Supplementary Figure 1:

Generation of KSHV latency locus transgenic mice. (A) Transgene fragment encompassing LANA, vCYC, vFLIP, KSHV miRNAs, and K12 was isolated from pDD801 for pronuclear injection. Transgene for LANA promoter[1] and LANA transgenic mice[2] was also shown in a and b. (B) Confirmation of transgene by Southern blot of tail DNA from three independent founder lines (i, ii, and iii). Genomic DNA was cut with PstI and EcoRV, followed by hybridization with LANA-specific probe (nucleotide sequence for amino acid 770 -1003). LANA was detected in all 3 founder lines. Lane 1 - 4 represent a transgene-negative mouse and three transgene-positive mice from founder line i, respectively. Genomic DNA from a C57BL/6 mouse and the transgene plasmid were used as negative (Neg.) and positive (Pos.) controls, respectively (lanes 10-11). (C) Founder–specific transgene integration. Genomic DNA was cut with SspI and hybridized to the same LANA probe in (B). Lanes 1-3 contain genomic DNAs belonging to independent founders, i, ii, and iii. (D) Confirmation of genotyping qPCR using LabChip® system. Gel electrophoresis was performed to verify qPCR data. Lane 1 and 3 show PCR products from a transgene-negative mouse (founder i) with LANA (lane 1) and apoB (lane 3) primer. Lane 2 and 4 represent PCR products from a transgene-positive mouse (founder i). wt or tg represents wild-type or KSHV latency transgenic mouse.

Supplementary Figure 2:

Transgene expression. (A, C) Kaposin was specifically detected in B cell follicles of Peyer's patches (PP) from a KSHV latency transgenic mouse. (B, D) no 1° indicates no primary antibody control reaction. Magnification 100X. (E-F) Higher magnification of

kaposin expression in the transgenic mouse. Magnification 400X. Arrows indicate cytoplasmic expression of kaposin on B cells in PP (A) but no reaction in staining without primary antibody (B). wt: wild-type mouse, tg: KSHV latency locus transgenic mouse.

Supplementary Figure 3:

Transgene expression. (A) vCYC was expressed in spleen from a KSHV latency transgenic mouse, but not from wild-type mouse spleen (C). Staining without primary antibody was shown in the transgenic mouse (B) or wild-type mouse (D). Xenograft tumor, which was formed in a SCID mouse after implantation of a PEL cell line, VG1, was stained as a positive control. Magnification 400X.

Supplementary Figure 4, related to Figure 2, 3, 4 and 5:

(A) Figure 2. Phenotype of KSHV latency locus transgenic mice. The numbers of the gated cells from transgenic (green), KSHV LANA transgenic (red) and littermate control mice (blue) were plotted for mature B cells ($CD19^+IgM^+IgD^+$), activated mature B cells ($CD19^+IgM^+IgD^+$FSC-hi), MZ B cells ($CD19^+IgM^+IgD^-$), activated MZ B cells ($CD19^+IgM^+IgD^-$FSC-hi), and activated mature B cells ($CD19^+IgM^+IgD^+$FSC-hi). WT (wild-type, n=9), CD19ko (CD19 knockout, n=4), LANA.125 (n=8) and LANA.151 (n=5) mean two independent lines of the KSHV LANA transgenic mice. TG.442 (n=9), TG.455 (n=6), TG.456 (n=5), and TG.633 (n=3) represent four independent lines of the KSHV latency locus transgenic mice. (B) Figure 3. MZ expansion in KSHV latency locus transgenic mice. The numbers of the gated cells from transgenic (red, n=9) and

littermate control mice (blue, n=5) were plotted for MZ B cells ($CD19^+CD21hiCD23^-CD24^+$, left), MZ B cells ($CD19^+CD21hiCD23^-IgD^-$, middle), and MZ precursor cells ($CD19^+IgD^+CD23^+CD21hi$; n=6(WT), n=9(TG)). (C) Figure 4. LPS-induced B cell expansion in KSHV latency locus transgenic mice. The numbers of activated GC B cells ($CD19^+CD71^+PNAhi$) and activated MZ B cells ($CD19^+CD21hiCD23^-CD69^+$) were plotted from LPS injected transgenic (n=6) and littermate control mice (n=6). TG_LPS; transgenic mice injected with LPS, TG_mock; transgenic mice injected with PBS, WT_LPS; littermate control mice injected with LPS, WT_mock; littermate control mice injected with PBS. (D) Figure 5. TD antigen-driven GC response in KSHV latency locus transgenic mice. The numbers of activated GC B cells ($CD19^+CD71^+PNAhi$) were plotted from NP-KLH immunized transgenic (n=6) and littermate control mice (n=6). WT_mock; littermate control mice immunized with PBS, TG_mock; transgenic mice immunized with PBS. WT_NP-KLH; littermate control mice immunized with NP-KLH, TG_NP-KLH; transgenic mice immunized with NP-KLH. The number of plasma cells ($CD19^-B220^-CD138^+$) were plotted from bone marrow (BM) and spleen (SP). WT; littermate control mice, TG; transgenic mice. *; $p \leq 0.05$, **; $p \leq 0.005$, ***; $p \leq 0.0005$.

