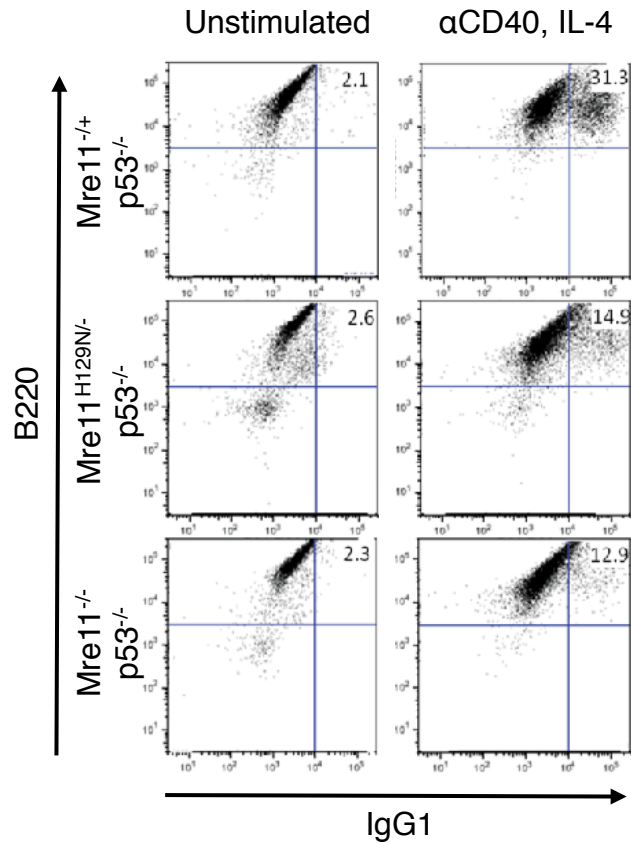
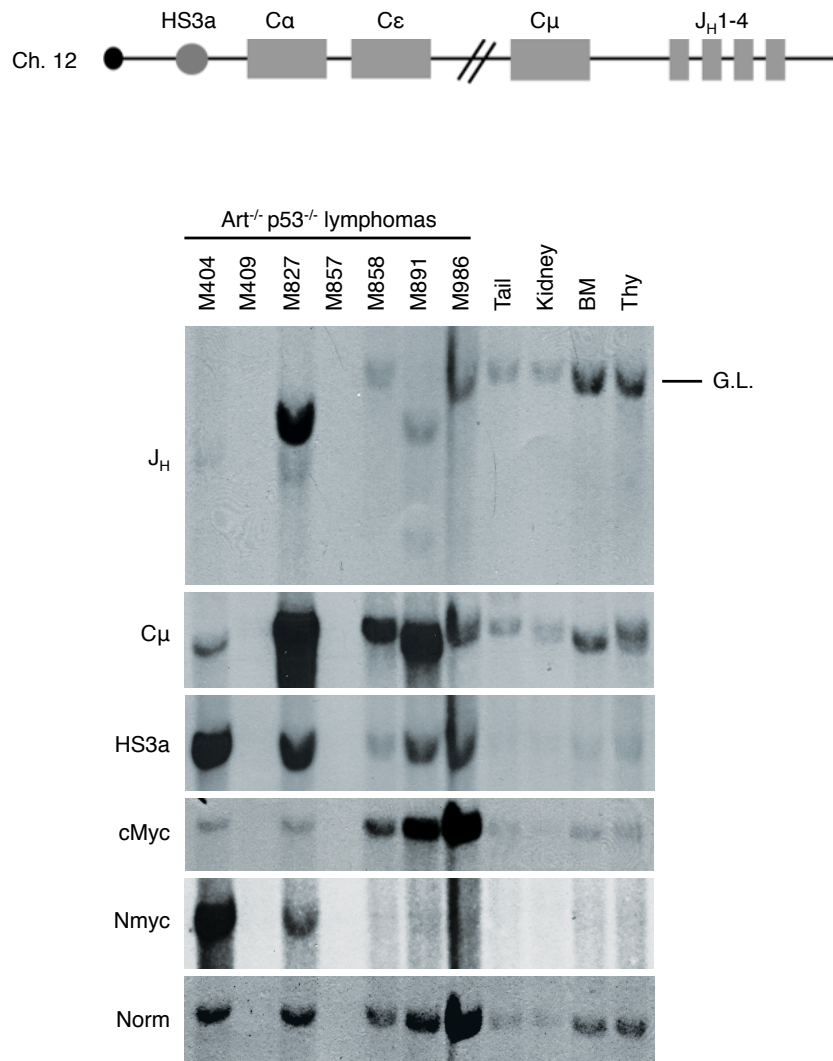


## Supplementary Figure 1



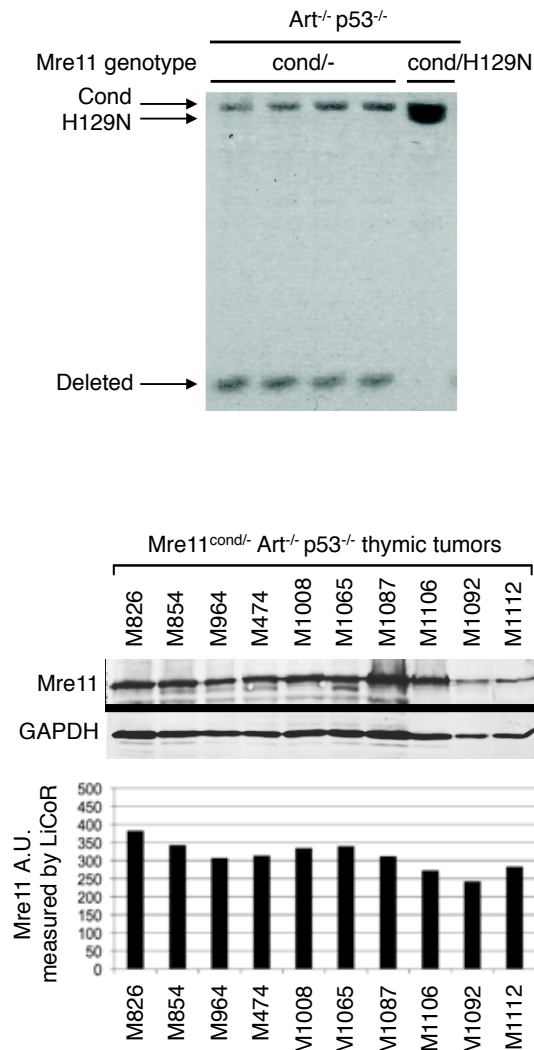
**Supplementary Figure 1: Class switching in Mre11/p53 mutant B cells.** Primary splenic B cells of the indicated genotypes were cultured then stimulated with  $\alpha$ -CD40/IL-4 to induce class switching. CSR to IgG1 was analyzed by flow cytometry with  $\alpha$ -B220 and  $\alpha$ -IgG1 antibodies. Representative plots are shown.

