

Figure S1.

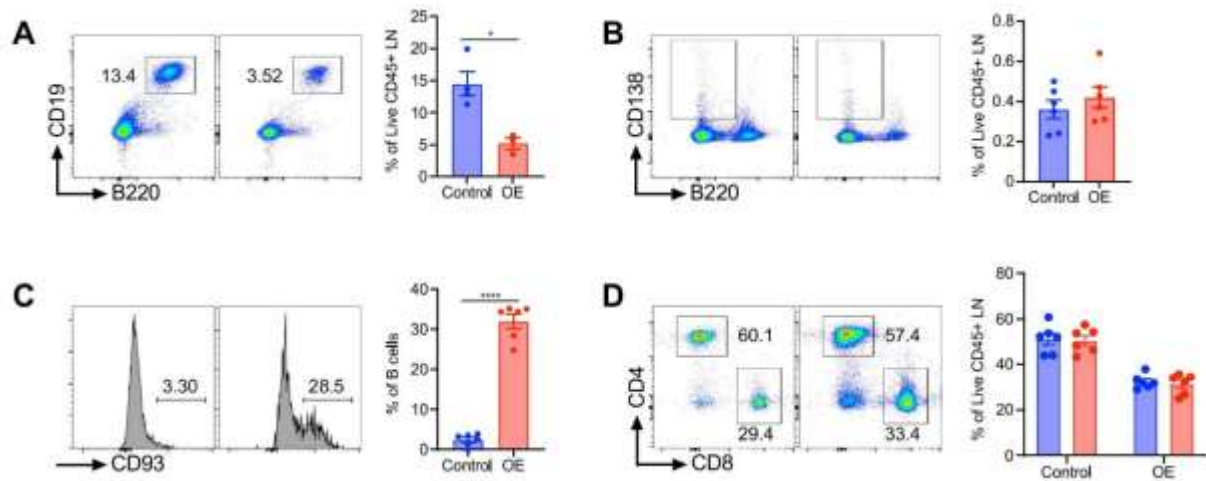


Figure S1. B cell populations are reduced within the lymph node. (A-D) Representative flow cytometry plot and quantitation of CD19+B220+ B cells, CD138+ plasma cells, CD93+ transitional B cells, and CD4+ vs CD8+ T cells. Data are presented as mean $\pm$ SEM. Statistical significance was determined using an unpaired two-tailed Student's t-test. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.001$.

Figure S2.

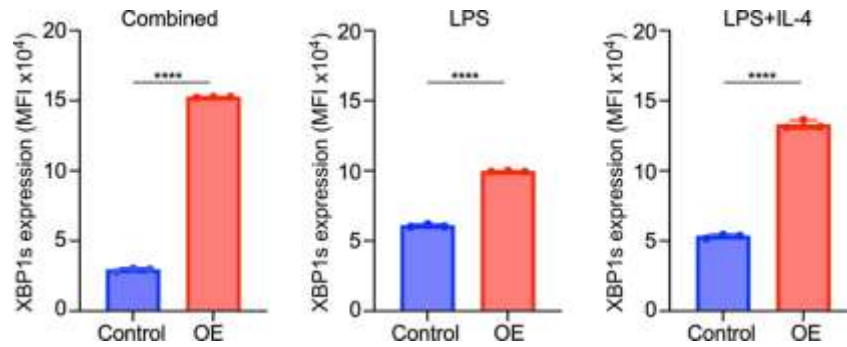


Figure S2. XBP1s MFI levels of stimulated B cells. MFI of XBP1s protein in B cells following BCR stimulation or LPS $\pm$ IL-4. Data are presented as mean $\pm$ SEM. Statistical significance was determined using an unpaired two-tailed Student's t-test. **** $p < 0.001$.

Figure S3.