Supplementary Figure 5:

KSHV latency locus transgenic mice show hyper-responsiveness to B cell stimulators. Proliferation was evaluated by incorporation of 5-ethynyl-2thynration was (EdU) into DNA using a Click-iT® EdU microplate assay kit (Invitrogen) according to the manufacturer's guide. Splenic B cells from the transgenic (n=5) and wild-type mice (n=5) were cultured with varying doses of anti-IgM, or anti-CD40 antibody, or LPS for 72

hours. Relative fluorescence unit (RFU) was measured and is expressed as ex vivo cell proliferation. *; $p \leq 0.05$.

Supplementary Figure 6:

Enlarged MZ in KSHV latency transgenic mice as ascertained by H&E stain. Panel WT shows a section of spleen in transgene negative littermate mouse; panel TG a section of transgene positive C57BL/6 mouse. Spleens were from untreated, 6-8 week old mice. The white arrows indicate the MZ. TG: transgenic mice, WT: wild-type mice. Magnification is 100X.

Supplementary Figure 7:

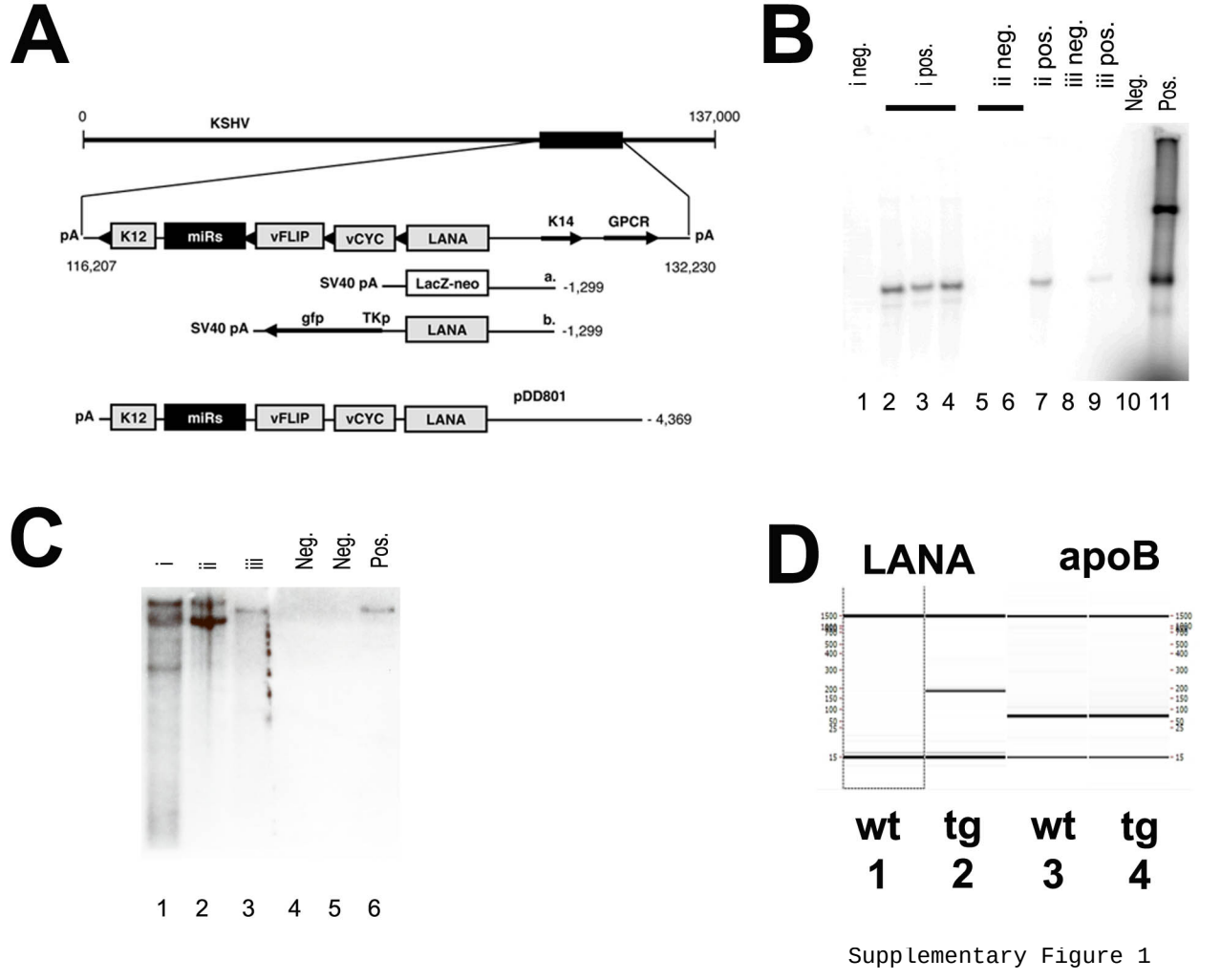
GC response of the KSHV latency transgenic mouse to a T-dependent antigen, NP-CGG. KSHV latency locus transgenic mice were immunized with NP-CGG. After 10 days, splenocytes were subject to FACS analysis. Activated GC B cells ($CD19^{+}CD71^{+}$PNAhi) were plotted (n=6). TG: transgenic mice, WT: wild-type mice.

