Supplementary Methods

Mice. Congenic CD45.1 mice, NSG mice (NOD.Cg-Prkdc^{scid} Il2rgtm^{1Wjl}/SzJ, as well as mice carrying transgenic Vav-Cre (B6.Cg-Tg(Vav1-icre)A2Kio/J), CD4-Cre (B6.Cg-Tg(Cd4-cre)1Cwi/BfluJ), OT-II TCR (B6.Cg-Tg(TcraTcrb)425Cbn/J) and targeted mutations of *Tet2* (B6;129S-*Tet2*$^{tm1.1Iaai}$/J) as well as congenic recipients (B6.SJL-*Ptprc*^{a} *Pepc*^{b}/BoyJ) were all purchased from Jackson Laboratories. For adoptive transfer, 5x10^{6} bone marrow cells were intravenously injected into CD45.1/CD45.2 congenic mice following irradiation with 1100 cGy from a Cs-137 source. Adoptive transfer into NSG mice was performed by intravenous injection of tumor cells without conditioning irradiation. All animals were handled according to Institutional Animal Care and Use Committee-approved protocol #10-035.

Quantitative PCR. For genomic DNA analysis, mouse tail DNA was extracted following cell lysis and proteinase treatment, and quantitative PCR against the indicated loci using SYBR® green. For quantitative analysis of transcript abundance in CD4^{+} cells, superficial inguinal lymph nodes from tgRhoA mice were enriched for CD4^{+} cells using a CD4 T-cell isolation kit (Stem Cell Technologies #19842). RNA was isolated using an RNEasy® plus mini kit (Qiagen USA) per manufacturer's instructions. Total RNA was used to generate cDNA using first strand synthesis with SuperScript™ III (ThermoFisher) per manufacturer's instructions using oligo dT primers. Human and Murine specific primers and probes were generated against RhoA using custom probes and PrimeTime® Gene Expression Master Mix (Integrated DNA Technologies). Primer sequences available in supplementary table 2.

Immunoblotting. Whole thymocytes harvested and washed with PBS and were lysed in RIPA Buffer + EDTA (Tris HCl 50 mM pH 7.4, NaCl 150 mM, NP-40 1%, Sodium Deoxycholate 0.5%, SDS 0.1%, EDTA 5mM, Boston Bioproducts, Ashland, MA) in the presence of ThermoHalt™ Protease and Phosphotase inhibitor (ThermoFisher). Samples were sonicated using a Qsonica

sonicator at pulse 2s on 2s off, with amplitude 35% for 30 seconds. Lysates were quantified using the Pierce™ BCA Protein Assay Kit (ThermoFisher). Proteins were separated using NuPage 4-12% gels (Invitrogen) and transferred to 0.2 μM Nitrocellulose membranes (Biorad). Immunoblots were probed with the anti-RhoA 67B9 Rabbit monoclonal antibody and anti-βactin 13E5 Rabbit monoclonal antibody (Cell Signaling Technology).

TCR Activation assays. Mixed Leukocyte Reactions were performed using co-culture of CD45.1 congenic C57Bl/6 splenocytes with sorted naïve splenic $CD4^+$ OT-II tgRhoA G17V or WT OT-II cells and either 5 mg/ml $OVA_{323-339}$ peptide (AnaSpec, Fremont, CA) or 50 ng/ml Phorbol Myristate-Acetate and 1 mg/ml Ionomycin (PMA-Ionomycin, Sigma) in RPMI 1640 Glutamax (ThermoFisher) supplemented with 10% FBS and L-glutamine (ThermoFisher) for 48 hours. Reagents were used fresh from supplier. Naïve cells were isolated following pre-depletion of mouse splenocytes with a EasySep™ mouse CD4 T-cell Isolation kit (Stem Cell Technologies #19842) followed by FACS sorting $B220^-CD4^+CD62L^+CD44^-CD25^-$. To detect activation markers, FACS of cell cultures was performed, and the indicated percentage of CD69 or CD25 positive cells was determined from a $CD45.2^+CD4^+$ cells.

Intracellular FACS. Following harvest and RBC lysis, primary mouse splenocytes were incubated in RPMI media for 3 hours at 37°. Following this splenocytes from each mouse were stained for CD4, B220, CD44, and CD62L as above. Following this, 1/3 of cells were set aside to serve as unstimulated controls for each. The remainder of the cells were placed on ice for 10 minutes followed by the addition of 10 μg/ml anti-CD3 (145-2C11, Biolegend) and 5 μg/ml anti-CD28 (37.51, Biolegend) antibody. Cells were incubated on ice for 10 minutes and then 10 μg/ml anti-Armenian hamster IgG (Poly4055, Biolegend) antibody was added followed by separation of cells into two equal aliquots and incubation on ice for 10 minutes. Cells were then transferred to 37° with the reactions stopped at the specified timepoints by addition of IC fixation buffer (ThermoFisher) with incubation for 30 minutes followed by addition of ice-cold methanol.

For intracellular staining, methanol and fixation buffer were removed, and cells were blocked with 2% Rat serum followed by staining with the indicated FACS antibody. Naïve cells were identified as $CD4^+/B220^{-/}CD62L^+/CD44^-$ by FACS and fluorescence intensity of intracellular proteins was compared. For adoptive transfer of tumor cells in everolimus experiments, splenocytes were used following RBC lysis. Cells were analyzed on a BD LSRFortessa.

Histology. All mouse tissues investigated for histology were fixed in a phosphate buffered solution containing 10% formalin and embedded in paraffin. Bones were decalcified following formalin fixation using Kristenson's Decalcification Solution. Standard 4-micron paraffin embedded tissue sections were stained using the Ventana Benchmark XT platform (Ventana Medical Systems, Inc., Tucson, AZ) with extended heat-induced epitope retrieval (CC1 Buffer). Antibody clone names are available in supplementary methods table 3 below.

Immunofluorescence. Mouse kidneys from tgRhoA or control littermates were harvested at 30 weeks of age and were flash frozen in OCT media as previously described[1]. 5 μm acetone-fixed frozen sections from spleen or kidney were air-dried and stained with indicated antibodies for 30 min at room temperature in a moist chamber. For assessment of IgG deposition in the kidney, >7 sections stained with FITC-conjugated anti-mouse IgG Ab (ThermoFisher) were examined for each experimental condition, verified for reproducibility and quantified as positively-stained using ImageJ software. Images were obtained using an Olympus FV3000 confocal microscope and UPLSAPO 10x objective at final magnification 400x using laser wavelength of 405.

Transcriptomic Analysis. For non-malignant T-cell analysis, primary mouse splenocytes were dissociated through a 70 μM strainer and then incubated with RBC lysis buffer (Qiagen). Cells from identical genotypes were pooled and enriched for CD4 cells using an EasySep™ mouse CD4 T-cell isolation kit (Stem Cell Technologies #19842). Naïve T-cells ($B220^-CD4^+CD62L^+CD44^-CD25^-$), activated T-cells ($B220^-CD4^+CD62L^-CD44^+$) or T_{FH} cells ($B220^-/CD4^+/CXCR5^+/PD\text{-}1^+$) were directly sorted into RLT plus buffer from a Qiagen RNEasy® Micro

kit (Qiagen #74004) and whole RNA was isolated following manufacturer's instructions. T_{FH} cells were isolated 6 days after intraperitoneal immunization with NP-40Ova + Alum. For Tumor samples, viably frozen samples were stained and sorted for T_{FH} cells ($B220^{-}CD4^{+}CXCR5^{+}PD\text{-}1^{+}$) directly into RLT plus buffer and whole RNA was extracted as above. cDNA was synthesized Clontech SmartSeq® v4 reagents from of RNA. Full length cDNA was fragmented to a mean size of 150bp with a Covaris M220 ultrasonicator and Illumina libraries were prepared from 2ng of sheared cDNA using Rubicon Genomics ThruPLEX® DNAseq reagents according to manufacturer's protocol. The finished dsDNA libraries were quantified by Qubit® fluorometer, Agilent TapeStation 2200, and RT-qPCR using the Kapa Biosystems library quantification kit. Uniquely indexed libraries were pooled in equimolar ratios and sequenced on an Illumina NextSeq500 run with single-end 75bp reads at the Molecular Biology Core Facilities. Sequenced reads were aligned to the UCSC mm9 reference genome assembly and gene counts were quantified using STAR (v2.5.1b). Differential gene expression testing was performed by DESeq2 (v1.10.1), normalized read counts (RPKM) were calculated using cufflinks (v2.2.1) and genome-wide variant calling was performed using VarScan (v2.4.2). All analysis was performed using the VIPER snakemake pipeline (https://bitbucket.org/cfce/viper/).

Mutation Confirmation. To confirm SNVs identified by VarScan analysis of transcriptomic data, candidate mutations were targeted by primers as noted in Supplemental Methods Table 2, designed to provide approximately 400 bp amplicons. DNA was obtained from sorted tumor populations or from mouse tail DNA purified using a DNEasy Blood and Tissue kit (Qiagen). Initial DNA amplification was performed with 100 pg of genomic DNA per reaction using Takara DNA PrimeSTAR™ (Takara Bio, Inc) with initial denaturing at 95° for 3 minutes followed by 95° for 10s followed by annealing at 55° for 5 seconds for 40 cycles. This was followed by a 72° extension for 5 minutes. Amplicons were purified by extraction from TAE agarose gels using a Qiaguick® gel extraction kit (Qiagen) per manufacturer's instructions. Sanger sequencing

reactions were performed by Eton Bioscience (Boston, MA) using the forward primer from each amplicon pair.

Vγ1 Sequencing. DNA amplification was initially performed from 10 ng of genomic DNA from sorted tumor populations or from purified C57/Bl6 tail or thymus DNA purified using a DNEasy Blood and Tissue kit (Qiagen) per manufacturer's instructions. DNA amplification was performed as described[2]. Flanking reactions were performed using primers for all Vγ sequences and primers for J1,2, and 3 as well as a second primer for J4 using KOD xtreme Hot Start DNA polymerase (Millipore) with initial denaturing reaction 94° for 4 minutes followed by 94° 30s, 60° 30s, and 72° 45s for 35 cycles followed by a 4 minute 72° extension. A nested reaction followed using 1/200 of the flanking reaction and a Vγ1 specific primer as well as primers recognizing primers for J1,2, and 3 as well as a second primer for J4 again using KOD Xtreme™ Hot Start DNA Polymerase. Reaction conditions were the same as for the flanking reaction except 72° extension time was limited to 30s. PCR reaction products were resolved on a TBE 12% bis-acrylamide gel and visualized with ethidium bromide.

Serum Protein Electrophoresis. SPEP reactions were performed using a Helena Laboratories SPIFE® 3000 using the SPIFE® kit per manufacturer's instructions.

Supplementary Methods References

1. Kim HJ, Verbinnen B, Tang X, Lu L, Cantor H. Inhibition of follicular T-helper cells by CD8(+) regulatory T cells is essential for self tolerance. *Nature*. 2010;467(7313):328-332.
2. Pereira P, Boucontet L. Rates of recombination and chain pair biases greatly influence the primary gammadelta TCR repertoire in the thymus of adult mice. *J Immunol*. 2004;173(5):3261-3270.

