

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
<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. F , t , r) with confidence intervals, effect sizes, degrees of freedom and P 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 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	EPIC EHR software (retrospective EMR review and clinical data aggregation) and REDCap 9.3.6 (clinical data aggregation).
Data analysis	R (version 3.6.3), ggplot2 (version 3.3.0), Graphpad Prism (version 8), SAS (version 9.4), Attune NxT (version 3.1.2), FlowJo (version 10.6, Tree Star).

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

All the flow cytometry data will be available via ImmPort website (study ID: SDY1648). All the data (viral load, antibody titer, ELISA data) used to generate figures and tables in this study are included in the Supplementary Information Table 1.

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	No statistical methods were used to calculate the sample size. Sample size was determined based on the number of patients admitted to Yale-New Haven Hospital (YNHH) between March 18th and May 9th that were enrolled and consented with the current study under IRB and HIC approved protocol #2000027690. Patients were identified through screening of EMR records for potential enrollment. Individuals with active chemotherapy against cancers, pregnant patients, patients with background hematological abnormalities, patients with autoimmune diseases (e.g. rheumatoid arthritis), and patients with a history of organ transplantation and on immunosuppressive agents were not included, and in total 98 patients were included in this study. Informed consent was obtained by trained staff and sample collection commenced immediately upon study enrollment. Clinical specimens were collected approximately every 4 days where an individual's clinical status permitted, and was continued until patient discharge or expiration.
Data exclusions	Two extreme outlier samples for cytokine ELISA in the entire study. Measurements from these individuals were outliers (beyond 1.5x the interquartile range) in more than half of the cytokines measured. This strongly suggested that a technical error occurred during these two experiments or poor sample quality. Likewise, for flow cytometry, data on myeloid panel and T cell surface staining panel for two individuals were outliers in more than half of the parameters measured, which suggested the poor staining quality during the experiments. Thus, data of these samples were excluded from the analyses.
Replication	The measurements were not replicated - longitudinal analyses of samples from human individuals.
Randomization	This is not relevant as this is an observational study.
Blinding	At the time of sample acquisition and processing, scientists were completely unaware of the patients' conditions. Blood acquisition is performed and recorded by a separate team. Information of patients' conditions are not available until after processing and analysing raw data by flow cytometry and ELISA. A clinical team, separate from the experimental team, performs chart review to determine patients' relevant statistics. Cytokines and facs analyses were blinded. Patients clinical information and clinical scores coding were only revealed after data collection.

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

Antibodies

Antibodies used	All antibodies used in this study are against human proteins. BB515 anti-hHLA-DR (G46-6) (1:400) (BD Biosciences), BV785 anti-hCD16 (3G8) (1:100) (BioLegend), PE-Cy7 anti-hCD14 (HCD14) (1:300) (BioLegend), BV605 anti-hCD3 (UCHT1) (1:300) (BioLegend), BV711 anti-hCD19 (SJ25C1) (1:300) (BD Biosciences), AlexaFluor647 anti-hCD1c (L161) (1:150) (BioLegend), Biotin anti-hCD141 (M80) (1:150) (BioLegend), PE-Dazzle594 anti-hCD56 (HCD56) (1:300) (BioLegend), PE anti-hCD304 (12C2) (1:300) (BioLegend), APCFire750 anti-hCD11b (ICRF44) (1:100) (BioLegend), PerCP/Cy5.5 anti-hCD66b (G10F5) (1:200) (BD Biosciences), BV785 anti-hCD4 (SK3) (1:200) (BioLegend), APCFire750 or PE-Cy7 or BV711 anti-hCD8 (SK1) (1:200) (BioLegend), BV421 anti-hCCR7 (G043H7) (1:50) (BioLegend), AlexaFluor 700 anti-hCD45RA (HI100) (1:200) (BD Biosciences), PE anti-hPD1 (EH12.2H7) (1:200) (BioLegend), APC anti-hTIM3 (F38-2E2) (1:50) (BioLegend), BV711 anti-hCD38 (HIT2) (1:200) (BioLegend), BB700 anti-hCXCR5 (RF8B2) (1:50) (BD Biosciences), PECy7 anti-hCD127 (HIL-7R-M21) (1:50) (BioLegend), PE-CF594 anti-hCD25 (BC96) (1:200) (BD Biosciences), BV711 anti-hCD127
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(HIL-7R-M21) (1:50) (BD Biosciences), BV421 anti-hIL17a (N49-653) (1:100) (BD Biosciences), AlexaFluor 700 anti-hTNF α (MAb11) (1:100) (BioLegend), PE or APC/Fire750 anti-hIFN γ (4S.B3) (1:60) (BioLegend), FITC anti-hGranzymeB (GB11) (1:200) (BioLegend), AlexaFluor 647 anti-hIL-4 (8D4-8) (1:100) (BioLegend), BB700 anti-hCD183/CXCR3 (1C6/CXCR3) (1:100) (BD Biosciences), PE-Cy7 anti-hIL-6 (MQ2-13A5) (1:50) (BioLegend), PE anti-hIL-2 (5344.111) (1:50) (BD Biosciences), BV785 anti-hCD19 (SJ25C1) (1:300) (BioLegend), BV421 anti-hCD138 (MI15) (1:300) (BioLegend), AlexaFluor700 anti-hCD20 (2H7) (1:200) (BioLegend), AlexaFluor 647 anti-hCD27 (M-T271) (1:350) (BioLegend), PE/Dazzle594 anti-hlgD (IA6-2) (1:400) (BioLegend), PE-Cy7 anti-hCD86 (IT2.2) (1:100) (BioLegend), APC/Fire750 anti-hlgM (MHM-88) (1:250) (BioLegend), BV605 anti-hCD24 (ML5) (1:200) (BioLegend), BV421 anti-hCD10 (HI10a) (1:200) (BioLegend), BV421 anti-hCD15 (SSEA-1) (1:200) (BioLegend), AlexaFluor 700 Streptavidin (1:300) (ThermoFisher), BV605 Streptavidin (1:300) (BioLegend).

