Ammonotelic teleosts and urea transporters

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UREA, A SMALL MOLECULE, IS an end product of nitrogen metabolism. In fish, it is mostly used as an osmolyte or excreted as a waste product of ammonia detoxification (22). Marine elasmobranch fish (dogfish, skate, and stingray) keep their plasma osmolality (~1,050 mosmol/kgH2O) slightly above that of teleosts, ammonia levels of 2–4 mM and maintain their tissue osmolality at 340 mosmol/kgH2O even in seawater (10). Since teleosts do not have high levels of urea and have a nephron that is not involved in urine concentration, most of the work pertaining to urea transport has been done in marine elasmobranchs. Recently, an eel urea transporter (eUT) present in the salt-secreting chloride cells of the gill of the Japanese eel was cloned and is thought to aid in urea excretion (11). Mistry et al. (10) report in this issue the discovery of another novel urea transporter in the Takifugu (puffer fish) genome and the cloning of its ortholog (eUT-C) from seawater-adapted eel kidney. The eUT-C is present in the basolateral membranes of renal proximal tubule cells of the kidney and is made up of 378 amino acid residues compared with 486 amino acid residues in the e-UT homolog from the gill. Both of these transporters are functionally similar as they are inhibited by phloretin and are not sensitive to forskolin or vasopressin treatments. The discovery of these two urea transporters by Mistry et al. in the eel, an ammonotelic teleost, raises more questions than it answers. Why does an ammonotelic teleost need a urea transporter?

Teleosts and elasmobranchs respond differently to severe osmotic stress. When a euryhaline elasmobranch is acclimated to a freshwater habitat, it reduces its plasma osmolality by excreting more urea and salts, increases its urinary output, and decreases the fractional reabsorption of urea in the kidney (5, 13, 15). In contrast, in teleosts such as eels acclimated to seawater, plasma osmolality and urea concentration increase. However, the magnitude of change is much less compared with marine elasmobranch fish acclimated to freshwater (10, 12). The serum osmolality changes from 297 ± 7 to 343 ± 15 mosmol/kgH2O, and urea concentration increases from 1.9 ± 0.4 to 3.7 ± 0.1 mM, respectively. They maintain their water balance by continuous drinking and intestinal absorption of seawater, coupled with excretion of excess salt via chloride cells in the gills (6). Recently, eel aquaporins (S-AQP and L-AQP) were shown to be strongly induced on the apical surface of columnar epithelial cells in the intestine of the Japanese eel on seawater acclimation, and these are thought to aid in water absorption (1).

Most teleosts are ammonotelic; however, they can be partially or fully ureotelic depending on their habitat. Two well-studied examples are the gulfood and Lake Magadi tilapia, the only fish living at pH ~10, where ammonia excretion is inopera due to high pH (14, 20). The gill is the major site of urea excretion, as reflected by the presence of urea transporters mtUP and tUP in the gills of Lake Magadi tilapia and gulfood fish, respectively (17, 18). In eel gills, eUT is strongly upregulated on seawater acclimation (11). Northern and Western blot analyses also showed that eUT-C is strongly induced in the kidney and stomach following seawater acclimation (8, 10). Mistry et al. (10) contend that eUT-C is involved in reabsorption of urea from proximal tubules and works in conjunction with gill eUT to effectively reduce urea levels in plasma. In teleosts, ammonia levels of 2 mmol/l can result in paralysis (8). In freshwater fish, the presence of an acidified boundary layer on the gill surface is thought to aid in trapping NH3 as NH4+, which ensures a favorable NH3 gradient across the gill. Eels acclimated to seawater have very low urine output, which, coupled with insignificant acidification of the gill boundary layer in seawater for efficient ammonia excretion, would result in ammonia toxicity (19). Mistry et al. (10) suggest that urea excretion may be a backup mechanism to prevent ammonia toxicity. However, in related European eel, branchial urea clearance was shown to decrease on seawater acclimation (9). This observation, combined with the basolateral location of the eUT in the gill led to the suggestion that eUT may be involved in urea retention (19). Although eUT-C is not sodium dependent, it is not clear whether eUT from the gill is sodium dependent so as to function as an active transporter to retain urea. Hence, actual urea flux measurements would be required to confirm these hypotheses. More molecular and physiological studies are required to understand the importance of eUT-C expression also seen in the stomach on seawater acclimation. Although the urea diet-fed rainbow trout was shown to absorb urea, it is not clear whether it was mostly due to passive diffusion or if there was also facilitated urea uptake (7). Recently, it was shown that urea excretion by teleosts is more widespread and that UT mRNA is expressed in the gills of a wide variety of teleosts (16). Isolation of purified apical and basal membrane vesicles from sites known to express UTs and use of cultured gill epithelia as models would aid in functional characterization of these transporters (2, 3, 21). However, molecular characterization of these channels would require functional expression and reconstitution of cloned urea transporters in a heterologous expression system. Clearly, additional work needs to be done to get at a complete physiological understanding of urea transporters present in fish in aquatic and marine habitats.

REFERENCES


