

Supplemental Table. 1.

Group	Age (week)	Experiment time (week)	Diet	Number	Drug/time (week)	Drug treated method
Pre-group	8	0	Normal salt	5	none	none
LS	8	8	Low salt	5	none	none
HS	8	8	High salt	5	none	none
HS+Saline	8	8	High salt	5	Saline/4	osmotic pump
HS+hydralazine	8	8	High salt	5	Hydralazine/4	water
HS+reCREG	8	8	High salt	5	reCREG protein/4	osmotic pump

Supplemental Table. 1. The information of every group.

Notes: Pre-group: before starting the high-salt diet, five rats were sacrificed, which were termed the Pre-group; Low salt (LS) and High salt (HS) group, which were treated with low-salt (0.3% NaCl) and high-salt (8% NaCl) diets. At week 4 of high-salt loading, HS rats were administered recombinant CREG1 protein (reCREG) (35 $\mu\text{g}/\text{kg}\cdot\text{d}$) (termed HS+reCREG group) and saline (termed HS+Saline group) via a subcutaneous osmotic pump, and were also administered hydralazine (20 $\text{mg}/\text{kg}\cdot\text{d}$) (termed HS+ hydralazine group) in drinking water.

Supplemental Table. 2.

Primer	sequences(5'to3')
GAPDH-F	TCAACGACCCCTTCATTGAC
GAPDH-R	ATGCAGGGATGATGTTCTGG
CREG-F	TGTCGGGAACTGTGACCAAG
CREG-R	CTTTAGTTGTTGAAATCTGTG
TGF β 1-F	GCAAGTCGCTCGTTCA
TGF β 1-R	GCCTTAGTTTGGACAGGATCTG
Foxp1-F	CTGGTGGCATTCCCTCTCTG
Foxp1-R	AAAGGCCCAAAGAGTCAAGTG

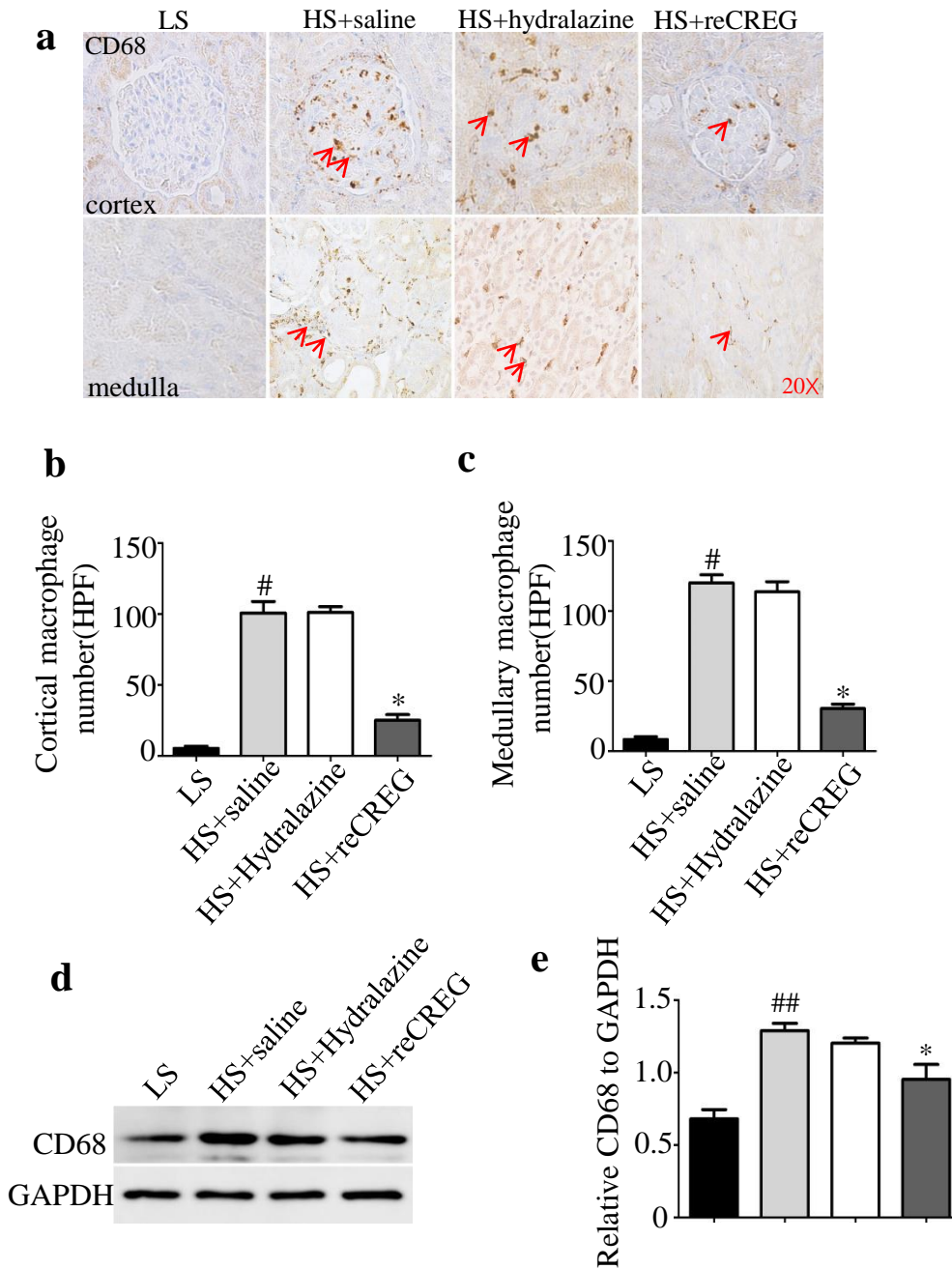
Supplemental Table. 2. Primer sequences for CREG, GAPDH, TGF- β 1, and Foxp1.

