

## 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](#).

Please do not complete any field with "not applicable" or n/a. Refer to the help text for what text to use if an item is not relevant to your study.

For final submission: please carefully check your responses for accuracy; you will not be able to make changes later.

### 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 collection was done by custom code written in LabVIEW 2019
Data analysis	Data analysis was performed in real-time in custom code written in LabVIEW 2019 and some plots were plotted using R-Studio or Origin 2020b

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 custom-made software for droplet analysis and sorting is provided in Supplementary Software 1 and 2 and can also be checked for updates on [www.epfl.ch/labs/lbmm/downloads/](http://www.epfl.ch/labs/lbmm/downloads/) or on <https://doi.org/10.5281/zenodo.6399980>. The design files for all the machined parts, 3D printed parts and microfluidic chips are provided in Supplementary Data 1 to 10 or on <https://doi.org/10.5281/zenodo.6399971>. Numeric data for all the experiments is Source Data 1 to 3, and Supplementary Data 11. Raw data can be found on <https://doi.org/10.5281/zenodo.6392149>.

## Human research participants

Policy information about [studies involving human research participants and Sex and Gender in Research](#).

Reporting on sex and gender	n/a
Population characteristics	n/a
Recruitment	n/a
Ethics oversight	n/a

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

## Life sciences study design

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

Sample size	Sample size was determined by the number of individual droplets analyzed during the experiment and is reported appropriately in the
Data exclusions	n/a
Replication	n/a
Randomization	n/a
Blinding	n/a

## Behavioural & social sciences study design

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

Study description	
Research sample	
Sampling strategy	
Data collection	
Timing	
Data exclusions	
Non-participation	
Randomization	

## Ecological, evolutionary & environmental sciences study design

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

Study description	
Research sample	
Sampling strategy	
Data collection	
Timing and spatial scale	

Data exclusions	
Reproducibility	
Randomization	
Blinding	

Did the study involve field work? ☒ Yes ☐ No

## Field work, collection and transport

Field conditions	
Location	
Access & import/export	
Disturbance	

## 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	n/a	Involved in the study
<input checked="" type="radio"/>	Antibodies	<input checked="" type="radio"/>	ChIP-seq
<input checked="" type="radio"/>	Eukaryotic cell lines	<input checked="" type="radio"/>	Flow cytometry
<input checked="" type="radio"/>	Palaeontology and archaeology	<input checked="" type="radio"/>	MRI-based neuroimaging
<input checked="" type="radio"/>	Animals and other organisms		
<input checked="" type="radio"/>	Clinical data		
<input checked="" type="radio"/>	Dual use research of concern		

## Antibodies

Antibodies used	
Validation	

## Eukaryotic cell lines

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

Cell line source(s)	HT-1080 fibrosarcoma cell line (DSMZ, cat. no. ACC 315, RRID: CVCL_0317)
Authentication	cell lines were not authenticated
Mycoplasma contamination	cell lines were not tested for mycoplasma contamination.
Commonly misidentified lines (See <a href="#">ICLAC</a> register)	n/a

## Palaeontology and Archaeology

Specimen provenance	
Specimen deposition	
Dating methods	

☐ Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.

Ethics oversight	
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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

Wild animals

Reporting on sex

Field-collected samples

Ethics oversight

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

Study protocol

Data collection

Outcomes

## 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 type="radio"/> | <input checked="" type="radio"/> Public health              |
| <input type="radio"/> | <input checked="" type="radio"/> National security          |
| <input type="radio"/> | <input checked="" type="radio"/> Crops and/or livestock     |
| <input type="radio"/> | <input checked="" type="radio"/> Ecosystems                 |
| <input type="radio"/> | <input checked="" type="radio"/> Any other significant area |

### Experiments of concern

Does the work involve any of these experiments of concern:

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

## 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*

Files in database submission	<input type="text"/>
Genome browser session (e.g. <a href="#">UCSC</a> )	<input type="text"/>

Methodology

Replicates	<input type="text"/>
Sequencing depth	<input type="text"/>
Antibodies	<input type="text"/>
Peak calling parameters	<input type="text"/>
Data quality	<input type="text"/>
Software	<input type="text"/>

Flow Cytometry

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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	<input type="text"/>
Instrument	<input type="text"/>
Software	<input type="text"/>
Cell population abundance	<input type="text"/>
Gating strategy	<input type="text"/>

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

Magnetic resonance imaging

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Experimental design

Design type	<input type="text"/>
Design specifications	<input type="text"/>
Behavioral performance measures	<input type="text"/>

Acquisition

Imaging type(s)	<input type="text"/>
Field strength	<input type="text"/>
Sequence & imaging parameters	<input type="text"/>
Area of acquisition	<input type="text"/>
Diffusion MRI	<input checked="" type="radio"/> Used <input type="radio"/> Not used

Preprocessing

Preprocessing software	<input type="text"/>
Normalization	<input type="text"/>
Normalization template	<input type="text"/>
Noise and artifact removal	<input type="text"/>
Volume censoring	<input type="text"/>

Statistical modeling & inference

Model type and settings	<input type="text"/>
Effect(s) tested	<input type="text"/>
Specify type of analysis:	<input type="text"/>

☐ 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

Functional and/or effective connectivity

Graph analysis

Multivariate modeling and predictive analysis