Supplementary Methods Table 1: Tg(Cd4-RHOA^{G17V})DWsk transgene sequence. RHOA G17V transgene in Blue

GCGGCCGCTCTAGAATTTCGACTCTAGTTGGGGTTCAAATTTGAGCCCCAGCTGTTAGCCCTCTGCAAAGAAAA
AAAAAAAAAAAAAAGAACAAAGGGCCTAGATTTCCCTTCTGAGCCCCACCCTAAGATGAAGCCTCTTCTTTCAAG
GGAGTGGGGTTGGGGTGGAGGCGGATCCTGTCAGCTTTGCTCTCTCTGTGGCTGGCAGTTTCTCCAAAGGGTA
ACAGGTGTCAGCTGGCTGAGCCTAGGCTGAACCCTGAGACATGCTACCTCTGTCTTCTCATGGCTGGAGGCAGC
CTTTGTAAGTCACAGAAAGTAGCTGAGGGGCTCTGGAAAAAAGACAGCCAGGGTGGAGGTAGATTGGTCCTAGA
ACAGCCGACTTAGTGGATCTGTTGGGCAACGTAATCTAAATTTTCCATTGATTAAATTGCTAACTTTTTTTTTTAAA
ACATGGCATTACTGCATAGGCAGCCTAGTCTGGCCTTGAGCTTGTGATTTTTCTGCCTAAATCACCCAGTGCTGG
GGTTACAGTTACATGCCCGTGCCCGTGCCCGTGCCTGTAAGCCTTGCCTCACGTTGACCTAACCAGGCTGTTTC
AGCTTTTTACGGCACCAAACAATAGTGACATTCCAGACTCCAGCTTGATTCTGCTCAGGCATTTTCAGTGACTTTG
GCATTTTTAATTTTTCAACTTCCCCAACAACTGGGGGTGGGAGGGAGGGACTCCTGAGGGCTGGCTTACGTCCG
CCGTGCAGAGGAGCCTCACGACCAGGCTTCCTGTCTTTTCATTTACGAACATCTGTGAAGGCAAAGCAAGACTC
TCTTCTTCACTAGGTACCTGTTTGCAAAGTCTCGAGCCCTCATATACACACACCTGTGCAAGAAGCAGAGTGAAG
GAAGGACTGGCCAGAGGTAAGAGGGACGTGTTCAACTTTGTTCTTTCAAGGAGCTGGAAGGGGCAGCTAATGT
GCCGGAATGTTCTGGATGCAGTTCTCTGTTCTCAGTTGTGGCCTGGGGTTCTCCTGTATTCCTCTTAGAACGGGT
CATGAACAGTGATCTCCCACTGGAATCATGAGCTTCGAAAGGCTCAGCAGTAAGCCCTTCTCATCTTTGCCTGCC
CATGGCCCCAAGTATAGTTTAGTGCTCAGAGCAGTAGGTGCCCCCTTGAACCACCCCAGGAAGAATGCAAAGTC
AGAGGGGTAGAAAGGCAGCTGGGACATGGTGGGGTGTGGGGGCAATAGTGGGGAGTGGAAAGCTGGGGAGA
GAGAAAATACAGAAATAATTTAGCAGAGGACTGAAGATTAGAAAGAGGAAACTTTGAGAATGGAAGAGACACTAA
AACAAAACAACAACAACAAAAAGAAACAGAAAACACAAGAAAAACAGAGTGGACGATATGCAATTAAAAAAAAAA
AACTTTCTTAAAAGTCTTCACCAAGGATCATGCAATCAAGAACACTGCAGGCCACATGGTCCATTTTGGGCTCGC
TCAATTTCATTTGTGTTGACGTGAGCTGTTAAACTCTTGTTTTCTTCTGTGAAGTTTTAGGGTTTTGGCTTGTTGTG
TTTTGTTTCTGAGGTTTCACTGTGTTGCCTGGGCTGGTCTCAATATCCTGGGCCCAGATGATATTATTGCTTCAGC
TTCCCCAGTAGCTGGGACCAAGGCACATGCCACTCTGTCTGGGCTGATATTTAGGGTTTTTGAAATGTTCTAAGG
GGACTCTGTTTTAGTTACCCTGGGTTAGGAGTTGAGGAGGGGATTTTATCAGAAAATGTTAAAACTGGCCCCTTA
TCTATGAATTGCTGTAAAGGGACACTTTTTTTTTTAAAAGTAGACATGTTAGAATAATTAATTCTAAGAGAATTAGT
CTTGGCTACAGACCCCAGAGGGCTTGGTACAAAGCGGTCATAAGTCAGGACTCTATTTCTCAAGATGGGGTGAG
CTTCCCTGTCTCCACACCCTCAGACCTTTCTCCTTCCCCAGAGCCACATGGTCTTGAAGTTATGTTGTGCCCCTG
AGTGTCCTTCAGTTCATAGACTTGTTCCCAGACAGTGGTCTCCTGAGGTTCATTCTGACCCTTCAAAATAGAAAG
GTTCCGTTGAGGTAATTCAAAAACTCTTCTGAGTGGAATAGCGGAATATCCTGGTCTCGTAGGGAACTCTTTTTG
GAAGCAAGGCTGGGAGAACCCGATGAGGGAGGCCAGTGCTATTTAGTGTTCTGACCATTTCCGATGCTATCTTA
GATTCTCTAGGTTAATACAAAATGGCCGCCCTGAACCACTAAAGAAAGATCCTCCGAGGAGCCAGATACCTAGAA
CCAGTTTTCCCTTTCAATCCGAGGCCCTCACAGAAGAGGCCTGCCTCTATGTACAGAGTCTTCCCCACGGTCAA
CCAGTTCTAGGAAGAGGCTCCAAGTGGCCTTCGGTCTCACTCTTGACCGCAGTGGTTGGCACATTTTAGACACT
TAATAAACATTTGTTGGGTTAAATACCTTGGATGGAGATGGGAAAGGGGATGACGGAAGGGAGGATGTAGATGT
GTCTGTAGGGTGTGAATGTTCAGTGCTGCTTACAGCATTGTTTAGACCTTTCTTTCTGAGTCAAGAGAAGCAGGG
GTTACAGAGCTCCCACCCACTGCCACCCACCCGCTGCGTGTAGGCACCCGAGGCAAAGGAGAGGGTGGCAGA
GGTTGCAGCCACTGAACCACAAGGGTCGCTTAGAGGGTCACATCTCTAGGAAGTTTATACGAAGCTAGGCAACA
GAGGAAGGGTGTGTGGCGGGGGGCACATCCCACAACTGGGCTAGAGTGGGCTGACTGGGGGGCCATGAGGA
GAAGATGAAAACGCATTCGGGACCACAGGCTGTCACTGTGGTGGGGCTGCTGTGCTGGAACTGTGCCCTCCTC
TCCCATCTCTGGGGGCCATGTGAGGGTGGCAGGAACCCCAAGTACCTTAAAAGGTGTGTGGTGTGTACTGTCAC
TTGATAACATCCCTTGTGTGGTCCCTCTCTTTGTTCTTTTGGTGTTGAGTTCTCTGCATGTATCTTGCCTTCTAGA
GTCTCTTCATTCCTATGCCTCTCCTTCTGACATGTTCTTGTCATGTGTTGATGGATCCTGTGAAGGGTGGTTGTTG
CTTACTGACTTTTCTTTGTCCCTTTCTCTTTCGCTCCTGTCTTCCCTTGAGGCTTCTGTGGTTGGTTTGTTGTTGTT
GTTGTTTGTTTGTTTGTTTGTTTTTTTCCAGAAAACATGTCCCCTCTCCCTCAACTCTGCAGCCAATTCCTCTCACA
TCCACCCTTCCGGTCCAGCCTATACTCCACAGCTTCCTGTCAGATCAAAGCTCCTGGAAGACCTACCAGAAGCC
AGGCTACTTGTTTACAGGGTAGAAGGAACCAGAGATCTTGGTGGCATCTGAGGAGAGGAAAGGGGAGAAAGAG
GAGATAGGGGGCACTCCAAGGGGAAGAGAACACTAAAGGCTGCAGCTCAGAGGAAGACATCCAAGGAGCTGAA
GGCCAAAGCACAAGCATGGAAAAATAGATTGAGAAATGCAGACATGAGCAGAGACGGGGGAGGGGGACATTGC
AGCCAGTCAGCTCTTGCATCCTTTCCCAGGGGTGACGTACACAGGATGCTGCGCTTACTCTTTATGAGATATAGC
GCCTCTGGGGAGGCTGAGGATGTGGGAATCAAAGGCCAGGTCTCTGGGGTAGCAGCGGAAACCTGAAGCACC
AATGCAGGCTGTGGCTGGAAACCCACAGCCTCCTCCACTGAGCCAATTCCCAGCGTGCGTTGGTGTGGGGCCA

GGAGCTGGAGACAGACTCCAAGGTTGTACAGTGAGGGAGAGAAAGTGCCTACCCTCTGGGGAAGAGCCAGGAA
TGCCCTCGTTCCTCCAGCATCTTTATCAGAGCTACGTGAATTTAGATCCCAAGGAGGAAGAGCCCAATAGAGACT
TGGTTTCTCTGTTAACTTCTACTCACCAGGGACTGACACACCCGCTCATCAAGGTTTTCCATCTAGGGTAGGGAC
AGCAGGAAACCTTCTTGGGCCTAGGCTGCTCCTTCAACTCTTATCACCCCACACCCTTCCCTTAAATGCTTTGCA
GGCCCTGGCCCAAGTCAACTGTGCCAACTTGTAATCTCCTCTGTGACTATAATGACTAGTCTCAGGCCTGCCTTC
CCCAGAAACCTCTCTTTTGGCTATTTCTCTTTCTAGTTCTCTGTTTAAACAAAATTTATTCTATATATCTATCTATCT
GTCTATCTATCTATCTATCTATCTATCTATCTATCTATCTATCTATCATCTACTTATCATCTGTCTAGCCATTTGAAG
CATCTTTGTGTTTTAGGTCCTGTTAGATTCTCCTTTCAGCCAGTGGAGGATCTGGACAGAGCTATTTCTTAGCTTC
CCCTAAGCCATGTTGTTAGAACGAATCCCCCACACCTCCTCTGAGTGCTACGTCTCCGTCAAGAATTATGTATGT
GGGATCCAGATGGCCCAGTGGATAAAACTGCAAGTGTCATGACCATGACCTGACTTCAAGGGATTGTGTAGAAA
GGGAGTTATCACAGTGTGAGGGACAGGGCTAAGGACACTAACCCGTATGTTGAGGGGCACAGACGCTAGCAAC
AACAGTGAAGTGTTTAAAAAGGCAAAAATCATGTTTCTAGAAGTCAGGAAGAGCCTAACTTGTGGACAAGGACCA
ACAGGCAGCAGTTGTAATGGGGCAGGGCAGAGGGAGAGCGGACACGCAGCTTTTGGCATCAAACACACCCAGA
GTGTGGATAGAGAGTAGGGAAATACTCTAGTCTCTGGCTAGGATACTCCCCTCTCTTTTTGACATTTCTCATTGG
CAGCCCCAAGTGGTCACTGGAGAGCCAGGAAGCCTAAAGGACACAGTTAGTAGCAGCCAGCTCCTTTGGTGGA
ATTTTGGGGACATGGTGGGGTGACTTGGCTCTATCCAGGCCAGGGCTGGGTGTGAGTATACACTTAGTGACTGG
CCTTCCTTCTCAGGTTCCCTCCTTCTCCCTCGCCCTTCTTTCCTTGAAGCTACATTTTTGTAATACTGAGGATAAG
ACCCAGGGCATGCAAAGCAGACCCTGTACCCCTGAGCTATGTCCTCGGCCTTCAGTGACCCATTTAAGGAACAG
AATCCAGGTACTGCGTATAGGAAGATGCACCAATGAGGTATTTGCCTCTGTTCATCCTATTTGGCTTAAATTAAAC
AGGGATATTATCCACTTCCACTGGTGCCAGCCTCGTGGTGGCTTAAGGCAGCTTGAGACTGTCATCTCTGTCCTT
GTAGAGTTCACGCTAGCGGGGAAGGGATTATGTGAATCACTCTCGGTTAAGGTGGCAGAGGCGACATGGCCAA
GAGAGCATCAAGAGAGAACTGATTGAGTTCAGAAAGGGCAGATTGCTACAGAGCAACACAGCAGGGGTTATTCA
AGGGGACAGAAAAATCAGGCTTGGGATAAAGAATAATAATTAACTCTTCGTGAATATCTTGCCTCACCAGCTCTG
GACCAGATTCCCTGTTGAGACTCACCCTTAATAGTCACTTCCCTGAGCCCCACTTAGAGCCTGGGCCGCTGGGT
TGCATTGCCTTCGTGCATGTGCGCATGCCCGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTATGT
GTGTGTGTGTATGCGTGTGTAAATAACAGTGATTTCACTCATCACCAGAACCAATCTCAACTCTTCTAGCTTGCCT
GTTAGGATTTATTGCCAGCCCCCAAATATGTTCCTATATATAGCCCCCTGTGCTGTGTTAGTTCTTAGCACTTCTA
GCACACCCCGAAGGACTGAGAACGGTCCTCTGAGGATGGCCTTGAACTCCCGATTTCCTGCCTCTTTCTACCTT
CTGTGCAGGGATTATCAGTATACACCACCACAGCTCGGACCACTCCATGGCCGGTGCTCCTGAACCCATGGCCT
CACACACACTAGGCAGATACTTACTAACCGAGCCACAGTCCCAAATGCTGCTTTTAATTTTTTTGGAAATTTTATA
TTAAAGCATTCCCATCCTTGCCACAGACGCAGAGTGGTGGATATAGCACTTGTCTAGTGTGTATGGCCCTGAGTT
CCATCTCAACAGAAAGTTTTATCAAAAATGAATATACCCGGCTGGTGACACCTTACCTTATCTGGTAAAGGTGTCT
GCTGCCAAGCCAAACCATCCCATTAGATCCCTAAGCCCCAAAATGGTGGAAGGAGAGAACTGACTCCCACAAGT
TGTCTTCCAACCTCCACGAAAGTGTAACATTTGATAACCAAATACACAAATAATTAGATTTATAGATAAGTAAATGA
ATAAGTAAATAAGATGAAAAAAATTAATGAATAACAAGCTCTGCACTCGCCACTTCAGTAAGAGACGTGTTTTGCT
TTCAGTTTGATGTTTTTCTCTTTCTTTCTTGAACATTTTATTTTTAGACAATTTTGTATATCTGTAAATACATTCTGAC
TATTCAGCTCCCACCATCTTCTCTTTCTCCCGAGTTGTCAACCCTCCCCTTCCCTGCAAACCTTGCTTCCCCTTTT
ATGTCTTTTTTGGTTTTGTTCTTTCATGACCCATCCAGTTTAACTAGGGCAGCCCCAGTGCATGGGTACAGAGCG
ATTCAGGGCATGGGTACAGAGCGATCCAGGGCACGGGCAAGACACCAGTGGCTACGCCGCTGAATACCATGAC
TGTTCTTCTTCTAGCCACTGCCCGCTGTCTGCTGCCCACTGCCCGCTGCCCATAGTTGCTCGGGGAGAGGCGG
GGCTGTGGCCTCCTGAGCTCCTGCCCATCCATGACTGGGCGCGGGGTCAGTGGTTTAAGGTTGGCAGGGGCCA
CAGCTTTCATTTGCCTTGCTTTTGGCCAGCAAGCAAGAGATGCATCAACACAAAAACAAAGAGCCAGGGGTCCA
GTTCAGTGATAGAACGCTTGCCCGGCAGGCACACACGGGGGTTGTGTCTCTGGCACCATGAAATGAATAGACAA
GCCAACTACGCAGCCTTGGTGCAAGGTCCACCCGTAAACCTAACATAGTAACTATTTGAAAATTACAGTTATCAG
GGTTAGGAGTGTGGTTCAGTAGTAGAAGAACACATATCTGATGCATGGGAATTTCTAGGTTATAGGCCCACTACT
GGGGGAAAACAAACAAAAAAATTACAATATCAGTAAAGGTGATATGATTTATAGGTGAAATAAAGCTATCTGGAAA
TGGTTTACTACAGTTTCTGAACTTGGACCTAAATGTGTGTGTGTATACATATAATTTTTATTTACATAAAATGTTGT
CAGTCTATGCTTATACTTTACTTTTTGTTTATTTATTTATGTGTATGGATGTTTTGTCTCCATGTGGGTCTGTGTGT
CACATGCATACCCTGGGACTAAGTTCCATACAGGCCACCAGTAAGTGCTAAGTATTGAACCCAGATCCCCGGGA
AGAGCAGCCAGTGCTCTTAAGGGCTGAGCCGTTGTTTCAGCCCCTGTTTCTACGTCTAACCAGAACAGACATCT
CAAGTAACAAGAGATGTTTCTCTATATGGAGTCTAATGGTTTCTTTTATGAACTACTTGTCCAAAGCTTCAAATAAT
TAACAAAACAACAAAACCCTTTCATAATATTGTCTCTTACAACTAGATTTGAGTGTATGTGAGTATGTATGTTTGAG
ATAGCATATTTGTGTGTGAGTACATATGTCCAGTTAGCATGTTTGTGTGTGTGTCCATGCCAGCTTTTTGGGTGTG
TGTTTGTATCCATGCCAACTTGCTCCAGAGATCATTTGCATAGTAAACACTTTATCTTCTGACCATCTCTCCAGTT

