

AID Is Required for the Chromosomal Breaks in *c-myc* that Lead to

c-myc/IgH Translocations

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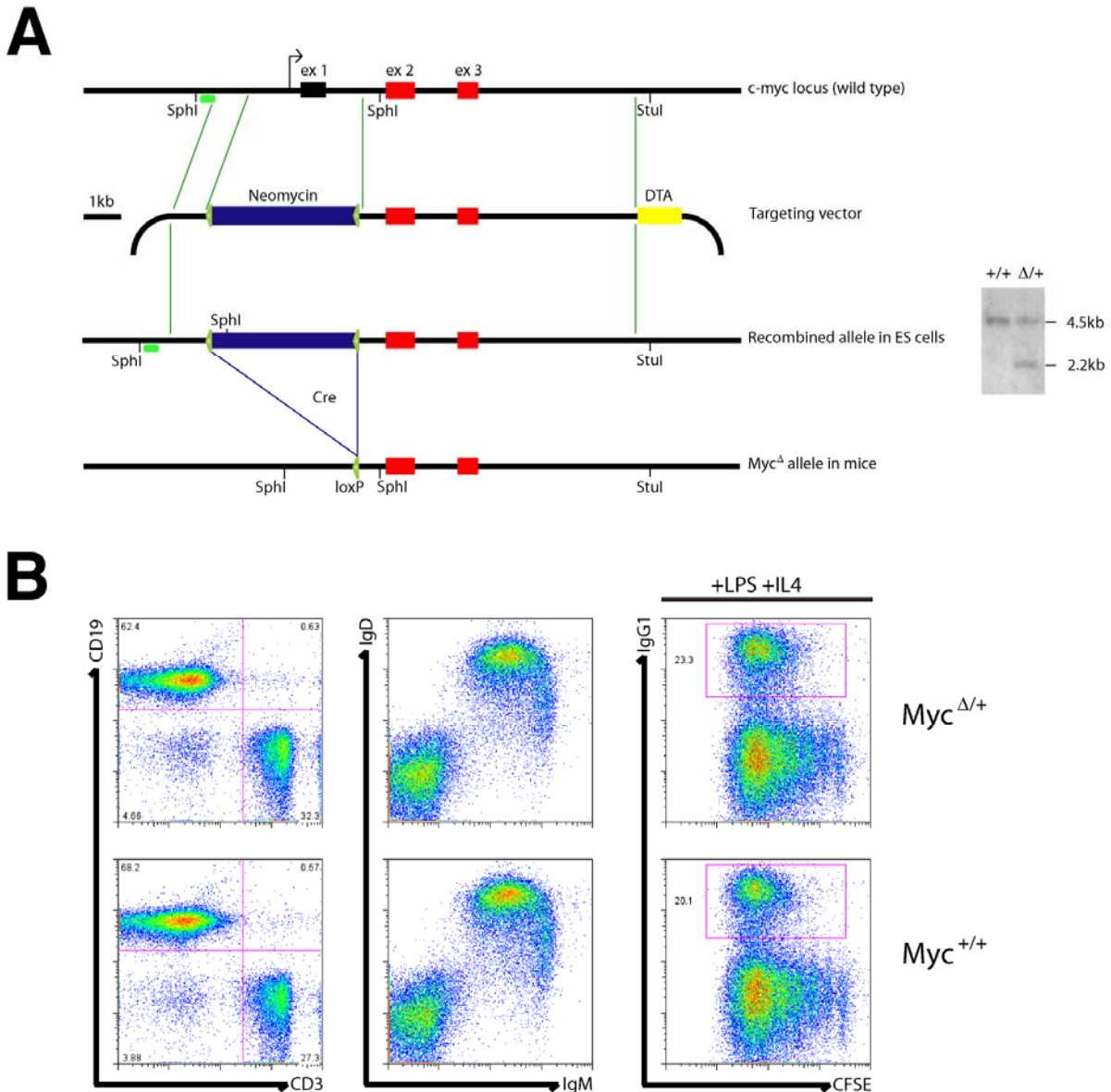


Figure S1. Knock-out strategy for the *Myc*^Δ allele.

(A) Targeting strategy is shown along with the genomic structure of the wild type murine *c-myc* locus, the targeting vector, the recombined allele in ES cells and in mice after removal of the neomycin-based ACN cassette (Bunting et al., 1999). Southern blot analysis of ES cell genomic DNA digested with SphI revealed proper integration upon hybridization with

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a radiolabeled probe (PCR product of 5-CATTCTGACTCCTTTTGCCC-3 and 5-TCAGAGGTGGCTATTCAGTTGC-3), yielding fragments of the indicated sizes. Diphtheria toxin A (DTA) was used for negative selection. The following primers were used for generating the targeting vector: short arm of homology, 5-GGCGCGCCTCACAAATCCGAGAGCCACAAC-3 and 5-GGCCGGCCTGCGCAGTCCAGTAA-3; long arm of homology, 5-TTAATTAACACCCAGTGCTGAATCGCTGC-3 and 5-GCGGCCGCCACCACTCTGTAGGAAATGCC-3. For genotyping, 35 cycles of PCR (95C, 45 s; 59C, 45 s; and 72C, 2 min) were performed with primers 5-GTGAAAACCGACTGTGGCCCTGGAA-3, 5-GGGGAGGGGGTGTCAAATAATAAGA-3 and 5-CAACCGCAGATGAGGTCTATGC-3. The size of the wild type allele is 0.4 kb, the Myc^{Δ} allele is 0.3 kb. (B) Flow cytometric analysis of splenocytes from age-matched wild type ($Myc^{+/+}$) and mutant ($Myc^{\Delta/+}$) mice reveals normal B lymphocyte development and activation in $Myc^{\Delta/+}$ mice. Immuno-staining was performed with the indicated markers on total spleen cells (left and center panels) or on LPS and IL-4 activated B cells labeled with CFSE to track cell division (right panels). Representative of three independent experiments.

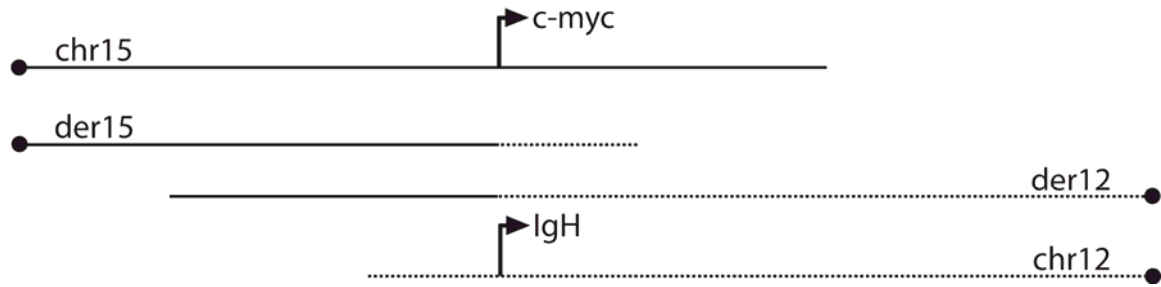


Figure S2. Diagram of balanced *c-myc/IgH* translocation.

Schematic representation of mouse chromosome 15 with *c-myc* transcribing towards the telomere and chromosome 12 with *IgH* transcribing towards the centromere. Centromeres are symbolized by circles. The derivative chromosomes der12 and der15, products of the balanced *c-myc/IgH* translocation, are also shown.

