(B) Publication Quality PDF
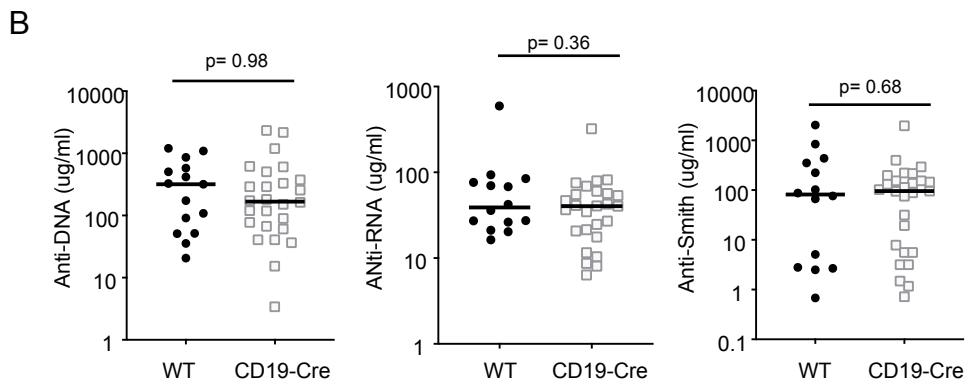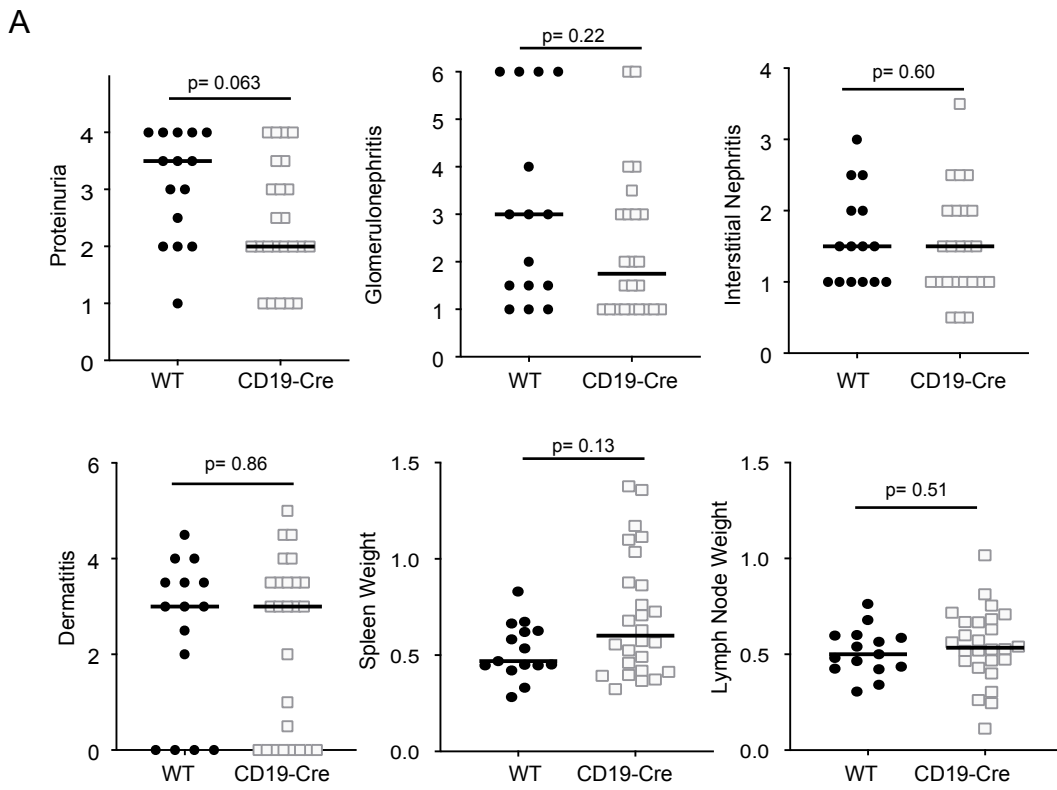
Supplemental Figure 1: **CD19-Cre knock-in allele does not alter disease phenotype, antibody profile, or cellular composition in MRL/*lpr* mice.**

(A) Evaluation of phenotypic markers of disease including proteinuria, glomerulonephritis, interstitial and perivascular renal infiltrates, dermatitis, spleen weight, and lymph node weight for CD19-Cre$^{-/-}$ vs CD19-Cre$^{+/-}$ n= 15 and 26 respectively.

