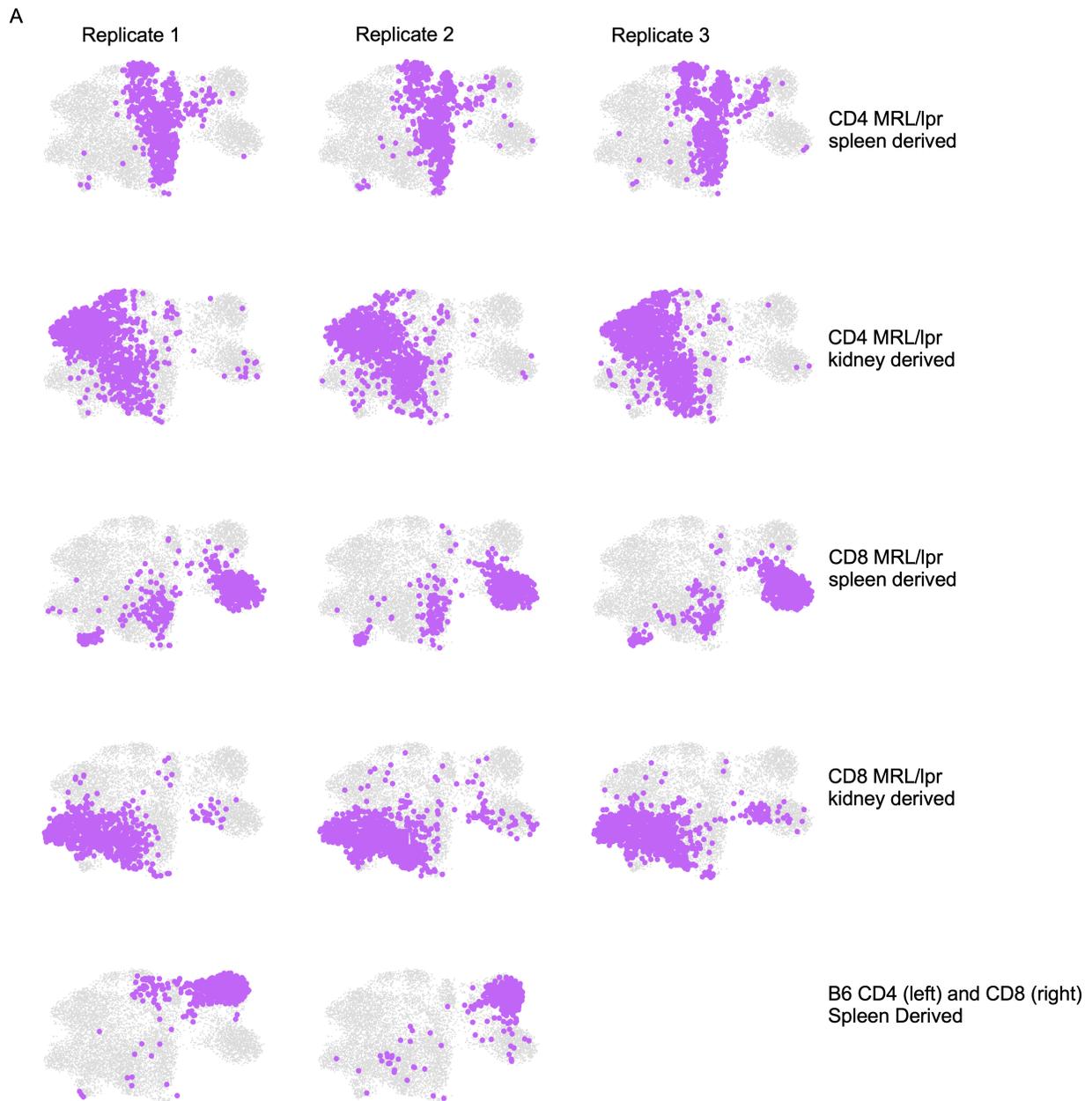
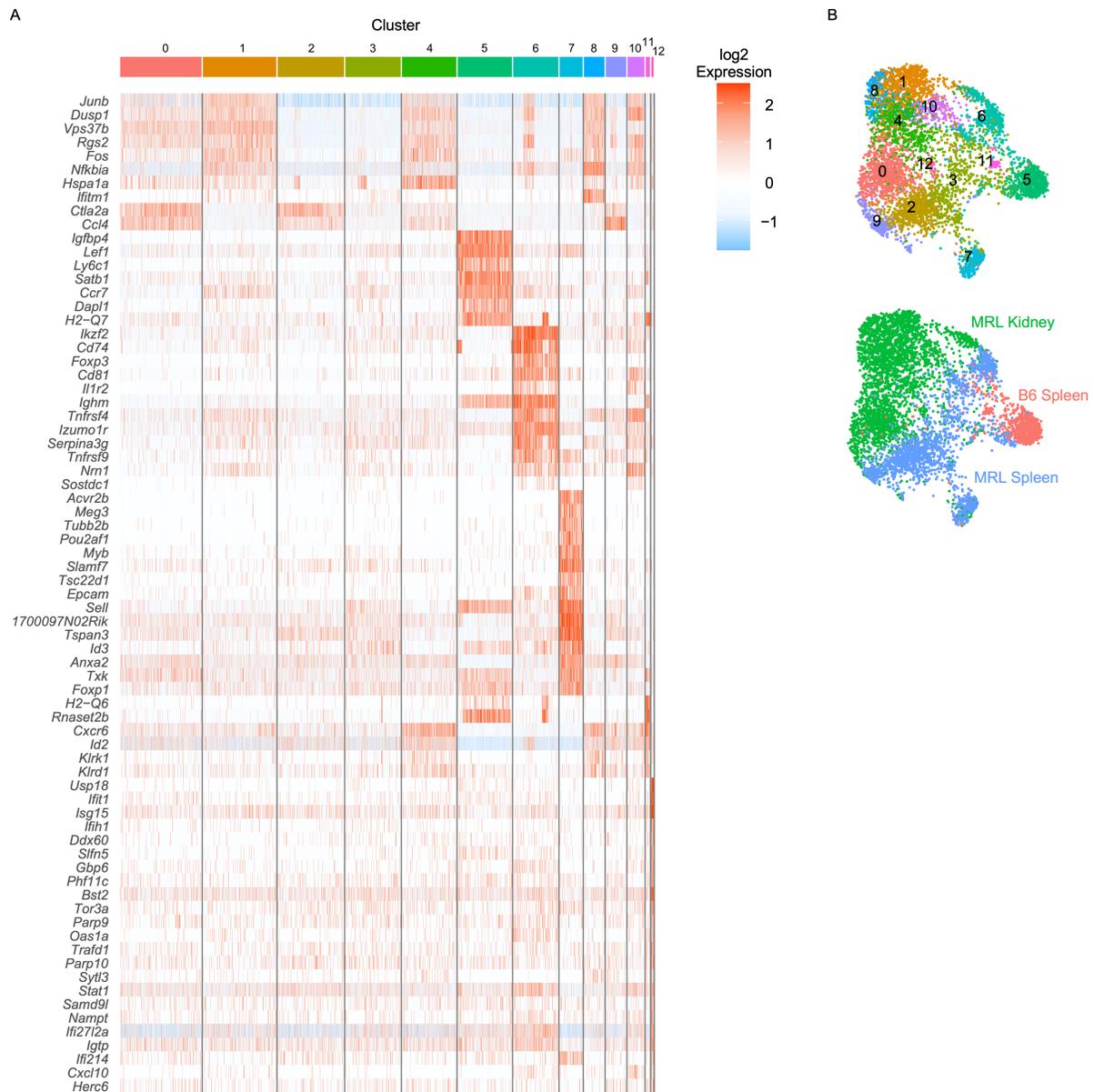


