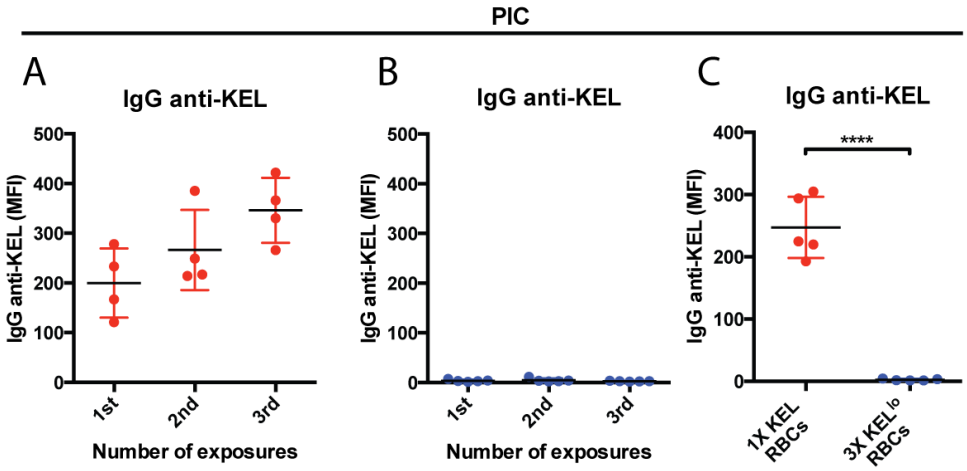
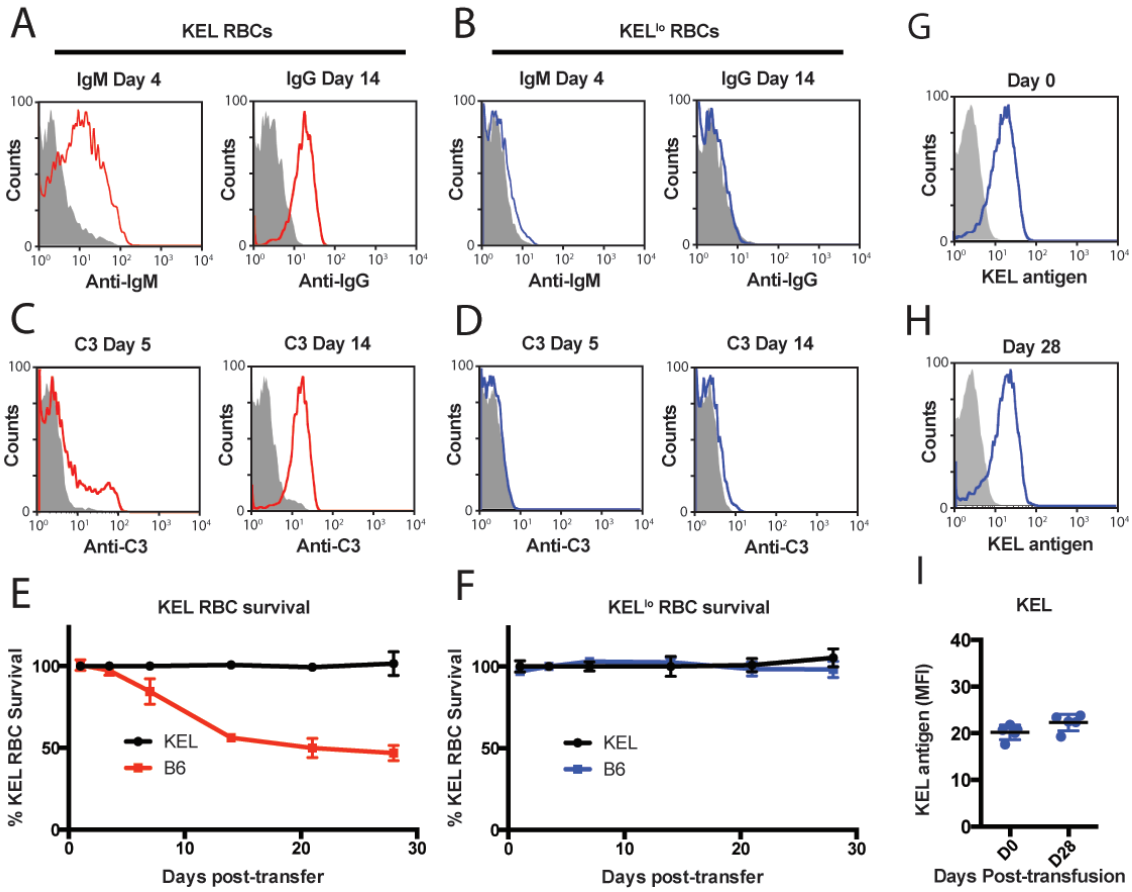
Supplemental Figure 1