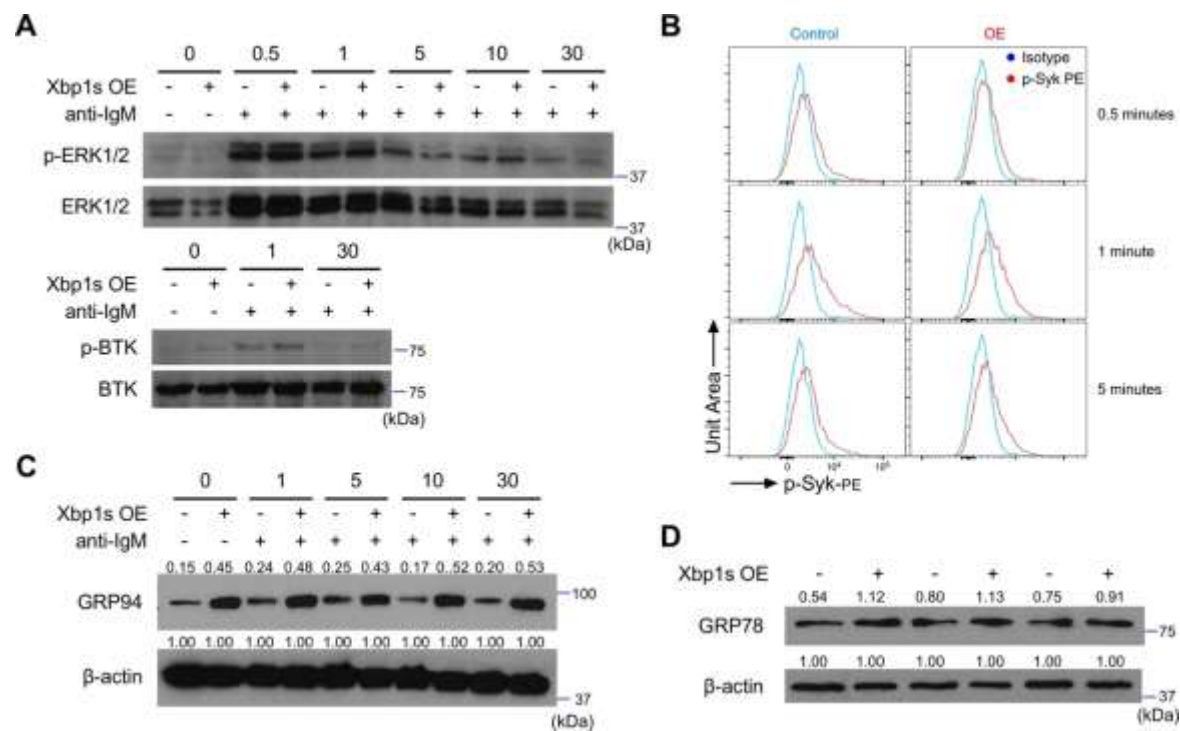


Figure S3. ER stress does not affect BCR signaling cascade. (A) Representative western blots of key signaling proteins p-ERK1/2 and p-BTK following 0.5, 1, 5, 10, or 30 minutes of anti-IgM stimulation. (B) Representative flow cytometry plots of p-Syk following 0.5, 1, 5 minutes of anti-IgM stimulation. (C) Representative western blots of GRP94 following 1, 5, 10, 30 minutes of stimulation. (D) GRP78 expression at steady-state in control and OE mice.

Figure S4.

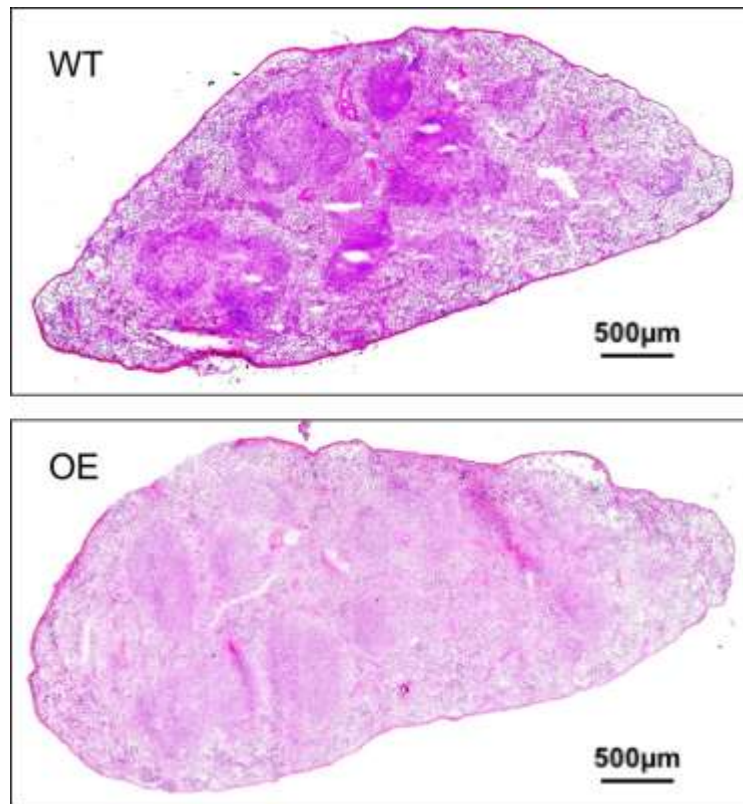


Figure S4. Baseline splenic architecture is preserved in XBP1s OE mice. Representative H&E staining of spleens from unimmunized control and OE mice showing preserved overall splenic architecture.

Figure S5.