Supplemental Table. 3.

antibody	company	Catalog numbers
CD68	Abcam	ab125212
TGF- β 1	Cell Signaling	3711S
CREG	Abcam	ab68341
GAPDH	Cell Signaling	5174T
cleaved caspase 3	Cell Signaling	9661T
Bcl2	Abcam	ab184925
Bax	Abcam	ab32503
collagen IV	Abcam	ab6586
fibronectin	Abcam	ab2413
Smad2/3	Abcam	ab202445
pSmad2	Abcam	ab53100
Smad7	Abcam	ab216428
Foxp1	Abcam	ab16645

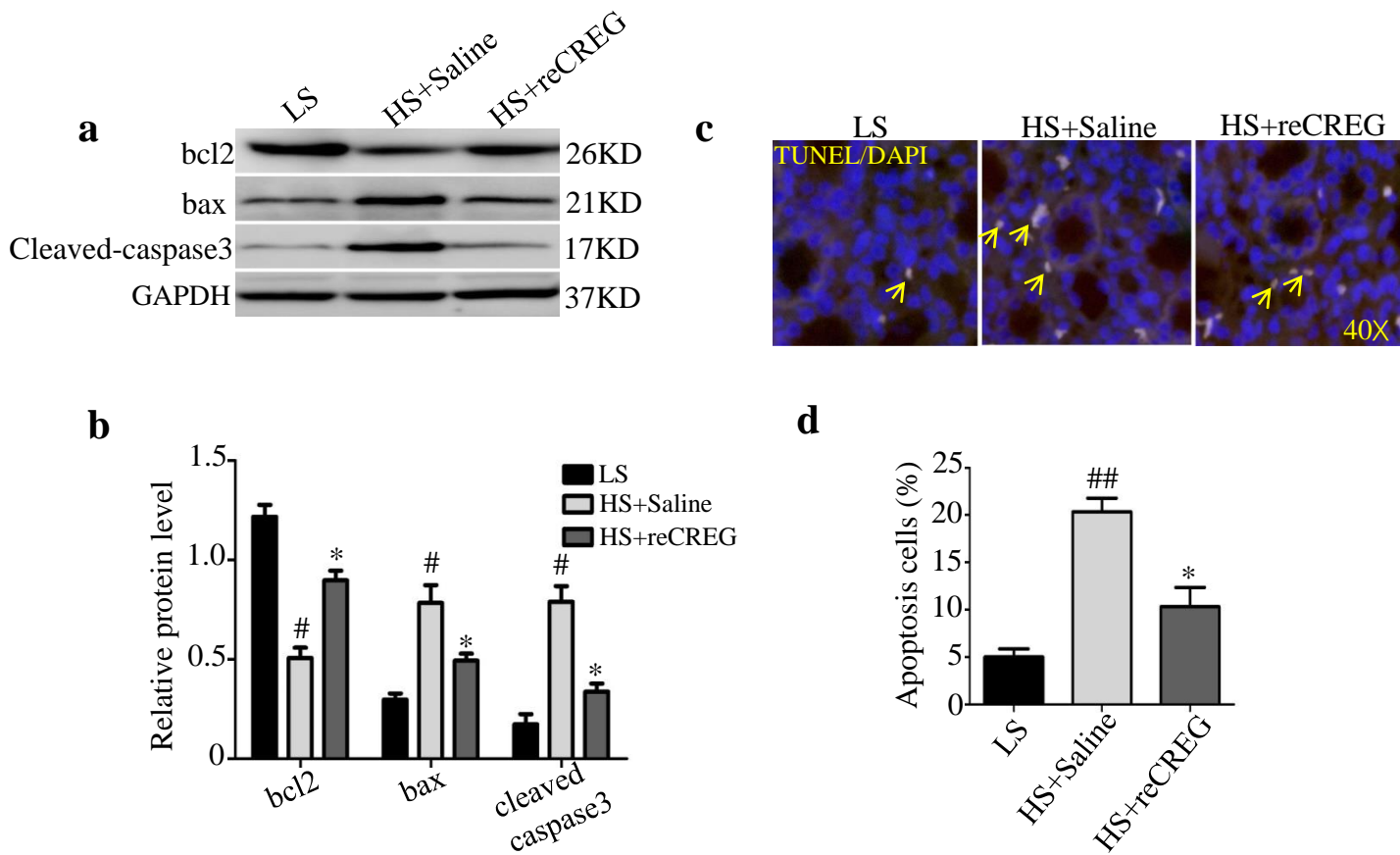
Supplemental Table. 3. The catalog numbers and company of all antibodies used for IHC and westerns.

