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# Structural and functional studies on bitter taste receptors

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The taste sensory system helps us to avoid ingestion of harmful substances. Taste perception is initiated by the physical interaction of tastants with the receptors located on the surface of taste receptor cells (TRCs) on the tongue and palate. In humans, tastants evoke five taste sensations: sweet, bitter, salty, sour and umami. Among the five taste modalities, ion channels transduce sour and salty signals, while bitter, sweet and umami tastes are mediated by G protein-coupled receptors (GPCRs). A distinct group of type 2 taste receptors (TAS2Rs) is responsible for bitter taste perception. TAS2Rs display low sequence identity (<20%) with other GPCRs and are classified as a separate class T GPCR subfamily. TAS2Rs recognize thousands of different bitter molecules. In humans, there are only ~25 TAS2Rs to cover this broad chemosensory space. Furthermore, the TAS2Rs are distributed, not only in the oral cavity, but also in extraoral tissues, including the upper and lower airways, gut, adipose tissue, brain, heart and immune cells. These ectopic bitter taste receptors are involved in a variety of physiological processes and are associated with different diseases. However, there are no bitter receptor structures solved so far. Here we report the cryo–electron microscopy structures of human TAS2R46 complexed with chimeric mini–G protein gustducin, in both strychnine-bound and apo forms. Several features of TAS2R46 are disclosed, including distinct receptor structures that compare with known GPCRs. This study provides a basis for further exploration of other bitter taste receptors and their therapeutic applications.