C1q/TNF-related protein-9 attenuates diabetic microangiopathy in db/db mice

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Introduction: This study was to investigate the protective effects of the adiponectin paralog CTRP9 on the diabetic microangiopathy and the underlying molecular mechanisms in db/db mice.

Methods: Our study contained diabetic nephropathy and diabetic retinopathy. The db/db mice (12 weeks old), a diabetic animal model, were randomly divided into DM group (n=20), DM+Ad-GFP group (n=20), DM+Ad-CTRP9 group (n=20), the non-diabetic db/m mice serve as control group. Adenovirus (Ad) vectors involving the green fluorescence protein (Ad-GFP) or full-length mice CTRP9 (Ad-CTRP9) at 3*10^8 (pfu) was respectively injected into db/db mice of DM+Ad-CTRP9 group and DM+Ad-GFP group via tail vein, at day 15 post injection, and the process was repeated, the db/m mice were treated with equivalent amounts of saline. We detected the biomarker of inflammation, apoptosis, oxidative stress, fibrosis in kidney and retina tissues, determined the breakdown of blood retina barrier using evens blue.

Result: The result showed that CTRP9 was reduced in kidney and retina tissues of diabetic mice. CTRP9 suppresses the expression of interleukin-1 beta, tumor necrosis factor-alpha, monocyte chemotactic protein-1 and adhesion molecules in the retina of db/db mice. CTRP9 can balance the expression of pigment epithelium-derived factor and vascular endothelial growth factor. CTRP9 can also inhibit the activation of nuclear factor Kappa B in the retina of db/db mouse. In addition, CTRP9 can prevent the breakdown of BRB and downregulation of tight-junction proteins in the retina of db/db mouse. In the kidney tissues, CTRP9 ameliorate renal dysfunction and injury at the structural and functional level in diabetic mice, inhibited glomerular and tubular glycogen accumulation and fibrosis, prevented the upregulation of TGF-β, α-SMA, fibronectin, collagen IV, laminin, promoted the expression of nephrin. Moreover, CTRP9 relieved hyperglycemia-mediated oxidative stress, reactive oxygen species level and apoptosis, inhibited the activation of MAPK/ERK/JNK signaling pathway.

Conclusion: In conclusion, our study, for the first time, suggest that CTRP9 has protective and therapeutic effect on diabetic nephropathy and diabetic retinopathy, providing a potentially effective clinical method for the treatment of patients with diabetic microangiopathy.