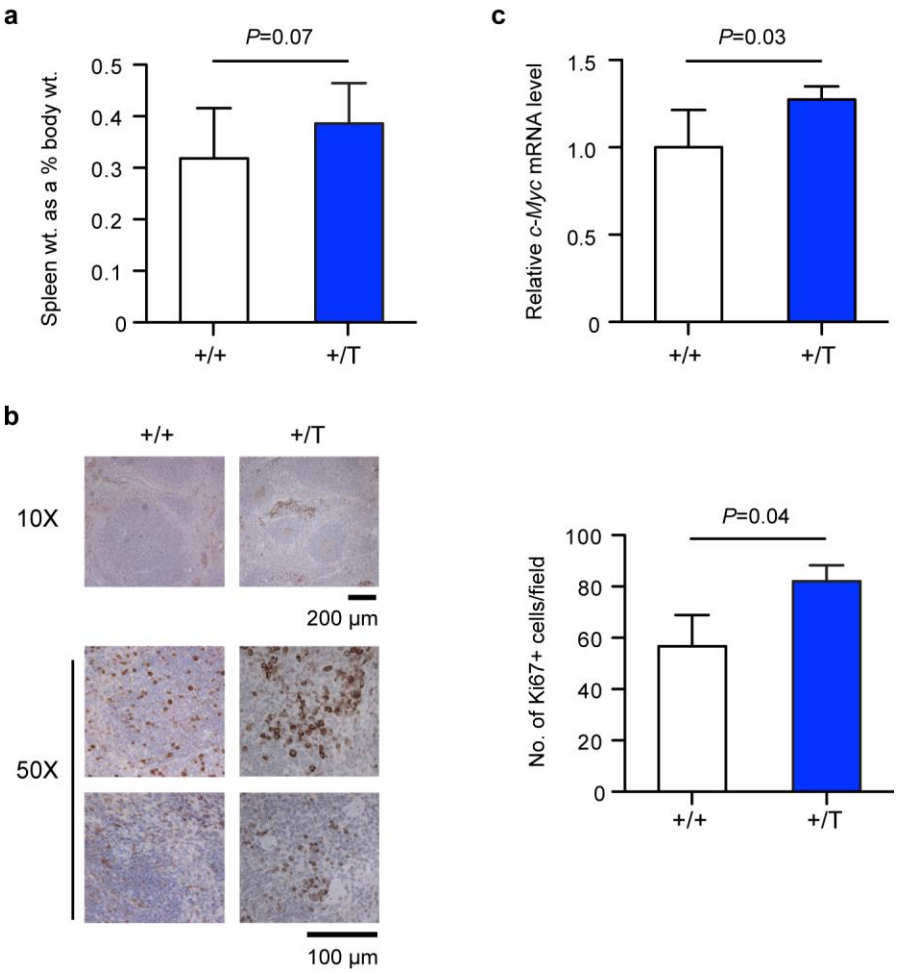
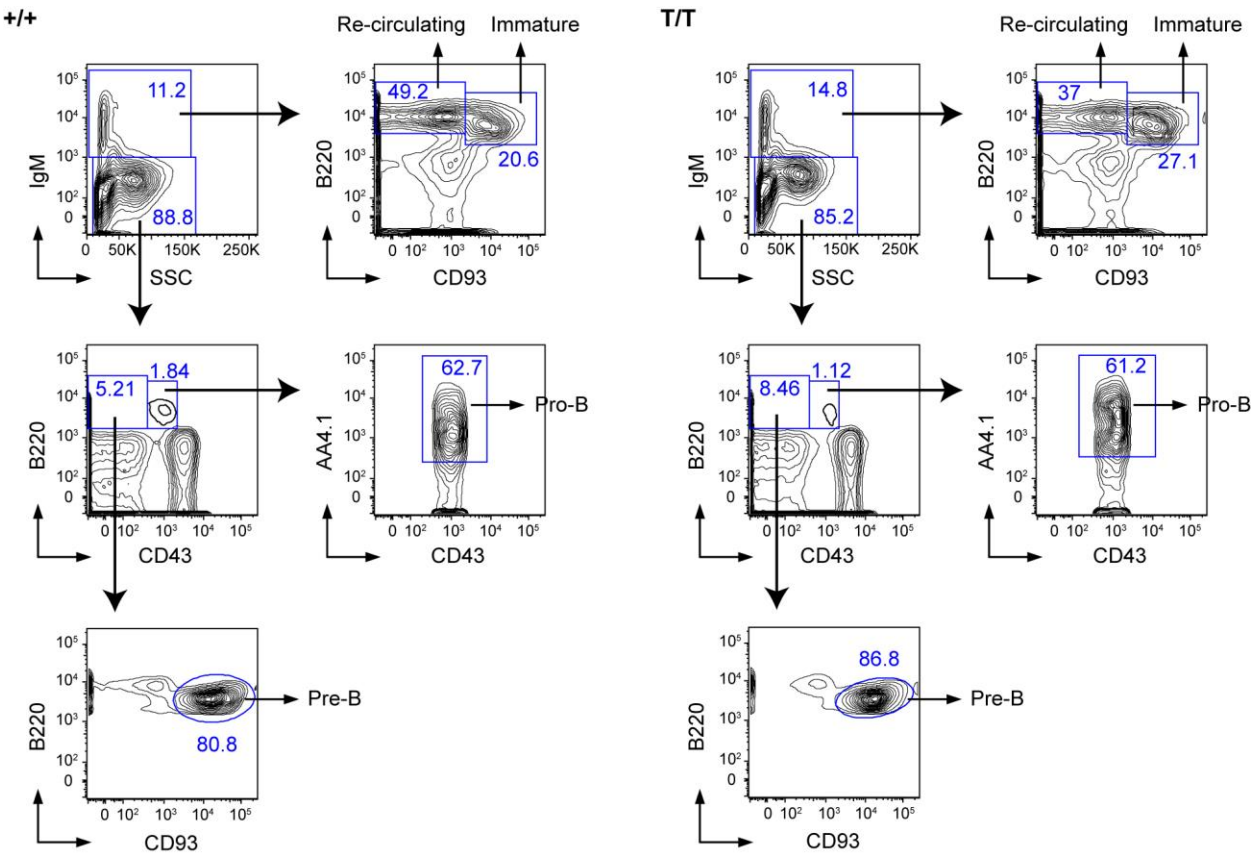
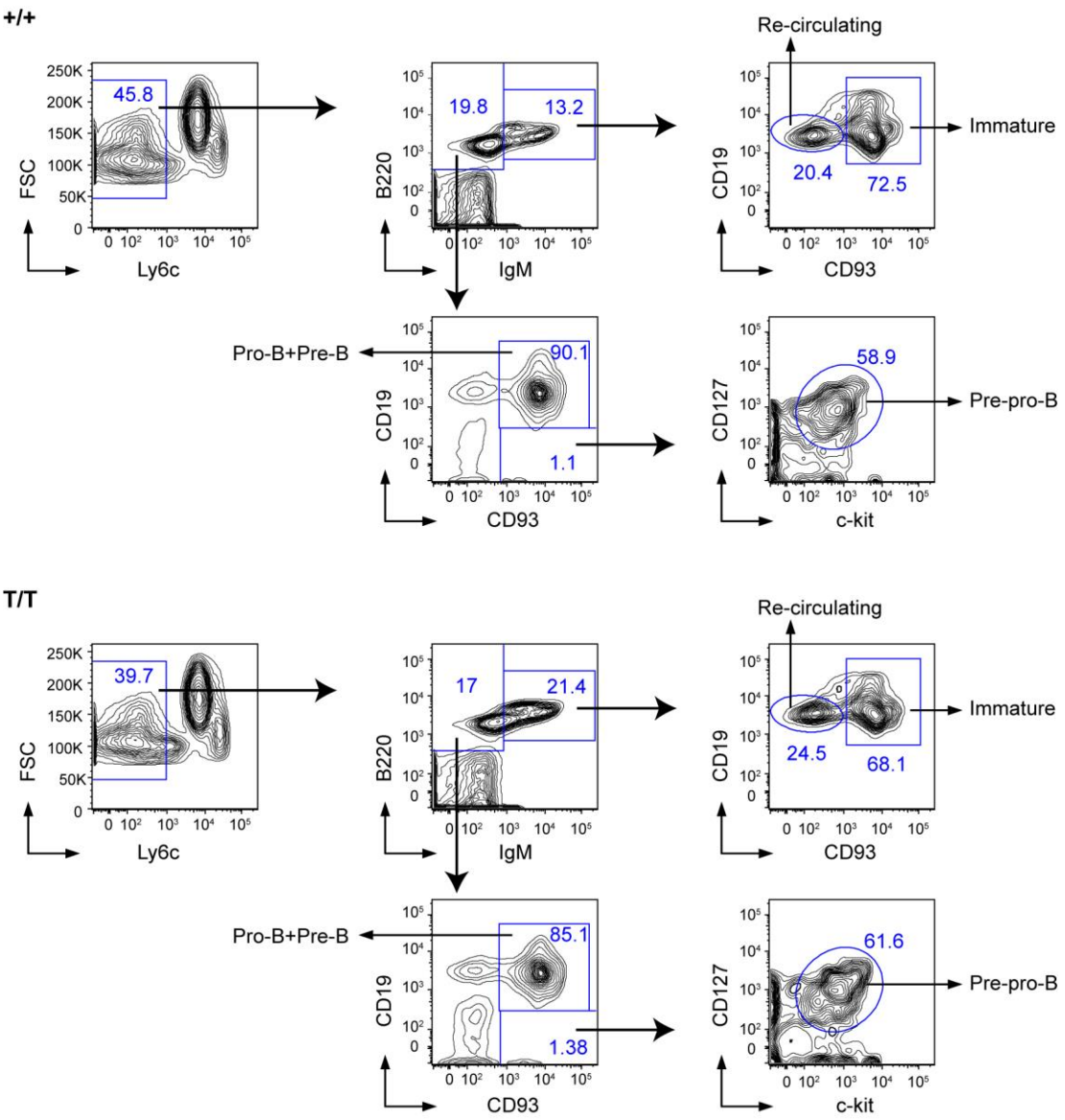


