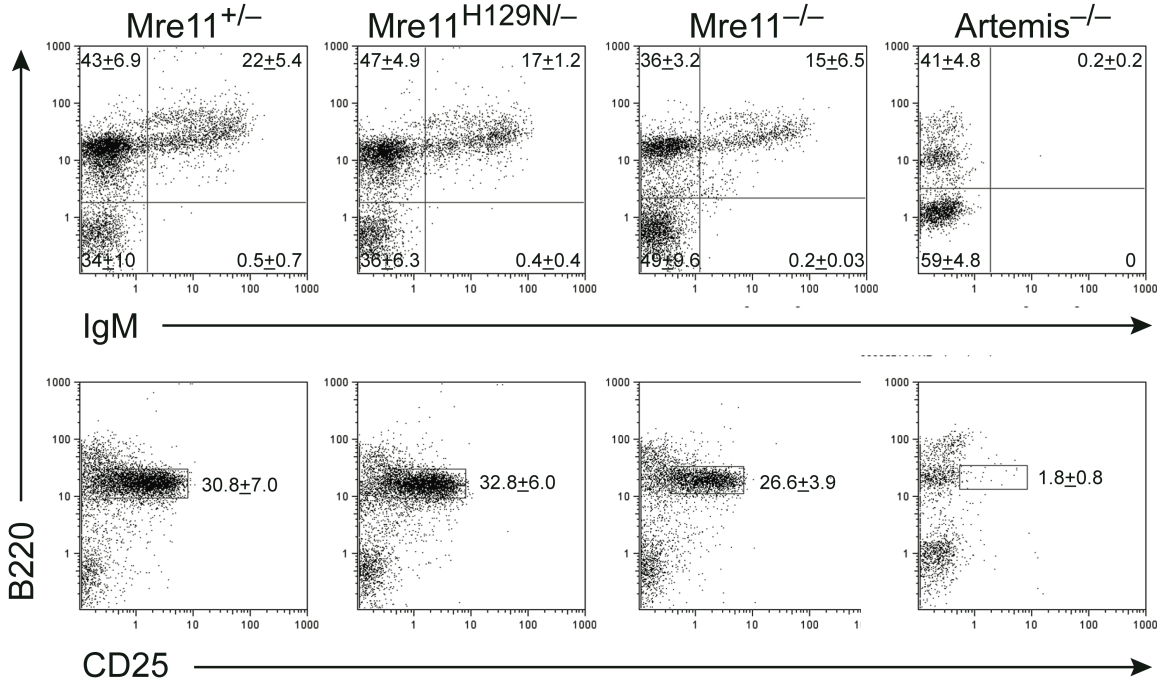
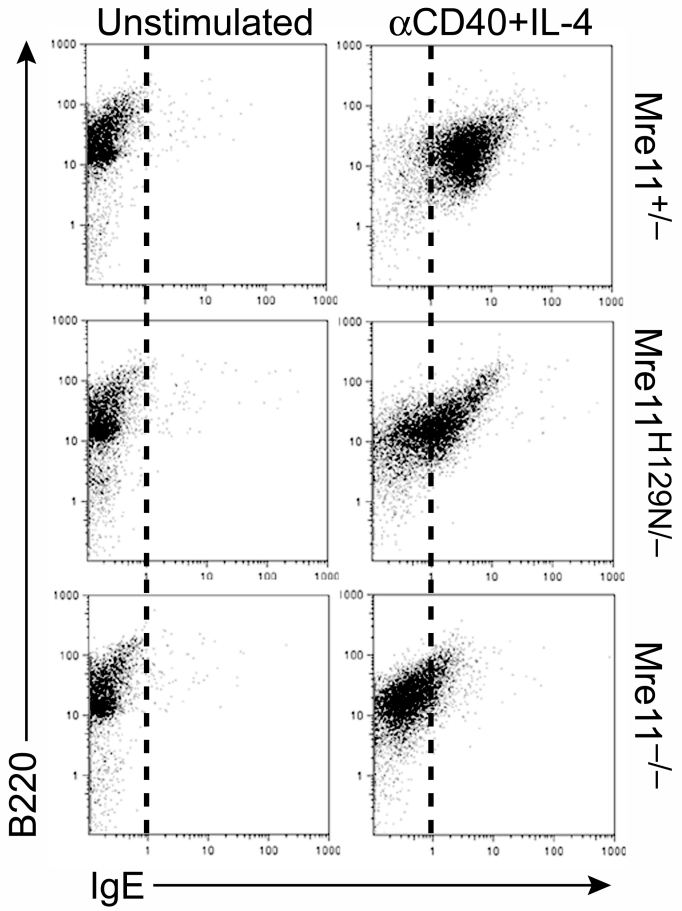
