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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 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	No software was used
Data analysis	No software was used

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 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

Raw data used for the figures of the manuscript will be made available upon 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

Life sciences study design

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

Sample size	Data about the frequency of subjects developing T cells and NT antibodies in response to the BNT162b2 vaccine were limited, thus this was an exploratory study. The phase 2/3 clinical trial [2] showed a 95% (95% CI: 90-98%) efficacy of the vaccine in protection from SARS-CoV-2 infection. Thus, adopting a conservative approach, we hypothesized a 90% rate of "full responders" developing both T cells specific for S protein and NT antibody. With a sample size of 150 subjects, the 95% confidence interval of the expected frequency is 84-94%. This correspond to a minimum number 126 "full responders" which should have been detected.
Data exclusions	No data were excluded from the analysis.
Replication	Samples were tested once because the amount of blood collected did not allow repeated measures.
Randomization	This is not a randomized study.
Blinding	Blinding is not applicable, because this is not a randomized study.

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
☒	☐ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☐	☒ Human research participants
☒	☐ Clinical data
☒	☐ Dual use research of concern

Methods

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

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	VERO C1008 (Vero 76, clone E6, Vero E6; ATCC1CRL-1586TM)
Authentication	The cell line used was not authenticated
Mycoplasma contamination	Cells were not tested for Mycoplasma contamination
Commonly misidentified lines (See ICLAC register)	Not applicable

Human research participants

Policy information about studies involving human research participants

Population characteristics	Among the 145 subjects enrolled in the study, 127 (87.6%) were SARS-CoV-2 naïve (30 males and 97 females) and 18 (12.4%) SARS-CoV-2 experienced (1 male and 17 females) before vaccination. The median age was 44 (range 21-69) years.
Recruitment	Healthcare workers of Fondazione IRCCS Policlinico San Matteo, Pavia receiving BNT162b2 vaccine were recruited.

Ethics oversight	Comitato Etico Area Pavia

Note that full information on the approval of the study protocol must also be provided in the 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	Peripheral blood mononuclear cells were isolated from heparin-treated blood by standard density gradient centrifugation.
Instrument	BD FACS Canto II
Software	DIVA
Cell population abundance	Not applicable
Gating strategy	FSC/SSC gate on lymphocytes; FSC-H/FSC-A for doublets exclusion; SSC/violet dye to exclude dead cells; SSC/CD3 PerCP 5.5 and gating on CD3+; CD4 APC-Cy7/CD8-FITC and gating on CD4+/CD8- or CD8+/CD4-; CD4 APC-Cy7/CXCR5-BV510 and gating on CXCR5+/CD4+

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