Structure, regulation and physiological roles of urea transporters.

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Abstract

Urea is the major constituent of the urine and the principal means for disposal of nitrogen derived from amino acid metabolism. Specialized phloretin-inhibitable urea transporters are expressed in kidney medulla and play a central role in urea excretion and water balance. These transporters allow accumulation of urea in the medulla and enable the kidney to concentrate urine to an osmolality greater than systemic plasma. Recently, expression cloning with Xenopus oocytes has led to the isolation of a novel phloretin-inhibitable urea transporter (UT2) from rabbit, and subsequently from rat kidney. UT2 from both species has the characteristics of the phloretin-sensitive urea transporter previously defined in kidney by in vitro perfused tubule studies. Based on these advances, Ripoche and colleagues cloned a homologous urea transporter (HUT11) from erythrocytes. UT2 and HUT11 predict 43 kDa polypeptides and exhibit 64% amino acid sequence identity. Since regulation of urea transport in the kidney plays an important role in the orchestration of the antidiuretic response, we have studied the regulation of urea transporter in rat kidney at the mRNA level. On Northern blots probed at high stringency, rat UT2 hybridized to two transcripts of 2.9 kb and 4.0 kb, which have spatially distinct distributions within the kidney. Northern analysis and in situ hybridization of kidneys from rats maintained at different physiologic states revealed that the 2.9 and 4.0 kb transcripts are regulated by separate mechanisms. The 4 kb transcript was primarily responsive to changes in the dietary protein content, whereas the 2.9 kb transcript was highly responsive to changes in the hydration state of the animal. We propose that the two UT2 transcripts are regulated by distinct mechanisms to allow optimal fluid balance and urea excretion.