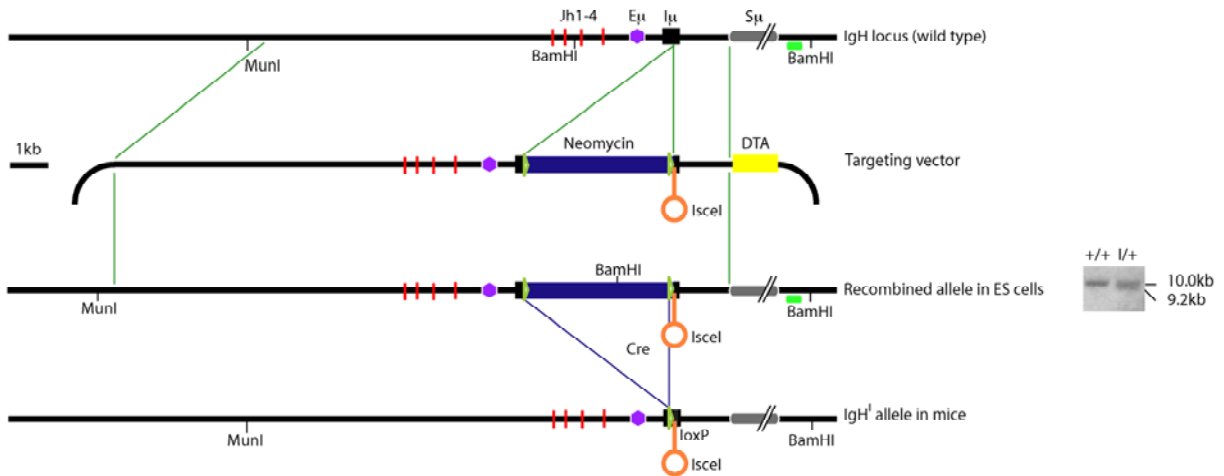
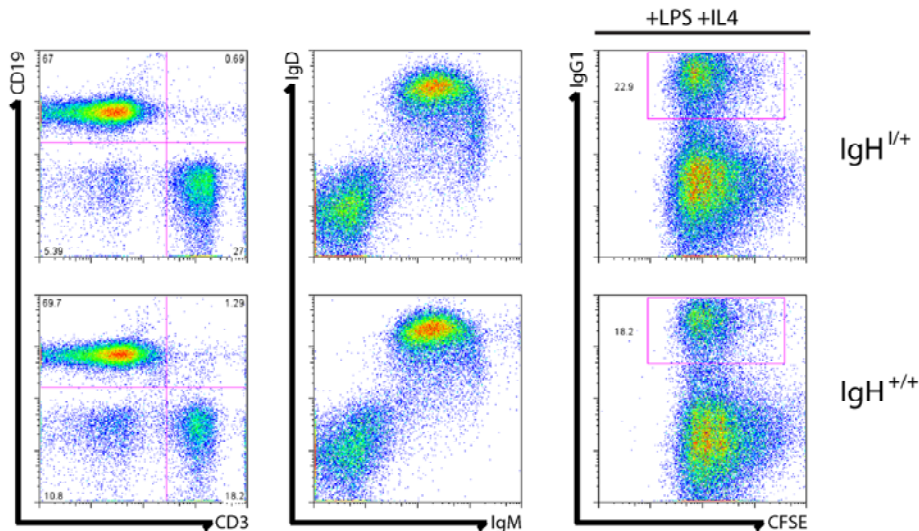
A**B**

Figure S3. Knock-in strategy for the IgH^I allele.

(A) The targeting strategy is shown along with the genomic structure of the wild type murine *IgH* locus, the targeting vector, the recombined allele in ES cells and in mice after removal of the neomycin-based ACN cassette (Bunting et al., 1999). Southern blot analysis of ES cell genomic DNA digested with BamHI revealed proper integration upon hybridization with a radiolabeled probe (PCR product of 5'-AAATGAGGAAGGCTGAGCAAGG-3 and 5'-AGGAAGGTGGGTTATGTTGGGG-3), yielding fragments of the indicated sizes. Diphtheria toxin A (DTA) was used for negative selection. The following primers were used for generating the targeting vector and introducing the I-SceI recognition sequence: long arm of homology, 5'-GGCGCGCCGATGAGAGCAGTGTAGGTCTATGGG-3 and 5'-GGCCGGCCCAGAAGCCACAACCATACATTCC-3; short arm of homology, 5'-GCGGCCGCAGTTACGCTAGGGATAACAGGGTAATATAGCCACCCATCCACCTGCTGC-3 (I-SceI site is underlined) and 5'-GCGGCCGCATTCCAGTTTGGCTCATCTCG-3. For genotyping, 35 cycles of PCR (95C, 45 s; 56C, 45 s; and 72C, 30 s) were performed with primers 5'-TGGGAATGTATGGTTGTGGCTTC-3 and

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5-GGAGAGGTCCAGAGTCTTTGTGTG-3. The size of the wild type allele is 0.1 kb, the IgH^I allele is 0.25 kb. (B) Flow cytometric analysis of spleen cells from age-matched wild type (IgH^{+/+}) and mutant (IgH^{I/+}) mice reveals normal B lymphocyte development and activation in IgH^{I/+} mice. Immuno-staining was performed with the indicated markers on total spleen cells (left and center panels) or on LPS and IL-4 activated B cells labeled with CFSE to track cell division (right panels). Representative of two independent experiments.