## Supplementary Figure 2



**Supplementary Figure 2. Southern blot analysis of IgH locus, *c-Myc* and *N-myc* in *Artemis*<sup>-/-</sup> *p53*<sup>-/-</sup> lymphomas.** Genomic DNA (gDNA) was isolated from primary lymph node tumors, digested with *Eco*RI and analyzed by Southern blotting. The membranes were hybridized with probes located within the IgH locus (diagrammed, top panel), *c-Myc* and *N-myc*, as described. Amplification of the IgH locus involving the J<sub>H</sub> cluster, C<sub>μ</sub>, and/or enhancer HS3a and *c-Myc* or *N-myc* was observed in the pro-B lymphomas analyzed. Data are representative of 7 *Artemis*<sup>-/-</sup> *p53*<sup>-/-</sup> pro-B tumors analyzed in this study.

## Supplementary Figure 3



**Supplementary Figure 3. *Mre11* conditional allele is retained in thymic tumors from *Art<sup>-/-</sup> p53<sup>-/-</sup>* mice with B-cell specific *Mre11* mutations. (A)** Representative PCR genotyping of the *Mre11* alleles of primary thymic tumors arising in *Art<sup>-/-</sup> p53<sup>-/-</sup> Cre+Mre11<sup>cond/-</sup>* and *Art<sup>-/-</sup> p53<sup>-/-</sup> Cre+Mre11<sup>cond/H129N</sup>* mice; Cond, band corresponding to undeleted conditional allele, Deleted, “-“ allele. The Cond and H129N allele are separated by 50bp and appear as a doublet. **(B)** Protein lysates of primary tumors were isolated and analyzed by western blotting with an  $\alpha$ -MRE11 antibody. Lower panel: Quantitation of MRE11 protein levels; Arbitrary units (A.U.) measured by LI-COR software.