CAAAATTAGGTATTTCTTAAGCAAAGGCAGCAGTCTCTCTCTCTCTCTTGGCTTTGTTGTTTGTTTGTTTGATTGAT
TGATTTTTTTGTTGTAGAACTTATGTAGAATAGGCTGACCTTGAGCATAGAGATCTACCTGGTTTTGCCTTCTGAG
TGCTGGGATTAAAGATGTATGCCACCCAAGAAGACAGGAGTAGGTGGGAGAGCACCCTCATAGAGGCAGTAGG
AGGAGATGGAGTAGGGGGTTTCTGAAGGGGAGACCTGGAAAGGGGAAAACATTTGAAACATAAACAATGAGAAT
AGCCAATAAAAAATAAAAAGAAACAGTATATGTATTTATAAAGAACACATTAGTGTGTATATATATACATGTATAAG
CATGTTAAATTTGTGTGTGTTTGTAAATCTACACATATATGTTCCATGAATATAATACTCTGCTGATAAACATTTAAT
GGTTGCCTCTCTAAAGCAAAACAAACAAAACACCCGATGGTCAATATTTGGCAACTTCCATGGTGTGAAGATTCC
TGCTGAGGCTGCTTTACCAGGACCCCTCCTGGTGACATCACTCACTGTAGAGCTGGGGAGAAAACTGCATAATC
AATTCTTGCCAATCACTGTGGAATGCTGCCAGTGCAGTGACAGATAACATACCTCCCCCAAAAGATGTGTGCCAC
CACCACCTGGCTATAATTTTATTAAAAGGCAAGTGGGTCCTTCTCCCCATACTTGAGATAGGGTCTTGTATAACCC
AGGTTAGCCTTGAGCTTACTATATAGCTGAGGCTGGCCTTGAACTGGGTGTTTGCCTGCATGTATGTACGCGTAC
CATGTGATTGGAGCCTGCTGAGGTCAGAAGAGGACACTGGATCCACAGTAATGGAATTACAGACATACCCATGT
AGGATCTCGGAATCGAACCTGGGACCTCCACAGGAGGAACAAGTGCTCACAACCCTTTAGTTTTATTTTTGAGAT
AGGGTTTCACAGTACAGTCCTTGCTGGCTTTGGACTCATGGTCCTCCTGCCTTGGCCTCCTAGCTACTAAGAGTG
TACACATATGCCTCTGTGCCAGGGTCGGAGACAATAACGGTGCACGTGAGGACCTAAAACCGTAGTTTGTCTTT
GACACCCAGGAATATACTTATTTCTGGGTCTCTGTCATGCACTGCTGCTATTGCTCAGGATGTTTAAATTGCTCTT
CAGCTACTGACATCACAGTCTTAGTTTGGCAGGACCTTTGGGGTGCATTACTGCAGGGTGCCCACTTTTGTGTAT
GCAGATAATGTTCTCTGGGTTGGTTATCAAGGTCCTGAGGAAGAGAAAGAGTTCTTGTGTGCCCCAGGCCCAAG
GAATACCTGAAGACTGATGATTTCTATCTTCCTCCGCCCCTGACATTTTTGTAGGCTCAGATTCCCAACCAACAAG
AGCTCAAGGAGTCGACGCAATGGCTGCCATCCGGAAGAAACTGGTGATTGTTGGTGATGGAGCCTGTGTAAAGA
CATGCTTGCTCATAGTCTTCAGCAAGGACCAGTTCCCAGAGGTGTATGTGCCCACAGTGTTTGAGAACTATGTGG
CAGATATCGAGGTGGATGGAAAGCAGGTAGAATTGGCTTTGTGGGACACAGCTGGGCAGGAAGATTATGATCG
CCTGAGGCCCCTCTCCTACCCAGATACCGATGTTATACTGATGTGTTTTTCCATCGACAGCCCTGATAGTTTAGA
AAACATCCCAGAAAAGTGGACCCCAGAAGTCAAGCATTTCTGTCCCAACGTGCCCATCATCCTGGTTGGGAATA
AGAAGGATCTTCGGAATGATGAGCACACAAGGCGGGAGCTAGCCAAGATGAAGCAGGAGCCGGTGAAACCTGA
AGAAGGCAGAGATATGGCAAACAGGATTGGCGCTTTTGGGTACATGGAGTGTTCAGCAAAGACCAAAGATGGAG
TGAGAGAGGTTTTTGAAATGGCTACGAGAGCTGCTCTGCAAGCTAGACGTGGGAAGAAAAAATCTGGGTGCCTT
GTCTTGTGAGTCGACGATTCCATGGATCATAATCAGCCATACCACATTTGTAGAGGTTTTACTTGCTTTAAAAAAC
CTCCCACACCTCCCCCTGAACCTGAAACATAAAATGAATGCAATTGTTGTTGTTAACTTGTTTATTGCAGCTTATA
ATGGTTACAAATAAAGCAATAGCATCACAAATTTCACAAATAAAGCATTTTTTTCACTGCATTCTAGTTGTGGTTTG
TCCAAACTCATCAATGTATCTTATCATGTCTGGATCCTCACATCCCAATCCGCGGCTCGACCAGCGGCC

Supplementary Methods Table 2	
Genomic quantitative PCR sequences	
mRhoA Genomic F	TCTTCAGACACACCAGCAGA
mRhoA Genomic R	CAACACACAATGGCACCGA
mTet2 genomic F	AAGAATTGCTACAGGCCTGC
mTet2 genomic R	TTCTTTAGCCCTTGCTGAGC
RHOA transgene F	CAGATATCGAGGTGGATGGAA
RHOA transgene R	GTTGGGACAGAAATGCTTGAC
Transcript quantitative PCR sequences	
Mouse RhoA Probe Sequence	TGGCCACGAGAGCTGCTCTGCAAGCT
Mouse RhoA F	GGCAAACAGGATTGGCGCTT
Mouse RhoA R	TCACAAGATGAGGCACCCAGAC
Human RHOA Probe Sequence	CCTGCCCAGCTGTGTCCCACAAAGCCA
Human RHOA F	GGACCAGTTCCCAGAGGTGT
Human RHOA R	GGGCCTCAGGCGATCATAATCTT
Mutation Analysis Primers	
mMaz F	CGACGTCTACCACCTGAACC
mMaz R	AGCCCTCAAACCAAGATTCC
mEomes F	ACACCTTCGGGAGCACCT
mEomes R	ACCCTGGCCGTAGGGATA
mCDC42 F	CGACCGCTAAGTTATCCACA
mCDC42 R	GCCCTCCTTACCTGTGTGAG

Supplementary Methods Table 3		
Flow Cytometry Antibodies:		
Antigen	**Clone**	**Vendor**
B220	RA3-6B2	BioLegend
CD3e	145-2c11	BioLegend
CD4	GK1.5	BioLegend
CD8	53-6.7	eBioscience
CD11b	M1/70	BioLegend
CD25	PC61.5	eBioscience
CD44	IM7	eBioscience
CD45.1	A20	BioLegend
CD45.2	104	BioLegend
CD62L	MEL-14	eBioscience
CD69	H1.2F3	eBioscience
CXCR5	SPRCL5	eBioscience
FoxP3	FJK-16s	eBioscience
ICOS	7E.17G9	eBioscience
Isotype Rat IgG 2a	RTK2758	BioLegend
Ly6G	Ly6G	eBioscience
PD-1 (CD279)	J43	eBioscience
RORgt	AFKJS-9	eBioscience
TCR beta	H57-597	eBioscience
Bcl6	K112-91	BD Biosciences
Phospho S6	Cupk43k	eBioscience
Phospho 4EBP1	V3NTY24	eBioscience
Phospho Akt	SDRNR	eBioscience
Immunohistochemistry Antibodies:		
Antigen	**Clone**	**Vendor**
Bcl6	D65C10	Cell Signaling Technologies
B220	RA3-6B2	BD Bioscience
CD3	SP7	Abcam
CD4	4SM95	eBioscience
MPO	polyclonal	Dako
Immunofluorescence Antibodies		
Antigen	**Clone**	**Vendor**
Mouse IgG	polyclonal	ThermoFisher (cat. A11001)

Supplementary Figure Legends

Supplementary Figure 1. TgRhoA G17V abrogates T-cell development in the Double Positive Stage. A. FACS analysis of CD69 and TCRβ in tgRhoA and WT littermate thymuses. Corresponding CD4 and CD8 profile of numbered populations as labeled. **B**. Differential counts of each population from individual thymuses, $CD69^{-}TCR\beta^{-}$ (p=0.3649), $CD69^{+}TCR\beta^{lo}$ (p=0.2828), $CD69^{+}TCR\beta^{hi}$ (p=0.0011), or $CD69^{-}/TCR\beta^{hi}$ (p=0.0021) and frequency of PD-1 expressing cells (p=0.6259, p=0.3276. p<0.0001, p<0.0001) respectively. p values from t-test with Welch's correction.

