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Reporting Summary

Nature Portfolio 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 Portfolio policies, see our [Editorial Policies](#) 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 EPU (v 3.6.0.6389)

Data analysis cryoSPARC (v 4.1.2), PHENIX (v 1.21.1-5286), Coot (v 0.9.8.1), ChimeraX (v 1.4), Chimera (1.17.1), Prism, Illustrator CS6, Endnote X9.

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 and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio [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 description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our [policy](#)

The cryo-EM density maps and atomic coordinates have been deposited in the Electron Microscopy Data Bank (EMDB) and Protein Data Bank (PDB) under accession numbers EMD-66695 [<https://www.ebi.ac.uk/pdbe/entry/emdb/EMD-66695>] and PDB: 9XB1 [<http://doi.org/10.2210/pdb9XB1/pdb>], for V1aR_apo; EMD-64555 [<https://www.ebi.ac.uk/pdbe/entry/emdb/EMD-64555>] and PDB: 9UWI [<http://doi.org/10.2210/pdb9UWI/pdb>], for V1aR_atosiban; EMD-64556 [<https://www.ebi.ac.uk/pdbe/entry/emdb/EMD-64556>] and PDB: 9UWJ [<http://doi.org/10.2210/pdb9UWJ/pdb>], for V1aR_balovaptan; EMD-64559 [<https://www.ebi.ac.uk/pdbe/entry/emdb/EMD-64559>] and PDB: 9UWL [<http://doi.org/10.2210/pdb9UWL/pdb>], for V1aR_SRX246. Source Data are provided with this paper.

Research involving human participants, their data, or biological material

Policy information about studies with [human participants or human data](#). See also policy information about [sex, gender \(identity/presentation\), and sexual orientation](#) and [race, ethnicity and racism](#).

Reporting on sex and gender	N/A
Reporting on race, ethnicity, or other socially relevant groupings	N/A
Population characteristics	N/A
Recruitment	N/A
Ethics oversight	N/A

Note that full information on the approval of the study protocol must also be provided in the manuscript.

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	For cryo-EM analysis, several thousand move stacks were collected for each sample in the study, which is sufficient to generate high-quality maps. For western blotting and protein purification, at least two times were repeated, and we didn't notice any variability. For experiments involving saturating binding and luciferase assay, a sample size n=3 was used as both biological repeat and technical repeat. For a single-molecule imaging experiment, three cells from two independent transfection experiments were used. All these sample sizes were used, as robust and reproducible data with small variation can be obtained.
Data exclusions	Cryo-EM data analysis involved removing images of poor-quality, and particles of poor quality were also removed during data analysis based on classification done in cryosparc. Both are common practices. Single-molecule experiments involved exclusion of disputed spots that can not be analyzed.
Replication	Each experiment was successfully repeated at least 2-3 times by independent experiments.
Randomization	For cryo-EM analysis, random positions on the grid were selected for data collection, and then millions of particles were picked randomly. For protein purification, immunoblotting, saturation binding, and luciferase assay, millions of cells from a particular transfection experiment were pooled and lysed for downstream experiments. For the single-molecule imaging experiment, cells with a similar expression level of the protein were randomly picked.
Blinding	Blinding was not applicable to the experiments in this study, and all analyses are adhered to pre-established protocols to minimize bias.

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 and archaeology
☒	☐ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

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

Antibodies

Antibodies used	anti-HA antibody used at 1:3000 dilution (Sigma, 3F10, #11867423001)
Validation	This commercial antibody was validated by the vendor, as well as in house by recombinant expressed HA-tagged protein.

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s)	U-2 OS (ATCC, HTB-96), HEK293T (ATCC, CRL-3216), Expi293F(Thermo Fisher Scientific, A14527), sf9 (Thermo Fisher Scientific, 11496015)
Authentication	No further authentications were performed for this study, only by the vendor.
Mycoplasma contamination	Mycoplasma contamination tests were performed routinely.
Commonly misidentified lines (See ICLAC register)	N/A

Plants

Seed stocks	N/A
Novel plant genotypes	N/A
Authentication	N/A