	G (pS)	PBr	PNO3	PI	pHi sensitivity
early DCT	9.5	0.46	0.50	0.9	+
late DCT	8.8	0.41	0.48	0.62	+
CNT	10.6	0.44	0.56	0.86	+
CCD	9.8	0.60	0.54	N.D.	+
CTAL	9	0.62	0.64	N.D.	+

The table gives the unit conductance and permeabilities (relative to chloride) of the chloride channels detected in various segments of the mouse nephron. Data from refs 2,3,4 and unpublished results (CTAL)

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Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

SA7

Acid- and volume-sensitive potassium channels in renal function

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A variety of acid- and volume-sensitive K^+ channels have been described which are implicated in important cellular functions. In the kidney, many studies have explored the role of pH-regulated KCNJ1 (ROMK) channels in the straight and convoluted distal tubule and of volume-, pH-, and ATP-regulated K^+ channels in the basolateral membrane of the proximal tubule. Here, we have focused on two pH- and volume-regulated K^+ channels of the 2P domain channel family, TASK2 (KCNK5) and TASK1 (KCNK3). TASK2 is strongly expressed in proximal tubules and papillary collecting ducts. Patch-clamp experiments on proximal tubular cells indicated that the TASK2-specific K^+ current is activated during bicarbonate transport. In *in vivo* experiments, TASK2-/- mice displayed mild metabolic acidosis which was caused by an increased renal bicarbonate excretion. Activation of TASK2 by transport-induced cell swelling and basolateral export of bicarbonate appears to be an important mechanism to adapt membrane potential and osmolyte export to the needs (1,2).
Aldosterone regulates ion transport in the distal nephron which is critical for water/salt balance and the control of arterial blood pressure. TASK1 is probably the most abundant K^+ channel in human adrenal glands. This channel has been proposed to contribute to the background conductance whose inhibition by angiotensin II stimulates aldosterone secretion. We investigated the contribution of TASK1 for this K^+ conductance using a TASK1-/- mouse as a tool. Female TASK1-/- mice exhibited severe hyperaldosteronism independent of salt intake, hypokalemia, and arterial 'low renin' hypertension. The aldosterone phenotype was accompanied by a severe adrenocortical zonation defect. Aldosterone synthase was totally absent in the zona glomerulosa but abundant in the deeper zona fasciculata. Also young male TASK1-/- mice displayed a zonation defect. In contrast to females, at adulthood male TASK1-/- mice had acquired normal zonation patterns highlighting the dynamics of the process of adrenocortical zonation. Interestingly, the hyperaldosteronism of female TASK1-/- mice was fully remediable by glucocorticoids indicating that in those mice aldosterone secretion is under the control of ACTH. These findings are reminiscent of glucocorticoid-remediable hyperaldosteronism in humans (3).
In conclusion, proximal tubular TASK2 channels stabilize the driving force and cell volume during ongoing Na+ and bicarbonate transport. We propose TASK2 as a novel candidate to underlie the clinical manifestations seen in proximal renal tubular acidosis syndrome. The acid-sensitive TASK1 channel is a pivotal factor for normal adrenocortical zonation, aldosterone secretion and, thereby, regulation of renal function. The phenotype of TASK1-/- mice underlines the potential of K^+ channels to influence cell differentiation and development.

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The support by the Deutsche Forschungsgemeinschaft (SFB699) is greatly acknowledged.

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SA8

Renal Na/Pi-cotransporter NaPi-IIa: a physiological and molecular overview

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Homeostatic balance of inorganic phosphate (Pi) has wide physiological implications. Plasma levels of Pi are kept constant by adjusting renal reabsorption/excretion to intestinal absorption. Both processes are mediated by members of the SLC34 gene family. NaPi-IIa/SLC34A1 and NaPi-IIc/SLC34A3 are responsible for renal reabsorption whereas intestinal absorption is mediated by NaPi-IIb/SLC34A2. NaPi-IIa and NaPi-IIc are expressed in the brush border membranes (BBM) of renal proximal tubules (PT) (1, 2). In the adult murine kidney, NaPi-IIa reclaims up to 80% of filtered Pi, with the 20% left attributed to NaPi-IIc (3). NaPi-IIa expression is reduced in animal models for X-linked hypophosphatemia (XLH), and in vitro studies indicate that similar defect could be involved in other phosphate wasting syndromes. However, such reductions on NaPi-IIa are probably secondary to defects on other factors collectively known as phosphatonins (FGF23, PHEX, FRP-4, and MEPE) (3). Recently, mutations in NaPi-IIc were linked to hereditary hypophosphatemic rickets with hypercalciuria. These findings indicate that