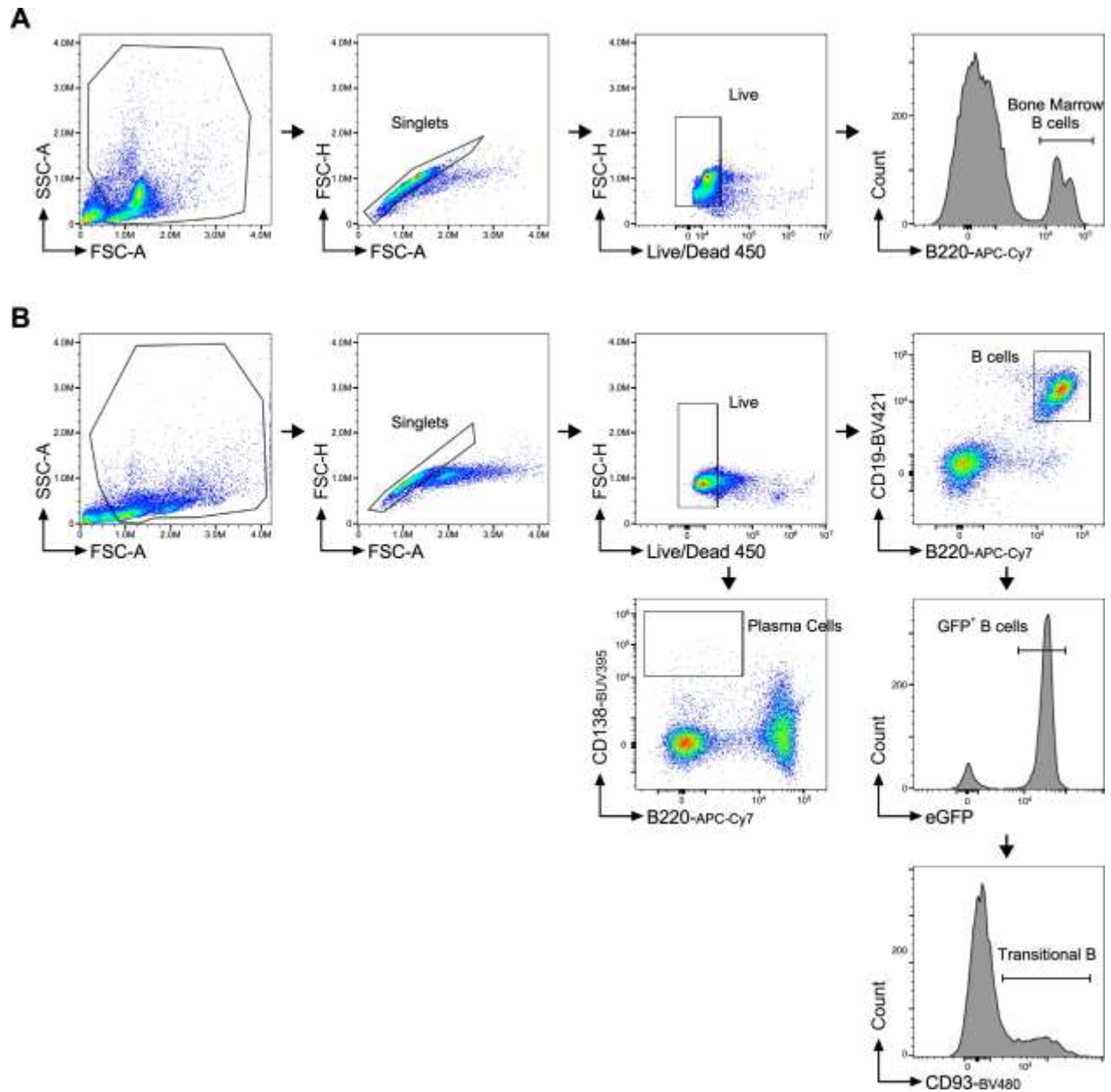


Figure S5 FACS gating strategy. (A) Bone marrow and (B) spleen gating strategies used to define B cell populations used in the manuscript.