(B) Serum concentrations of anti-nucleosome, anti-Sm and anti-RNA IgG from CD19-Cre$^{-/-}$ vs CD19-Cre$^{+/-}$ MRL/*lpr* mice. Scatter plots display data from individual mice with black lines representing median values. No comparisons were statistically significant by two-tailed Mann-Whitney test. (C) Percentage of cells from each lineage represented as mean and standard deviation with associated p-values as determined by two-tailed Mann-Whitney test.
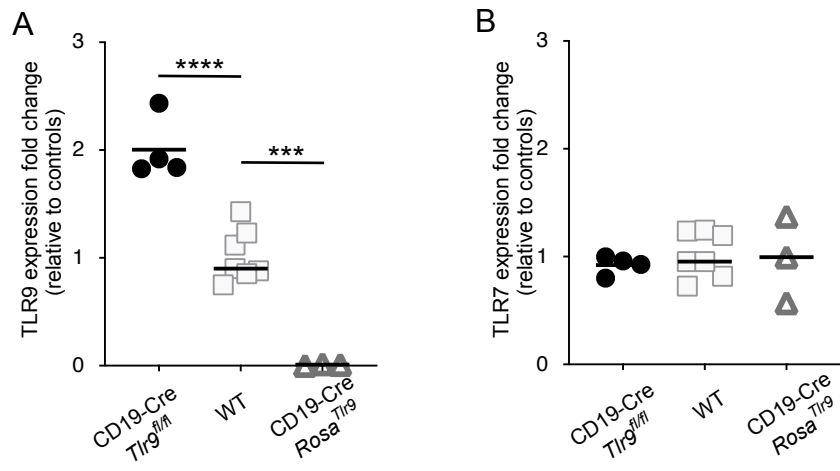
Supplemental Figure 2: **TLR9 expression does not alter TLR7 transcription.**

(A) qPCR analysis of TLR9 expression in sorted B cells from CD19-Cre *Rosa$^{Tlr9}$* mice (n=4) control MRL/*lpr* (n=7) and mice and CD19-Cre *Tlr9$^{fl/fl}$* mice (n=3). (B) qPCR analysis of TLR7 expression in sorted B cells from CD19-Cre *Rosa$^{Tlr9}$* mice (n=4) control MRL/*lpr* (n=7) and mice and CD19-Cre *Tlr9$^{fl/fl}$* mice (n=3). Scatter plots display fold change mRNA expression data from individual mice with black lines showing median values. *** $p<0.001$,**** $p<0.0001$ one-tailed Mann-Whitney U test.

A



B



C

|  | CD19-Cre neg | CD19-Cre + | p-value |
|---|---|---|---|
| B cells (% of total cells) | 33 ± 11 | 24 ± 13 | 0.17 |
| Plasmablasts (% of total cells) | 2.1 ± 1.1 | 1.9 ± 1.2 | 0.54 |
|  |  |  |  |
| B cell Subets |  |  |  |
| Follicular (as a % of B cells) | 37 ± 12 | 36 ± 10 | 0.88 |
| Marginal Zone (as a % of B cells) | 36 ± 6 | 34 ± 13 | 0.97 |
| Germinal Center (as a % of B cells) | 0.7 ± 1.5 | 0.5 ± 0.8 | 0.73 |
|  |  |  |  |
| CD8 T cells (% of total cells) | 13 ± 4 | 12 ± 4 | 0.71 |
| Naïve CD8 T cells (as a % of CD8 T cells) | 13 ± 4 | 14 ± 4 | 0.92 |
|  |  |  |  |
| CD4 T cells (% of total cells) | 16 ± 2 | 15 ± 4 | 0.38 |
| Naïve CD4 T cells (as a % of CD8 T cells) | 4.8 ± 3.1 | 4.1 ± 2.6 | 0.59 |

Supplemental Figure 1

A

TLR9 expression fold change (relative to controls)

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CD19-Cre *Tlr9*$^{fl/fl}$    WT    CD19-Cre *Rosa*$^{Tlr9}$

B

TLR7 expression fold change (relative to controls)