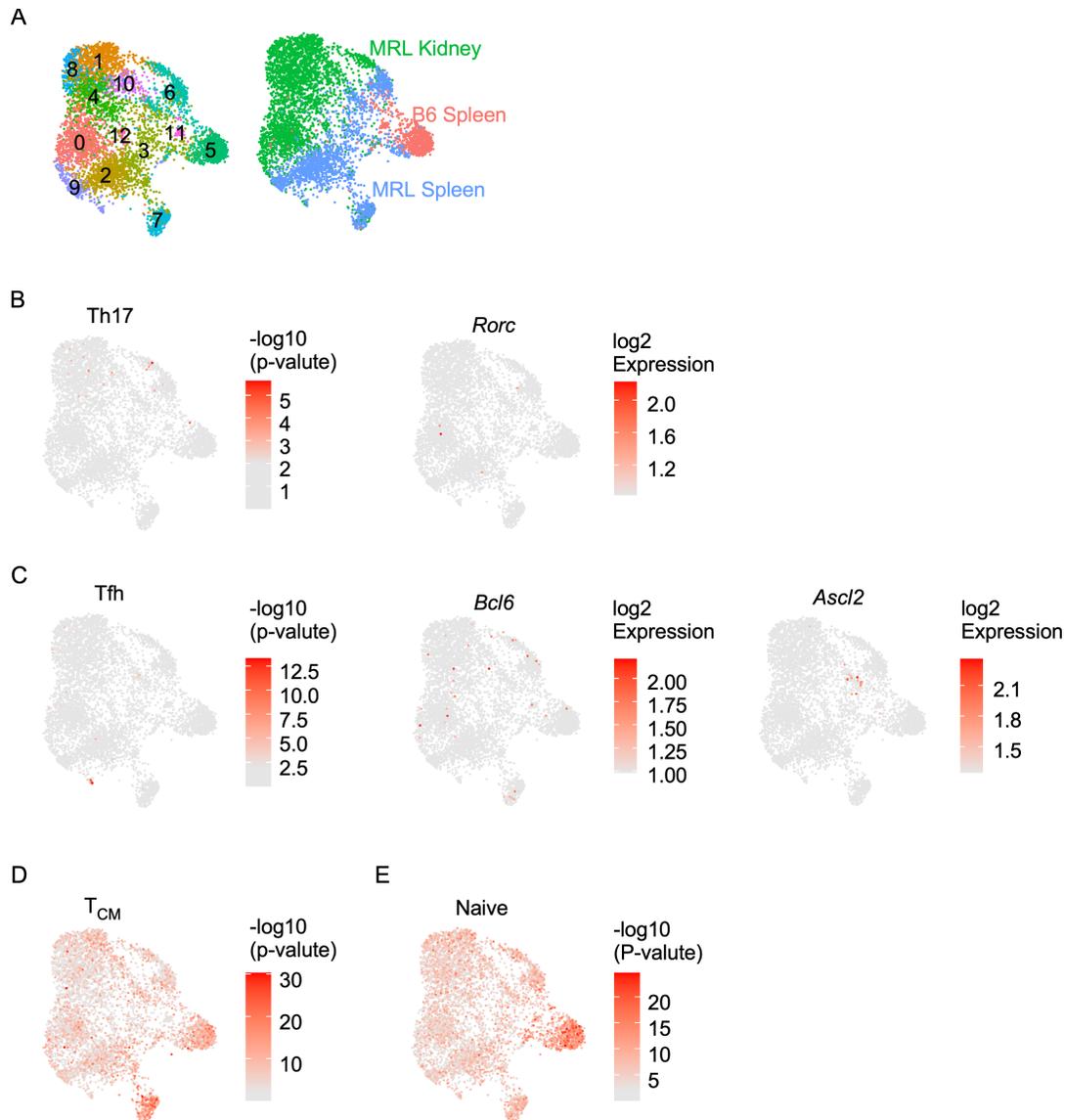
## Supplemental Data:



Supplemental Figure 1: *Analytics methodology* (A) Cell source determined using HTO for each of the 14 individual sorted populations was overlaid on the UMAP projection (as per Fig 1B) and organized based on replicates to exhibit the equal contribution of each replicate to the observed clusters.

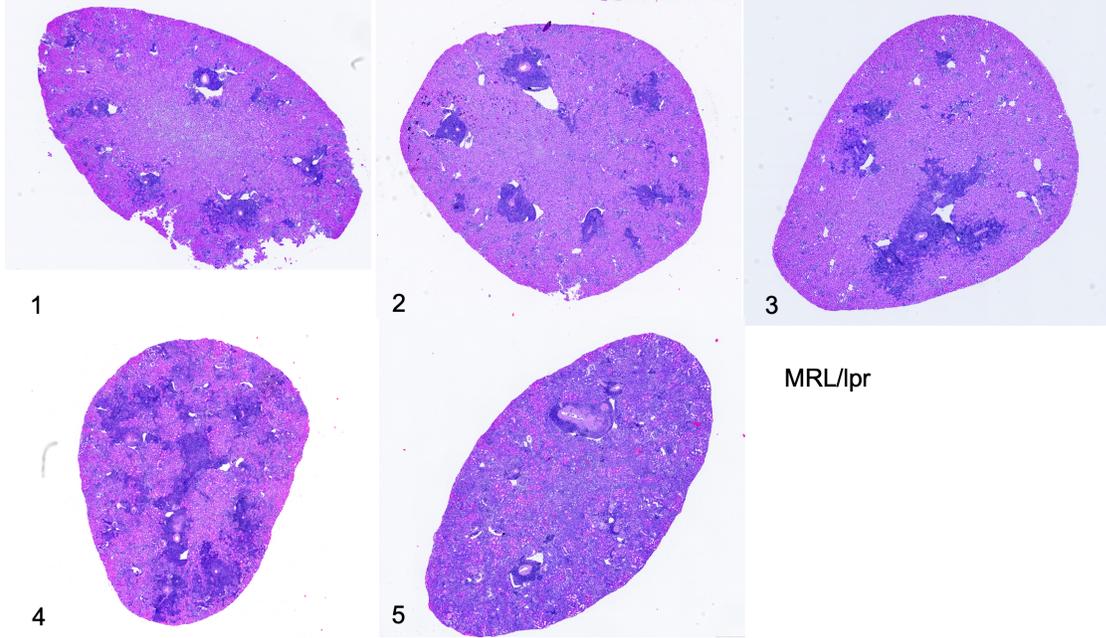


Supplemental Figure 2: *Top DEGs associated with CD4 T cell clusters.* (A) Heat map shows top (Fold change > 1 and FDR < 0.01) significant differentially expressed genes (rows) associated with the 13 CD4 clusters and their expression at the single cell level (columns), colored according to expression level. (B) With UMAP projection of CD4 T cells from Main-seq outlining 13 clusters, and overlay of cell source as determined by HTO (as defined in Figure 2).

