THE SODIUM-ACTIVATED SODIUM CHANNEL (Na⁺) EXPRESSED BY THE THICK ASCENDING LIMB AND COLLECTING DUCT CELLS OF THE RAT KIDNEY IS UPREGULATED DURING HIGH SALT INTAKE

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Increased dietary salt triggers oxidative stress and exacerbates hypertension and kidney injury in angiotensin II (Ang II)-dependent hypertension; however the mechanism for sensing increased extracellular Na⁺ concentration remains unclear. A Na⁺-activated Na⁺ channel (Na⁺), recently discovered in the brain, operates as a sensor of extracellular fluid Na⁺ concentration. We have identified in the Sprague Dawley (SD) rat kidney a specific PCR product of 448 bp and a protein of 190 KDa which identity with the Na⁺ was confirmed by DNA sequencing. By using immunofluorescence, specific Na⁺ immunoreactivity was expressed on the luminal side of tubular epithelial cells of collecting ducts (CD) and thick ascending limb (TAL), co-localizing respectively with aquaporin (AQP)-2, a marker of principal cells, and with Tamm-Horsfall, a marker for the TAL cells. To determine the effect of a high salt (HS) diet on the Na⁺ expression, we quantified its protein levels by Western blot in renal medullary extracts from 15 male SD rats (175-200 g; controls, normal salt diet; n=5, and rats subjected to 8% HS for 7 and 14 days; n=5 each subgroup). Seven days of HS diet increased the Na⁺ protein levels 74±16 % (p<0.05) but they were downregulated at 14 days compared to controls. These data indicate that the Na⁺ in the CD and TAL cells is upregulated by HS and suggest a role in monitoring changes in tubular fluid Na⁺ concentration.

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