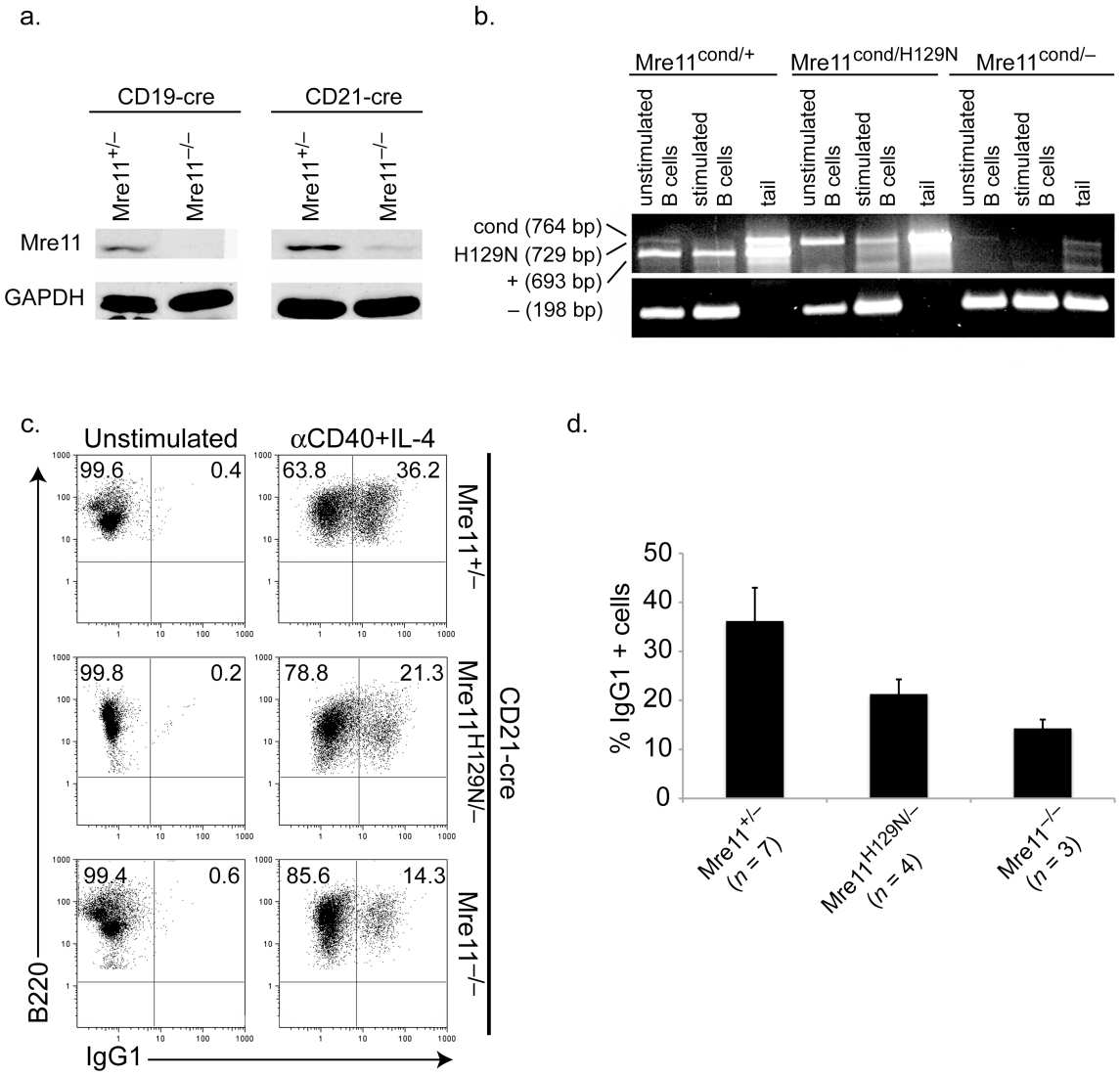