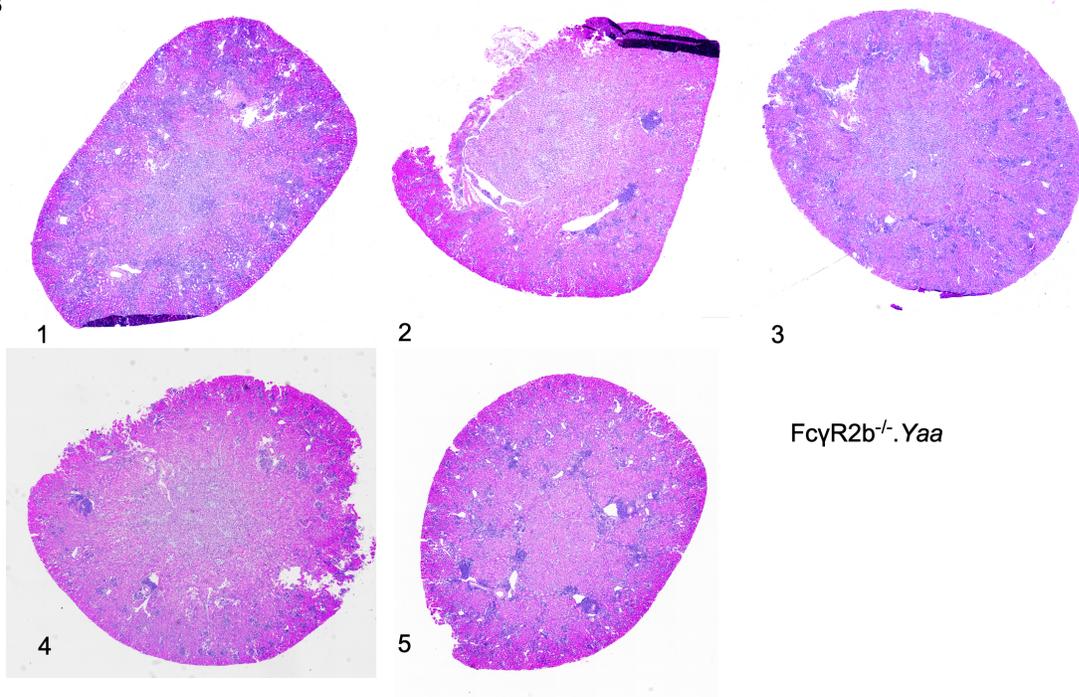


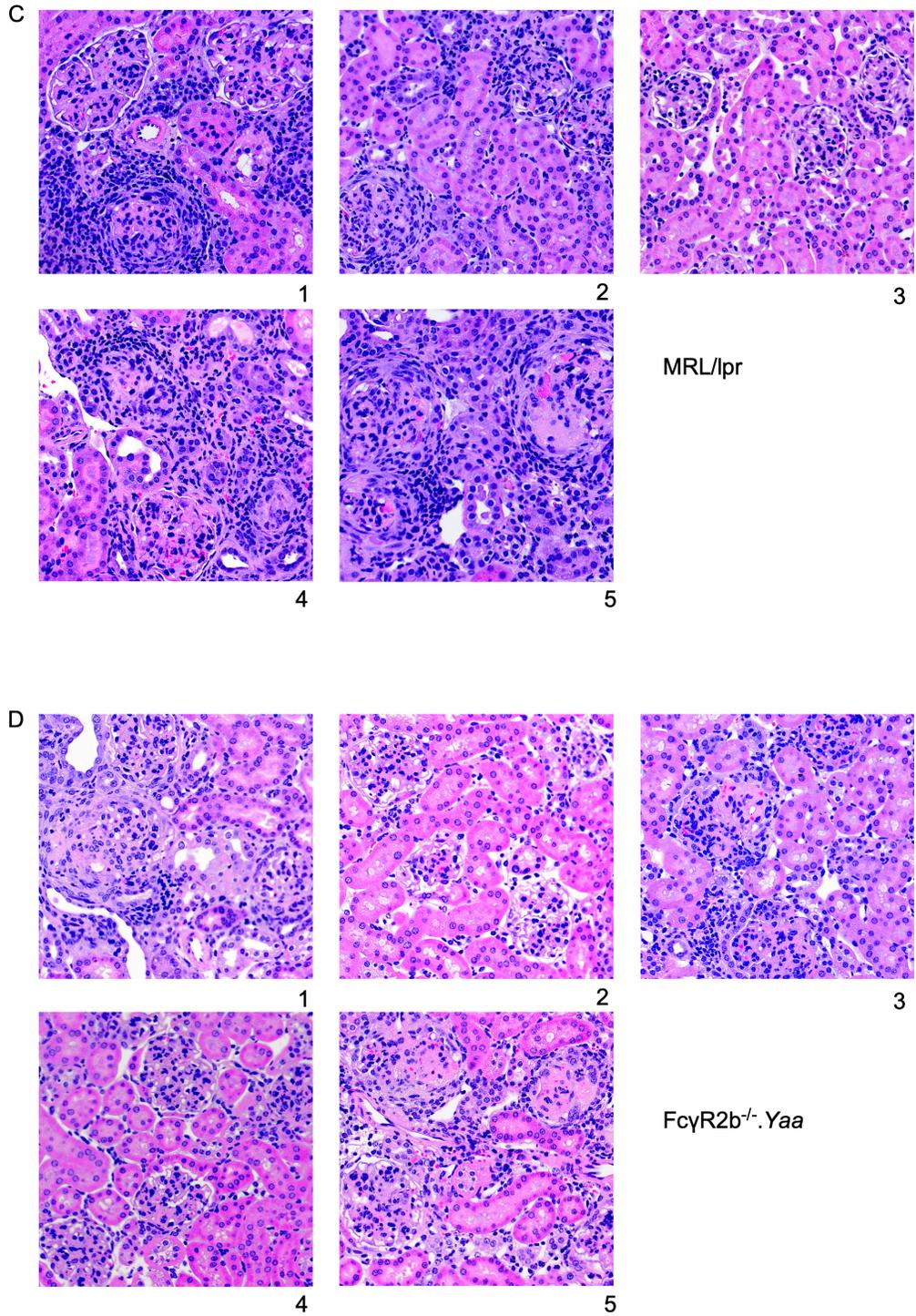
Supplemental Figure 3: GSEA and gene expression mapping identifies clusters and cells with a naïve and  $T_{CM}$  signature but not Th17 or Tfh populations. GSEA performed in each cell by Wilcox-test using published reference signature genes (Table S1) and related TF expression is mapped onto the (A) CD4 UMAP and HTO defined cell source to identify CD4 T cell phenotypes. (B) Th17 gene signature and associated TF *Rorc*; (C) Tfh gene signature and associated transcription factors *Bcl6* and *Ascl2*; and gene signatures for (D)  $T_{CM}$  and (E) naïve populations.

