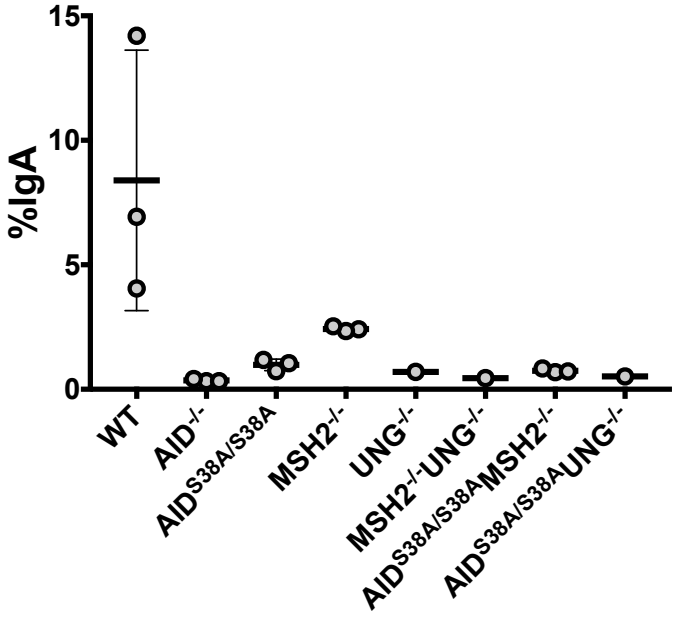
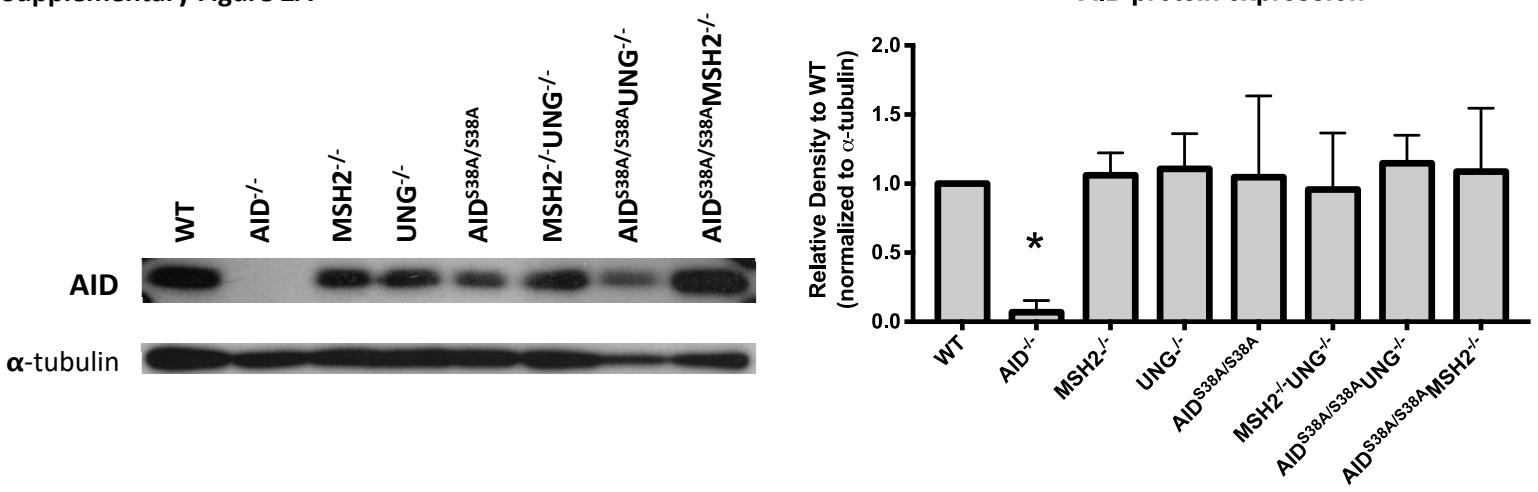
Supplementary Figure 1