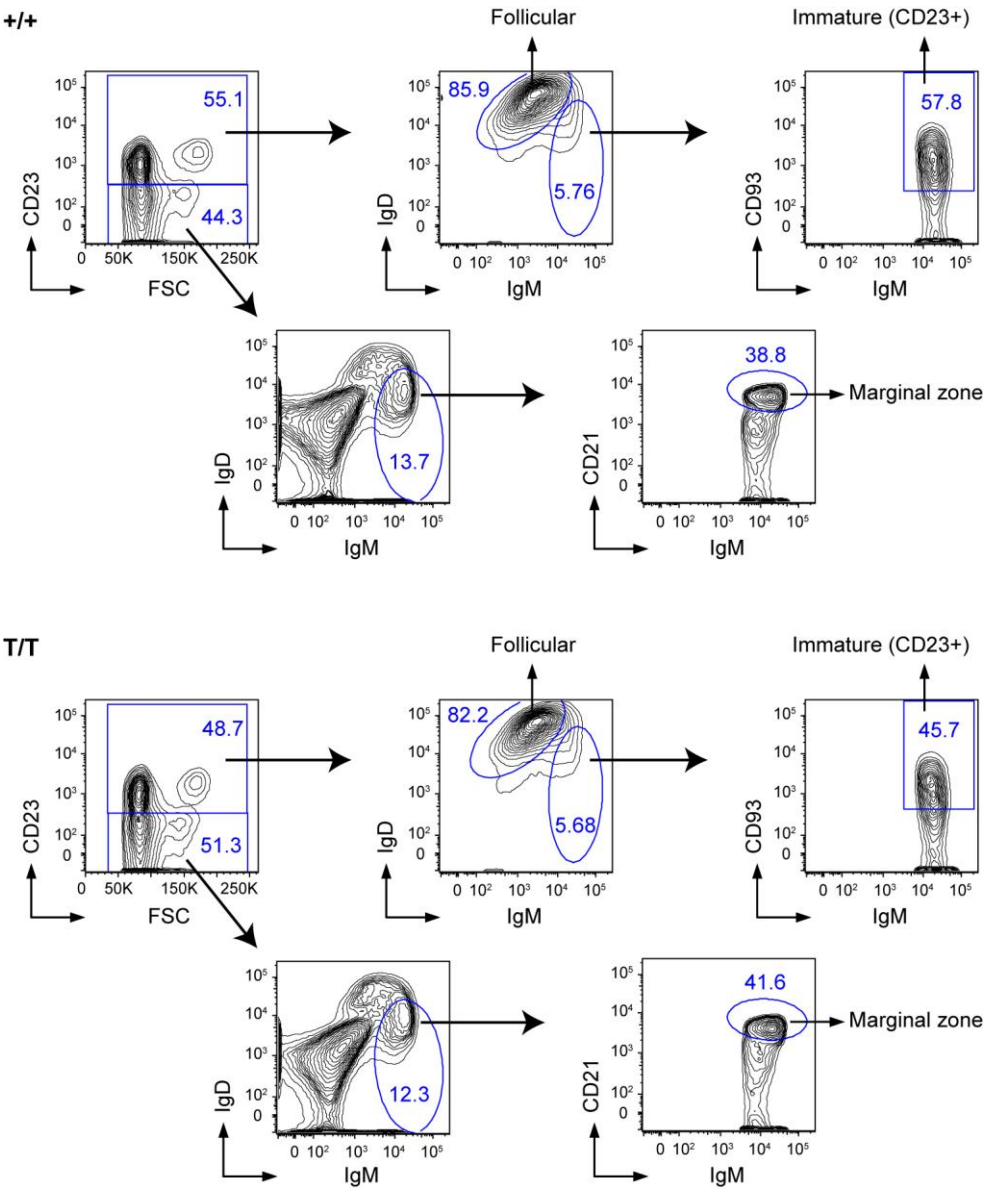
Supplementary Figure S1. Characterization of spleen cells in heterozygous *Smurf2*$^{+/T}$ mice. (**a**) Relative gross weight of spleen to body weight in spleen of 2-month-old wild-type (+/+) (N=12) and *Smurf2*$^{+/T}$ (+/T) mice (N=11). (**b**) Representative Ki-67 staining of spleen sections of 2-month old wild-type and *Smurf2*$^{+/T}$ mice and quantitation of Ki-67 positive cells in 10 randomly selected fields. (**c**) Quantitative RT-PCR analysis of c-Myc expression in spleen of 2-month old wild-type and *Smurf2*$^{+/T}$ mice. Error bars are standard deviations. Student *t*-test is used for statistical analysis.