A

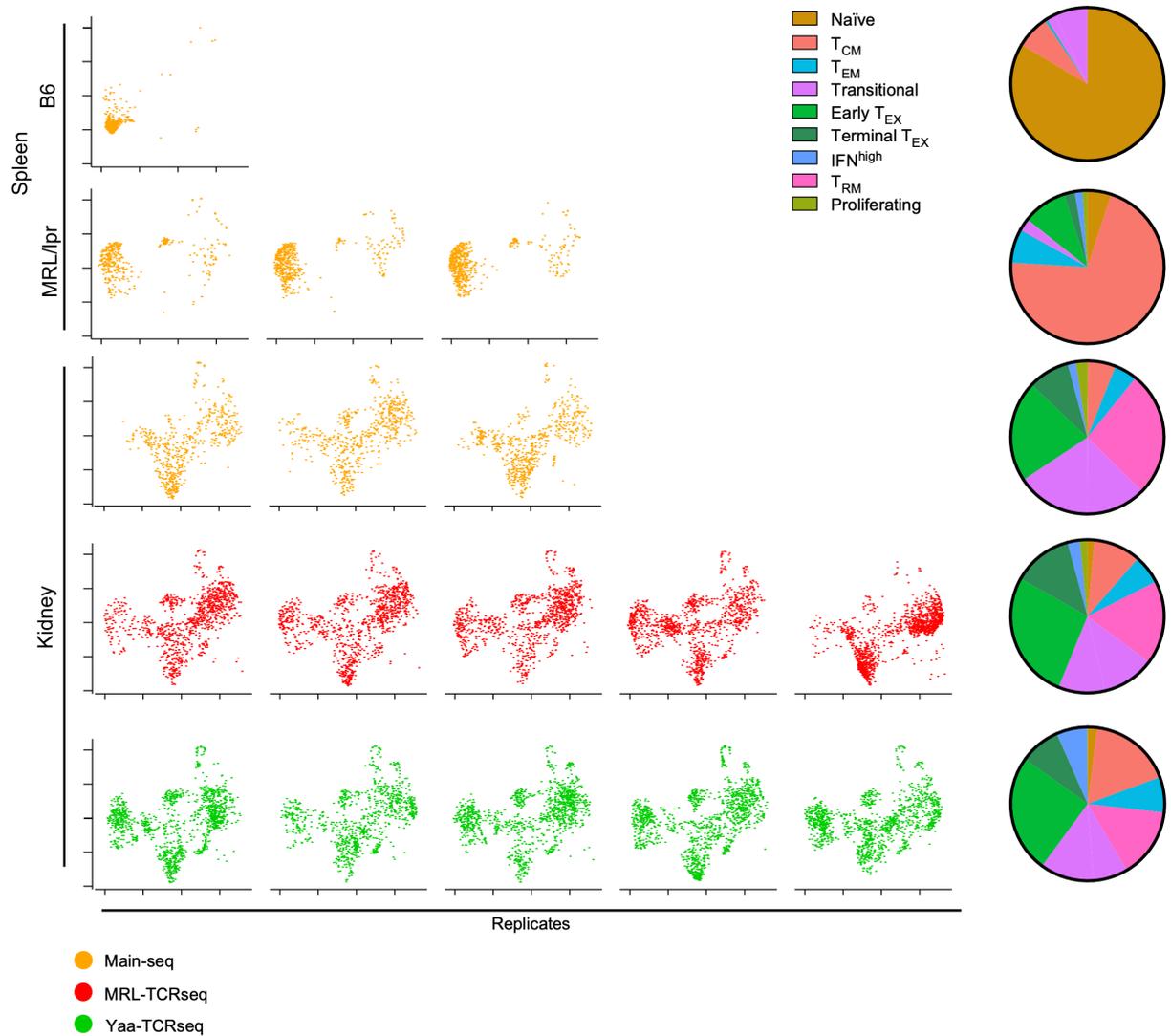


B



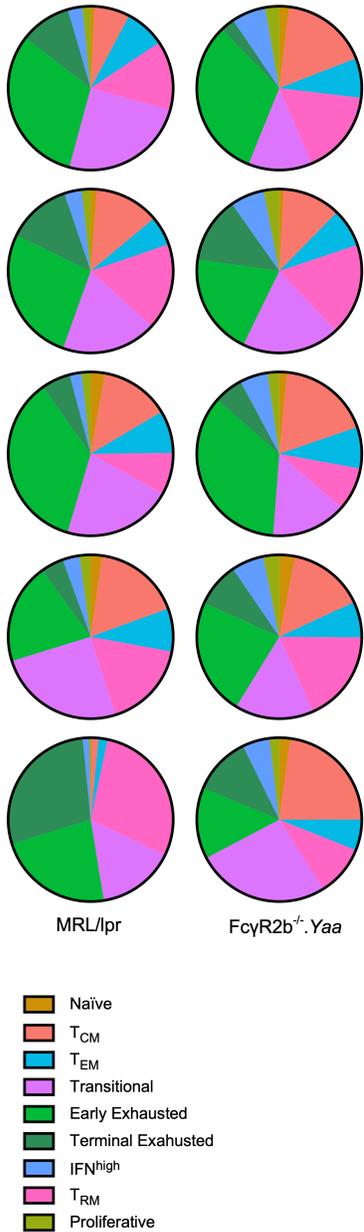


Supplemental Figure 4: H&E stained cross section of kidneys from mice analyzed in (A) cohort 2 (MRL-TCRseq), and (B) cohort 3 (Yaa-TCRseq), with high resolution 20x images of representative glomeruli for (C) cohort 2 mice (MRL-TCRseq), and (D) cohort 3 (Yaa-TCRseq). Associated disease scoring is included in Supplemental Table 2.