CD19-Cre *Tlr9*$^{fl/fl}$    WT    CD19-Cre *Rosa*$^{Tlr9}$

Supplemental Figure 2

Supplemental Table 1: Deletion Efficiency *Tlr9* of Cre lines on the MRL/lpr background

| Strain | Cell Type | n | % Deletion Efficiency | Assay |
|---|---|---|---|---|
| CD19-Cre *Tlr9$^{fl/fl}$* | B cell | 2 | 96.3 | qPCR |
| | cDC | 2 | 0 | |
| | pDC | 2 | 0 | |
| | plasmablast | 2 | 6.0 | |
| LysM-Cre *Tlr9$^{fl/fl}$* | cDC | 6 | 26.5 | qPCR |
| | B cell | 6 | 12.3 | |
| | T cell | 6 | 8.0 | |
| | Macrophages | 6 | 58.2 | |
| | Neutrophils | 6 | 69.3 | |
| MRP8-Cre *Tlr9$^{fl/fl}$* | B cell | 5 | 4.5 | qPCR |
| | Macrophages | 5 | 2.3 | |
| | Neutrophils | 5 | 90.6 | |
| | T cell | 5 | 0.0 | |
| CD11c-Cre *Tlr9$^{fl/fl}$* | cDC | 2 | 95.8 | qPCR |
| | pDC | 2 | 91.7 | |
| | B cell | 2 | 62.8 | |
| | plasmablast | 2 | 93.2 | |

Supplemental Table 2: Percent cell composition of MRL/*lpr* spleens from indicated strains

| | *Tlr9*$^{fl/fl}$ | CD19-Cre *Tlr9*$^{fl/fl}$ | *Tlr9*$^{fl/fl}$ | LysM-Cre *Tlr9*$^{fl/fl}$ | *Tlr9*$^{fl/fl}$ | MRP8-Cre *Tlr9*$^{fl/fl}$ | *Tlr9*$^{fl/fl}$ | CD11c-Cre *Tlr9*$^{fl/fl}$ | ROSA$^{Tlr9}$ | CD19-Cre ROSA$^{Tlr9}$ |
|---|---|---|---|---|---|---|---|---|---|---|
| B cells | 27.5 ± 12 | 19.2 ± 11.8 | 21.8 ± 11.8 | 23.0 ± 13.0 | 34 ± 13 | 31 ± 15 | 31 ± 11 | 27.7 ± 9.9 | 21.1 ± 8.1 | 19.1 ± 10.8 |
| Plasmablasts | 2.1 ±1.2 | 2.1 ± 1.7 | 1.7 ± 0.8 | 1.8 ± 1.1 | 1.26 ± 069 | 0.99 ± 0.82 | 2.9 ± 1.1 | 4.5 ± 1.6 | 1.82 ± 0.81 | 1.83 ± 1.03 |
| cDCs | 0.50 ± 0.16 | 0.58 ± 0.21 | 0.37 ± 0.20 | 0.36 ± 0.17 | 0.31 ± 0.16 | 0.28 ± 0.12 | 0.72 ± 0.22 | 0.70 ± 0.29 | 1.19 ± 0.49 | 1.24 ± 0.42 |
| pDCs | 0.26 ± 0.11 | 0.26 ± 0.17 | 0.11 ± 0.1 | 0.11 ± 0.08 | 0.11 ± 0.04 | 0.11 ± 0.05 | 0.26 ± 0.11 | 0.23 ± 0.12 | 0.12 ± 0.05 | 0.14 ± 0.05 |
| CD4 T cells | 15.3 ± 2.7 | 16.7 ± 3.5 | 10.0 ± 2.4 | 9.8 ± 2.9 | 10.7 ± 2.7 | 12.6 ± 3.0 | 17.3 ± 1.7 | 17.7 ± 3.2 | 10.9 ± 2.65 | 11.3 ± 3.1 |
| CD4 naïve T cells (% of Total CD4) | 5.9 ± 2.4 | 3.6 ± 1.5 | 6.9 ± 4.9 | 6.8 ± 5.0 | 6.1 ± 2.6 | 7.7 ± 3.4 | 2.7 ± 1.5 | 1.96 ± 1.21 | 7.8 ± 3.3 | 7.7 ± 5.0 |
| CD8 T cells | 10.0 ± 2.2 | 9.9 ± 3.5 | 10.1 ± 3.4 | 10.4 ± 3.8 | 10.1 ± 3.3 | 10.9 ± 4.5 | 10.2 ± 2.7 | 10.0 ± 2.8 | 11.5 ± 3.7 | 10.1 ± 3.3 |
| CD8 naïve T cells (% of Total CD8) | 13.9 ± 3.5 | 11.0 ± 4.2 | 14.0 ± 6.4 | 11.9 ± 6.1 | 15.4 ± 3.6 | 16.3 ± 3.6 | 8.3 ± 4.7 | 5.96 ± 3.9 | 15.0 ± 3.9 | 15.2 ± 5.0 |
| CD11b+ | 4.25 ± 1.45 | 4.6 ± 1.8 | 6.0 ± 3.2 | 6.3 ± 3.0 | 7.4 ± 2.6 | 7.6 ± 2.2 | 3.81 ± 0.82 | 3.9 ± 1.3 | 6.7 ± 1.7 | 7.64 ± 2.2 |
| Macrophages | 0.94 ± 0.43 | 1.15 ± 0.57 | 0.83 ± 0.47 | 0.84 ± 0.34 | 1.11 ± 0.55 | 1.13 ± 0.55 | 0.97 ± 0.36 | 0.99 ±0.47 | 1.29 ± 0.55 | 1.51 ± 0.73 |
| Monocytes | 0.75 ± 0.29 | 0.85 ± 0.64 | 0.73 ± 0.38 | 0.72 ± 0.35 | 0.79 ± 0.47 | 0.78 ± 0.4 | 0.68 ± 0.22 | 0.67 ± 0.24 | 0.83 ± 0.62 | 0.96 ± 0.52 |
| Neutrophils | 1.17 ± 0.73 | 1.16 ± 0.81 | 3.3 ± 2.2 | 3.5 ± 2.1 | 4.0 ± 1.6 | 4.1 ± 1.6 | 0.89 ± 0.25 | 0.91 ± 0.36 | 3.55 ± 0.88 | 4.3 ± 1.5 |

