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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 our <u>Editorial Policies</u> and the <u>Editorial Policy Checklist</u>.

Statistics

For a	all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.
n/a	Confirmed
	\boxtimes The exact sample size (<i>n</i>) 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. <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	Estimates of effect sizes (e.g. Cohen's <i>d</i> , Pearson's <i>r</i>), indicating how they were calculated
	Our web collection on <u>statistics for biologists</u> contains articles on many of the points above.

Software and code

Policy information about availability of computer code			
Data collection	GraphPad Prism 8 for windows 64-bit (Version 8.4.3)		
Data analysis	GraphPad Prism 8 for windows 64-bit (Version 8.4.3)		

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 Research guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a <u>data availability statement</u>. 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 analyzed during this study are included in this article (and its supplementary files). The detailed study design of the phase I clinical trial was published previously. The full trial protocol can be accessed by submitting an enquiry to Merck & Co. via the website: http://engagezone.msd.com/doc/ ProcedureAccessClinicalTrialData.pdf.

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

For a reference copy of the document with all sections, see <u>nature.com/documents/nr-reporting-summary-flat.pdf</u>

Ecological, evolutionary & environmental sciences

Life sciences study design

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

Sample size	It is a sub-study of a previous phase I clinical trial (NCT01986010, registered on November 18th, 2013). The trial was a 2-part, single-blind, randomized, placebo-controlled, dose-escalating study, conducted at 9 clinical sites in the United States. In this sub-study, to characterize the vaccine-induced monoclonal antibodies, we selected, at random, six vaccinated participants from: the 30U intramuscular injection group (n = 3, seronegative, without adjuvant, enrolled in Virginia Commonwealth University), the 30U intradermal injection group (n = 3, without adjuvant, enrolled in University of Texas Medical Branch), and the two placebo controls of the intradermal injection group (n = 2, without adjuvant, enrolled in University of Texas Medical Branch)
Data exclusions	No data was excluded
Replication	Three replications in each group for the antibody characterization of this study.
Randomization	The subjects were randomly picked from the indicated groups.
Blinding	The investigators were not blinded in the data collection in this study

Reporting for specific materials, systems and methods

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	n/a	Involved in the study
	Antibodies		ChIP-seq
	Eukaryotic cell lines		Flow cytometry
	Palaeontology and archaeology		MRI-based neuroimaging
	Animals and other organisms		
	Human research participants		
	Clinical data		
	Dual use research of concern		

Antibodies

Antibodies used	All antibodies are generaged in house.
Validation	viral neutralization assay and viral antigen binding assay

Eukaryotic cell lines

olicy information about <u>cell lines</u>			
Cell line source(s)	Both ARPE-19 and MRC-5 are purchased from ATCC		
Authentication	None of the cell lines uses were authenticated		
Mycoplasma contamination	All cell lines are negative for mycoplasma contamination		
Commonly misidentified lines (See <u>ICLAC</u> register)	n/a		

Palaeontology and Archaeology

Specimen provenance	Provide provenance information for specimens and describe permits that were obtained for the work (including the name of the issuing authority, the date of issue, and any identifying information).
Specimen deposition	Indicate where the specimens have been deposited to permit free access by other researchers.
Dating methods	If new dates are provided, describe how they were obtained (e.g. collection, storage, sample pretreatment and measurement), where they were obtained (i.e. lab name), the calibration program and the protocol for quality assurance OR state that no new dates are provided.
Tick this box to confi	rm that the raw and calibrated dates are available in the paper or in Supplementary Information.
Ethics oversight	Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.

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

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research Laboratory animals For laboratory animals, report species, strain, sex and age OR state that the study did not involve laboratory animals. Wild animals Provide details on animals observed in or captured in the field; report species, sex and age where possible. Describe how animals were caught and transported and what happened to captive animals after the study (if killed, explain why and describe method; if released, say where and when) OR state that the study did not involve wild animals. Field-collected samples For laboratory work with field-collected samples, describe all relevant parameters such as housing, maintenance, temperature, photoperiod and end-of-experiment protocol OR state that the study did not involve samples collected from the field. Ethics oversight Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.

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

Human research participants

Policy information about studies involving human research participants			
Population characteristics	The informations were listed in supplementary Table 1. Age range 20s-40s; inculde both male and female, are HCMV seronegative at the time of enrollment of this study.		
Recruitment	The subjects in this study are recruited by two seperate clinical sites, and are HCMV seronegative subjects. Healthy subjects eligible for inclusion in this sub-study were over 18 years of age with bodyweight more than 50 kg and body mass index 19 - 32 kg/m2.		
Ethics oversight	Western Institutional Review Board, Inc.; Institutional Review Board of UTMB		

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

Clinical data

Policy information about <u>cl</u>	inical 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	NCT01986010, registered on November 18th, 2013		
Study protocol	The full trial protocol can be accessed by submitting an enquiry to Merck & Co. via the website: http://engagezone.msd.com/doc/ ProcedureAccessClinicalTrialData.pdf.		
Data collection	We selected, at random, six vaccinated participants from: the 30U intramuscular injection group (n = 3, seronegative, without adjuvant, enrolled in Virginia Commonwealth University), the 30U intradermal injection group (n = 3, seronegative, without adjuvant, enrolled in University of Texas Medical Branch), and the two placebo controls of the intradermal injection group (n = 2, without adjuvant, enrolled in University of Texas Medical Branch). Human memory B cells were isolated from these subjects, the cells culture and screening of HCMV specific antibodies were performed. We characterized the antibodies for the binding the neutralizing to HCMV.		
Outcomes	Primary outcome: The serum neutralizign titer of the subject after vaccination. Secondary outcome: The binding specificity the neutralizing activity of vaccine induced monoclonal antibodies from the subjects		