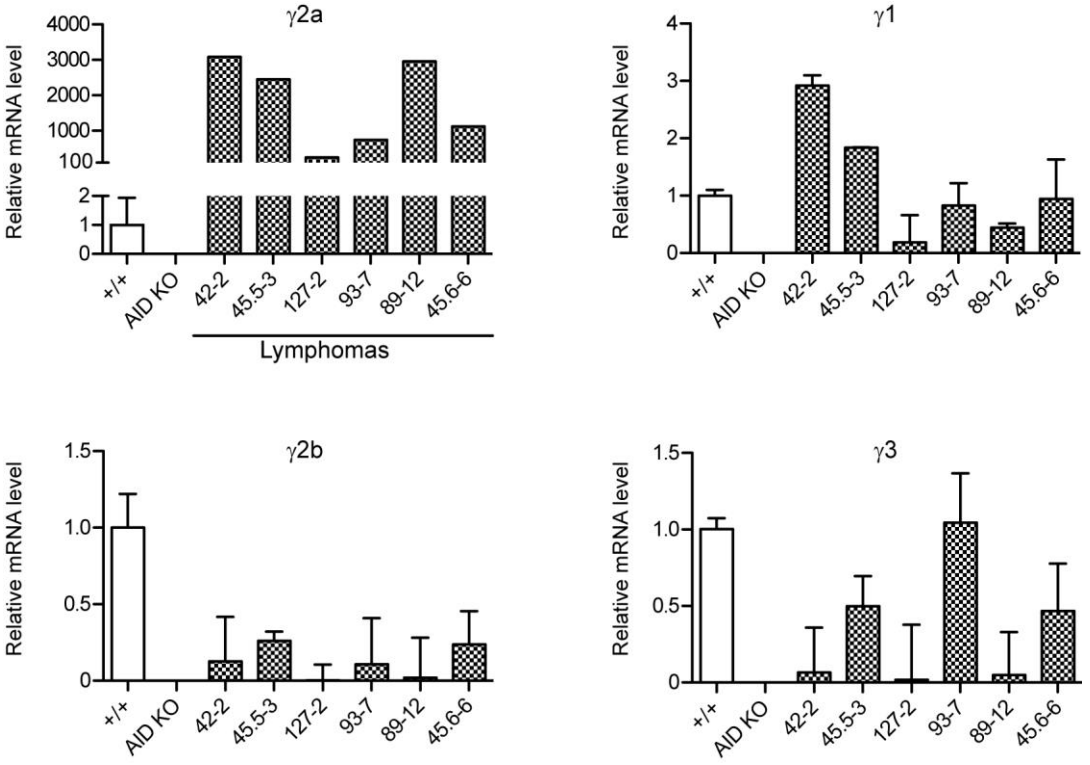
Supplementary Figure S2. Characterization of B-cell development in the bone marrow of Smurf2-deficient mice. Representative FACS analysis of bone marrow cells from 2-month old wild-type (+/+) and *Smurf2*$^{T/T}$ (T/T) mice. Live cells (propidium iodide excluding) are displayed. Sequential gating strategies are indicated by arrows. Frequency of each gated population as a percent of displayed cells is shown.



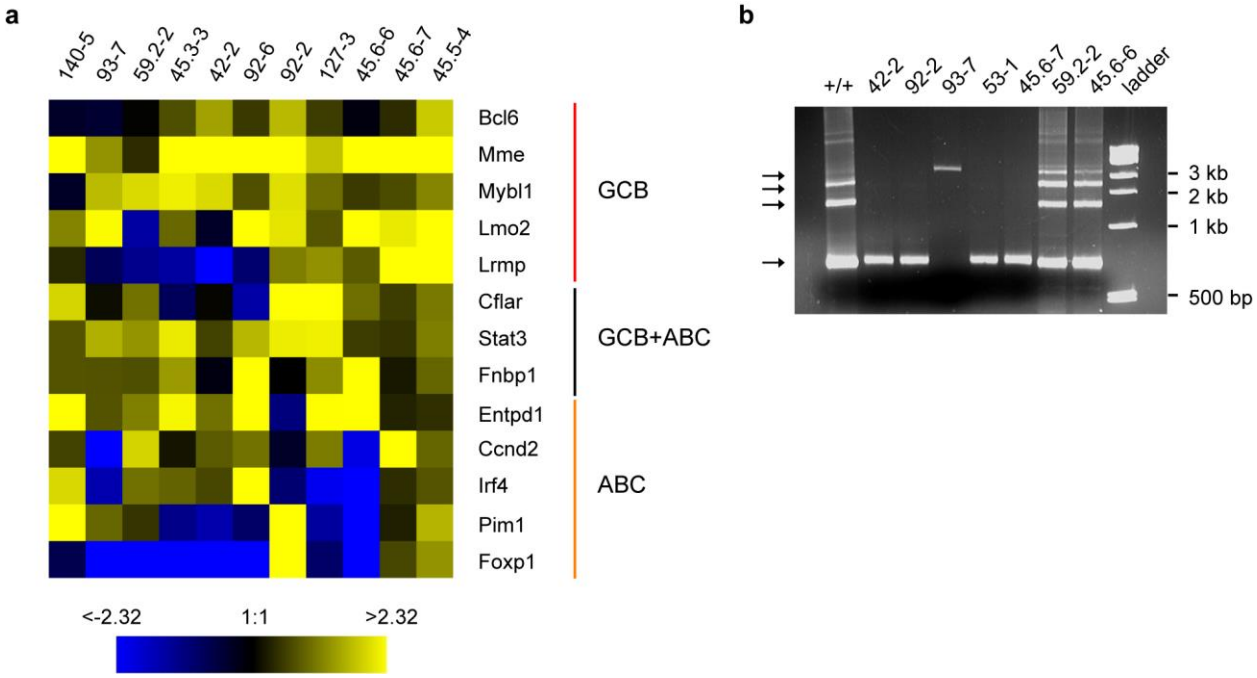
Supplementary Figure S3. Characterization of B-cell development in the bone marrow of Smurf2-deficient mice. Representative FACS analysis of bone marrow cells from 2-month old wild-type (+/+) and *Smurf2*$^{T/T}$ (T/T) mice. Live cells (propidium iodide excluding) are displayed. Sequential gating strategies are indicated by arrows. Frequency of each gated population as a percent of displayed cells is shown.



