



**Supplementary Figure 1. Time course for PP242 inhibition of mTOR signaling.** Wild-type, 8-12 week old mice were injected with 30 mg/kg PP242 (n=3 per time point) or vehicle (n=2 per time point). To determine duration of mTOR inhibition, kidneys were excised 1, 3 and 5 hours post-IP injection. Each lane represents a separate mouse. A) 100 $\mu$ g of kidney cytosolic extract was used to assess phosphorylation of SGK1, Akt and rpS6 by Western blot. Arrows indicate phosphorylated SGK1. SGK1 KO lysate was used as a control to confirm SGK1 expression.

**SUPPLEMENTARY TABLE 1. Urinary electrolytes in rapamycin-treated mice**

	<b>Vehicle (6)</b>	<b>rapamycin (6)</b>
<b>Body mass (g)</b>	22.3 +/- 0.6	22.4 +/- 0.3
<b>U volume (<math>\mu</math>L)</b>	231.2 +/- 30.2	202.5 +/- 32.3
<b>UNa (mmol/L)</b>	20.3 +/- 1.9	26.5 +/- 7.4
<b>UK (mmol/L)</b>	263.1 +/- 29.5	247.6 +/- 47.7
<b>UCI (mmol/L)</b>	119.2 +/-17.4	124 +/- 21.6
<b>UNa*V (mmol)</b>	4.67 +/- 0.8	5.97 +/- 2.2
<b>UK*V (mmol)</b>	61.1 +/- 12	50.9 +/- 11.7
<b>UCI*V (mmol)</b>	28.2 +/- 6.6	25.6 +/- 6.2
<b>UNa/UK</b>	0.08 +/- 0.01	0.11 +/- 0.02
<b>UCr (mg/dl)</b>	49.3 +/- 4	49.6 +/- 5.4
<b>Uglucose (mg/dl)</b>	81.3 +/- 7.3	72.7 +/- 9.8

Wild-type, 8-12-wk-old, male mice were treated with vehicle or rapamycin (1.5 mg/kg). Following IP injection, mice were placed in balance cages for 6h under conditions of free access to food and water. Urine was collected and urinary electrolytes, glucose and creatinine, were measured. Numbers in parentheses indicate 'n'. Creatinine is abbreviated 'CR'. Data represent mean +/- SEM; differences were determined by unpaired Student's *t* test.

**SUPPLEMENTARY TABLE 2. Urinary electrolytes in AZD8055-treated mice**

	<b>Vehicle (6)</b>	<b>AZD8055 (6)</b>
<b>Body mass (g)</b>	23 +/- 0.3	22.4 +/- 0.4
<b>U volume (<math>\mu</math>L)</b>	219.75 +/- 35	459.8 +/- 50.8*
<b>UNa (mmol/L)</b>	18.2 +/- 2.2	63.7 +/- 8*
<b>UK (mmol/L)</b>	279.4 +/- 41.7	113.3 +/- 7.4*
<b>UCI (mmol/L)</b>	144.5 +/- 25.8	113.7 +/- 5.3
<b>UNa*V (mmol)</b>	4.2 +/- 0.9	28.5 +/- 4*
<b>UK*V (mmol)</b>	62.8 +/- 13.6	50.4 +/- 4
<b>UCI*V (mmol)</b>	32.6 +/- 7.9	51.2 +/- 4.7
<b>UNa/UK</b>	0.07 +/- 0.01	0.57 +/- 0.07*
<b>UCr (mg/dl)</b>	47.7 +/- 3.9	14.9 +/- 1.6*
<b>Uglucose (mg/dl)</b>	88.3 +/- 6.4	1726.3 +/- 285.5*

Wild-type, 8-12-wk-old, male mice were treated with vehicle or AZD8055 (15 mg/kg). Following IP injection, mice were placed in balance cages for 6h under conditions of free access to food and water. Urine was collected, and urinary electrolytes, glucose and creatinine were measured. Numbers in parentheses indicate 'n'. Creatinine is abbreviated 'CR'. Data represent mean +/- SEM; differences were determined by unpaired Student's *t* test. \**p* < 0.05, Veh vs. AZD8055.

**SUPPLEMENTARY TABLE 3. Urinary electrolytes in SGK1 KO mice treated with diuretics and PP242**

	Amiloride		Hydrochlorothiazide	
	Vehicle (7)	PP242 (8)	Vehicle (7)	PP242 (7)
<b>Body mass (g)</b>	23.5 +/- 0.9	24.0 +/- 1.1	25.1 +/- 1.1	26.1 +/- 1.5
<b>U volume (<math>\mu</math>L/6h)</b>	348.7 +/- 30.8	372.7 +/- 47.6	393.6 +/- 55.3	601.9 +/- 81.2
<b>UNa (mM)</b>	97.3 +/- 10.2	80.8 +/- 7.2	163.7 +/- 17.1	145.6 +/- 12.1
<b>UK (mM)</b>	72.5 +/- 4.5	60.9 +/- 8.2	194.0 +/- 19.5	150.0 +/- 21.6
<b>UCI (mM)</b>	50.4 +/- 5.9	39.0 +/- 5.5	259.4 +/- 24.7	185.4 +/- 24.3*
<b>UNa*V (mmol/6h)</b>	32.4 +/- 2.0	30.9 +/- 3.6	61.0 +/- 6.0	82.9 +/- 6.7*
<b>UK*V (mmol/6h)</b>	25.2 +/- 2.6	23.0 +/- 3.6	75.6 +/- 12	82.2 +/- 6.1
<b>UCI*V (mmol/6h)</b>	17.0 +/- 2.1	15.8 +/- 3.1	97.5 +/- 11	103.2 +/- 8.9
<b>UNa/UK</b>	1.36 +/- 0.1	1.39 +/- 0.1	0.88 +/- 0.1	1.03 +/- 0.1
<b>UCr (mg/dl)</b>	24.3 +/- 2.2	16.0 +/- 1.4	30.8 +/- 2.3	25.5 +/- 3.4
<b>Uglucose (mg/dl)</b>	33.0 +/- 4.7	1223 +/- 562*	54.7 +/- 5.1	61.7 +/- 9.6

SGK1 KO mice, 8-12 weeks of age, were pre-treated overnight with either amiloride or HCTZ to block ENaC or NCC, respectively. The next morning, mice were IP injected with amiloride plus PP242 or HCTZ plus PP242. Following IP injection, mice were placed in balance cages for 6h under conditions of free access to food and water. Urine was collected, and urinary electrolytes, glucose and creatinine were measured. Numbers in parentheses indicate 'n'. Creatinine is abbreviated 'CR'. Data represent means +/- SEM; differences were determined by unpaired Student's *t* test. \*  $p < 0.05$  Veh vs PP242.