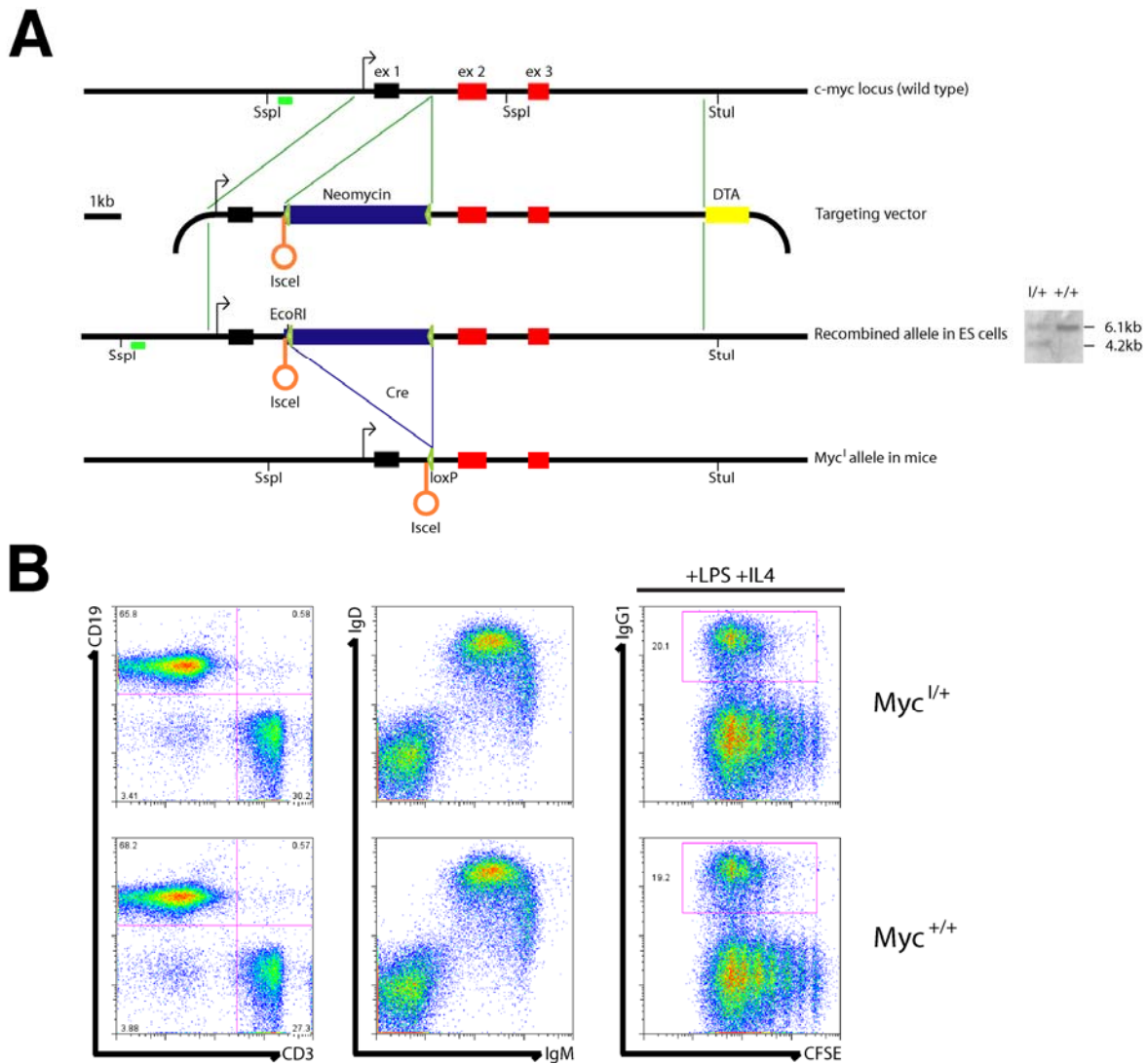


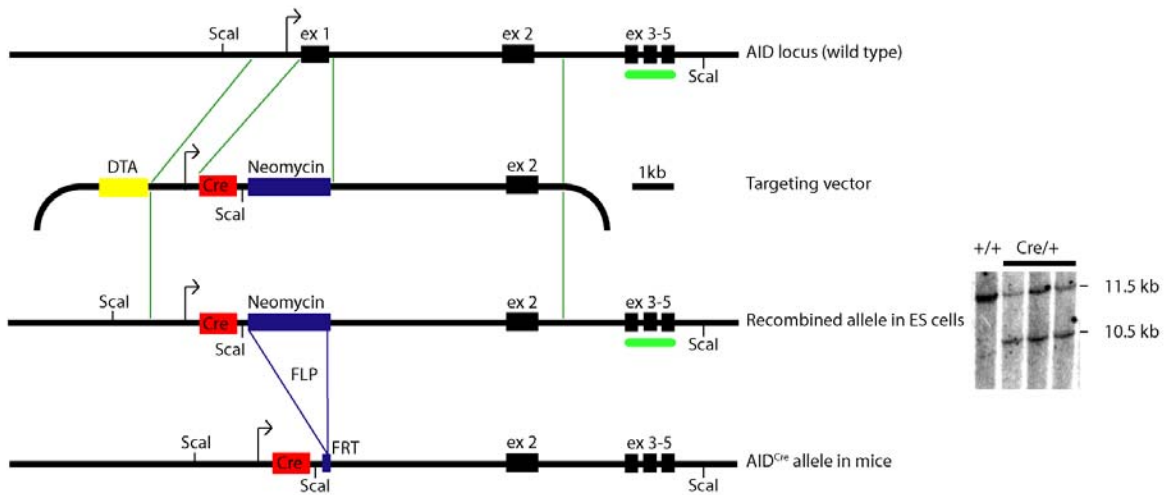
Figure S4. Knock-in strategy for the Myc^I allele.

(A) The targeting strategy is shown along with the genomic structure of the wild type murine *c-myc* locus, the targeting vector, the recombined allele in ES cells and in mice after removal of the neomycin-based ACN cassette (Bunting et al., 1999). Southern blot analysis of ES cell genomic DNA digested with *SspI* revealed proper integration upon hybridization with a radiolabeled probe (PCR product of 5-CATTCTGACTCCTTTTGCCC-3 and 5-TCAGAGGTGGCTATTCAGTTGC-3), yielding fragments of the indicated sizes. Diphtheria toxin A (DTA) was used for negative selection. The following primers were used for generating the targeting vector and introducing the I-SceI recognition sequence: short arm of homology, 5- GGCCGGCCGGGAGACCTACAGGGGAAAGAGCCG-3 and 5-GGCCGGCCATTACCCTGTTATCCCTACAGGGCGTCTTCCCTCTCCCCG-3 (I-SceI site is underlined); long arm of homology, 5-TTAATTAACACCCAGTGCTGAATCGCTGC-3 and 5-GCGGCCGCCACCACTCTGTAGGAAATGCC-3. For genotyping, 35 cycles of PCR (95C, 45 s; 58C, 45 s; and 72C, 45 s) were performed with primers 5-TTGGGGGAAACCAGAGGGAATCC-3 and 5-GGGAGGGGGTGTCAAATAATAAGAG-3. The size of the wild type allele is 0.25 kb, the Myc^I allele is 0.35 kb. (B) Flow cytometric analysis of spleen cells from age-

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matched wild type (Myc^{+/+}) and mutant (Myc^{I/+}) mice reveals normal B lymphocyte development and activation in Myc^{I/+} mice. Immuno-staining was performed with the indicated markers on total spleen cells (left and center panels) or on LPS and IL-4 activated B cells labeled with CFSE to track cell division (right panels). Representative of two independent experiments.

A



B

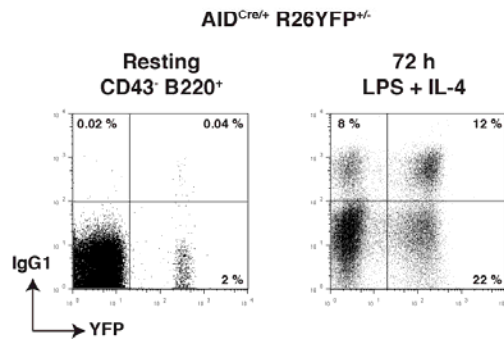


Figure S5. Targeted insertion of Cre recombinase into the mouse *aicda* locus ($AID^{Cre/+}$ mice).

The targeting strategy is shown along with the genomic structure of the wild type murine *aicda* locus, the targeting vector, the recombined allele in ES cells and in mice after germline deletion of the selection cassette by crossing with FLP^{er} mice. The inserted Cre recombinase DNA contains a nuclear localization signal, an SV40 T-antigen intron and an HSV thymidine kinase polyA signal. Expression of the neomycin resistance gene is driven by the PGK promoter. To increase the frequency of targeting, the neomycin DNA lacked a polyA and included the splice donor sequence of AID's exon 2. Southern blot analysis of ES cell genomic DNA digested with ScaI revealed proper integration upon hybridization with a radiolabeled probe (amplified with primers 5-CTGGCTGCCACGTGGAATTGTTG-3 and 5-TCCCAACATACGAAATGCATCTC-3), yielding fragments of the indicated sizes. Diphtheria toxin A (DTA) was used for negative selection. The following primers were used for generating the targeting vector: short arm of homology, 5-ATAAGAATGCGGCCGCACATTCAGAGCAAGCCGCAGTGGTG-3 and 5-CCTTAATTAATAGTACTCCAAATCTCAGGACAAGTCAAGGC-3; long arm of homology, 5-CCATTAATTAAGCAGAGCTAGAGCCGGCTTGTGGTAATAAC-3 and 5-GGCGCGCCGTGACTGTAATAACTGCAATCGTAATAGG-3; Cre recombinase DNA, combined PCR with the products of 5-GGCATAAAACTGAGTGTAACAAACGGAAGGAAC-3 and 5-

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GACACCTTCCTCTTCTTCTTGGGCATATCGGTCTCCAGCGTGACTTTCTTG-3 with
5-CAAGAAAGTCACGCTGGAGACCGATATGCCCAAGAAGAAGAGGAAGGTGTC-
3 and 5-

CCTTAATTAATACGCGTCGATCGAGTACTCGACCGAACAAACGACCCAACAC-3.

The frt-flanked Neomycin cassette was removed in vivo by crossing to FLPer mice (a gift by Dr. Susan Dymecki (Rodriguez et al., 2000)). For genotyping, 35 cycles of PCR (95C, 45 s; 57C, 45 s; and 72C, 1 min) were performed with primers

5-GGACCCAACCCAGGAGGCAGATGT-3,

5-CACTCGTTGCATCGACCGGTAATG-3 and

5-CCTCTAAGGCTTCGCTGTTATTACCAC-3. The wild type allele is 0.5 kb, the AID^{Cre}

allele is 0.3 kb. (B) Flow cytometric analysis of splenic B cells from AID^{Cre/+}, ROSA26-

STOP-YFP^{+/-} (Srinivas et al., 2001) mice prior and after stimulation with LPS and IL-4

shows regulated activity of Cre.

