

## 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

Data analysis

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 XL-MS dataset has been deposited on the ProteomeXchange Consortium via the PRIDE [41] repository with the dataset identifier PXD053636 and 10.6019/PXD053636 [<https://proteomecentral.proteomexchange.org/cgi/GetDataset?ID=PX053636>]. The Mass Photometry raw and treated files generated in this study will be made fully available upon request. CryoEM maps generated in this study have been deposited at the Electron Microscopy Data Bank (EMDB) under accession

codes EMD-50815 [https://www.ebi.ac.uk/emdb/EMD-50815], EMD-50816 [https://www.ebi.ac.uk/emdb/EMD-50816], EMD-50817 [https://www.ebi.ac.uk/emdb/EMD-50817] and EMD-50818 [https://www.ebi.ac.uk/emdb/EMD-50818]. 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	<input type="text" value="Does not apply to our manuscript"/>
Reporting on race, ethnicity, or other socially relevant groupings	<input type="text" value="Does not apply to our manuscript"/>
Population characteristics	<input type="text" value="Does not apply to our manuscript"/>
Recruitment	<input type="text" value="Does not apply to our manuscript"/>
Ethics oversight	<input type="text" value="Does not apply to our manuscript"/>

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](https://www.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="We followed the common sample sizes in the relevant literature"/>
Data exclusions	<input type="text" value="No data was excluded"/>
Replication	<input type="text" value="We confirm that replications were successful"/>
Randomization	<input type="text" value="Does not apply to our manuscript, we did not work with patient data"/>
Blinding	<input type="text" value="Does not apply to our manuscript, we did not work with patient data"/>

## 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 type="checkbox"/> Eukaryotic cell lines
<input type="checkbox"/>	<input type="checkbox"/> Palaeontology and archaeology
<input type="checkbox"/>	<input type="checkbox"/> Animals and other organisms
<input type="checkbox"/>	<input type="checkbox"/> Clinical data
<input type="checkbox"/>	<input type="checkbox"/> Dual use research of concern
<input type="checkbox"/>	<input type="checkbox"/> Plants

### Methods

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

## Antibodies

Antibodies used	<input type="text" value="mouse monoclonal anti-HA antibody (Roche Diagnostics, Cat. # 12013819001, 1:1000 dilution), mouse monoclonal anti-Myc antibody (Covalab, ID Covalab: mab20008; Clone 9E10, batch number: 527700, Cat. # 00115009, dilution: 5 µg/ml)"/>
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## Validation

Anti-HA-Peroxidase, High Affinity (3F10) recognizes the 9-amino acid sequence YPYDVPDYA, derived from the human influenza hemagglutinin (HA) protein. This epitope is also recognized in fusion proteins regardless of its position (N-terminal, C-terminal or internal). The anti-Myc antibody HRP conjugate recognizes the EQKLISEEDL peptide

## Eukaryotic cell lines

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

Cell line source(s)	Not relevant to our manuscript
Authentication	Not relevant to our manuscript
Mycoplasma contamination	Not relevant to our manuscript
Commonly misidentified lines (See <a href="#">ICLAC</a> register)	Not relevant to our manuscript

## Palaeontology and Archaeology

Specimen provenance	Not relevant to our manuscript
Specimen deposition	Not relevant to our manuscript
Dating methods	Not relevant to our manuscript
<input type="checkbox"/> Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.	
Ethics oversight	Not relevant to our manuscript

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

## Animals and other research organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research, and [Sex and Gender in Research](#)

Laboratory animals	Not relevant to our manuscript
Wild animals	Not relevant to our manuscript
Reporting on sex	Not relevant to our manuscript
Field-collected samples	Not relevant to our manuscript
Ethics oversight	Not relevant to our manuscript

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

## Clinical data

Policy information about [clinical studies](#)

All manuscripts should comply with the ICMJE [guidelines for publication of clinical research](#) and a completed [CONSORT checklist](#) must be included with all submissions.

Clinical trial registration	Not relevant to our manuscript
Study protocol	Not relevant to our manuscript
Data collection	Not relevant to our manuscript
Outcomes	Not relevant to our manuscript

## Dual use research of concern

Policy information about [dual use research of concern](#)

### Hazards

Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

- | No                                  | Yes                      |                            |
|-------------------------------------|--------------------------|----------------------------|
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Public health              |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | National security          |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Crops and/or livestock     |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Ecosystems                 |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Any other significant area |

### Experiments of concern

Does the work involve any of these experiments of concern:

- | No                                  | Yes                      |   |
|-------------------------------------|--------------------------|---|
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Demonstrate how to render a vaccine ineffective                             |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Confer resistance to therapeutically useful antibiotics or antiviral agents |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Enhance the virulence of a pathogen or render a nonpathogen virulent        |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Increase transmissibility of a pathogen                                     |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Alter the host range of a pathogen  |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Enable evasion of diagnostic/detection modalities                           |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Enable the weaponization of a biological agent or toxin                     |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Any other potentially harmful combination of experiments and agents         |

## Plants

Seed stocks

Not relevant to our manuscript

Novel plant genotypes

Not relevant to our manuscript

Authentication

Not relevant to our manuscript

## ChIP-seq

### Data deposition

- Confirm that both raw and final processed data have been deposited in a public database such as [GEO](#).
- Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links

*May remain private before publication.*

Not relevant to our manuscript

Files in database submission

Not relevant to our manuscript

Genome browser session  
(e.g. [UCSC](#))

Not relevant to our manuscript

### Methodology

Replicates

Not relevant to our manuscript

Sequencing depth	Not relevant to our manuscript
Antibodies	Not relevant to our manuscript
Peak calling parameters	Not relevant to our manuscript
Data quality	Not relevant to our manuscript
Software	Not relevant to our manuscript

## Flow Cytometry

### Plots

Confirm that:

- The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).
- The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).
- All plots are contour plots with outliers or pseudocolor plots.
- A numerical value for number of cells or percentage (with statistics) is provided.

### Methodology

Sample preparation	Not relevant to our manuscript
Instrument	Not relevant to our manuscript
Software	Not relevant to our manuscript
Cell population abundance	Not relevant to our manuscript
Gating strategy	Not relevant to our manuscript

- Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.

## Magnetic resonance imaging

### Experimental design

Design type	Not relevant to our manuscript
Design specifications	Not relevant to our manuscript
Behavioral performance measures	Not relevant to our manuscript

### Acquisition

Imaging type(s)	Not relevant to our manuscript
Field strength	Not relevant to our manuscript
Sequence & imaging parameters	Not relevant to our manuscript
Area of acquisition	Not relevant to our manuscript
Diffusion MRI	<input type="checkbox"/> Used <input checked="" type="checkbox"/> Not used

### Preprocessing

Preprocessing software	Not relevant to our manuscript
Normalization	Not relevant to our manuscript
Normalization template	Not relevant to our manuscript

Noise and artifact removal

Volume censoring

### Statistical modeling & inference

Model type and settings

Effect(s) tested

Specify type of analysis:  Whole brain  ROI-based  Both

Statistic type for inference

(See [Eklund et al. 2016](#))

Correction

### Models & analysis

n/a | Involved in the study

Functional and/or effective connectivity

Graph analysis

Multivariate modeling or predictive analysis