nature research

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Life Sciences Reporting Summary

Nature Research wishes to improve the reproducibility of the work we publish. This form is published with all life science papers and is intended to promote consistency and transparency in reporting. All life sciences submissions use this form; while some list items might not apply to an individual manuscript, all fields must be completed for clarity.

For further information on the points included in this form, see Reporting Life Sciences Research. For further information on Nature Research policies, including our data availability policy, see Authors & Referees and the Editorial Policy Checklist.

Experimental design

1. Sample size

   Describe how sample size was determined.

   Sample size to achieve adequate power was chosen based on our previous studies with similar methods.

   Described in material and method section (mice, page 17).

2. Data exclusions

   Describe any data exclusions.

   No exclusion of sample was done.

3. Replication

   Describe whether the experimental findings were reliably reproduced.

   All the experiment was repeated minimum twice and all attempts at replication were successful.

4. Randomization

   Describe how samples/organisms/participants were allocated into experimental groups.

   We randomized the mice from different cages and different time points to exclude cage or batch variation.

5. Blinding

   Describe whether the investigators were blinded to group allocation during data collection and/or analysis.

   Experiments and data analysis was performed without aforementioned genotype or treatment information.

Note: all studies involving animals and/or human research participants must disclose whether blinding and randomization were used.

6. Statistical parameters

   For all figures and tables that use statistical methods, confirm that the following items are present in relevant figure legends (or the Methods section if additional space is needed).

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement (animals, litters, cultures, etc.)
☐	☒	A description of how samples were collected, noting whether measurements were taken from distinct samples or whether the same sample was measured repeatedly.
☐	☒	A statement indicating how many times each experiment was replicated
☐	☒	The statistical test(s) used and whether they are one- or two-sided (note: only common tests should be described solely by name; more complex techniques should be described in the Methods section)
☒	☐	A description of any assumptions or corrections, such as an adjustment for multiple comparisons
☐	☒	The test results (e.g. *p* values) given as exact values whenever possible and with confidence intervals noted
☐	☒	A summary of the descriptive statistics, including central tendency (e.g. median, mean) and variation (e.g. standard deviation, interquartile range)
☐	☒	Clearly defined error bars

See the web collection on statistics for biologists for further resources and guidance.

Software

Policy information about availability of computer code

7. Software

Describe the software used to analyze the data in this study.	GraphPad Prism 5 was used for statistical analysis. FlowJo v.10.0.8 was used for flow cytometry analysis. MiXCR and CD-HIT software packages were used for sequencing. Bio-Plex manager software was used for cytokine analysis.

For all studies, we encourage code deposition in a community repository (e.g. GitHub). Authors must make computer code available to editors and reviewers upon request. The *Nature Methods* guidance for providing algorithms and software for publication may be useful for any submission.

Materials and reagents

Policy information about availability of materials

8. Materials availability

Indicate whether there are restrictions on availability of unique materials or if these materials are only available for distribution by a for-profit company.	NGS data was deposited at BioProject under the accession numbers SAMN06927868-77. All other materials are available commercially as described. Cathepsin s inhibitor, RO5461111. RO5461111 is only available from Hoffman La-Roche.

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).	We used antibodies which were validated from published database (multiple publications from independent groups). anti-STAT3: 124H6, Cell Signaling anti-BLIMP-1:sc-13206, Santa Cruz anti-p10: cat#HAF016, R&D Systems anti-Actin: mAbcam8226, Abcam anti-mouse IgG AF488: Cat#1010-30, Sourthen Biotech anti-CXCR5: J252D4, Biolegend anti-PD1:EF12.2H7, Biolegend anti-CD4:GK1.5, BDPharmingen anti-TCRb: H57-597, BDPharmingen anti-CD11c:N418, eBioscience anti-CD8a:53-6.7, Biolegend anti-MHC II:M5/114.15.2, eBioscience anti-SiglecH:eBio440c, eBioscience anti-CD3: 17A2, Biolegend anti-CD44:IM7, Biolegend anti-CD62L: MEL-14, Biolegend anti-B220: RA3-6B2, eBioscience anti-GL7: Cat# 553666, BDPharmingen anti-CD138: 281-2, BDPharmingen anti-ICOS1: C398.4A, Biolegend anti-BCL6: BCL-DWN, eBioscience anti-IL-2: JES6-5H4, Biolegend IL-21R-Fc: Cat# 991-R2, R&D System anti-IL-6: MP5-20F3, eBioscience