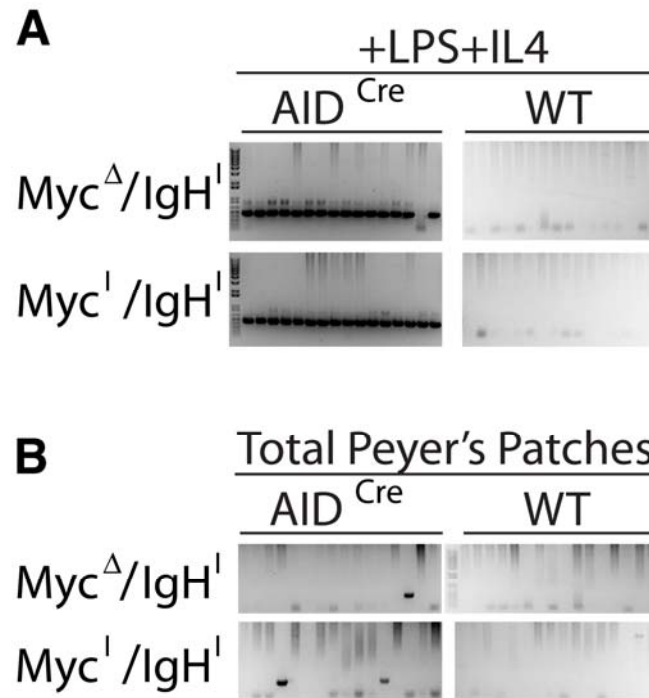


Figure S6. AID^{Cre} mediated translocations *in vivo*.

(A) Agarose gel with 0.5 kb PCR products corresponding to precise loxP-to-loxP *c-myc/IgH* translocations (as verified by sequencing). B cells of the indicated genotypes were stimulated with LPS and IL-4. 100,000 cells were assayed in each lane. (B) Agarose gel with 0.5 kb PCR products corresponding to precise loxP-to-loxP *c-myc/IgH* translocations (as verified by sequencing). DNA from total Peyer's Patches from mice with the indicated genotypes were analyzed. 100,000 cells were assayed in each lane.

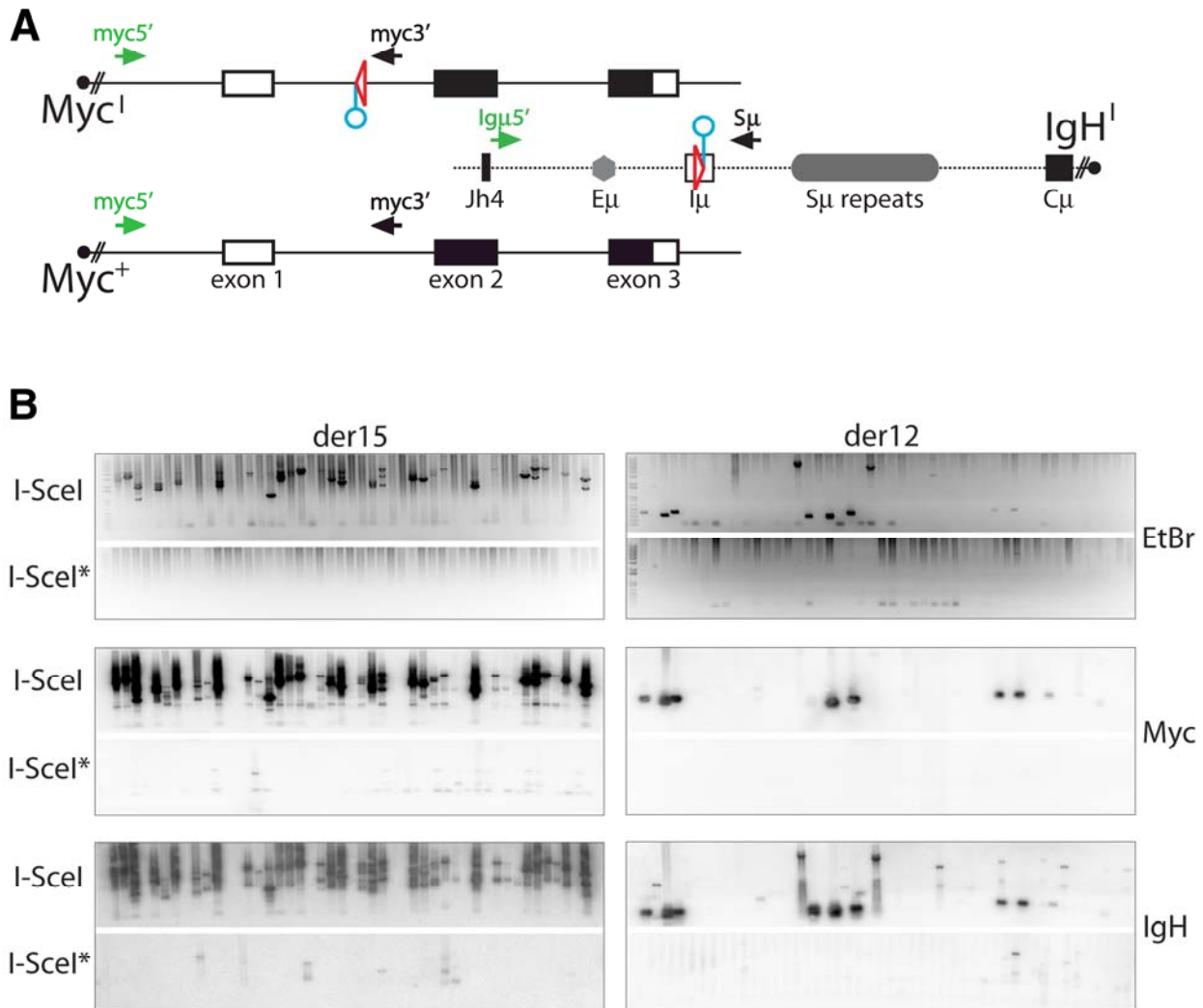


Figure S7. I-SceI induced translocations in AID deficient B lymphocytes: Southern Blot.

(A) Schematic representation of the Myc^l , Myc^+ and IgH^l alleles with the PCR primers for detecting der12 and der15 *c-myc/IgH* translocations. Circles point to recognition sequences for I-SceI. (B) I-SceI rescues translocation in the absence of AID. Representative ethidium bromide (EtBr) stained agarose gels from Figure 4B were Southern blotted and oligo-probed for *c-myc* and *IgH*, as indicated, to verify translocations.

