Supplementary Information

Table S1 illustrates the complete haemodynamic parameters and plasma concentrations in WT and KO animals, in the absence or presence of chromanol or clofilium. The majority of haemodynamic parameters and plasma concentrations recorded in WT and KO animals, in the absence or presence of chromanol or clofilium were not significantly different between each treatment group. However, the GFR in clofilium treated animals (both WT and KO) were significantly lower than equivalent control (vehicle) animals. In addition, the plasma osmolality of KO animals was significantly lower than WT, while treating KO animals with clofilium increased plasma osmolality. The only other difference observed was that the plasma K^+ of KO animals increased with clofilium.

In addition to the differences described in the paper, there were significant differences in additional renal parameters between WT and KO mice, Table S2. KO mice demonstrated an increased osmolar clearance, Na^+ clearance and urine Na^+ and Cl^- output. The renal handling of K^+ and glucose was not different in KO animals. These differences were mimicked by exposing WT mice to chromanol, Table S2. Like KO animals, chromanol-treated WT mice also had increased osmolar clearance, Na^+ clearance, urine Na^+ and Cl^- output. However, the addition of chromanol to KO animals was without effect on these parameters. Infusion of clofilium was also associated with a fall in GFR and a decrease in urinary K^+ loss (Tables S1 and S2). Unlike chromanol, the pattern of response to clofilium was the same for both WT and KO animals (Tables S1 and S2).

Table S1: Haemodynamic parameters and plasma concentrations

Treatment	N	Weight (g)	MAP (mmHg)	HCT (%)	GFR (µl/min)	PNa (mM)	PCl (mM)	PK (mM)	PGluc (mM)	Posm (mOsmoles/ kgH$_2$O)
WT$_{vehicle}$	8	23 ± 1	119 ± 4	40 ± 1	480 ± 48	156 ± 3	117 ± 2	4.0 ± 0.2	8.4 ± 2.0	320 ± 8
KO$_{vehicle}$	9	23 ± 1	138 ± 11	41 ± 1	423 ± 34	155 ± 3	118 ± 1	4.0 ± 0.1	10.8 ± 1.5	$297 \pm 6*$
WT + chromanol	6	24 ± 2	128 ± 6	44 ± 1	402 ± 18	151 ± 2	120 ± 1	4.2 ± 0.1	10.9 ± 1.0	307 ± 9
KO + chromanol	9	23 ± 1	119 ± 5	41 ± 1	393 ± 19	149 ± 2	118 ± 1	4.2 ± 0.1	13.1 ± 2.0	301 ± 4
WT + clofilium	10	23 ± 1	136 ± 7	41 ± 1	$279 \pm 19*$	154 ± 3	118 ± 2	4.2 ± 0.1	10.9 ± 1.4	321 ± 3
KO + clofilium	9	26 ± 2	142 ± 8	42 ± 1	$267 \pm 18\#$	156 ± 1	120 ± 2	$4.5 \pm 0.1\#$	10.2 ± 0.8	$324 \pm 7\#$
F value (P value)		1.47 (0.22)	1.97 (0.10)	2.00 (0.10)	**10.56 (<0.001)**	1.65 (0.17)	0.64 (0.67)	**2.55 (0.04)**	1.05 (0.40)	**4.18 (0.003)**

* Indicates a significant difference to WT (P<0.01), # indicates a significant difference to KO (P<0.01), F values in bold are significant

MAP = mean arterial pressure, HCT = haematocrit, GFR = glomerular filtration rate, P indicated plasma concentration of Na$^+$, Cl$^-$, K$^+$ and glucose.

Posm = plasma osmolality

Table S2: Renal parameters

Treatment	N	C_{osm} (µl/min)	C_{Na} (µl/min)	UV_{Na} (µmol/min)	C_{Cl} (µl/min)	UV_{Cl} (µmol/min)	C_K (µl/min)	UV_K (µmol/min)	C_{Gluc} (µl/min)	UV_{Gluc} (nmol/min)
WT$_{vehicle}$	8	18.7 ± 1.7	9.9 ± 1.3	1.55 ± 021	15.8 ± 2.5	1.84 ± 0.2	90.2 ± 7.4	0.36 ± 0.04	1.37 ± 0.24	9.4 ± 1.3
KO$_{vehicle}$	9	21.9 ± 1.8*	13.7 ± 1.9*	2.13 ± 0.30*	19.1 ± 2.5*	2.23 ± 0.3*	94.1 ± 9.4	0.38 ± 0.04	0.99 ± 0.17	9.6 ± 1.6
WT + chromanol	6	24.1 ± 3.2*	16.7 ± 1.0*	2.53 ± 0.16*	23.2 ± 1.8*	2.78 ± 0.2*	102 ± 9.1	0.43 ± 0.04	1.29 ± 0.17	13.7 ± 1.7
KO + chromanol	9	21.0 ± 1.5	14.2 ± 1.4	2.12 ± 0.21	19.4 ± 1.8	2.28 ± 0.2	80.8 ± 8.4	0.34 ± 0.04	1.77 ± 0.32#	21.0 ± 6.8#
WT + clofilium	10	15.4 ± 1.2	10.3 ± 1.0	1.58 ± 0.15	13.8 ± 1.3	1.62 ± 0.1	46.7 ± 5.0*	0.20 ± 0.03*	0.99 ± 0.16	11.7 ± 2.8
KO + clofilium	9	16.5 ± 1.4#	12.2 ± 1.1	1.90 ± 0.16	16.1 ± 1.6	1.93 ± 0.2	53.0 ± 6.7#	0.24 ± 0.03#	0.96 ± 0.11	9.5 ± 1.0
F value (P value)		**4.16 (0.003)**	**3.58 (0.008)**	**3.11 (0.02)**	**2.98 (0.02)**	**3.38 (0.01)**	**10.13 (<0.001)**	**7.27 (<0.001)**	**2.80 (0.03)**	**3.01 (0.02)**

* Indicates a significant difference to WT ($P<0.05$), # indicates a significant difference to KO ($P<0.01$), F values in bold are significant

C = clearance of Na^+, Cl^-, K^+ and glucose, C_{osm}= osmolar clearance, UV = urinary excretion of Na^+, Cl^-, K^+ and glucose.