Dual use research of concern

Policy information about <u>dual use research of concern</u>

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	
\ge		Public health
\ge		National security
\ge		Crops and/or livestock
\ge		Ecosystems
\ge		Any other significant area
Experiments of concern		

Does the work involve any of these experiments of concern:

No	Yes
\boxtimes	Demonstrate how to render a vaccine ineffective
\boxtimes	Confer resistance to therapeutically useful antibiotics or antiviral agents
\boxtimes	Enhance the virulence of a pathogen or render a nonpathogen virulent
\boxtimes	Increase transmissibility of a pathogen
\boxtimes	Alter the host range of a pathogen
\boxtimes	Enable evasion of diagnostic/detection modalities
\boxtimes	Enable the weaponization of a biological agent or toxin
\boxtimes	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.	For "Initial submission" or "Revised version" documents, provide reviewer access links. For your "Final submission" document, provide a link to the deposited data.
Files in database submission	Provide a list of all files available in the database submission.
Genome browser session (e.g. <u>UCSC</u>)	Provide a link to an anonymized genome browser session for "Initial submission" and "Revised version" documents only, to enable peer review. Write "no longer applicable" for "Final submission" documents.

Methodology

Replicates	Describe the experimental replicates, specifying number, type and replicate agreement.
Sequencing depth	Describe the sequencing depth for each experiment, providing the total number of reads, uniquely mapped reads, length of reads and whether they were paired- or single-end.
Antibodies	Describe the antibodies used for the ChIP-seq experiments; as applicable, provide supplier name, catalog number, clone name, and lot number.
Peak calling parameters	Specify the command line program and parameters used for read mapping and peak calling, including the ChIP, control and index files used.
Data quality	Describe the methods used to ensure data quality in full detail, including how many peaks are at FDR 5% and above 5-fold enrichment.
Software	Describe the software used to collect and analyze the ChIP-seq data. For custom code that has been deposited into a community repository, provide accession details.

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	Describe the sample preparation, detailing the biological source of the cells and any tissue processing steps used.
Instrument	Identify the instrument used for data collection, specifying make and model number.
Software	Describe the software used to collect and analyze the flow cytometry data. For custom code that has been deposited into a community repository, provide accession details.
Cell population abundance	Describe the abundance of the relevant cell populations within post-sort fractions, providing details on the purity of the samples and how it was determined.
Gating strategy	Describe the gating strategy used for all relevant experiments, specifying the preliminary FSC/SSC gates of the starting cell population, indicating where boundaries between "positive" and "negative" staining cell populations are defined.

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	Indicate task or resting state; event-related or block design.	
Design specifications	Specify the number of blocks, trials or experimental units per session and/or subject, and specify the length of each trial or block (if trials are blocked) and interval between trials.	
Behavioral performance measures	State number and/or type of variables recorded (e.g. correct button press, response time) and what statistics were used to establish that the subjects were performing the task as expected (e.g. mean, range, and/or standard deviation across subjects).	

Acquisition

F

Normalization

Normalization template

Noise and artifact removal

Imaging type(s)	Specify: functional, structural, diffusion, perfusion.
Field strength	Specify in Tesla
Sequence & imaging parameters	Specify the pulse sequence type (gradient echo, spin echo, etc.), imaging type (EPI, spiral, etc.), field of view, matrix size, slice thickness, orientation and TE/TR/flip angle.
Area of acquisition	State whether a whole brain scan was used OR define the area of acquisition, describing how the region was determined.
Diffusion MRI Used Not used	
Preprocessing	
Preprocessing software	Provide detail on software version and revision number and on specific parameters (model/functions, brain extraction, segmentation, smoothing kernel size, etc.).

-	ilized/standardized, describe the approach(es): specify linear or non-linear and define image types use
transformation OF	indicate that data were not normalized and explain rationale for lack of normalization.

Describe the template used for normalization/transformation, specifying subject space or group standardized space (e.g. original Talairach, MNI305, ICBM152) OR indicate that the data were not normalized.

Describe your procedure(s) for artifact and structured noise removal, specifying motion parameters, tissue signals and physiological signals (heart rate, respiration).

Define your software and/or method and criteria for volume censoring, and state the extent of such censoring.

Statistical modeling & inference

Model type and settings	Specify type (mass univariate, multivariate, RSA, predictive, etc.) and describe essential details of the model at the first and second levels (e.g. fixed, random or mixed effects; drift or auto-correlation).	
Effect(s) tested	Define precise effect in terms of the task or stimulus conditions instead of psychological concepts and indicate whether ANOVA or factorial designs were used.	
Specify type of analysis: Whole brain ROI-based Both		
Statistic type for inference (See <u>Eklund et al. 2016</u>)	Specify voxel-wise or cluster-wise and report all relevant parameters for cluster-wise methods.	
Correction	Describe the type of correction and how it is obtained for multiple comparisons (e.g. FWE, FDR, permutation or Monte Carlo).	

Models & analysis

n/a Involved in the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the study Image: Second state of the state of the study Image: Second state of the study Image: Second state of the study	is
Functional and/or effective connectivity	Report the measures of dependence used and the model details (e.g. Pearson correlation, partial correlation, mutual information).
Graph analysis	Report the dependent variable and connectivity measure, specifying weighted graph or binarized graph, subject- or group-level, and the global and/or node summaries used (e.g. clustering coefficient, efficiency, etc.).
Multivariate modeling and predictive analysis	Specify independent variables, features extraction and dimension reduction, model, training and evaluation metrics.