nature research

Corresponding author(s): Bruce D. Levy

Last updated by author(s): Oct 3, 2019

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 Authors & Referees 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	Gen5 Software from BioTek, Flowjo Software version 10.1 (Tree star), MATLAB, Micromanager
Data analysis	R packages, Graphpad prism, SPSS software, Microsoft Excel, Origin, ImageJ

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/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

The data supporting the results in this study are available within the paper and its Supplementary Information. The raw patient data are available from the authors, subject to approval from the Institutional Review Board of Partner's Healthcare.

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

Life sciences study design

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

Sample size	Based on power calculations, we estimated that we needed up to 20 samples in each group to detect a significant difference in leukocyte phenotypes and function.
Data exclusions	Samples were excluded if technical matters affected data collection.
Replication	Biospecimens from healthy subjects were subjected to repeated testing to establish the cell functional assays developed for this study. Once established, the methods for cell-based assays were replicated by multiple investigators over the duration of the study. Biological replication was assessed by obtaining biospecimens from multiple healthy subjects and two distinct sepsis cohorts.
Randomization	Randomization is not relevant to this pre-clinical study.
Blinding	Laboratory investigators were blinded to the diagnosis of patients until data collection and analyses were completed. Patients were assigned to disease group by an independent group of clinical investigators after completion of the laboratory analyses.

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
☒	☐ Animals and other organisms
☐	☒ Human research participants
☒	☐ Clinical data

Methods

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

Antibodies

Antibodies used	The following antibodies to human proteins were used, with clones noted in parentheses: anti-CD45 PerCP (HI30), anti-CD66b Pacific blue (G10F5), anti-CD16 APC-Cy7 (3G8), anti-CD69 FITC (FN50), anti-CD62L Brilliant Violet 510 (DREG-56), anti-CD42b Alexa Flour 700 (HIP1) (all from BioLegend) and anti-CD14 APC (61D3) and anti-CD11b PE-Cy7 (ICRF44) (from Thermofisher).
Validation	The antibodies used are commercially available and were validated by the manufacturers (Biolegend and Thermofisher). Anti-CD45 PerCP (HI30) - Audigé A, et al. 2017. BMC Immunology. Anti-CD66b Pacific Blue (G10F5) - Gunn BM, et al. 2018. Cell host & microbe. Anti-CD16 APC-Cy7 (3G8) - Felices M, et al. 2018. JCI Insight. Anti-CD69 FITC (FN50) - Shifrut E. 2018. Cell. Anti-CD62L Brilliant Violet 510 (DREG-56) - Charles N, et al. 2010. Nat. Med. Anti-CD42b Alexa Flour 700 (HIP1) - Meyer Dos Santos S, et al. 2011. Blood. Anti-CD14 APC (63D3) - Kan B, et al. 2018. Nat. Commun. Anti-CD11b PE-Cy7 (ICRF44) - Ormel PR, et al. 2018. Nat. Commun. More information can be found on the manufacturer's website (Biolegend and Thermofisher).

Human research participants

Policy information about studies involving human research participants

Population characteristics	Biospecimens were obtained from volunteer healthy human subjects and from two sepsis patient cohorts (ROCI and STEM), as detailed in Methods. Subject characteristics are provided in Table 1.
Recruitment	Recruitment details are provided in Methods.
Ethics oversight	The study was approved by the Brigham and Women's Hospital Institutional Review Board. Details are provided in Methods.

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	Sample preparation is detailed in Methods.
Instrument	BD Fortessa
Software	Flowjo
Cell population abundance	Cell sorting via flow cytometry was not performed.
Gating strategy	Cells were first gated for FSC/SSC, then for live, CD45+ cells, then for cell population-specific markers, as indicated in Methods.

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