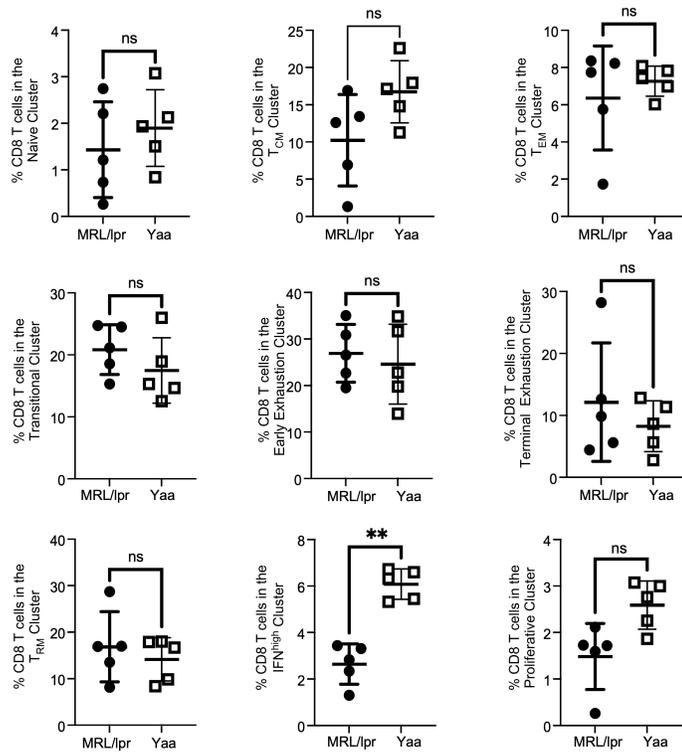


Supplemental Figure 5: *Cluster contribution by mouse and cohort.* Mouse by mouse contribution to combined CD8 UMAP cluster as defined in Figure 5. Each row of UMAP plots represents a single source and origin. The cohort derivation of each UMAP plot is color-coded according to the legend. Pie charts to the right represent relative phenotypically-identified cluster distribution of T cells within combined cells from each source/origin.

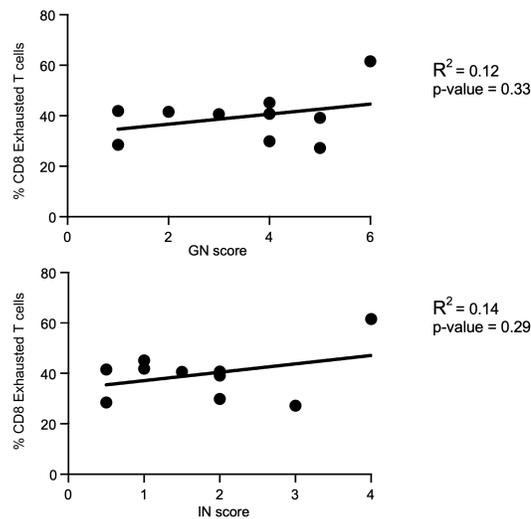
A



B

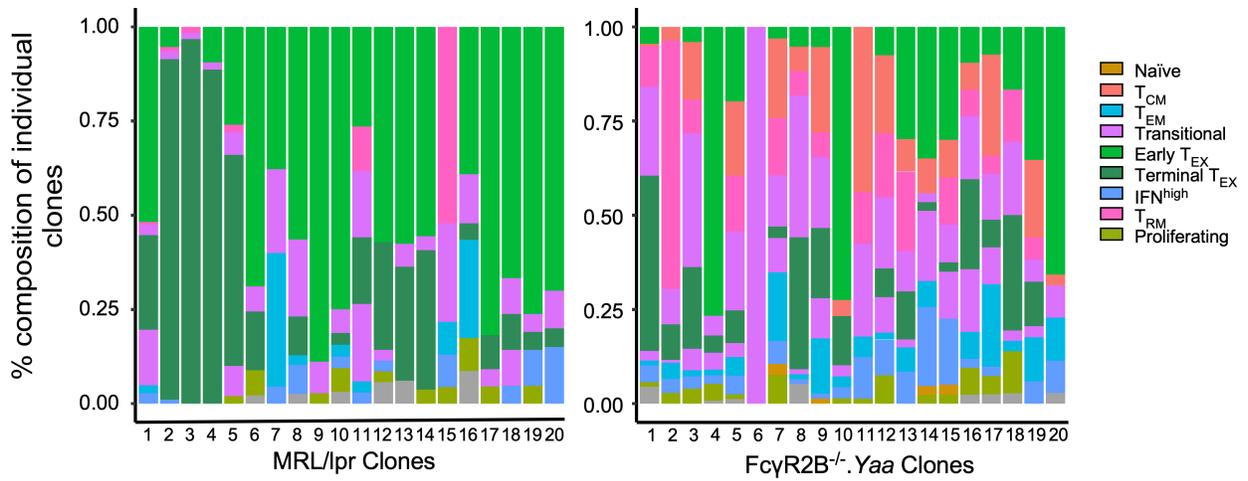


C



Supplemental Figure 6: *CD8 Cluster distribution does not differ by mouse model or based on histologic disease.* (A) Pie charts represent relative phenotypically-identified cluster distribution of CD8 T cells defined in Figure 5 for each mouse assessed in cohort 2 and 3. (B) Dot plot represents percent of CD8 T cells from MRL/lpr and FcγR2B<sup>-/-</sup>:Yaa (Yaa) models in each outlined cluster. Statistics were determined using Two-way Anova with repeat measures corrected for multiple comparisons using Bonferroni adjustment (\*\*

indicates p-value <0.01). (C) Linear regression analysis of % exhausted T cells in each mouse and corresponding histologic disease score, either glomerulonephritis (GN) or interstitial nephritis (IN), with no analysis reaching statistical significance.



Supplemental Figure 7. *Progeny of the same T cell transition between different clusters within the kidney suggesting dynamic progression between T cell states.* Bar graphs represent the top 20 CD8 T cell clones from the MRL/lpr (left panel) and FcγR2B<sup>-/-</sup>.Yaa (right panel) models with the relative distribution of these clones within the putative T cell clusters as defined in Fig. 8 B/C.

