

Supplementary information

HnRNP A1 and A2B1 enforce *Ezh2* mRNA splicing to promote germinal center B cell responses

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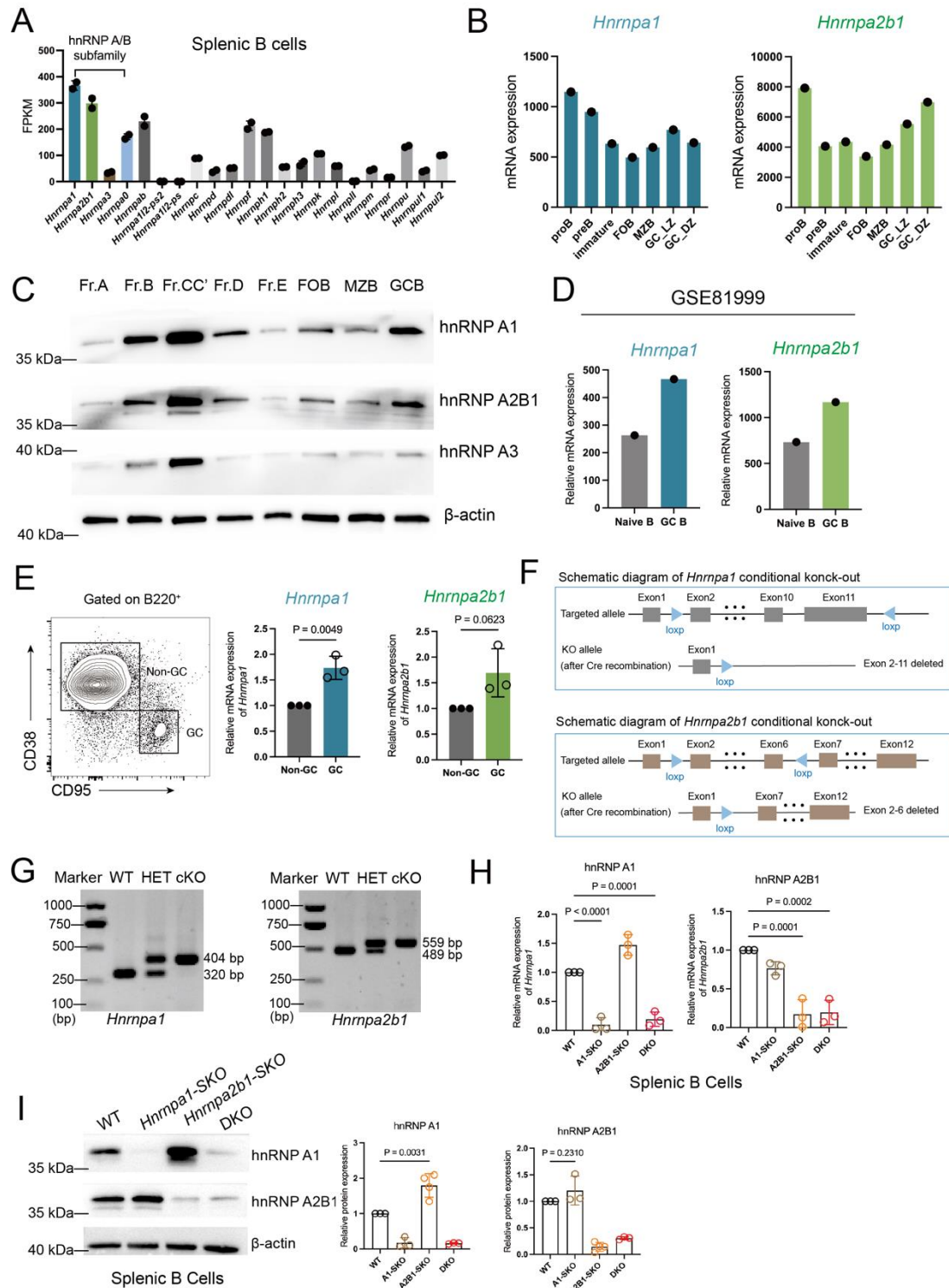
Supplementary Table 1

List of reagents and resources used in this study

Supplementary Table 2

Primer sequences used in this study

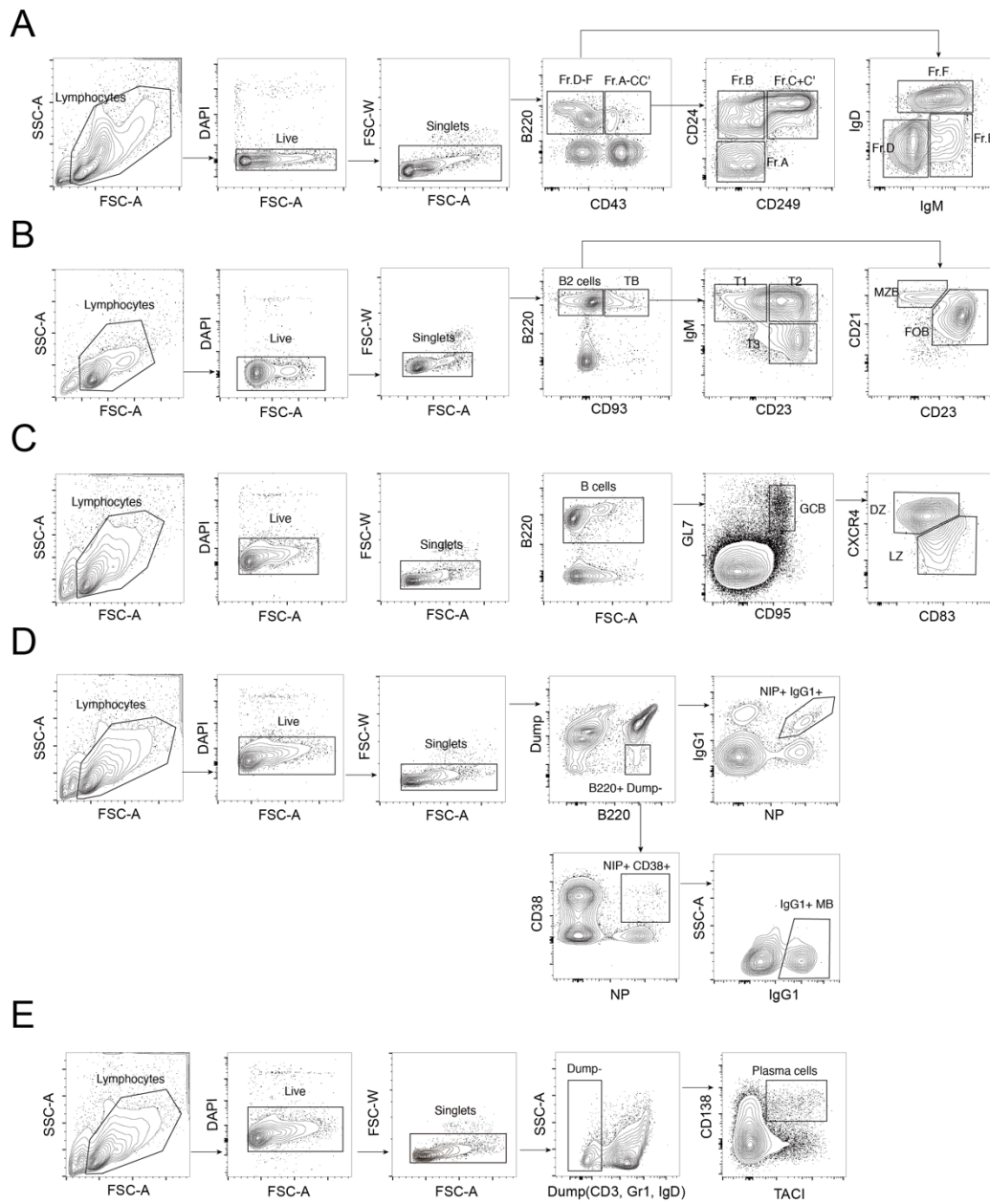
Supplementary Figure 1 (Supplementary Fig. 1)