Supplementary Figure 8:

Analysis of band intensity for IgH rearrangement PCR. PCR product was analyzed using LabChip® system. Band intensity defined as concentration of each band was plotted for each PCR sample. Cell line i and ii means mouse lymphoma cell lines; K46 and M12. WT; wild-type.

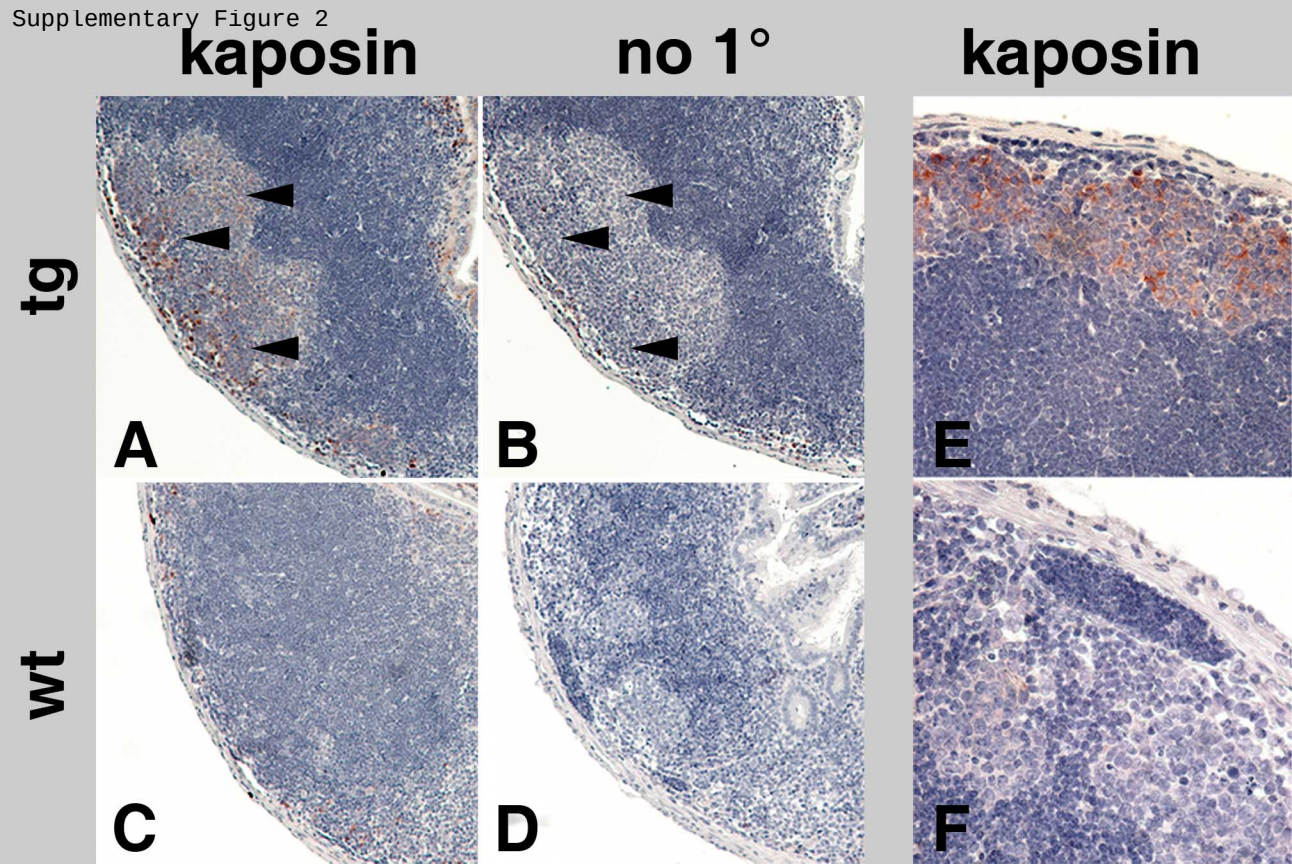
1. Jeong JH, Hines-Boykin R, Ash JD, Dittmer DP. Tissue specificity of the Kaposi's sarcoma-associated herpesvirus latent nuclear antigen (LANA/orf73) promoter in transgenic mice. *J Virol*. 2002;76(21):11024-11032.