Table S1. Key Resources Table

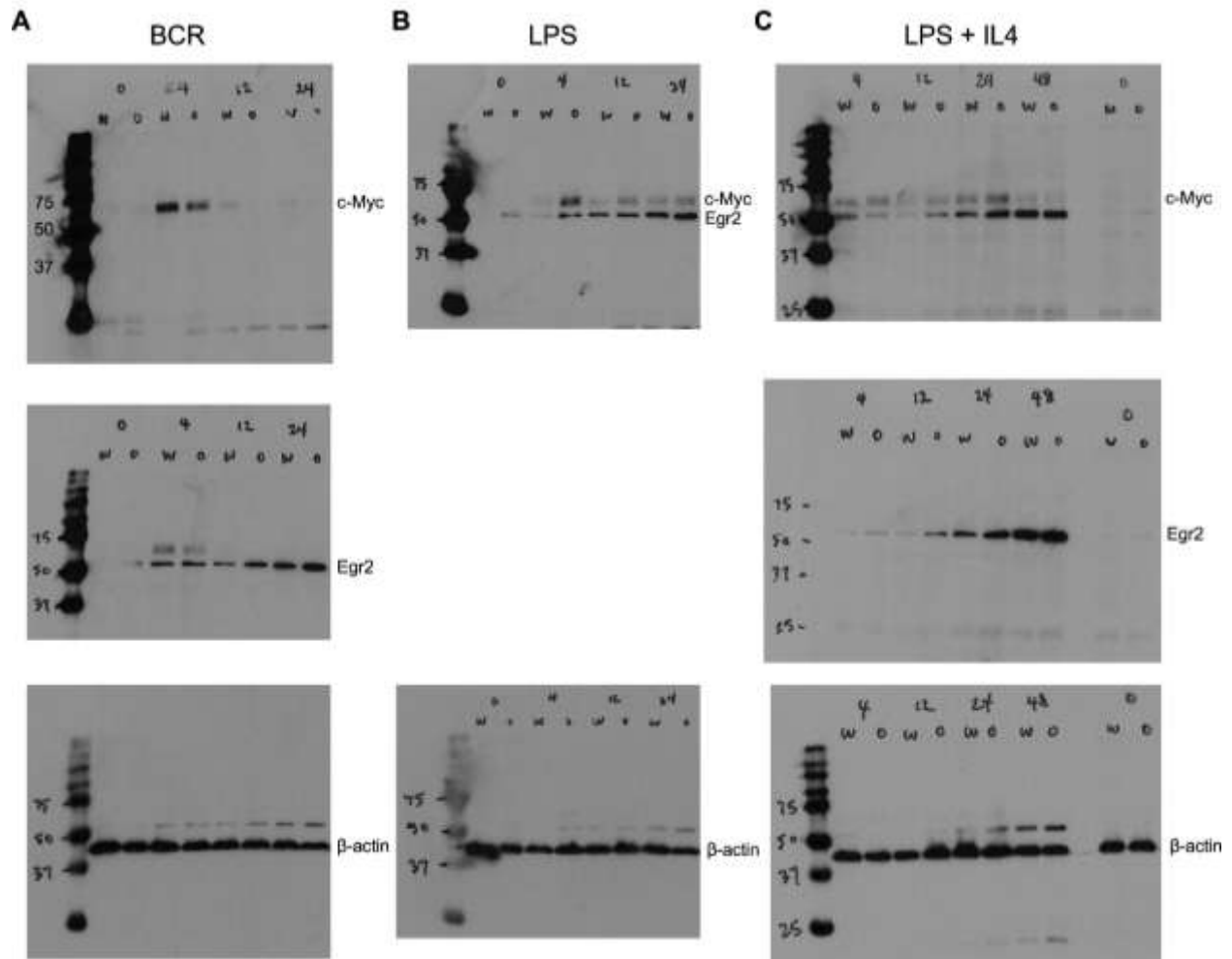
REAGENT or RESOURCE	SOURCE	IDENTIFIER
Antibodies		
Rat monoclonal anti-B220, APC-Cy7	BD Biosciences	Cat#: 552094; RRID:AB_394335
Rat monoclonal anti-B220, FITC	Thermo Fisher Scientific	Cat#: 11-0452-85; RRID:AB_465055
Hamster monoclonal anti-CD3, BUV395	BD Biosciences	Cat#: 563565; RRID:AB_2738278
Rat monoclonal anti-CD4, BV421	BD Biosciences	Cat#: 740007; RRID:AB_2739779
Rat monoclonal anti-CD8, BUV805	BD Biosciences	Cat#: 612898; RRID:AB_2870186
Rat monoclonal anti-CD11b, BV605	BD Biosciences	Cat#: 563015; RRID:AB_2737951
Hamster monoclonal anti-CD11c, BUV805	BD Biosciences	Cat#: 749038; RRID:AB_2873432
Rat monoclonal anti-CD16/32, unconjugated	BioLegend	Cat#: 101320; RRID:AB_1574975
Rat monoclonal anti-CD19, BV421	BioLegend	Cat#: 115538; RRID:AB_11203527
Rat monoclonal anti-CD21/35, Alexa Fluor® 700	BioLegend	Cat#: 123431; RRID:AB_2860649
Rat monoclonal anti-CD21/35, APC	BD Biosciences	Cat#: 561770; RRID:AB_10892818
Rat monoclonal anti-CD23, BUV563	BD Biosciences	Cat#: 741228; RRID:AB_2870782
Rat monoclonal anti-CD23, PE	Thermo Fisher Scientific	Cat#: 12-0232-83; RRID:AB_465594
Rat monoclonal anti-CD24, BUV563	BD Biosciences	Cat#: 749336; RRID:AB_2873710
Rat monoclonal anti-CD43, PE-Cy7	BD Biosciences	Cat#: 562866; RRID:AB_2737852
Rat monoclonal anti-CD44, APC	Thermo Fisher Scientific	Cat#: 17-0441-83; RRID:AB_469391
Rat monoclonal anti-CD45, Alexa Fluor® 700	BD Biosciences	Cat#: 565478; RRID:AB_2739257
Rat monoclonal anti-CD93, BUV661	BD Biosciences	Cat#: 741574; RRID:AB_2870995
Rat monoclonal anti-CD138, BUV395	BD Biosciences	Cat#: 740240; RRID:AB_2739987
Rat monoclonal anti-CD138, BV785	BioLegend	Cat#: 142534; RRID:AB_2814047
Rat monoclonal anti-GFP, AF488	BioLegend	Cat#: 338007; RRID:AB_2563287
Rat monoclonal Gr-1, APC	BD Biosciences	Cat#: 553129; RRID:AB_398532

