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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

Chef Instrument name : CHEF00520
Chef Script Version/263
Chef Package Version/IC.5.0.1

Torrent Suite/5.0.4
DataCollect/3220
OIA/5002
OS/30
Graphics/52
Ion Chef/IC.5.0.1

Flow Cytometry
Summit/software v4.3
ImageStream Sysyem Software INSPIRE/2.0

Q-PCR
QuantStudio 12K Flex Software/v1.2.2

Microscope
Leica Application Suite/4.9.0
ZEN (blue edition)/ 2.1

Data analysis

Flow Cytometry
FlowJo/10.4.1
Java/1.8.0_151
IDEAS/6.0

#Microscope
ImageJ/1.52a
java/1.8.0_45
ZEN (blue edition)/ 2.1

Data analysis and visualization
Prism/6.0h
Ingenuity Pathway Analysis/01-13
Morpheus
Gephi/0.9.1
Circos/0.69-3
Bespoke coding (Perl)/Code available on request

Affymetrix
Bioconductor/1.18.5
limma/3.24.15
oligo/1.32.0

Ion Proton ChIPseq NGS
java/1.8.0_45
fastqc/0.11.2
IGVTools/2.3.57
samtools/0.1.19
bedtools/2.24.0
bamtools/2.3.0
bedGraphToBigWig/315
picard/1.118
findPeaks/3.1.8
MEME Suite/ 4.11.2

Illumina RNAseq NGS
fastqc/0.11.2
STAR/2.5.1b
picard/1.118
java/1.8.0_45
samtools/0.1.19
bedtools/2.24.0
bamtools/2.3.0
HTSeq/0.6.1p1
subread/1.4.6-p2
trimmomatic/0.35

Illumina RNAseq NGS - Synovial tissue
RR/3.4.4
Shiny/1.1.0
Kallisto/0.43.0
tximport/1.4.0
DESeq2/1.14.1

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 sets generated during the current study for Mircoarray data are available in ArrayExpress: https://www.ebi.ac.uk/arrayexpress/experiments/E-MTAB-7682

- The data sets generated during the current study for ChIP-seq are available in ArrayExpress: https://www.ebi.ac.uk/arrayexpress/experiments/E-MTAB-6273
Username: Reviewer_E-MTAB-6273
Password: 7tBavowV

- Other datasets used for the analysis are available in GEO: GSE40463, GSE60482, GSE65621

- Data associated with the study is available in the webside: http://jones-cytokinelab.co.uk/NI2019/index.shtml
user: reviewer
pass: reviewer

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 were determined through experience :
- Microarray data: we have 2 sample per condition. One of them was used for microarray and the other one for qPCR validation.
- ChIP: we have 2 sample per condition. One of them was used for sequencing and the other one for qPCR validation.

For micrroarray and ChIP-seq techniques, qPCR analysis help to correct the biases of the preferences of the biochip and sequencer for certain sequences and for the bioinformatic processes that are used to analyse the data.

- FACs analysis: at least biological triplicates.
- RNA-seq synovial tissue: sample size was determined based on pilot RNA-seq of 29 synovial samples.

Data exclusions

Not data excluded

Replication

All attempts at replication were successful. Experiments have been repeated by different authors and in some cases different techniques have been used - e.g., flow cytometry and immunohistochemistry or Chip-seq and ChIP-qPCR.

Randomization

Mouse studies - Studies of antigen-induced arthritis were conducted on male mice to ensure optimal priming of the disease model (>98% penetrance). Since the experimental design was not established to compared difference in responses between groups of mice no randomisation was applied.

Human studies - Synovial biopsies were obtained from patients entered into an open-label randomised controlled clinical trial of biological drug intervention. Patients enrolled to the study were stratified according to the synovial pathology, and were randomised to receive specific biological drug therapy after all clinical screening protocols were conducted. Our study was not subject to this randomisation since we were interested in the synovial gene expression profile associated with defined pathotypes prior to drug treatment. These analyses were independent of the biological drug intervention underpinning the wider trial design.