Supplementary Figure 2. **Flow cytometric evaluation of tgRhoA tail-skin hematopoietic cells.** A. Flow cytometric plots and percentage of $CD45^{+}$ (**A**) $CD4^{+}TCR\beta^{+}$ (p=0.0031) and (**B**) $CD11b^{+}Ly6G^{+}$ (p=0.0147) cells recovered from tail skin in WT or tgRhoA littermates. **C.** Mean Fluorescence Intensity (MFI) of RORγt (red) in tgRhoA $CD4^{+}$ cells compared to isotype control (black) (p=0.0076). p values from t-test with Welch's correction.

Supplementary Figure 3. Fibrotic tail and ear phenotypes from adoptive transfer of tgRhoA Bone Marrow. Gross images of WT and tgRhoA mice, and immunohistochemical characterization of tgRhoA tail tips using indicated stains. Scale bars represent 50 μM. Images taken 100x.

Supplementary Figure 4. Follicular regulatory T cells in tgRhoA mice. **A**. FACS of splenic CD4, CD3, CXCR5, PD-1 and Foxp3 as indicated. Cells were fixed and permeabilized after surface stains. **B.** Percentage (p=0.0065) and absolute counts (p=0.5970) of tgRhoA or WT T_{FR} cells. p values from t-test with Welch's correction.

Supplementary Figure 5. **T_{FH} compartments from lymph nodes of tgRhoA mice**. **A.** Lymph Node $CD4^+$ cell expression of CXCR5 and PD-1 in CD4 cells from 10-week old WT versus tgRhoA littermates. **B.** ICOS expression in $CD4^+CXCR5^+PD\text{-}1^+$ from WT and tgRhoA littermates. Naïve CD4 T cells in both plots are from WT splenocytes. **C.** Percent of $CD4^+$ cells that are $CXCR5^+PD\text{-}1^+$ (p=0.0061). **D.** ICOS MFI among $CD4^+CXCR5^+PD\text{-}1^+$ from both genotypes (p=0.0129). **E.-H.** The same approaches in **A.-D.** applied to 30-week old mice. p=0.0040 for (**G**)**.** p=0.0054 for (**H**).

Supplementary Figure 6. Analysis of mouse plasma does not reveal immunoglobulin clonality. **A**. Primary serum protein electrophoresis readouts from plasma of 30-week old mouse cohort examined in Figure 3 and Supplementary Figure 5. Note that gamma peak of WT sample third from left and tgRhoA sample second from left are affected by an artifact visible in the bottom-right and top-right portions of the gels (black arrowheads) respectively. **B**. Gamma globulin percentage of each plasma sample.

Supplementary Figure 7. Tail inflammation and fibrosis associated with tgRhoA cells is maintained on a *Tet2*-deleted background. A. Tails from *Tet2*$^{fl/fl}$; Vav-Cre^+ sacrificed at 12-14 months of age. **B.** Tails from tgRhoA; *Tet2*$^{fl/fl}$; Vav-Cre^+ mice sacrificed at 6-12 months of age. Scale bars represent 1 cm.

Supplementary Figure 8. Tet2-deficient T_{FH} cells do not enrich for mTORc1 signatures. GSEA Hallmark analysis for *Tet2*$^{fl/fl}$; Vav-Cre^+ T_{FH} cells compared to WT T_{FH} cells. Top 10 enriched gene sets by normalized enrichment score shown.

Supplementary Figure 9. tgRhoA naïve T-cells show increased mTORc1 signaling. Quantification of MFI of WT (red) or tgRhoA (blue) naïve splenic CD4 T cells following 5 minutes (**A**) or 30 minutes (**B**) of CD3 and CD28 activation. All p values calculated using unpaired t-test.

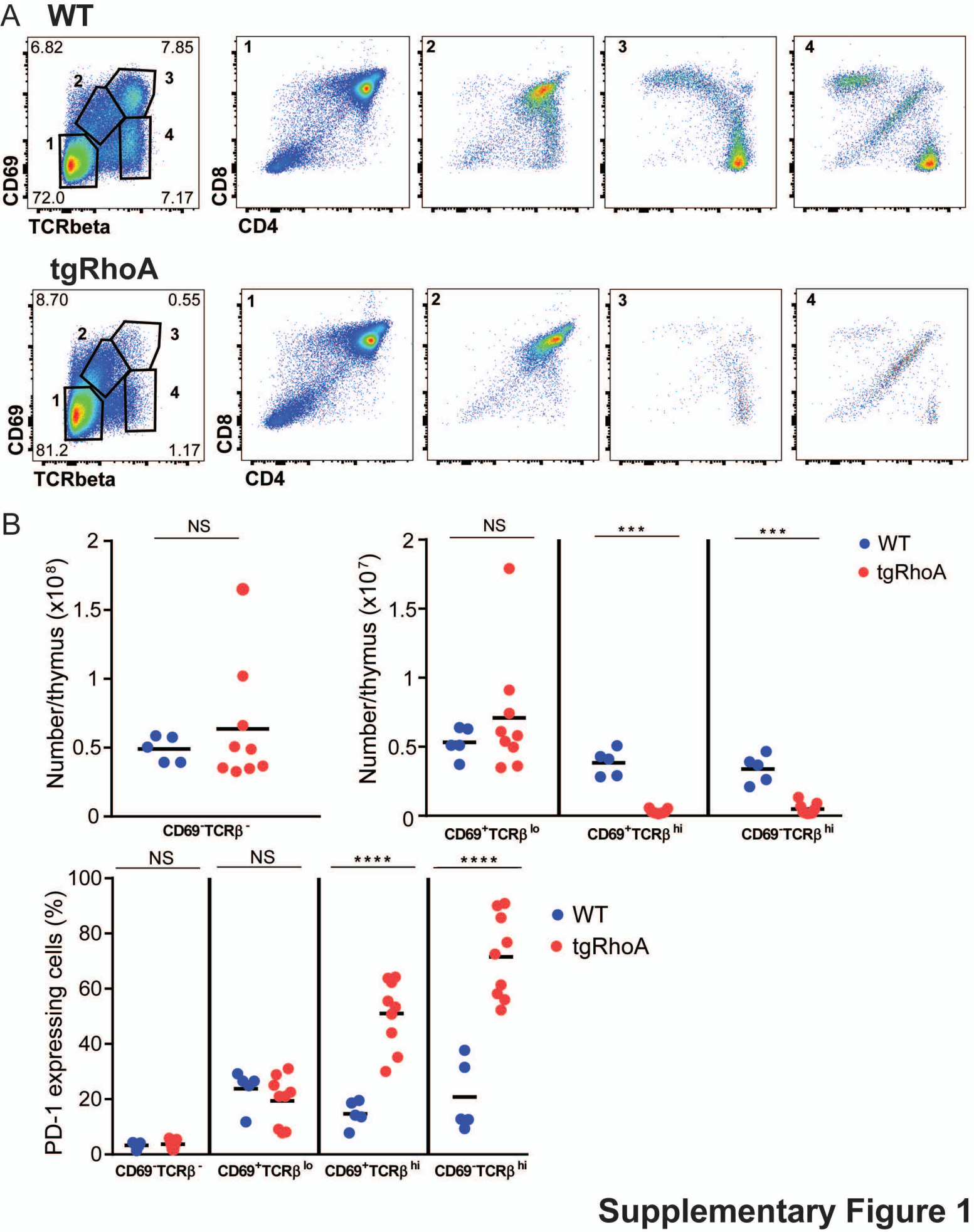
Supplementary Figure 10. **Features of tgRhoA; Vav-Cre^{+}; *Tet2*$^{fl/fl}$; OT-II tumors**.

A. Lymph node histology of four tgRhoA; *Tet2*$^{fl/fl}$; Vav-Cre^{+}; OT-II tumors with stains as indicated. Time of mouse death Tumor 1 = 231d, Tumor 2 = 270d, Tumor 3 = 195d. Tumor 4 = 197d. Scale bar represents 100 μM. Images taken at 100x and 400x (H&E, all IHC). Black arrows on 400x H&E mark High Endothelial Venules (HEVs). **B**. Double stain for CD4 (brown) and Bcl6 (red) from tumor samples as indicated. Black arrows indicate double-stained cells. Scale bar represents 100 μM. Images taken at 1000x. **C**. Sanger sequencing from spleens of primary tumor cells showing detected SNVs compared to C57Bl/6 WT mice. Each mutation is linked to the same tumor as is labeled in section **B**. RNAseq was not performed on tumor 4, so no mutational analysis is available. Additional sanger sequencing from a second passage of Tumor 1 is also shown. **D**. PCR products of Vγ1 rearrangements from Tumors 1-3, DNA isolated from mouse tail (genomic control), and DNA from WT thymus.

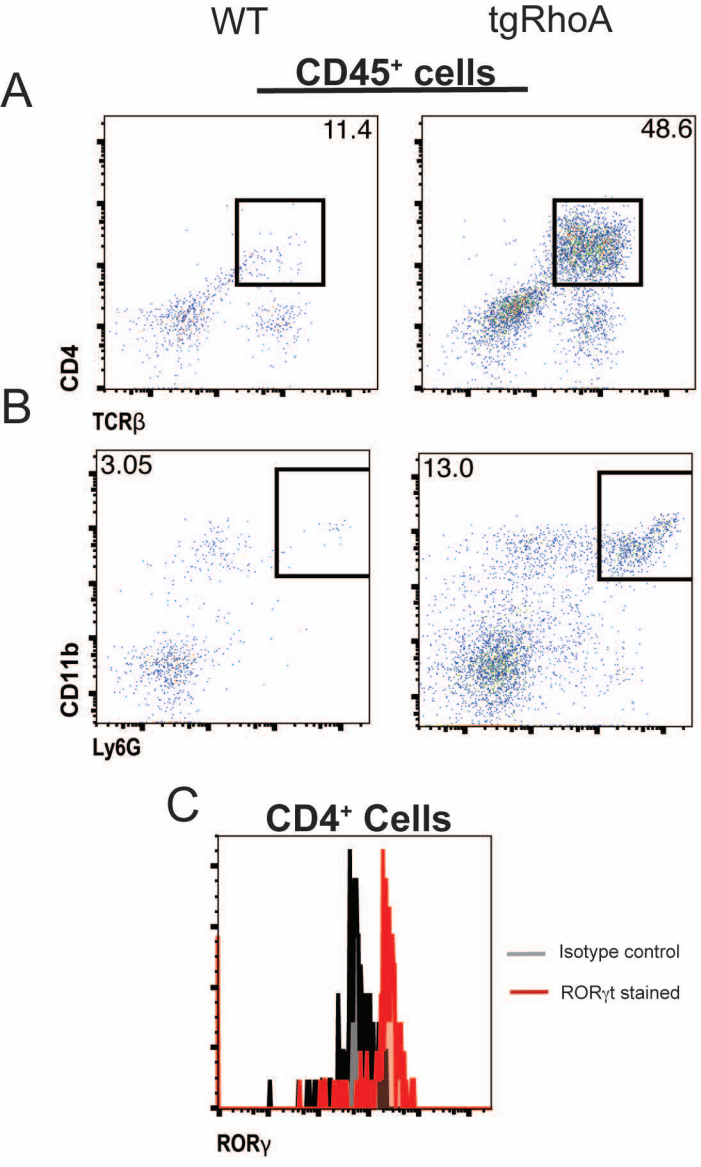
Supplementary Figure 11. Spontaneous T-cell tumors from tgRhoA; *Tet2*$^{fl/fl}$; CD4-Cre^{+} mice. Staining of enlarged mesenteric lymph node (LN) by H&E (**A**) and immunohistochemistry markers as indicated (**B**). Scale bar is 20 μM. The mouse was not injected with NP40-Ovalbumin and died at 380 days after birth. **C**. Flow cytometry of the lymph node and spleen with indicated markers. **D**. Flow cytometry of a spleen from a second mouse of the same genotype with enlarged mesenteric lymph node with the indicated markers that died at 694 days.

Supplementary Figure 12. **Gene expression analysis of tgRhoA and *Tet2*-deleted tumor populations reveals activation of the mTORc1 pathway**. **A**. Principal component analysis of technical replicates of tgRhoA; *Tet2f*$^{l/fl}$; Vav-Cre^{+}; OT-II tumors (Tumor 1, Tumor 2, Tumor 3) or a spontaneous T-cell tumor from a tgRhoA; *Tet2*$^{fl/fl}$; CD4-Cre^{+} tumor from a mouse that died at 380 days sorted for CD4^{+}CXCR5^{+}PD-1^{+}B220^{-} cells compared with untransformed *Tet2*$^{fl/fl}$; Vav-Cre^{+} CD4^{+}CXCR5^{+}PD-1^{+}B220^{-} cells 5 days after immunization with NP40-Ova/Alum. GSEA Hallmark analysis for Tumor 1 (**B**), Tumor 2 (**C**) based on differential gene expression analysis compared with *Tet2*$^{fl/fl}$; Vav-Cre^{+} CD4^{+}CXCR5^{+}PD-1^{+}B220^{-} cells.