# Supplementary Figure 4

A

IgH sequence	Junction	Myc sequence
Mre11 <sup>+/+</sup>		
<p>1222 bp- ends in exon 3- of J<sub>4</sub></p> <p>CCTCAGTACCCTGCTCCTCAGGATAAGGAATGGCTCTCCAGGCTTTAT            TTTAAACCTTTGTTATGGAGTTTCTGTGCATTGCAGACTAATCTTGGATATT            TGTCCTGGAGGAGCCGGCTGAGAGAAGTTGGGAAATAAAGCTGCTAGGG            ATCTCAGAGCCCTTAGGACAGATTAICTCCACATCTTTGAAAACTAAGAAT            CTGTGTGATGGTGTGGTGGAGCTCCCTGATGATGGATAGGGACTTTGG            AGGCTCATTGAGGAGATGCTAAACAATCTCTAGGCTGGAGGATAGTT            GGGCTGTAGTGGAGTTTTCAGTTTAAAGATAAAGTATAGCTGGGA            ATATACTCAGSACCACCTTTGTGACAGCATTATACAGTATCCGATGCATA            NGACAAGAAGTGGAGTGGGCACTTTCTTANATTTGTGAGAAATGTTCC            AACTANATTTTAAACCTCATTGTGGTAGGAGAGCTGTCTACTGAT            TGAGTCAAGGAGAAAGGCATCTGCGCTCGGTCTCAAAGGGTAGTGGCT            GCTCAGAGGCTGGTGGAGCTGCAAAAGTCCAGCTTTCAAAGGAACA            CAGAAGTATGTATGAATATAGAAGATGTGCTTTAATCTTAAAGTGGT            TCCTAGGAAAAATGTTAAATCTGTACTTTAAATGTGAGAGGTTTTC            AGTACTCATTTTTAAATGCTCAAAATTTTGTCAATCAATTTGAGGCTGTG            TTTGTGTAGAACTGACATCTTAAAGTTTANCCGAGGAAATGGAGTGGG            CTCTCTCATGCCCTATTAGAACTGACTTTTAAACAATAAATAAAGTTTAA            AATTTTAAATGAATTTGAGCANTGTGAGTGGAGTCAAGATGGCCGATC            AGAACCAAGACCTTCAAGAGCTGGCAGGAAGCAGGTCTATGGCAAG            GCTATTTGGGAAAGGGAATAAANCCACTAGGTAACCTGTAGCTGTGGT            TTGAAAAGTGGTTTGAACCCCTGTCCAGCCGCCCAACNAAAGTCC            AGGCCGAAACAAACNCCCTGGGNNANTTGCATTNCTAAANANNTGNA            GAATCCCCNAACTNNGANANGGCCCNNTTAACTNTTGGAGTTCACC            TTTAATTTNACCTGAAAAANTCCANTNCCCAAACTTANGTT</p>	<p>Not detectable-translocation too large</p>	<p>986 bp, ends in exon 1</p> <p>TGTGGAGGTGTATGGGGTGTAGACCGGCAGAGACTCTCCCGGAGGAGC            CGGGTAGAGCGCACCCGCCCTTTACTTGGACTGCGCAGGGAGACCT            ACAGGGGAAAGAGCCGCTCCACACCACCCGCGGGTGGAAAGTCCGAAC            CGGAGGTGCTGGAGTGTGTGTGGGGGGGGGGGAAATCTGCCTTTTGG            CAGCAATTTGGGGGGGGGGTGTGTCTGCGAAAGAAATGTGCCAGTCAACA            TAACGTACGACCAAGGCAAAATACCAATGCTTCCCGCGAGATGGT            TGGCTGTTTATCCCTAAGTGGCTCTCAAGTATACGTGGAGTGAATGGT            GAGCAATTTAATAAAATCCAGACATCTTTTCTGCTCATAGACCTCATCTG            CGTTGATCACCTCTATCACTCCACACACTGAGCCGGGCTCTAGATAA            CTCAATCTGCTGCTTCCCTTCTAAATCTGTTTCCCGAGCTTATA            GAGACCGCTTCCCGCCGGGACGTGGTGAAGGCTCCGAGGATCATGG            CGTATTGTGTGAGCGGAGGAGCTTCCACCTCGGTGACTATATACGC            AGGCAAGAACAACATTTAGCCGAGCGTCCGCCCAACACCTCAG            AAAGGAAAGGACTAGCGCCGAGCAAGAAATGTGCGGCCGACAG            TTAATCATGCTGGCTTACTTGTTTACACCCCGGAGCCGAGTCTGGG            CTCCGGGGGCTGAAGCTCTCTCTCTTCCCGGCTCCCACTAGCC            CCTCCGAGTTTCCCAAGCAAAAGNNGGGGAAGGAGGAGGAGGAAAA            AAAAAATTANAGAGAGTGGGGAAGGANAANAANAAGATCTCTGGGCTAA            TCCCGCCCAACCCGCTTANNATTTCCGGGGTCTGCCGNCNCTAA            GGACCCNTGGGNTGCNCTGCTTCAACCTNCCCGGTCGCA</p>
<p>1202 bp- ends in exon 3' of J<sub>4</sub></p> <p>CCTCAGTGAAGAATGGCTCTCCAGGCTTTTATTTAACCTTTGTTATGGA            GTTTTCTGAGCATTGCAGACTAATCTTGGATATTGCTCCCTGAGGAGCCG            GCTGAGAGAAGTTGGGAAATAAAGTCTCAGGATCTCAGAGCCTTTAGGA            CAGATTATCCACATCTTTGAAAACATAAGAACTGTGCTGATGGTGTGGT            GGAGTCCCTGGATGATGGATAGGGACTTTGGAGGCTCATTGAGGGAAGA            TGCTAAAACAATCTCAGTGGCCGAGGGATAGTTGGGCTGTAGTTGGAGAT            TTTCAATTTTGAATAAAGTGTAGCTGGCAATATACTCAGGACCACT            TCTGTGACAGCATTATACAGTATCCGATGCATAGGGCAAAAGAGTGGAGT            GGGGCACTTTCTTAGATTGTGAGGAATGTTCCACACTAGATTGTTTAA            CTTCAATTTGTTGAAGGAGGCTGTCTAGTATTGAGTCAAGGAGGAAAG            GCATCTAGCCCTCGGCTCAAAGAGGATGCTGCTCAGAGAGGCTTGGT            GGAGCCTGCAAAAGTCCAGCTTTCAAAGGAACAGAAATGTATGATGG            AATATAGAAGATGTTGCTTTTACTCTTAAAGTGGTTCCTAGGAAGAATG            AAATACTGTGACTTAAATGTTGAGAGGGTTTTCAAGTACTCATTTTTAA            TGCCAAAATTTTGTCAATCAATTTGAGGCTCTGTTGTGTAGAACTGACA            TTAATTAAGTTTAAACCGAAGTGGAGTGGGCTCTCTCATACCTTATC            AGAACTGACTTTTAAACAATAAATAAATTAAGTTTGAATATTTTAAATGA            AGCAATGTTGAGTGTGAGTCAAGATGGCCGATCAGAACCAAGCAACCTG            CAGCAGCTGGCAGGAAGCAGGTGATGGCAAGGCTATTGGGGAAGGG            