Results: Compared with normal control group, the cells exposed to HG showed up-regulated Notch pathway protein and mRNA expression, up-regulated TGF-β-1 and FN mRNA expression. Cordyceps sinensis and DAPT inhibited HG-induced mesangial cell proliferation, down-regulated the Notch pathway, TGF-β-1 and FN expressions.

Conclusion: We found that high glucose can upregulate the expression of Notch signaling in GMC while also up-regulate the expression of TGF-β-1 and FN. Activation of the Notch signaling pathway could induce TGF-β-1 signaling pathway, which is involved in the pathogenesis of diabetic nephropathy. Our experiments indicate that Cordyceps sinensis may inhibit high glucose-induced mesangial cell TGF-β-1 and FN overexpression, inhibit the activation of Notch signaling pathway. However there is no convincing evidence to prove that Cordyceps sinensis can inhibit the mesangial cell proliferate through the the Notch signaling pathway. Thus, additional studies using animal models are wanted to confirm our study in vitro results.

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0179
Long Non-coding RNA Expression Profiles in Diabetic Nephropathy
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Objective: The LncRNA and mRNA expression profiles of normal group, diabetes mellitus, diabetic nephropathy patients were investigated by Arraystar human LncRNA/mRNA microarray.

Methods: We obtained serum samples from 21 diabetic nephropathy patients proven by renal biopsy as nodular diabetic glomerulosclerosis, 9 diabetic patients without microalbuminuria (DM) and 19 healthy controls (N). Serum LncRNA/mRNA expression levels were analyzed with Arraystar Human LncRNA/mRNA V3.0 expression spectrum biochips. Agilent Feature Extraction (version 11.0.1.1) software was used to extract the information contained in the microarray images obtained. GeneSpring GX (Agilent Technologies, version 12.0) software was used to further screen the obtained original expression information of LncRNA and mRNA.

Results: The urinary microalbumin/creatinine ratio and serum creatinine in diabetic nephropathy patients were higher than that of diabetic patients and healthy control (p < 0.05). 245 lncRNAs were upregulated and 680 LncRNAs were downregulated in serum of diabetic patients compared with that of healthy controls. 45 lncRNAs were upregulated and 813 lncRNAs were downregulated in serum of diabetic nephropathy patients compared with that of diabetic patients. Among them, along with the progression of diabetes and diabetic nephropathy, lncRNA-ARAP1-AS2 was gradually increased (2.82 times in DM/N and 2.47 times in DN/DM), lncRNA-ARAP1-AS1 were gradually reduced (2.24 times in DM/N, 4.79 times in DN/DM).

Conclusion: The downregulation of lncRNA-ARAP1-AS1 and upregulation of lncRNA-ARAP1-AS2 upregulated ARAP1 mRNA expression and may involve in the pathogenesis of DN.

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0182
Inhibiting Core Fucosylation of Megalin and TGF-β receptor II Protects Against Proximal Tubular Epithelial Cell Injury Caused by Albumin
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Objective: Albuminuria is a strong risk factor for renal interstitial injury that impairs proximal tubular epithelial cells (PTECs) through both albumin endocytosis and non-endocytosis mechanisms in diabetic nephropathy. Megalin is essential for albumin endocytosis mechanism whereas transforming growth factor-β receptor II (TGFβRII) is responsible for albumin non-endocytosis mechanism. We try to find a common target to inhibit both endocytic and non-endocytic injury pathway.

Methods: Both megalin and TGFβRII are glycoproteins modified by core fucosylation. We investigated the role of core fucosylation in albumin induced-injury to HK-2 cells. RNAi was performed to suppress expression of megalin, TGFβRII and FUT8 genes. FACS and confocal microscopy were performed to observe effect of siRNAs on endocytosis of BSA. Western blot, ELISA and FACS were performed to determine changes in levels of megalin, TGFβRII, p-Smad2/3, monocyte chemotactic protein 1 (MCP-1), nuclear factor-kB (NF-kB), reactive oxygen species (ROS), TGFβRII, Fibronectin, Collagen I and apoptosis after incubation with bovine serum albumin (BSA) for different time.

