nature portfolio

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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	No software was used
Data analysis	Flow cytometry: Downstream analyses included SPICE v6.1 for polyfunctionality, PCA and UMAP for dimension reduction (nearest neighbours = 15; min dist = 0.5) followed by clustering/annotation using PhenoGraph v4.0.3 (k = 30). Single-cell RNA sequencing analysis: Cell Ranger v6.1.1 (10x Genomics), Seurat v5.1.0 using the Read10X function. TCR analysis: Cell Ranger "filtered_contig_annotations" files were imported into R v4.4.1 and Rstudio v2024.04.2+764 and analysed with scRepertoire v2.2.1 using CTstrict and CTaa definitions. The functions clonalProportion, highlightClones, and clonalDiversity were used to generate plots. Statistics: All descibed in the manuscript. Statistical analyses were performed using GraphPad Prism v9.5.1 and R v4.3.2. Normality was assessed using the Shapiro–Wilk test. Non-parametric comparisons between two groups were performed using the two-tailed Mann–Whitney U test. For non-parametric comparisons across three or more groups, two-tailed Kruskal–Wallis tests with Dunn's post hoc correction were used. Correlations were assessed using two-tailed Spearman rank correlation. Permutation tests (10,000 iterations) were used to compare population profiles in SPICE.

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 data are included in the Supplementary Information or available from the authors as a Source Data file.

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	We report % Male in Table 1.Cohort characteristics
Reporting on race, ethnicity, or other socially relevant groupings	Ethnicity was reported (Table 1) because adaptive immune responses, particularly T cell–mediated immunity, are influenced by host genetic factors such as human leukocyte antigen (HLA) variation. The distribution of HLA alleles differs across populations with distinct ancestral backgrounds, which can shape antigen presentation and downstream immune responses. Reporting ethnicity therefore provides important context for interpreting variability in immune outcomes and supports transparency, reproducibility, and generalizability of the findings.
Population characteristics	Age
Recruitment	Described in the Material and Methods section under cohort
Ethics oversight	Swedish Ethical Review Authority in Stockholm (Dnr. 2016/2543-21/1).

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	Dependent on number of HIV infected children in Stockholm
Data exclusions	Clearly descibed in the result section.
Replication	n/a
Randomization	n/a
Blinding	Blinded until summarizing results

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
[ ]	[x] Antibodies
[x]	[ ] Eukaryotic cell lines
[x]	[ ] Palaeontology and archaeology
[x]	[ ] Animals and other organisms
[ ]	[x] Clinical data
[x]	[ ] Dual use research of concern
[x]	[ ] Plants

Methods

n/a	Involved in the study
[x]	[ ] ChIP-seq
[ ]	[x] Flow cytometry
[x]	[ ] MRI-based neuroimaging

Antibodies

Antibodies used: Included in the supplemental material

Validation: All antibodies used in the study has been validated before use.

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: n/a

Study protocol: n/a

Data collection: n/a

Outcomes: n/a

Plants

Seed stocks: n/a

Novel plant genotypes: n/a

Authentication: n/a

Flow Cytometry

Plots

Confirm that:

[x] The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

[x] 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).

[x] All plots are contour plots with outliers or pseudocolor plots.

[x] A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation: Detailed in material and methods

Instrument: Identified in material and methods and supplementary table 1

Software: Identified in material and methods and supplementary table 1

Cell population abundance: Identified in material and methods and supplementary table 1

Gating strategy | Included in S. Fig 2

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