# Relaxin ameliorates salt-sensitive hypertension and renal fibrosis in rats

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Relaxin (RLX), belonging to the insulin family, has been known as a pregnancy-related hormone. Although potent vasodilatory and anti-fibrotic properties of RLX are recently reported, the involvement and effects on salt-sensitive hypertension have not been elucidated.

First, we examined the expression of RLX and RLX receptor (RXFP1) protein and mRNA in kidneys in Dahl salt-sensitive (DS) rats and Dahl salt-resistant (DR) rats before and after 8-week 8% NaCl diet. Then, we examined the effects of RLX treatment on blood pressure and renal histology, nNOS and TGF-ß expression in DS and DR rats placed on an 8% NaCl diet.

By immunohistochemistry, the expression of RLX receptor (RXFP1) was observed in the distal tubular epithelium and vascular endothelial cells. RLX and RXFP1 mRNA was detected in kidneys by RT-PCR. RXFP1 protein in the cortex was significantly increased in DS rats compared with DR rats after feeding high salt diet, whereas there was no difference in RXFP1 between DS and DR rats before salt loading. The administration of RLX (4 μg/h) to male DS rats for 8 weeks significantly reduced systolic blood pressure from 227.0 ± 18.9 mmHg in control DS to 166.7 ± 18.5 mmHg in RLX treated rats ($p<0.004$) and urinary protein from 228.0 ± 162.7 in control rats to 87.5 ± 54.2 mg/day in RLX treated rats ($p<0.05$). Histologic studies revealed the amelioration of tubulointerstitial fibrosis assessed using a point counting method (38.4 ± 6.0 % in RLX treated rats vs. 49.1 ± 10.0 % in DS rats, $p<0.02$) and arterial thickening in rats received RLX. RLX-treated kidneys showed increased nNOS expression and decreased glomerular and tubulointerstitial TGF-ß, phosphorylated Smad2 expression compared to saline control.

These results suggest that RLX might directly act on the kidney and turn salt-sensitivity to salt-resistance, at least, in part by up-regulating nNOS and can be a potential therapeutic substance for salt-sensitive hypertension.