Validation

All antibodies used in this study are commercially available, and all have been validated by the manufacturers and used by other publications. Likewise, we titrated these antibodies according to our own staining conditions. The following were validated in the following species: BB515 anti-hHLA-DR (G46-6) (BD Biosciences) (Human, Rhesus, Cynomolgus, Baboon), BV785 anti-hCD16 (3G8) (BioLegend) (Human, African Green, Baboon, Capuchin Monkey, Chimpanzee, Cynomolgus, Marmoset, Pigtailed Macaque, Rhesus, Sooty Mangabey, Squirrel Monkey), PE-Cy7 anti-hCD14 (HCD14) (BioLegend) (Human), BV605 anti-hCD3 (UCHT1) (BioLegend) (Human, Chimpanzee), BV711 anti-hCD19 (SJ25C1) (BD Biosciences) (Human), AlexaFluor647 anti-hCD1c (L161) (BioLegend) (Human, African Green, Baboon, Cynomolgus, Rhesus), Biotin anti-hCD141 (M80) (BioLegend) (Human, African Green, Baboon), PE-Dazzle594 anti-hCD56 (HCD56) (BioLegend) (Human, African Green, Baboon, Cynomolgus, Rhesus), PE anti-hCD304 (12C2) (BioLegend) (Human), APCFire750 anti-hCD11b (ICRF44) (BioLegend) (Human, African Green, Baboon, Chimpanzee, Common Marmoset, Cynomolgus, Rhesus, Swine), PerCP/Cy5.5 anti-hCD66b (G10F5) (BD Biosciences) (Human), BV785 anti-hCD4 (SK3) (BioLegend) (Human), APCFire750 or PE-Cy7 or BV711 anti-hCD8 (SK1) (BioLegend) (Human, Cross-Reactivity: African Green, Chimpanzee, Cynomolgus, Pigtailed Macaque, Rhesus, Sooty Mangabey), BV421 anti-hCCR7 (G043H7) (BioLegend) (Human, African Green, Baboon, Cynomolgus, Rhesus), AlexaFluor 700 anti-hCD45RA (HI100) (BD Biosciences) (Human), PE anti-hPD1 (EH12.2H7) (BioLegend) (Human, African Green, Baboon, Chimpanzee, Common Marmoset, Cynomolgus, Rhesus, Squirrel Monkey), APC anti-hTIM3 (F38-2E2) (BioLegend) (Human), BV711 anti-hCD38 (HIT2) (BioLegend) (Human, Chimpanzee, Horse), BB700 anti-hCXCR5 (RF8B2) (BD Biosciences) (Human), PE-Cy7 anti-hCD127 (HIL-7R-M21) (BioLegend) (Human), PE-CF594 anti-hCD25 (BC96) (BD Biosciences) (Human, Rhesus, Cynomolgus, Baboon), BV711 anti-hCD127 (HIL-7R-M21) (BD Biosciences) (Human), BV421 anti-hIL-17a (N49-653) (BD Biosciences) (Human), AlexaFluor 700 anti-hTNF α (MAb11) (BioLegend) (Human, Cat, Cross-Reactivity: Chimpanzee, Baboon, Cynomolgus, Rhesus, Pigtailed Macaque, Sooty Mangabey, Swine), PE or APC/Fire750 anti-hIFN γ (4S.B3) (BioLegend) (Human, Cross-Reactivity: Chimpanzee, Baboon, Cynomolgus, Rhesus), FITC anti-hGranzymeB (GB11) (BioLegend) (Human, Mouse, Cross-Reactivity: Rat), AlexaFluor 647 anti-hIL-4 (8D4-8) (BioLegend) (Human, Cross-Reactivity: Chimpanzee, Baboon, Cynomolgus, Rhesus), BB700 anti-hCD183/CXCR3 (1C6/CXCR3) (BD Biosciences) (Human, Rhesus, Cynomolgus, Baboon), PE-Cy7 anti-IL-6 (MQ2-13A5) (BioLegend) (Human), PE anti-hIL-2 (5344.111) (BD Biosciences) (Human), BV785 anti-hCD19 (SJ25C1) (BioLegend) (Human), BV421 anti-hCD138 (MI15) (BioLegend) (Human), AlexaFluor700 anti-hCD20 (2H7) (BioLegend) (Human, Baboon, Capuchin Monkey, Chimpanzee, Cynomolgus, Pigtailed Macaque, Rhesus, Squirrel Monkey), AlexaFluor 647 anti-hCD27 (M-T271) (BioLegend) (Human, Cross-Reactivity: Baboon, Cynomolgus, Rhesus), PE/Dazzle594 anti-hlgD (IA6-2) (BioLegend) (Human), PE-Cy7 anti-hCD86 (IT2.2) (BioLegend) (Human, African Green, Baboon, Capuchin Monkey, Common Marmoset, Cotton-topped Tamarin, Chimpanzee, Cynomolgus, Rhesus), APC/Fire750 anti-hlgM (MHM-88) (BioLegend) (Human, African Green, Baboon, Cynomolgus, Rhesus), BV605 anti-hCD24 (ML5) (BioLegend) (Human, Cross-Reactivity: Chimpanzee), BV421 anti-hCD10 (HI10a) (BioLegend) (Human, African Green, Baboon, Capuchin monkey, Chimpanzee, Cynomolgus, Rhesus), BV421 anti-hCD15 (SSEA-1) (BioLegend) (Human), AlexaFluor 700 Streptavidin (1:300) (ThermoFisher), BV605 Streptavidin (1:300) (BioLegend).