AAAAAAACCACTAGGTAACCTGTAGCTGTGGTTTGAAGAAGTGGTTT            AAACACTGTGTCAGCCCNCCCAAGGAAAGTCCAGGCTGAAACCAACNC            CACTGGGNNANTNGCATTTCTAAAAAANTTGAAGNATCCGCGNAACTGGA            NAGNCCNCTTAACTTGAAGNATCCACCCTTAAATTAACCTGAAAANTT            CNAGTNNCCCAACCTAAGTTT</p>	<p>Not detectable-translocation too large</p>	<p>1088 bp, ends in exon 1</p> <p>TGTGGAGGTGTATGGGGTGTAGACCGGCAGAGACTCTCCCGGAGGAGC            CGGGTAGAGCGCACCCGCCCTTTACTTGGACTGCGCAGGGAGACCT            ACAGGGGAAAGAGCCGCTCCACACCACCCGCGGGTGGAAAGTCCGAAC            CGGAGGTGCTGGAGTGTGTGTGGGGGGGGGGGAAATCTGCCTTTTGG            CAGCAATTTGGGGGGGGGGTGTGTGGAAGAATGTGCCAGTCAACA            TAACGTACGACCAAGGCAAAATACGCAATGCTTCCCGCGAGATGGAG            TGGCTGTTTATCCCTAAGTGGCTCTCAAGTATACGTGGCAAGTGAATGCT            GAGCAATTTAATAAAATCCAGACATCTTTTCTGCTCATAGACCTCATCTG            CGTTGATCACCTCTATCACTCCACACACTGAGCCGGGCTCTAGATAA            CTCAATCTGCTGCTTCCCTTCTAAATCTGTTTCCCGAGCTTATA            GAGACCGCTTGGCCCGCCGGGACGTGGTGAAGGATGTGCCAGTCAAG            AAAGGAAAGGACTAGCGCCGAGCAAGAAATGTGCGGCCGACAG            TTAATCATGCTGGCTTACTTGTTTTACACCCCGGAGCCGAGTCTGGG            CTGCGGGGCTGAGGCTCTCATCTCTTCCCGGCTCCCACTAGCCCC            CTTCCCGAGTTTCCAAAGCAAAAGGGCGGGGAAGCAGAGGAGGAAAA            AGATNANAGAGGTTGGGNAAGGANAAGAAAGATCTCTGGGCTAATC            CCGCCCAACCCCTTTTATTTCCGGGGGCTGTCNCGGCCNAAAGACC            CTTGGGCTGCTGCTGCTCANCTGCGGGGCTCCNANTGCTCCTCAATCAA            NTTCCTCCCTGCTGCTGCTGAAAGGCAAGGGCTTCCCAACCCCTT            GCGGGGAAAAAAGGGAAGGGNAGGATCTCT</p>
<p>1105 bp- ends in exon 3' of J<sub>4</sub></p> <p>CCTCAGTACCCTGCTCCTCAGATAAGGAATGGCTCTCCAGGCTTTATTT            TAACCTTTGTTATGGAGTTTCTGAGCATTGCAGACTAATCTTGGATATTGT            CCTGAGGAGCCCGCTGAGAGAATTTGCAAAATAAAGTCTTAGGGATC            TCAAGCCCTTAGAGACTGATATCTCCACATCTTTGAAAACATAAGAACTC            TGTGATGTTTGGTGGAGTCCCTGGATGATGGATAGGACTTTGGAGG            CTCAITTTAGGGAGATGCTAAACAATCTCTAGGCTGCTGGAGGATGTTGGG            GCTGTAGTGGAGATTTTCAGTTTAAAGATAAAGTATAGCTGCGGAATAT            ACTTCAGGACCCTCTGTGACAGCATTATACAGTATCCGATGCATAGGG            ACAAGAGTGGAGTGGGCACTTTCTTAGATTGTGAGGAATGTCCACA            CTAGATTGTTTAAACCTCATTTTGGGAAGGAGAGCTGCTTAGTGAATGA            GTCAGGGGAGAAAGGATCTAGCCCTGGTCAAAGAGGATGTTGCTGCT            TAGAGAGTCTGGTGGAGCTCAAAGGATCCAGCTTTCAAAGGAACAGAG            AAGTATGTATGGAATATAGAAGATGTTGCTTTACTCTTAAAGTGGTCC            TAGAAAATAAGTTAAACTGTGACTTTTAAAGTGGAGGTTTCAAGT            ACTCATTTTTAAATGCTCAAATTTTGTCAATCAATTTGAGGCTGTTGTT            GTGTAGAACTGACATCTTAAAGTTTAAACCGGAAATGGAGTGGAGGCT            TCTCATCCCTATTAGAACTGACTTTTAAACAATAAATAAATTAAGTTTAA            AATAAATTTTAAATGAGCAATGTTGAGTGGAGTCAAGATGGCCGATCAG            CCAAGAACCTGTCAGCAGCTGGCAGGAAGCAGGTGATGTTGGCAAGGCTA            TTTGGGNNAGAAAATAAACNCTAGGTAACCTGTANCTGTGGTTGAA            AANTGGTTTGAACNCTGTGTCACCCCAACNAAAGTCCAGCTGAN            CAAAACNCCCTGGGANTTGCATTC</p>	<p>Not detectable-translocation too large</p>	<p>920 bp, ends in exon 1</p> <p>TGTGGAGGTGTATGGGGTGTAGACCGGCAGAGACTCTCCCGGAGGAGC            CGGGTAGAGCGCACCCGCCCTTTACTTGGACTGCGCAGGGAGACCT            ACAGGGGAAAGAGCCGCTCCACACCACCCGCGGGTGGAAAGTCCGAAC            CGGAGGTGCTGGAGTGTGTGTGGGGGGGGGGGAAATCTGCCTTTTGG            CAGCAATTTGGGGGGGGGGTGTGTGGAAGAATGTGCCAGTCAACA            ACTGTACGACCAAGGCAAAATACCAATGCTTCCCGCGAGATGGAGT            GCTGTTTATCCCTAAGTGGCTCTCAAGTATACGTGGCAAGTGAATGCTGA            GCAATTTAATAAAATCCAGACATCTTTTCTGCTCATAGACCTCATCTGCG            GTTATCACCTCTATCACTCCACACACTGAGCCGGGCTCTAGATAACT            CATTGTTGCTGCTTCCCTTCTAAATCTGTTTCCCGAGCTTATAGCA            GACGCTGGCCCGCCGGGACGTGGTGAAGGATGTGCCAGTCAATGGCG            TATTGTGTGAGCGGAGCAGTGTCCACCTCGGTGACTGATATAGCAG            GGCAAGAACAGTTCAGCCGAGGCTGCGCCGAAACACCTGACAGAA            GGAAGAGGACTAGCGCCGAGCAAGAAATGTTGCCGGGCGGCTGATTA            ATTATGCTGCGCTTACTGTTTACACCCCGGAGCCGAGTCTGGGCTG            GGGGCTGANGCTTCTCTCTCTTCCCGGCTCCCACTAGCCCCCT            CCGAGTTTCCAAAGCAAAAGGGCGGGGAANAGGAGGAAAGAAAA            AAATNANANAGAGTGGGGAAGGANAANAANAATCTCTGGCNTA            ATCCCCGCCCAACCC</p>