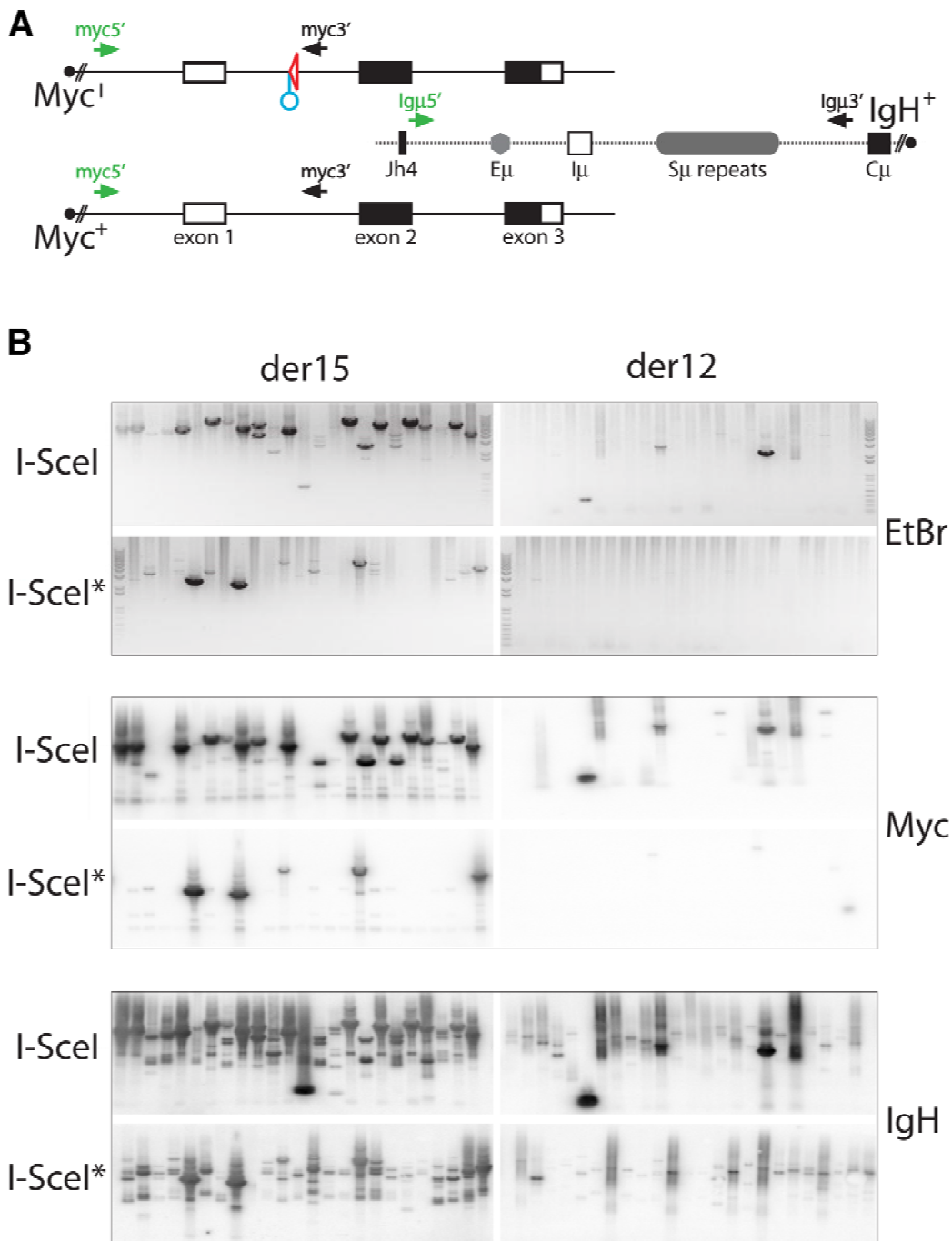


Figure S8. I-SceI mediated translocations in $Myc^{I/+}$, AID proficient B lymphocytes: Southern Blot.

(A) Schematic representation of the Myc^I , Myc^+ and IgH^+ alleles with the PCR primers for detecting der12 and der15 $c-myc/IgH$ translocations. Circles point to recognition sequences for I-SceI. (B) I-SceI mediated translocations in the presence of AID. Representative ethidium bromide (EtBr) stained agarose gels from Figure 5B were Southern blotted and oligo-probed for $c-myc$ and IgH , as indicated, to verify translocations. $Myc^{I/+}$ B cells were stimulated with LPS and IL-4 and infected with retroviruses encoding I-SceI or I-SceI* control. 100,000 cells were assayed in each lane.

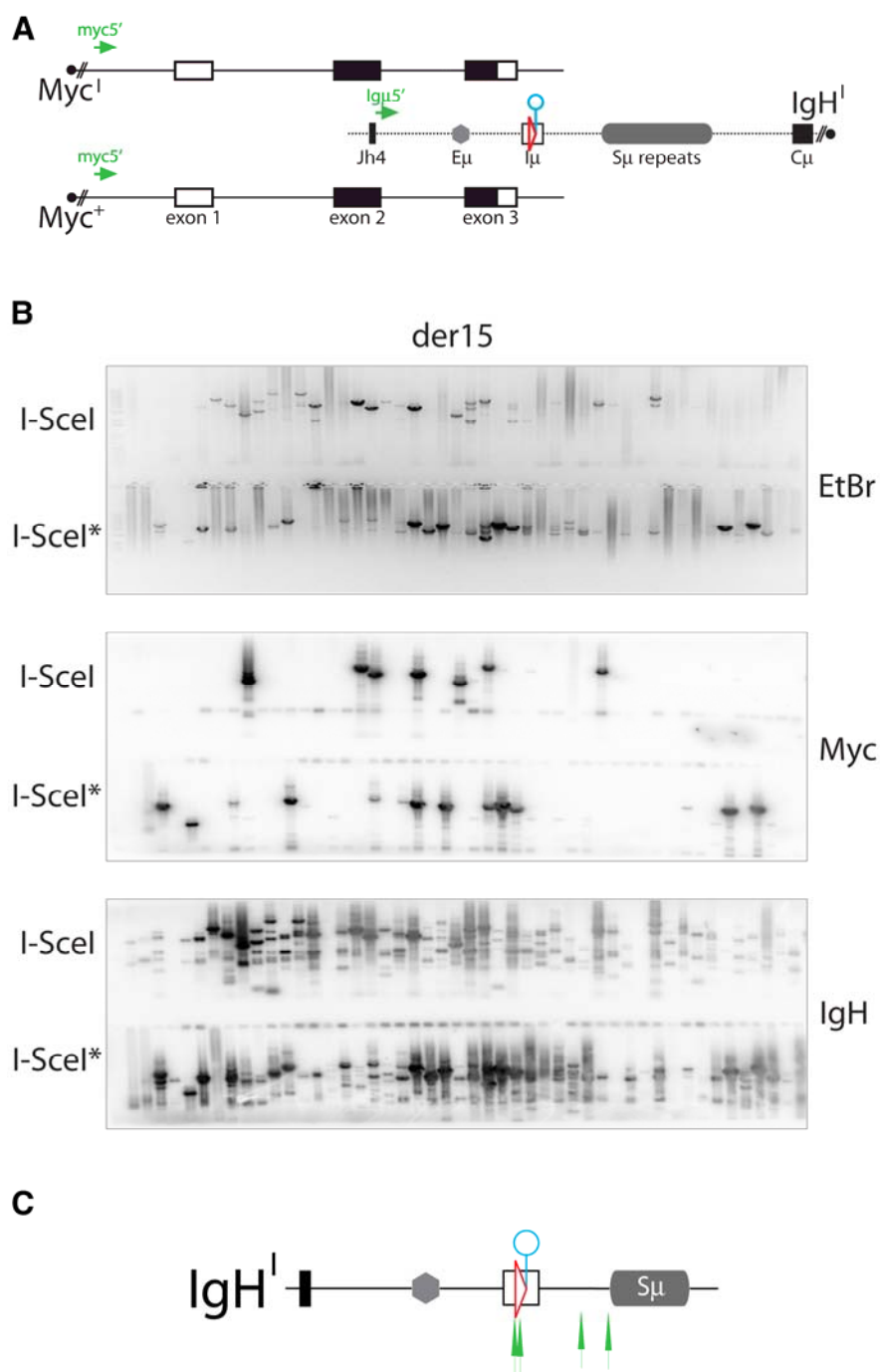


Figure S9. I-SceI mediated translocations in *IgH*^{I/+}, AID proficient B lymphocytes. (A) Schematic representation of the *Myc*⁺ and *IgH*^I alleles with the PCR primers for detecting der15 *c-myc/IgH* translocations. Circles point to recognition sequences for I-SceI. (B) I-SceI mediated translocations in the presence of AID. Representative ethidium bromide (EtBr) stained agarose gel with PCR products corresponding to *c-myc/IgH* translocations was Southern blotted and oligo-probed for *c-myc* and *IgH*, as indicated, to identify translocations. *IgH*^{I/+} B cells were stimulated with LPS and IL-4 and infected with retroviruses encoding I-SceI or I-SceI* control. 100,000 cells were assayed in each lane. Two independent experiments. (C) Map of translocation breakpoints from stimulated *IgH*^{I/+} B cells infected with I-SceI. Arrows point to *c-myc/IgH* der15 breakpoints at the *IgH*^I allele.