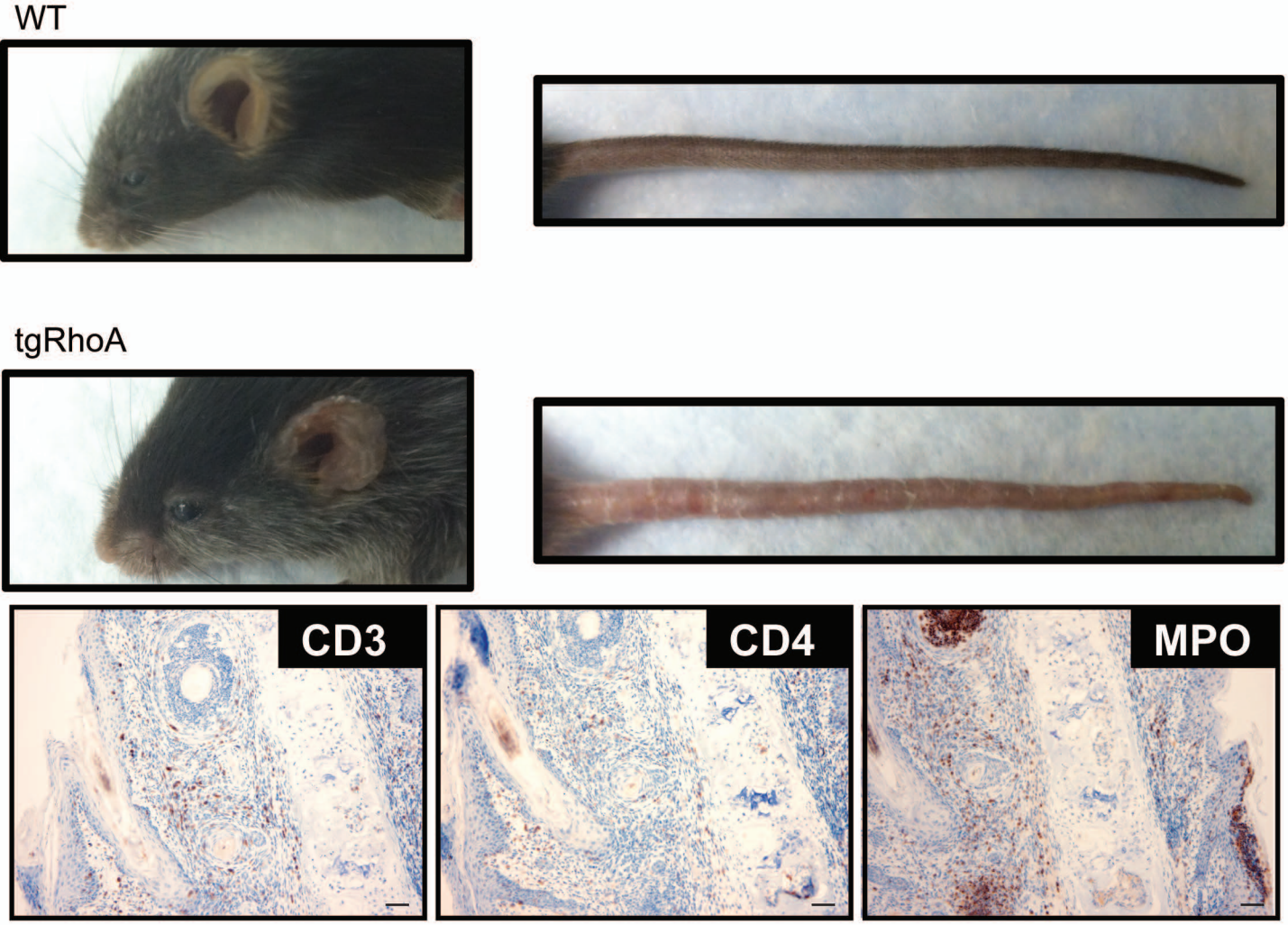
Supplementary Figure 13. Molecular features of tgRhoA; *Tet2*$^{fl/fl}$; Vav-Cre^{+}; OT-II tumors. **A**. GSEA enrichment plots of T_{FH} signatures enriched in tgRhoA; *Tet2*$^{fl/fl}$; Vav-Cre^{+}; OT-II tumors. **B.** FACS of CD4^{+} Tumor 1 cells for Bcl6 (blue) or isotype control (black). **C.** FACS of ICOS in CD4^{+} Tumor 1 cells (blue) compared to unstained Tumor 1 CD4^{+} cells (black). **D.** Foxp3 in CD4^{+} Tumor 1 cells (blue) compared to splenic CD4^{+}/Foxp3^{+} cells (red) isotype control. CD4^{+} tumor cells stained by isotype control in black. All histograms display frequency of events as percentage of cells within the population indicated.



