

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 (<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 <i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>
☐	☒ 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>
☒	☐ 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 <i>d</i> , Pearson's <i>r</i>), 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	ELISA samples were quantified using a Magellan3, Tecan Life Sciences at 450nm wavelength. ADCC data was collected by flow cytometry using an Attune NxT flow cytometer, Invitrogen and analysed by FlowJo v10.
Data analysis	Univariate analysis was carried out using Graphpad Prism 9. Multivariate analysis and generalized additive mixed models were performed with RStudio Version 2024.04.2+764 with R version 4.4.1.Packages used: corrplot version 0.95 dplyr version 1.1.4 factoextra version1.0.7 FactoMineR version2.11 ggnewscale version 0.5.0 ggplot2 version3.5.1 ggrepel version 0.9.5 itsadug version2.4.1 lmtest version 0.9.40 Matrix version1.7-0 mgcv version1.9-1 missMDA version1.19 qgraph version1.9.8 readxl version1.4.3 scales version1.3.0

tidyr version 1.3.1
 tidyverse version 2.0.0
 vegan version 2.6-10
 writexl version 1.5.0
 xlsx version 0.6.5

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](#)

Data from ELISA responses with background subtracted are indicated in the main text and supplementary figures. Deidentified raw data that support this study are available.

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

Table 1 reports the age and sex balance in the study cohort, with Supplementary Table 1 reporting the age and sex in a subcohort. Sample sizes were determined by sample availability from an opportunistic observational study. Age and sex were used to analyse and categorise data. They were self-reported.

Reporting on race, ethnicity, or other socially relevant groupings

Race, ethnicity and other social groupings were not included in our analysis.

Population characteristics

Described in table 1

Recruitment

Participants were recruited based on available patients with RT-PCR confirmed COVID-19 infection in Hong Kong. All participants provided informed consent or assent. Their blood was collected at various time-point after disease onset, and there was no bias to the recruitment or collection. As participation was voluntary, circulation of SARS-CoV-2 was limited during the study period in Hong Kong leading to small infection waves in 2020, most cases were mild or asymptomatic in Hong Kong, our cohort may have self selection bias to mild COVID-19 as described in table 1 especially in children. Symptom severity, age and sex were all used to analyse data in figure 5 and supplementary figure 9.

Ethics oversight

The COVID-19 patient study was approved by the institutional review board of the respective hospitals, viz. Kowloon West Cluster (KW/EX-20-039 (144-27)), Kowloon Central / Kowloon East cluster (KC/KE-20-0154/ER2) and HKU/HA Hong Kong West Cluster (UW 20-273, UW20-169), Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee (CREC 2020.229).

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

This is an opportunistic study that determined the sample size. We used n=257 samples from 146 pediatric participants with heterogeneity in terms of age and symptomatology. These pediatric samples were compared to 122 samples from 85 infected adults. n=12 uninfected children and n=48 pre-pandemic controls were included as age matched controls.

Data exclusions

Only samples which were tested for most serological assays were included in multiparametric analyses, with sample information in supplementary table 1. Participants with responses below the negative cut off were excluded from IgG avidity analysis.

Replication

Experiments were repeated, but not all samples for each run.

Randomization

Samples were not randomised as grouping was based on RT-PCR positivity and age.

Blinding

Blinding was not carried out as grouping was based on RT-PCR positivity and age.

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	ELISA: IgG-HRP (1:5,000, clone G18-145; lot 1103324; BD Biosciences), IgM-HRP (1:1,000, clone HP6083, lot VI310774; Invitrogen), IgA-HRP (1:1000, clone BFG-267, lot SG2410745; Invitrogen) ADCC assay: anti-CD56-PE (clone 5.1H11, dilution 1:200, lot 362508, Biolegend) and anti-CD107a-APC (clone H4A3, dilution 1:50, Biolegend)
Validation	Product specification websites for each antibody include multiple references. All antibodies were titrated by us prior to use to ensure antibodies in use are working well.

Eukaryotic cell lines

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

Cell line source(s)	NK-92-FcγR3a-bearing cell line, provided by Fox Chase Cancer Center, originating from a 50-year-old Caucasian male.
Authentication	Morphology check by microscope, only cells at early passage have been used, CD56 and CD16 positivity and used in a functional assay for CD107a degranulation.
Mycoplasma contamination	In-house mycoplasma testing was performed and confirmed to be negative.
Commonly misidentified lines (See ICLAC register)	None

Plants

Seed stocks	N/A
Novel plant genotypes	N/A
Authentication	N/A

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

NK-92 cells from Fox Chase Cancer centre were frozen in LN2, thawed and passaged in MEM-alpha media, and used in ADCC degranulation assays as detailed in methods.

Instrument

flow cytometry (AttuneNXT Invitrogen)

Software

FlowJo v10

Cell population abundance

Debris and doublets were excluded from analysis of cell line.

Gating strategy

Gating strategy with positive and negative populations shown in supplementary figure 7.

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