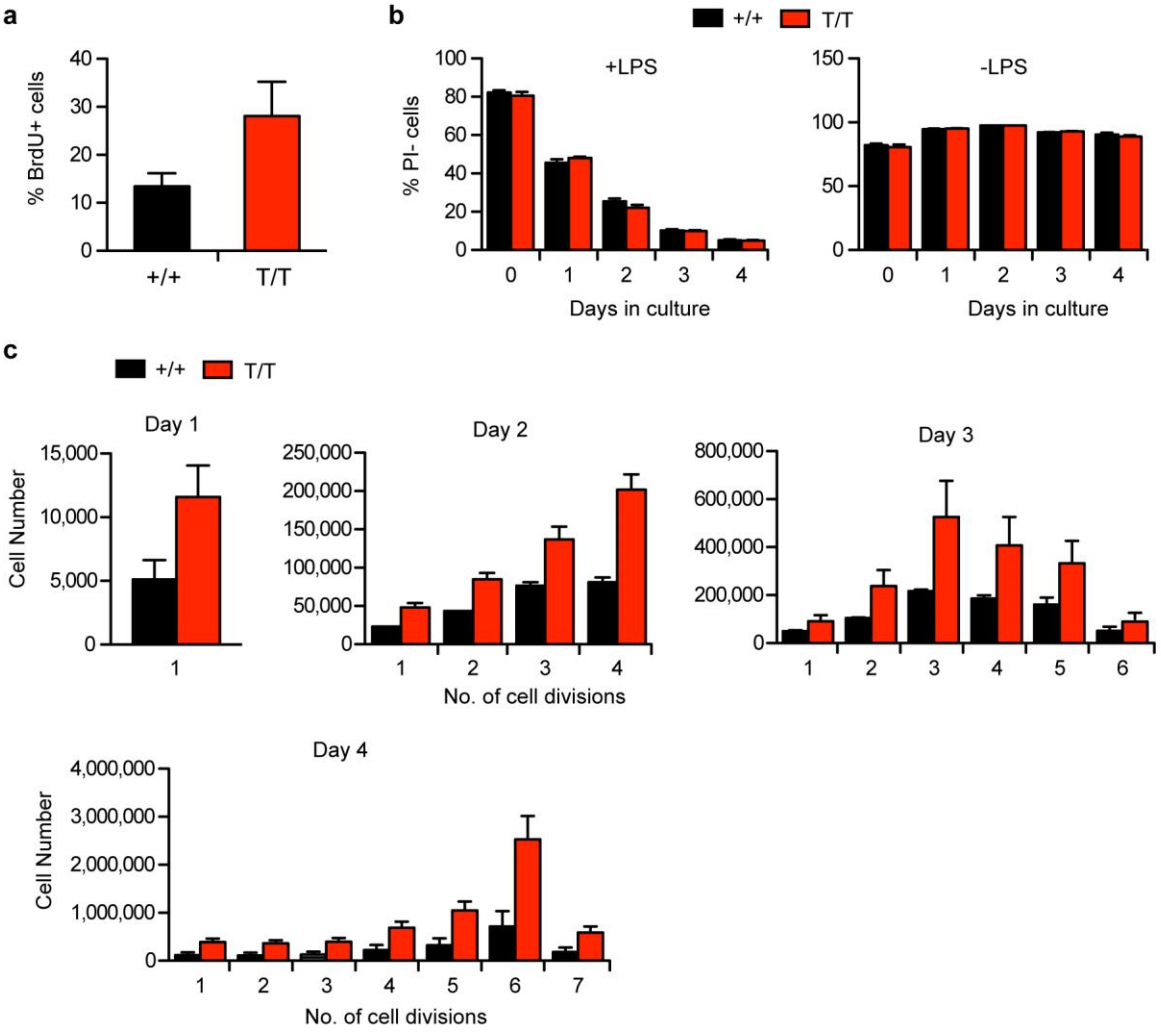
Supplementary Figure S4. Characterization of B cells in the spleen of Smurf2-deficient mice. Representative FACS analysis of splenic cells from 2-month old wild-type (+/+) and *Smurf2*$^{T/T}$ (T/T) mice. Live cells (propidium iodide excluding) are displayed. Sequential gating strategies are indicated by arrows. Frequency of each gated population as a percent of displayed cells is shown.



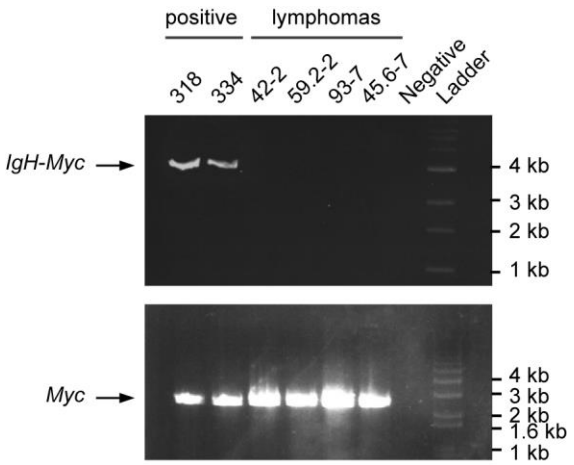
Supplementary Figure S5. Analysis of class switch recombination in representative lymphomas. Post-switch transcripts (γ1, γ2a, γ2b and γ3) of mouse immunoglobulin heavy chain locus are analyzed by quantitative RT-PCR. Splenic cells from wild-type and activation-induced cytidine deaminase (AID) knockout mice are used as controls. Error bars are standard deviations of 3 independent experiments.



