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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 <u>Authors & Referees</u> and the <u>Editorial Policy Checklist</u>.

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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
	\square 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.
\boxtimes	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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
\boxtimes	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
\boxtimes	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
\boxtimes	\square Estimates of effect sizes (e.g. Cohen's d , Pearson's r), indicating how they were calculated
	Our web collection on <u>statistics for biologists</u> contains articles on many of the points above.
So	ftware and code
Poli	cy information about <u>availability of computer code</u>

Data analysis

Data were analyzed with commercially available and open-source programs as stated in the methods section. Descriptive statistics were calculated with Prism 8 and R program. Statistical tests were performed with SAS v9.4

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

Data collection

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

No unique software was used for data collection.

- A list of figures that have associated raw data
- A description of any restrictions on data availability

The authors declare that the data supporting the findings of this study are available within the main and supplemental figures. All data is available in the Source Data File.

Field-spe	ecific re	eporting		
Please select the or	ne below that i	s the best fit for your research. If you are not sure, read the appropriate sections before making your selection.		
∑ Life sciences	B	Behavioural & social sciences Ecological, evolutionary & environmental sciences		
For a reference copy of t	the document with	all sections, see <u>nature.com/documents/nr-reporting-summary-flat.pdf</u>		
Life scier	nces stu	udy design		
All studies must dis	close on these	points even when the disclosure is negative.		
Sample size	We used group	os of 5 or 8 macaques.		
Data exclusions	No data were e	excluded.		
Replication	magnitude inst	binding study was repeated to confirm results. Within binding studies we tested multiple dilutions of antibodies to confirm the binding nitude instead of relying on single data points. Neutralization assays have been validated to be reproducible and group geometric means hown to identify the group trend.		
Randomization	Macaques were	e distributed in groups to balance age, gender and weight whenever possible		
Blinding	Neutralization, binding, and competition assays were performed by laboratories independent from the discovery laboratory. No other data was supplied until after the assay was complete. Statistics were not calculated until the study was complete, and were done so by statisticians independent from the discovery researchers.			
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 Methods				
Policy information	about <u>cell lines</u>			
Cell line source(s)	ThermoFisher and the Farzan Laboratory at Scripps		
Authentication		Each cell line is provided with a certificate of analysis. Cell identity is verified by morphology or fluorescent markers expressed.		
Mycoplasma con	tamination	All cell lines undergo mycoplasma testing every 60 days.		
Commonly miside (See <u>ICLAC</u> register)	y misidentified lines register) None to report.			
Animals and	other org	ganisms		
Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research				
Laboratory anima	Laboratory animals Macca mulatta. Males and females were used in the studies. Macaques had various ages.			

Wild animals

Field-collected samples

The study did not involve wild animals.

The study did not involve collection of samples from animals in the field.

Ethics oversight

The macaque studies were performed at Bioqual. Prior to study commencement, all procedures and materials to be used in the study were approved by the Bioqual IACUC. The Duke University Institutional Biosafety Committee approved protocols for research involving recombinant DNA.

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