Supplemental Figure 1: KEL^{lo} RBCs fail to induce detectable anti-KEL antibodies in the presence of PIC. (A,B) C57BL/6 KEL negative recipients were exposed to one, two or three doses of KEL (A) or KEL^{lo} (B) RBCs in the presence of PIC, followed by examination of IgG anti-KEL antibody formation. (C) C57BL/6 KEL negative recipients were exposed to a normal dose of KEL RBCs or 3 times the normal dose of KEL^{lo} RBCs in the presence of PIC, followed by evaluation of IgG anti-KEL antibodies. Data were analyzed using student t-test. Error bars indicate SEM. ****$P < 0.0001$.

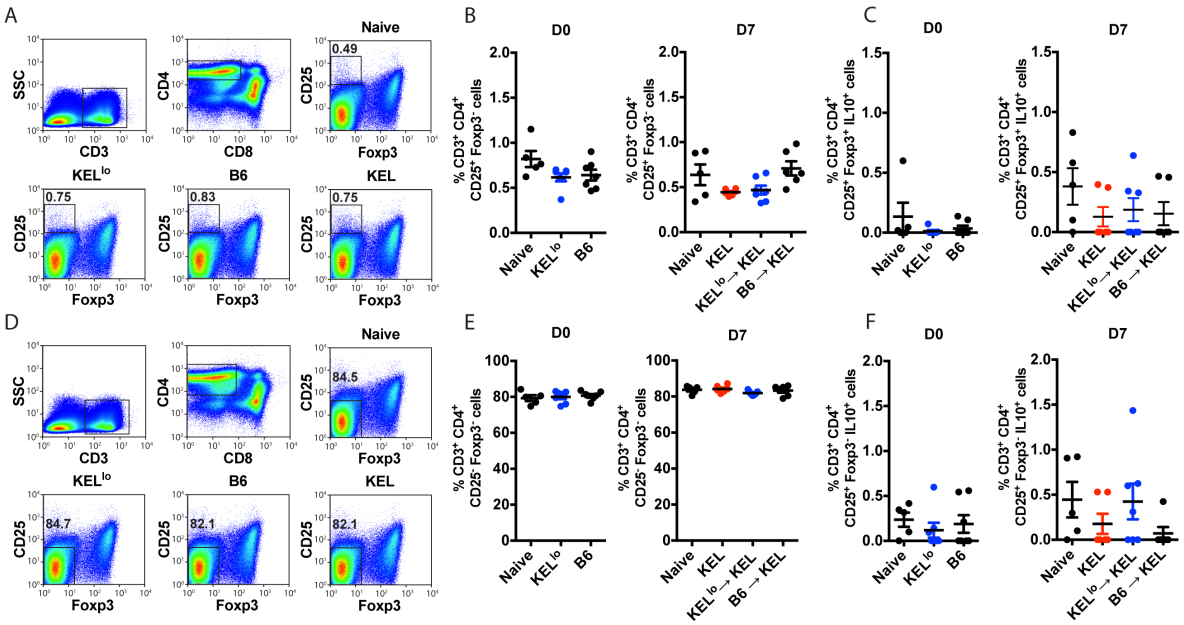
Supplemental Figure 2



Supplemental Figure 2: KEL^{lo} RBCs fail to induce antibody engagement, complement fixation, experience accelerated clearance or alteration to antigen levels following transfer. (A) Detection of IgM or IgG on the surface of KEL RBCs 4 days (IgM) or 14 days (IgG) following transfer into C57BL/6 KEL negative recipients. (B) Detection of IgM or IgG on the surface of KEL^{lo} RBCs 4 days (IgM) or 14 days (IgG) following transfer into C57BL/6 KEL negative recipients. (C) Detection of complement component 3 (C3) on the surface of KEL RBCs 4 days or 14 days following transfer into C57BL/6 KEL negative recipients. (D) Detection of C3