Supplementary Figure 1. Construction and validation of *Hnmpa1* and *Hnmpa2b1* conditional knockout mice. **A** RNA expression profiles of hnRNP family members in wild-type naïve B cells, based on RNA-seq analysis ($n = 2$). **B** Expression patterns of hnRNP A1 and A2B1 across various B cell populations, derived from RNA-seq datasets in the Immunological Genome Project. **C** Protein expression profiles of hnRNP A1, A2B1, and A3 in

B cell subsets at different developmental stages. Representative results from two independent experiments are shown. **D** Histogram comparing *Hnrnpa1* and *Hnrnpa2b1* expression levels between naïve B cells and Germinal center (GC) B cells, based on data from the dataset GSE81999. **E** qRT-PCR analysis of *Hnrnpa1* and *Hnrnpa2b1* expression in flow cytometry-sorted non-GC and GC B cells ($n = 3$). **F** Schematic diagram illustrating the loxP-based conditional knockout strategy. loxP sites were inserted flanking exon 2 and exon 11 of *Hnrnpa1*, and exons 2–6 of *Hnrnpa2b1*. Conditional knockout mice were generated by crossing floxed lines with *Cd19^{cre/+}* mice, enabling gene deletion from the pro-B cell stage. **G** RT-PCR validation of loxP site insertion in *Hnrnpa1* and *Hnrnpa2b1* alleles. The data shown are representative images from two independent experiments. **H** qRT-PCR analysis showing efficient depletion of *Hnrnpa1* and *Hnrnpa2b1* transcripts in single knockout (SKO: hnRNP A1-SKO and hnRNP A2B1-SKO) and double knockout (DKO) B cells compared to WT ($n = 3$). Data are pooled from three independent experiments. Each dot represents an individual mouse. $p < 0.0001$ (hnRNP A1: WT vs A1-SKO = 5.30×10^{-5}). **I** Western blot validation of the knockout efficiency of hnRNP A1 and hnRNP A2B1 proteins in splenic CD19⁺ B cells from WT, SKO, and DKO mice. The right panel shows densitometric quantification; protein levels were normalized to the β -actin loading control and expressed as fold change relative to the WT group (WT, A1-SKO, DKO $n = 3$; A2B1-SKO: $n = 4$). Data are representative of two independent experiments (left panels); Right: densitometric quantification of protein levels normalized to β -actin. All data are presented as mean $\pm$ SEM and are pooled from three independent experiments (**E**, **H**, **I**). Statistical significance was determined using an unpaired two-tailed Student's *t*-test (**E**) or one-way ANOVA followed by Tukey's multiple comparisons test (**H**, **I**).

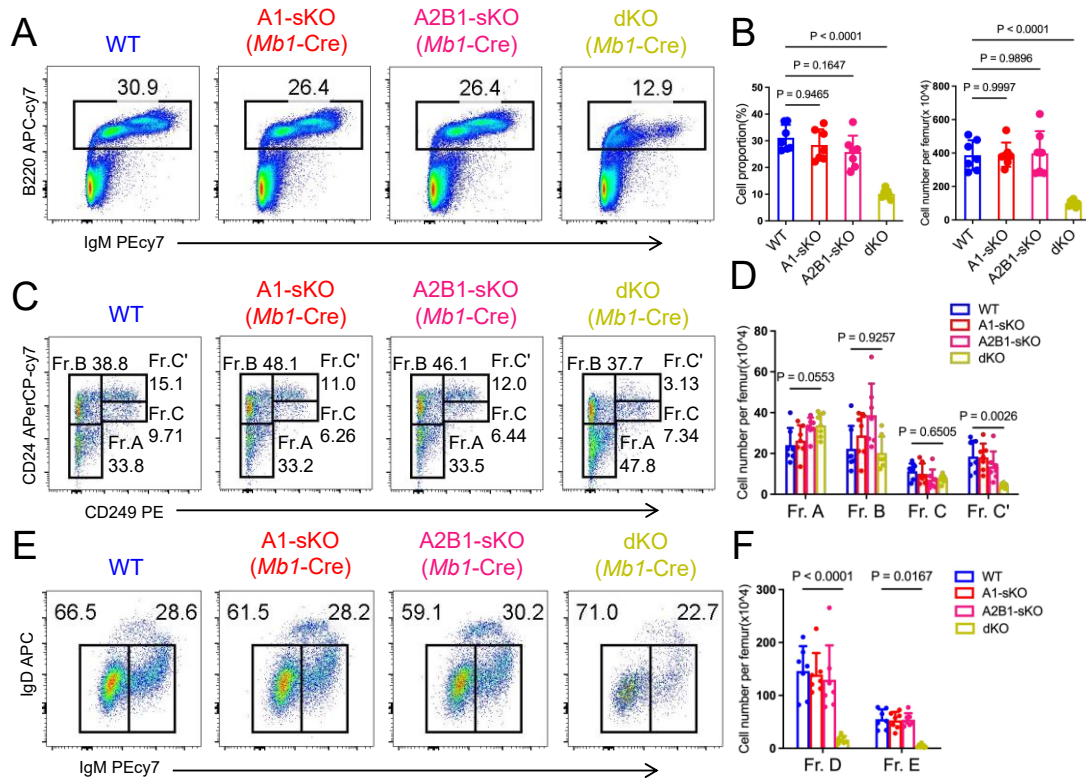
Supplementary Figure 2 (Supplementary Fig. 2)



Supplementary Figure 2. Gating strategies. **A** Gating strategy for different developmental stages of B cells in the bone marrow. Various B cell subsets in the bone marrow of *Hnrnpa1^{ff} Hnrnpa2b1^{ff}* (WT), *Hnrnpa1^{ff} Cd19^{Cre/+}* (A1-SKO), *Hnrnpa2b1^{ff} Cd19^{Cre/+}* (A2B1-SKO), and *Hnrnpa1^{ff}Hnrnpa2b1^{ff} Cd19^{Cre/+}* (DKO, double knockout) mice were analyzed based on Hardy's gating strategy. This gating strategy corresponds to the data presented in Fig. 1A, 1C, 1E and Supplementary Fig. 3A, 3C, 3E. **B** Gating strategy for different development stages of B cells in spleen. This gating strategy corresponds to the data presented in Fig. 1G and 1I. **C** Gating strategy for germinal center (GC), LZ (Light Zone), and DZ (Dark Zone) B cells. GC: B220⁺ CD38⁻ CD95⁺ GL7⁺; LZ: B220⁺ CD38⁻ CD95⁺ GL7⁺ CD83^{high} CXCR4^{low}; DZ: B220⁺ CD38⁻ CD95⁺ GL7⁺ CD83^{low} CXCR4^{high}. This gating strategy was applied to: GC B cell subset analysis, BCL6 expression, and proliferation analysis in Fig. 3A, 3I, 3K, 3M and Fig. 7A, 7D; GC B cell sorting in Supplementary Fig. 1C, Supplementary Fig. 1E; proliferation and apoptosis analysis