Human research participants

Policy information about [studies involving human research participants](#)

Population characteristics

Fifty-one female (age 64.0 $\pm$ 16.9) and 47 male (age 61.9 $\pm$ 16.7) patients were included. The detailed demographic information can be found in Extended Data Table 1.

Recruitment

Patients admitted to the Yale New Haven Hospital (YNHH) between the 18th of March through the 9th of May 2020, were recruited to the Yale IMPACT study (Implementing Medical and Public Health Action Against Coronavirus CT) after testing positive for SARS-CoV2 by qRT-PCR. (serology was further confirmed for all patients enrolled). Patients were identified through screening of EMR records for potential enrollment with no self selection. Informed consent was obtained by trained staff and sample collection commenced immediately upon study enrollment. Clinical specimens were collected approximately every 4 days where an individual's clinical status permitted, and was continued until patient discharge or expiration.

Ethics oversight

Yale Human Research Protection Program Institutional Review Boards. Informed consents were obtained from all enrolled patients and healthcare workers. • Our research protocol was reviewed and approved by the Yale School of Medicine IRB and HIC (#2000027690). Informed consent was obtained by trained staff and records maintained in our research database for the duration of our study. There were no minors included on this study.

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

Freshly isolated PBMCs were stained for live and dead markers, blocked with Human TruStan FcX , stained for surface markers and then fixed with PFA 4%. For intracellular cytokine staining following stimulation , cells were surface stained, washed and fixed in 4% PFA. After permeabilization with 1X Permeabilization Buffer cells were stained for intracellular cytokines analysis.

Instrument

Cells were acquired on an Attune NXT (ThermoFisher).

Software

Data were analysed using FlowJo software version 10.6 software (Tree Star).

Cell population abundance

Cell population abundance: Cells populations were reported in various formats including as a number or concentration of the patient's blood sample (x106cells/mL), as a proportion of live, single PBMC (% of Live), or as a proportion of a parent gate (% of CD4 T cells, % of Monocytes, etc.). The full gating path for clarification is included in the extended figures.

Gating strategy

SSC-A and FSC-A parameters were used to select leukocytes from isolated PBMCs. Live and dead cells were defined based on aqua staining. Singlets were separated based on SSC/ FSC parameters. Leukocytes were gated based on to identify lymphocytes (CD3/CD4/CD8/CD19/CD56 markers), granulocytes (CD16,CD14, HLA-DR markers) and pDCs, and cDCs (CD304, CD1c, CD141). TCR-activated T cells, Terminally-differentiated T cells, and additional subsets.were defined using HLA-DR, CD38, CCR7,CD127, PD1, TIM-3, CXCR5, CD45RA, CD25. Intracellular T cell gating strategy to identify CD4 and/or CD8 T cells secreting TNFa, IFN-γ, IL-6, IL-2, GranzymeB, IL-4, and/or IL-17 were defined using the specif markers: CD3, CD4, CD8, TNF, IFN, IL-6, IL-2, IL-4, IL-17 and granzyme B.

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