on the surface of KEL^{lo} RBCs 4 days or 14 days following transfer into C57BL/6 KEL negative recipients. (E) Examination of KEL RBC clearance following transfer into C57BL/6 KEL positive (black) or KEL negative (red) recipients. (F) Examination of KEL^{lo} RBC clearance following transfer into C57BL/6 KEL positive (black) or KEL negative (blue) recipients. (G-H) Detection of KEL antigen on the surface of KEL^{lo} RBCs 0 days (G) or 28 days (H) following transfer into C57BL/6 KEL negative recipients. (I) Quantitation of KEL antigen level on KEL^{lo} RBCs 0 days or 28 days following transfer into C57BL/6 KEL negative recipients.

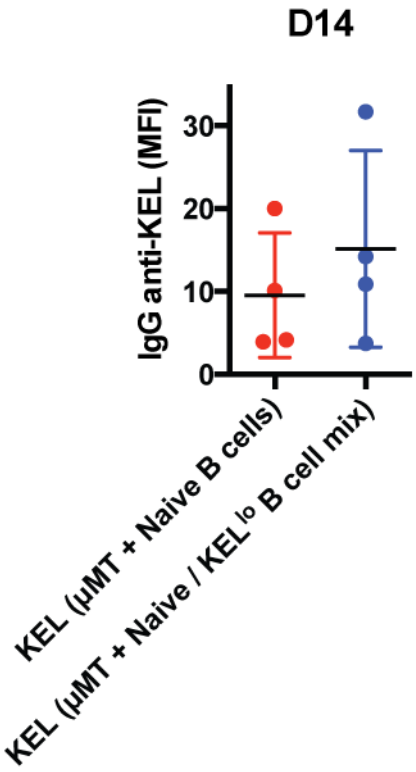
Supplemental Figure 3



Supplemental Figure 3: KEL^{lo} RBC exposure fails to induce detectable change in cytokine secretion of regulatory T cells (Tregs). (A) Representative flow cytometric examination of CD25^{+} Foxp3^{-} T regulatory 1 (Tr1) cells following exposure to PBS, C57BL/6 (B6), KEL or KEL^{lo} RBCs. (B) Quantitation of CD25^{+} FoxP3^{-} Tr1 cells in PBS, C57BL/6 (B6) or KEL^{lo} RBC treated recipients in the absence (D0 = Day 0) or presence (D7 = Day 7) of a subsequent KEL RBC transfusion. (C) Quantitation of IL10 production by CD25^{+} Foxp3^{+} T cells following exposure to PBS, C57BL/6 (B6) or KEL^{lo} RBC (D0 = Day 0), or following KEL RBC challenge of each recipient group (D7 = Day 7). (D) Representative flow cytometric plots of CD25^{-} FoxP3^{-} T cells post PBS, C57BL/6 (B6), KEL^{lo}, or KEL RBC transfusion. (E) Quantitative analysis of CD25^{-} FoxP3^{-} T cells in PBS, C57BL/6 (B6) or KEL^{lo} RBC

treated recipients prior to (D0 = Day 0) and following (D7 = Day 7) exposure of a subsequent KEL RBC transfusion. (F) Quantitation of IL10 production of $CD25^{+}$ $Foxp3^{-}$ T cells following exposure to PBS, C57BL/6 (B6) or KEL^{lo} RBC (D0 = Day 0), or following KEL RBC challenge of each recipient group (D7 = Day 7).

Supplemental Figure 4



Supplemental Figure 4: Co-transfer of B cells from KEL^{lo} recipients along with naïve B cells fails to inhibit anti-KEL antibody production following KEL RBC transfer. Examination of anti-KEL antibody production following KEL RBC transfusion into µMT recipients adoptively transferred with B cells from C57BL/6 naïve (µMT + Naïve B cells) or a 1:1 ratio ($5x10^7$ each) B cells from C57BL/6 naïve or KEL^{lo} treated recipients (µMT + Naïve/KEL^{lo} recip. B cell mix).