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STAT3 Mediates Autophagy and Extracellular Matrix Synthesis in Human Glomerular Mesangial Cells Exposed to High Glucose

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Ojectives: To explore the effect of STAT3 pathway on the autophagy of human glomerular mesangial cells (HGMC) and expression of extracellular matrix Collagen IV cultured in high glucose.
Methods: HGMC were cultured in normal (5 mmol/L) or high glucose (30 mmol/l) for 12—72 hours, and then S3I-201 (an inhibitor of STAT3 activity) or STAT3-siRNA transfection were added into HGMC. STAT3, p-STAT3 and autophagy marker proteins LC3 and p62 protein expression was evaluated by western blot, autophagesomes was detected by electron microscopic and the expression of collagen IV was detected by ELISA in each group.
Results: High glucose significantly reduced the generation of autophagosome and altered expression of LC3 and p62 at 24 h (LC3 II/LC3I and LC3II decreased, p62 increased obviously), consistently high glucose exposure significantly increased protein levels of STAT3, p-STAT3 and collagen IV. These changes were reversed by S3I - 201 or STAT3-siRNA transfection.
Conclusion: High glucose can inhibit autophagy activity of human glomerular mesangial cells and induce up-regulation expression of Collagen-IV. Inhibition of STAT3 pathway can reduce the inhibition of autophagy activity and synthesis of collagen IV by high glucose.

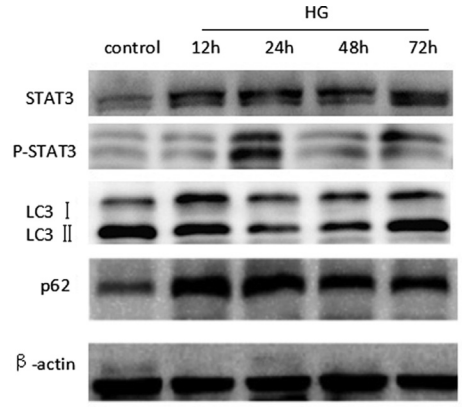

Fig. 1 High glucose inhibits autophagy activity and induces STAT3 activation of human glomerular mesangial cells at 24 h.

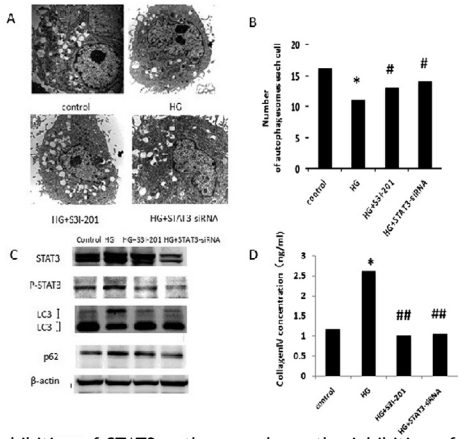

Fig. 2 Inhibition of STAT3 pathway reduces the inhibition of autophagy activity and synthesis of collagen IV by high glucose. (A, B) Autophagesomes were detected by electron microscopic (*P $<$ 0.01 vs control, #P $<$ 0.05 vs high glucose). (C) Analysis of stat3, p-stat3, LC3 and p62 by Western blot. (D) Expression of Collagen IV was detected by ELISA (*P $<$ 0.01 vs control, ##P $<$ 0.01 vs high glucose).

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0212

Ursolic Acid Improves the Podocytes Injury Caused by High Glucose

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Objective: Autophagy plays an important role in maintaining podocytes homeostasis. Reduced autophagy may result in limited renal cell function during exposure to high glucose. In this study, we investigated the effects of ursolic acid (UA) on autophagy and podocytes injury induced by high glucose.
Methods: Conditionally immortalized murine podocytes were cultured in media containing high glucose, and we determined the effect of the PI3K inhibitor LY294002 and ursolic acid treatment on protein expression. miR-21 expression was detected using RT-qPCR. Activation of the PTEN-PI3K/Akt/mTOR pathway, expression of autophagy-associated proteins and expression of podocytes specific proteins were determined by Western blot. Immunofluorescence was used to monitor expression of podocytes specific proteins and LC3 accumulation. Autophagosomes were observed using electron microscopy.
Results: During exposure to high glucose condition, autophagy was reduced in podocytes. Increased miR-21 expression, decreased PTEN expression, and activation of the PI3K/Akt/mTOR pathway were observed during exposure to high glucose. Ursolic acid and LY294002 reduced podocytes injury through autophagy rescue. Our data suggest ursolic acid inhibits miR-21 expression and increases PTEN expression, thereby inhibiting Akt and mTOR and restoring autophagy levels.
Conclusion: Our data suggest that podocytes injury is associated with reduced autophagy levels during exposure to high glucose. Ursolic acid reduces podocytes injury by increasing autophagy through miR-21 inhibition and PTEN expression.

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0227

Influence of Shenkang Injection on Hemodynamics of Kidney in Patients with Early Diabetic Nephropathy

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Objective: To observe the influence of Shenkang injection on renal artery peak velocity in systole (Vs) and resistance indices (RI) of patients with early diabetic nephropathy.
Methods: A total of 58 early diabetic nephropathy patients were randomly divided into conventional treatment group (A group) and Shenkang Injection-treated group (B group), 29 cases in each group. To detect the level of UAER between before and after treatment, color Doppler ultrasound were used to cheek and analyze the chief renal arteries and intersegmental arteries Vs and RI of patients. Moreover, 25 healthy subjects were measured for control.
Results: (1) Vs of patients with early diabetic nephropathy was significantly lower than that in normal control group, RI was significantly higher than that in normal control group ($P < 0.01$). (2) Vs of B group was significantly higher than that before ($P < 0.01$), and RI was significantly lower than that before ($P < 0.05$). All the improvements were better than those in A group. The A group had no significant difference with treated before ($P > 0.05$). UAER of B group was significantly lower than that before and better than that of A group ($p < 0.01$).
Conclusion: Shenkang injection can increase renal artery peak velocity in systole, decrease resistance indices, improve renal ischemia state, decrease urine protein, and has curative effect on diabetic nephropathy in earlier stage.

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0264

Effect Of Glucagon-like Peptide-1 Receptor Agonists on Regulation of Blood Pressure and Water-Sodium Metabolism in Rats with Diabetic Nephropathy

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Objective: To observe the effect of glucagon like peptide-1 receptor agonist liraglutide on blood pressure and water-sodium metabolism in rats