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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	Automated data collection on the Titan Krios was performed using AutoEmation2 (developed by Jianlin Lei at Tsinghua University)
Data analysis	The following software were used in this study: MotionCor and MotionCor2, CTFFIND4, RELION 3.0.5, UCSF Chimera 1.14, ResMap, Coot 0.8.9, PyMOL 2.1.1, Phenix 1.16, MODELLER 9v4, GROMACS 2018.1, AMBER18, CPPTRAJ (AMBER18), Matplotlib 3.0.2, AutoDock Vina

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

All data generated or analyzed during this study are included in this published article and its Supplementary Information. Sequences of constructs used in this study are listed in Supplementary Figure 2 and described in Methods. The cryo-EM density maps for the alpha2B-G protein complexes with scFv16 have been deposited in the Electron Microscopy Data Bank under accession codes EMDB-9911 and EMDB-9912 respectively. The coordinates for the models have been deposited in the Protein Data Bank under accession codes 6K41 and 6K42, respectively.

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 sizes were not predetermined by statistical methods. For cryoEM data, sample sizes were determined by availability of microscope. Cryo-EM data was collected until we were able to refine a high-resolution structure that allowed us to obtain a high-resolution reconstruction within the confines of limited microscope time.
Data exclusions	No data was systematically excluded. The process of generating 3D maps from cryo-EM particles involves sorting for particles that are damaged, have low signal, or are in minority conformations that are unlikely to refine correctly. This is implemented in RELION 3.0.5. These exclusion criteria were predetermined.
Replication	No replication studies were attempted, nor were necessary. Our primary data is a cryo-EM structure that was calculated according to standard procedures and does not need replicates.
Randomization	No randomization was necessary for this study. Our primary data is a calculated cryo-EM structure that was calculated according to standard procedures with freely available software and does not need randomization.
Blinding	No blinding was used or necessary during data collection or analysis. As above, Our primary data is a calculated cryo-EM structure that was calculated according to standard procedures with freely available software and did not require blinding. We calculated our initial model ab-initio to avoid bringing model bias into our map calculation, and in a sense, blinded the software.

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

Antibodies

Antibodies used	scFv16 is the property of F. Hoffmann-La Roche Ltd (Roche) and a plasmid for expressing the ScFv is available upon request by material transfer agreement from Hoffmann-La Roche. The development and expression of the ScFv is described in Maeda, S. et al. Development of an antibody fragment that stabilizes GPCR/G-protein complexes. Nat Commun 9, 3712 (2018).
Validation	Binding of this scFv fragment was confirmed by size exclusion chromatography and electron microscopy. This antibody fragment was generated for the purposes of this study. Most of the scFv could be built into density and register was confirmed.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	Sf9, Expression Systems, Cat 94-001S. Tni Cells (Hi-5), Expression Systems, Cat 94011S.
Authentication	Cell lines are maintained by the supplier. No additional authentication was performed by the authors of this study.
Mycoplasma contamination	Cell lines are tested by manufacturer for contamination, but were not further tested by the authors of this study

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