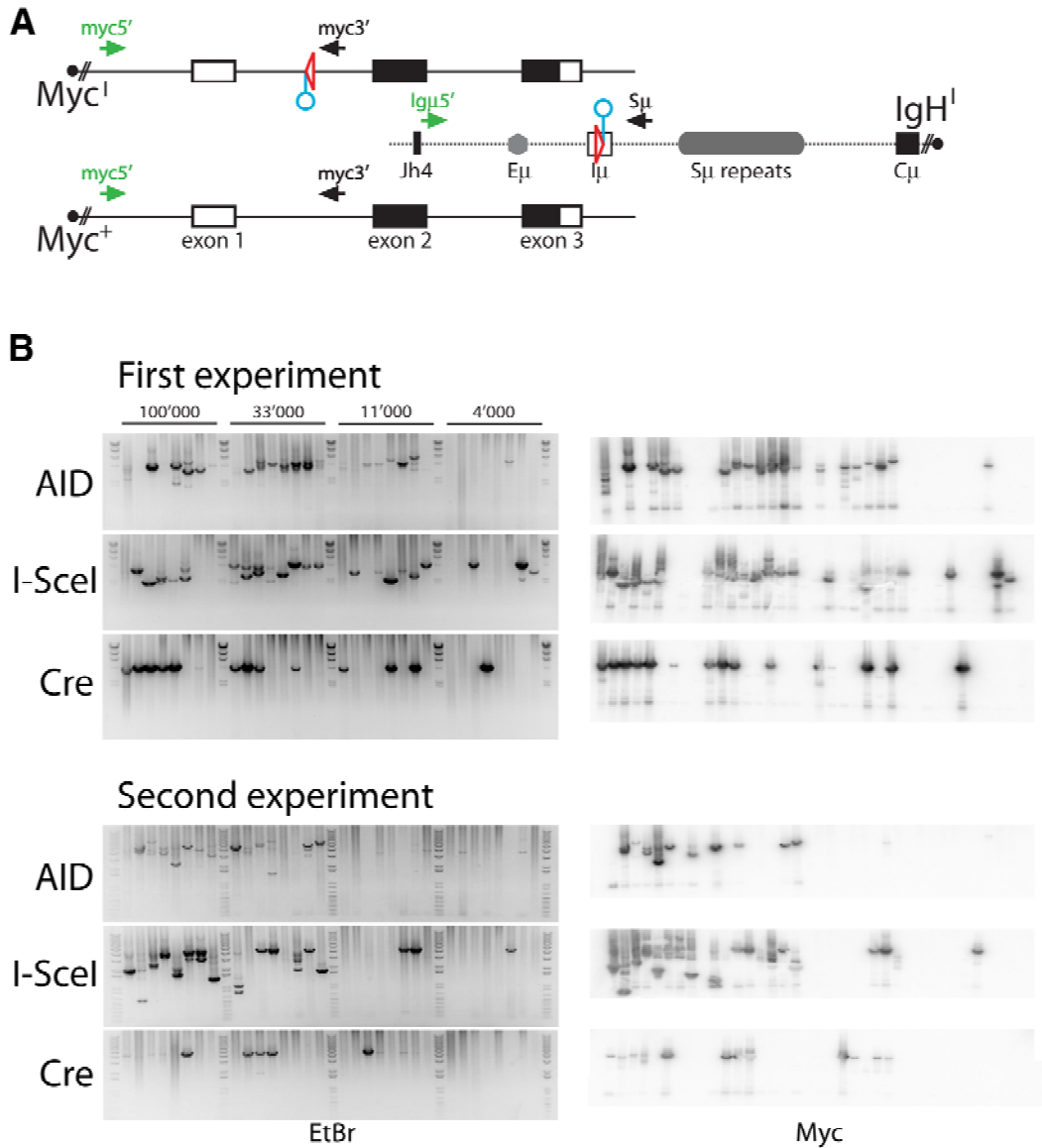


Figure S10. Comparing translocations by retroviral AID, I-SceI and Cre in AID^{-/-} cells: Southern Blot.

(A) Schematic representation of the *Myc*^l, *Myc*⁺ and *IgH*^l alleles with the PCR primers for detecting der15 *c-myc/IgH* translocations. Triangles represent loxP sites, circles point to recognition sequences for I-SceI. (B) AID, I-SceI, or Cre mediated translocations in the absence of AID. Ethidium bromide (EtBr) stained agarose gels from two independent experiments were blotted and oligo-probed for *c-myc*, as indicated, to identify translocations (see also figure 6B).

Table S1. Summary of mutation data in *c-myc*.

Genotype	Retrovirus	Frequency of unique mutations¹	Mutations at C/G (%)²	Transitions at C/G (%)³
Wild type	-	0.3 x 10 ⁻⁴ (87'890) ⁴	33.3	100
AID ^{-/-}	AID	1.2 x 10 ⁻⁴ (101'541) ⁵	66.7	75
AID ^{-/-}	empty	<0.07 x 10 ⁻⁴ (136'800) ^{4,5}	-	-

¹ Frequency of unique mutations (number of analyzed nucleotides).

² Percentage of mutations at C or G.

³ Percentage of C or G mutations that are transitions.

⁴ p = 0.08 with Student's T-Test.

⁵ p = 0.0005 with Student's T-Test.

Table S2. Translocation breakpoints from *Myc*^{l/+} *IgH*^{l/+} *AID*^{-/-} B cells infected with I-SceI. 50 nucleotides surrounding each breakpoint are shown, with the homology to germline sequence indicated by vertical bars. I-SceI site sequences are highlighted in blue, insertions are green, microhomologies are yellow. Shaded in light grey are extended microhomologies if single nucleotide gaps are tolerated. Numbers on the right indicate the distance in base pairs between the breakpoint and the center of the corresponding I-SceI allele. The top 8 sequences are from der12, the remaining 13 from der15 translocations.

<i>Myc</i> ^l	AGTTATAAGCTTTCGCGAGCTCGAA TCCGA TCCGAATTCTTAATTAACAC	75
285-1	GGCTTACCATTGCGGTGCCTGGTT TCCGA TCCGAATTCTTAATTAACAC	
<i>IgH</i> ^l	GGCTTACCATTGCGGTGCCTGGTT TCCGA GAGGTCCAGAGTCTTTGTGT	95
<i>Myc</i> ^l	TAACAGGGTAAT GGCCGGCCCAAGG G CGAATTCATAACTTCGTATAATGT	22
285-3	GTGCCTGGTTTCGGAGAGGT CCAGA GCGAATTCATAACTTCGTATAATGT	
<i>IgH</i> ^l	GTGCCTGGTTTCGGAGAGGT CCAGA GCTTTGTGTGGAATTGTTCCCTTCA	84
<i>Myc</i> ^l	ACAGGGTAAT GGCCGGCCCAAGGCGAATTCATAACTTCGTATAATGT	24
285-4	AATTGTTTCCTTCAAAG ATTAATTA GAATTCATAACTTCGTATAATGT	
<i>IgH</i> ^l	AATTGTTTCCTTCAAAGCCACCGAGGCTGGCTGGTCCATGAGCAGCCAGG	57
<i>Myc</i> ^l	GAAGACGCCCTG TAGGGATAACAGG GTAATGGCCGGCCCAAGGGCGAAT	4
285-7	GGTGGATGGGTGGCTAT ATTACCCT GTAATGGCCGGCCCAAGGGCGAAT	
<i>IgH</i> ^l	GGTGGATGGGTGGCTAT ATTACCCT G TATCCCTA GCGTAACTGCGGCC	-1
<i>Myc</i> ^l	TTAACACCCAGTGTGAATCGCTGC AGGGT CTCTGGTGCAGTGGCGTGC	118
285-8	TGGAATTGTTTCCTTCAAAGCCACCG AGGGT CTCTGGTGCAGTGGCGTCA	
<i>IgH</i> ^l	TGGAATTGTTTCCTTCAAAGCCACCG AGGCT GGCTGGTCCATGAGCAGCC	48
<i>Myc</i> ^l	TTCGCGAGCTCGAATCGGATCCGAAT TCTTAATTAACACCCAGT GCTGA	86
285-9	TGGATGGGTGGCTAT ATTACCCTGT TCTTAATTAACACCCAGT GCTGA	
<i>IgH</i> ^l	TGGATGGGTGGCTAT ATTACCCTGT TATCCCTA GCGTAACTGCGGCCG	-2
<i>Myc</i> ^l	CTTCGTATAATGTATGCTATACGAAG GTTAT AAGCTTTCGCGAGCTCGAAT	51
285-10	GGTGGATGGGTGGCTAT ATTACCCT GTTAT AAGCTTTCGCGAGCTCGAAT	
<i>IgH</i> ^l	GGTGGATGGGTGGCTAT ATTACCCT GTTATCCCTA GCGTAACTGCGGCCG	-4
<i>Myc</i> ^l	ACAGGGTAAT GGCCGGCCCAAGGG GA AATTCATAACTTCGTATAATGTAT	24
299-2	AAGCCACCGAGGCTGGCTGGTCCAT GA AATTCATAACTTCGTATAATGTAT	
<i>IgH</i> ^l	AAGCCACCGAGGCTGGCTGGTCCAT GAG CAGCCAGGTGGATGGGTGGCTA	33
<i>Myc</i> ^l	CAAAAGGCAGATTCACCCCCCC CC CACACACACTCCAGCACCTCCGG	2178
299-5	TCTAGAGCTAGCGGCCGAGTT CC CACACACACTCCAGCACCTCCGG	
<i>IgH</i> ^l	TCTAGAGCTAGCGGCCGAGTT CC TAGGGATAACAGGGTAAT ATAGCC	10
<i>Myc</i> ^l	GCTCCGGGTGTAAACAGTAATAG GC AGCATGAATTAAGTGCAGCGCCCG	1632
299-8	CTCTGTGTGAACTCCCTCTGGCCCT GC AGCATGAATTAAGTGCAGCGCCCG	
<i>IgH</i> ^l	CTCTGTGTGAACTCCCTCTGGCCCT GC TATTGTTGAATGGCCAAAGGT	231