**Supplementary Figure 4: Sequences of cloned PCR products from IgH:MyC PCR amplification.** PCR was performed on genomic DNA from activated splenic B lymphocytes. PCR products cloned and sequenced from all genotypes contained sequences from both IgH and Myc. B lymphocyte genotypes were as follows: (A) p53<sup>-/-</sup>Mre11<sup>+/+</sup> (B) p53<sup>-/-</sup>Mre11<sup>-/H129N</sup> (C) p53<sup>-/-</sup>Mre11<sup>-/-</sup>. (B) and (C) are shown on the following pages.



# Supplementary Figure 4 (continued)

**B**

IgH sequence	Junction	Myc sequence
<b>Mre11<sup>Δ/H129N</sup></b>		
<p style="text-align: center;">983 bp- ends in exon 3' of J<sub>H</sub>4</p> <p>CCTCAGGTAAGAATGGCCTCTCCAGGCTTTATTTTAAAC            CTTTGTATGGAGTTTCTGAGCATTGCAGACTAATCTTG            GATATTTGCCCTGAGGGAGCCGGCTGAGAGAAGTTGG            GAAATACAACGTCTAGGGATCTCAGAGCCTTTAGGACA            GATTATCTCCACATCTTGGAAAACTAAGAATCTGTGTGA            TGGTGTGGTGGAGTCCCTGGATGATGGGATAGGGACTT            TGGAGGCTCATTGGAGGAGATGCTAAAACAATCCTATG            GCTGGAGGGATAGTTGGGGCTGTAGTTGGAGATTTTCAG            TTTTGAATAAAAGTATTAGCTGCGGAATATACTTCAGGA            CCACCTCTGTGACAGCATTTATACAGTATCCGATGCATAG            GGACAAAGAGTGGAGTGGGGCCTTTCTTTAGATTTGTG            AGGAATGTTCCACACTAGATTGTTAACTTCATTGTTG            GAAGGAGAGCTGTCTAGTATTGATGCAAGGGAGAAAG            GCATCTAGCCTCGGTCTCAAAGGGTAGTTGCTGTCTAG            AGAGGCTGTTGGAGCCTGCAAAAGTCCAGCTTTCAA            GAAACACAGAAGTATGTGTAGGAATATTAGAAGATGTTG            CTTTACTGCTTAAAGTTGGTCTAGGAAAAATAGTAAAT            ACTGTGACTTTAAATGTGAGAGGGTTTTCAAGTACTCAT            TTTTTAAATGTCCAAAATTTTTGTCAATCAATTTGAGGTC            TTGTTTGTGAGAACTGACATTACTTAAAGTTAACCGAG            GAATGGGAGTGGAGCTCTCTACACCTATTCCAGAACTG            ACTTTTAAACAATAATAAATTAAGTTTAAATATTTTAAATGA            ATTGAGCAATGTTGAGTTGGAGTCAAGATGGCCGATCAG            AACCAGAACACCTGCAGCAGCTGGCAGGAAGCAGGTCA            TGTGGCAAGGCTATTTGGGGAAGGAAAAATAA</p>	<p>Not detectable- translocation too large</p>	<p style="text-align: center;">1015 bp, ends in exon 1</p> <p>TGTGGAGGTGTATGGGGTGTAGACCGGCAGAGACTCCTC            CCGGAGGAGCCGGGTAGAGCGCACCCGCCCACTTTA            CTGGACTGCGCAGGGAGACCTACAGGGGAAAGAGCCGC            CTCCACACCACCCGCCGGGTGGAAGTCCGAACCGGAGG            TGCTGGAGTGTGTGTGGGGGGGGGGGAATCTGCCT            TTTGGCAGCAAATTTGGGGGGGGGGTCTGTTCTGGAAG            AATGTGCCAGTCAACATAACTGTACGACCAAAGGCAAAA            TACACAATGCCTTCCCGCGAGATGGAGTGGCTGTTTATC            CCTAAGTGGCTCTCAAAGTATACGTGGCAGTGGATTGCT            GAGCAATTTAATAAAATTCAGACATCGTTTTTCTCGCAT            AGACCTCATCTGCGGTTGATCACCCTCTACTCCACAC            ACTGAGCGGGGGCTCCTAGATAACTATTGTTCTGCTCCTT            CCCCCTTTCTAAATCTGTTTTCCCGAGCCTTAGAGAGAG            GCCTGGCCGCCCGGACGTGCGTGACGCGGTCCAGGG            TACATGGCGTATTGTGTGGAGCGAGGCAGCTTTCCACC            TGCGGTGACTGATATACGACGGCAAGAACACCTTTCAG            CCGAGCGCTGCGCCGAACAACCGTACAGAAAGGGAAA            GGACTAGCGCGCAGCAAGAGAAAATGTCGGGCGCGC            AGTTAATTCATGCTGCGCTATTACTGTTTACACCCCGGAG            CCGGAGTACTGGGCTGCGGGGTGAGGCTCCTCCTCCT            CTTTCCCGGCTCCCCACTAGCCCCCTCCCGAGTTCCC            AAAGCANAGGGCGGGGNAAGCGAGAGGAGGAAAAA            AATAGAGAGAGGTGGGAAAGGANAAAAAATTTTC            TCTGGCTAAATCCCCCGCCCCANCCCGCCCCTTTTTA            TATTTCCCGGGGGNTCTGCCCGGGCCCAANGGACC            CCCCCTGGGGGTNGCCGCTTTGCTTCTCCANNCTTGCC            CGGGGG</p>
<p style="text-align: center;">1135 bp- ends in exon 3' of J<sub>H</sub>4</p> <p>CCTCAGTACCCTCTCCTCAGGTAAGAATGGCCTCTCCA            GGTCTTTATTTTAACTTTTGTATGGAGTTTCTGAGCAT            TGACAGACTAATCTTGGATATTTGTCCTGAGGGAGCCGG            CTGAGAGAAGTTGGGAAATAACTGTCTAGGGATCTCAG            AGCCTTTAGGACAGATTATCTCCACATCTTTGAAAACTA            AGAATCTGCGTGATGTTGTTGGTGGAGTCCCTGGATGAT            GGGATAGGGACTTTGGAGGCTCATTGAGGGAGATGCTA            AAACAATCCTATGGCCGGAGGGATAGTTGGGGCTGTAGT            TGGAGATTTTCAGTTTTAGAAATAAAGTGTAGCTGCGG            AATATACTCAGGACCCTCTGTGACAGCATTATACAG            TATCCGATGCATAGGGACAAAGAGTGGAGTGGGGCCTT            TCTTTAGATTTGTGAGGAATGTTCCACACTAGATTGTTAA            AACTTCATTTGTTGGAAGGAGAGCTGCTTAGTGATTGAG            TCAAGGGAGAAAGGCATCTAGCCTCGGTCTCAAAGGGT            AGTTGCTGTCTAGAGAGGCTGTTGGAGCCTGCAAAAG            TCCAGCTTTCAAAGGAACACAGAAGTATGTATGGAATA            TTAGAAGATGTTGCTTTACTCTTAAAGTTGGTTCTTAGGA            AGAATAGCTAAATACTGTGACTTTAAATGTGAGAGGGTT            TTCAAGTACTCATTTTTTAAATGTCCAAAATTTTTGTCAAT            CAATTTGAGGCTTTGTTGTGTAGAACTGACATTACTTAA            GTTTAACCGAGGAATGGGAGTGGGGCTCTCTACACCT            ATTCAGAACTGACTTTTAAACAATAATAAATTAAGTTTGAAT            ATTTTAAATGAATTGAGCAATGTTGAGTNGGAGTCAAGA            TGCCGATCAGAACAGAACACCTGCAGCAGCTGGCAG            GAAGCAGTCTGTGGCAAGGCTATTTGGGGAAGGGAA            AATAAACCNCTAGGTAACCTGTANCTGGGGTTTGAANAA            TGGTTTNNANCACTCTGTCCAGCCCCCAACCGAAAAGT            CNAGGCTGACNAANNCCCTGGGTAATGCATTCNAAA            ANAGTNGAGNATCNCCCAAACTGGA</p>	<p>Not detectable- translocation too large</p>	<p style="text-align: center;">974 bp, ends in exon 1</p> <p>TGTGGAGGTGTATGGGGTGTAGACCGGCAGAGACTCCTC            CCGGAGGAGCCGGGTAGAGCGCACCCGCCCACTTTA            CTGGACTGCGCAGGGAGACCTACAGGGGAAAGAGCCGC            CTCCACACCACCCGCCGGGTGGAAGTCCGAACCGGAGG            TGCTGGAGTGTGTGTGGGGGGGGGGGAATCTGCCT            TTTGGCAGCAAATTTGGGGGGGGGGTCTGTTCTGGAAG            AATGTGCCAGTCAACATAACTGTACGACCAAAGGCAAAA            TACGCAATGCTTCCCGCGAGATGGAGTGGCTGTTTAT            CCTAAGTGGCTCTCAAAGTATACGTGGCAGTGGATTGCT            TGAGCAATTTAATAAAATTCAGACATCGTTTTTCTGCA            TAGACCTCATCTGCGGTTGATCACCCTCTACTCCACA            CACTGAGCGGGGCTCCTAGATAACTATTGTTCTGCTCC            TTCCCCTTTCTAAATCTGTTTTCCCGAGCCTTAGAGAG            AGCCCTGGCCGCCCGGACGTGCGTGACGCGGTCCAG            GGTACATGGCGTATTGTGTGGAGCGAGGCAGCTGTTCCA            CCTGCGGTGACTGATATACGACGGGCAAGAACACAGTTC            AGCCGAGCGCTGCGCCGAACAACCGTACAGAAAAGGGA            AAGGACTAGCGCGCAGCAAGAGAAAATGGTCGGGCGC            GCAGTTAATTCATGCTGCGCTATTACTGTTTACACCCCG            AGCCGGAGTACTGGGCTGCGGGGTGANGCTCCTCATC            CTCTTTCCCGGCTCCCCACTAGCCCCCTCCCGAGTTTC            CCAAAGCAAANGGCGGGGAANCNANAGGAGGAAAAA            NATANANAGANGTNGGNAANGGAAAAAATAATNCT            CTGGCTAATCCCCGCCACCCGCCCTTTTATATTCCNNGG            GGTCTNCCCCGGCCAAAGACCCCTGGGGCTTGCNCT            GCTT</p>

