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Functional Interaction between TAS2R Receptors and G-Protein α Subunits Expressed in Taste Receptor Cells

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Bitter taste perception is a conserved chemical sense against the ingestion of poisonous substances in mammals. It could be mediated by G protein-coupled receptors that need the appropriate G proteins to transduce the signals. TAS2R receptors and a G protein α subunit, α–gustducin are believed to be key molecules for its perception (Margolskee, 2002; Montmayeur and Matsunami, 2002), but little is known about the molecular basis for its interaction. In the present study, we used a heterologous expression system to determine a specific domain of gustducin necessary to TAS2R coupling. Two chimeric Gα16 proteins harboring 37 and 44 gustducin-specific sequences at their C termini (G16/gust37 and G16/gust44) responded to different TAS2R receptors with known ligands in dose-dependent manner, but G16, G16/gust 23, G16/gust11 and G16/gust5 did not exhibit any responses (Figure 1). The former two chimeras contained a predicted β6 sheet, an α5 helix and an extreme C-terminus of gustducin, and all the domains were indispensable to the expression of TAS2R activity. Taste receptor cells express a variety of Gαi subunit, but these functions are not well known. We next expressed G16 protein chimeras with the corresponding domain from other Gαi proteins, cone-transducin (Gαt2), Gαi2 and Gαz (G16/t2, G16/i2 and G16/z). As a result, G16/t2 and G16/i2 produced specific responses of TAS2Rs, but G16/z did not (Figure 1). Since Gαt2 and Gαi2 are expressed in taste receptors cells, these may be also involved in bitter taste perception via TAS2R receptors. The present Gα16-based chimeras could be powerful tools to analyze the functions of many orphan G protein-coupled taste receptors.

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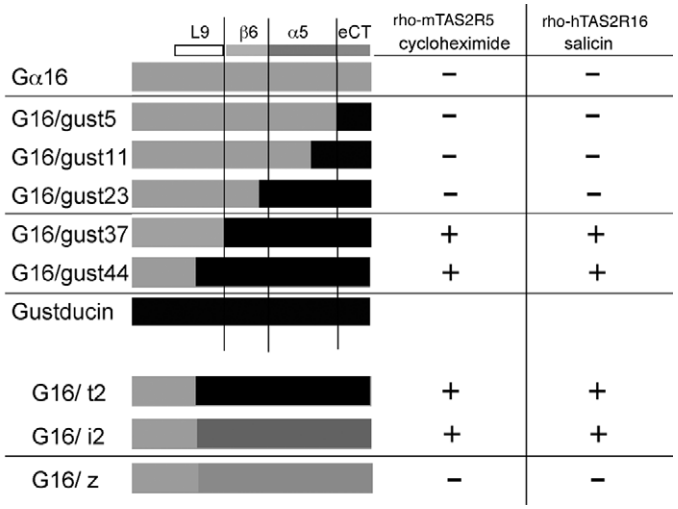

Figure 1 Schematic illustrations of chimeric G16/gust proteins with different lengths of C terminal amino acids found in gustducin and G16-based chimeras with C-terminal 44 amino acids of Gαt2, Gαi2 or Gαz and their abilities to couple to TAS2Rs indicated. '+' specifically responded to the ligand in dose dependent manner; '–' did not exhibit any responses even at 1000-fold higher ligand concentration. Putative secondary structure on the basis of the Gαt1 crystal structure is indicated by the bars above the G protein sequences. eCT, extreme C terminus.