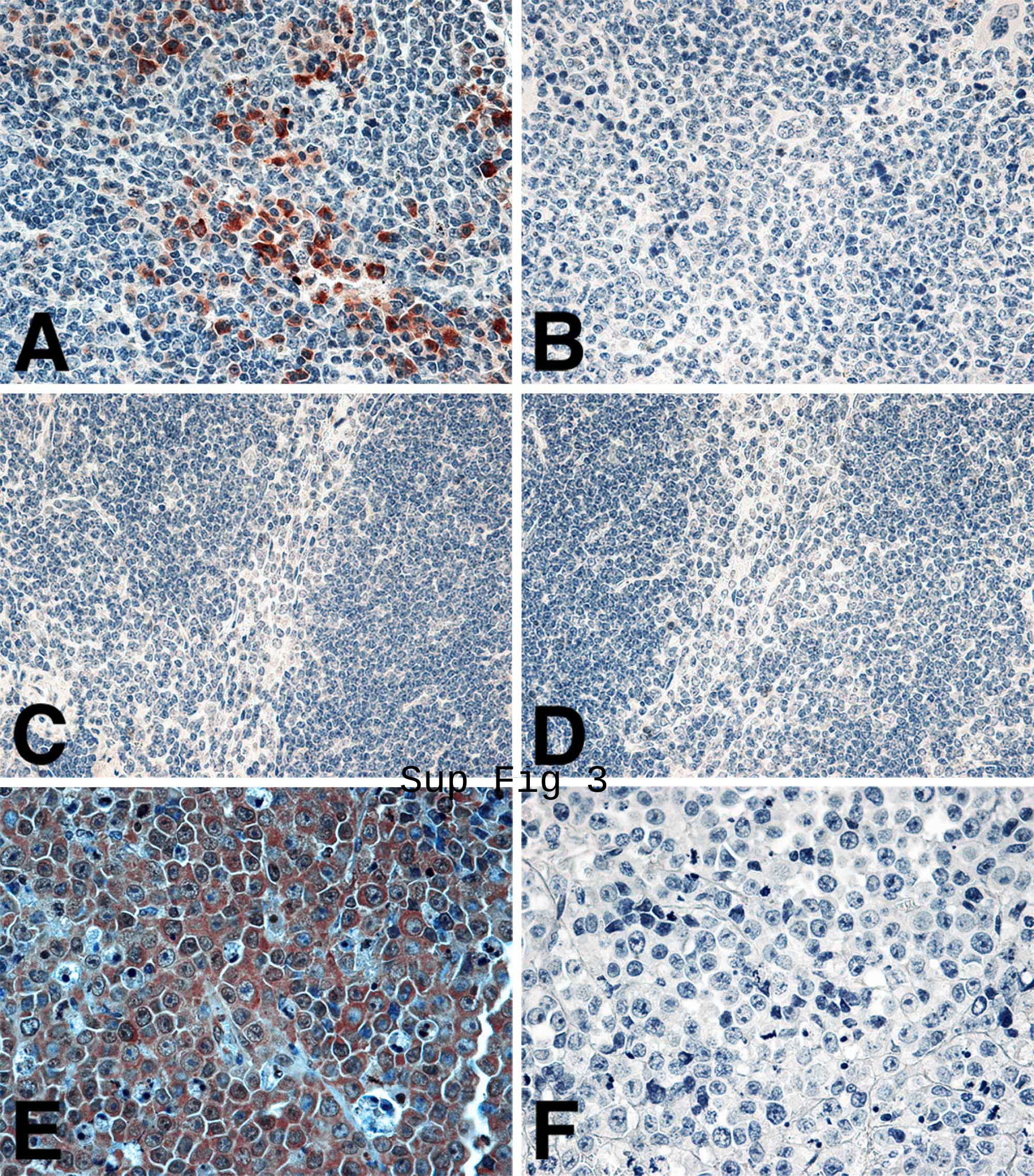
2. Fakhari FD, Jeong JH, Kanan Y, Dittmer DP. The latency-associated nuclear antigen of Kaposi sarcoma-associated herpesvirus induces B cell hyperplasia and lymphoma. *J Clin Invest*. 2006;116(3):735-742.