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Myc ^I	GCAGGAGGGGAGCTGAGTGAGGCGA GTCGGACC CGGCAGCTGAGAGCAGC	1365
299-11	TGGGAATGTATGGTTGTGGCTTCTG GTCGGACC CGGCAGCTGAGAGCAGC	
IgH ^I	TGGGAATGTATGGTTGTGGCTTCTG GGCCGGCC GAATTCGGATCCGATTC	124
Myc ^I	GAACGAATGAGTTATCTAGGAGCC CCGCT CAGTGTGTGGAGTGATAGAG	1910
1212-1	GCTTCTGGGCCGGCCGAATTCGGAT CCGCT CAGTGTGTGGAGTGATAGAG	
IgH ^I	GCTTCTGGGCCGGCCGAATTCGGAT CCGAT TCGAGCTCGCGAAAGCTTAT	104
Myc ^I	CCTT TTGGT CGTACAGTTAT GTGGACTGGG CACATFCTTTCCAGAACGACC	2104
1212-2	CCCTCTGGCCCTGCTTAT GTGGAA TGGGCACATFCTTTCCAGAACGACC	
IgH ^I	CCCTCTGGCCCTGCTTAT GTGGAA TGGGC CAAAGG CTCTGAGACCAGGCT	211
Myc ^I	GGGGTGTAACAGTAATAGCGCAGC ATGAAT TAACTGCGCGCCCGACCAT	1637
1212-4	CGTATAGCATAcATTATACGAAGTT ATGAAT TAACTGCGCGCCCGACCAT	
IgH ^I	CGTATAGCATAcATTATACGAAGTT ATGAAT CTTAATTAATCTAGAGCT	46
Myc ^I	CGCCCAGCCATTTTCTCTTGCTCGC CGCTAG TCCTTTCCCTTTCTGTAC	1678
1212-15	AAGTTATGAATTCTTAATTAATCTA GAGCTAG TCCTTTCCCTTTCTGTAC	
IgH ^I	AAGTTATGAATTCTTAATTAATCTA GAGCTAG CGGCCGAGTTACG CTAG	25
Myc ^I	ATAAAGGGCGGGTGGCGGGGATTA GCCAGAGA ATCTCTCTTTCTCCCTT	1456
1212-16	ATCTAGAGCTAGCGGCCGAGTTAC GCTAGAGA ATCTCTCTTTCTCCCTT	
IgH ^I	ATCTAGAGCTAGCGGCCGAGTTAC GCTAGGGA TAAcAGGGTAAT ATAGC	7
Myc ^I	ATTAGCCAGAGAATCTCTCTTTCT CCCT TCCCCACCTCTCTATTTTTT	1474
1212-17	NTGGACTTTGGGTCTCCACCCAG ACT TCCCCACCTCTCTATTTTTT	
IgH ^I	CTGGACTTTGGGTCTCCACCCAG ACT GGGAATGTATGGTTGTGGCTTC	149
Myc ^I	GGTCTATGCAGGAAAACGATGTCTGGAATTTTATTAAAATTGCTCAGCA	1982
1212-18	TTNNNNGCCAGTCCACATGCTCTGT AA ATTTTATTAAAATTGCTCAGCA	
IgH ^I	TTCTAAGCCAGTCCACATGCTCTGTGTGA ACTCCCT CTGGCCCTGCTTAT	248
Myc ^I	TTTCTGTACGGTTGTT CGGGCGCAGCGCT CGGCTGAACTGTGTTCTTGCC	1717
1212-23	AATCTAGAGCTAGCGGCCGAGTTA CGCT CGGCTGAACTGTGTTCTTGCC	
IgH ^I	AATCTAGAGCTAGCGGCCGAGTTA CGCTAGGGATAACAGGGTAAT ATAG	9
Myc ^I	CAGCGTCTCTCTAAGGCTGGGGAA AACAG AATTTAGAAAGGGGAAGGA	1854
1212-27	TAGCGGCCGAGTTACGCT TAGGGAT AACAG AATTTAGAAAGGGGAAGGA	
IgH ^I	TAGCGGCCGAGTTACGCT TAGGGAT AACAGGGTAAT ATAGCCACCCATCC	-2
Myc ^I	CTCTTGCTCGCGCTAGTCCTTT CC TTTCTGTACGGTTGTT CGGGCGC	1690
1212-28	TTCTTAATTAATCTAGAGCTAGCG CC TTTCTGTACGGTTGTT CGGGCGC	
IgH ^I	TTCTTAATTAATCTAGAGCTAGCG CC GCAGTTACGCTAGGGATAACAGG	20

Table S3. Translocation breakpoints from Myc^{l/+} B cells infected with I-SceI. 50 nucleotides surrounding each breakpoint are shown, with the homology to germline sequence indicated by vertical bars. I-SceI site sequences are highlighted in blue, insertions are green, microhomologies are yellow. Shaded in light grey are extended microhomologies if single nucleotides gaps are tolerated. In 5 cases the breakpoint falls in the repetitive switch μ region, but cannot be precisely mapped. Numbers on the right indicate the distance in base pairs between the breakpoint and the center of the I-SceI site at the Myc^l allele. The top 12 sequences are from der12, the remaining 3 from der15 translocations.

