

1 *Supporting Information for*

2 **Ligand Dependent and G Protein Dependent Properties for the Sweet Taste Heterodimer,**

3 **TAS1R2/1R3**

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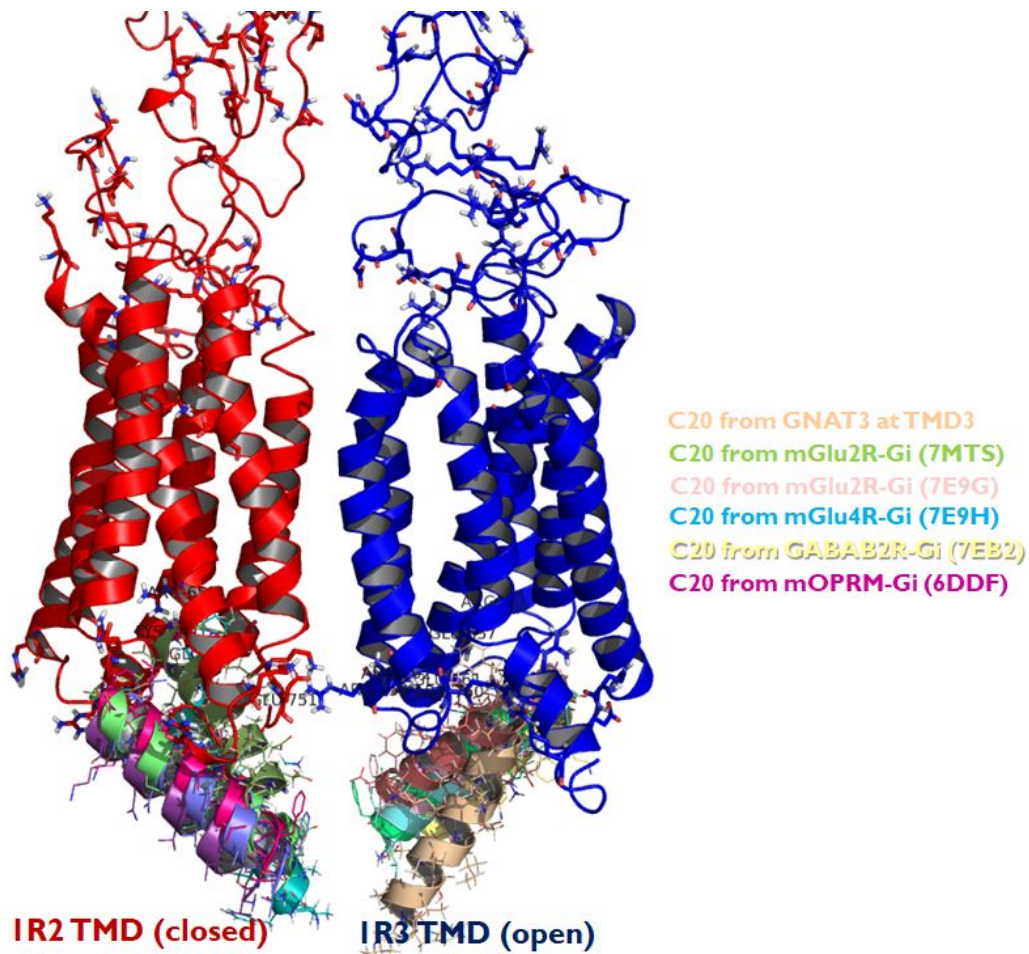
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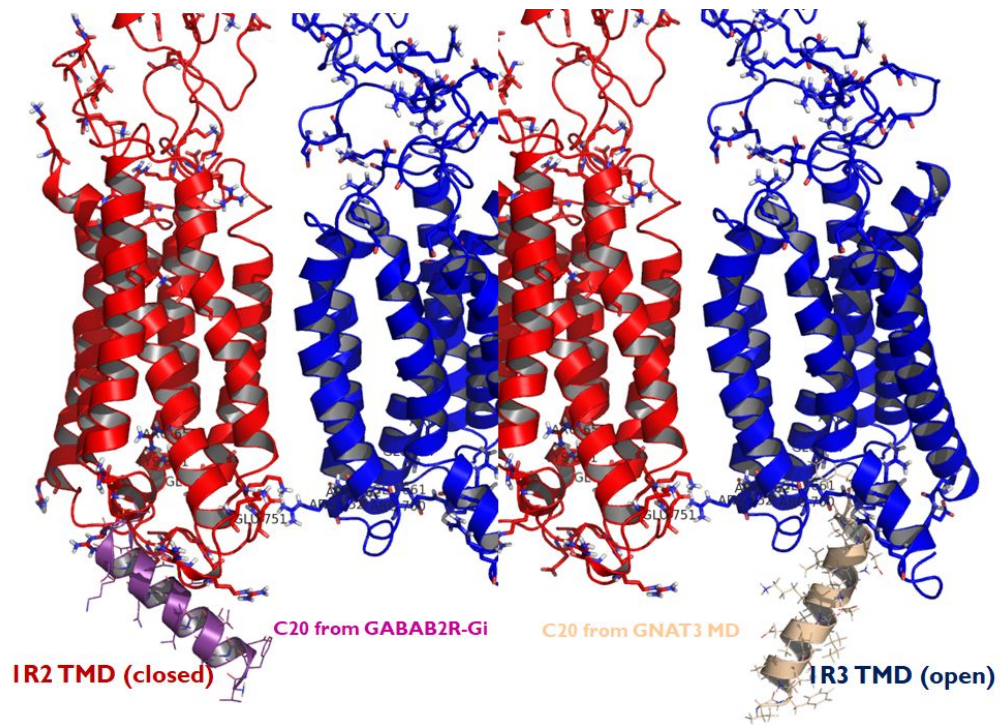
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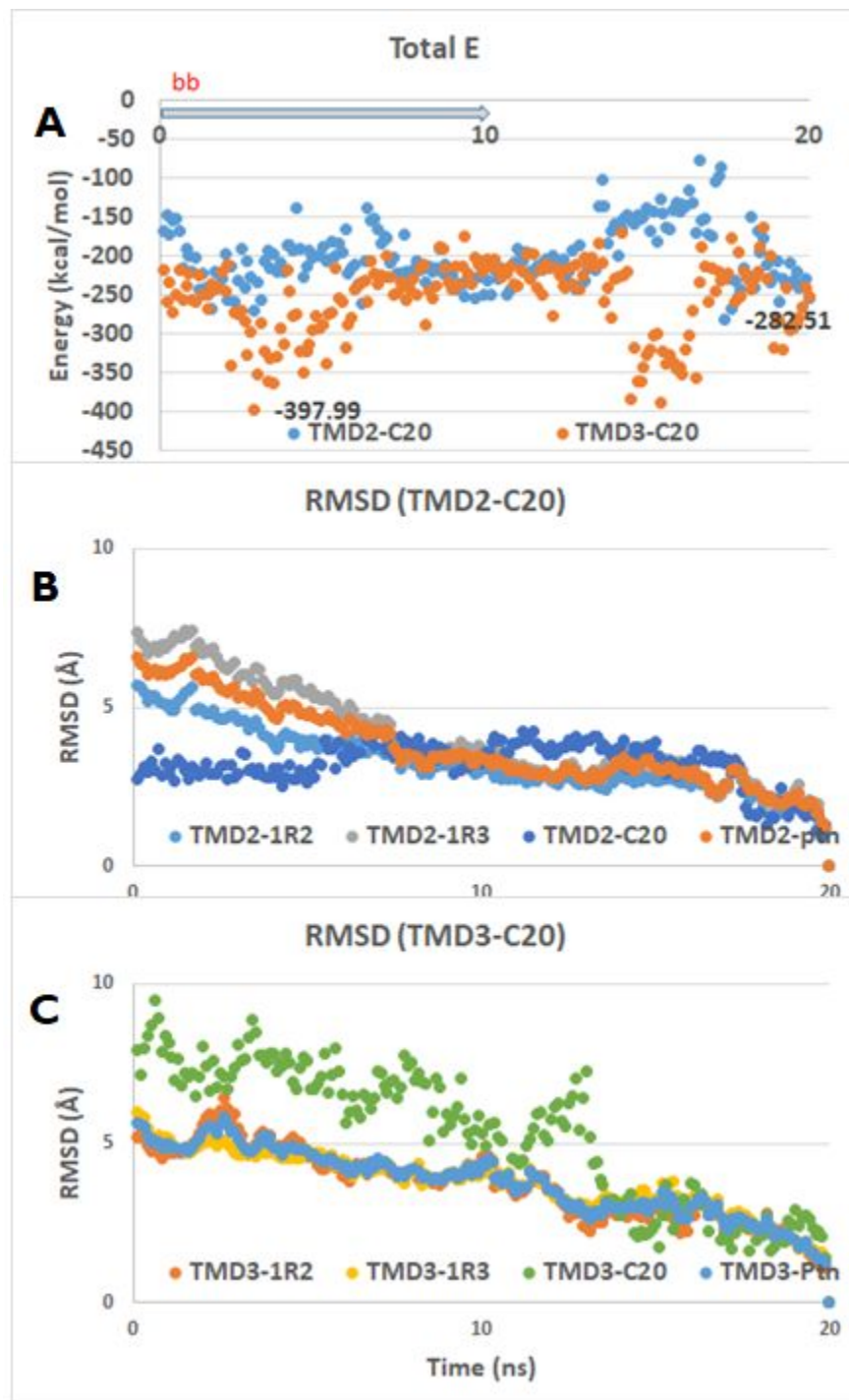
14 **Figure S1.** The various initial positions of the C-terminal α -helices of the C20 G protein peptide at the
15 cytoplasmic transmembrane domain (TMD) of closed taste receptor TAS1R2 (red) and open IR3
16 (blue) between helix 3 and 6 prior to MD simulations. The initial positions of GNAT3 C20 were
17 generated after aligning the experimental structures of GPCR-G protein complexes, four class C
18 mGlu2R-Gi (PDB ID: 7MTS,¹² 7E9G¹³), mGlu4R-Gi (PDB ID: 7E9H)¹³, GABAB2R-Gi (PDB ID:
19 7EB2)¹⁴, and one class A OPRM-Gi (PDB ID 6DDF)¹⁵. We also included our predicted structure
20 of the GNAT3-TAS1R3/IR3 homodimer complex from molecular dynamics.¹⁶

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23 **Figure S2.** The best initial positions of the C-terminal α -helices of C20 G protein peptide at the cytoplasmic
 24 transmembrane domain (TMD) of closed taste receptor TAS1R2 (red) and open TAS1R3 (blue)
 25 between helix 3 and 6. The best C20 orientation for the TMD2 is from GABAB2R-Gi (PDB ID:
 26 7EB2)¹⁴ in the class C GPCR-like non-canonical way, while the best C20 orientation for TMD3 is
 27 from our predicted structure of the GNAT3-TAS1R3/1R3 homodimer complex in the class A
 28 GPCR-like canonical way.¹⁶



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30 **Figure S3.** (A) Interaction energy between C20 and TAS1R2 or TAS1R3 over 20 ns (B and C) The root
 31 mean square deviation (RMSD) of the TAS1R2/1R3-C20 complex when C20 binds at 7
 32 transmembrane domain (TMD) of TAS1R2 (TMD2-C20) or TAS1R3 (TMD3-C20).