# Supplementary Figure 4 (continued)

C

IgH sequence	Junction	Myc sequence
Mre11 <sup>Δ</sup>		
<p>1151 bp- ends in exon 3' of J<sub>H</sub>4            CTTTGAAAAACTAAGAATCTGTGTGATGGTGTGGTGGAG            TCCTTGGATGATGGGATAGGGACTTTGGAGGCTCATTTG            AGGGAGATGCTAAACAATCCTATGGCTGGAGGGATAGTA            GGGGCCGTAGTTGGAGATTTTCAGTTTTAGAAATAAAAGT            ATTAGCTGCGGAATATACTTCAGGACCACCTCTGTGACAG            CATTATACAGTATCCGATGCATAGGGACAAGAGTGGAG            TGGGGCACTTTCTTTAGATTTGTGAGGAATGTTCCACACT            AGATTGTTTAAACTTCATTTGTTGGAAGGAGAGCTGTCT            TAGTGATTGAGTCAAGGGAGAAAGGCATCTAGCCTCGGT            CTCAAAGGGTAGTTGCTGTCTAGAGAGGCTGGTGGAG            CCTGCAAAAGTCCAGCTTTCAAAGGAACACAGAAGTATG            TGTATGGAATATTAGAAAGATGTTGCTTTTACTCTTAAAGTTG            GTTCTAGGAAAAATAGTAAATACTGTGACTTTAAATGT            GAGAGGGCTTTCAAGTACTCATTTTTTAAATGTCCAAAAT            TTTTGTCAATCAATTTGAGGCTTTGTTTGTAGAACTGAC            ATTACTTAAAGTTTAAACCGAGGAATGGGNAGTGAGGCTCT            CTCATACCTTATTCANAAGTACTTTTAAACAATAATAAAT            AAGTTTTAAATATTTTTAAATGAATTTGAGCAATGTTGAN            TTNGGANTCAANATGGCCCAATCANAACCAAAACACCT            GCANCACTGGCAAGAAACAAGGTCAATGTGGCNAAGG            CTTTTTGGGGGAAAGGNAAAAATAAAACCNC TAGGTAAA            ACTTNGTAACTTTNGTTTTGAAAAAATTTGTTTTNAA            AAANCTNTGTNCCANCCCCCCCCAAACCCGAAANGTTC            NNGNCTTNAANCAAACCCNCCTGGGGTTAATTTGCAN            TTTCCNAAAAAATTTGAAGAAATTCNNCCNAAAACTGGA            AANGGNCCCNCTTTTTANCTTTTTGANTTCANCTTTTT            ANTTTTNANCTNGAAAAATTTANNTTCCCNAACTTAA            ANTTTTTCCNCTTTTAAAGGNTTTTAAATNCTTTTTCAA            AATTTGGNTTTTTTAAAAAATNAAGGA</p>	<p>GGGGGG            GA/            CTTTGAAAA            A</p>	<p>185 bp, ends 5' of exon 1            TGTGGAGGTGTATGGGGTGTAGACCGGCAGAGACTCCTCC            CGGAGGAGCCGGGTANAGCGCACCCGCCCACTTTACTG            GACTGCGCAGGGAGACCTACAGGGGAAAGAGCCGCTCCA            CACCACCCCGGGTGGAAAGTCCGAACCGGAGGTGCTGG            AGTGTGTGTGGGGGGGGGGGA</p>
<p>1222 bp- ends in exon 3' of J<sub>H</sub>4            CCTCAGTCACCGTTCCTCAGGATAAGGAATGGCCTCT            CCAGGTCTTTATTTTAACTTTTGTATGGAGTTTTCTGTG            CATTGCAGACTAATCTTGGATATTTGTCCCTGAGGGANCC            GGCTGAGAGAAGTTGGGAAATAAACTGTCTAGGGATCTC            AGAGCCTTTAGGACAGATTATCTCCACATCTTTGAAAAAC            TAAGAATCTGTGTGATGGTGTGGTGGAGTCCCTGGATG            ATGGGATAGGGACTTTGGAGGCTCATTGAGGGAGATGC            TAAACAATCCTATGGCTGGAGGGATAGTTGGGGCTGTAG            TTGGAGATTTTCAGTTTTTGAATAAAAAGTATTAGCTGCCG            AATATACTTCAAGACCACCTCTGTGACAGCATTATACAGT            ATCCGATGCATANGGACAAAGAGTGGAGTGGGGCACTTT            CTTTANATTTGTGAGGAATGTTCCACACTANATTTTAA            ACTTCAATTTGTTGGAAGGAGAGCTGTCTTAGTGATTGAGT            CAAGGGAGAAAGGCATCTAGCCTCGGTCTCAAAGGGTA            GTTGCTGTCTAGAGAGGCTGGTGGAGCCTGCAAAAGTC            CAGCTTTCAAAGGAACACAGAAGTATGTGTATGGAATATTA            GAAGATGTTGCTTTTACTCTTAAAGTTGGTTCCTAGGAAA            ATAGTTAAATACTGTGACTTTAAAAATGTGAGAGGGTTTTCA            AGTACTCATTTTTTAAATGTCCAAAATTTTTGTCAATCAAT            TTGAGGCTTTGTTGTGTAAGACTGACATTAAGTTTT            ANCCGAGGAATGGGAGTGGAGCTCTCTCATGCCCTATTC            AGAACTGACTTTTAAACAATAATAAATTAAGTTTTAAATATTTT            TAAATGAATTGAGCANTGTTGAGTTGGAGTCAAGATGGCC            GATCAGAACCAGAACACCTGCANCACTGGCAGGAAGC            AGGTCATGTGGCAAGGCTATTTGGGGAAAGGAAAATAA            ANCCACTAGGTAACCTGTAGCTGTGGTTTTGAAAAAGTGGT            TTGAAACCTCTGTCCAGCCCCCAACNAAAGTCCAG            GCCGAACAAAACNCCNCTGGGNNANTTGCATTNCTAAA            ANANNTGNAGAATCCCCNAACTNNGGANANGGCCCNNT            TTAACNTTGGAGTTCACCTTTAATTTNACCTTGA AAAAN            TCCANTTNC CCAAACTTANGTT</p>	<p>Not            detectable-            translocation            too large</p>	<p>996 bp, ends in exon 1            TGTGGAGGTGTATGGGGTGTAGACCGGCAGAGACTCCTCC            CGGAGGAGCCGGGTAGAGCGCACCCGCCCACTTTACTG            GACTGCGCAGGGAGACCTACAGGGGAAAGAGCCGCTCCA            CACCACCCCGGGTGGAAAGTCCGAACCGGAGGTGCTGG            AGTGTGTGTGGGGGGGGGGGAATCTGCCTTTTGGCAG            CAAATTTGGGGGGGGGGTCTGTTCTGAAAGAATGTGCCA            GTCAACATAACTGTACGACCAAGGCAAAATACACAATGCCT            TCCCCGCGAGATGGAGTGGCTGTTTATCCCTAAGTGGCTCT            CCAAGTATACGTGGCAGTGAATGCTGAGCAATTTAATAAA            ATTCCAGACATCGTTTTCTGTCATAGACCTCATCTGCCGTT            GATCACCTCTATCACTCCACACTGAGCGGGGGCTCCTA            GATAACTATTGTTCTGCTCCTCCCCCTTTCTAAATCTGTTT            TCCCCAGCCTTAGAGAGACGCTGGCCGCCGGGACGTGC            GTGACCGGGTCCAGGGTACATGGCGTATTGTGTGGAGCGA            GGCAGCTGTTCCACCTGCGGTGACTGATATACGAGGGCAA            GAACACAGTTCAGCCGAGCGCTGCGCCGAAACACCGTAC            AGAAAGGGAAGGACTAGCGCGGAGCAAGAGAAAATGGT            CGGGCGCGAGTTAATTCATGCTGCGCTATTACTGTTTACAC            CCGGAGCCGGAGTACTGGGCTGCGGGGGTGAAGCTCC            TCCTCCTTTTCCCGGCTCCCCACTAGCCCCCTCCGAG            TTCCCCAAGCAAAGGNNGGGGAAAGCGAGAGGAGGAAAA            AAAAATTANAGAGAGGTGGGGAAAGGGAANAAAAGATTCT            CTGGGCTAATCCCCGCCCAACCCGCTTTANNTTCCGG            GGGGTCTGCCCGNCCAAGGACCCNNTGGGNTGCNCTGC            TTCTCAACCTNCCCGGGTCCGA</p>