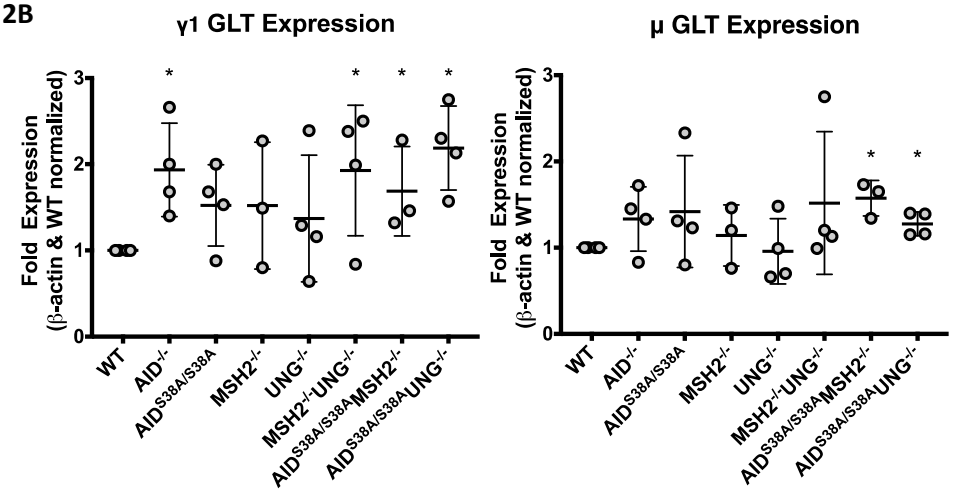


Supplementary Figure 1. CSR to IgA is absent in *AID$^{S38A/S38A}$MSH2$^{-/-}$* and *AID$^{S38A/S38A}$UNG$^{-/-}$* mice. Splenic B cells were purified from mice of the indicated genotypes, stimulated for CSR to IgA, and analyzed for surface IgA by flow cytometry after four days in culture.