Supplemental Fig. 1.



Supplemental Fig. 1. ReCREG inhibits macrophage infiltration into kidney cortex and medulla. a-c Immunohistochemical staining was showed the expression of CD68 in renal cortex and medulla; d, e Western blotting revealed that the expression of CD68 protein. [#] $P < 0.05$, ^{##} $P < 0.05$ versus LS; ^{*} $P < 0.05$ versus HS+Saline. Data are expressed as mean \pm SEM, $n = 5$.

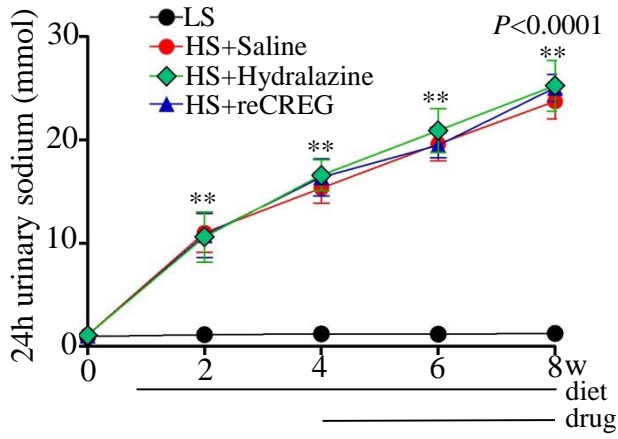
Supplemental Fig. 2.



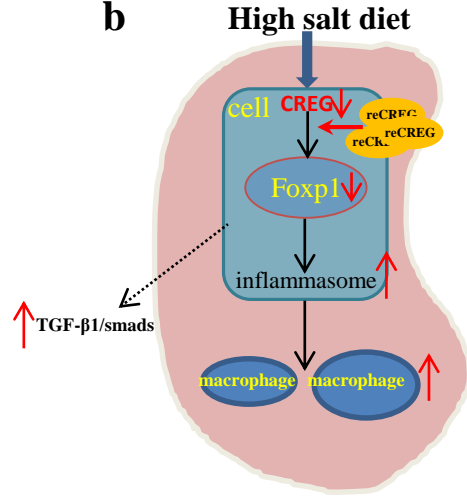
Supplemental Fig. 2. ReCREG reduces high-salt-induced renal-cell apoptosis. a, b Western blotting was used to analyze the expression of bcl2, bax, and cleaved caspase 3 in the different groups at week eight; c, d Level of renal cells apoptosis was evaluated by TUNEL staining. # $P < 0.05$, ## $P < 0.01$ versus LS; * $P < 0.05$ versus HS+Saline. Data are expressed as mean \pm SEM, $n = 5$.

Supplemental Fig. 3.

a



b



Supplemental Fig. 3. A 24h urinary sodium was supervised; b A schematic picture was demonstrated how CREG protected the kidney function. $**P < 0.01$ versus LS, Data are expressed as mean \pm SEM, n=5.

Assessment of renal-cell apoptosis

Terminal deoxyribonucleotidyl transferase-mediated dUTP-biotin nick end labeling (TUNEL) was used to analyze renal-cell apoptosis. An in situ Cell Death Detection Kit (Roche Diagnostics, Indianapolis, USA) was used to detect apoptotic nuclei, and 4'6-diamidino-2-phenylindole (DAPI) (Sigma) was used to label cell nuclei. An apoptotic index was assigned using the percentage of apoptotic cells.

Western blotting

Briefly, kidney samples were dissected and homogenized. The homogenized tissues were lysed in RIPA buffer (Thermo Scientific, USA) and then centrifuged at $12,000 \times g$ for 10 min at $4^{\circ} C$. Equal amounts of sample were separated by SDS-PAGE (at 150 V for 1 h), and then proteins were transferred into a polyvinylidene difluoride membrane. After 5% non-fat dry milk in TBST blocking, the membrane was incubated with antibodies against GAPDH (Cell Signaling), cleaved caspase 3 (Cell Signaling), Bcl2 (Abcam), Bax (Abcam), collagen IV (Abcam), fibronectin (Abcam), Smad2/3 (Abcam), pSmad2 (Abcam), Smad7 (Abcam), and Foxp1 (Abcam) at $4^{\circ} C$ overnight, all antibodies were diluted 1:1000. After washing, the membrane was incubated with Goat anti-rabbit (Thermo, USA) (1:5000) for 2 hours at $25^{\circ} C$ as described previously [11], the catalog numbers of all antibodies were listed in supplemental Table 2.