## Supplementary Figure 5:

A

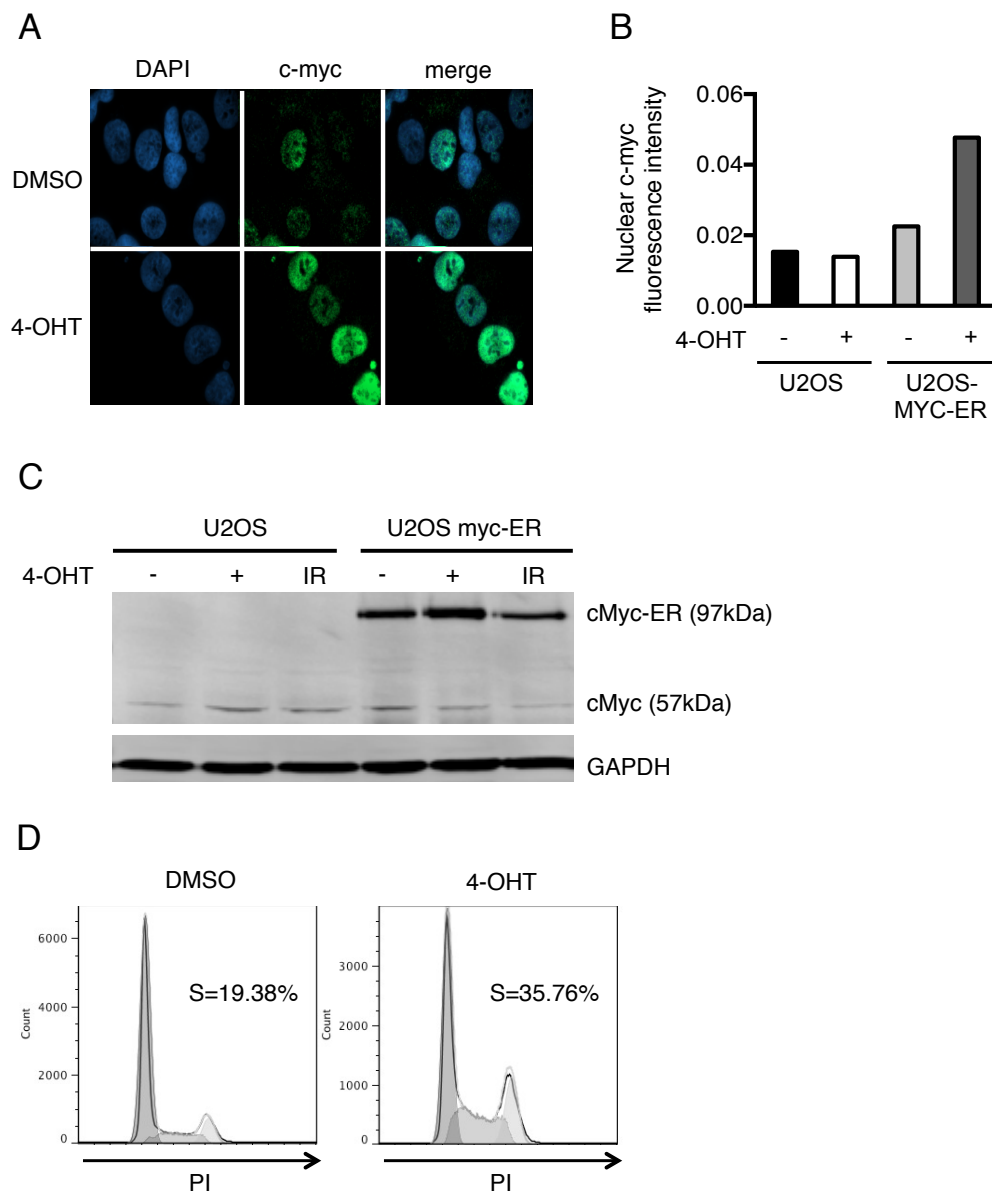
Genotype	Microhomology (A-NHEJ)	Blunt (C-NHEJ)
Mre11 <sup>+/-</sup>	14	7
Mre11 <sup>-/-</sup>	7	5
Mre11 <sup>H129N</sup>	6	9

B

	DR-GFP	MMP-24
Mre11 <sup>+/-</sup>	5' GAGCTGTTACCCGGGTGGTGCCCAT	<b>CCTGG</b> 3'
		3' <b>GGACC</b> GCAAAGACTCATTTCAAAACCTCTTCTCT 5'
	5' GGATCCACCCGGTCGCCACCATGGT	<b>GAG</b> 3'
		3' <b>CTC</b> ATTTCAAAACCTCTTCTCTCT 5'
	5' ACGTAAACGGCCACAAGTTCAGCGTGTC	3' <b>CTTCCCGTCCGACC</b> GTCCTCTTCCGTCCAACG 5'
	5' AGGAGCTGTTACCCGGGTGGTGCCCAT	3' <b>GCAACCTGC</b> TTTCTCTGCCAGCCTGCCCTTC 5'
Mre11 <sup>-/-</sup>	5' GGAGCTGTTACCCGGGTGGTGCCCA	<b>CCA</b> 3'
		3' <b>GGTCTGACTGAAAGAGGACTGTGGTTG</b> 5'
	5' AGCTGGACGGCGACGTAAACGGCCACA	<b>AGTT</b> 3'
		3' <b>TCAACGGGACGAATTAATTCGGGAGACCTCTCAGTCTG</b> 5'
	5' AGGGCGAGGAGCTGTTACCCGGGTGG	3' <b>CGGGACGAATTAATTCGGGAGACCTCTCAGTCTGC</b> 5'
	5' GGGGTGGTGCCCATCCTGGTCGAGCTGGAC	3' <b>TTAATGGACCGCAAAGACTCATTTCAAAACCTCTT</b> 5'
Mre11 <sup>-/-</sup> + Mre11 <sup>H129N</sup> cDNA	5' CTGCTACCCGTGATCAGGCAGAGCAGG	<b>AGG</b> 3'
		3' <b>TCCGGTCTGGGTCTGACTGAAAGAGGACTGTG</b> 5'
	5' AAGGGCGAGGAGCTGTTACCCGGGTGGT	<b>GCCC</b> 3'
		3' <b>CGGGACGAATTAATTCGGGAGACCTCTCAGTCTGC</b> 5'
	5' CCCGGCACCGAGAAGCCCAGGAGCAGGAG	3' <b>GCAAAGACTCATTTCAAAACCTCTTCTCTTC</b> 5'
	5' CACAAGTTCAGCGTGCCGGCGAGGGC	3' <b>CTCAACGGGACGAATTAATTCGGGAGACCTCTCA</b> 5'