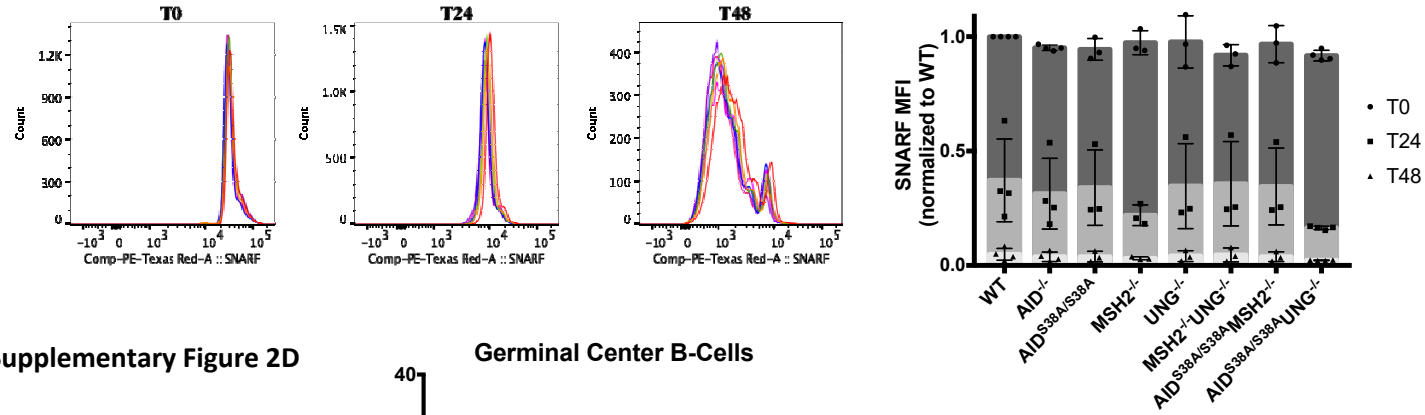
Supplementary Figure 2A



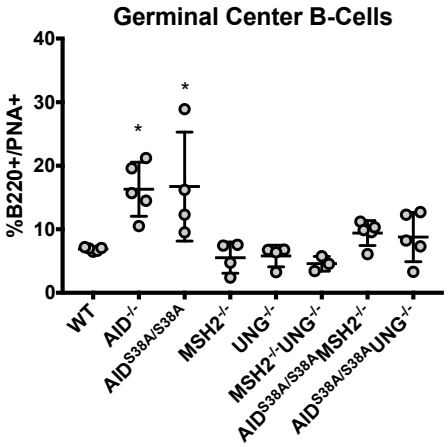
Supplementary Figure 2B



Supplementary Figure 2C

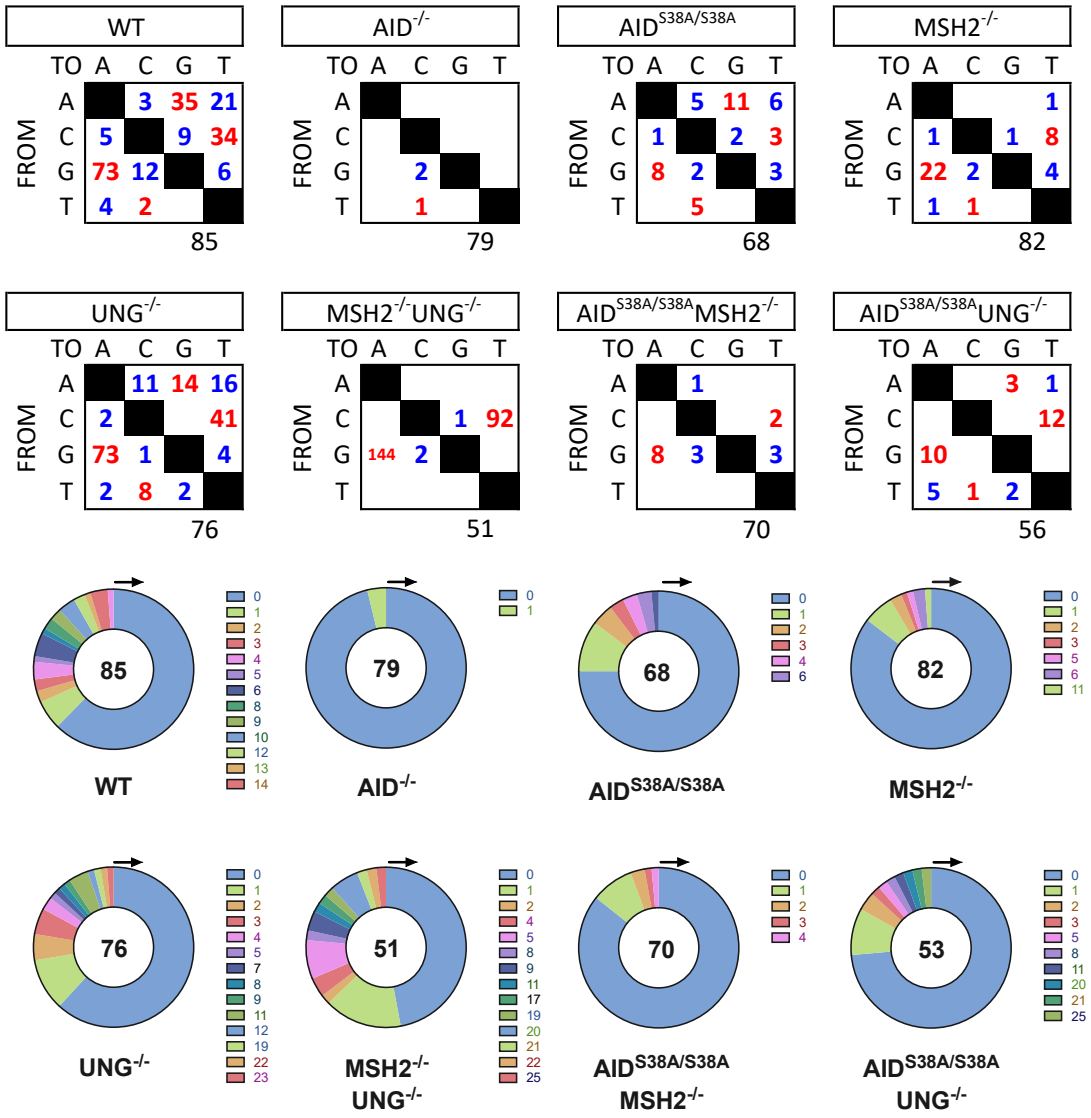


Supplementary Figure 2D

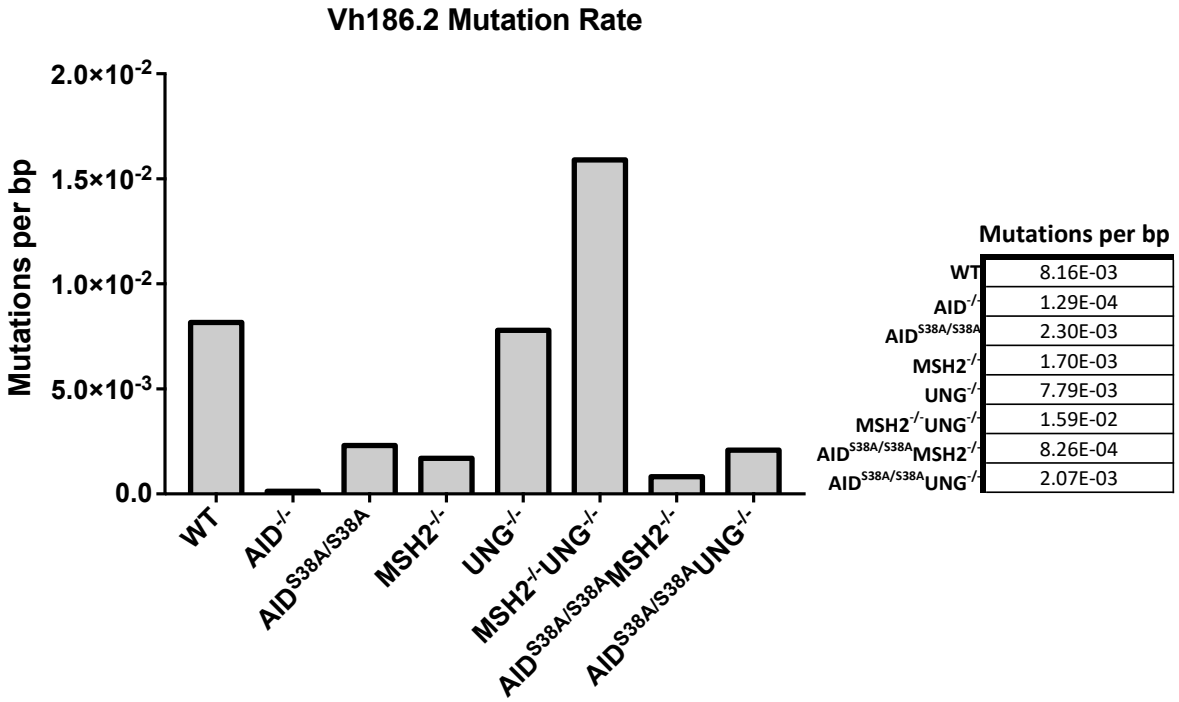


Supplementary Figure 2. Altered CSR and SHM in *AID*$^{S38A/S38A}$*MSH2*$^{-/-}$ and *AID*$^{S38A/S38A}$*UNG*$^{-/-}$ B cells is not due to defects in AID expression, germline transcription, cell proliferation, or GCBC formation. Purified splenic B cells from mice of the indicated genotype were stimulated for CSR to IgG1 *in vitro*. (**A**) AID protein expression was analyzed by immunoblot and quantified by densitometric analysis of three immunoblots. Only *AID*$^{-/-}$ B cells had significantly reduced (P<0.0001) AID protein expression. (**B**) Germline transcription was analyzed by quantitative RT-PCR. cDNA from IgG1-stimulated splenic B cells was analyzed for γ1 and μ GLT expression and normalized to β-actin expression. *AID*$^{S38A/S38A}$*MSH2*$^{-/-}$ and *AID*$^{S38A/S38A}$*UNG*$^{-/-}$ B cells demonstrated significantly increased γ1 and μ GLT