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eLife's transparent reporting form

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Sample-size estimation

- You should state whether an appropriate sample size was computed when the study was being designed
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- If no explicit power analysis was used, you should describe how you decided what sample (replicate) size (number) to use

Please outline where this information can be found within the submission (e.g., sections or figure legends), or explain why this information doesn't apply to your submission:

For the radioligand binding and functional studies, no statistical analysis was used to determine appropriate sample size. The high reproducibility of these data mean that a replicate value of $n \ge 3$ is used throughout literature and is sufficient to observe a biological effect.

Replicates

- You should report how often each experiment was performed
- You should include a definition of biological versus technical replication
- The data obtained should be provided and sufficient information should be provided to indicate the number of independent biological and/or technical replicates
- If you encountered any outliers, you should describe how these were handled
- Criteria for exclusion/inclusion of data should be clearly stated
- High-throughput sequence data should be uploaded before submission, with a private link for reviewers provided (these are available from both GEO and ArrayExpress)

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For the radioligand binding data the mean of at least three independent experiments performed in triplicate are shown along with 95% confidence intervals. For BRET data, the mean of at least nine independent experiments in triplicate or quadruplicate are shown along with SEM. No outliers were excluded. This information is shown in the legend of table 1 and Fig. 3.

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Statistical reporting

- Statistical analysis methods should be described and justified
- Raw data should be presented in figures whenever informative to do so (typically when N per group is less than 10)
- For each experiment, you should identify the statistical tests used, exact values of N, definitions of center, methods of multiple test correction, and dispersion and precision measures (e.g., mean, median, SD, SEM, confidence intervals; and, for the major substantive results, a measure of effect size (e.g., Pearson's r, Cohen's d)
- Report exact p-values wherever possible alongside the summary statistics and 95% confidence intervals. These should be reported for all key questions and not only when the p-value is less than 0.05.

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For the radioligand binding data the mean of at least three independent experiments is provided with the 95% confidence intervals. No further statistical analysis is performed. For BRET data, the mean of at least nine independent experiments are shown along with SEM. One-way ANOVA followed by Tukey's multiple comparisons test was performed. These details are presented in table 1 and Fig. 3.

(For large datasets, or papers with a very large number of statistical tests, you may upload a single table file with tests, Ns, etc., with reference to sections in the manuscript.)

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- Indicate how samples were allocated into experimental groups (in the case of clinical studies, please specify allocation to treatment method); if randomization was used, please also state if restricted randomization was applied
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No randomization or masking was incorporated into the experimental procedure or analysis of the radioligand binding and functional experiments.

Additional data files ("source data")

- We encourage you to upload relevant additional data files, such as numerical data that are represented as a graph in a figure, or as a summary table
- Where provided, these should be in the most useful format, and they can be uploaded as "Source data" files linked to a main figure or table
- Include model definition files including the full list of parameters used
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Please indicate the figures or tables for which source data files have been provided:



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2019