Rat monoclonal anti-IgD, BV711	BioLegend	Cat#: 405731; RRID:AB_2563342
Goat polyclonal anti-mouse IgG, BV510	BioLegend	Cat#: 405331; RRID:AB_2616858
Rat polyclonal anti-mouse IgG, FITC	Thermo Fisher Scientific	Cat#: 11-4011-85; RRID:AB_465218
Donkey polyclonal anti-rabbit IgG1, PE	Thermo Fisher Scientific	Cat#: 12-4739-81; RRID:AB_1210761
Rat monoclonal anti-IgG1, PE	BD Biosciences	Cat#: 550083; RRID:AB_393553
Rat monoclonal anti-IgG1, APC	BioLegend	Cat#: 406610; RRID:AB_10696420
Rat monoclonal anti-IgM, BV605	BioLegend	Cat#: 406523; RRID:AB_2563358
Mouse monoclonal anti-NK1.1, BV605	BD Biosciences	Cat#: 563220; RRID:AB_2738077
Rat monoclonal anti-PDCA-1, BV421	BioLegend	Cat#: 127023; RRID:AB_2687109
Mouse monoclonal anti-XBP-1S, PE	BD Biosciences	Cat#: 562642; RRID:AB_2687882
Rat monoclonal anti-CD40, unconjugated	BD Biosciences	Cat#: 553787; RRID:AB_395051
Goat anti-mouse IgM, unconjugated	Jackson ImmunoResearch Labs	Cat#: 115-006-020; RRID:AB_2338469
Peanut agglutinin (PNA), Biotinylated	Vector Laboratories	Cat#: B-1075; RRID:AB_2313597
Goat anti-rabbit IgG, HRP	Cell Signaling	Cat#: 7074; RRID:AB_2099233
Rabbit monoclonal anti-Egr2, unconjugated	Abcam	Cat#: ab108399; RRID:AB_10862073
Rat monoclonal anti-Grp94, unconjugated	Enzo	Cat#: ADI-SPA-850; RRID:AB_10615091
Rabbit polyclonal anti-Grp78, unconjugated	Proteintech	Cat#: 11587-1-AP; RRID:AB_2119855
Rabbit monoclonal anti-Irf4, unconjugated	Cell Signaling	Cat#: 15106; RRID:AB_2798709
Rabbit monoclonal anti-c-Myc, unconjugated	Cell Signaling	Cat#: 5605; RRID:AB_1903938
Rabbit monoclonal anti-phospho-p38, unconjugated	Cell Signaling Technologies	Cat#: 4511; RRID:AB_2139682
Rabbit monoclonal anti-phospho-p44/42 MAPK, unconjugated	Cell Signaling Technologies	Cat#: 4370; RRID:AB_2315112
Rabbit monoclonal anti-phospho-Syk, unconjugated	Cell Signaling Technologies	Cat#: 2710; RRID:AB_2197222
Chemicals, peptides, and recombinant proteins		
Mouse IL-4	Peprtech	Cat#: 214-14-20UG
Mouse IL-21	Peprtech	Cat#: 210-21-10UG
Lipopolysaccharides from <i>Escherichia coli</i> O55:B5	Sigma-Aldrich	Cat#: L2637-5MG
Human Serum Albumin	Sigma-Aldrich	Cat#: A5843-5G