expression levels as compared to WT B cells (γ1: P=0.041 and 0.003, respectively; μ: P=0.002 and 0.007, respectively) (**C**) B cell proliferation was analyzed by dilution of SNARF. Splenic B cells from mice (n ≥ 3) of the indicated genotypes were stained with SNARF 24 hours post-stimulation with LPS+IL4 and assayed for SNARF fluorescence at 0 hour (T0), 24 hours (T24), and 48 hours (T48) post-staining. Mean fluorescence intensity (MFI) was calculated for each sample in FlowJo. Paired, two-tailed Student's *t*-test did not demonstrate a difference between B cell proliferation for each mutant genotype as compared to WT B cells. (**D**) Peyer's patch GCBCs (B220^{+}PNA^{hi}) from mice of the indicated genotypes were analyzed by flow cytometry. A two-tailed, Student's *t*-test was used to determine statistical difference from WT (*P<0.05).

Supplementary Figure 3A

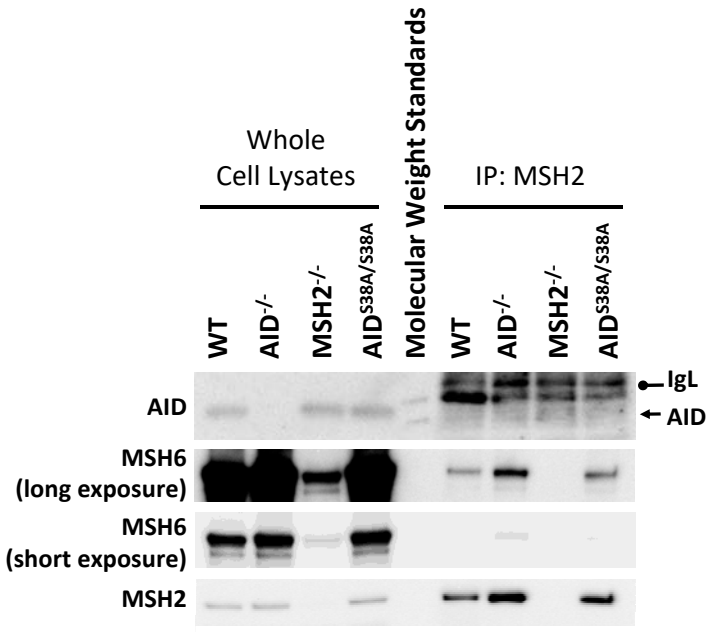


Supplementary Figure 3B



Supplementary Figure 3. ***AID*$^{S38A/S38A}$*MSH2*$^{-/-}$ and *AID*$^{S38A/S38A}$*UNG*$^{-/-}$ B cells mutate V_H186.2.** Peyer's patch from mice of the indicated genotypes were isolated and cDNA was synthesized from the extracted RNA to analyze for mutations within V_H186.2. (**A**) The total number of transition (red) and transversion (blue) mutations at A, C, G, and T base pairs is summarized in the tables. The total number of sequences analyzed is indicated below each table. The number of mutations per PCR amplicon is depicted in the pie charts. (**B**) The V_H186.2 mutation frequency is depicted in the bar graph and calculated by dividing the number of mutations by the total number of base pairs sequenced.

Supplementary Figure 4



Supplementary Figure 4. AID does not co-immunoprecipitate with MSH2. Protein extracts of purified WT, *AID*$^{-/-}$, *MSH2*$^{-/-}$, *AID*$^{S38A/S38A}$ B cells 72 hours post-stimulation with LPS+IL4 were immunoprecipitated for MSH2 and analyzed for AID interaction. Immunoblots of anti-MSH2 immunoprecipitates or whole cell lysates were probed with antibodies to AID, MSH6, or MSH2. As previously described [54], the loss of MSH2 reduces MSH6 protein levels. The expected position of the AID protein is indicated with an arrow and the IgL chain is indicated with a knob.