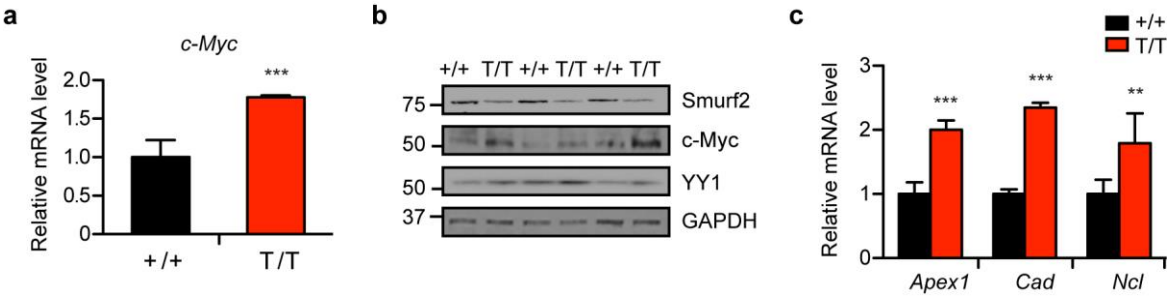
Supplementary Figure S6. Characterization of lymphomas from Smurf2-deficient mice. (**a**) Quantitative RT-PCR analysis of gene expression in lymphomas generated in Smurf2-deficient mice. Genes whose expression is characteristic of DLBCL[57, 58] including the germinal center B cell-like (GCB) and activated B cell-like (ABC) subgroups are selected for analysis. Relative expression in wild-type mice is set to be 1 after normalization with β-actin. The relative expression in lymphoma samples as compared to wild-type mice is $\log_2$ transformed and displayed in a heatmap. (**b**) Analysis of mouse immunoglobulin heavy chain (*IgH*) locus rearrangements in spleens containing B-cell lymphomas from Smurf2-deficent mice. Rearrangements of the $V_HJ588(D)J_H$ region of *IgH* are analyzed by genomic PCR. A wild-type (+/+) mouse spleen is used as a control. Arrows indicate 4 major bands corresponding to rearrangements using each one of the 4 J_H segments.



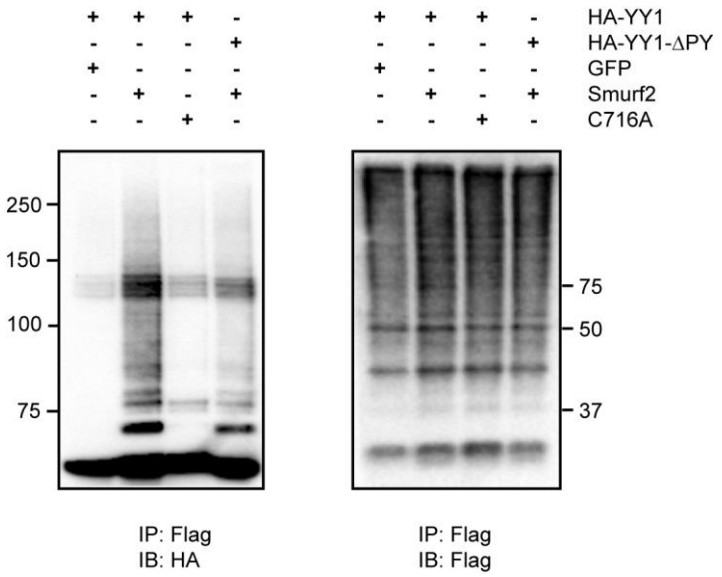
Supplementary Figure S7. Characterization of splenic B-cell proliferation in 2-month old wild-type (+/+) and *Smurf2*$^{T/T}$ (T/T) mice. (**a**) BrdU incorporation is determined in total splenic cells using flow cytometry. (**b**) Viability of splenic B (B220^{+}) cells with or without 5 μM lipopolysaccharide (LPS) treatment. Cell viability is determined as percent of propidium iodide-negative B220^{+} cells in flow cytometry. (**c**) Number of cells undergoing different number of cell divisions in response to LPS treatment is determined by carboxyfluorescein succinimidyl ester (CFSE) staining and flow cytometry. Error bars are standard deviations of 3 independent experiments.



