Conclusion: These findings demonstrate a novel mechanism that reducing the activity of Cdk5 attenuates TIF by blocking the ERK1/2/PPARγ pathway and inhibiting EMT in DN. Targeting Cdk5 might be an alternative to suppress renal TIF in DN.

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0160
MicroRNA-130b Improves Renal Tubulointerstitial Fibrosis via Repression of Snail-Induced Epithelial-Mesenchymal Transition in Diabetic Nephropathy
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Objectives: To investigate the role of microRNA-130b (miR-130b) in mediating renal tubulointerstitial fibrosis (TIF) in diabetic nephropathy (DN).

Methods: Total 86 renal biopsy tissue samples obtained from the Division of Nephrology in Nanfang Hospital and Department of Renal Pathology in King Medical Diagnostics Center in Guangzhou from 2013 to 2014 were used for analysis. Expressions of Snail, E-cadherin, Vimentin and Collagen IV were examined and TIF was evaluated in these renal biopsy samples using immunohistochemistry and Masson’s Trichrome stain (MTS), respectively. Correlations between plasma miR-130b and biological parameters including serum β2-microglobulin (β2-MG), blood urea nitrogen (BUN) and creatinine were analyzed. Effects of activating or inhibiting miR-130b and Snail on downstream gene expressions and epithelial-to-mesenchymal transition (EMT) were investigated using in vitro and in vivo approaches.

Results: Plasma miR-130b downregulation exhibited clinical and biological relevance as it was linked to increased serum creatinine and β2-microglobulin, increased Snail expression and deteriorated tubulointerstitial fibrosis in renal biopsies of DN patients (Figure 1). MiR-130b inhibitor caused Snail upregulation and enhanced molecular features of epithelial-to-mesenchymal transition (EMT) in high glucose (30 mM) cultured NRK-52E cells. In contrast, miR-130b mimic downregulated Snail expression and increased epithelial hallmarks. Notably, Snail was identified as an miR-130b direct target and inversely correlated with E-Cadherin expression. Furthermore, the miR-130b-dependent effects were due to Snail suppression that in turn deregulated E-cadherin, vimentin, and collagen IV, key mediators of EMT. These effects were reproduced in streptozotocin-induced diabetic rats (Figure 2).

Conclusion: Thus, we propose a novel role of the miR-130b-SNAIL axis in fostering EMT and progression toward more deteriorated renal tubulointerstitial fibrosis in DN. Detection of plasma miR-130b and its association with SNAIL can be extrapolated to quantifying the severity of renal tubulointerstitial fibrosis. Targeting miR-130b could be evaluated as a potential therapeutic approach for DN.

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0175
The Effect of High Glucose on the Notch Signal Pathway in Rat Mesangial Cell and the Interventive Effect of the Extract of Cordyceps sinensis
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Objective: To investigate the underlying mechanism of Cordyceps sinensis attenuates diabetic mesangial cells injury induced by high glucose (HG).

Methods: Rat glomerular mesangial cells were cultured in normal glucose and HG, HG with DAPT or HG with Cordyceps sinensis. The cell proliferation was detected by MTT and the ratio of total protein content to cell number. The TGF-β and FN were detected by RT-qPCR. The Notch pathway was detected by western blotting and RT-qPCR.
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: Compared with normal control group, the cells exposed to HG showed up-regulated Notch pathway protein and mRNA expression, up-regulated TGF-β and FN mRNA expressions. Cordyceps sinensis and DAPT inhibits HG-induced mesangial cell proliferation, down-regulated the Notch pathway, TGF-β, 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 and FN. Activation of the Notch signaling pathway could induce TGF-β 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 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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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 (TGF-βRII) 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 TGF-βRII 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, TGF-βRII 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, TGF-βRII, p-Smad2/3, monocyte chemotactic protein 1 (MCP-1), nuclear factor-kB (NF-kB), reactive oxygen species (ROS), TGF-βRII, 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 TGF-βRII 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 TGF-βRII, suppressed activation of TGF-βRII/TGF-βRII/Smad2/3 signaling pathway after incubation for 24 h, followed by downregulation of fibronectin and collagen I.

Conclusion: Inhibiting core fucosylation of megalin and TGF-βRII 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.

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

Fig. 2 Inhibiting core fucosylation of megalin suppressed endocytosis of BSA in HK-2 cells.