Supplementary Figure 1. MRN deficiencies generated by CD19-Cre do not block early B cell development. Flow cytometric analyses of bone marrow using the indicated antibodies. Artemis deficiency was used as a control for early developmental block resulting from defective V(D)J recombination. Three mice of each genotype were analyzed. Numbers in the quadrants represent the averages +/- S.E.M. B220/IgM positive populations reflect B cells having supported successful V(D)J recombination at the heavy and light chain loci. B220/CD25 positive populations have supported heavy chain, but not light chain, recombination.



Supplementary Figure 2. Requirement of MRN for switching to IgE. Representative flow cytometric analysis of class switching from IgM to IgE in B cells cultured with IL-4 and anti-CD40 for four days. IgE positivity cannot be quantitated precisely due to IgE antibody binding to Fc receptors.



Supplementary Figure 3. Conversion of Mre11^{cond} to Mre11^{-} by CD21-Cre. (a) Western blot analyses comparing Mre11 protein levels in CD19-Cre and CD21-Cre containing mice. Enriched splenic B cells stimulated with IL-4 and anti-CD40 were used. More residual Mre11 protein was reproducibly observed in CD21-Cre relative to CD19-Cre Mre11$^{-/-}$ B cell cultures. (b) PCR analyses confirming conversion of Mre11^{cond} to Mre11^{-} by CD21-Cre in B lymphocytes. Primers used are depicted in figure 1a. (c) Flow cytometric analyses of class switching from IgM to IgG1 in mice harboring CD21-

Cre, which begins expression in mature IgM+ B cells. Numbers in upper right quadrants represent the average percentage of IgG1+ cells from three to five mice of each genotype. (d) Bar graph depicting direct comparisons of IgG1+ cell populations in (c) (average +/- S.D).

Figure S 4 Mre11+/-

Blunt

IgG1

GTGTCTTTTGAGTACCGTTGTC | TGGGTCACTCACATTTAACTTT
GTGTCTTTTGAGTACCGTTGTC | GT | TCCAGGGCAGCCAGGACAGGTG
GGTGACCCAGGCAGAGCAGC | TCCAGGGCAGCCAGGACAGGTG

TGCTCTGTGTGAACTCCCTCTG | GCCCTGCTTATTGTTGAATGGG
TACTCTGTGTGAACTCCCTCTG | T | CAGGACAGGTGGAAGTGTGGTGA
GGCAGAGTAGCTACAGGGAGC | CAGGACAGGTGGAAGTGTGGTGA

ACAGCTGTACAGAATTGAGAAA | GAATAGAGACCTGCAGTTGAGG
ACAGCTGTACAGAATTGAGAAA | T | AAGTGTGGAGACCCAGGCAGAG
ACAGGTAAGCAGGGACAGGTGG | AAGTGTGGAGACCCAGGCAGAG

GAAGAAAAGATGTTTTTAGTTT | TTATAGAAAACACTACTACATT
GAAGAAAAGATGTTTTTAGTTT | AGGGCAGCCAGGACAGGTGGAA
GTGACCCAGGCAGAGCAGCTCC | AGGGCAGCCAGGACAGGTGGAA

CAGTAAGGAGGGACCCAGGCTA | AGAAGGCAATCCTGGGATTCTG
CAGTAAGGAGGGACCCAGCTTA | TATAGGGCAGCCAGGACAGGTG
GTGGTGACCCAGGCAGAGCAGC | TATAGGGCAGCCAGGACAGGTG

GGTAGGCCTGGACTTTGGGTCT | CCCACCCAGACCTGGGAATGTA
GGTAGGCCTGGACTTTGGGTCT | ATAG | GGGTGCCAGGACAGGTACAAG
AATATCCAGGCAGAACAGGTCCA | GGGTGCCAGGACAGGTACAAG