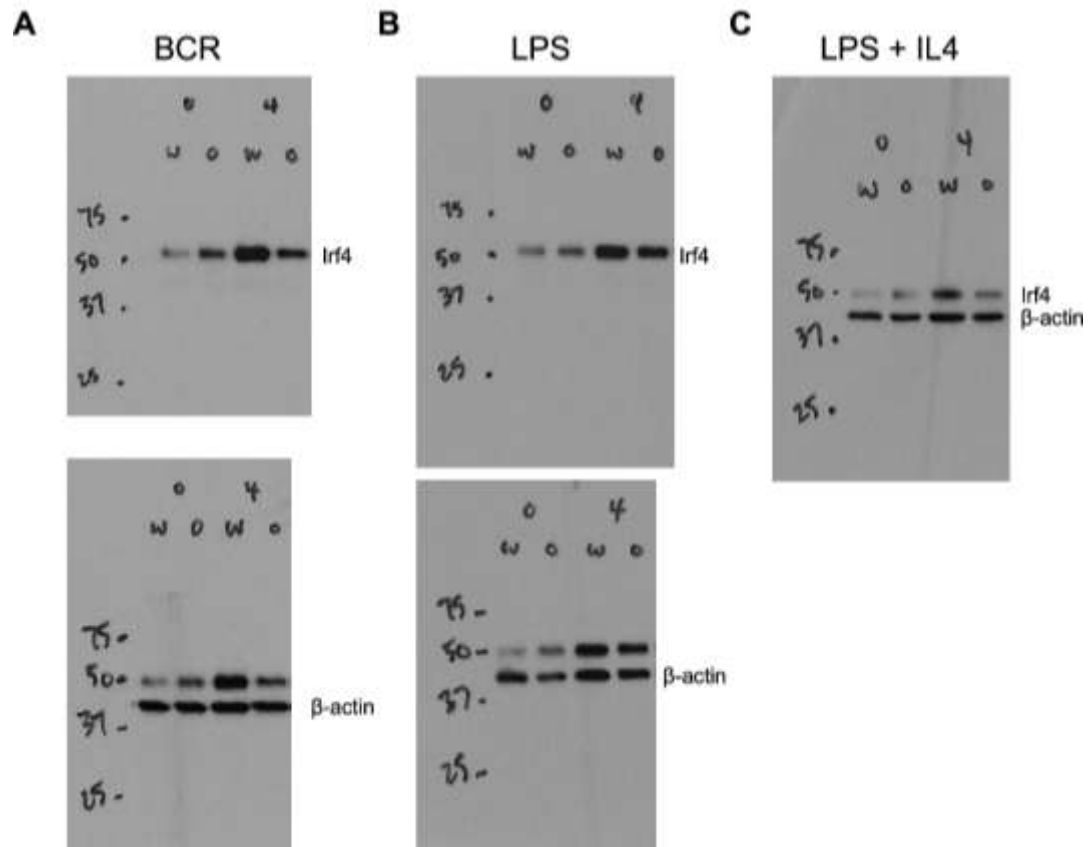
Bovine Serum Albumin	Sigma-Aldrich	Cat#: A3294
Critical commercial assays		
CD19 MicroBeads, mouse	Miltenyi Biotec	Cat#: 130-121-301
LS Columns	Miltenyi Biotec	Cat#: 130-042-401
QuadroMACS separator	Miltenyi Biotec	Cat#: 130-091-051
Foxp3 / Transcription Factor Staining Buffer Set	Thermo Fisher	Cat#: 00-5523-00
CellTrace Violet Cell Proliferation Kit, for Flow Cytometry	Invitrogen	Cat#: C34571
Ghost Dye Violet 450	Tombo Biosciences	Cat#: 13-0863-T100
Ghost Dye Violet 510	Tombo Biosciences	Cat#: 13-0870-T100
Ghost Dye Violet 780	Tombo Biosciences	Cat#: 13-0865-T100
7-AAD Viability Staining Solution	eBioscience	Cat#: 00-6993-50
SBA Clonotyping System-C57BL/6-HRP	Southern Biotech	Cat#: 5300-05B
Mouse Immunoglobulin Panel	Southern Biotech	Cat#: 5300-01
BD OptEIA	BD Bioscience	Cat#: 555214
RNeasy Plus Mini Kit	Qiagen	Cat#: 74134
SuperScript™ III First-Strand Synthesis System	Invitrogen	Cat#: 18080-051
PerfeCTa SYBR® Green FastMix	Quantabio	Cat#: 95072-012
RIPA Lysis and Extraction Buffer	Thermo Scientific	Cat#: 89900
Phenylmethylsulfonyl fluoride	Thermo Scientific	Cat#: 36978
Halt™ protease and phosphatase inhibitor cocktail	Thermo Scientific	Cat#: 78440
Pierce ECL Western Blotting Substrate	Thermo Scientific	Cat#: 32106
Experimental models: Organisms/strains		
Mouse: CD19-Cre Rosa26 ^{LSL-XBP1s} -eGFP	This paper	N/A
Mouse: CD19-Cre	Liu et al., 2008.	N/A
Oligonucleotides		
Rosa26 Forward	Integrated DNA Technologies	AGTCGCTCTGAGT TGTTATCA
Rosa26 Reverse	Integrated DNA Technologies	TGAGCATGTCTTT AATCTACCTCGAT G
Rosa26 Mutant Reverse	Integrated DNA Technologies	GTCAATGGAAAGT CCCTATTGGCGT
CD19c (CD19 Forward)	Integrated DNA Technologies	AACCAGTCAACAC CCTTCC
CD19d (CD19 Reverse)	Integrated DNA Technologies	CCAGACTAGATAC AGACCAG
Cre7 (CD19cre)	Integrated DNA Technologies	TCAGCTAGACCAG AGACGG
Mouse Nur77 Forward	Integrated DNA Technologies	GTGCAGTCTGTGG TGACAATGC
Mouse Nur77 Reverse	Integrated DNA Technologies	CAGGCAGATGTAC TTGGCGCTT
Mouse Egr2 Forward	Integrated DNA Technologies	CCTTTGACCAGAT GAACGGAGTG