Grey comparisons indicate statistically significant differences $p<0.05$ by Mann Whitney

Supplemental Table 3: Cell counts from MRL/*lpr* spleens from indicated strains

| | $Tlr9^{fl/fl}$ | CD11c-Cre $Tlr9^{fl/fl}$ | $Tlr9^{fl/fl}$ | CD19-Cre $Tlr9^{fl/fl}$ | ROSA$^{Tlr9}$ | CD19-Cre ROSA$^{Tlr9}$ |
|---|---|---|---|---|---|---|
| B cells | 93 ± 42 | 88 ± 29 | 75 ± 33 | 56 ± 31 | 65 ± 27 | 58 ± 41 |
| Plasmablasts | 10.1 ± 6.9 | 17.0 ± 11.6 | 6.2 ± 4.0 | 6.4 ± 5.5 | 5.3 ± 2.7 | 4.8 ± 2.2 |
| cDCs | 2.7 ± 2.0 | 1.5 ± 1.8 | 1.4 ± 0.6 | 1.8 ± 0.8 | 4.3 ± 2.9 | 4.1 ± 1.7 |
| pDCs | 0.93 ± 0.64 | 0.75 ± 0.50 | 0.73 ± 0.35 | 0.83 ± 0.55 | 0.47 ± 0.23 | 0.48 ± 0.27 |
| CD4 T cells | 62 ± 44 | 63 ± 33 | 44 ± 14 | 57 ± 22 | 38 ± 12 | 39 ± 18 |
| CD4 naïve T cells | 1.7 ± 1.5 | 1.2 ± 0.9 | 2.5 ± 1.4 | 1.8 ± 1.5 | 3.0 ± 1.7 | 3.6 ± 3.3 |
| CD8 T cells | 36 ± 25 | 33 ± 12 | 29 ± 10 | 33 ± 16 | 40 ± 15 | 38 ± 24 |
| CD8 naïve T cells | 3.0 ± 2.3 | 2.2 ± 1.8 | 4.1 ± 1.8 | 4.0 ± 2.0 | 6.2 ± 3.0 | 6.1 ± 4.2 |
| CD11b+ | 13 ± 8 | 14 ± 9 | 12 ± 7 | 16 ± 10 | 24 ± 8 | 26 ± 13 |
| Macrophages | 3.3 ± 2.0 | 3.4 ± 1.9 | 2.6 ± 1.7 | 4.0 ± 2.5 | 4.6 ± 2.0 | 5.2 ± 3.9 |
| Monocytes | 2.3 ± 1.6 | 2.4 ± 1.6 | 2.2 ± 1.4 | 3.3 ± 3.2 | 2.8 ± 2.1 | 3.2 ± 1.6 |
| Neutrophils | 3.3 ± 2.5 | 3.5 ± 2.8 | 3.5 ± 3.0 | 4.5 ± 4.7 | 12.6 ± 3.5 | 14.5 ± 6.6 |

Grey comparisons indicate statistically significant differences dark grey $p < 0.05$, light grey $p < 0.1$ by Mann Whitney