Blinding

Blinding was not performed. Data reported are not subjective. Computational analysis was not performed 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

Protein name / Supplier / Catalog number / Clone / Lot number/Dilution
STAT1 / Santa Cruz Biotechnology / sc-592 / p84-p91/ K0414/5ugr
STAT3 / Santa Cruz Biotechnology / sc-482 / C-20/ D1315/5ugr
CD3 APC-Cy7 / BD Biosciences / 560590 / 17A2 / 6027584/1:200
CD4 PerPCP-Cy5.5 / eBioscience / 45- 0042-82 / RM4-5/ E08292-1632/1:200

CD25 PE / eBioscience / 12-0251-83 / PC61.5 / E01155-1631/1:200
CD44 APC/ eBioscience / 17-0441-83 / IM7 / E07147-1631/1:200
CD62L FITC / eBioscience / 11-0621-85 / MEL-14 / E00377-1633/1:200
CD62L PE-Texas / Life technologies / RM4317 / MEL-14 / 1662867/1:200
CD126 APC / Biolegend / 115812 / D7715A7 / B143205/1:100
CD127 PE-Cyanine7 / eBioscience / 25-1271-82 / A7R34 / E07599-1635/1:200
TCR APC / BD Biosciences / 553174 / H57-597 / 38374/1:100
gp130 APC / R&D Systems / FAB4681A / 125623 / AAOK0108081/1:100
IFNgamma eFluor450 / eBioscience / 48-7311-80 / XMG1.2 / E10945-1633/1:200
IL-4 PE / eBioscience / 12-7041-82 / 11B11 / E02067-1633/1:200
IL-17A PE / Biolegend / 506904 / TC11-18H10.1 / B173240/1:200
IL-21 Recombinant mouse IL-21R Fc Chimera / R&D / 596-MR //EFS0417031/1:40
R-Phycoerythrin AffiniPure F(ab')$_2$ Fragment Goat Anti-Human IgG, Fcγ Fragment Specific / Jackson Immuno Research / 109-116-098 / Polyclonal / 111933/1:200
CD3 APC-Cy7 / BioLegend / 300426 / UCHT1 / B214151/1:200
CD4 PE / eBioscience / 12-0049042 / RPA-T4 / 4298927/1:200
CD45RA FITC / BioLegend / 304106 / HI100/1:200
CD45RO PE-Cy7 / BioLegend / 304230 / UCHL1 / B160500/1:200
CD62L PE-CF594 / BD Biosciences / 562301 /DREG-56/1:200
CD197 (CCR7) PerCP-Cy5.5 / BioLegend / 353220 / G043H7 / B198880/1:200
pY STAT1 (pY701) FITC / BD Biosciences / 612596 / 4a / 6078703/1:10
pY-STAT3 (pY705) PE / BD Biosciences / 557815 / 4_P-STAT3 / 5309547/1:10
pY-STAT5 (pY694) 488/BD Biosciences / 612598 / 47/Stat5 / 5212980/1:10
pS-STAT1 (pS727) FITC / BD Biosciences / 560191 / K51-856 /5141653/1:10
pS STAT3 (pS727) PE / BD Biosciences / 558557 / 49_p-Stat3 / 4269803/1:10
Ptpn2 / R&D Systems / AF1930 / Polyclonal / 1:50

Validation

Antibody validation was based on descriptions provided by the manufacturer. Concentrations were derived from preliminary dose dependent assessments - based on our own pilot studies and on-going experience. Where appropriate, studies used isotype control antibodies as described.

- Santa Cruz antibodies:
STAT1: sc-592
STAT3: sc-482
Both of them were validated in our laboratory by ChIP-qPCR (see supplemental material) but they have been used in many different laboratories for the same technique:
1. Iwata, S., et al. (2017). "The Transcription Factor T-bet Limits Amplification of Type I IFN Transcriptome and Circuitry in T Helper 1 Cells." Immunity 46(6): 983-991 e984.
2. Mahendrarajah, N., et al. (2017). "HSP90 is necessary for the ACK1-dependent phosphorylation of STAT1 and STAT3." Cell Signal 39: 9-17.
3. Hirahara, K., et al. (2015). "Asymmetric Action of STAT Transcription Factors Drives Transcriptional Outputs and Cytokine Specificity." Immunity 42(5): 877-889.
4. Nakayamada, S., et al. (2014). "Type I IFN induces binding of STAT1 to Bcl6: divergent roles of STAT family transcription factors in the T follicular helper cell genetic program." J Immunol 192(5): 2156-2166.
5. Hutchins, A. P., et al. (2012). "Genome-wide analysis of STAT3 binding in vivo predicts effectors of the anti-inflammatory response in macrophages." Blood 119(13): e110-119.