**Table 1:** Gene Sets used for UMAP GSEA

| Profile      | Cytotoxic CD4 | Exhausted            | Th1     | Th17      | Th2 long      | TRM          | Tperiph | Hypoxia | Treg    | TEM     | TCM   | T naive    | Tfh           |
|--------------|---------------|----------------------|---------|-----------|---------------|--------------|---------|---------|---------|---------|-------|------------|---------------|
| Citation     | 13            | 14                   | 15      | 15        | 16            | 17           | 17      | 18      | 19      | 20-22   | 20-22 | 21         | 23            |
| <b>Genes</b> | Gzma          | 0610010F05RIK        | Ifng1   | Ahr       | Plac8         | Cdh1         | Sid1    | Bnip3   | Foxp3   | Cx3cr1  | Cd28  | ABLIM1     | Il21          |
|              | Gzmb          | 0610037D15RIK        | Il18r1  | Irf4      | Igfbp7        | Cd244        | Rasgrp2 | Prodh   | Ctla4   | Id2     | Tiam1 | ACTN1      | Plagl1        |
|              | Prf1          | 1110035E04RIK        | Cxcr6   | Nfx1      | Pdcd1         | Itga1        | S1pr1   | Idh1    | Il2ra   | Stat4   | Cpne2 | ACVR1C     | Sostdc1       |
|              | Gzmb          | 1190002F15RIK        | Il18rap | Rora      | Il5           | LOC641050    | Cmah    | Prodh2  | Il2rb   | Cc4     | Cdh1  | ADD3       | Ttc39c        |
|              | Nkg7          | 1200009F10RIK        | Klrc1   | Rorc      | Arg1          | Skil         | Fam65b  | Pdk2    | Tnfrsf4 | Ccl5    | F2r1  | ADSL       | Popdc2        |
|              | Gnly          | 1700009P17RIK        | Il12rb2 | Il21      | Il1r1         | Sik1         | Ly6c2   | IDH1    | Tnfrsf9 | Lgals1  | Sesn3 | AIF1       | Myo1f         |
|              | Klrg1         | 1700012B09RIK        | Etv5    | Il12      | Gata3         | Litaf        | Elovl7  | IDH2    | Itgae   | Lgals3  | Sell  | ALS2CR13   | Sostdc1       |
|              | Klrb1         | 1700012D01RIK        | Hoxp    | Il17f     | Bhlhe40       | Chn2         | Eomes   | BNIP3L  | Ccr6    | Klrc1   | Ccr7  | ALS2CR13   | Dntt          |
|              | Itgal         | 1700017B05RIK        | Onecut2 | Il17a     | Gclc          | Ctla4        | Fgf13   | MX11    | Cd83    | Itgal   | Cd27  | AMY2B      | Scppdh        |
|              |               | 1700019E19RIK        | Tbx21   | Il2       | Ltb4r1        | LOC641050    | Klre1   | PDK1    | Klrg1   | Itgb1   | Eomes | APBB1      | Cdc25c        |
|              |               | 1700106N22RIK        | Ifng    | Inhba     | Rnf128        | Icos         | S1pr5   | SLC2A1  | Penk    | Klrc1   | Tcf7  | APEX1      | Rab39b        |
|              |               | 1810009J06RIK.GM2663 | Csf1    | Pgf       | Fgl2          | Inpp4b       | Slamf6  | P4HA2   | Cst7    | Gzma    | Stat3 | ARH        | Cxcr3         |
|              |               | 2010107G23RIK        | Il34    | Il2ra     | Serpinb6a     | Tmem123      | Tlr1    | Hif1a   | Ahr     | Gzmb    | Id3   | ARMCX1     | Gldc          |
|              |               | 201011110RIK         |         | Ptgrn     | Pparg         | Vps37b       | Usp33   |         | Il1r1   | Prf1    |       | ATM        | Aurkb         |
|              |               | 2210403K04RIK        |         | Tfrc      | Nfk1          | Nr4a2        |         |         | Ikzf4   | Il2rb   |       | ATM        | Angptl2       |
|              |               | 2310016C08RIK        |         | Tnfrsf13b | Ccr8          | Itgae        |         |         | Ikzf2   | Il18rap |       | ATP8A2     | Zdhhc2        |
|              |               | 2310039F13RIK        |         |           | Cxcr6         | Rgs1         |         |         | Ebi3    |         |       | AXIN2      | Pf1           |
|              |               | 2310046K01RIK        |         |           | Tagln2        | Xcl1         |         |         |         | Tbx21   |       | B4GALT3    | Aspm          |
|              |               | 2310079F09RIK        |         |           | Zcchc10       | Rgs2         |         |         |         | Prdm1   |       | BACH2      | Zdhhc2        |
|              |               | 2500002B13RIK        |         |           | Ctla2a        | LOC100503878 |         |         |         | Klf2    |       | BEX2       | Aurkb         |
|              |               | 2610024B07RIK        |         |           | Cd200r1       | Nr4a1        |         |         |         | Rora    |       | BNIP3      | Ces2d-ps      |
|              |               | 2700007P21RIK        |         |           | Litaf         | Hspa1a       |         |         |         |         |       | BTBD11     | Ces2c         |
|              |               | 2700008G24RIK        |         |           | Rgs1          |              |         |         |         |         |       | CABC1      | Tmbim1        |
|              |               | 2810433K01RIK        |         |           | Il6           |              |         |         |         |         |       | CACNA1I    | Cdc25c        |
|              |               | 2900001G08RIK        |         |           | Id2           |              |         |         |         |         |       | CAMK4      | Ispd          |
|              |               | 290026A02RIK         |         |           | Rgs2          |              |         |         |         |         |       | CCND3      | Slc29a4       |
|              |               | 3830408D07RIK        |         |           | Rgcc          |              |         |         |         |         |       | CCR7       | Angptl2       |
|              |               | 4831426I19RIK        |         |           | Il4           |              |         |         |         |         |       | CD164L1    | Slc43a1       |
|              |               | 4930422G04RIK        |         |           | Mns1          |              |         |         |         |         |       | CDR2       | Il1r1         |
|              |               | 4930429F24RIK        |         |           | Msmo1         |              |         |         |         |         |       | CGI-30     | Perp          |
|              |               | 4930434E21RIK        |         |           | Sdf2          |              |         |         |         |         |       | CHKA       | Ttk           |
|              |               | 4930520O04RIK        |         |           | Paxbp1        |              |         |         |         |         |       | CKAP4      | Gas2l3        |
|              |               | 5330409N07RIK        |         |           | Gm5127        |              |         |         |         |         |       | CLNS1A     | 6330403K07Rik |
|              |               | 5330426P16RIK        |         |           | Il17rb        |              |         |         |         |         |       | CNN3       | Ifng          |
|              |               | 5730469M10RIK        |         |           | Hif           |              |         |         |         |         |       | COH1       | Melk          |
|              |               | 5830415L20RIK        |         |           | Fam213a       |              |         |         |         |         |       | CPT1B      | Coro2b        |
|              |               | 5830456J23RIK        |         |           | Il13          |              |         |         |         |         |       | CRLF3      | Aspm          |
|              |               | 5830474E16RIK        |         |           | Dusp6         |              |         |         |         |         |       | CTL2       | Chst2         |
|              |               | 6030487A22RIK        |         |           | Lgals3        |              |         |         |         |         |       | CUGBP2     | Cenpe         |
|              |               | 6230409E13RIK        |         |           | Epas1         |              |         |         |         |         |       | DAF        | Osbpl3        |
|              |               | 6430537I21RIK        |         |           | Tnfsf11       |              |         |         |         |         |       | DEAF1      | Zdhhc2        |
|              |               | 9230110C19RIK        |         |           | Plk3          |              |         |         |         |         |       | DGKA       | Il2           |
|              |               | 9230116N13RIK        |         |           | Stx12         |              |         |         |         |         |       | DHRS3      | Klrc1         |
|              |               | 9430037O13RIK        |         |           | Cysl1r1       |              |         |         |         |         |       | DKFZP434B1 | D930003E18Rik |
|              |               | 9430087J23RIK        |         |           | Egr1          |              |         |         |         |         |       | DKFZP564M  | LOC102641248  |
|              |               | 9530053H05RIK        |         |           | Tusc3         |              |         |         |         |         |       | DOCK10     | Maf           |
|              |               | 9630010G10RIK        |         |           | Rbpj          |              |         |         |         |         |       | DSCR1L2    | Alcam         |
|              |               | 9630013D21RIK        |         |           | Aprt          |              |         |         |         |         |       | EFHC1      | 2810417H13Rik |
|              |               | A930012M21RIK        |         |           | Ldha          |              |         |         |         |         |       | EIF2S3     | Cadm1         |
|              |               | A930012O16RIK        |         |           | Samsn1        |              |         |         |         |         |       | EIF3S6     | Cebpa         |
|              |               | A930026I22RIK        |         |           | 4932438H23Rik |              |         |         |         |         |       | ESD        | S100a8        |
|              |               | AA407881             |         |           | Degs1         |              |         |         |         |         |       | EZH1       | Alcam         |
|              |               | AA408396             |         |           | Adck5         |              |         |         |         |         |       | FCER1G     | Tpx2          |
|              |               | ABCB1B               |         |           | Ramp1         |              |         |         |         |         |       | FKBP5      | LOC102641248  |
|              |               | ABCB9                |         |           | Cib2          |              |         |         |         |         |       | FLJ00133   | Maf           |
|              |               | ACADSB               |         |           |               |              |         |         |         |         |       | FLT3LG     | Dcl1          |
|              |               | ACTR3B               |         |           |               |              |         |         |         |         |       | FOXP1      | Angptl2       |
|              |               | ADAMTS6              |         |           |               |              |         |         |         |         |       | FRAG1      | Acvr1         |
|              |               | ADSSL1               |         |           |               |              |         |         |         |         |       | FXYD5      | Rad54b        |
|              |               | AGL                  |         |           |               |              |         |         |         |         |       | FYB        | Nusap1        |
|              |               | AI120166             |         |           |               |              |         |         |         |         |       | GCN5L2     | Cd109         |
|              |               | AI836003             |         |           |               |              |         |         |         |         |       | GPR155     | Clec4b1       |
|              |               | AI845619             |         |           |               |              |         |         |         |         |       | GPRASP1    | Tbx21         |
|              |               | AIFM2                |         |           |               |              |         |         |         |         |       | HA-1       | Rab26         |
|              |               | AK3L1.LOC100047616   |         |           |               |              |         |         |         |         |       | HABP4      | Il18rap       |
|              |               | AKR1B8               |         |           |               |              |         |         |         |         |       | HAPLN3     | Lrr1          |
|              |               | AKTIP                |         |           |               |              |         |         |         |         |       | hIAN2      | Srpk3         |
|              |               | ALG6                 |         |           |               |              |         |         |         |         |       | hIAN6      | Tpx2          |
|              |               | ALS2CR4              |         |           |               |              |         |         |         |         |       | HIPK1      | Rora          |
|              |               | AMIGO1               |         |           |               |              |         |         |         |         |       | HIST1H4E   | Enpp2         |
|              |               | AMOTL2               |         |           |               |              |         |         |         |         |       | HNRPDL     | Lanc13        |
|              |               | ANGPTL2              |         |           |               |              |         |         |         |         |       | HOK1       | Ryk           |
|              |               | ANKRD46              |         |           |               |              |         |         |         |         |       | HPCAL4     | Synpo         |
|              |               | ANUBL1               |         |           |               |              |         |         |         |         |       | HRMT1L1    | Mpp2          |
|              |               | ANXA5                |         |           |               |              |         |         |         |         |       | HSF2       | Igfbp4        |
|              |               | APBB1                |         |           |               |              |         |         |         |         |       | HSPBAP1    | Npd1          |
|              |               | APLP1                |         |           |               |              |         |         |         |         |       | ICAM2      | Cenpf         |
|              |               | APOLD1               |         |           |               |              |         |         |         |         |       | IL23A      | Myo1f         |
|              |               | AQP1                 |         |           |               |              |         |         |         |         |       | IL6ST      | Dhrs3         |
|              |               | AREG                 |         |           |               |              |         |         |         |         |       | IMAP1      | Gm9861        |
|              |               | ARFGAP3.LOC100045474 |         |           |               |              |         |         |         |         |       | IMPDH2     | Litaf         |
|              |               | ARG1                 |         |           |               |              |         |         |         |         |       | INADL      | Cxcr5         |
|              |               | ARHGAP21             |         |           |               |              |         |         |         |         |       | INPP5A     | Gm5593        |
|              |               | ARHGEF5              |         |           |               |              |         |         |         |         |       | IRS2       | Ccnb1         |
|              |               | ARHGEF9              |         |           |               |              |         |         |         |         |       | ITGA6      | Cela1         |
|              |               | ARL4D                |         |           |               |              |         |         |         |         |       | ITPKB      | Txinb         |
|              |               | ARNT2                |         |           |               |              |         |         |         |         |       | JAK3       | Kdelc2        |
|              |               | ARPC1B.GM5637        |         |           |               |              |         |         |         |         |       | KCTD12     | Dcl1          |
|              |               | ATF4                 |         |           |               |              |         |         |         |         |       | KIAA0303   | 5330417C22Rik |
|              |               | ATF5                 |         |           |               |              |         |         |         |         |       | KIAA0582   | Gpr83         |
|              |               | ATG16L2              |         |           |               |              |         |         |         |         |       | KIAA0748   | Gng3          |
|              |               | ATHL1                |         |           |               |              |         |         |         |         |       | KIAA0922   | Aicda         |