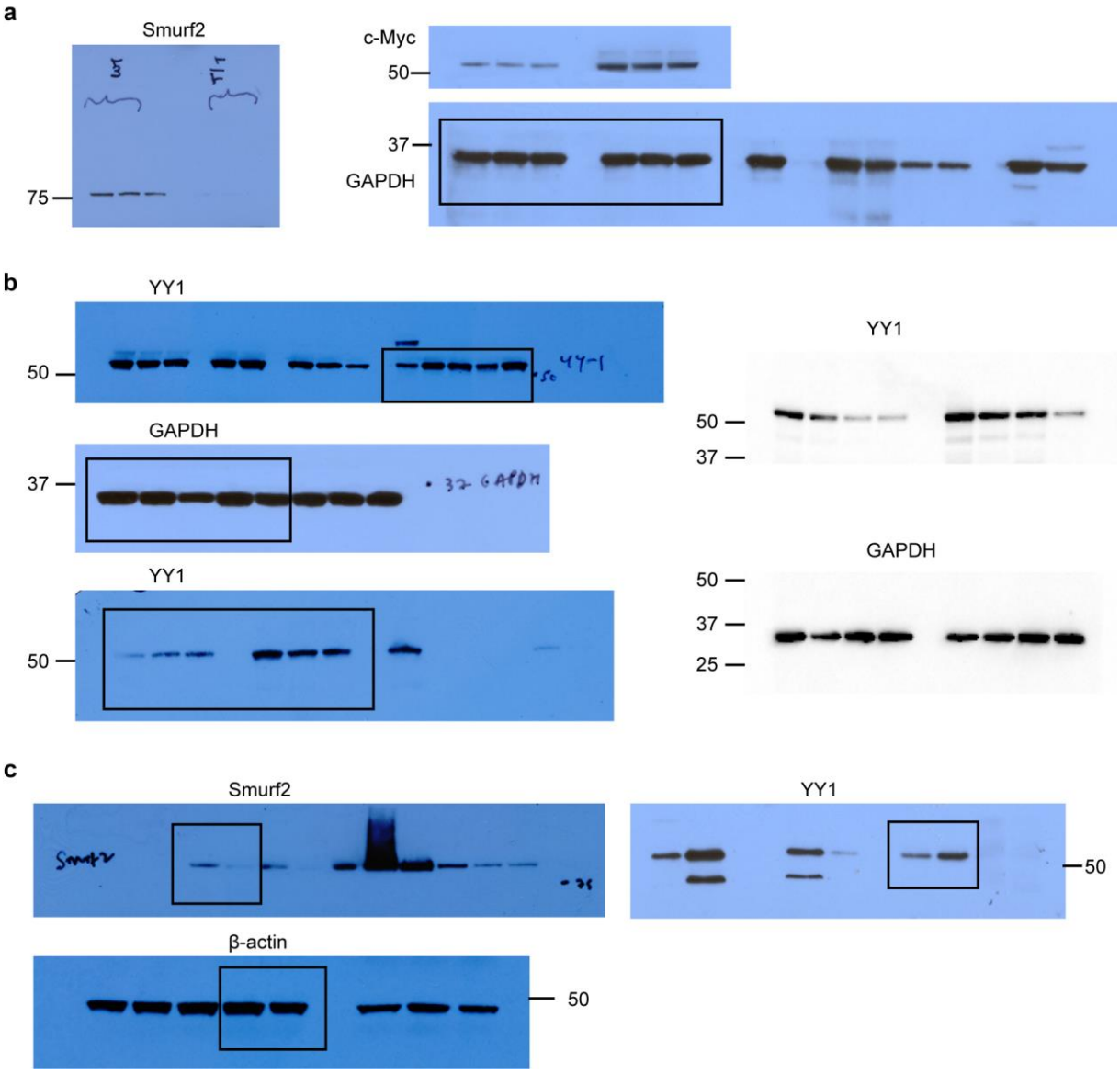
Supplementary Figure S8. Characterization of *IgH-Myc* translocation in lymphomas of Smurf2-deficient mice. Genomic PCR is used to detect *IgH-Myc* translocation in lymphomas generated in Smurf2-deficient mice and two lymphoma samples (318 and 334) with known *IgH-Myc* translocation as positive controls. Amplification of the *Myc* locus is used as a control.



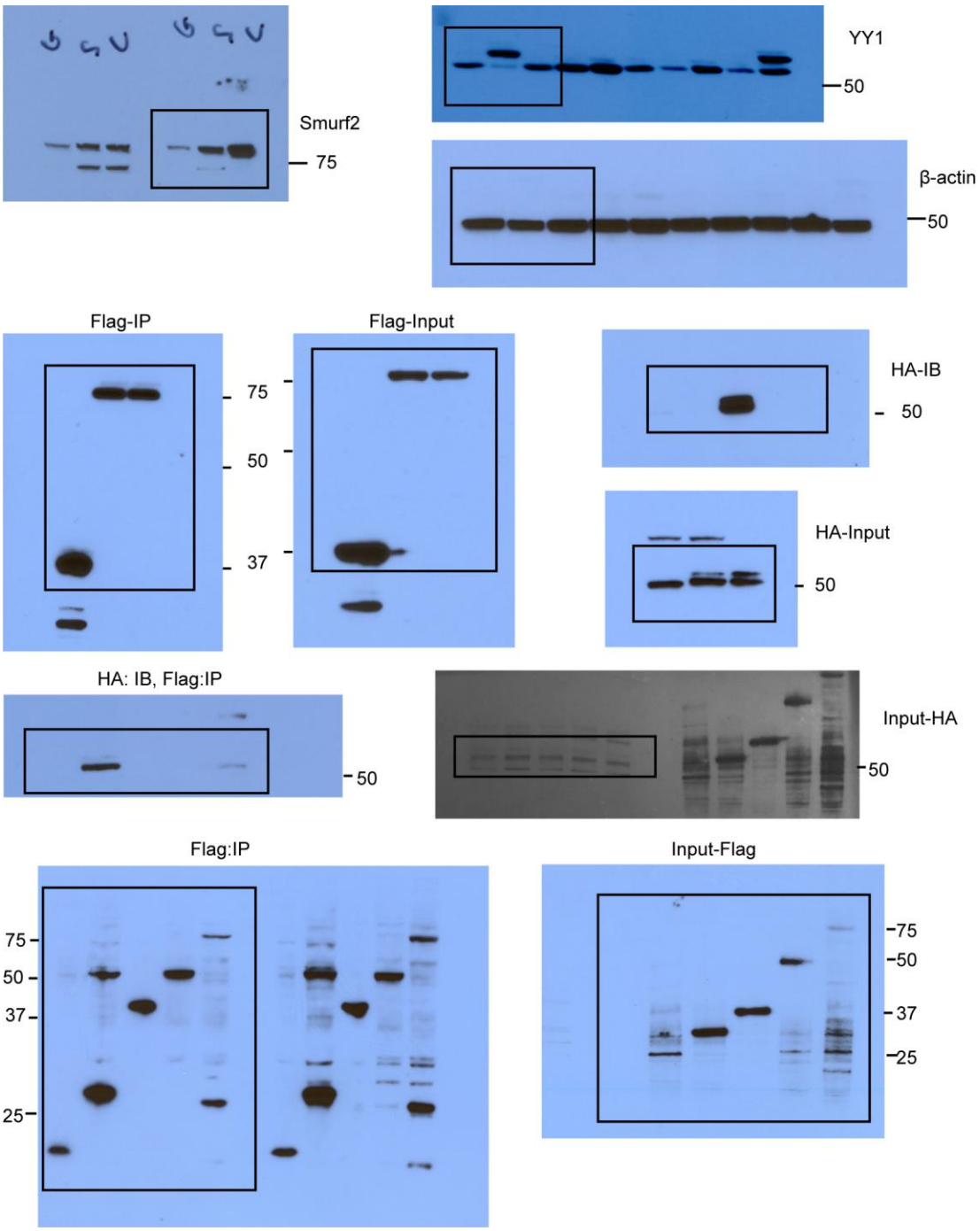
Supplementary Figure S9. Characterization of c-Myc and YY1 expression in liver of 2-month old wild-type (+/+) and *Smurf2*$^{T/T}$ (T/T) mice. (**a**) Quantitative RT-PCR analysis of c-Myc expression. (**b**) Western blot of c-Myc and YY1 proteins in 3 littermate pairs. (**c**) Quantitative RT-PCR analysis of c-Myc target genes. Error bars are standard deviations of 3 independent experiments. Student *t*-test is used to compare *Smurf2*$^{T/T}$ samples with wild-type samples. Statistical significance is indicated as: ** (P<0.01) and *** (P<0.001). Larger images of immunoblots are shown in Supplementary Figure S14a.