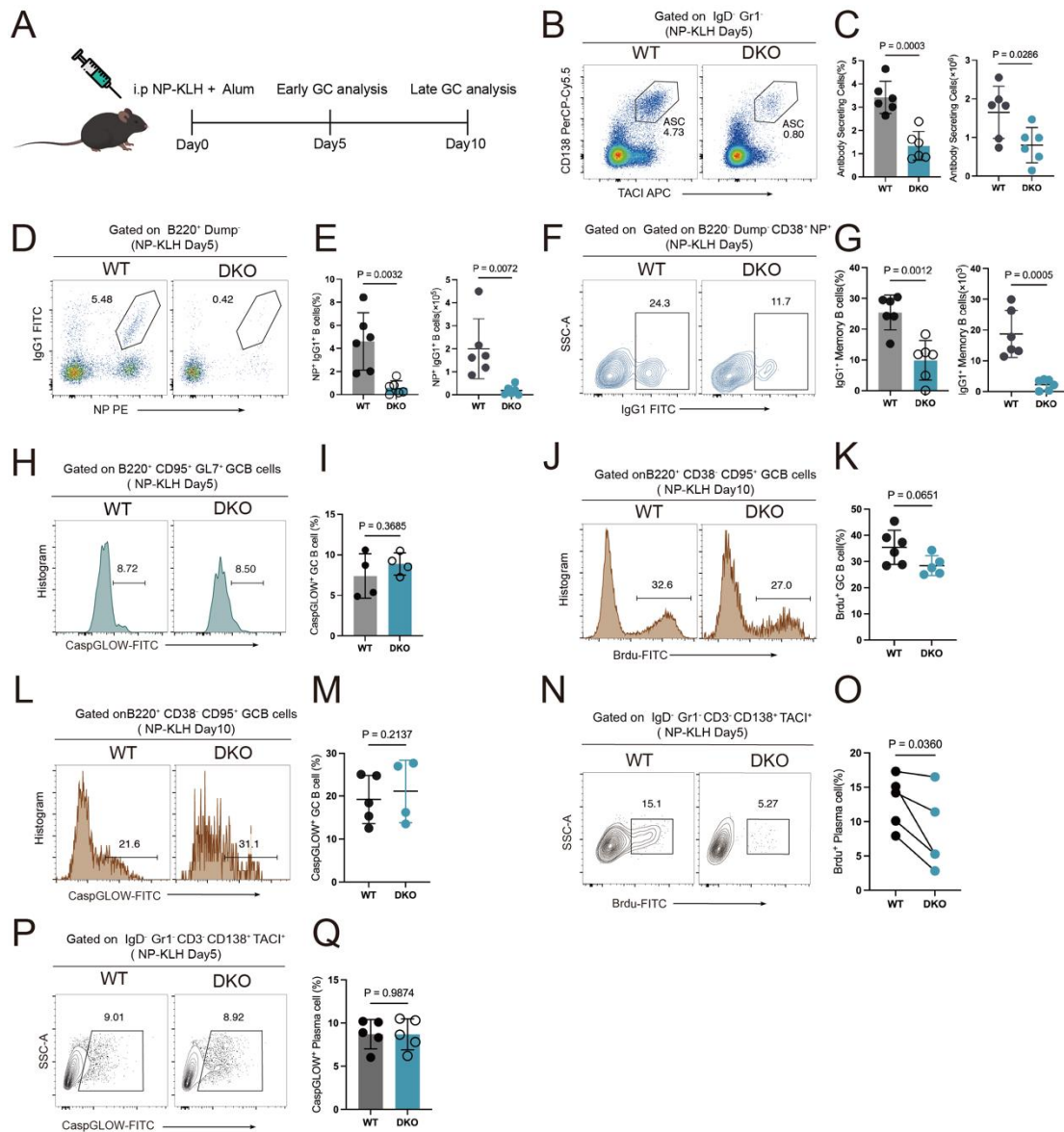
of GC B cells in Supplementary Fig. 4H, 4J, 4L; GC B cell sorting in Supplementary Fig. 5F, 5G; and GC B cell analysis and sorting in Supplementary Fig. 8A, 8C, 8D. **D** Gating strategy for NP⁺ IgG1⁺ B cells and CD38⁺ Memory B cells. Dump: IgM, IgD, CD3, Gr1 and CD138. This gating strategy corresponds to memory B cell and NP⁺ IgG1⁺ B cell analysis at day 10 post NP-KLH immunization in Fig. 3C, 3E; and at day 5 post NP-KLH immunization in Supplementary Fig. 4D, 4F. **E** Gating strategy for CD138⁺ TACI⁺ plasma cells. Dump: IgD, CD3 and Gr1. This gating strategy corresponds to plasma cell analysis at day 10 post NP-KLH immunization in Fig. 3G; and plasmablast proliferation and apoptosis analysis at day 5 post NP-KLH immunization in Supplementary Fig. 4B, 4N, 4P.

Supplementary Figure 3 (Supplementary Fig. 3)



Supplementary Figure 3. B cell development is impaired in Mb1-Cre-mediated hnRNP A1/A2B1 double knockout mice. **A–B** Representative flow cytometry plots (A) and quantification (B) of the proportion and number of total B cells in the bone marrow of WT, A1-sKO (*Hnrnpa1^{ff} Mb1^{Cre/+}*), A2B1-sKO (*Hnrnpa2b1^{ff} Mb1^{Cre/+}*), and dKO (*Hnrnpa1^{ff} Hnrnpa2b1^{ff} Mb1^{Cre/+}*) mice ($n = 7$). $p < 0.0001$ (Cell proportion: WT vs dKO = $1.10\text{e-}7$; Cell number: WT vs dKO = $7.78\text{e-}6$). **C–D** Representative flow cytometry plots (C) and quantification (D) of Fr. A–C' B cells in the bone marrow of WT, A1-sKO, A2B1-sKO, and dKO mice ($n = 7$). **E–F** Representative flow cytometry plots (E) and quantification (F) of Fr. D–E B cells in the bone marrow of WT, A1-sKO, A2B1-sKO, and dKO mice ($n = 7$). $p < 0.0001$ (Fr. D Cell proportion: WT vs dKO = $7.80\text{e-}9$). Each dot represents an individual mouse (**B**, **D**, **F**). Absolute cell numbers were calculated based on total cell counts obtained from a single mouse femur (**B**, **D**, **F**). Data are presented as mean $\pm$ SEM and are pooled from three independent experiments (**B**, **D**, **F**). Statistical significance was determined using one-way ANOVA followed by Dunnett's multiple comparisons test (**B**) or two-way ANOVA followed by Dunnett's multiple comparisons test (**D** and **F**).

