# Endocrine regulation of cell proliferation and apoptosis in the esophagus of euryhaline fishes

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**EFFECTS OF HYPEROSMOTIC STRESS AND ARGININE VASOTOCIN ON EXPRESSION OF AN UREA TRANSPORTER IN THE KIDNEY AND URINARY BLADDER OF THE MARINE TOAD**

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Anuran amphibians accumulate a large amount of urea in their body fluids and maintain hyper-osmolality to tolerate a severe dehydration under dry and hyper-saline environments. To clarify the mechanisms of urea retention and effects of arginine vasotocin (AVT) on urea reabsorption, we examined molecular structure, distribution and functional expression of the urea transporter (UT) following exposure to dry and hyper-saline conditions in the kidney and urinary bladder of the marine toad (Bufo marinus). Bufo UT cDNA cloned from the kidney encodes a 390 amino acid residue protein, and the mRNA and protein were abundantly expressed in the kidney and urinary bladder. Immunohistochemically, the UT is localized at the apical membrane of epithelial cells along the early distal tubule, known as the diluting segment, in the kidney. When toads were acclimated to dry and hyper-saline environments for 7 days, plasma concentrations of urea and AVT were significantly elevated, and there were significant correlations among the plasma concentrations of urea and AVT, and the level of Bufo UT mRNA expression in both the kidney and urinary bladder. These results suggest that the Bufo UT probably contributes to urea reabsorption in the kidney and urinary bladder in response to hyperosmotic stresses and an increase of circulating plasma AVT level.

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**ENDOCRINE REGULATION OF CELL PROLIFERATION AND APOPTOSIS IN THE ESOPHAGUS OF EURYHALINE FISHES**

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In the seawater (SW)-acclimated euryhaline fishes, the ion/water permeability of the gastrointestinal tract is generally greater than that of freshwater (FW)-acclimated fish. The esophageal epithelium of SW fishes is simple columnar in form, whereas that of FW fishes is stratified. To understand how environmental and hormonal stimuli affect the gastrointestinal-tract differentiation, we examined the esophageal cell turnover of Mozambique tilapia and amphibious mudskipper transferred to various environments. In both species, increased apoptosis was found throughout the esophageal epithelium during SW acclimation, whereas cell proliferation occurred randomly over the epithelium in FW. There was no significant change in the mudskipper kept out of water. In vivo treatment of the mudskipper with prolactin (PRL) induced the epithelial cell proliferation. Triiodothyronine or a teleostean mineralocorticoid candidate, 11-deoxycorticosterone, showed no significant effect on cell turnover. Cortisol stimulated both epithelial cell proliferation and apoptosis. In the tilapia, glucocorticoid receptor (GR) was observed in the epithelia including the apoptotic and proliferating cells, whereas the PRL receptor expression was high in FW and seemed to be localized in the proliferating cells. Thus, it is likely that in the esophageal epithelium of these fishes, PRL and cortisol induce cell proliferation in FW, whereas cortisol-GR stimulates apoptosis during SW acclimation.