Results: After 4 h incubation with BSA, albumin endocytosis increased, followed by upregulation of ROS, MCP-1 and NF-kB. Inhibiting core fucosylation of megalin suppressed endocytosis of BSA, subsequently, it suppressed described endocytic injury above. In contrast, after 24 h incubation with BSA, expression of megalin decreased to 55%, while that of TGFβRII increased to 1.5-fold of its original level. At the 24-h time point, inflammation and oxidative stress were weaker than that at the 4-h time point, the expression of fibronectin and collagen I was significantly upregulated. Inhibiting core fucosylation of TGFβRII, suppressed activation of TGFβRII/TGFβRII/Smad2/3 signaling pathway after incubation for 24 h, followed by downregulation of fibronectin and collagen I.

Conclusion: Inhibiting core fucosylation of megalin and TGFβRII could inhibit albumin endocytosis and non-endocytosis injury to PTECs simultaneously, regulating core fucosylation is likely an effective strategy for preventing against albumin-induced injury to PTECs in diabetic nephropathy.

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Fig. 1 Effect of incubation with BSA on expression of megalin, TGFβRII, MCP-1, TGFβRII and p-Smad2/3 in HK-2 cells.

Fig. 2 Inhibiting core fucosylation of megalin suppressed endocytosis of BSA in HK-2 cells.
To Observe the Curative Effect of Alprostadil Combined with Candesartan in the Treatment of Early Diabetic Nephropathy

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Objective: To observe the clinical curative effect of Alprostadil Injection combined with candesartan in the treatment of early diabetic nephropathy.

Methods: The 78 cases of early diabetic nephropathy patients were randomly divided into three groups: alprostadil group 26 cases, candesartan losartan group 26 cases, alprostadil combined with candesartan losartan group 26 cases, continuous medication for 2 weeks, the control of blood glucose, blood lipids and other treatment of each phase is same.

Results: Compared with before treatment, significantly reduced alprostadil group, the Candesartan group and combination group of urinary total protein and albumin, serum creatinine, blood urea nitrogen (P < 0.01); Comparison between groups, alprostadil group and candesartan group urine total protein and albumin to reduce the difference no significant, United Group, urinary total protein, albumin, serum creatinine and blood urea nitrogen and alprostadil group and candesartan group were significantly reduced (P < 0.01).

Fig. 3 Inhibiting core fucosylation of megalin down-regulated the expression of MCP-1 and NF-κB, decreased levels of ROS and suppressed cell apoptosis, while it increased the level of TGF-β1.

Fig. 4 FUT8 siRNA inhibited albumin-induced injury after incubation for 4 h.

Fig. 5 Inhibiting core fucosylation of TGFβII suppressed the activation of TGFβII/Smad2/3 in HK-2 cells.

Fig. 6 FUT8 siRNA inhibited expression of megalin, TGFβRII, MCP-1, NF-κB and TGF-β1 and decreased cellular apoptosis after incubation for 24 h.

Fig. 7 FUT8 siRNA decreased Col 1, FN and cellular apoptosis after HK-2 cells were incubated for 24 h.

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0188
To Observe the Curative Effect of Alprostadil Combined with Candesartan in the Treatment of Early Diabetic Nephropathy

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Objective: To observe the clinical curative effect of Alprostadil Injection combined with candesartan in the treatment of early diabetic nephropathy.

Methods: The 78 cases of early diabetic nephropathy patients were randomly divided into three groups: alprostadil group 26 cases, candesartan losartan group 26 cases, alprostadil combined with candesartan losartan group 26 cases, continuous medication for 2 weeks, the control of blood glucose, blood lipids and other treatment of each phase is same.

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