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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	Illumina Basespace; RTA (Illumina, version 1.17); bcl2fastq2 (version 2.17);
Data analysis	MATLAB (R2017b); IGV (version 2.4.10); hisat2 (version 2.1.0); StringTie (version 1.3.3b); bowtie2 (version 2.2.9); MACS2 (version 2.1.3); Barcode Splitter (version 0.18.0); Cutadapt (version 2.5); Circos (version 0.69-6); fastqc (version 0.11.5); Transloc Pipeline (version NA); featureCount (version 1.5.3); Picard MarkDuplicates (version 2.10.3); Juicer (version 1.5.6); Juicebox (version 1.11). Flow cytometry data were acquired using FACSDiva or BD Accuri C6 Plus Software and analyzed using FlowJo.

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

All sequencing data were deposited in NCBI Bioproject PRJNA544488

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 calculation was not performed, sample sizes were chosen according to previous publications.
Data exclusions	Data were not excluded from analyses.
Replication	All our attempts were reproducible, with similar trends. We used at least two independent biological replicates per experiments.
Randomization	Pairs of mice (littermates) were chosen randomly. Randomization was not used for molecular analyses.
Blinding	This project did not required blind experimentations or analyzes for our conclusions.

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

For flow cytometry we used:
Fc block BD Biosciences 553142 2.4G2
GL7 BD Biosciences 561530 GL7
anti-B220 BD Biosciences 557683 RA3-6B2
anti-IgG1 BD Biosciences 550083 A85-1
For ChIP experiments we used:
anti-CTCF Abcam ab70303 Rabbit polyclonal
anti-Rad21 Abcam ab992 Rabbit polyclonal
anti-RNA pol II S5 ab5131 Rabbit polyclonal
IgG control Abcam ab171870 Rabbit polyclonal
For DRIP experiments we used:
S9.6 Kerafast ENH001

Validation

These commercial antibodies are validated by the suppliers, see comments found on their websites:
GL7: Application Flow cytometry (Routinely Tested)
anti-B220: Application Flow cytometry (Routinely Tested)
anti-IgG1: Application Flow cytometry (Routinely Tested)
Flow cytometry antibodies are commonly used by many investigators, have been previously validated in our lab and we used various negative controls (non-B cells for anti-B220, resting cells for anti-IgG1 and GL7).
For ChIP these commercial antibodies are validated by the supplier, see comments found on their websites:
anti-CTCF: Tested applications Suitable for: IHC-Fr, WB, IP, IHC-P
anti-RNA pol II S5: Tested applications Suitable for: WB, ChIP, ICC/IF
anti-RAD21: Published in many articles, including this one: Nature. 2017 November 02; 551(7678): 51–56. doi:10.1038
IgG isotype control was used as control for ChIP experiments.
For DRIP this commercial antibody has been published by many groups, including these articles:

Chromatin Immunoprecipitation (ChIP) Analysis: Bhatia, V., et al. (2014). Nature. 511(7509):362-365; Skourti-Stathaki, K., et al. (2011). Mol. Cell. 42(6):794-805; El Hage, A., et al. (2014). PLoS Genet. 10(10):e1004716.
RNase H treatment was used as control for DRIP experiments as control.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	We generated Abelson cell lines from Exosc3 COIN mice. Plat-E cells are commercially available (Cell Biolabs, Inc).
Authentication	We validated the presence of the Exosc3 COIN alleles by PCR and GFP expression after tamoxifen treatment. Plat-E cells were not authenticated directly, but indirectly by their potential to produce retrovirus used to generate the Abelson cell lines, which was successful.
Mycoplasma contamination	Not tested.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used in this study.

Animals and other organisms

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

Laboratory animals	We used mouse models (mus musculus) from C57BL/6 genetic background, male or female littermates, 6 to 12 weeks-old.
Wild animals	This study did not involve wild animals.
Field-collected samples	No field-collected samples were used in this study.
Ethics oversight	All mouse experiments were approved by the IACUC of Columbia University.

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.*	https://www.ncbi.nlm.nih.gov/bioproject/544488 http://52.20.87.23/public/Dis3_project/
Files in database submission	ChIP-seq data for CTCF and RAD21; Hi-C data; LAM-HTGTS data; RNA-sequencing data; DRIP-seq data
Genome browser session (e.g. UCSC)	No longer applicable.

Methodology

Replicates	ChIP were performed from 2 independent B cell stimulations with similar results.
Sequencing depth	Dis3 Het CTCF 1: Total number of reads: 277269112; uniquely mapped reads: 181363235; length of reads: 75; paired-end; Dis3 CC CTCF 1: Total number of reads: 323080414; uniquely mapped reads: 202822439; length of reads: 75; paired-end; Dis3 Het CTCF 2: Total number of reads: 108537202; uniquely mapped reads: 78254424; length of reads: 75; paired-end; Dis3 CC CTCF 2: Total number of reads: 139114676; uniquely mapped reads: 92826574; length of reads: 75; paired-end; Dis3 Het Rad21 1: Total number of reads: 177074158; uniquely mapped reads: 114990944; length of reads: 75; paired-end; Dis3 CC Rad21 1: Total number of reads: 213033106; uniquely mapped reads: 139331414; length of reads: 75; paired-end; Dis3 Het Rad21 2: Total number of reads: 154156806; uniquely mapped reads: 33511956; length of reads: 38; paired-end; Dis3 CC Rad21 2: Total number of reads: 107569862; uniquely mapped reads: 21304281; length of reads: 38; paired-end;
Antibodies	anti-CTCF Abcam ab70303 Rabbit polyclonal anti-Rad21 Abcam ab992 Rabbit polyclonal IgG control Abcam ab171870 Rabbit polyclonal
Peak calling parameters	-f BAMPE -g mm -q 0.05
Data quality	IgG control samples and public ChIPseq data were used to evaluate the data quality.
Software	Illumina Basespace; MATLAB (R2017b); IGV (version 2.4.10); bowtie2 (version 2.2.9); MACS2 (version 2.1.3); Cutadapt (version 2.5); featureCount (version 1.5.3); Picard MarkDuplicates (version 2.10.3).

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	Primary B cells were collected from Peyer's patches or spleen. Splenocytes were depleted from CD43+ cells using MACS beads and columns, and activated in vitro. Then cells were washed in PBS, resuspended in FACS buffer (PBS with 2% FBS) containing Fc block (clone 2.4G2, BD Biosciences) for 5 mins at room temperature, and then incubated for 30 mins at 4°C with antibodies , washed in cold PBS and resuspended in FACS buffer for analysis or complete media for cell sorting.
Instrument	Cells were analyzed on a BD LSR Fortessa or BD Accuri C6 Plus. Cell sorting was done using BD FACS Aria II or Bio-Rad S3e cell sorters.
Software	BD FACSDiva™ Software and BD Accuri™ C6 Plus Software were used for data aquisition. FACS data were analyzed using FlowJO.
Cell population abundance	About 50,000 germinal center cells were obtained post-sorting. We validated the quality of these experiments by analyzing RNA-sequencing data (including germinal center markers).
Gating strategy	Lymphocytes (FSC/SSC gate) were analyzed as singlet cells (FSC-A/FSC-H gate), live cells (using either the dead cell exclusion dye 7AAD or DAPI from BD Biosciences) and then as B220+ and GL7+ for germinal center B cells, and GFP+ for our Dis3 reporter system (Fig. 2a).

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