

## 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

No software was used for data collection.

Data analysis

Statistical comparisons between groups using  $t$ -, Mann-Whitney- or log-rank tests were conducted using Prism 7.0 (GraphPad Software, Inc, San Diego, CA). Probit modeling and bootstrap analyses were conducted in R version 3.4.4.

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

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 analysed during the study are included in the article and its supplementary information or source data files.

### 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

## Life sciences study design

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

Sample size	A total of 30 rhesus macaques ( <i>Macaca mulatta</i> ) was used to perform the penile and vaginal challenge studies. Ten control animals, which were challenged with SHIV162P3 via the penile route in the absence of any bNAb infusion, were reported previously in a manuscript describing development of the penile SHIV challenge model (Garber DA, et al. PLoS One 13, e0194837 (2018)). Group sizes of up to 6 macaques, among groups of animals that were administered bNAb(s), is consistent with other published studies utilizing repeated limiting-dose virus challenge models.
Data exclusions	No data were excluded.
Replication	All samples were assayed in duplicate for vRNA or TZM-bl neutralization assays.
Randomization	Animals were allocated by gender into study arms as required by the study design (penile vs vaginal challenge). Within each arm, animals were assigned randomly to treatment or control groups.
Blinding	Blinding was not relevant in this study - animal samples were analysed using objective, standardized assays that included appropriate controls.

## 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
<input type="checkbox"/>	<input checked="" type="checkbox"/> Antibodies
<input type="checkbox"/>	<input checked="" type="checkbox"/> Eukaryotic cell lines
<input checked="" type="checkbox"/>	<input type="checkbox"/> Palaeontology
<input type="checkbox"/>	<input checked="" type="checkbox"/> Animals and other organisms
<input checked="" type="checkbox"/>	<input type="checkbox"/> Human research participants
<input checked="" type="checkbox"/>	<input type="checkbox"/> Clinical data

### Methods

n/a	Involved in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> ChIP-seq
<input checked="" type="checkbox"/>	<input type="checkbox"/> Flow cytometry
<input checked="" type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging

### Antibodies

Antibodies used	10-1074 and 3BNC117 were generated by the Nussenzweig laboratory
Validation	Neutralization activities of bNAbs against challenge viruses were determined using TZM-bl cell assay.

### Eukaryotic cell lines

Policy information about [cell lines](#)

Cell line source(s)	TZM-bl: NIH AIDS Reagent Program
Authentication	Not authenticated
Mycoplasma contamination	Not tested
Commonly misidentified lines (See <a href="#">ICLAC</a> register)	No commonly misidentified cell lines were used in the study.

### Animals and other organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research

Laboratory animals	Rhesus macaques ( <i>Macaca mulatta</i> ) or Indian- or Chinese-genetic origin, as indicated; male or female; 4.8-10.7 years old
Wild animals	The study did not involve wild animals.
Field-collected samples	The study did not involve samples collected from the field.

## Ethics oversight

The study was approved by the Institutional Animal Care and Use Committee of the Centers for Disease Control and Prevention (protocol 2804GARMONC) and was performed in compliance with the Public Health Service Policy on Humane Care and Use of Laboratory Animals, the Animal Welfare Act and the Guide for the Care and Use of Laboratory Animals.

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