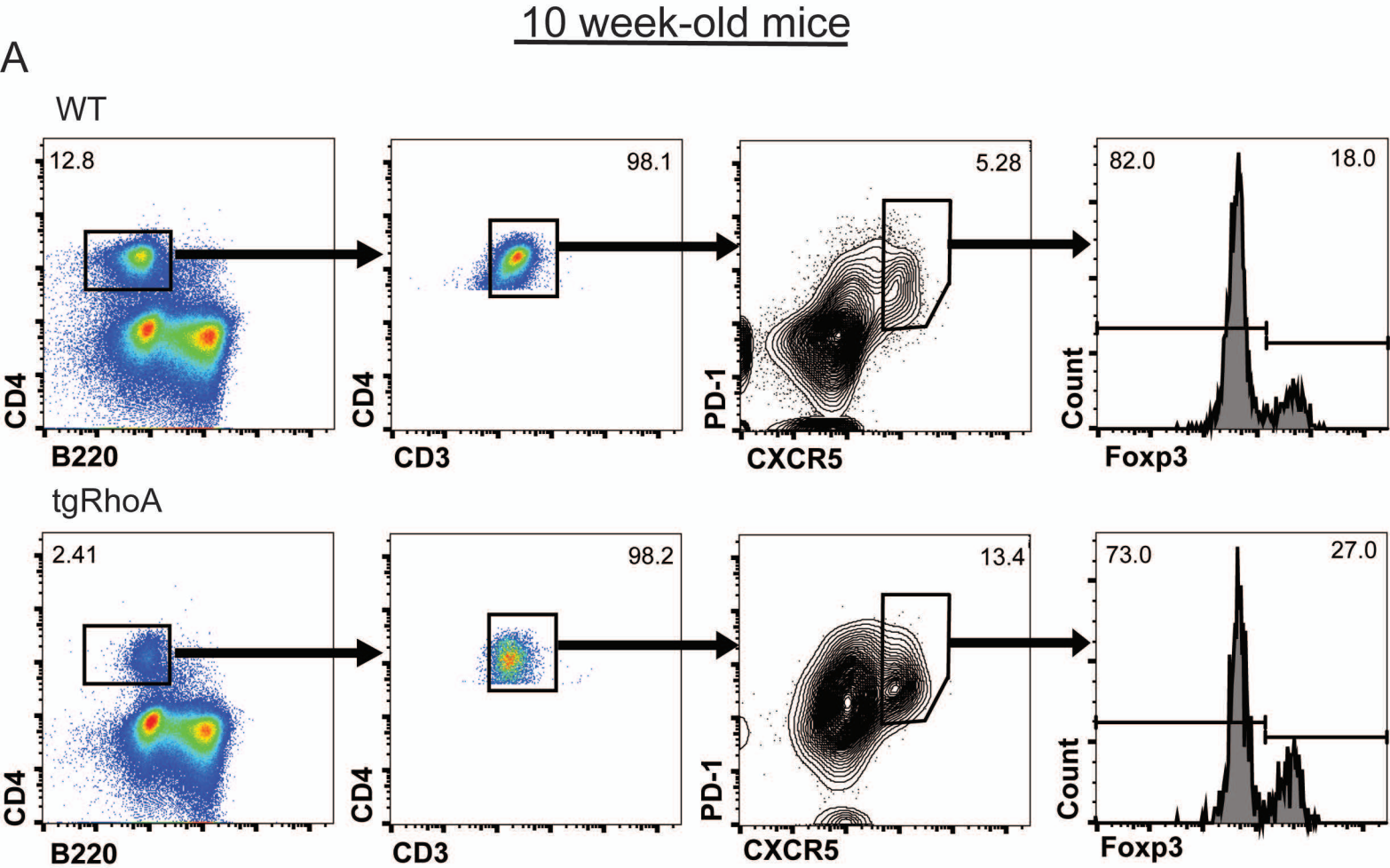
Supplementary Figure 1

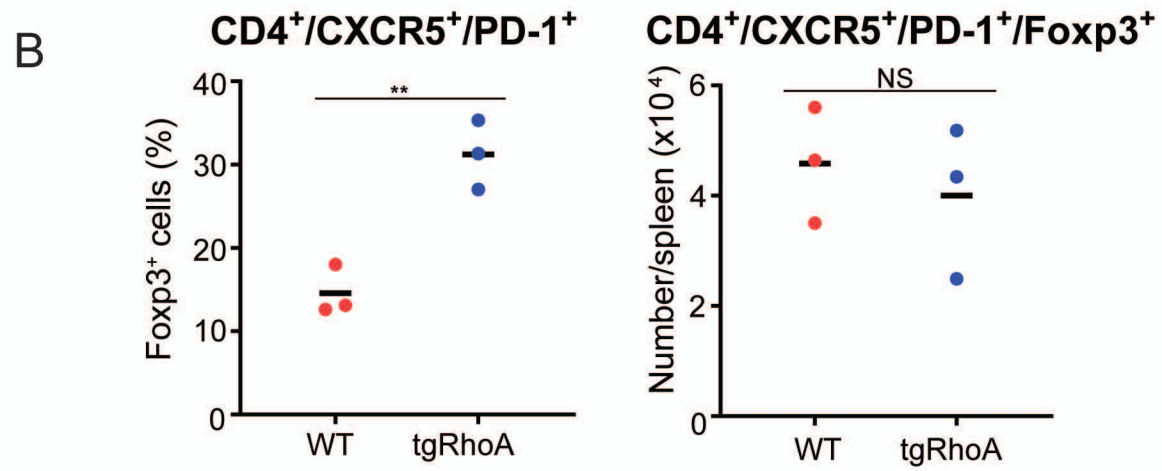


Supplementary Figure 2

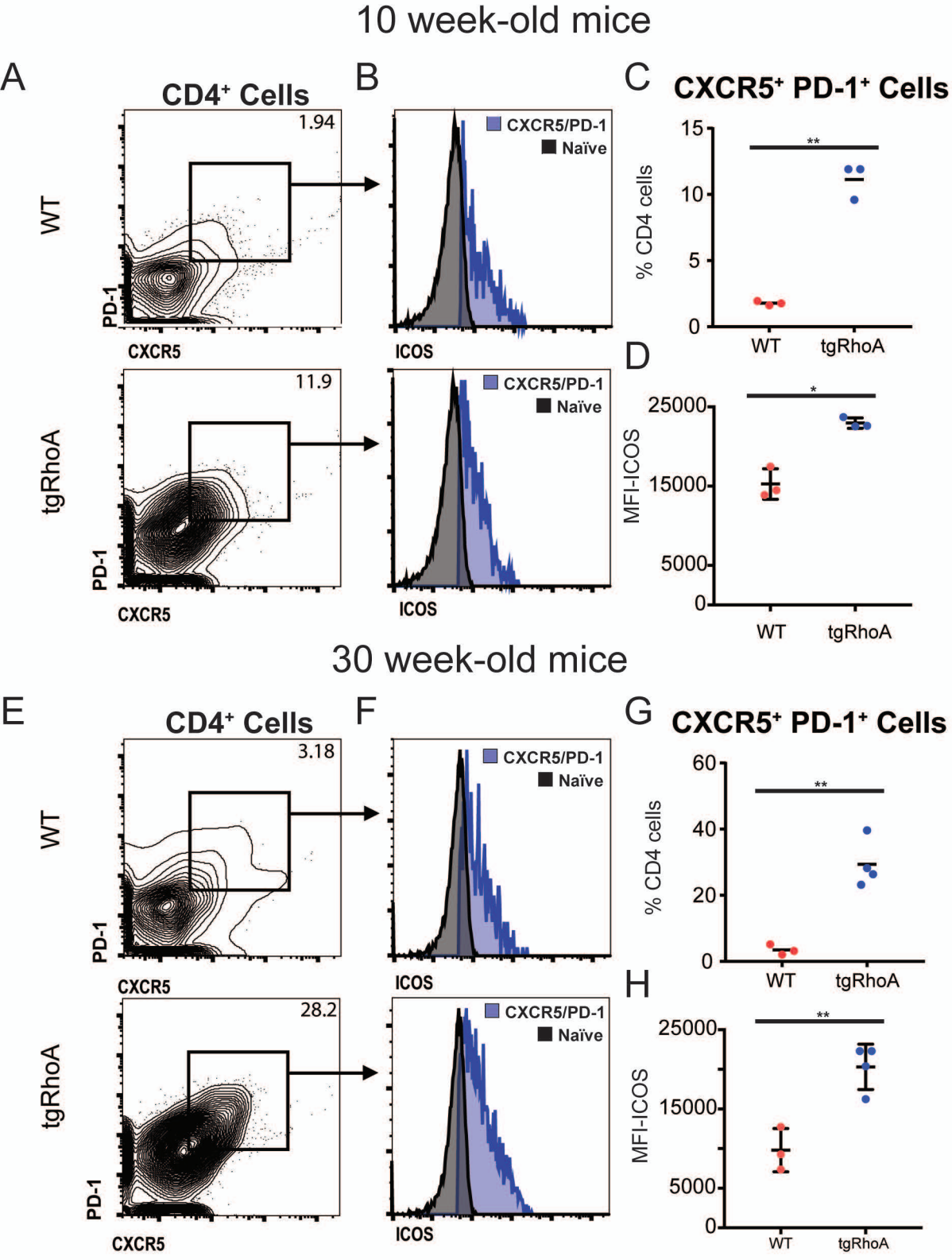


Supplementary Figure 3





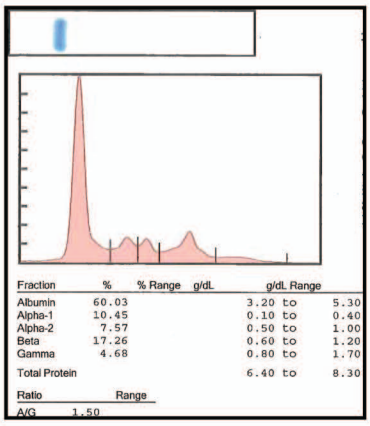
Supplementary Figure 4



Supplementary Figure 5

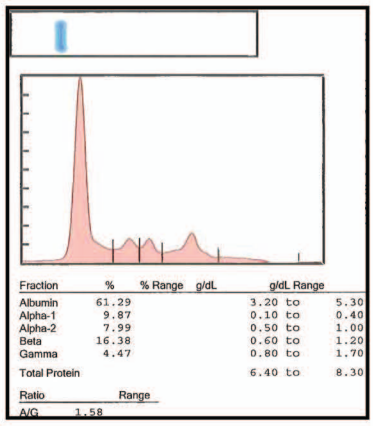
A

WT



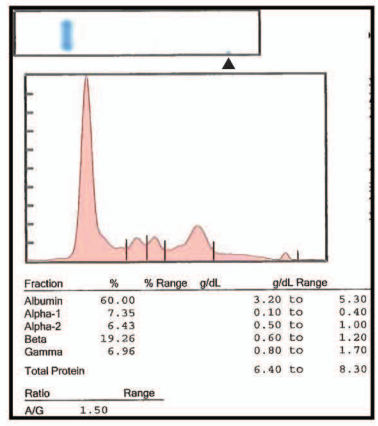
Fraction	%	% Range	g/dL	g/dL Range
Albumin	60.03			3.20 to 5.30
Alpha-1	10.45			0.10 to 0.40
Alpha-2	7.57			0.50 to 1.00
Beta	17.26			0.60 to 1.20
Gamma	4.68			0.80 to 1.70
Total Protein				6.40 to 8.30

Ratio	Range
A/G	1.50



Fraction	%	% Range	g/dL	g/dL Range
Albumin	61.29			3.20 to 5.30
Alpha-1	9.87			0.10 to 0.40
Alpha-2	7.99			0.50 to 1.00
Beta	16.38			0.60 to 1.20
Gamma	4.47			0.80 to 1.70
Total Protein				6.40 to 8.30

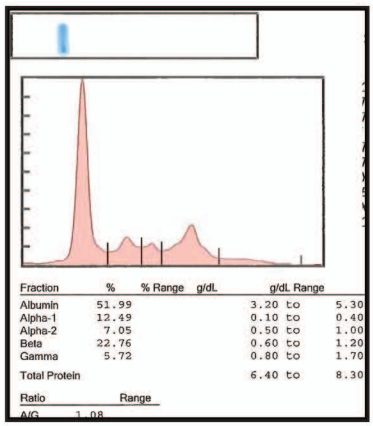
Ratio	Range
A/G	1.58



Fraction	%	% Range	g/dL	g/dL Range
Albumin	60.00			3.20 to 5.30
Alpha-1	7.35			0.10 to 0.40
Alpha-2	6.43			0.50 to 1.00
Beta	19.26			0.60 to 1.20
Gamma	6.96			0.80 to 1.70
Total Protein				6.40 to 8.30

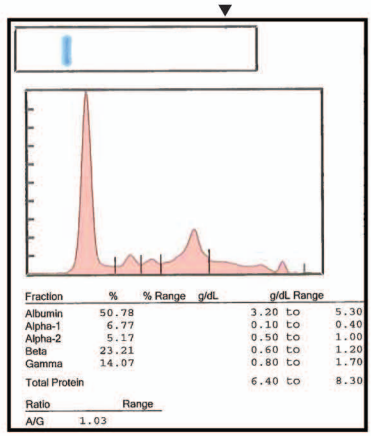
Ratio	Range
A/G	1.50

tgRhoA



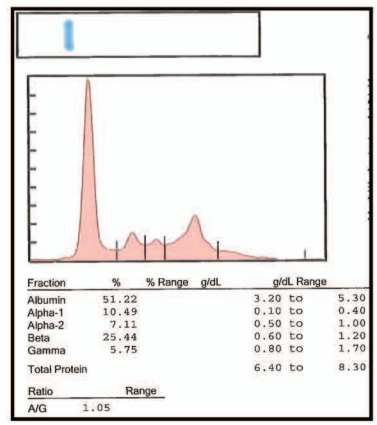
Fraction	%	% Range	g/dL	g/dL Range
Albumin	51.99			3.20 to 5.30
Alpha-1	12.49			0.10 to 0.40
Alpha-2	7.05			0.50 to 1.00
Beta	22.76			0.60 to 1.20
Gamma	5.72			0.80 to 1.70
Total Protein				6.40 to 8.30

Ratio	Range
A/G	1.08



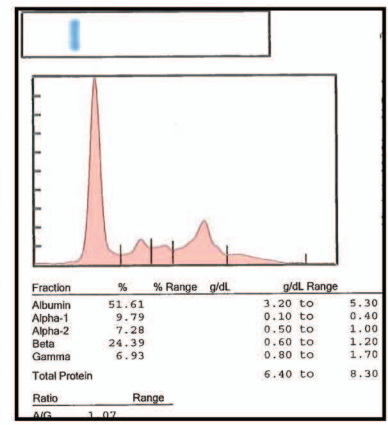
Fraction	%	% Range	g/dL	g/dL Range
Albumin	50.78			3.20 to 5.30
Alpha-1	6.77			0.10 to 0.40
Alpha-2	5.17			0.50 to 1.00
Beta	23.21			0.60 to 1.20
Gamma	14.07			0.80 to 1.70
Total Protein				6.40 to 8.30

Ratio	Range
A/G	1.03



Fraction	%	% Range	g/dL	g/dL Range
Albumin	51.22			3.20 to 5.30
Alpha-1	10.49			0.10 to 0.40
Alpha-2	7.11			0.50 to 1.00
Beta	25.44			0.60 to 1.20
Gamma	5.75			0.80 to 1.70
Total Protein				6.40 to 8.30

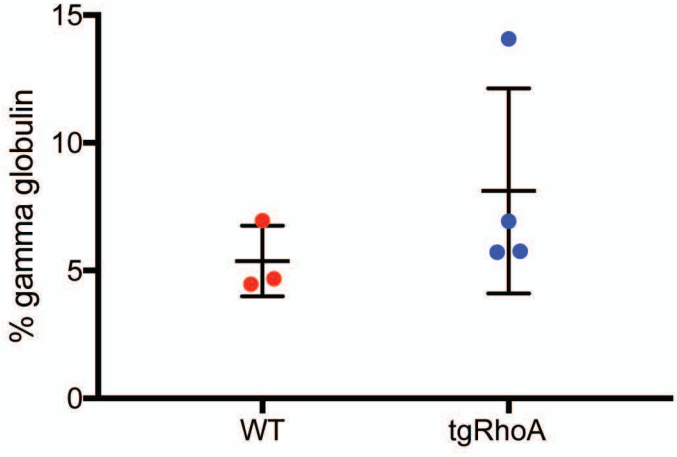
Ratio	Range
A/G	1.05



Fraction	%	% Range	g/dL	g/dL Range
Albumin	51.61			3.20 to 5.30
Alpha-1	9.79			0.10 to 0.40
Alpha-2	7.28			0.50 to 1.00
Beta	24.39			0.60 to 1.20
Gamma	6.93			0.80 to 1.70
Total Protein				6.40 to 8.30

