

Corresponding author(s): Florian Greten

Last updated by author(s): Aug 25, 2025

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 SecuTrial; <https://www.secutrial.com/>

Data analysis GraphPad Prism, Version 10; SAS® Version 9.4 with SAS Enterprise Guide Version 8.3

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](#)

scRNAseq data of participant PBMCs are publicly available in the NCBI Sequence Read Archive (SRA) under BioProject accession number PRJNA1169651. The minimum de-identified dataset to generate the graphs that support the findings are available from the corresponding author.

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	Intervention groups were randomised according to sex, hence both intervention groups included the same sex distribution, which is displayed in the Extended Data Set. Due to sample size limitations, no specific gender-based analysis were performed.
Reporting on race, ethnicity, or other socially relevant groupings	No specific measurements were taken or intended to include or exclude participants of a certain ethnicity. Participants were enrolled based on inclusion and exclusion criteria, which did not specifically include ethnicity. Definition of ethnicity was self-reported by the participants and stored in the eCRF. All participants identified as caucasian.
Population characteristics	Populations characteristics are displayed in the Extended Data set.
Recruitment	Participants were recruited from health care workers and scientific staff from the Georg-Speyer-Haus and University Hospital Frankfurt, respectively. Additional participants were recruited via social media advertisement previously approved by the institutional review board. Participants were recruited from 03/2023 to 12/2023. The study only included participants that met all inclusion and exclusion criteria (healthy, aged adults), and the results may not generalize to other diseases or age groups.
Ethics oversight	Our study was approved and monitored by the local IRB of the University of Frankfurt, Germany (Ethikkommission des Fachbereichs Medizin der Goethe-Universität, approval number 2022-745_2)

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	Sample size estimates were based on statistical simulations by Jacques et al (doi: 10.1096/fj.201901997RR) where a comprehensive literature review was performed to assess range of effect size for 80% power when oxidative function of muscle cells was studied. According to these statistical simulations, 24 participants are considered sufficient for interventions with an expected 11% effect size. Likewise, the sample size chosen (n=50) is comparable to a similar study in the literature (doi: 10.1172/JCI138538) that focused on immune health and mitochondrial function.
Data exclusions	No data was excluded for the primary endpoint analysis, rendering n=25 per group. For cytokine measurements, samples that did not provide any measurable levels were excluded from analysis (1-2 measurements per group), which is specified in the paper.
Replication	For each assay, each participants was only measured once; hence all replicates correspond to biological replicates, not technical replicates. These biological replicates ranged from n=12-25. Only statistically significant findings were used to draw conclusions. This marks a proof-of-concept phase I study which has addressed the primary and secondary aims. Thus, future trials are needed to confirm these findings and its potential translation to other cohorts and diseases.
Randomization	Upon study participant inclusion and informed consent, randomization was performed double-blind at the study site, using the eCRFs (Secutrial) web-based, in-built randomization platform. A static stratified block randomization algorithm was used, randomizing participants according to age, gender and BMI. For this block-based randomization strategy, a block size of four was used. All participants received the allocated intervention.
Blinding	The investigational product was blinded into a study code by an unblinded person at the sponsor site, who was not involved in trial design, data collection, analysis or interpretation of the data. Data collection and analysis was performed blinded. Unblinding was performed after analysis of primary and secondary endpoints.

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	Detailed information regarding antibodies used including clone, vendors and catalogue numbers are provided in the Methods section and the Supplementary Information.
Validation	The commercially-available antibodies are field standards and have been validated by the respective vendor. A list of antibodies for the staining panels has been provided in the Supplementary Information. The antibody mixes for the broad immune profiling were concomittantly tested on a "standard" sample (healthy, frozen PBMC) with known immune cell distribution to ensure validity of the staining and gating strategy. A gating strategy showing positive/negative separation is provided in the Supplementary Information.

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	The study was registered prior to the enrollment of the first participant on clinicaltrials.gov : NCT05735886.
Study protocol	The study protocol is made available with the paper.
Data collection	The data was collected at Georg-Speyer-Haus, Frankfurt and University Hospital, Frankfurt from 2023-2024. Informed consent was obtained from all participants. Participants were healthy volunteers; therefore we cannot exclude self-selection bias and inclusion of participants that inherently aim to live a healthier lifestyle.
Outcomes	Primary outcomes: 1) Change in percentages of CD3+ T-cell immune cell population In particular, number of CD8+ T memory stem cells and naïve-like T cells (flow cytometry) [Time Frame: 28 days] 2) Change in Mitochondrial activity in CD3+ T-cells Mitochondrial function evaluated via SCENITH metabolic profiling (flow cytometry) [Time Frame: 28 days] Secondary outcomes: 1) Change in pro and anti-inflammatory cytokine levels (IL-6, TNF-α, IL-1β, IL-10) in plasma measured by bead-based flow cytometry [Time Frame: 28 days] 1. Change in percentages of other immune cell populations (B cells, NK cells, Macrophages, DCs etc.) via flow cytometry [Time Frame: 28 days] 2. Change in Mitochondrial content on CD3 T-cell populations via Mitotracker staining using flow cytometry [Time Frame: 28 days] 3. Change in gene-expression: single cell analysis of CD3+ T-cells [Time Frame: 28 days] 4. Change in PBMC's immune function assessment (cytokine secretion, bacterial engulfment) via flow cytometry [Time Frame: 28 days] 5. Change in Lipid profile [Time Frame: 28 days] 6. Number of adverse events [Time Frame: 28 days]

Plants

Seed stocks	Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.
Novel plant genotypes	Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.
Authentication	Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosaicism, off-target gene editing) were examined.

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	Spectral flow cytometry to broadly analyze immune composition was performed on PBMCs from 25 UA and 25 placebo individuals from our cohort. Flow cytometry staining was performed in three batches to minimize to batch-related effects. PBMC were thawed and allowed to recover for 3 hours in uncoated cell culture dishes. All samples for any particular donor series were thawed together. Cells were stained with the panel shown in the Supplementary Figures.
Instrument	Data was acquired by Cytex Aurora, generating FCS files.
Software	FCS files were exported into FlowJo (BD, Version 10) for further analysis
Cell population abundance	Alive abCD8+ cells ranged from 30,000 - >200,000.
Gating strategy	Cells were identified by a initial SSC/FSC plot, followed by identification of single cells via FSC-H/FSC-A. Next, alive CD45+ cells were gated by the use of an anti-CD45 antibody and viability dye. A representative gating strategy depicting these steps is provided in the Supplementary Information.

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