Mouse Egr2 Reverse	Integrated DNA Technologies	GAAGGTCTGGTTT CTAGGTGCAG
Mouse Egr3 Forward	Integrated DNA Technologies	CTGACAATCTGTA CCCCGAGGA
Mouse Egr3 Reverse	Integrated DNA Technologies	GCTTCTCGTTGGT CAGACCGAT
Mouse Dusp1 Forward	Integrated DNA Technologies	CAACCACAAGGCA GACATCAGC
Mouse Dusp1 Reverse	Integrated DNA Technologies	GTAAGCAAGGCAG ATGGTGGCT
Mouse Socs3 Forward	Integrated DNA Technologies	GGACCAAGAACCT ACGCATCCA
Mouse Socs3 Reverse	Integrated DNA Technologies	CACCAGCTTGAGT ACACAGTCG
Mouse Tnfaip3 Forward	Integrated DNA Technologies	AGCAAGTGCAGGA AAGCTGGCT
Mouse Tnfaip3 Reverse	Integrated DNA Technologies	TTTCAGCCTTGAG GCTACCTGTG
Mouse Prdm1 Forward	Integrated DNA Technologies	AAGACGTTCCGGTC AGCTCTCCA
Mouse Prdm1 Reverse	Integrated DNA Technologies	CTGGCACTCATGT GGCTTCTCT
Mouse Irf4 Forward	Integrated DNA Technologies	GAACGAGGAGAAG AGCGTCTTC
Mouse Irf4 Reverse	Integrated DNA Technologies	GTAGGAGGATCTG GCTTGTCGA
Mouse Myc Forward	Integrated DNA Technologies	TCGCTGCTGTCCT CCGAGTCC
Mouse Myc Reverse	Integrated DNA Technologies	GGTTTGCCTCTTC TCCACAGAC
Mouse CD69 Forward	Integrated DNA Technologies	GGGCTGTGTTAAT AGTGGTCCTC
Mouse CD69 Reverse	Integrated DNA Technologies	CTTGCAGGTAGCA ACATGGTGG
Mouse CD86 Forward	Integrated DNA Technologies	ACGTATTGGAAGG AGATTACAGCT
Mouse CD86 Reverse	Integrated DNA Technologies	TCTGTCAGCGTTA CTATCCCGC
Mouse Pax5 Forward	Integrated DNA Technologies	TGACGCAGGTGTC ATCGGTGAG
Mouse Pax5 Reverse	Integrated DNA Technologies	ATTCGGCACTGGA GACTCCTGA
Mouse Eif2ak3 Forward	Integrated DNA Technologies	CCGATGTCAGTGA CAACAGCTG
Mouse Eif2ak3 Reverse	Integrated DNA Technologies	AAGACAACGCCAA AGCCACCAC
Mouse ATF6 Forward	Integrated DNA Technologies	GTCCAAAGCGAAG AGCTGTCTG
Mouse ATF6 Reverse	Integrated DNA Technologies	AGAGATGCCTCCT CTGATTGGC

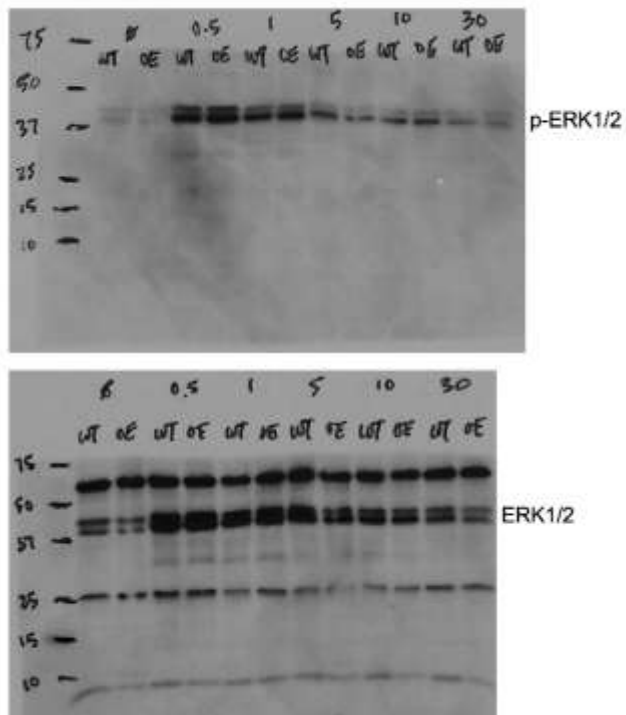
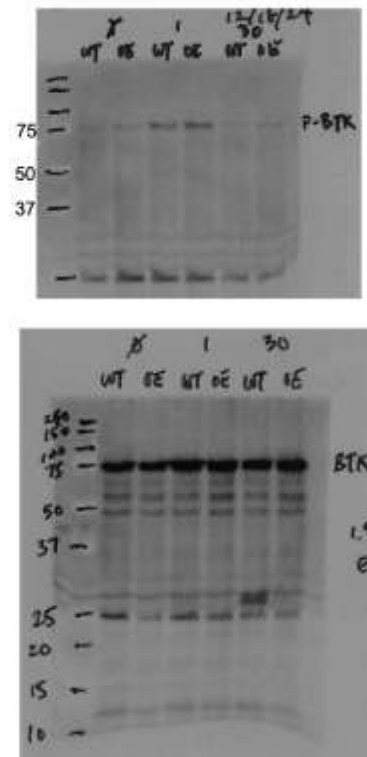
Mouse Xbp1s Forward	Integrated DNA Technologies	GACAGAGAGTCAA ACTAACGTG
Mouse Xbp1s Reverse	Integrated DNA Technologies	GTCCAGCAGGCAA GAAGGT
Mouse Gapdh Forward	Integrated DNA Technologies	ACCCCAGCAAGGA CACTGAGCAAG
Mouse Gapdh Reverse	Integrated DNA Technologies	GGCCCCTCCTGTT ATTATGGGGGT
Software and algorithms		
FlowJo 10.8.1	BD Biosciences	https://www.flowjo.com/
GraphPad Prism 10	GraphPad Software	https://www.graphpad.com/
ImageJ 1.54g	ImageJ	https://imagej.net/ij/
OMIQ	Dotmatics	https://www.omiq.ai/