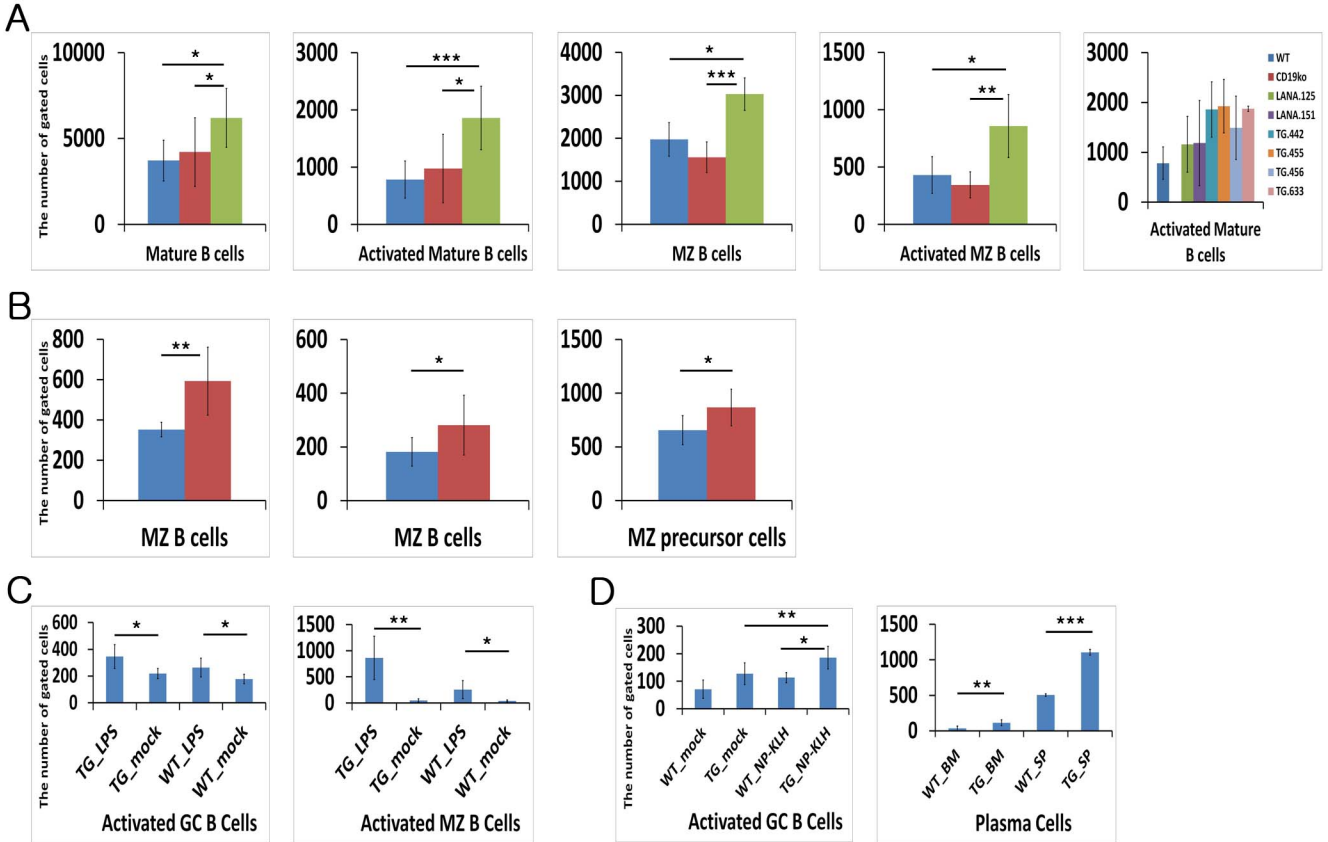
Supplementary Figure 1

Supplementary Figure 2

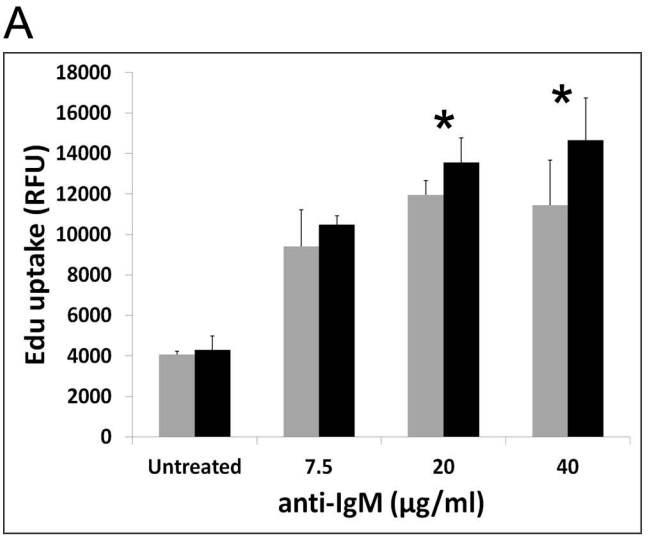