- BD Biosciences: Flow cytometry antibodies are routinely tested by the company.
CD3 APC-Cy7: 560590
TCR APC: 553174
CD62L PE-CF594: 562301
pY STAT1 (pY701) FITC: 612596
pY-STAT3 (pY705) PE: 557815
pY-STAT5 (pY694) 488: 612598
pS-STAT1 (pS727) FITC: 560191
pS STAT3 (pS727) PE: 558557

- eBioscience (now in ThermoFisher Scientific): Validation standards for reproducibility
Thermo Fisher Scientific is committed to adopting validation standards for our antibody portfolio that are tested for both target specificity and functional application. By supporting the International Working Group for Antibody Validation (IWGAV), and adopting their recommendations, we're doing our part to ensure reproducibility and proper functionality in the scientific community.
CD4 PerPCP-Cy5.5: 45- 0042-82
CD25 PE: 12-0251-83
CD44 APC: 17-0441-83
CD62L FITC: 11-0621-85
CD127 PE-Cyanine7: 25-1271-82
IFNgamma eFluor450: 48-7311-80
IL-4 PE: 12-7041-82
CD4 PE: 12-0049042
CD62L PE-Texas: RM4317

- Biolegend antibodies: Each lot of these antibodies are quality control tested and/or validated by immunofluorescent staining with flow cytometric analysis. (https://www.biolegend.com/en-us/advanced-search?GroupID=&PageNum=1&PID=81&isLiveSearch=true&Applications=KO%2fKD-WB)

CD126 APC: 115812
IL-17A PE: 506904
CD3 APC-Cy7: 300426
CD45RA FITC: 304106
CD45RO PE-Cy7: 304230
CD197 (CCR7) PerCP-Cy5.5: 353220

- R&D Systems antibody: Flow cytometry antibodies are routinely tested by the company.
gp130 APC: FAB4681A

References:
1. Narazaki, M. et al. (1993) Blood 82:1120.
2. Taga, T. and T. Kishimoto (1997) Annu. Rev. Immunol. 15:797.

- IL-21 Recombinant mouse IL-21R Fc Chimera (R&D) and R-Phycoerythrin AffiniPure F(ab')$_2$ Fragment Goat Anti-Human IgG, Fcγ Fragment Specific (Jackson Immuno Research): Both of them were validated in our laboratory and also has been used in other laboratories:
1. Suto A., et al. (2008). "Development and characterization of IL-21-producing CD4+ T cells." J Exp Med 205(6):1369-79.

- Ptpn2 (R&D Systems):
For Flow cytometry isotype control antibodies was used. For immunohistoquemistry also we stained with an IgG control and antibody concentration was assessed.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	CHO cell line
Authentication	Cell line was used by Biovan company: Biovian facilities are EMA certified and FDA inspected for cGMP production of investigational and commercial products.
Mycoplasma contamination	Cell line was used by Biovan company: Biovian facilities are EMA certified and FDA inspected for cGMP production of investigational and commercial products.
Commonly misidentified lines (See ICLAC register)	Cell line was used by Biovan company: Biovian facilities are EMA certified and FDA inspected for cGMP production of investigational and commercial products.

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals	- Inbred 8-10 weeks wild type C57BL/6 male mice were purchased from Charles River UK. - C57BL/6 IL-6 receptor deficient mice (Il6ra-/-) mice were bred under approved UK Home Office guidelines in Cardiff University. Male mice were used for experiments at the age of 8-10 weeks. - Ptpn2fl/fl, Lck-Cre:Ptpn2fl/fl, and Ptpn22-/- mice were bred and housed at the Peter MacCallum Cancer Centre (Melbourne, Australia). All male mice were 8-12 weeks of age.
Wild animals	The study did not involve wild animals
Field-collected samples	The study did not involve samples collected from the field
Ethics oversight	Inbred wild type C57BL/6 male mice were purchased from Charles River UK. C57BL/6 IL-6 receptor deficient mice (Cd126-/-) mice have been described previously and were bred under approved UK Home Office guidelines in Cardiff University7. Ptpn2fl/fl, Lck-Cre:Ptpn2fl/fl, and Ptpn22-/- mice were bred and housed at the Peter MacCallum Cancer Centre (Melbourne, Australia). All procedures were performed in accordance with the NHMRC Australian Code of Practice for the Care and Use of Animals, and approved by the Peter MacCallum Animal Ethics and Experimentation Committee (Ethics number: AEEC 570). Antigen-induced arthritis was performed under the UK Home Office-approved project licences PPL 30/2928 and PB3E4EE13.