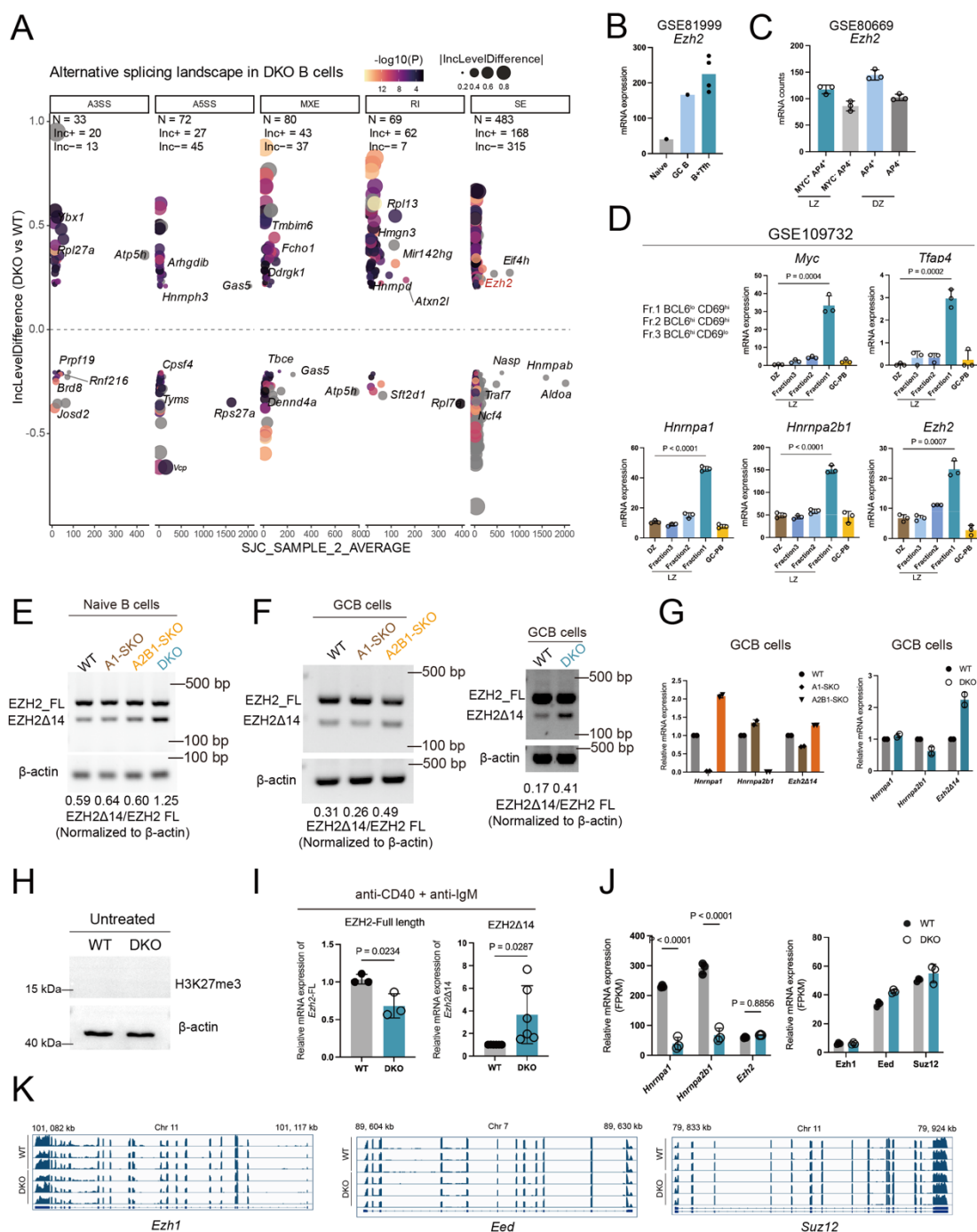
Supplementary Figure 4 (Supplementary Fig. 4)



Supplementary Figure 4. Early GC formation depends on hnRNP A1 and A2B1. **A** Schematic diagram of the immunization protocol. Mice were intraperitoneally injected with NP-KLH/Alum. **B–C** Representative flow cytometry plots (**B**) and quantification (**C**) of the proportion and number of antibody-secreting cells in the spleen days 5 post NP-KLH/Alum immunization ($n = 6$). **D–E** Representative flow cytometry plots (**D**) and quantification (**E**) of the proportion and number of NP-specific class-switched B cells in the spleen on day 5 post NP-KLH/Alum immunization ($n = 6$). **F–G** Representative flow cytometry plots (**F**) and quantification (**G**) of the proportion and number of IgG1⁺ memory B cells in the spleen on day 5 post-immunization ($n = 6$). **H–I** Representative flow cytometry plots (**H**) and quantification (**I**) showing the proportion of CaspGLOW⁺ apoptotic germinal center (GC) B cells in *Hnnrnpa1^{fl/fl} Hnnrnpa2b1^{fl/fl}* (WT) and *Hnnrnpa1^{fl/fl} Hnnrnpa2b1^{fl/fl} Cd19^{Cre/+}* (DKO, double knockout) mice day 5 post NP-KLH/Alum immunization ($n = 4$). **J–K** Representative flow cytometry plots (**J**) and quantification (**K**) of BrdU⁺ GC B cells from spleens of WT and DKO mice 10 days after

NP-KLH/Alum immunization (WT: $n = 6$; DKO: $n = 5$). **L–M** Representative flow cytometry plots (**L**) and quantification (**M**) of CaspGLOW⁺ GC B cells from spleens of WT and DKO mice 10 days after NP-KLH/Alum immunization (WT: $n = 5$; DKO: $n = 4$). **N–O** Representative flow cytometry plots (**N**) and quantification (**O**) of BrdU⁺ plasmablasts in the spleens of WT and DKO mice on day 5 after NP-KLH/Alum immunization ($n = 5$). **P–Q** Representative flow cytometry plots (**P**) and quantification (**Q**) of CaspGLOW⁺ plasmablasts in the spleens of WT and DKO mice on day 5 after NP-KLH/Alum immunization ($n = 5$). Each dot represents an individual mouse (**C, E, G, I, K, M, O, Q**). Data are presented as mean $\pm$ SEM. Data are pooled from two independent experiments (**I, O, Q**) or from three independent experiments (**C, E, G, K, M**). Statistical significance was determined using an unpaired two-tailed Student's *t*-test (**C, E, G, I, K, M, Q**) or paired two-tailed Student's *t*-test (**O**).

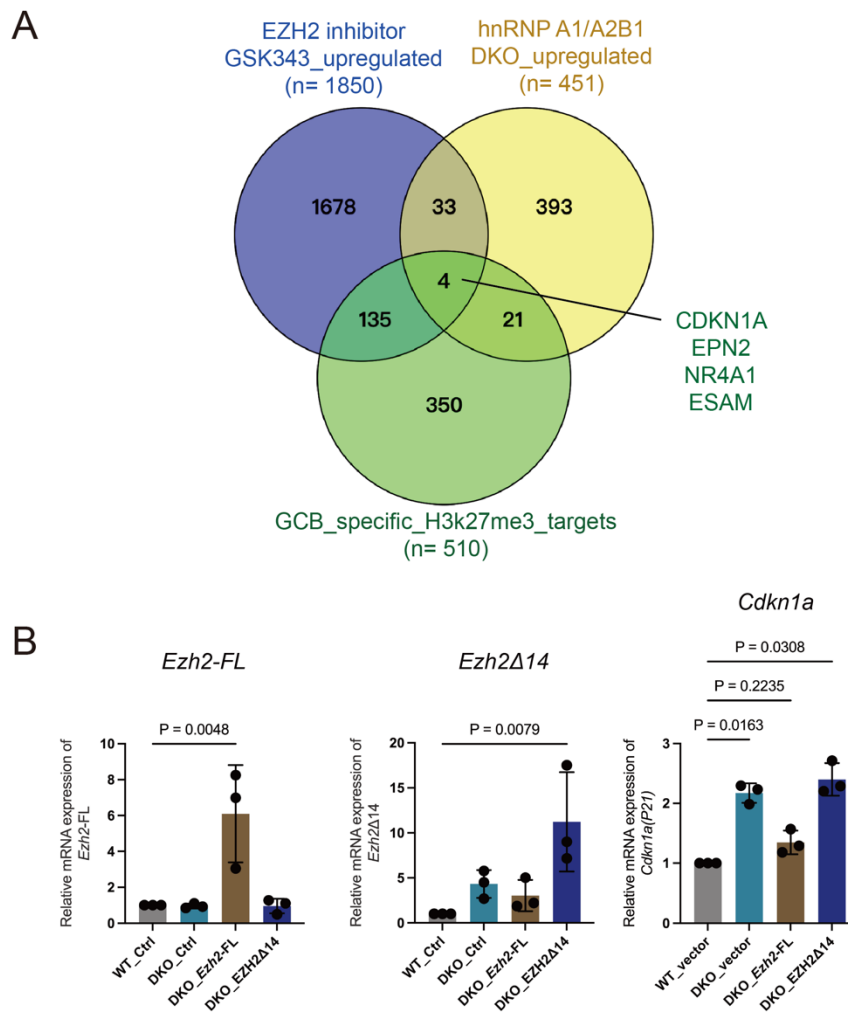
Supplementary Figure 5 (Supplementary Fig. 5)