AAGAAAAGATGTTTTTAGTTTT | TATAGAAAACACTACTACATTC
AAGAAAAGATGTTTTTAGTTTT | GTGACCCAGGCAGAGCATCTAT
AGCCAGGACAGGTGGAAATGTG | GTGACCCAGGCAGAGCATCTAT

IgE

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AACTGGAATGAACTTCATTAAT | GGCCCGGCTAAGCTAAGTAAGG
TGGACTGAATTGGCCTAAGATG | GGCCCGGCTAAGCTAAGTAAGG

CTGGACTTTGGGTCTCCCACCC | AGACCTGGGAATGTATGGTTGT
CTGGACTTTGGGTCTCCCACCC | GAGCTGGGCCAGGCTGGTATGA
CTGGTCCAAGTTGGGCTAAACA | GAGCTGGGCCAGGCTAGTATGA

AGGCAATCCTGGGATTCTGGAA | GAAAAGATGTTTTTAGTTTTTA
AGGCAATCCTGGGATTCTGGAA | T | TGGGTTAAACTAGGTTGCACTG
GTTAACCTGGGCTGGACCATAC | TGGGTTAAACTAGGTTGCACTG

ACAGCTGTACAGAATTGAGAAA | GAATAGAGACCTGCAGTTGAGG
ACAGCTGTACAGAATTGAGAAA | TC | GCGGGCGGGGCTAGGCTGGGC
AGGCAAGGCTGAGCTAGGCTGGG | CGGGGCGGGGCTAGGCTGGGC

GGCCAGCAGGTCGGCTGGACTA | ACTCTCCAGCCACAGTAATGAC
GGCCAGCAGGTCGGCTGGACTA | TTTTGTATATTCGGTTGAAATG
GGCAGGGCTGGACTGAGCTAGC | TTTTGTATATTCGGTTGAAATG

GATTCAGCCGAAACTGGAGAGG | TCCTCTTTTAACTTATTGAGTT
GATTCAGCCGAAACTGGAGAGG | CAAG | TTGACCTGGCATGAGCTTAACT
AGCAGGACTGGCCTGGCCTGGA | TTGACCTGGCATGAGCTTAACT

Microhomology

IgG1

TTGAGTACCGTTGTCTGGGTCACTCACATTTAACTTTCCTTG
TTGAGTACCGTTGTCTGGGT**CA**AGACAGGTGGAAGTGTGGGG
CACAGTAGCTATAGGGGAGCCAAGACAGGTGGAAGTGTGGGG

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GCCAGACTCATAAAGCTTGCTGAGCAAAATTAAGGGAACAAGGT
GCCAGACTCATAAAGCTTGCT**G**CAGCCAGGACAGGTGGGAGTG
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CTCTACTTCAGTTATACATGTGGGTTTGAATTTTGAATCTATTC
CTCTACTTCAGTTATACAT**GTG**TGGGGATCCAGGTAAGGCT
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GCCGCTAAGCTAAACTAGGCTGGCTTAACCGAGATGAGCCAAAC
GCCGCTAAGCTAAACTAGGC**TG**ACACAGGCAGAGCAGCTCAT
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GGTATGGATACGCAGAAGGA**AG**CAGGTATAGGGAGCCAGGAC
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GTAAGCCAGAGGCAGCCAC**AGC**AAGGACAGGGAAACTATAG
CCAGGCAGAGCAGTACCTTAGGAGCAAGGACAGGGAAGCTATAG

IgE

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GAACTTCATTAA**TCTAAGTTGA**TTTGAGTTGGCT
TGGCTGAGCTGAGTCAAGATGGTCTGAGTTGATTTGAGTTGGCT

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CTAGGTTGAATAGAGCTA**AACT**GAGCAGGACTGGCCTGGC
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GGATACGCAGAAGGAAGGCCA**C**GGGGCGGGGCTAGGCTGGGCA
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ATTAAGGGAACAAGGTTGAGA**G**GCTGGGCGGGGCGGGGCTAGG
TTAGCTAGGCAAGGCTGAGCTAGGCTGGGCGGGGCGGGGCTAGG