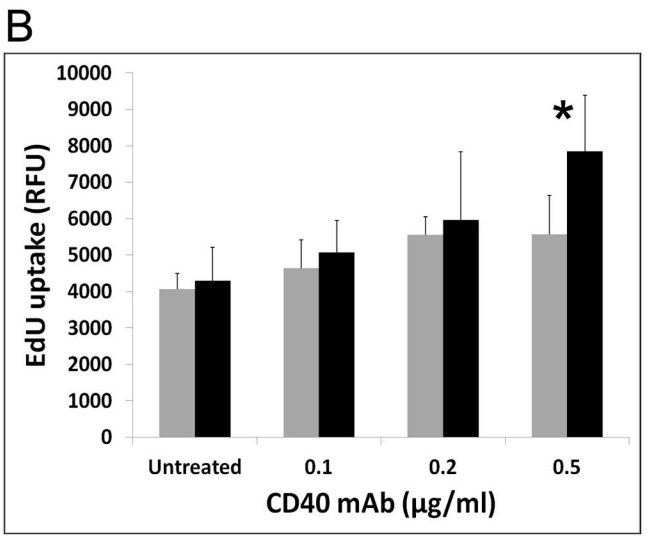


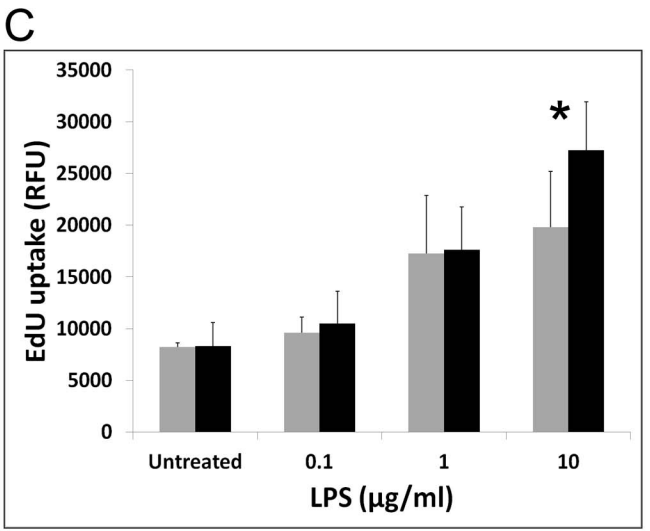
Sup Fig 3