Supplementary Figure 5. hnRNP A1/A2B1 knockout does not alter the expression or alternative splicing of other PRC2 components. **A** Bubble plots were generated for significantly altered genes across multiple types of alternative splicing events based on the following filtering criteria: $|\text{inclusion level difference}| > 20\%$, $P < 0.05$, and skipping junction counts (SJC) > 10 . The x-axis represents SJC_SAMPLE2_AVERAGE, denoting the average skipping junction counts in the DKO group, where higher values indicate more pronounced splicing changes. The y-axis represents the inclusion level difference, with larger values reflecting greater alterations in exon inclusion. Bubble size corresponds to the absolute value

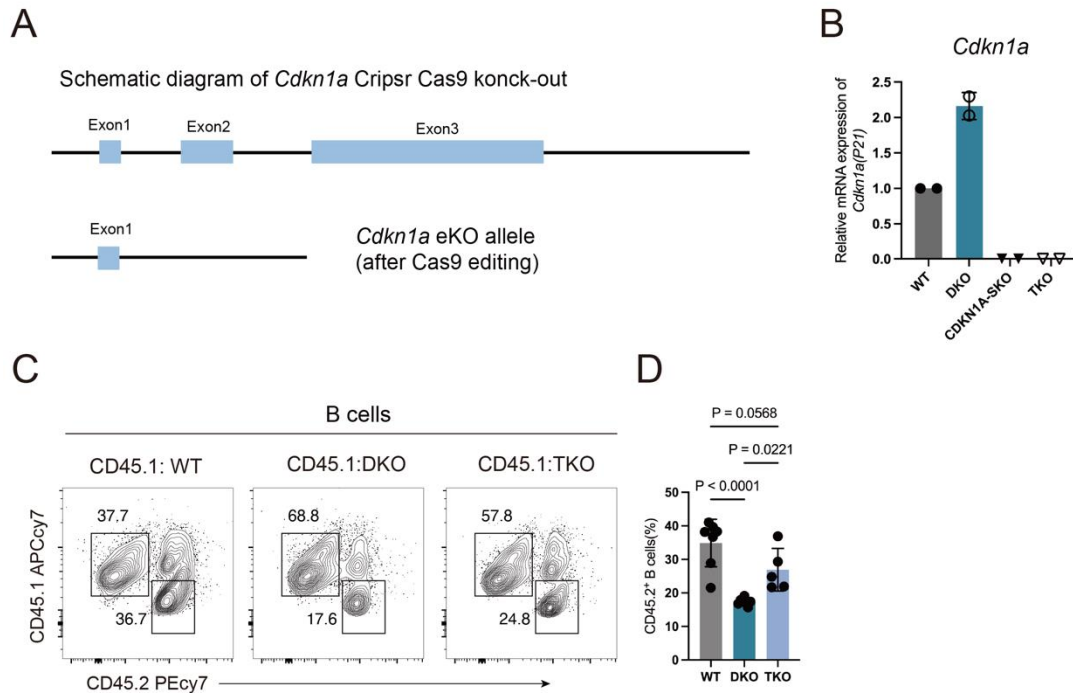
of the inclusion level difference, while bubble color represents the P-value. **B** Expression levels of *Ezh2* in naïve B cells, germinal center (GC) B cells, and T follicular helper (Tfh)-GC B cell co-cultured cells, derived from RNA-seq dataset GSE81999. **C** *Ezh2* expression patterns across various B cell subsets from dataset GSE80669. **D** RNA expression levels of *Myc*, *Tfap4*, *Hnrnpa1*, *Hnrnpa2b1*, and *Ezh2* in distinct GC B cell subsets (Fraction 1: Bcl6^{low} CD69^{high}; Fraction 2: Bcl6^{high} CD69^{high}; Fraction 3: Bcl6^{high} CD69^{low}) based on dataset GSE109732. $p < 0.0001$ (*Hnrnpa1*: DZ vs Fraction 1 = 5.42e-6; *Hnrnpa2b1*: DZ vs Fraction 1 = 6.44e-5). **E** Semi-quantitative RT-PCR analysis of *Ezh2* exon 14 splicing in splenic CD19⁺ B cells isolated from *Hnrnpa1^{ff} Hnrnpa2b1^{ff}* (WT), *Hnrnpa1^{ff} Cd19^{Cre/+}* (A1-SKO), *Hnrnpa2b1^{ff} Cd19^{Cre/+}* (A2B1-SKO), and *Hnrnpa1^{ff} Hnrnpa2b1^{ff} Cd19^{Cre/+}* (DKO, double knockout) mice. Data are representative of two independent experiments. **F** Semi-quantitative PCR analysis of *Ezh2* alternative splicing in GC B cells from WT, A1-SKO, A2B1-SKO, and DKO mice day 7 post NP-KLH/Alum immunization. The gel image shows the relative abundance of *Ezh2*Δ14 and *Ezh2*-FL isoforms. Data are representative of two independent experiments. **G** qRT-PCR analysis of RNA expression levels of *Hnrnpa1*, *Hnrnpa2b1*, and *Ezh2*Δ14 in germinal center B cells from WT, A1-SKO, A2B1-SKO, and DKO mice day 7 post NP-KLH/Alum immunization ($n = 2$). **H** B cells from the spleens of WT and DKO mice were analyzed for H3K27me3 expression by immunoblot. Data are representative of two independent experiments. **I** qRT-PCR using isoform-specific primers to detect the expression levels of *Ezh2*Δ14 and *Ezh2*-FL in B cells from WT and DKO mice after 48 hours of stimulation with anti-CD40 (1 μg/ml) and anti-IgM (2 μg/ml) (*Ezh2*-FL: $n = 3$; *Ezh2*Δ14: $n = 6$). **J** RNA-seq quantification of *Hnrnpa1*, *Hnrnpa2b1*, and PRC2 core components (*Ezh2*, *Ezh1*, *Eed*, *Suz12*) in unstimulated B cells from WT and DKO mice ($n = 3$). $p < 0.0001$ (*Hnrnpa1*: 7.04e-9; *Hnrnpa2b1*: 1.11e-9). **K** RNA-seq-based alternative splicing analysis of *Ezh1*, *Eed*, and *Suz12* in unstimulated WT and DKO B cells ($n = 3$). Data are presented as mean ± SEM. Data are pooled from two independent experiments (**G**, **J**). Data are pooled from at least three independent experiments (**I**). Statistical significance was determined using an unpaired two-tailed Student's *t*-test (**D**, **I**) or two-way ANOVA followed by Sidak's multiple comparisons test (**J**).

