Evidence that taurine modulates osmoregulation by modification of osmolarity sensor protein ENVZ – expression

H. Moenkemann1, O. Labudova2, K. Yeghiazarian1, H. Rink3, H. Hoeger3, and G. Lubec1

1Department of Pediatrics and 3Institute for Animal Breeding, University of Vienna, Austria
2Department of Radiobiology, University of Bonn, Federal Republic of Germany

Accepted November 2, 1998

Summary. Although the involvement of taurine in osmoregulation is well-documented and widely accepted, no detailed mechanism for this function has been reported so far.

We used subtractive hybridization to study mRNA steady state levels of genes up- or downregulated by taurine. Rats were fed taurine 100mg/kg body weight per day for a period of three days and hearts (total ventricular tissue) of experimental animals and controls were pooled and used for mRNA extraction. mRNAs from two groups were used for subtractive hybridization. Clones of the subtractive library were sequenced and the obtained sequences were identified by gen bank assignment.

Two clones were found to contain sequences which could be assigned to the osmolarity sensor protein envZ, showing homologies of 61 and 65%. EnvZ is an inner membrane protein in bacteria, important for osmosensing and required for porine gene regulation. It undergoes autophosphorylation and subsequently phosphorylates OmpR, which in turn binds to the porine (outer membrane protein) promoters to regulate the expression of OmpF and OmpC, major outer membrane porines.

This is the first report of an osmosensing mechanism in the mammalian system, which was described in bacteria only. Furthermore, we are assigning a tentative role for taurine in the osmoregulatory process by modifying the expression of the osmoregulatory sensor protein ENVZ.

Keywords: Amino acids – Taurine – Osmoregulation – Rat – Osmolarity sensor protein ENVZ

Introduction

The role of taurine for osmoregulation from microorganisms to the animal kingdom including Man in several organ systems, under physiological and
pathophysiological conditions, is unequivocally accepted (Solis et al., 1988; Law, 1991; Schaffer and Azuma, 1992; Pasantes-Morale et al., 1993; Moran et al., 1994; Burg, 1995; Walz and Allen, 1987; Trachtman et al., 1988; Wade et al., 1988; Oja and Saransaari, 1996; Lehmann, 1989; Graham and Wilkinson, 1992; Harris et al., 1993; Burg, 1994; Hilgier et al., 1996). The mechanisms for the osmoregulatory process are, however, not fully elucidated yet. All cells are able to keep their volume within a very limited range using volume regulatory mechanisms involving changes in the concentration of osmolytes of which taurine may be of particular importance. Cell swelling in excitable tissues may occur as a result of depolarization or fluctuations in osmolarity. These conditions lead to taurine release. Detailed mechanisms for taurine release and the released taurine’s actions remain to be elucidated. Pasantes–Morales and Schousboe (Pasantes-Morales and Schousboe, 1997) stressed this problem in a recent review citing a large body of evidence excluding the participation of the taurine high affinity carrier: Using a number of inhibitors of anion exchangers it has been demonstrated that both volume regulation and taurine release in brain cells are inhibited by these drugs, implicating an anion channel in the process. Also the Ca++ dependence of taurine release remains a controversial issue but recent studies suggest that the releasing process is not associated with Ca++ or Ca++ – channels, whereas the Ca++calmodulin system or other second messengers may well be involved. Taurine also contributes to volume regulation after shrinkage of brain cells by increasing its intracellular concentration. This effect maybe accomplished by an upregulation of the sodium-taurine cotransporter along with reduced passive fluxes and increased endogenous synthesis.

GarciaRomeu and coworkers suggest a role for the anion exchange AE1 in cell volume regulation (GarciaRomeu et al., 1996; Motaïs et al., 1997): Molecular cloning and functional expression of AE1 from the trout erythrocyte shows that this anion exchanger can function as a channel mediating taurine fluxes. In the erythrocyte, the channel activation depends on the conditions as the cell is swollen: when swelling is caused by an accumulation of electrolytes, the channel is not activated and regulation is mediated by potassium and chloride via a KCl cotransporter. When swelling is caused by hypotonic shock, the AE1 channel mediating taurine fluxes becomes activated allowing volume recovery by releasing both, taurine and other ions. Deleuze and coworkers propose an osmoregulatory effect and regulation of the whole body fluid-balance through modulation of vasopressin release (Deleuze et al., 1988). This mechanism would involve glycine receptors of which taurine can be regarded as a major natural agonist, in the supraoptic nucleus, the main site of magnocellular neurons representing the neuroendocrine regulatory loop of vasopressin (Hussy et al., 1997).

We used the molecular biological technique of subtractive hybridization approach to search for taurine – inducible genes which may be related to osmoregulation in the heart, which is probably the best studied organ in taurine research. Subtractive hybridization was employed to subtract mRNAs steady state levels in heart of taurine treated rats from control rats and vice versa. We found that two clones of the subtractive library contained