cellular process, physiological process and metabolism by using Gene Ontology (GO). The pathway analysis was performed by KEGG, and 135 pathways were found significantly altered in the TSF group. The top pathways mainly included tight junction, Wnt signaling pathway, Drug metabolism-cytochrome P450, MAPK signaling pathway and TGF-beta signaling pathway.
Conclusion: Thus, the current study revealed that TSF might improve kidney injury type 2 DN by multiple signaling pathways.

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0073

Tangshen Formula Attenuates Hepatic Steatosis in db/db Mice by Mechanisms Involving AMPK/SREBP Pathway

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Objectives: AMP-activated protein kinase (AMPK), which regulates whole-body energy metabolism and has emerged an attractive target metabolism syndrome, especially on lipid metabolic disorder in type 2 diabetes. To evaluate the role of Tangshen Formular (TSF) in regulating liver dyslipidemia in diabetes, db/db mice were randomized to a standard diet (SD) or SD plus TSF for 12 weeks and db/m mice as a control.
Methods and results: we demonstrated that TSF significant suppressed mice weight gain and liver steatosis with lipid accumulation (Oil Red O &HE staining results). These changes were accompanied by modulation of insulin and AMPK/SREBP signaling. The administration of TSF increased the phosphorylation of AMPK and decreased SREBP-1 nuclear translocation. Moreover, the target genes of SREBP-1 such as FAS, ACC, and SCD1, at both mRNA and protein levels were also decreased in mouse received TSF. TSF also potently inhibited de novo lipogenesis and stimulated fatty acid combustion in mice liver with downregulation of hepatic gluconeogenesis/lipogenesis genes (PGC-1α, Acadm, Acox1).
Conclusion: TSF may be a potential promising theraputic approach to attenuate fatty liver, dyslipidemia and obesity-related diseases.

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0076

C-Reactive Protein Exacerbates Diabetic Kidney Fibrosis by Enhancing CD32-Smad3-mTOR Signaling in Human CRP-Tg/db/db Mice

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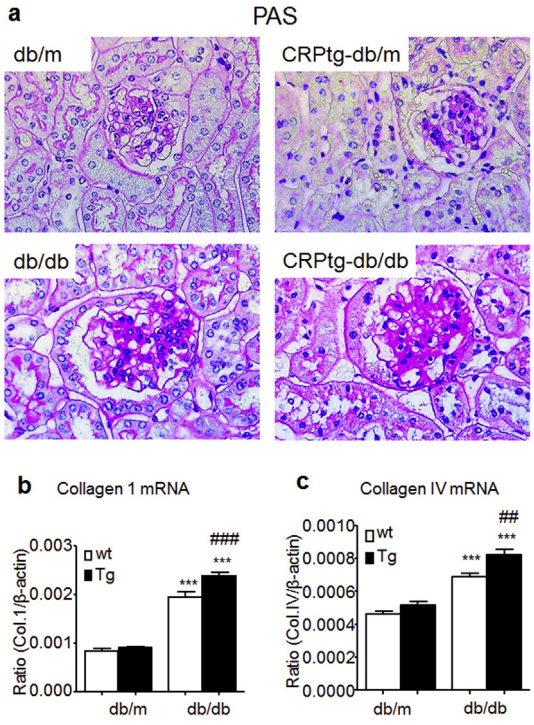
Objective: Type 2 diabetic kidney disease is a leading cause of end-stage renal failure. Emerging evidence shows that patients with type-2 diabetic nephropathy (T2DN) is highly correlated with elevated serum levels of C-reactive protein (CRP). In this study, we hypothesized that CRP may be pathogenic and promote T2DN in a novel mouse model of db/db mice with over-expressing human CRP gene (CRPtg-db/db).
Methods: Human CRPtg-db/db mice and their littermate controls including db/db, db/m and CRPtg-db/m mice were generated by crossing db/m mouse with CRPtg mouse that expresses human CRP. Fasting blood glucose, body weight, blood pressure and 24-h urine microalbumin levels were measured every 4 weeks over the 36-week period and renal fibrosis was examined at 36 weeks. In addition, signaling mechanisms of CRP-mediated DN was investigated in vivo and in vitro.
Results: Compared with littermate db/db mice, CRPtg-db/db mice developed higher blood glucose with more severe diabetic kidney injury including: a marked increase in microalbuminuria and deposition of collagen I, IV and connective tissue growth factor (CTGF) within the diabetic kidney. Exacerbation of renal fibrosis in CRPtg-db/db mice was associated with a marked activation of TGF-b/Smad3 and mTOR signaling. Further studies in cultured HK-2 cells revealed that addition of CRP induces activation of Smad3 through its receptor CD32b via both TGF-b-dependent mechanism and ERK/P38 MAPK signaling. Activated Smad3 then bound directly to mTOR and stimulated fibrosis, which was blocked by an anti-CD32b neutralizing antibody or by an mTOR inhibitor (rapamycin).
Conclusion: CRP is pathogenic and exacerbates diabetic kidney fibrosis in a mouse model of T2DN. CRP may promote T2DN via the CD32b-Smad3-mTOR signaling pathway.



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0089

Autophagy Modulates Mitochondrial Morphogenesis in Diabetic Renal Tubules

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Objective: Autophagy attenuates glomerular damage through protection of glucose-induced podocyte injury but its role in diabetic tubules remains unclear. Glucose produces oxidative stress and causes mitochondrial fragmentation in renal tubules. However, information on the interplay between autophagy and mitochondrial morphogenesis in diabetic tubules is limited. This study aimed to examine the crosstalk between these two mechanisms in diabetic tubulopathy.
Methods: Diabetic mice were induced by high fat high sucrose (HFHS) diet. H&E stain was used to illustrate diabetic tubulopathy. Renal tubular cell (HK2) culture models were used to investigate the regulating mechanisms of autophagy on mitochondrial morphology. Transmission electron microscope (TEM) was used to demonstrate autophagosome formation. Western blot and flow cytometry were used to assay the LC3B-II expressions. Pharmacology inhibition and RNAi were used to investigate the role of autophagy in HK2 cells cultured in the presence or absence of glucose. Mitochondrial morphology were stained by mitotracker and analyzed by confocal microscopy. TUNEL assay was used to examine the cellular apoptosis in glucose-treated HK2 cells.