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Amiloride-Sensitive Salt-Sensing Mechanism in Taste Buds

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Summary

Sodium taste promotes salt ingestion by mediating attraction to sodium salts, and excessive dietary sodium intake has been linked to elevated blood pressure. Thus, understanding the mechanisms of the perception of sodium taste is important to devise strategies to reduce salt consumption. The amiloride-sensitive epithelial Na^+ channel (ENaC) has been identified as the Na^+ sensor in taste cells dedicated to sodium taste, a.k.a. sodium cells. However, the identity of sodium cells and their intracellular signal transduction cascade downstream of ENaC, including the involvement of action potentials and Ca^{2+} signals and neurotransmission mechanism, have remained unknown. Therefore, we continue to lack understanding of the cellular and molecular basis of the peripheral perception of sodium taste. In this study, we have discovered the identity of sodium cells and elucidated the underlying mechanism of sodium sensing in taste buds. We demonstrate that a subpopulation of taste cells expressing ENaC generate action potentials in response to Na^+ influx through ENaC, and possess a channel synapse with afferent gustatory neurons involving CALHM1/3, a voltage-gated neurotransmitter-release channel. Furthermore, conditional knockout of ENaC in CALHM1-expressing cells and conventional *Calhm3* knockout in mice negate the animals' ability to perceive sodium taste. In summary, cells expressing ENaC and CALHM1/3 constitute sodium cells, in which the entry of Na^+ induces depolarization for action potential discharge driving voltage-dependent neurotransmitter release via the CALHM1/3-dependent channel synapse. We also revealed the structures of the channel synapse and CALHM channels, further deepening our understanding of sodium taste mechanisms.