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.	HEK293 purchased from ATCC
b. Describe the method of cell line authentication used.	Authenticated by ATCC.
c. Report whether the cell lines were tested for mycoplasma contamination.	not tested since we used newly purchased cell line.
d. If any of the cell lines used in the paper are listed in the database of commonly misidentified cell lines maintained by ICLAC, provide a scientific rationale for their use.	No commonly misidentified cell line was used.

Animals and human research participants

Policy information about studies involving animals; when reporting animal research, follow the ARRIVE guidelines

11. Description of research animals

Provide details on animals and/or animal-derived materials used in the study.

Blimp-1 flox/flox; Cre-Tg and IL-6 +/-; Blimp-1 flox/flox; Cre-Tg mice are on C57BL/6 genetic background, both female and male, from 6 weeks old through 8 month old. (page 17)

Policy information about studies involving human research participants

12. Description of human research participants

Describe the covariate-relevant population characteristics of the human research participants.

IRB approval number is provided in Material and Method (page 17). Both female and male (hormonally active, age 55 and younger) individuals were included. Participants were genotyped and registered in the Genotype and Phenotype Registry at The Feinstein Institute for Medical Research. Any genotyped individuals with chronic inflammatory disorders, cancers or under hormonal therapy were excluded.

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Flow Cytometry Reporting Summary

Form fields will expand as needed. Please do not leave fields blank.

Data presentation

For all flow cytometry data, confirm that:

☒ 1. The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

☒ 2. 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).

☒ 3. All plots are contour plots with outliers or pseudocolor plots.

☒ 4. A numerical value for number of cells or percentage (with statistics) is provided.

Methodological details

5. Describe the sample preparation.	For blood samples (Fig. 1C), mouse blood was obtained and PBMCs were prepared by Ficoll gradient centrifugation. For samples from spleen (Fig. 5A, Fig. 6B, Fig. 7A-B, and Supplementary Fig. 4), splenocytes were prepared by through nylon mash and RBCs were removed (RBC lysing buffer). In vitro stimulated cells (Fig. 2D and Fig. 4A) were collected after stimulation. All the staining was performed in immediately after collection in ice-cold staining buffer. Dead cells were excluded by live-dead staining.
6. Identify the instrument used for data collection.	BD LSRII new (7-3-2-2)
7. Describe the software used to collect and analyze the flow cytometry data.	FACSDiva software was used for data collection and FlowJo software v.10.0.8 was used for analyses.
8. Describe the abundance of the relevant cell populations within post-sort fractions.	FACSAria instrument was used for cell sorting. Purity of post-sorted samples was 90-95% for all samples. Abundance of population is variable depending on samples; 50,000 for Fig 1C, 1-2 millions for Fig.2D, 0.1-0.2 millions of cells for Fig. 5B and Fig. 7D.
9. Describe the gating strategy used.	All the samples was analyzed from live cell population except the case of intracellular staining (Fig. 4c). Positive and negative population was defined by isotype control staining. Specific gating strategies which were used: Fig.1C (from the live cells, lineage markers negative, and CD11chiMHCIIhi cells, Fig. 2B,D (from live cells, GFP-positive population was defined by null transfected GFP negative cells), Fig 4A (T alone without stimulation was defined as a positive population and CFSE-unlabelled T cells was used as a negative population), Fig. 4C (unstimulated T cells stained with IL-2 and IL-21 was one negative control and stimulated T cells stained with isotype controls was another negative control), Fig. 4D (DC cultured with unlabeled OVA was a negative control), Fig 5A (for BCL-6 intracellular staining, isotype control staining was a negative control, otherwise all other gating strategy is described in the figure), Fig. 6B (for B and T cell, lymphocyte population was

defined from FSC/SSC gating, otherwise specific gating strategies are described in the figure), Fig. 7A (cells were analyzed from lymphocyte gating defined by FSC/SSC gating), Fig. 7B-C (broad lymphocyte gating was applied to include plasmablast).

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