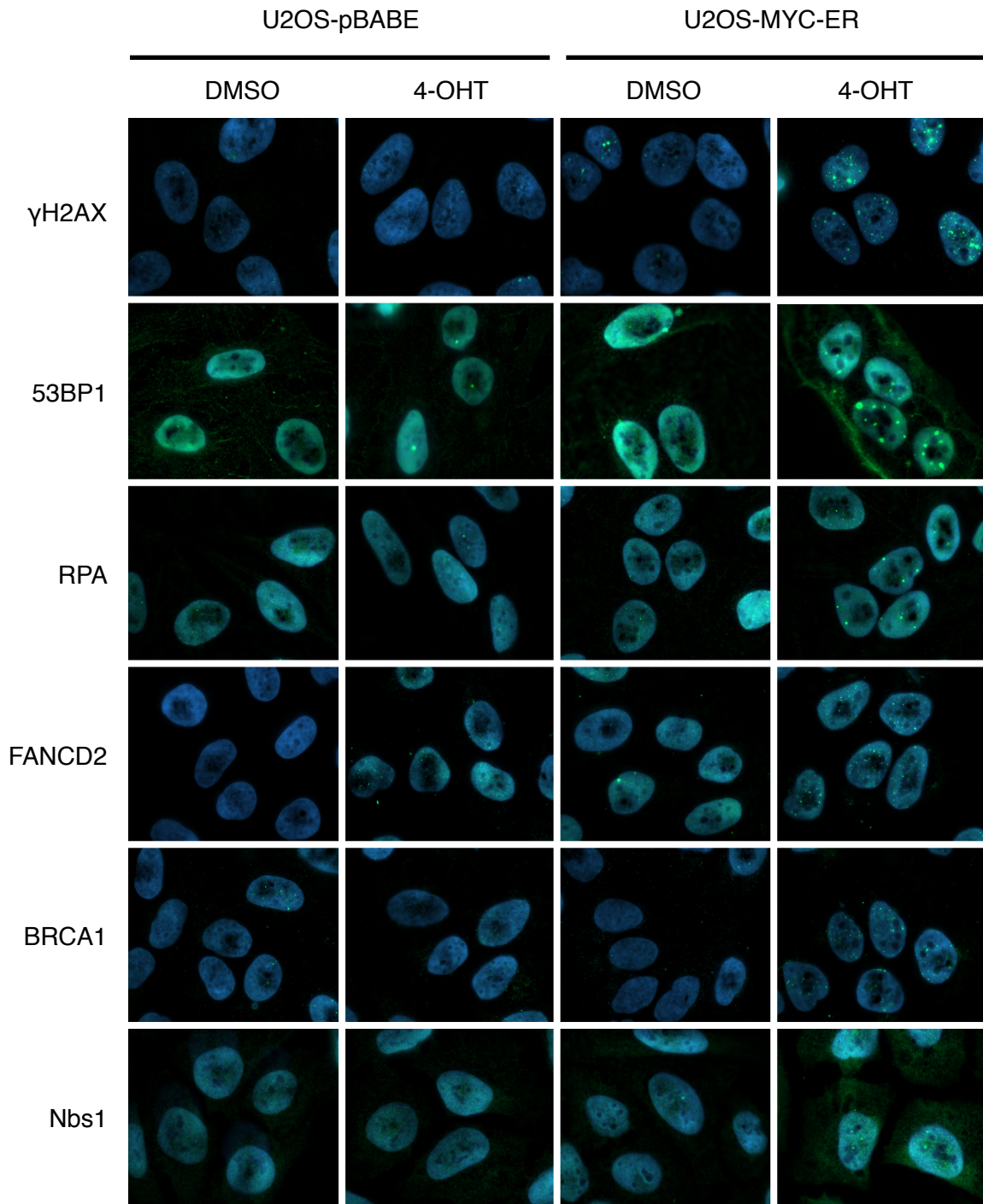
**Supplementary Figure 5: DR-GFP:MMP24 translocation junctions.** (A) Number of junctions with microhomologies (A-NHEJ) and blunt (C-NHEJ) recovered from MEFs of the indicated genotypes. (B) Representative sequences of A-NHEJ and C-NHEJ joins for each genotype. DR-GFP flanking sequences, left; MMP-24 flanking sequence, right (Bold); microhomologies, box.

## Supplementary Figure 6



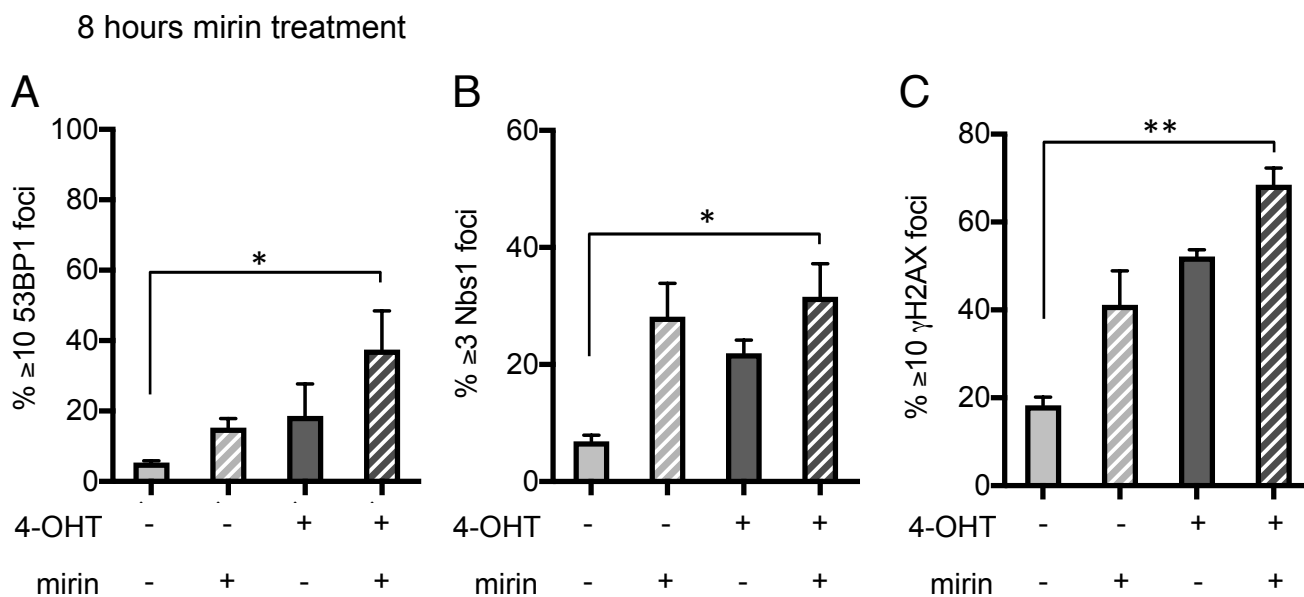
**Supplementary Figure 6: Inducible MYC overexpression.** U2OS and U2OS-MYC-ER cells were treated with DMSO or 200nM 4-OHT for 72 hours to induce MYC localization to the nucleus. (A) Immunofluorescent images of nuclear MYC. (B) Fluorescence intensity of nuclear MYC was quantitated using Applied Spectral Imaging software. (C) Western blot analysis of MYC-ER. Cell lysates from untreated and 4-OHT treated cells were analyzed by western blotting using an  $\alpha$ -MYC antibody. The MYC-ER fusion protein (97kDa) is overexpressed compared to the endogenous MYC protein (57kDa). GAPDH, loading control. (D) Flow cytometry analysis. DNA content was analyzed by fixing cells and staining with propidium iodide. Percent indicates cells in S-phase of the cell cycle.

## Supplementary Figure 7



**Supplementary Figure 7: DNA repair foci induced by MYC overexpression.** U2OS cells harboring pBABE (empty vector) or pBABE-MYC-ER were treated with DMSO or 200nM 4-OHT to induce MYC localization to the nucleus. DNA repair proteins (indicated at left) were detected by immunofluorescence microscopy (green); DAPI, blue. Representative images of nuclear foci from Figure 4C-H are shown.

## Supplementary Figure 8



### Supplementary Figure 8: Quantitation of DNA repair foci in mirin treated cells

**overexpressing MYC.** U2OS-cMycER cells were treated with DMSO or 75 $\mu$ M mirin for 8 hours after 72 hours 200nM 4-OHT treatment, and localization of DNA repair foci was examined by immunofluorescence microscopy. Percentages of nuclei with indicated DNA repair foci are plotted. Mean  $\pm$  SEM of 3 independent experiments. \*,  $p < 0.05$ ; \*\*,  $p < 0.01$ ; paired t-test.