 in diabetic kidney is examined using SIRT1 heterozygotes (C57BL/J6). Urinary albumin excretion, kidney histology and extracellular fibrosis were examined in both normal and diabetic mice treated with SIRT1 knockdown or control siRNA.

Results: SIRT1 knockdown increased albuminuria and extracellular fibrosis in diabetic mice compared to control siRNA. In addition, the expression of SIRT1 was significantly increased in diabetic mice treated with control siRNA compared to normal mice, while the expression of SIRT1 was significantly decreased in diabetic mice treated with SIRT1 knockdown compared to control siRNA.

Conclusion: SIRT1 deficiency contributes to albuminuria and extracellular fibrosis in diabetic kidney damage. This study provides evidence for the role of SIRT1 in diabetic nephropathy and suggests potential therapeutic targets for the treatment of diabetic kidney disease.

http://dx.doi.org/10.1016/j.hkjn.2015.08.031