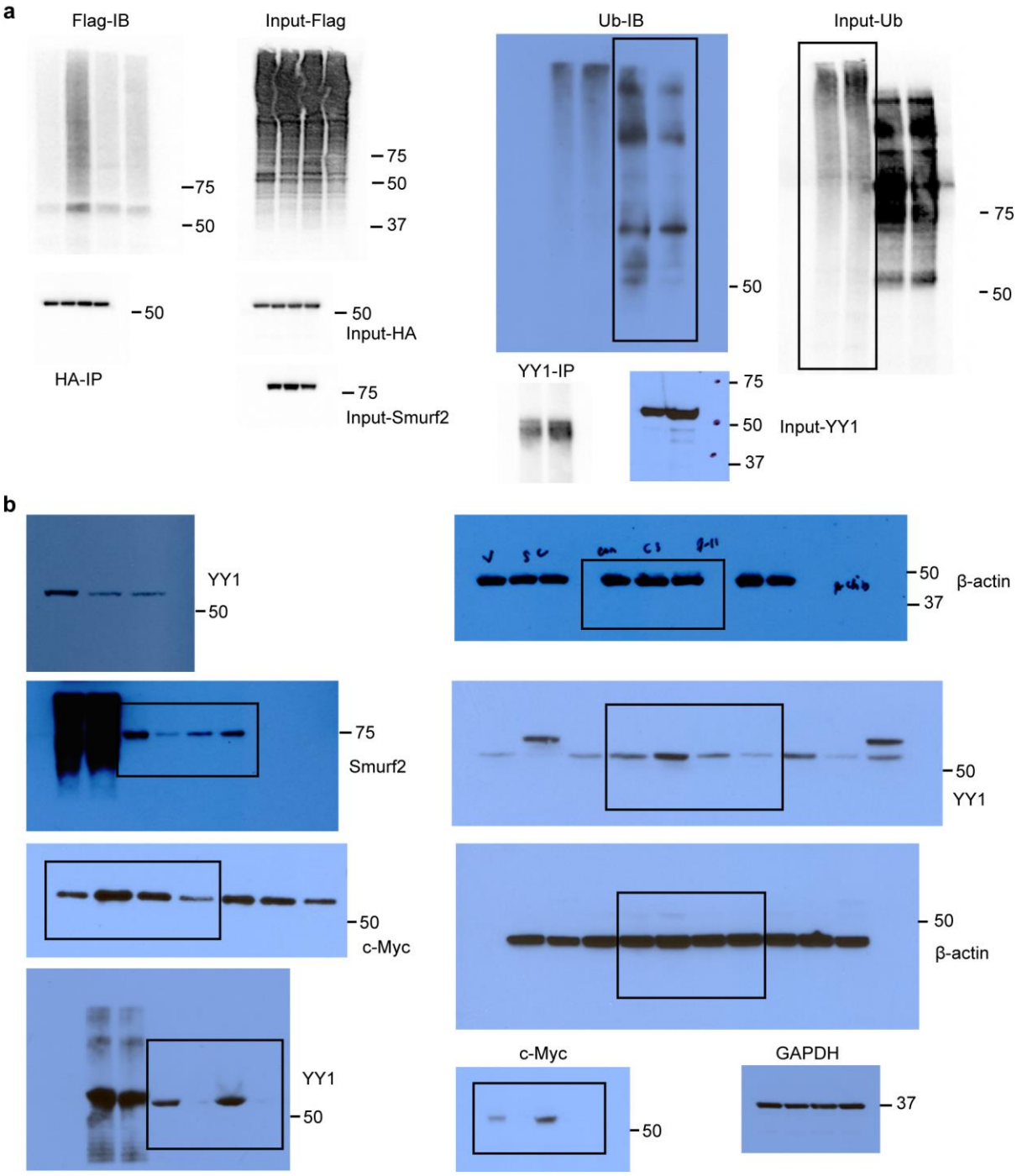
Supplementary Figure S10. Smurf2 mediates ubiquitination of YY1. 293T cells are transfected with HA-YY1 (or ΔPY), 3xFlag-Ub and Smurf2 (or C716A). IP with anti-Flag antibody is followed by IB with anti-HA antibody to detect poly-ubiquitinated YY1.



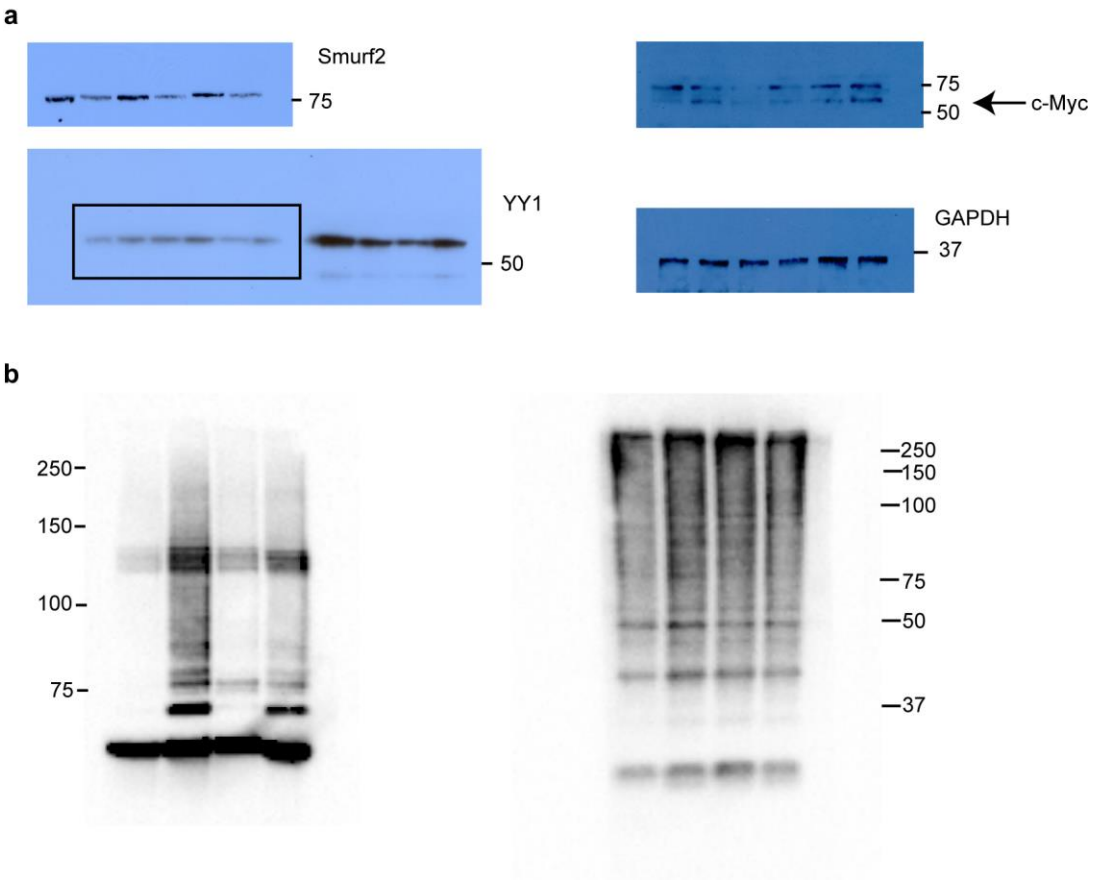
Supplementary Figure S11. (**a**) Western blot images of the selected portion displayed in Figure 5b. (**b**) Western blot images of the selected portion displayed in Figure 6. The original image for GAPDH in Figure 6b is shown in panel (**a**). (**c**) Western blot images of the selected portion displayed in Figure 7a. Images for Figure 6c were obtained on Bio-Rad Chemidoc, and all others were scanned from films.



