

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
<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

Processing of the raw Illumina sequencing data was performed using the CellRanger versions 2.0.2, 2.1.0 and 2.1.1 (10X Genomics). Flow cytometry data was acquired with BD FACSDiva software (version 8.0). Fluorescence images were acquired with Zeiss AxioVision 4.8 software (Carl Zeiss).

Data analysis

Seurat R package (v2.3.4) for single-cell RNA seq analysis; Monocle (v2.10.1) for trajectory analysis; Loupe V(D)J Browser (v2.0.1) for single cell T cell receptor V(D)J analysis; GraphPad Prism v.8.2.0 (GraphPad Software Inc.) and R (v3.5.2) for statistics; ImageJ (v1.52k) for image handling; FlowJo v10 (FlowJo, LLC) for flow cytometry analysis.

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

Source data for Figures 1-4 and Extended Data Figures 1, 2, and 4 are provided with the paper. The matrix and raw data for scRNAseq reported in this paper have been deposited in NCBI's Gene Expression Omnibus and are accessible through GEO Series accession number GSE132802 (<https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE132802>).

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 sample size calculation was performed. Cell capture for single cell analysis was aimed to obtain as many cells as possible for each run, which maximum is theoretically 50-60% of 10,000 input cells. The number of cells analyzed (patient + healthy volunteer(s)) totalled over 12,000 cells and thus provided robust statistical analysis on clustering and differentially expressed genes.
Data exclusions	1) Flow cytometry analysis; any doublets defined by FSC and SSC and ZombieAque-positive dead cells were excluded. 2) For single cell analysis, multiplets or fragmented cells and dying or stressed cells were excluded. Multiplets or fragmented cells during filtration were defined using the numbers of genes and unique molecular index (UMI) counts. Dying or stressed cells were defined by percentages of mitochondrial genes. Thresholds for exclusions in each dataset are defined in Supplementary Table 5.
Replication	For in vitro studies, three biological replicates were performed and experiments were repeated at least twice. For HHV6b detection in PBMC or sorted blood subsets, PCR quantification was performed without technical replicates in two different sampling points.
Randomization	No randomization was performed.
Blinding	The investigators were not blinded.

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	Anti-CD3-APC-Cy7 (clone HIT3a, Biolegend, #300317), anti-CD4-APC (clone RPA-TA, Biolegend, #350514), anti-CD8- PerCP-Cy5.5 (clone SK1, Biolegend, #344709), anti-CCR4-PE-Cy7 (clone L291H4, Biolegend, #359409), anti-CCR7-FITC (clone G043H7, Biolegend, #353215), anti-CCR10-PE (clone 314305, R&D #FAB3478P-025), anti-CD45RO-BUV395 (clone UCHL1, BD Biosciences, #564292), anti-CD4-PE-Cy7 (RPA-TA, Biolegend, #300512), anti-CD8-BV421 (clone RPA-T8, Biolegend, #301036), anti-CD3-Alexa Fluor 488 (clone UCHT1, Biolegend, #300415), anti-CCR10-unconjugate (polyclonal, Invitrogen, #PA5-32694), anti-JAK3 (clone 1A1, Bioss Inc, # bsm-54067R), anti-Phosphorylated-STAT1 (Ty701) (clone 58D6, Cell Signaling, #9167), goat anti-mouse IgG-Alexa Fluor 488 (Invitrogen, #A28175), goat anti-rabbit IgG-Alexa Fluor 568 (Invitrogen, #A-11011).
Validation	All of the above antibodies have been documented and validated by the manufacturer to be specific for the indicated molecules.

Human research participants

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

Population characteristics	This manuscript describes a 45-year-old male patient that was diagnosed as having drug-induced hypersensitivity syndrome or drug reaction with eosinophilia and systemic symptoms (DiHS/DRESS) initially at Walter Reed National Military Medical Center and subsequently at Washington Hospital Center, further confirmed at the National Institutes of Health. 5 healthy volunteers participated for skin biopsy and one age-matched and sex-matched blood sample was obtained from the NIH Blood Bank.
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Recruitment

The patient was referred to the National Institutes of Health from Walter Reed National Military Medical Center. Healthy volunteers were recruited through a tissue-acquisition protocol at the NIH (NCT00001505).

Ethics oversight

National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institute of Allergy and Infectious Diseases

Note that full information on the approval of the study protocol must also be provided in the manuscript.

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

Provide the trial registration number from ClinicalTrials.gov or an equivalent agency.

Study protocol

Note where the full trial protocol can be accessed OR if not available, explain why.

Data collection

Describe the settings and locales of data collection, noting the time periods of recruitment and data collection.

Outcomes

Describe how you pre-defined primary and secondary outcome measures and how you assessed these measures.

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

For phenotyping of PBMC, PBMCs were freshly isolated using density gradient centrifugation from heparinized peripheral blood. For lymphocyte transformation test, cultured PBMCs were collected then stained using fluorochrome-labeled antibodies.

Instrument

BD LSR II

Software

FACSDiva (BD, ver 8.0) for cell acquisition and FlowJo software (FlowJo, LLC) version 10 for analysis.

Cell population abundance

PBMCs were sorted only for viral detection, and due to the limited number of cells (e.g. CD4+ central, effector and naive T cells), the purity of cells after cell sorting was not confirmed. Purity of live cells after dead cell exclusion that were processed for single cell RNAseq was also not determined because loss of cells were a bigger issue than minor dead cell contaminants.

Gating strategy

Cells were excluded for doublets based of SSC and FSC, excluded for dead cell staining (Zombie Aqua) and then gated for CD45+ cells. Positivity for expression of cell surface molecules of interest were determined with isotype controls.

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