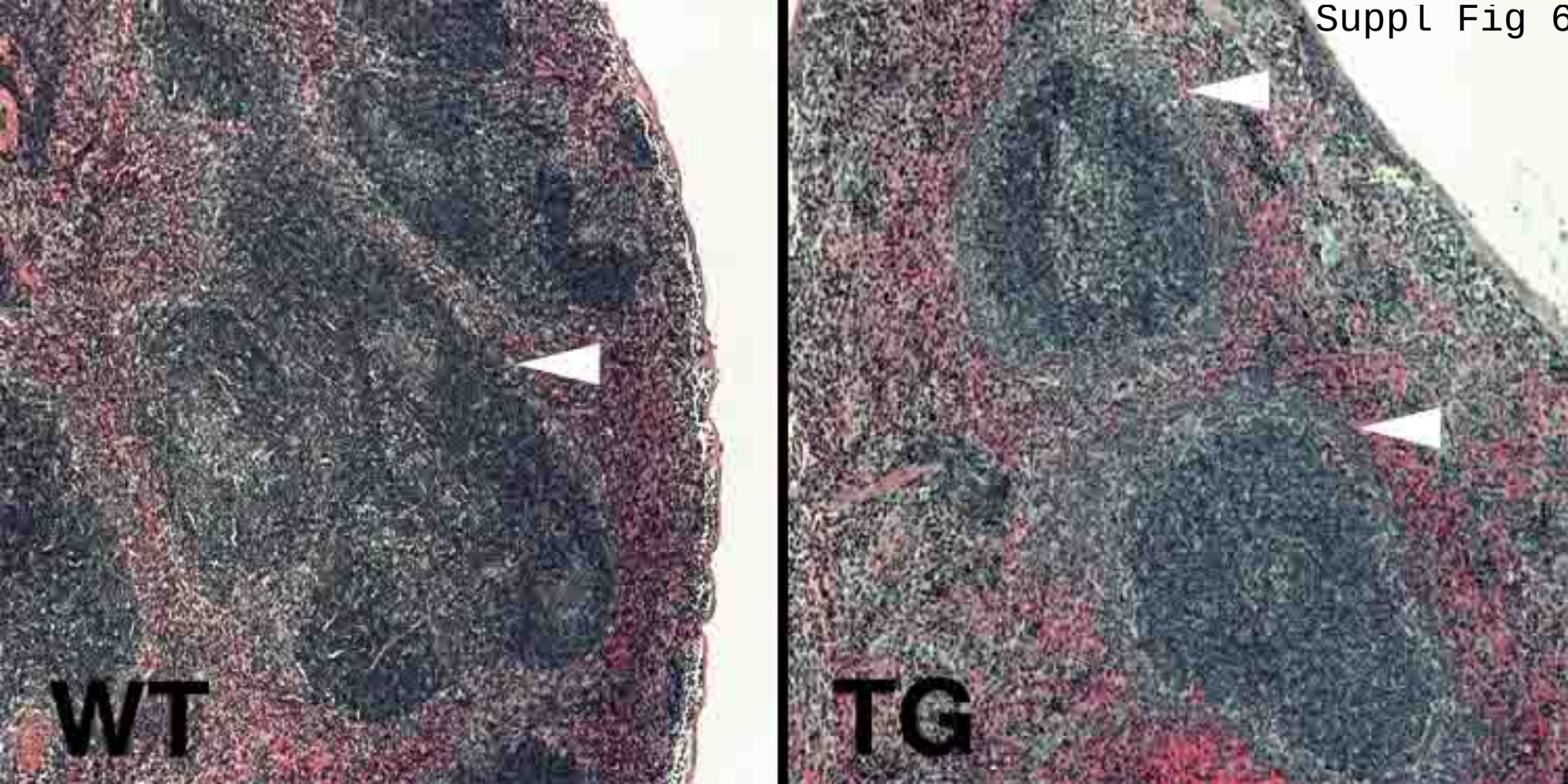
Supplementary Figure 4

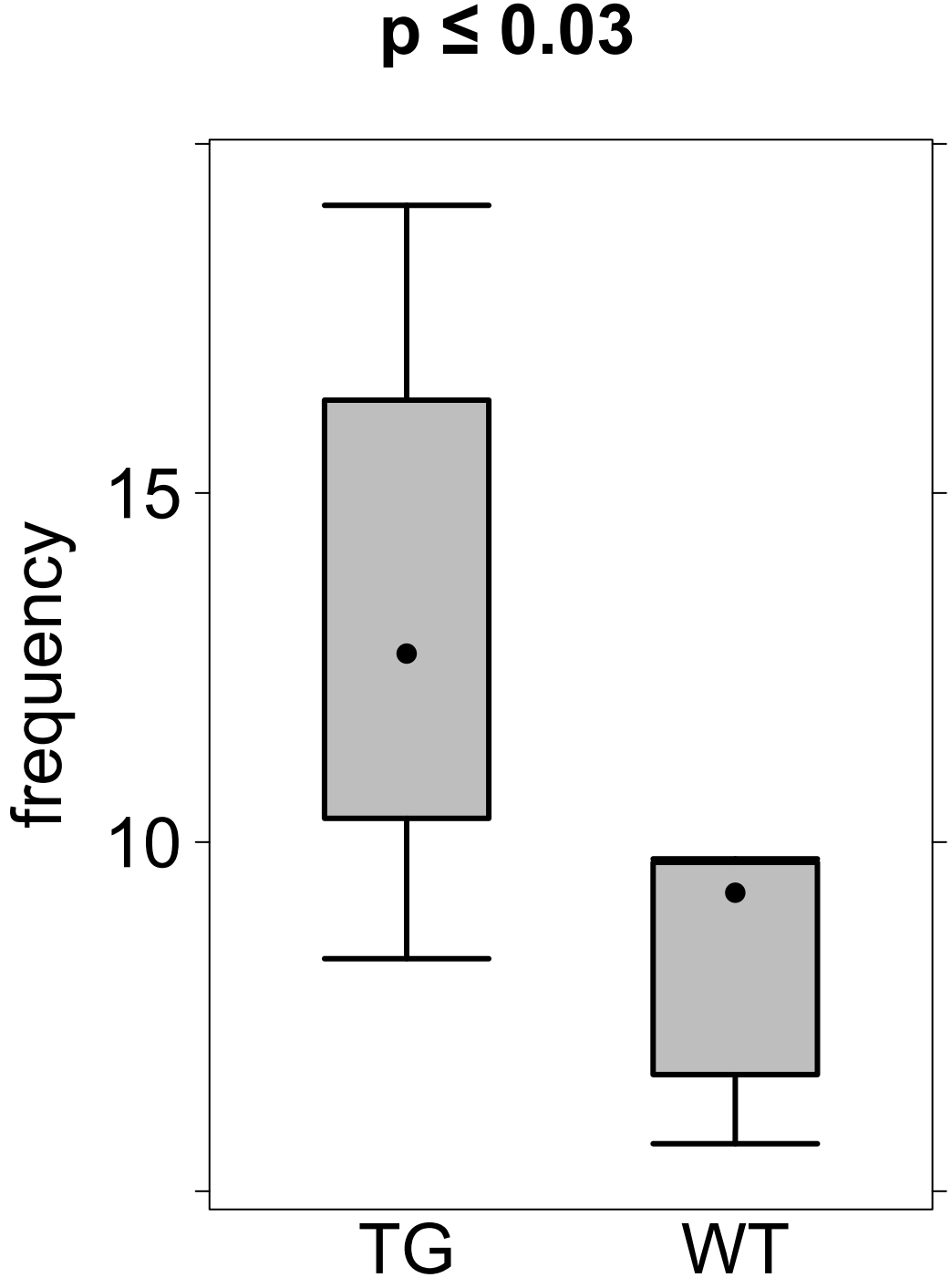




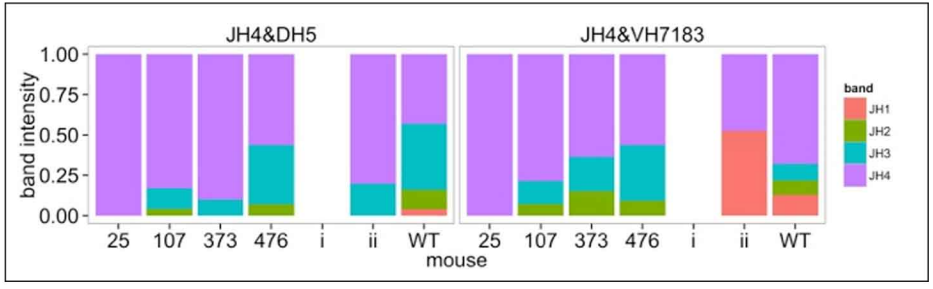


Supplementary Figure 5


WT
TG



Supplementary Figure 7



Supplementary Figure 8