Ratio	Range
A/G	1.07

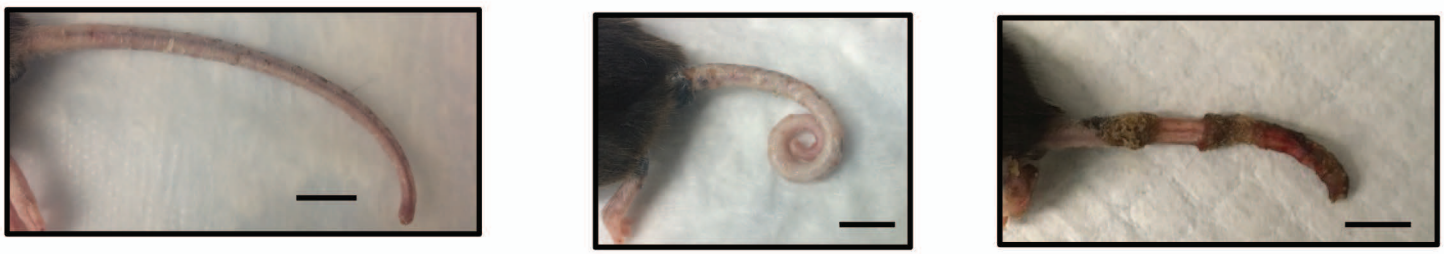
B



Supplementary Figure 6

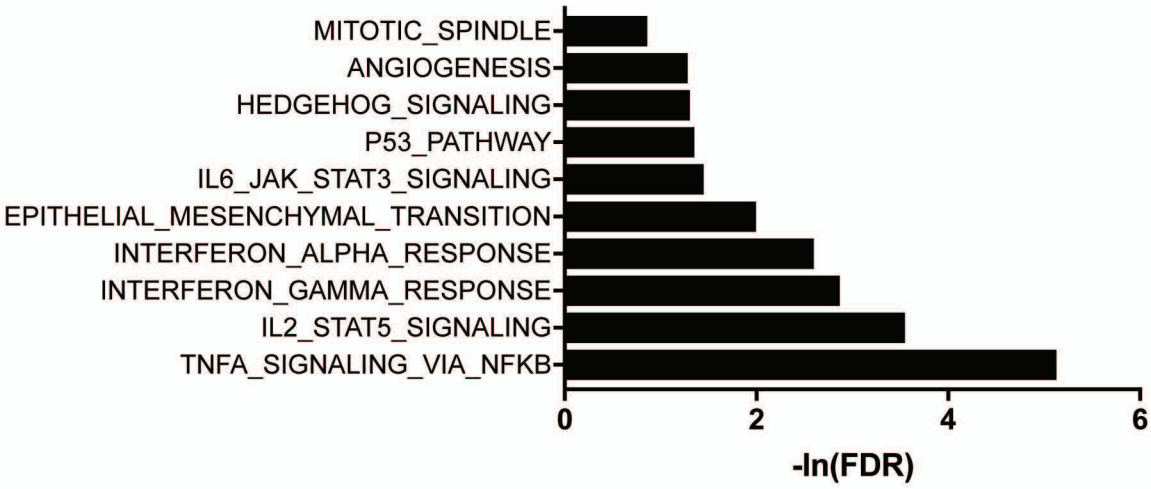
A *Tet2*$^{fl/fl}$; Vav-Cre^{+}

B tgRhoA; *Tet2*$^{fl/fl}$; Vav-Cre^{+}



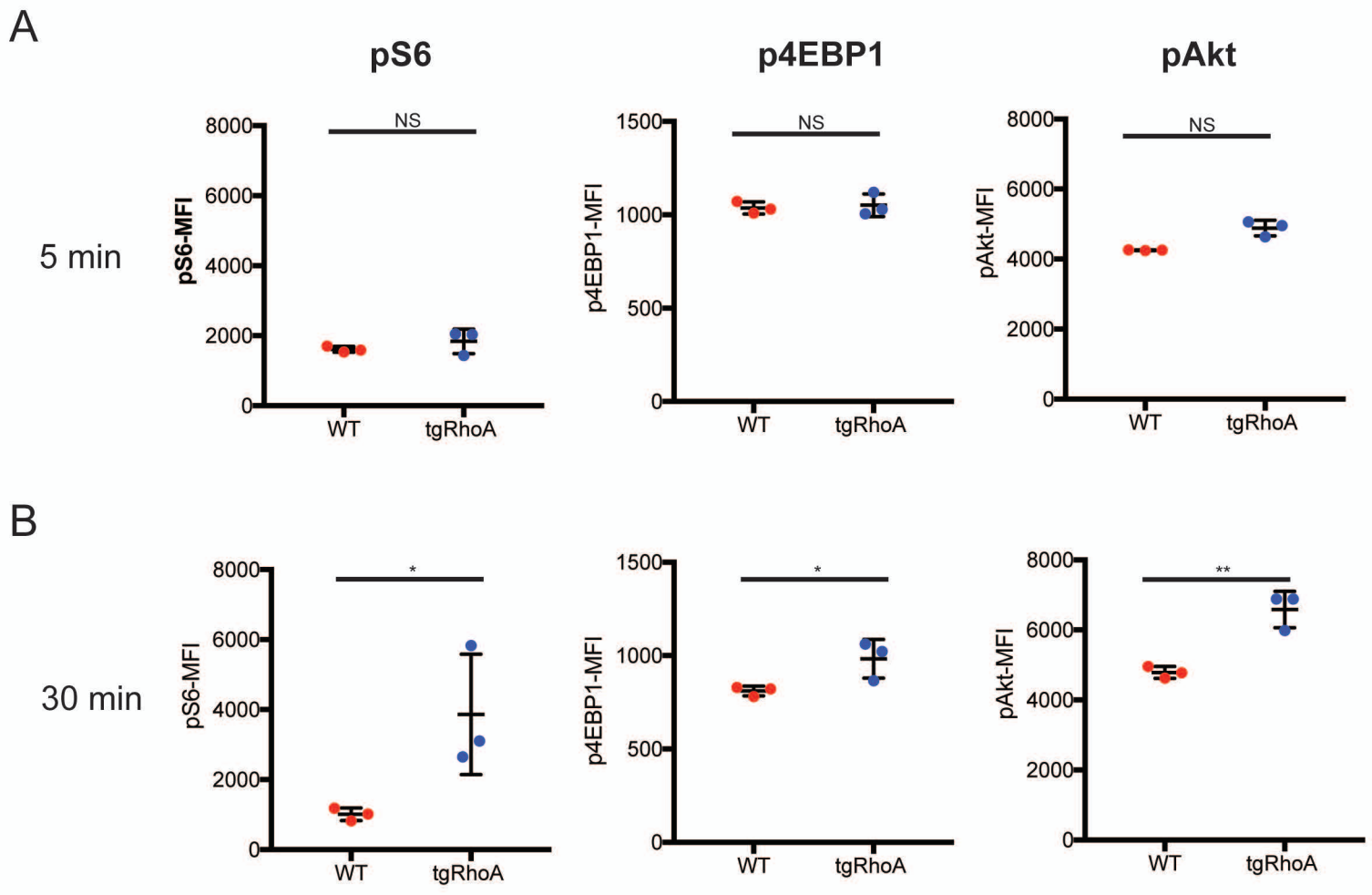
1 cm

Supplementary Figure 7

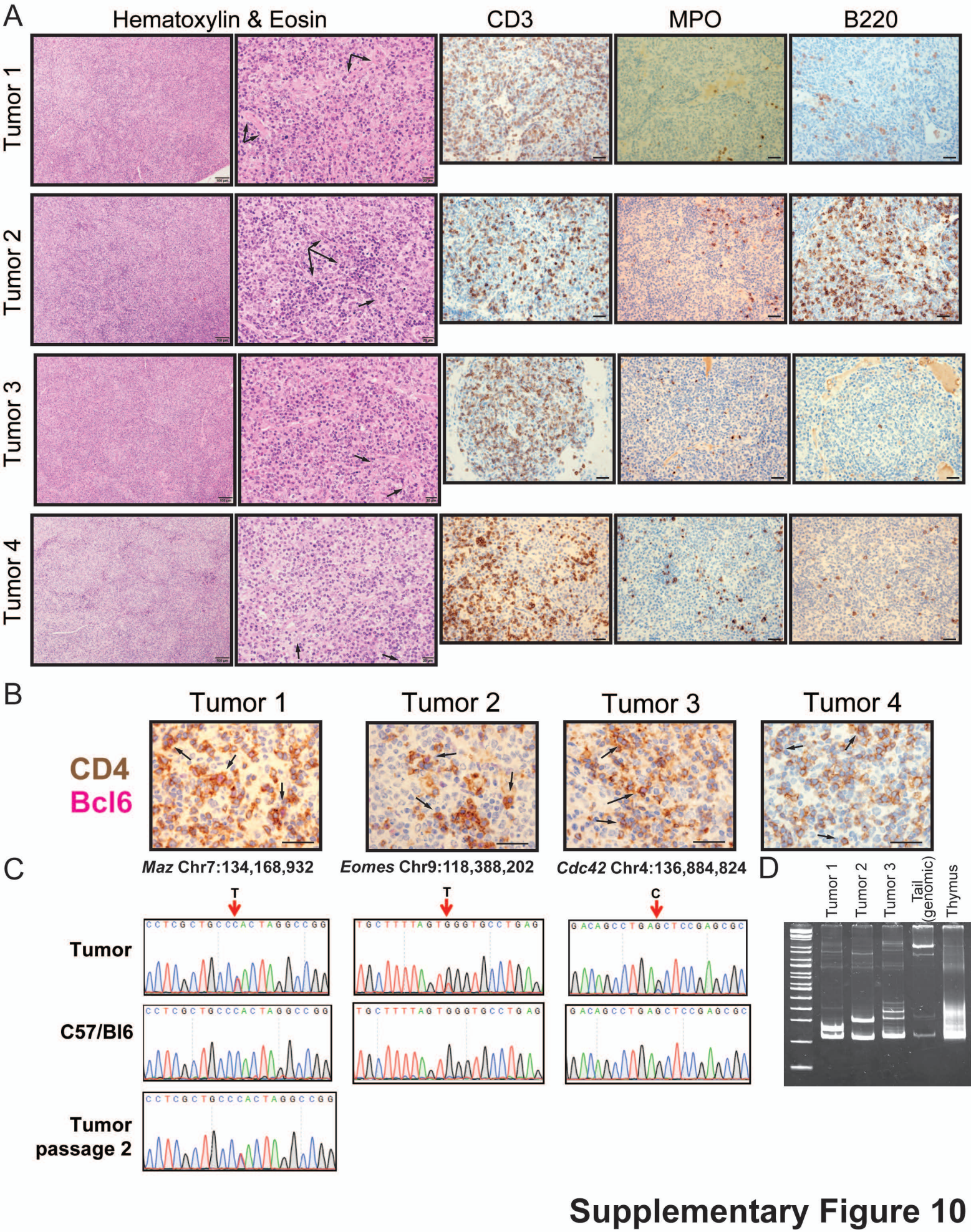


Supplementary Figure 8

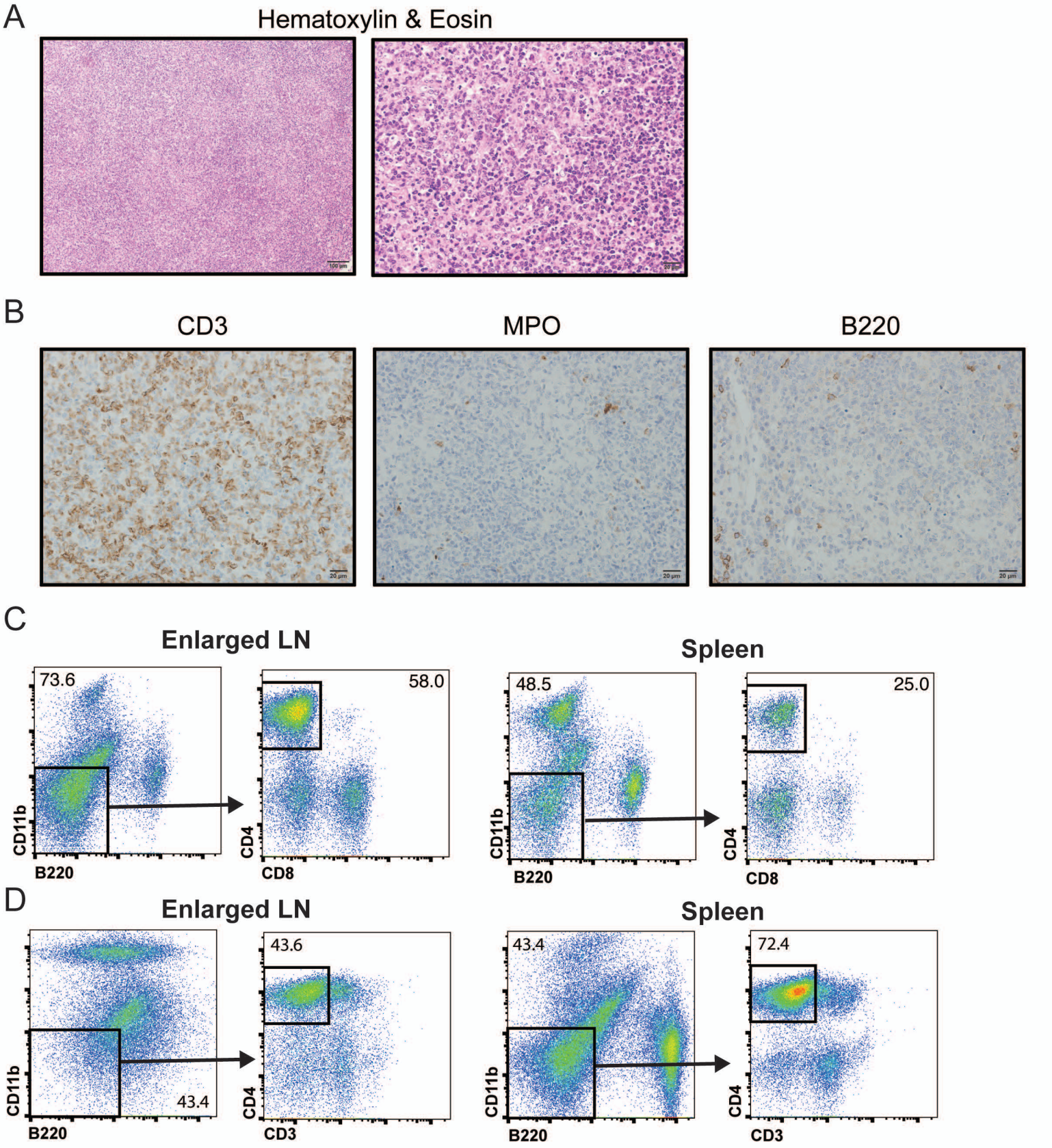
Splenic CD4 Naïve T cells



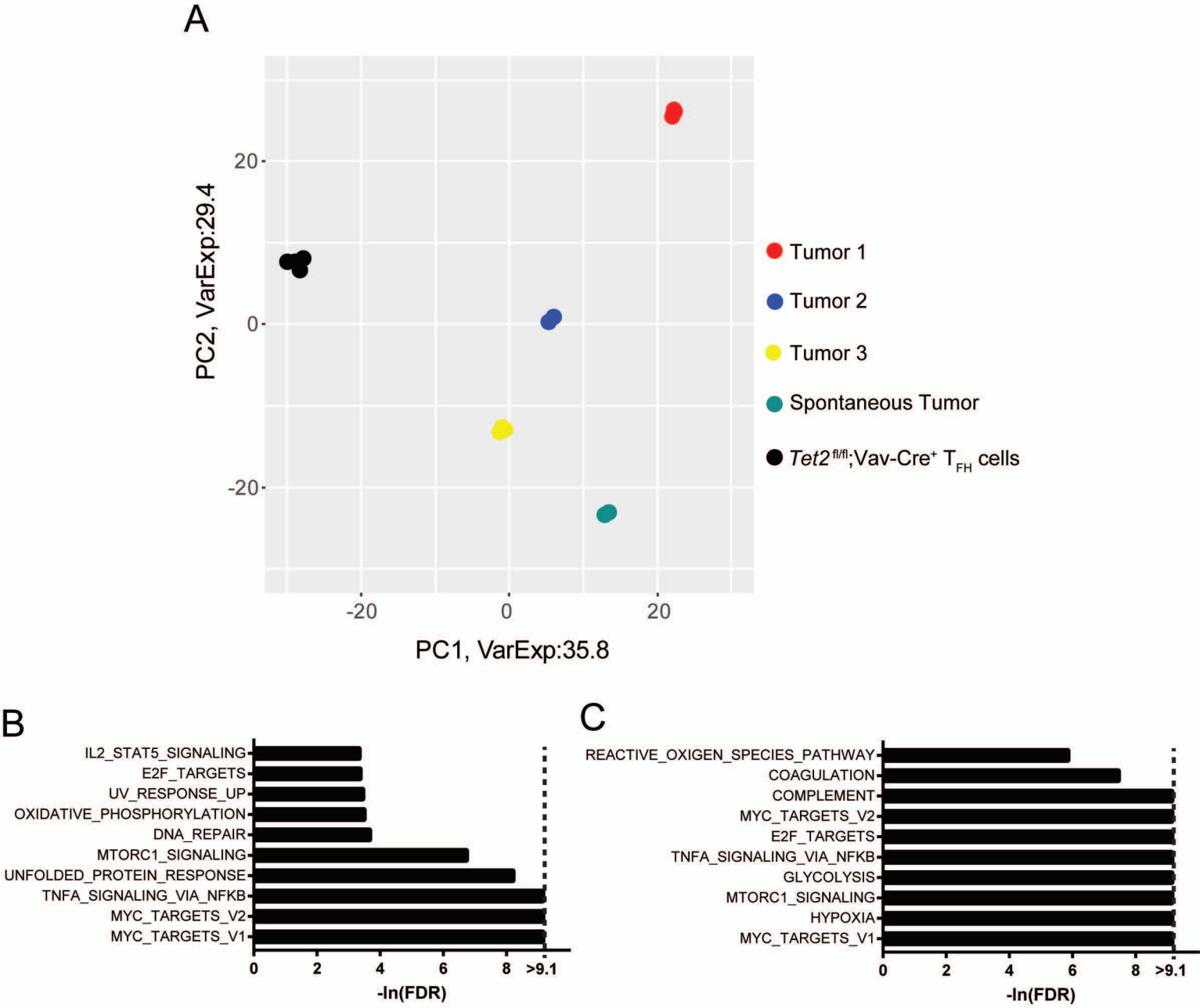
Supplementary Figure 9



Supplementary Figure 10



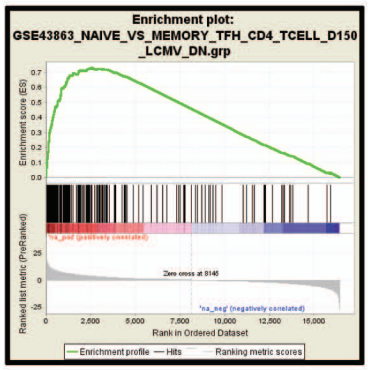
Supplementary Figure 11



Supplementary Figure 12

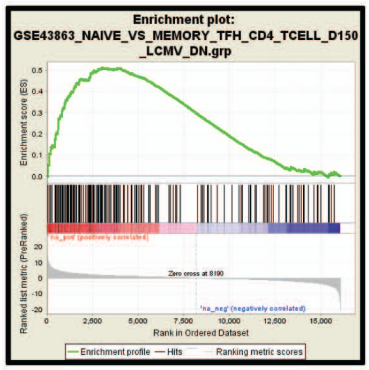
A

Tumor 1



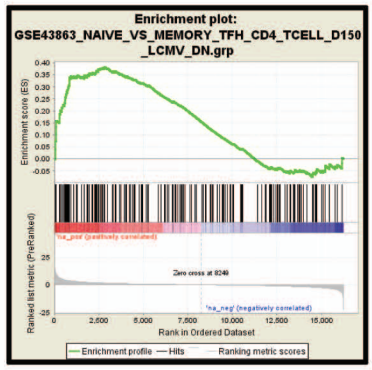
NES: 2.916
Nominal p value: <0.001

Tumor 2

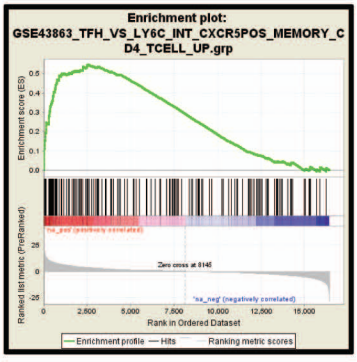


NES: 2.060
Nominal p value: <0.001

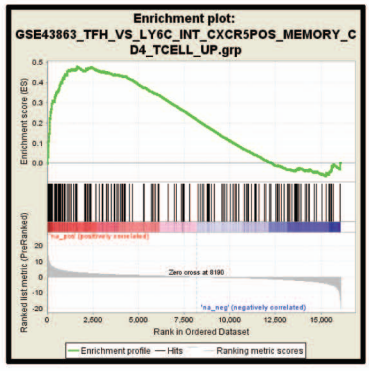
Tumor 3



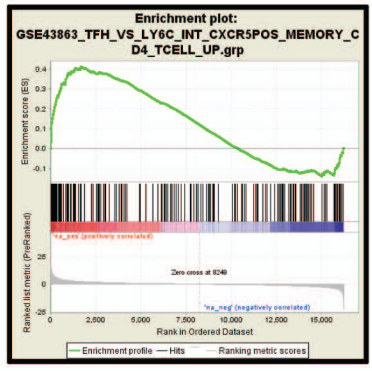
NES: 1.485
Nominal p value: 0.0067



NES: 2.146
Nominal p value: <0.001

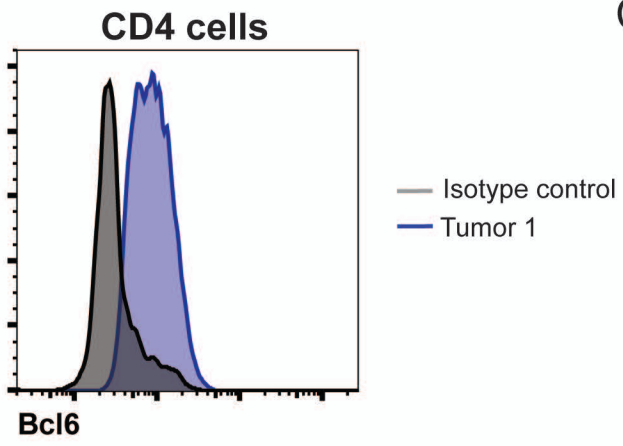


NES: 1.935
Nominal p value: <0.001

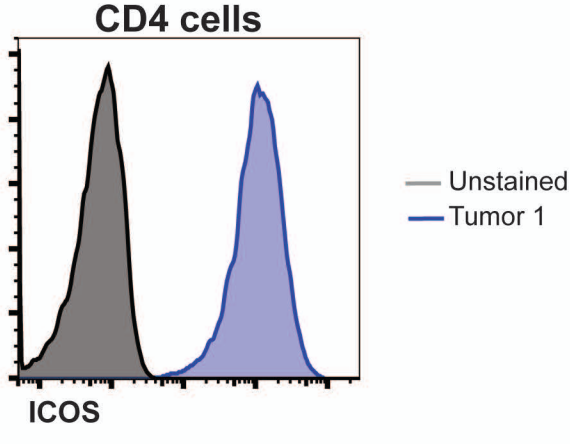


NES: 1.577
Nominal p value: 0.0027

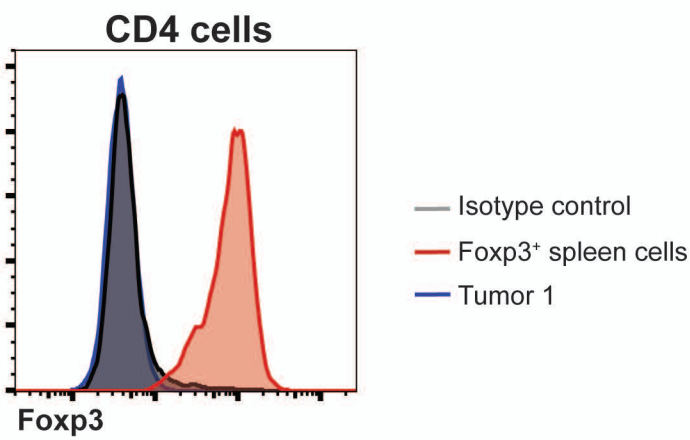
B



C



D



Supplementary Figure 13

Supplementary Table 2: Effector T-cell gene expression signatures of activated tgRhoA $CD4^+$ cells. Transcriptomes from pooled $B220^-CD4^+CD62L^-CD44^+$ cells sorted from tgRhoA or WT littermate mice were subjected to differential gene expression analysis followed by gene set enrichment analysis (GSEA) using gene sets from murine effector cell populations (Figure 4A and B). Positive values indicate enrichment in tgRhoA cells, while negative values indicate enrichment in WT cells. ES = Enrichment Score, NES = Normalized Enrichment Score, nominal p and false discovery rate (FDR) q values per GSEA output.

