

**Supplementary Table 1. ECL1 distance constraints and other constraints used in Modeller.** The ECL1 constraints were used to control the orientation of the ECL1 helix in line with the variability data (Baldwin et al., 1997; Vohra et al., 2013) and were chosen by visual analysis. Torsional constraints applied to the C<sub>α</sub> coordinates were also used to constrain the backbone conformation of the 4 C-terminal residues of Gs, namely Y391-L394.

GLP-1/GLP-1R position (A)	GLP-1R/GLP-1 position (B)	constraint
TM2; M204; C <sub>α</sub>	GLP-1; V26; C <sub>α</sub>	r <sub>AB</sub> ≤ 8.0
ECL1; W214; C <sub>α</sub>	GLP-1; V16; C <sub>α</sub>	r <sub>AB</sub> ≥ 12.0
ECL1; W214; C <sub>α</sub>	TM2; W203; C <sub>α</sub>	r <sub>AB</sub> ≥ 5.0
ECL1; H212; C <sub>α</sub>	GLP-1; F12; C <sub>α</sub>	r <sub>AB</sub> ≥ 10.0
ECL1; H212; C <sub>α</sub>	GLP-1; V16; C <sub>β</sub>	r <sub>AB</sub> ≥ 12.0
ECL1; H212; C <sub>α</sub>	GLP-1; M13; C <sub>α</sub>	r <sub>AB</sub> ≥ 12.0
ECL1; H212; C <sub>α</sub>	GLP-1; L20; C <sub>α</sub>	r <sub>AB</sub> ≥ 12.0
ECL1; Q213; C <sub>α</sub>	GLP-1; H19; C <sub>β</sub>	r <sub>AB</sub> ≥ 10.0
ECL1; D215; C <sub>α</sub>	GLP-1; V16; C <sub>β</sub>	r <sub>AB</sub> ≥ 12.0
TM3; C226; C <sub>α</sub>	ECL2; C296; C <sub>α</sub>	disulfide
GLP-1; D15	GLP-1; L33	helix
Helix 8; T378	Helix 8; S392	helix
TM2; V194	TM3; A209	helix
TM3; A221	TM3; F232	helix

Baldwin, J. M.; Schertler, G. F.; Unger, V. M. An alpha-carbon template for the transmembrane helices in the rhodopsin family of G-protein-coupled receptors. *Journal of Molecular Biology* **1997**, 272, 144-164.

Vohra, S.; Taddese, B.; Conner, A. C.; Poyner, D. R.; Hay, D. L.; Barwell, J.; Reeves, P. J.; Upton, G. J.; Reynolds, C. A. Similarity between class A and class B G-protein-coupled receptors exemplified through calcitonin gene-related peptide receptor modelling and mutagenesis studies. *J R Soc Interface* **2013**, 10, 20120846.