

## 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

AMBER16, Modeller

Data analysis

Pymol, VMD, Clonanalyst

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

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

### 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](http://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	<input type="text" value="n/a"/>
Data exclusions	<input type="text" value="n/a"/>
Replication	Data are reported as the mean and standard deviation from a minimum of two replicate measurements (T <sub>m</sub> , SPR, BLI data). Data shown in Figure 1c for CH01, PG9, and CH31 Ab pairs are the result of single measurements by CD and with replicate measurements by DSC reported in Supplementary Table 1. Differences in the magnitude of derived T <sub>m</sub> values were observed when both platforms were used (CD versus DSC) and all T <sub>m</sub> values are reported in the Supplemental Information section. When comparing two antibodies of the same lineage (UCA vs bnAb), both CD and DSC gave similar trends.
Randomization	<input type="text" value="n/a"/>
Blinding	<input type="text" value="n/a"/>

## 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

- n/a  Involved in the study
- Antibodies
- Eukaryotic cell lines
- Palaeontology
- Animals and other organisms
- Human research participants
- Clinical data

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

## Antibodies

Antibodies used	All antibodies were produced in-house at the Duke Human Vaccine Institute and expression and purification methods are referenced in the article. The following antibody was used in SPR assays to capture mAbs on the sensor surface- goat anti-human IgG antibody, Fc, Supplier - Millipore-Sigma, Catalogue # AP113.
Validation	The above antibody manufactured by Millipore-Sigma lists on their website that this antibody is validated for use in ELISA, IP, WB for the detection of human IgG.

## Eukaryotic cell lines

Policy information about [cell lines](#)

Cell line source(s)	Freestyle 293 cells from Invitrogen was used to express Env gp120 and gp140 proteins
Authentication	Manufacturer of the cell line provides authentication information on their website
Mycoplasma contamination	Mycoplasma contamination screening is described on the manufacturer's website
Commonly misidentified lines (See <a href="#">ICLAC</a> register)	<i>Name any commonly misidentified cell lines used in the study and provide a rationale for their use.</i>