tgRhoA Activated vs. WT Activated CD4 T cells					
NAME	**SIZE**	**ES**	**NES**	**NOM p-val**	**FDR q-val**
GSE11924_TFH_VS_TH1_CD4_TCELL_UP	178	0.387319	1.702261	0	0.001334668
GSE11924_TFH_VS_TH17_CD4_TCELL_UP	178	0.382948	1.647299	0	0.001805377
GSE11924_TH2_VS_TH17_CD4_TCELL_UP	156	0.350138	1.504572	0.005	0.012112328
NAME	**SIZE**	**ES**	**NES**	**NOM p-val**	**FDR q-val**
GSE11924_TFH_VS_TH1_CD4_TCELL_DN	148	-0.38113	-1.6933	0	0.001002004
GSE11924_TFH_VS_TH17_CD4_TCELL_DN	168	-0.33352	-1.54664	0	0.006838678
GSE11924_TFH_VS_TH2_CD4_TCELL_DN	158	-0.32184	-1.46159	0.00262467	0.011959632

Supplementary Table 3: Cause of death in mouse cohorts

Cohort	Day of death from birth	Cohort 1 (genotype below)	Cohort 2 (genotype below)
		tgRhoA*; Tet2*$^{fl/fl}$; Vav-Cre^{+}; OT-II TCR^{+}	***Tet2***$^{fl/fl}$**; Vav-Cre^{+}; OT-II TCR^{+}**
1	147	Died with no tumor (iatrogenic)	
1	231	Died with T-cell Tumor (Tumor 1)	
1	156	Died with Myeloid Proliferation	
1	171	Died with indeterminate tumor[*]	
1	205	Died with Myeloid Proliferation	
1	283	Died with Myeloid Proliferation	
1	270	Died with T-cell Tumor (Tumor 2)	
1	197	Died with T-cell Tumor (Tumor 4)[#]	
1	195	Died with T-cell Tumor (Tumor 3)	
1	228	Died of unknown cause[^]	
2	266		Died with Myeloid Proliferation
2	302		Died with Myeloid Proliferation
2	245		Died with Myeloid Proliferation
2	294		Died with T-cell Tumor
2	358		Died with T-cell Tumor
2	405		Died with Myeloid Proliferation
2	326		Died of unknown cause[^]
2	235		Died of indeterminate tumor[*]
2	121		Died with no tumor (iatrogenic)
2	349		Died with T-cell Tumor

[*] Indeterminate Tumors had histologic features of both B-cell and myeloid proliferation

[^] Mice died of unknown cause due to corpse not being recovered

[#] Histology revealed T-cell tumor identity but RNAseq was not included in analysis