Supplementary Figure 6 (Supplementary Fig. 6)



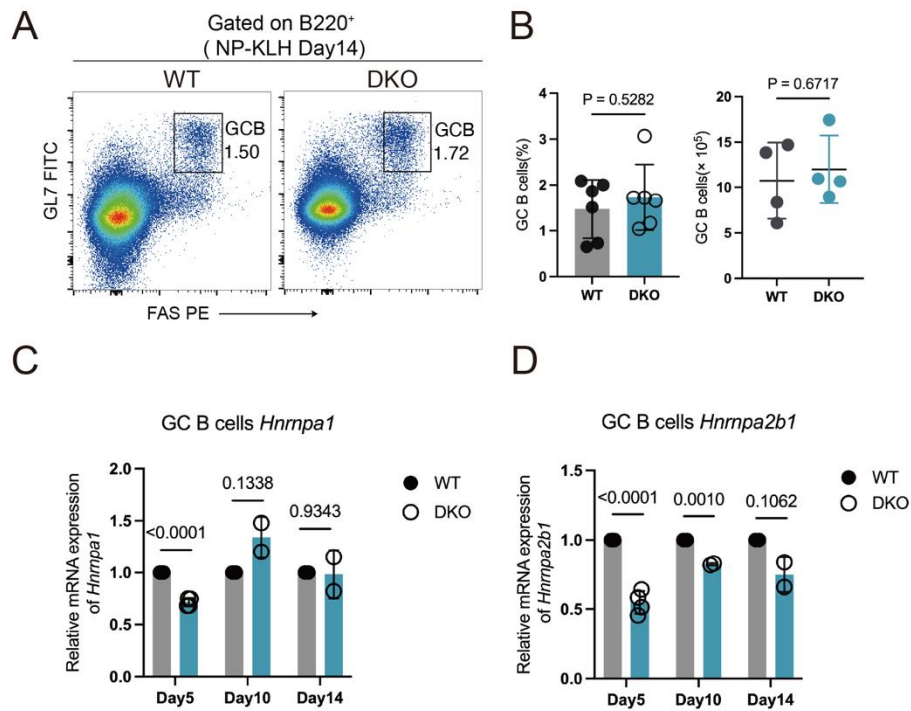
Supplementary Figure 6. *Cdkn1a* is a potential downstream target of the hnRNP A1/A2B1–EZH2 regulatory axis in B cells. **A** Venn diagram showing the overlap among three gene sets: genes upregulated following treatment with the EZH2 inhibitor GSK343 (from GSE45982), H3K27me3-specific target genes in GC B cells, and differentially expressed genes in B cells from *Hnrnpa1^{ff}Hnrnpa2b1^{ff}Cd19^{Cre/+}* (DKO, double knockout) mice. *Cdkn1a* was identified as a common target across all three datasets, indicating its regulation by the hnRNP A1/A2B1–EZH2 axis. **B** WT and DKO B cells were reconstituted with an empty vector (Vector), the full-length *Ezh2* isoform (*Ezh2*-FL), or the EZH2 exon 14–deleted isoform (*Ezh2*Δ14), followed by qRT-PCR analysis of expression levels of *Ezh2*-FL, *Ezh2*Δ14, and *Cdkn1a* (n = 3). Data are presented as mean ± SEM and are pooled from three independent experiments (**B**). Statistical significance was determined by one-way ANOVA with Dunnett's post-hoc multiple comparisons test (**B**).

Supplementary Figure 7 (Supplementary Fig. 7)



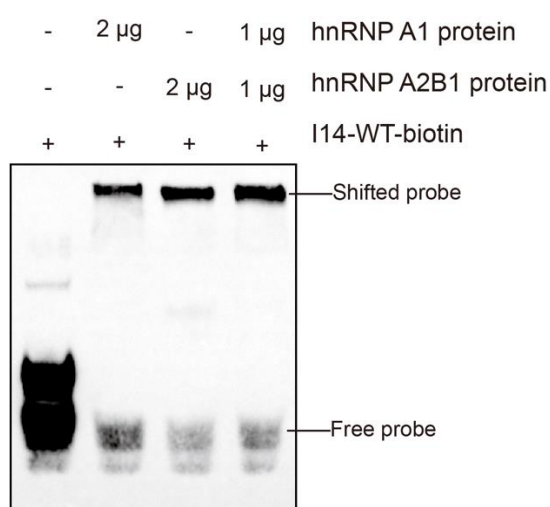
Supplementary Figure 7. *Cdkn1a* deletion partially rescues the B cell defects in hnRNP A1/A2B1-deficient mice. **A** Schematic illustrating the generation of triple knockout (TKO) mice: *Cdkn1a*^{-/-} mice were crossed with *Hnrnpa1*^{fl/fl} *Hnrnpa2b1*^{fl/fl} *Cd19*^{Cre/+} (DKO, double knockout) mice to produce *Hnrnpa1*^{fl/fl} *Hnrnpa2b1*^{fl/fl} *Cd19*^{Cre/+} *Cdkn1a*^{-/-} (TKO) mice. **B** qRT-PCR analysis confirming *Cdkn1a* depletion in WT, DKO and TKO B cells ($n = 2$). **C–D** Bone marrow chimera experiments. **C** Representative flow cytometry plots of CD45.2⁺ B cells. **D** Quantification of the frequency of CD45.2⁺ B cells (WT: $n = 7$; DKO: $n = 7$; TKO: $n = 5$). $p < 0.0001$ (WT vs DKO: 4.90×10^{-5}). Each dot represents an individual mouse (**B**, **D**). Data are presented as mean $\pm$ SEM and are pooled from two independent experiments (**B**) or three independent experiments (**D**). Statistical significance was determined by one-way ANOVA with Tukey's post-hoc multiple comparisons test (**D**).

Supplementary Figure 8 (Supplementary Fig. 8)



Supplementary Figure 8. Cells that escape Cre-mediated knockout outcompete hnRNP A1/A2B1-deficient cells. **A-B** Representative flow cytometry plots (**A**) and quantification (**B**) showing the proportion and number of germinal center (GC) B cells in the spleens of immunized mice on day 14 post NP-KLH/Alum immunization ($n = 6$). **C-D** qRT-PCR analysis of *Hnrnpa1* and *Hnrnpa2b1* transcript levels in GC B cells isolated on days 5, 10, and 14 post NP-KLH/Alum immunization (Day 5: $n = 4$; Day 10 and Day 14: $n = 2$). $p < 0.0001$ (*Hnrnpa1*_Day 5: 6.14×10^{-6} ; *Hnrnpa2b1*_Day 5: 3.31×10^{-5}). Each dot represents an individual mouse (**B**, **C**, **D**). Data are presented as mean $\pm$ SEM and are pooled from three independent experiments (**B**, **C**, **D**). Statistical analysis was performed using an unpaired two-tailed Student's *t*-test (**B**, **C**, **D**).

Supplementary Figure 9 (Supplementary Fig. 9)



Supplementary Figure 9. Independent binding of hnRNP A1 and A2B1 to *Ezh2* exon 14 RNA without cooperative complex formation. EMSA was performed using in vitro–reconstituted hnRNP A1, hnRNP A2B1, or both proteins, incubated with wild-type *Ezh2* pre-mRNA probe. Data are representative of two independent experiments.