|                     |           |               |
|---------------------|-----------|---------------|
| ATL3                | KIAA1078  | Mki67         |
| ATP10A              | KIAA1189  | Ndr4          |
| ATP2B2              | KIAA1729  | Kif4          |
| AV249152            | KIAA1971  | Osbp13        |
| AW555355            | KIF2      | Ccnb2         |
| B230312A22RIK       | KIFAP3    | Endod1        |
| B3GALT5             | KLF7      | Birc5         |
| B4GALT1             | LASS6     | Endod1        |
| B4GALT5             | LCHN      | Cnn3          |
| B830008J18RIK       | LDHB      | Fads2         |
| B930095G15RIK       | LEF1      | Srxn1         |
| BACE2               | LENG10    | Kif11         |
| BAIAP2L1            | LEPROTL1  | S100a4        |
| BARD1               | LETMD1    | Zbtb32        |
| BB557941            | LGTN      | Lacc1         |
| BC010981            | LIAS      | Pbk           |
| BC023744            | LISCH7    | 8-Mar         |
| BC046404            | LKAP      | Tnfsf14       |
| BC068157            | LNPEP     | Gm3924        |
| BCL2L1              | LOC129293 | Endod1        |
| BCL2L15             | LOC143903 | Bmp7          |
| BCL6B               | LPAAT-e   | Gm34221       |
| BCMO1               | LRRC5     | Ctla2b        |
| BEND6               | LRRN3     | Alcam         |
| BMPR2               | LT44H     | Myo1f         |
| BNIP3               | LTB       | Plek          |
| BRCA2               | LY96      | Optn          |
| BSPRY               | LYPLAL1   | Srxn1         |
| BTBD10.LOC100047893 | MAGEH1    | Gstt3         |
| C130057M05RIK       | MAL       | Gm5593        |
| C1QL3               | MAML2     | Ccnb1         |
| C230098O21RIK       | MAN1C1    | Zdhc2         |
| C76533              | MDS2      | Bub1          |
| C77545              | MEST      | Jdp2          |
| C80258              | MGC15763  | Tmem2         |
| CABLES1             | MGC17330  | 8030451A03Rik |
| CALCB               | MMS19L    | Chrd1         |
| CALD1               | MPHOSPH9  | Cdca8         |
| CAMK2N1             | MRPL1     | Soat2         |
| CAMK4               | MSL3L1    | S100a6        |
| CAPSL               | MTRF1     | Atp1b1        |
| CAR13               | MTUS1     | Morn4         |
| CAR6                | MYB       | Klrc1         |
| CAV1                | MYC       | Spag5         |
| CAV2                | NDE1      | Tjp2          |
| CCDC112             | NDFIP1    | Igfbp4        |
| CCDC122             | NDUFB5    | Ccna2         |
| CCDC21              | NELL2     | Ampd1         |
| CCDC34              | NGFRAP1   | Runx2         |
| CCL1                | NKX3-1    | Stfa3         |
| CCL27A              | NOG       | Igfbp4        |
| CCR8                | NRCAM     | Gm17619       |
| CD200R4             | NUCB2     | Tshz2         |
| CD34                | PCSK5     | Gpm6a         |
| CD70                | PDK1      | Ncapp         |
| CD93                | PHEMX     | Tk1           |
| CDC14A              | PIK3CD    | Kitl          |
| CDC14A.LOC100047731 | PLAC8     | Morc1         |
| CDC25C              | RAC2      | Dtl           |
| CDK6                | RAPGEF6   | Aifm2         |
| CENPA               | RASA2     | Gm36401       |
| CENPI               | RASA4     | Adam19        |
| CENPP               | RIN3      | Stil          |
| CETN4               | RNU22     | Kif14         |
| CHAC1               | SAMHD1    | Igfbp4        |
| CHST10              | SP110     | Ccnb1         |
| CHST12              | STK4      | Gzmk          |
| CIAPIN1             | STX16     | Proser2       |
| CILP2               | SUMF2     | Ccna2         |
| CKAP2               | T3JAM     | Rragd         |
| CLDN12              | TM4SF8    | Pawr          |
| CLEC4D              | TPP2      | Pif1          |
| CNNM2               | TTC11     | Ccnf          |
| CNRIP1              | USP52     | Esco2         |
| CNTLN               | VPS35     | 2810417H13Rik |
| COCH                | WDR42A    | Gna15         |
| COL1A2              | ZFP90     |               |
| COPZ2               | ZNF291    |               |
| CPA2                | ZNF44     |               |
| CPE.LOC100046434    |           |               |
| CRYBG3              |           |               |
| CSF2                |           |               |
| CTNND2.LOC100045979 |           |               |
| CTSC                |           |               |
| CTSD                |           |               |
| CXCL1               |           |               |
| CXCL2               |           |               |
| CXCL3               |           |               |
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ORC4L  
PEX11A  
PHF23  
PHKA2  
PIGN  
PLEKHH1  
POLH  
POLK  
POPC2  
PRKACA  
PRMT1  
RAB27A  
RAB7  
RIN3  
RNASEH2C  
RNF170  
RPS6KC1  
S100A10  
SDCCAG10  
SRP54A.SRP54B.SRP54C  
SUDS3  
SYT11  
TARSL2  
TBC1D2B  
TBC1D7  
TM9SF3  
TMBIM4  
TMEM180  
TMEM29  
TMEM39A  
TNFSF14  
TRAPPC1  
TRAPPC4  
TRPT1  
TSEN2  
TSGA14