Supplementary Figure S12. Western blot images of the selected portion displayed in Figure 7b,c. All images were scanned from films.



Supplementary Figure S13. (**a**) Western blot images of the selected portion displayed in Figure 7d,e. (**b**) Western blot images of the selected portion displayed in Figure 8. Images for Figure 7d,e except Ub-IB and Input-YY1 were obtained on Bio-Rad Chemidoc, and all others were scanned from films.



Supplementary Figure S14. (**a**) Western blot images of the selected portion displayed in Supplementary Figure S9. An arrow points to the right-sized band in the c-Myc image. (**b**) Western blot images of the selected portion displayed in Supplementary Figure S10. Images for Supplementary Figure S10 were obtained on Bio-Rad Chemidoc, and all others were scanned from films.

Supplementary Table S1 Somatic mutations in the rearranged V_H186.2 transcripts of mouse immunoglobulin heavy chain μ isotype in lymphomas derived from spleen of Smurf2-deficient mice. [a]

	# chains		Mutations per 10^3 bases [b]											
	Seq	Mut	Total (306 bp)				CDR1+2 (66 bp)				Framework (228 bp)			
			Total	R [c]	S [c]	R/S [c]	Total	R	S	R/S	Total	R	S	R/S
WT Sp [d]	10	8	33.0	23.9	9.1	2.6	62.1	57.6	4.5	12.8	25.9	15.4	10.5	1.5
42-2	6	6	61.5	48.5	13.0	3.7	108.6	103.5	5.1	20.3	50.4	34.4	16.0	2.2
45.6-6 [e]	6	6	78.4	56.6	21.8	2.6	184.3	159.1	25.2	6.3	49.7	28.5	21.2	1.3
127-2	3	3	63.2	38.1	25.1	1.5	146.5	111.1	35.4	3.1	39.5	16.1	23.4	0.7
93-7	3	3	73.0	50.1	22.9	2.2	181.8	156.6	25.2	6.2	42.4	19.0	23.4	0.8

[a] The region that was used to determine mutation frequency corresponds to amino acid residues -4 to 98 in V_H186.2 μ transcripts. Nucleotide replacements at the V_HD_H junctions were not scored as mutations.

[b] Mutation frequency was calculated by dividing the accumulated number of mutations in a given region with the total number of nucleotides sequenced for the region, length of which is shown in parentheses.

[c] R and S stand for replacement and silent mutations, respectively. R/S indicates ratio of replacement to silent mutations.

[d] Spleen from a wild-type mouse.

[e] A deletion of 128 bp, in addition to point mutations, was found in a clone derived from tumor 45.6-6. This clone was not used in calculation of mutations listed in the table.

Supplementary Table S2 Antibody sources and dilutions for immunohistochemistry, Western and immunoprecipitation.

Antibody (catalog #)	Source	Dilution
B220 (ab64100)	Abcam	1:50
Ki-67 (NCL-Ki67p)	Leica	1:1000
Smurf2 (ab53316)	Epitomics	1:2000
c-Myc (46-0603)	Invitrogen	1:5000
YY1 (sc-281)	Santa Cruz Biotechnology	1:5000 (Western)
YY1 (sc-7341)	Santa Cruz Biotechnology	1:500 (IP)
HA (sc-7392)	Santa Cruz Biotechnology	1:5000
Ubiquitin (sc-271289)	Santa Cruz Biotechnology	1:500
β-actin (sc-47778)	Santa Cruz Biotechnology	1:10,000
GAPDH (sc-25778)	Santa Cruz Biotechnology	1:2000
Flag (A8592)	Sigma	1:5000

Supplementary Table S3 Antibody sources and dilutions for flow cytometry.

Antibody	Source	Dilution
CD16/32	Bio-X-Cell	1 μg/10^6 cells
B220-APC or -biotin (RA3-6B2)	eBioscience	1:50
CD19-PE-TR (ID3)	Invitrogen	1:200
CD21-FITC (7G6)	eBioscience	1:50
CD23-biotin (B3B4)	eBioscience	1:25
CD24-FITC (30-F1)	Sothern Biotech	1:50
CD43-PE (S7)	eBioscience	1:200
CD93-PE-Cy7 (AA4.1)	eBioscience	1:100
CD95-PE (15A7)	eBioscience	1:200
CD117(c-kit)-PE-Cy5.5 (2B8)	eBioscience	1:200
CD127-PE (A7R34)	eBioscience	1:50
IgD-PE or -biotin (11-26)	eBioscience	1:50
IgM-APC, -biotin or -PE-Cy7 (II/41)	eBioscience	1:100
IgG2a-PE (m2a-15F8)	eBioscience	1:100
Ly6C-FITC (AL21)	BD Biosciences	1:30
anti-BrdU-FITC	BD Biosciences	1:100

Supplementary References

57. Alizadeh AA*, et al.* Distinct types of diffuse large B-cell lymphoma identified by gene expression profiling. *Nature* **403**, 503-511 (2000).

58. Wright G, Tan B, Rosenwald A, Hurt EH, Wiestner A, Staudt LM. A gene expression-based method to diagnose clinically distinct subgroups of diffuse large B cell lymphoma. *Proc Natl Acad Sci U S A* **100**, 9991-9996 (2003).