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Exendin-4, GLP-1 Receptor Agonist, Ameliorates the Development of Renal Injury and High Salt-Sensitivity of Blood Pressure in Type 2 Diabetic Mice

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Summary

The metabolic syndrome is associated with the development of increased risk for chronic kidney disease (CKD). Here, we examined the renal injury in metabolic syndrome and type 2 diabetes by using mice under a high fat diet (HFD) or type 2 diabetic db/db mice. In addition, we examined the effect of Exendin-4, glucagon-like peptide 1 (GLP-1) analog on the renal abnormalities.

HFD induced core characteristics of metabolic syndrome syndrome and renal abnormalities, including such as glomerulosclerosis and albuminuria. In addition, the urinary sodium excretion in response to salt-loading was significantly attenuated by HFD. The db/db mice also showed albuminuria, glomeruloscrelosis and mesangial expansion. Treatment with Exendin-4 attenuated the developments of hyperglycemia and hypertension, and subsequently ameliorated the increases in urinary albumin excretion, mesangial expansion and glomerulosclerosis. In db/db mice, urinary sodium excretion in response to sodium-loading was delayed, and high-salt-induced hypertension was observed. In contrast, these alterations in response to salt-loading in db/db mice were attenuated by Exendin-4. These result indicated that GLP-1 signaling regulates salt-sensitivity, and Exendin-4 can ameliorate the development of nephropathy through the improvements of high salt-sensitivity.