Sequences of CSR joins from Mre11+/– stimulated B cells

Figure S5 Mre11 H129N/-

Sequences of CSR joins from Mre11H129N/– stimulated B cells

Figure S6 Mre11 -/-

Blunt

IgG1

AGAATCAGTAAGGAGGGACCCA | GGCTAAGAAGGCAATCCTGGGA
AGAATCAGTAAGGAGGGACCCA | CAGGACAGGTGGAAATGTGGTG
GGCAGAGCAGCTCCAGGGGAGC | CAGGACAGGTGGAAATGTGGTG

AGCCAGCCTCGGTGGCTTTGAA | GGAACAATTCCACACAAAGACT
AGCCAGCCTCGGTGGCTTTGAA | AGGACAGGTGGAAGTGTAGGGA
GCAGAGTAGCTCTTAGGGAGCC | AGGACAGGTGGAAGTGTAGGGA

CTGAAATGAGATACTCTGGAGT | AGCTGAGATGGGGTGAGATGGG
CTGAAATGAGATACTCTGGAGT | CAGGACAGGTGGGAGTGTGGTG
GGCAGAGCAGCTGCAGGGCAGC | CAGGACAGGTGGGAGTGTGGTG

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AATTAAGGGAACAAGGTTGAGA | TGACCCAGGCAGAGCAGCTGC
AACCAGGACAGGTGGAAGTGTGG | TGACCCAGGCAGAGCAGCTGC

CAGTAAGGAGGGACCCAGGCTA | AGAAGGCAATCCTGGGATTCTG
CAGTAAGGAGGGACCCAGTCTA | CAGGAAAGGTGGAAGTGTGGTG
GGCAGAGCAGCTCCATGGCAGC | CAGGACAGGTGGAAATGTGGTG

AGCTGGGCCGCTAAGCTAAACT | AGGCTGGCTTAACCGAGATGAG
AGCTGGGCCGCTAAACTAAACT | CAGGGAAGCTATAGGAAAACCA
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TGAGATGGGTGGGCTTCTCTGA | CCAGGACAGGTGGGAGTGTGGG
AGGCAGAGCATCTATAGGGGAG | CCAGGACAGGTGGGAGTGTGGG

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AATTGAGAAAGAATAGAGACCT | ATAGAAGTTTGTTA | AATTCAGGCAGAGCAGTGCCTT
CCAAGACAACTAGAAGTGTGTG | AATCCAGGCAGAGCAGTGCCTT

IgE

GCTGGGCCGCTAAGCTAAACTA | GGCTGGCTTAACCGAGATGAGC
GCTGGGCCGCTAAGCTAAACTA | TAAGGCTGCCCTGAACTGAGCA
AGATGGGCCCGGCTAAGCTAAG | TAAGGCTGCCCTGAACTGAGCA

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GTTTAATGAATTTGAGGTTGCC | GGCTGAGCTGAGTCAAGATGGT
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CTGAGCAAAATTAAGGGAACAA | GGTTGAGAGCCCTAGTAAGCGA
CTGAGCAAAATTAAGGGAACAA | ACTGGGCTGAGCTAAGTTGCAC
GACCTGAGCTAGGGTAGGCTGG | ACTGGGCTGAGCTAAGTTGCAC

Microhomology

IgG1

ACCCAGGCTAAGAAGGCAATCCTGGGATTCTGGAAGAAAAGATG
ACCCAGGCTAAGAAGACAATC**C**AGATGCAGGGCAGCCAGGACA
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IgE

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AGGTTGAATAGAGCTAAACT**CT**GAGCTAGGGTAGGCTGGACT
AGCTGGTCTACACTAGCCTGACCTGAGCTAGGGTAGGCTGGACT

CAAAATTAAGGGAACAAGGTTGAGAGCCCTAGTAAGCGAGGCTC
CAAAATTAAGGGAACAAGGTT**G**CTGGGTAGACTAGGCTGAGC
TGGGTTAAACTAGGTTGCACTGGCTGGGTTAGACTTGGCTGAGC

Sequences of CSR joins from Mre11–/– stimulated B cells