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

Human research participants

Policy information about studies involving human research participants

Population characteristics	- 3 healthy Caucasian male, age between 35-50 for Flow cytometry analysis. - 87 synovial samples were acquired through a minimally invasive US-guided synovial biopsy from patients presenting with early RA naïve to therapy from the Pathobiology of Early Arthritis Cohort (PEAC). Ethical approval was granted by the King's College Hospital Research Ethics Committee (REC 05/Q0703/198) for RNA - seq ans histology. The cohort has more females (80%) than males, this was not planned but is a reflection of the increased prevalence of rheumatoid arthritis in female (http://www.peac-mrc.mds.qmul.ac.uk/docs.php). All patients underwent ultrasound-guided synovial biopsy of an affected joint at baseline.

Sections of paraffin embedded RA synovial tissue were stained with standard Haematoxylin and Eosin (H&E) and graded as either a lymphoid, myeloid or fibroid phatotypes.

Recruitment

- Healthy male: request was circulated around the university for healthy participants
- Synovial samples: recruitment protocol from the Pathobiology of Early Arthritis Cohort (PEAC) (http://www.peac-mrc.mds.qmul.ac.uk/docs/RECRUITMENT%20-%20Protected.pdf). As described above, the cohort has more females (80%) than males due to the increased prevalence of rheumatoid arthritis in female; that could be a bias factor for the results.

Ethics oversight

Ethical approval was granted by the King's College Hospital Research Ethics Committee (REC 05/Q0703/198).

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

ChIP-seq

Data deposition

☒ Confirm that both raw and final processed data have been deposited in a public database such as GEO.

☒ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links
May remain private before publication.

Submitted to ArrayExpress - https://www.ebi.ac.uk/arrayexpress/experiments/E-MTAB-6273/

Username: Reviewer_E-MTAB-6273
Password: 7tBavowV

Files in database submission

BAM

S1.Nv.IL6.Input
S1.Nv.IL6.IP
S1.EM.IL6.Input
S1.EM.IL6.IP
S3.Nv.IL6.Input
S3.Nv.IL6.IP
S3.EM.IL6.Input
S3.EM.IL6.IP

Genome browser session
(e.g. UCSC)

http://www.ensembl.org/Mus_musculus/Gene/Summary?db=core;g=ENSMUSG00000004040;r=11:100885098-100939540

Log in: JonesSA@cardiff.ac.uk
Password: reviewer2018

Methodology

Replicates

One replicate per sample with the ChIP-qPCR validation (supplemental data) for each sample and ChIP (STAT1 and STAT3).
Samples were obtained after sorting and treated with IL-6 [20ng/ml] for 30 min:
Naive CD4 T-cells: S1.Nv.IL6.Input - S1.Nv.IL6.IP - S3.Nv.IL6.Input - S3.Nv.IL6.IP
Effector memory CD4 T-cells: S1.EM.IL6.Input - S1.EM.IL6.IP - S3.EM.IL6.Input - S3.EM.IL6.IP

Sequencing depth

Library preparation followed the manufacturer's recommended protocol (Ion ChIP-Seq Library Preparation on the Ion Proton System. Publication Number 4473623 (Revision B)).

For the amplification PCR we used as it is suggested:
Nick repair -72°C for 20 min
Denature - 95°C for 5 min
Cycling (18 cycles) - 97°C 15 sec, 60°C 15 sec and 70°C for 1 min
Holding - 70°C for 5 min and 4°C ∞

The sequencing coverage was the following:
Sample name - total reads - mapped reads - reads length (bp)
S1.Nv.IL6.Input - 75818935 - 71155423 - 169
S1.Nv.IL6.IP - 74584503 - 65458907 - 167
S3.Nv.IL6.Input - 48912438 - 48362832 - 154
S3.Nv.IL6.IP - 57492786 - 52997712 - 161
S1.EM.IL6.Input - 52430613 - 40704114 - 130
S1.EM.IL6.IP - 53318561 - 31330388 - 138
S3.EM.IL6.Input - 44336863 - 35004431 - 134
S3.EM.IL6.IP - 61400306 - 41996444 - 142

Antibodies

The antibodies used for ChIP-seq are:

Protein name / Supplier / Catalog number / Clone / Lot number
STAT1 / Santa Cruz Biotechnology / sc-592 / p84-p91/ K0414
STAT3 / Santa Cruz Biotechnology / sc-482 / C-20/ D1315

Both of them were validated in our laboratory by ChIP-qPCR (see supplemental material) but they have been used in many different laboratories for the same technique:

1. Iwata, S., et al. (2017). "The Transcription Factor T-bet Limits Amplification of Type I IFN Transcriptome and Circuitry in T Helper 1 Cells." Immunity 46(6): 983-991 e984.
2. Mahendrarajah, N., et al. (2017). "HSP90 is necessary for the ACK1-dependent phosphorylation of STAT1 and STAT3." Cell Signal 39: 9-17.
3. Hirahara, K., et al. (2015). "Asymmetric Action of STAT Transcription Factors Drives Transcriptional Outputs and Cytokine Specificity." Immunity 42(5): 877-889.
4. Nakayamada, S., et al. (2014). "Type I IFN induces binding of STAT1 to Bcl6: divergent roles of STAT family transcription factors in the T follicular helper cell genetic program." J Immunol 192(5): 2156-2166.
5. Hutchins, A. P., et al. (2012). "Genome-wide analysis of STAT3 binding in vivo predicts effectors of the anti-inflammatory response in macrophages." Blood 119(13): e110-119.

Peak calling parameters

HOMER: default parameters used

preprocessing
makeTagDirectory tag.dir rmdup.bam -format sam

peak finding
findPeaks tag.dir -style factor -o peaks.out -i tag.input -F 4 -P 0.0001 -fdr 0.05

catering for transcription factor binding, peak calling
-style factor
peak fold-enrichment (default value used 4)
-F 4
poisson p-value threshold (default value used 0.0001)
-P 0.0001
false discovery rate
-fdr 0.05

Data quality

Fold-enrichment = 4 (software published default value).
FDR = 0.05.
For these parameters, number of peaks called per condition:
S1.Nv.IL6.IP vs S1.Nv.IL6.Input = 2952
S1.EM.IL6.IP vs S1.EM.IL6.Input = 954
S3.Nv.IL6.IP vs S3.Nv.IL6.Input = 1056
S3.EM.IL6.IP vs S3.EM.IL6.Input = 1085

Software

Reads from the Ion Proton where mapped in situ using company-supplied software and default settings
bowtie2

Sequencing read quality assessment
fastqc

Duplicate read filtering
picard-tools MarkDuplicates
samtools

Duplicate read quality assessment
bamtools

bam to bigwig conversion for data visualisation
bedtools
bedGraphToBigWig

data visualisation
IGV

peaking calling
Homer findPeaks

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	Murine CD4 T-cells from total splenocytes were enriched by negative magnetic selection (Miltenyi Biotec) before purification of naïve (CD4+CD25−CD44loCD62LhiCD127hi), central memory (CD4+CD25−CD44hiCD62LhiCD127hi), effector (CD4+CD25 −CD44loCD62LloCD127lo-int) or effector memory (CD4+CD25−CD44hiCD62LloCD127int-hi) T-cells using a BD FACS ARIA II (BD Biosciences)
Instrument	BD FACS ARIA II (BD Biosciences) was used for sorting cells. After the experiments cells were acquired on a CyAn ADP analyzer (Beckman-Coulter) or BD FACS CANTO II (BD Biosciences)
Software	To collect the data we used Summit (software v4.3, Beckman-Coulter) or ImageStream imaging flow cytometer (Amnis). We analyzed the acquired samples with Summit using FlowJo 10 (TreeStar) and software IDEAS for the ImagStream samples.
Cell population abundance	We calculate the purity of our sorted populations running the samples after sorting. T-cell subset purity was >98%. Example of the purity strategy used is in the Supplementary information.
Gating strategy	1. FSC/SSC gates were used to selected live-lymphocyte population. 2. FSC-H/FSC-A was used to indicate the singlets. 3. CD4-PerCP-Cy5.5 positive vs CD25-PE negative cells were used from here to select CD4 Tcells. 4. Using the markers CD62L vs CD44 we were able to sort the 4 different populations: naïve: CD4+ CD25- CD44low CD62Lhigh central memory CD4+ CD25− CD44high CD62Lhigh effector CD4+ CD25− CD44low CD62Llow effector memory CD4+ CD25− CD44high CD62Llow An example of the gating used is in the Supplementary information

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