Supplemental Table 2:

Experimental Mice used

Main-seq

| Background | Mouse number | Age at Sacrifice | Proteinuria | Gender |
|------------|--------------|------------------|-------------|--------|
| MRL/lpr    | 1            | 21 weeks         | 4           | F      |
| MRL/lpr    | 2            | 21 weeks         | 2.5         | F      |
| MRL/lpr    | 3            | 21 weeks         | 1           | F      |
| C57Bl/6    | 4            | 8 weeks          | 0           | F      |

MRL-TCRseq

| Background | Mouse number | Age at Sacrifice | Proteinuria | Gender | GN score | IN Score |
|------------|--------------|------------------|-------------|--------|----------|----------|
| MRL/lpr    | 1            | 20.5 weeks       | 4           | F      | 3.5      | 1.5      |
| MRL/lpr    | 2            | 21 weeks         | 2.5         | F      | 3        | 1.5      |
| MRL/lpr    | 3            | 21 weeks         | 1           | F      | 2        | 1        |
| MRL/lpr    | 4            | 25.5 weeks       | 4           | F      | 5        | 2.5      |
| MRL/lpr    | 5            | 25.5 weeks       | 4           | F      | 6        | 3        |

Yaa-TCRseq

| Background                      | Mouse number | Age at Sacrifice | Proteinuria | Gender | GN score | IN Score |
|---------------------------------|--------------|------------------|-------------|--------|----------|----------|
| <i>FcyR2b<sup>-/-</sup>.Yaa</i> | 1            | 23.5 weeks       | 4           | M      | 5        | 2        |
| <i>FcyR2b<sup>-/-</sup>.Yaa</i> | 2            | 24 weeks         | 4           | M      | 2        | 0.5      |
| <i>FcyR2b<sup>-/-</sup>.Yaa</i> | 3            | 23.5 weeks       | 2.5         | M      | 4        | 1        |
| <i>FcyR2b<sup>-/-</sup>.Yaa</i> | 4            | 23.5 weeks       | 3           | M      | 3        | 0.5      |
| <i>FcyR2b<sup>-/-</sup>.Yaa</i> | 5            | 23 weeks         | 2           | M      | 4        | 2        |