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Peripheral Coding and Neurotransmission of Salty Taste

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Summary

Although the pathogenesis of hypertension is multifactorial, high salt intake is the best known factor. Therefore, understanding the mechanism of tasting salt which controls our salt intake is crucial for prevention of hypertension. However, the peripheral mechanisms of salty taste sensing and neurotransmission in the taste bud are largely known. Salty taste sensation involves at least two pathways: amiloride-sensitive (AS) and amiloride-insensitive (AI) pathways. AS salty taste is known to utilize epithelial sodium channel (ENaC) as the Na^+ sensor but its cellular basis and neurotransmission mechanisms are unknown. AI salty taste is known to recruit sour and bitter taste pathways but its salt sensor molecule and neurotransmission mechanisms remain to be identified. This study is aimed at elucidating (1) the neurotransmission mechanism of salty taste and (2) the cellular basis of AS salty taste. Regarding (1), type II taste bud cells sense sweet, bitter, umami, and AI salty tastes and transmit the taste information to the afferent nerves by releasing ATP as the neurotransmitter. Although Calcium homeostasis modulator 1 (CALHM1) is the essential component of the ATP release channel in type II taste cells, involvement of unknown interacting partner(s) of CALHM1 has been suggested. We found that CALHM1 and CALHM3, a CALHM1 paralog, form a novel heteroligomeric ion channel, that biophysical and pharmacological properties of the CALHM1/3 channel are identical to those of the ATP release channel in type II taste cells, that CALHM1 and CALHM3 are co-expressed in type II taste cells, and that genetic elimination of CALHM3 diminishes sweet, bitter, umami, and AI salty taste sensation. These data lead to the conclusion that a CALHM1/3 heteroliomer is the neurotransmitter release ion channel for AS salty taste. Regarding (2), AS salty taste is sensed in fungiform taste buds by a taste cell population which is different from sweet, bitter, umami, and sour cells. However, the properties of AS salty taste cells are unknown. We found that ENaC and the CALHM1/3 channel is co-expressed in fungiform taste buds. This result suggests that AS salty taste is mediated by CALHM1/3-expressing taste cells and thereby CALHM1/3 mediates the neurotransmission of AS salty taste.