

## Molecular mechanisms underlying sodium reception in the brain

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### Summary

Mammals feel thirsty or salt appetite when the correct balance between water and sodium in the body fluid has been disrupted, but little is known about the sensing mechanism in the brain for the control of salt homeostasis. It has been postulated that the existence of both osmoreceptor and specific sodium receptor is essential to encompass the experimental data. In the osmoreception, stretch-sensitive channels and aquaporin-4 in the magnocellular neurosecretory cells, glial cells and ependymal cells in the supraoptic nucleus and subfornical organ (SFO) are thought to be involved. Here, we show that  $\text{Na}_x$  channel in the circumventricular organs (CVOs) is a candidate for the specific sodium receptor, using ion-imaging and whole-cell patch-clamp techniques.  $\text{Na}_x$  is a newly identified type of sodium channel that is sensitive to an increase in the extracellular sodium concentration, and is likely to be the sodium-level sensor of body fluids in the brain.

Furthermore, we examined the localization of  $\text{Na}_x$  throughout the visceral organs at the cellular level. In visceral organs including lung, heart, intestine, bladder, kidney and tongue, a subset of Schwann cells within the peripheral nerve trunks were highly positive for  $\text{Na}_x$ . An electron microscopic study indicated that these  $\text{Na}_x$ -positive cells were non-myelinating Schwann cells. In the lung,  $\text{Na}_x$ -positive signals were also observed in the alveolar type II cells, which actively absorb sodium and water to aid gas exchange through the alveolar surface. It was thus suggested that  $\text{Na}_x$  sodium channel is involved in controlling the local extracellular sodium level through sodium absorption activity.