C1q/TNF-Related Protein-9 improves diabetes-induced cardiac perivascular fibrosis by inhibiting endothelial-to-mesenchymal transition

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Introduction: C1q/TNF-Related Protein-9 (CTRP9) attenuates adverse cardiac remodeling partially by inhibiting interstitial fibrosis, endothelial cells respond by endothelial-to-mesenchymal transition (EndMT) plays a significant role in CF of diabetes. However, little is known about CTRP9-associated EndMT.

Methods: we investigated the potential role and mechanism of CTRP9 in diabetes-induced EndMT. After treated with Ad-GFP or Ad-CTRP9 for 4 weeks of 16-week-old db/db mice, untreated db/db mice and age-matched controls were sacrificed in 20 weeks. EndMT related markers, histopathological staining were detected. In vitro, high glucose (HG)-induced human umbilical vein endothelial cells (HUVECs) were treated with gCTRP9/short-hairpin CTRP9 to explore the mechanism of CTRP9 in the function of EndMT.

Result: We observed that diabetes decreased CTRP9 expression, and promoted the progression of EndMT and aggravated collagen deposition in vivo. Whereas CTRP9 overexpression improved the process without affecting the cardiac function of diabetic mice. In vitro, HG induced EndMT and production of collagenII, TGF-β1, CTGF, gCTRP9 ameliorated HG–induced EndMT in HUVECs. Conversely, silencing CTRP9 further exacerbated HG–induced EndMT. These protective effects of CTRP9 on EndMT were likely mediated by inactivating Smad2/Smad3 and inhibiting Snail signaling pathways.

Conclusion: Taken together, our results showed that CTRP9 alleviates diabetes-induced EndMT partially via Smad2/3 and Snail pathways.