Supplementary Table 1. List of reagents and resources used in this study

REAGENT OR RESOURCE	SOURCE	IDENTIFIER	
ANTIBODIES			DILUTIONS
Rat Anti-Mouse CD45R	eBioscience	Cat#47-0452-82; RRID: AB_1518810	1:100
Rat anti-mouse CD93(AA4.1) Biotin	eBioscience	Cat#13-5892-85; RRID: AB_466768	1:100
Rat anti-mouse CD21/CD35 Percp-Cy5.5	BD Pharmingen	Cat#562797; RRID: AB_2737802	1:100
Rat anti-mouse CD23 APC	Biolegend	Cat#101620; RRID: AB_2563439	1:100
Rat anti-mouse CD43 FITC	eBioscience	Cat#11-0431-85; RRID: AB_465041	1:100
Rat anti-mouse CD24 Percp-Cy5.5	BD Pharmingen	Cat# 562360; RRID: AB_11151895	1:100
Rat anti-mouse CD249 (BP1) PE	BD Pharmingen	Cat# 553735; RRID: AB_395018	1:100
Rat anti-mouse IgD Biotin	eBioscience	Cat#13-5993-85; RRID: AB_466861	1:100
Rat anti-mouse IgM PE-Cy7	eBioscience	Cat#25-5790-82; RRID: AB_469655Rat	1:100
Rat anti-mouse IgD FITC	eBioscience	Cat#11-5993-85; RRID: AB_465347	1:100
Mouse Anti-Human CD38 Percp-Cy5.5	BD Pharmingen	Cat#551400; RRID: AB_394184	1:100
CD95 (APO-1/Fas) Monoclonal Antibody (15A7), APC	eBioscience	Cat#17-0951-82; RRID: AB_10717405	1:100
CD95 (APO-1/Fas) Monoclonal Antibody (15A7), PE	eBioscience	Cat#12-0951-81; RRID: AB_465788	1:100

GL7 Monoclonal Antibody (GL-7 (GL7)), eFluor™ 660	eBioscience	Cat#50-5902-82; RRID: AB_2574252	1:100
FITC Rat Anti-Mouse GL7	BD Pharmingen	Cat#553666; RRID: AB_394981	1:100
CD83 Monoclonal Antibody (Michel-17), FITC	eBioscience	Cat#11-0831-82; RRID: AB_465141	1:100
PE/Cyanine7 anti-mouse CD83	Biolegend	Cat#121518; RRID: AB_2566123	1:100
Brilliant Violet 605™ anti-mouse CD184 (CXCR4)	Biolegend	Cat#146519; RRID: AB_2687359	1:100
Ly-6G/Ly-6C Monoclonal Antibody (RB6-8C5), FITC	eBioscience	Cat#11-5931-82; RRID: AB_465314	1:100
Biotin Rat Anti-Mouse CD138	BD Pharmingen	Cat#553713; RRID: AB_394999	1:100
CD267 (TACI) Monoclonal Antibody (ebio8F10-3), APC	eBioscience	Cat#17-5942-82; RRID: AB_842758	1:100
Biotin anti-mouse CD3	Biolegend	Cat#100244; RRID: AB_2563946	1:100
Biotin Rat Anti-Mouse IgM	BD Pharmingen	Cat#553406; RRID: AB_394843	1:100
Ly-6G/Ly-6C Monoclonal Antibody (RB6-8C5), Biotin	eBioscience	Cat#13-5931-85; RRID: AB_466801	1:100
Rat anti-mouse CD38 APC	eBioscience	Cat#17-0381-82; RRID: AB_469382	1:100
FITC Rat Anti-Mouse IgG1	BD Pharmingen	Cat#553443; RRID: AB_394862	1:100

Rat Anti-Mouse IgG1-BIOT	SouthernBiotech	Cat#1144-08; RRID: AB_2794640	1:100
Rat Anti-Mouse IgM-BIOT	SouthernBiotech	Cat#1140-08; RRID: AB_2794630	1:100
PE Hamster Anti-Mouse CD69	BD Pharmingen	Cat#553237; RRID: AB_394726	1:100
APC anti-mouse CD40 Antibody	Biolegend	Cat#124612; RRID: AB_1134072	1:100
MHC Class II (I-A/I-E) Monoclonal Antibody (M5/114.15.2), FITC	eBioscience	Cat#11-5321-82; RRID: AB_465232	1:100
PE Hamster Anti-Mouse CD80	BD Pharmingen	Cat#553769; RRID: AB_395039	1:100
FITC Rat Anti-Mouse CD86	BD Pharmingen	Cat#553691; RRID: AB_394993	1:100
BCL6-PE	eBioscience	Cat#12-5453-82	1:100
HRP-conjugated anti-IgG1	SouthernBiotech	Cat#1071-05	1:1000
HRP-conjugated anti-IgG2b	SouthernBiotech	Cat#1091-05	1:1000
HRP-conjugated anti-IgG3	SouthernBiotech	Cat#1101-05	1:1000
HRP-conjugated anti-IgM	SouthernBiotech	Cat#1021-05	1:1000
HRP-conjugated anti-IgA	SouthernBiotech	Cat#1040-05	1:1000
beta Actin Rabbit PolyAb	proteintech	Cat#20536-1-AP	1:5000
Mouse anti-hnRNP A1	Santa Cruz Biotechnology	Cat#sc-32301	1:1000
Mouse anti-hnRNP A2B1	Santa Cruz Biotechnology	Cat#sc-53531	1:1000
Rabbit anti-EZH2/KMT6 pAb	ABclonal	Cat#A5743; RRID: AB_2769389	1:1000

Rabbit anti-EZH2/KMT6 mAb	ABclonal	Cat#A19577; RRID: AB_2862678	1:1000
Rabbit anti-H3K27me3 mAb	ABclonal	Cat#A22396;	1:1000
Rabbit anti-CDKN1A mAb	Cell Signaling Technology	Cat#2947;	1:1000
Streptavidin PE	eBioscience	Cat#12-4317-87	1:100
Streptavidin Percp-Cy5.5	eBioscience	Cat#45-4317-82	1:100
Streptavidin APC	Biolegend	Cat#405207	1:100
Streptavidin AP	SouthernBiotech	Cat#7100-04	1:1000
Streptavidin HRP	SouthernBiotech	Cat#7105—05	1:1000
Goat Anti-Rabbit IgG (H+L), HRP Conjugate	TransGen	Cat#HS101-01	1:5000
Goat Anti-Mouse IgG (H+L), HRP Conjugate	TransGen	Cat#HS201-01	1:5000
CHEMICALS, PEPTIDES, AND RECOMBINANT PROTEINS			
Anti-NIP-BSA PE	This paper	N/A	1:100
NP-KLH (Keyhole Limpet Hemocyanin)	Biosearch Technologies	Cat: N-5060-25	
Imject Alum adjuvant	Thermo Scientific	Cat#77161	
Alhydrogel® adjuvant 2%	invivogen	Cat#vac-alu-50	
Lipopolysaccharides	Sigma-Aldrich	Cat#L7895	
Purified NA/LE hamster anti-mouse CD40	BD Pharmingen	Cat#553721	
AffiniPure F(ab')2 fragment goat anti-mouse IgM	JacksonImmunoRe search Laboratories	Cat#115-006-075	
Goat Anti-Mouse Ig, Human ads-UNLB	SouthernBiotech	Cat#1010-01	
neomycin	Aladdin	N109017	
CRITICAL COMMERCIAL ASSAYS			
CaspGLOW Kit	BioVision	Cat#K180-100	
TMB Substrate Set	Biolegend	Cat#421101	
Substrate for ELISpot	mabtech	Cat#3650-10	

