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Corresponding author(s): Christopher G Tate

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Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see Authors & Referees and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☒	☐ The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☒	☐ A description of all covariates tested
☒	☐ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☒	☐ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☒	☐ For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐ Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	serialEM 3.8.0 beta EPU 2.3.0.79
Data analysis	RELION 3.0.7 RELION 3.1 SIDESPLITTER Warp 1.0.6 CCP-EM v1.3 REFMAC5 PHENIX 1.17.1-3660 eLBOW (via PHENIX) Coot 0.9-pre EL Chimera 1.13.1 Pymol 2.2.2 Molprobity (via PHENIX) EMRinger (via PHENIX) GESAMT (ccp4 suite 7.0.077) GraphPad Prism 7 Zen Lite 8.1.0484

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

Structures of formoterol-bound β1AR-Nb80 and formoterol-bound β1AR- βarr1-Fab30 have been deposited in the Protein Data Bank with accession numbers 6IBL and 6TKO respectively. The cryo-EM data for 6TKO has also been deposited in the Electron Microscopy Data Bank (EMDB-10515). All other data are contained within the paper and its supporting data.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	Sample size was not predetermined. For the cryo-EM structure, the number of images and particles used were determined by the amount of time available on the electron microscope and which gave us a high-resolution structure.
Data exclusions	During the generation of the 3D cryo-EM structure, particles that did not align well with the major population (i.e. they were damaged, poor signal to noise, different conformation, lacking a subunit) were excluded from the data set. Inclusion of 'bad' particles would have had a detrimental effect on the overall resolution of the structure. No exclusions were made in biochemical assays.
Replication	Structure determination does not require replication because it represents the average structure of 400,000 molecules. All biochemical assays had a number of independent experiments performed with an appropriate number of replicates (as reported in the manuscript).
Randomization	All variables could be controlled and so randomization was not required.
Blinding	No blinding was attempted or needed.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology
☒	☐ Animals and other organisms
☒	☐ Human research participants
☒	☐ Clinical data

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	Trichoplusia ni (Expressions Systems & Thermo Fisher)
Authentication	The cell lines were not authenticated by the authors as this was performed by the supplier.
Mycoplasma contamination	The cell lines were not tested by the authors for mycoplasma contamination as this was performed by the supplier.

Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used