nature portfolio

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Last updated by author(s): Sep 21, 2023

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	Clinical data was collected and stored in commercially available REDCap (https://www.project-redcap.org) and exported for analyses in Microsoft Excel. Python 3.9.2 was used to combine immunological parameters and clinical data.
Data analysis	GraphPad Prism 10.0.2 was used for most of the data analysis, including box and whiskers plots, two-tailed Mann Whitney-U tests, Wilcoxon Rank test two-tailed Fisher exact test, ROC curves and bar charts. UMAP for 8-cytokine release assay was generated using R version 4.3.0, incorporated as additional parameters and converted to FCS files and loaded into FlowJo to generate heatmaps.

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

All aggregate data supporting the findings of this study are available within the paper and its supplementary materials. Subject-level data are not publicly available

to preserve individuals' confidentiality; they can be made available on reasonable request from the corresponding authors (Y.Z. and E.E.O.), subject to prior consent by individual subjects. A data transfer agreement will be required for accessing such subject-level data.

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	Sex was not considered for enrollment, and is reported in aggregate here based on extraction from parent or patient report.
Reporting on race, ethnicity, or other socially relevant groupings	Race and ethnicity were not considered for enrollment, and is reported in aggregate here based on extraction from parent or patient report.
Population characteristics	The study took place in the National University Hospital, a tertiary academic medical centre in Singapore. Healthy children aged 5 to 12 years old, eligible for BNT162b2 vaccination, were recruited from the general population between 20 December 2021 and 8 March 2022.
Recruitment	Children were recruited through advertisements around the National University Hospital, Singapore and in the community.
Ethics oversight	The study protocol was approved by the National Healthcare Group Domain Specific Review Board (NHG-DSRB) (2021/00945, 2021/00984).

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

Life sciences study design

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

Sample size	No sample size calculation was performed as the study is a cohort study.
Data exclusions	No data was excluded.
Replication	This natural experiment of primary vaccination of children during the SARS-CoV-2 pandemic could not be replicated.
Randomization	Randomisation was not relevant to our study, as all subjects received the same vaccine.
Blinding	Blinding was not relevant to our study, as all subjects received the same vaccine.

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
☐	☒ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

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

Antibodies

Antibodies used	For the standard curve for Anti-Spike IgG ELISA: Anti-SARS-CoV-2 RBD Neutralising Antibody, Acrobiosystems HRP-IgG secondary antibody (Life Technologies).
Validation	As per manufacturer

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 applicable as this was an observational study, not a clinical trial.
Study protocol	Full protocol available upon request.
Data collection	All clinical data were obtained through parental/child interviews during pre-determined study visits at pre-vaccination baseline, day 10, 3 months, 6 months, and 1 year post-vaccination. In addition, parents were trained to administer a SARS-CoV-2 ART testing at home if the child developed symptoms suggestive of COVID-19 anytime during the 1-year follow-up period, according to prevailing national guidelines for active surveillance and community treatment during the COVID-19 pandemic in Singapore. ART kits were certified by the Health Sciences Authority of Singapore and freely distributed by the Ministry of Health, Singapore.
Outcomes	Levels of binding and neutralising antibody titres; spike (S)-specific memory B cell (MBC) and S-reactive T cell responses over 1 year; SARS-CoV-2 infections

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	Thawed PBMCs were first enriched for B cells using pan B cell isolation kit (Miltenyi, Germany), according to manufacturer's guidelines. Biotinylated full-length Wuhan-Hu-1 S proteins (Miltenyi, Germany) were incubated with fluorescently labeled streptavidin (SA) for 15 minutes at room temperature.. Cells were stained with an antibody cocktail containing CD3, CD19, CD21, CD27, CD38, CD138, CD71, IgA, IgG, IgD, IgM and 7-AAD for 30minutes at 4°C prior to acquisition.
Instrument	BD LSR Fortessa
Software	Flowjo 10.8.1
Cell population abundance	Final population of interest was 0.001% - 1% of total B cells.
Gating strategy	CD3-CD19+IgD-CD27+CD38-/+S bispecific cells were identified using gating strategy in SUpplementary figure 1.

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