BrdU Staining Kit for Flow Cytometry	eBioscience	Cat#8812-6600-42	
FITC BrdU Kit	BD Pharmingen	Cat#559619	
CFSE Cell Division Tracker Kit	Biolegend	Cat#423801	
ClonExpress MultiS one Step Cloning Kit	Vazyme	Cat#C113	
CD43 Microbeads	Miltenyi	Cat#130-049-801	
Streptavidin MicroBeads	Miltenyi	Cat#130-048-101	
EasySep™ Mouse CD19 Positive Selection Kit II	STEMCELL Technologies	Cat#18000	
Streptavidin Magnetic Beads	MCE	Cat#HY-K0208	
ChIP-Grade Protein G Magnetic Beads	Cell Signaling Technology	Cat#9006S	
Annexin v-FITC/PI apoptosis Detection kit	Yeasen	Cat#40302ES60	
Hifair® III 1st Strand cDNA Synthesis Kit (gDNA digester plus)	Yeasen	Cat#11139ES60	
RNAiso Plus	TaKaRa	Cat#9108	
Hieff UNICON® Universal Blue qPCR SYBR Green Master Mix	Yeasen	Cat#11184ES60	
MiniBEST Universal Genomic DNA Extraction Kit	TaKaRa	Cat#9765	
Clear Flat-Bottom Immuno Nonsterile 384-Well Plates	Thermo Scientific™	Cat#464718	
MultiScreenHTSIP Filter Plate, 0.45 µm, white, non-sterile	Merck Millipore	Cat#MSIPN4W50	
Fetal Bovine Serum (Prime, Uruguay)	Excell	Cat#FSP500	
Gibco™ BASIC DMEM, High Glucose, Pyruvate	Gibco™	Cat#C11995500BT	
Gibco™ BASIC RPMI 1640 Medium	Gibco™	Cat#C11875500BT	
HyClone™ Penicillin-Streptomycin 100X solution	HyClone™	Cat#SV30010	
EXPERIMENTAL MODELS: ORGANISMS/STRAINS			

C57BL/6NCya- <i>Hnrnpa2b1</i> ^{em1flox} /Cy a	Cyagen	Cat#S-CKO-1160 2	
C57BL/6JGpt- <i>Hnrnpa1</i> ^{em1Cflox} /Gpt	Gempharmatech	Cat #T013507	
CD19-Cre: B6N. 129P2- <i>Cd19</i> ^{tm1(cre)Cgn} /J	The Jackson Laboratory	RRID: IMSR_JAX:01895 8	
MB1-Cre: B6.C(Cg)- <i>Cd79a</i> ^{tm1(cre)Reth} /EhobJ	The Jackson Laboratory	RRID: 020505	
C57BL/6Smoc- <i>Cdkn1a</i> ^{em1Smoc}	Shanghai Model Organisms Center, Inc.	Cat #NM-KO-190774	
CD45.1 mice	Shanghai Model Organisms Center, Inc.	Cat. No. NM-KI-210226	

Supplementary Table 2. Primer sequences used in this study

Used for	Gene	Oligonucleotide(5'-3')
qRT-PCR	Actb-qF	CGTGAAAAGATGACCCAGATCA
	Actb-qR	CACAGCCTGGATGGCTACGT
	Hnrnpa2b1-KO-qF	CTGGAAAACCAGGAGCCCAT
	Hnrnpa2b1-KO-qR	CTTTCCAGACTGCCTATCGGT
	Hnrnpa1-qP-qF	GGAAGAGTTGTGGAACCTAAGAGAG
	Hnrnpa1-qP-qR	CTCGTAGGTGATGTTCTTCAGTGTC
	Ezh2-FL-qF	ACTGAAAAAGGACGGCTCCTCT
	Ezh2-FL-qR	AGCGGTTTTGACACTCTGAACTAC
	Ezh2 Δ 14-qF	AACTGAAAAAGGGTCAAAACCGCT
	Ezh2 Δ 14-qR	TACTGTCCCAATGGTCAGCAGC
	Cdkn1a-qF	CGGTGTCAGAGTCTAGGGGA
	Cdkn1a-qR	AGGATTGGACATGGTGCCTG
EZH2/EZH2 Δ 14 gene cloning	mEzh2-cF	GCGCCGGAATTAGATCTCGCCACCATGGGCCA GACTGGGAAG
	mEzh2-cR	GCGGAATTCGTTAACCTCGATCAAGGGATTTC ATTTCTCGTTC
RT-PCR	Actb-RTPCR-F	CGGACTGTACTGAGCTGCG
	Actb-RTPCR-R	ACGCGACCATCCTCCTCTTA
	AS-EZH2-F'	GTTGTGGGCTGCACACTGC
	AS-EZH2-R'	CTTTTTAGAGCCCCGCTGAATGC
RIP	Ezh2-RIP-qF	CTAAGGAGTTTGCTGCTGCTCTTACTG
	Ezh2-RIP-qR	GGTCTGCTACTGTTATTCGGAAGTCTT
ChIP	ChIP-P21-F1	ACATCCATTCCACTCGGAACCTC
	ChIP-P21-R1	GCGACGTAGGGGACAGAGG
	ChIP-P21-F2	GCCTATTTCCCCCTCCTCAC
	ChIP-P21-R2	GTTTCGGGAGGTGGGTCTGTTG
miniGene	miniGene-cF	GCGCCGGAATTAGATCTCTCGTTGTGGGCTGCA CACTGC
	miniGene-cR	GGGCGGAATTCGTTAACCTCCTTTTAGAGCCC CGCTGAATGC
	miniGene-M1-cF	TGTAGTTCAGAGTGTCCCTATTTGTTGCTTT
	miniGene-M1-cR	AAAGCAACAAATAGGGACACTCTGAACTACA
	miniGene-M3-cF	GCATGAGAACTGAACCCGCTTTTGGTC
	miniGene-M3-cR	GACCAAAAGCGCCTTCAGTTCTCATGC

	R	
	miniGene-M1+ M3-cF	AGAGTGTCCCTATTTGTTGCTTTGGTGCAATTGC ATGAGAACTGAACCCGCTTTTGGTC
	miniGene-M1+ M3-cR	GACCAAAAGCGGGTTCAGTTCTCATGCAATTGC ACCAAAGCAACAAATAGGGACACTCTGAA
	miniGene-M1+ M2+M3-cF	AGAGTGTCCCTATTTCTTGCTTTGGTGCAATTGC ATGAGAACTGAACCCGCTTTTGGTC
	miniGene-M1+ M2+M3-cR	GACCAAAAGCGGGTTCAGTTCTCATGCAATTGC ACCAAAGCAAGAAATAGGGACACTCTGAA
EMSA	Hnrnpa1-pet28- F	TGCCGCGCGGCAGCCATATGGGGGGTGGATCT GGGGGTGGATCTATGTCTAAGTCCGAGTCTCCC
	Hnrnpa1-pet28- R	TGGTGGTGGTGCTCGAGTGCGGCCGCAAGCTT TTAGAACCTCCTGCCACTGCC
	Hnrnpa2b1-pet 28-F	TGCCGCGCGGCAGCCATATGGGGGGTGGATCT GGGGGTGGATCTATGGAGAGAGAAAAGGAACA G
	Hnrnpa2b1-pet 28-R	TGGTGGTGGTGCTCGAGTGCGGCCGCAAGCTT TTAATATCTGCTCCTTCCACC
Genotyping	Cd19-Cre-gF	CCTGGAAAATGCTTCTGTCCG
	Cd19-Cre-gR	CAGGGTGTTATAAGCAATCCC
	Hnrnpa1-gF	CTGAATATAGCGGGATGTGACGTGT
	Hnrnpa1-gR	CAACAAAGGGCACAGGTTAGTCG
	Hnrnpa2b1-gF	GAGCTACCAGAAACACTATTTGGAG
	Hnrnpa2b1-gR	CCTGTTTCCAAATTCACCACTTCC
	Cdkn1a-F1	CAGGGTAGGGAGACCACTGGA
	Cdkn1a-F2	AAACGGATGCAGATGGGTTGA
	Cdkn1a-R	CTTGCAGGTGCTTTTCCACC