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Reception Mechanism of Bitter Taste Receptors for High Salt

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Summary

This study aims to understand the mechanisms that bitter taste receptors respond to high salt. The bitter taste receptor T2R is a G-protein-coupled receptor (GPCR), which consists 25 subtypes in human. Although they have a common feature, seven-transmembrane structure, they differ in sequence features from the generic GPCRs (class A GPCRs). So T2Rs are classified as class T GPCR. In class A GPCRs, the residue in position 2.50, based on generic GPCR numbering, is a negatively charged Asp and is known to hold Na^+ in the structure in a paired form with the Asp. However, the residue at position 2.50 in T2R is a positively charged Arg, which is the opposite of that in class A GPCRs. This suggests that T2R is capable of interacting with Cl^-. On the other hand, electrophysiological experiments on the mouse tongue have shown that the aversive taste against high salt (>150 mM) is a complex taste originating from sour and bitter cells. The individuals a bitter receptor signalling factor knocked out, lost their signal to high salt is also halved (although stimulation on the sour cell side remains) (Oka et al., Nature, 2013). Based on these findings, I conducted research on the assumption that one of the repellent signals for high salt concentrations is caused by the reception of Cl^- by bitter taste receptors.

Despite attempts to measure this in cultured cells, it was difficult to obtain a response to high salt due to osmotic pressure. After examining various conditions, we succeeded in obtaining bitter taste receptor-specific cellular responses by preparing a buffer based on N-methyl-D-glucamine and gluconic acid and containing the same level of minerals as saliva.

Using this buffer, the responses of 25 bitter taste receptors to 100 mM NaCl were measured, with some T2Ra responding well and others showing no response.

Although various responses to high salt were obtained, these differences could not be elucidated because constructing measurement system wasted much time. Based on the structure of T2R46, which has already been clarified, and the structure of T2R14, which has been reported very recently, we will continue to verify how these different responses are brought about, using MD simulations and other methods.