Myc ^l	CCCTTGGGCCGGCCATTACCCTGTTATCCCTACAGGGCGTCTTCCCTCTC	-2
108A	 CCCTTGGGCCGGCCATTACCCTGTTGAGCTGAGCTGGGTGAGCTGAGCTG	
IgH	GGCCTGCTGCTGGGCTGGCATAGCTGAGTTGAACTTAAATGAGGAAGGCT	
Myc ^l	GCCCTTGGGCCGGCCATTACCCTGTTATCCCTACAGGGCGTCTTCCCTCT	-1
112A	 GCCCTTGGGCCGGCCATTACCCTGTAGTTGGGTGAGCTGAGCTGAGCTG	
IgH	AGCTGGAGTGAGCTGAGCTGAGGTGAAC TGGGTGAGCTGAGCTGAGCTG	
Myc ^l	CGCCCTTGGGCCGGCCATTACCCTGTTATCCCTACAGGGCGTCTTCCCTCT	0
113A	 CGCCCTTGGGCCGGCCATTACCCTGAGCTGGGCTAGCTGACATGGATTAT	
IgH	AGCTGGGATGAGGTAGGCTGGGATGAGCTGGGCTAGCTGACATGGATTAT	
Myc ^l	CGCCCTTGGGCCGGCCATTACCCTGTTATCCCTACAGGGCGTCTTCCCTCT	0
114A	 CGCCCTTGGGCCGGCCATTACCCTGAGCTGGGTGAGCTGAGCTGAGCT	
IgH	GAGCTGAGCTGAGCTGGGTGAGCTGAGCTGGGTGAGCTGAGCTGAGCT	
Myc ^l	CCCTTGGGCCGGCCATTACCCTGTTATCCCTACAGGGCGTCTTCCCTCTC	-2
116A	 CCCTTGGGCCGGCCATTACCCTGTTCTGAGCTGGGTGAGCTGAGCTGA	
IgH	GGTGAAGCTGAGCTGGGTGAGCTGAGCTGGGTGAGCTGAGCTGA	
Myc ^l	CATTATACGAAGTTATGAATTCGCCCTTGGGCCGGCCATTACCCTGTTAT	22
1034-4	 CATTATACGAAGTTATGAATTCGCCAGCTGAGCTGAGCTGAGCTGAGCTG	
IgH	S μ -TGAGCTGAGCTGAGCTGAGCTGAGCTG	
Myc ^l	GCCCTTGGGCCGGCCATTACCCTGTTATCCCTACAGGGCGTCTTCCCTCT	-1
1034-8	 GCCCTTGGGCCGGCCATTACCCTGTGGGTGAGCTGGGTAAAGCTGAGCTG	
IgH	S μ -TGGGTGAGCTGGGTAAAGCTGAGCTG	
Myc ^l	GGTGTAAATTAAGAATTCGGATCCGATTCGAGCTCGGAAAGCTTATAAC	83
1034-9	 GGTGTAAATTAAGAATTCGGATCCGAGCTGAGCTGANCTGGGTAAAGCTG	
IgH	S μ -GTGAGCTGAGCTGAGCTGGGTAAAGCTG	
Myc ^l	ATGAATTCGCCCTTGGGCCGGCCATTACCCTGTTATCCCTACAGGGCGTC	7
1034-10	 ATGAATTCGCCCTTGGGCCGGCCATTCCCAGCTCAGCCAGCTCAGCTC	
IgH	S μ -CACCCAGCTCAGCCAGCTCAGCTC	
Myc ^l	TTCGCCCTTGGGCCGGCCATTACCCTGTTATCCCTACAGGGCGTCTTCCC	1
1108-10	 TTCGCCCTTGGGCCGGCCATTACCCTAGCTGAGCTGGGTGAGCTGAGCT	
IgH	S μ -TGAGCTGAGCTGGGTGAGCTGAGCT	

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Myc ^I	CGCCCTTGGGCCGGCCATTACCCTGTTATCCCTACAGGGCGTCTTCCCTC	-1
1108-11	CGCCCTTGGGCCGGCCATTACCCTGTTCCAGCTCAGCCCAGCTCAGCCCAG	
IgH	GAGCTGAGCTGAGCTGGGGTGAGCTGCCAGCTCAGCCCAGCTCAGCCCAG	
Myc ^I	TCGTATAGCATACATTATACGAAGTTATGAATTCGCCCTTGGGCCGGCCA	32
1108-12	TCGTATAGCATACATTATACGAAGTTGGACTCAACTGGGCTGGCTGATGG	
IgH	CTGGATGATCTGGTGTAGGGTGATCTGGACTCAACTGGGCTGGCTGATGG	
Myc ^I	CCTCGGCGGGGAGAGGGAAGACGCCCTGTAGGGATAACAGGGTAATGGCC	13
11-10-13	CCTCGGCGGGGAGAGGGAAGACGCCATCTCAGCTCATCTGTGCTTTTITAG	
IgH	TAGAAGCACTCAGAGAAGCCACCCATCTCAGCTCAGCTGTGCTTTTITAG	
Myc ^I	GGGAGAGGGAAGACGCCCTGTAGGGATAACAGGGTAATGGCCGGCCCAAG	5
11-10-17	GGGAGAGGGAAGACGCCCTGTAGGGGTTTTCTATAAAAACTAAAAACATC	
IgH	AGTTGTAGATCAAGAATGTAGTAGTGTTTTTCTATAAAAACTAAAAACATC	
Myc ^I	CGGCGGGGAGAGGGAAGACGCCCTGTAGGGATAACAGGGTAATGGCCGGC	10
681-6	CGGCGGGGAGAGGGAAGACGCCCTGGGGTCAGCTGAGCAAGAGTGAGTAG	
IgH	GAACTGAGCTGTGTGAGCTGAGCTGGGGTCAGCTGAGCAAGAGTGAGTAG	

Table S4. Translocation breakpoints from uninfected wild type B cells. 50 nucleotides surrounding each breakpoint are shown, with the homology to germline sequence indicated by vertical bars. Insertions are green, microhomologies are yellow. Shadowed in light grey are extended microhomologies if single nucleotides gaps are tolerated. In 4 cases the breakpoint falls in the repetitive switch μ region, but cannot be precisely mapped. The top 5 sequences are from der12, the remaining 6 from der15 translocations.

Myc	CTAGCGCAGTGAGGAGAAGCAAAATTGGGACAGGGATGTGACCGATTTCGT
931-1	TCAGCTCACCCAGCTCAGCTCACCTGGGACAGGGATGTGACCGATTTCGT
IgH	TCAGCTCACCCAGCTCAGCTCACCC - S μ
Myc	CAGACTCTGGTGGTCTTTCCCTGTGTTCCTTCTGCGTCTTGAATGTAGCGG
931-4	TCACCTAGNTCAGCTCACCCAGCTCTTCTGCGTCTTGAATGTAGCGG
IgH	TCACCTAGCTCAGCTCACCCAGCTCAG - S μ
Myc	TGAGGGGTCAAACCGGAGGTTCGCTTCGTGGTGGCCAAAGAAAGCCCTTG
931-6	AAGCACTCAGAGAAGCCACCCATCTCGTGGTGGCCAAAGAAAGCCCTTG
IgH	AAGCACTCAGAGAAGCCACCCATCTCAGCTCAGCTGTGCTTTTATAGAGC
Myc	TTTGGGAGCGAGAAGGCTCCGTAGCTTCTGACTTACCAGTCTCTGAGAGG
931-7	TCACCTAGCTCAGCTCACCCAGCTTCTGACTTACCAGTCTCTGAGAGG
IgH	TCACCTAGCTCAGCTCACCCAGCTCA - S μ
Myc	TCGTTCTGTTGGTGGCCAAAGAAAGCCCTTGAATCCTGAGGTCTTTGGAG
931-8	CAGCTCAGCTCAGCTCAGCCAGCTCTTGAATCCTGAGGTCTTTGGAG
IgH	CAGCTCAGCTCAGCTCAGCCAGCTCAGCTCAGCTCACCCAGCTCAGCT
Myc	TTCTGACTTACCAGTCTCTGAGAGGGCATTAAATTTACAGCTTGGTGCAT
237	TTCTGACTTACCAGTCTCTGAGAGGATGCATCGGATACTGTATAAAATGCT
IgH	GTGCCCACTCCACTCTTTGTCCCTATGCATCGGATACTGTATAAAATGCT
Myc	CAGTTAATTCATGCTGCGCTATTACGTTTACACCCCGAGCCGAGTAC
268	CAGTTAATTCATGCTGCGCTATTACCCAGCTCAGCTCACCTAGCTCAGC
IgH	CTCACCCAGCTTAGCTCAGCTCACCCAGCTCAGCTCACCTAGCTCAGC
Myc	AAACCCCGTAAGCACAGATCTGGTGGTCTTTCCCTGTGTCTTTCTGCG
274	AAACCCCGTAAGCACAGATCTGGTGGTCTTTCTCAATTCTGTACAGCTGTGGC
IgH	TGGCCTCAACTGCAGGTCTTATTCTTTCTCAATTCTGTACAGCTGTGGC
Myc	GGTTAGGACAGTCTTTCTTCCATTCTGTGCTTTTGACACTTTTCTCAAG
276	GGTTAGGACAGTCTTTCTTCCATTCTGTGCTTTTGACACTTTTCTCAAG
IgH	GGTCCCTGAAGCTGATCTGCCAGGATCCGCCCAATCTAGCTGATTTGTC
Myc	TCTCTGAGAGGGCATTAAATTTCAAGCTTGGTGCATTTCTGACAGCCTGG
278	TCTCTGAGAGGGCATTAAATTTCAACTCATTAACCACATGAGTNGTA
IgH	GAAGTACATTTACTGGCAACTTCAATTCATTAACCACATGAGTNGTA