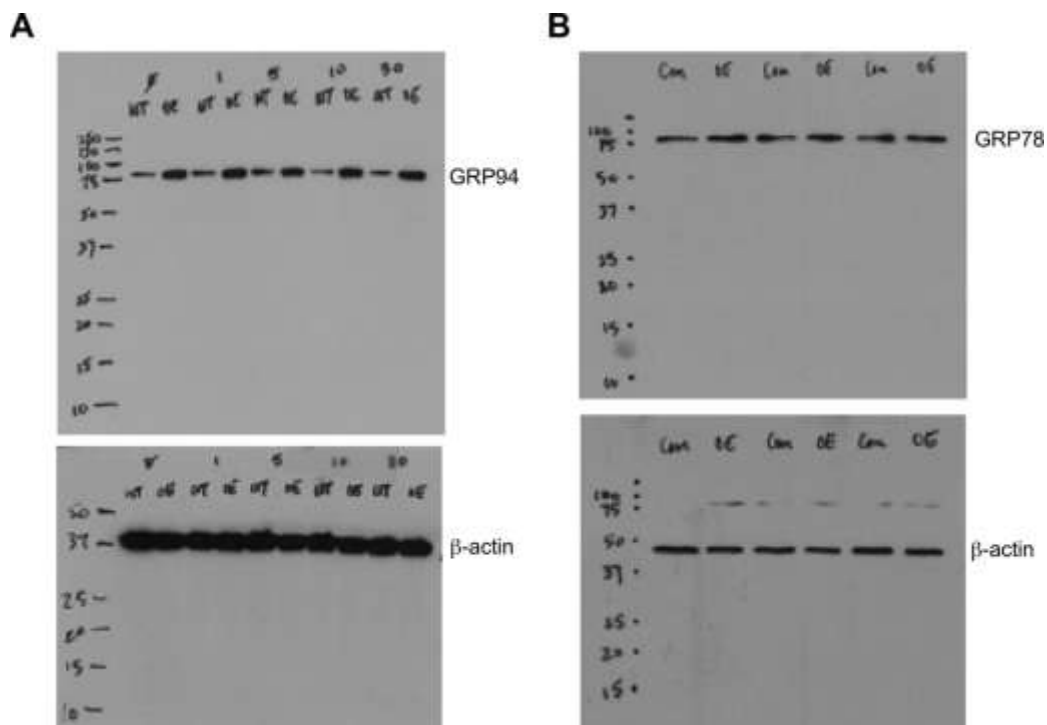
Supplemental Western 1 (Related to Figure 6). **(A)** Full-length blots showing expression of c-MYC, Egr2, and beta-actin in control versus OE isolated B cells with BCR activation. **(B, C)** Full-length blots showing expression of c-MYC, Egr2, and beta-actin in control versus OE B cells with LPS (B) and LPS+IL-4 (C) activation.



Supplemental Western 2 (Related to Figure 6). Full-length blots showing expression of IRF4 and beta-actin in control versus OE isolated B cells activated with BCR (A), LPS (B), and LPS+IL-4 (C).

A**B**

Supplemental Western 3 (Related to Figure S3). **(A)** Full-length blots showing expression of p-ERK1/2 and ERK1/2 in control versus OE isolated B cells after anti-IgM activation. **(B)** Full-length blots showing expression of p-BTK and BTK in control versus OE B cells after anti-IgM activation.



Supplemental Western 4 (Related to Figure S3). **(A)** Full-length blots showing expression of GRP94 and beta-actin in control versus OE isolated B cells after anti-IgM stimulation. **(B)** Full-length blots showing expression of GRP78 and beta-actin in control versus OE B cells at steady state.