

Supplementary Table S1 Gene sets of IFN- γ response, effector genes, cytolytic score

| | | | | |
|--------------------------------|---------|----------|----------|---------|
| IFN- γ Response (M5913) | Il10ra | Trim26 | H2-Eb2 | Cdkn1a |
| Stat1 | Pla2g4a | Vcam1 | Gbp4 | Irf4 |
| Isg15 | Trim21 | Cd274 | Lcp2 | Nfkb1 |
| Ifit1 | Usp18 | Ciita | H2-M3 | Batf2 |
| Mx2 | Ptgs2 | Nampt | Mt2 | H2-K1 |
| Ifit3b | Epsti1 | Selp | Ripk1 | Lats2 |
| Ifi35 | C1s2 | Gpr18 | Klrk1 | Irf5 |
| Irf7 | Ddx58 | Fpr1 | Upp1 | Slamf7 |
| Ifit2 | Il15 | Helz2 | Psmb2 | Isoc1 |
| Oas2 | Nlrc5 | Psme2 | Tdrd7 | P2ry14 |
| Tap1 | Nmi | Serping1 | Hif1a | Stat3 |
| Eif2ak2 | Ido1 | Ccl5 | Eif4e3 | Ncoa3 |
| Rsad2 | Psmb10 | Rnf31 | Vamp8 | H2-K1 |
| Mx2 | Cxcl11 | Sod2 | Pfkip | Il6 |
| Irf1 | Itgb7 | Trim25 | Cd38 | Gzma |
| Oas3 | Samhd1 | Lap3 | Zbp1 | Ifnar2 |
| Tnfsf10 | Herc6 | Psma3 | Bank1 | Cd74 |
| Irf9 | Cmpk2 | Peli1 | Tor1b | Rapgef6 |
| Cxcl10 | Samd9l | Cfb | Rbck1 | Casp4 |
| Ifi44 | Rtp4 | Cd86 | Pde4b | Fas |
| Bst2 | Ptpn2 | Txnip | Mvp | Ogfr |
| Xaf1 | Parp14 | H2-Aa | Il7 | Arl4a |
| Sp110 | Tnfaip2 | Gch1 | Bpgm | Sri |
| Oasl1 | Ifitm2 | Pnp | Cmtr1 | Lysmd2 |
| Psmb8 | Plscr1 | Ccl7 | Auts2 | Csf2rb |
| Ifi44l | Socs1 | Ptpn6 | B2m | St3gal5 |
| Ifitm3 | Casp1 | Sppl2a | Ripk2 | C1ra |
| Ddx60 | Icam1 | Il4ra | Cd69 | Casp3 |
| Lgals3bp | Wars | Pnpt1 | Myd88 | Cmklr1 |
| Gbp3 | Psme1 | Dhx58 | Psma2 | Nfkbia |
| Irf8 | Isg20 | Btg1 | Pim1 | Mettl7b |
| Psmb9 | Irf2 | Casp8 | Nod1 | St8sia4 |
| Pml | Trim14 | Ifi30 | Cfh | Xcl1 |
| Ifih1 | Fcgr1 | Ccl12 | Tapbp | Il2rb |
| Ube2l6 | March1 | Fgl2 | Slc25a28 | Vamp5 |
| Ifi27 | Socs3 | Casp7 | Ptpn1 | Il18bp |
| Adar | Jak2 | Sectm1a | Tnfaip3 | Znfx1 |
| Ly6e | H2-DMA | Il15ra | Sspn | Arid5b |
| Stat2 | Parp12 | Cd40 | Nup93 | Apol6 |
| Cxcl9 | Tnfaip6 | Trafd1 | Mthfd2 | Stat4 |

| | | | | |
|----------------------------|-----------|---------|----------|---------|
| Effector Geneset (GSE9650) | Cdk1 | Gng11 | Mapk3 | Reps1 |
| Nlrp1a | Cdkn2c | Gnpda1 | Mapre2 | Rfc4 |
| Acot7 | Cdkn3 | Gzma | Mbd2 | Rhpn2 |
| Actb | Chd7 | Gzme | Mdfic | Rnf14 |
| Actc1 | Commd1 | Gzmk | Med12l | Rnf19b |
| Actn4 | Cox17 | Haspin | Mis18bp1 | Rora |
| Acyp2 | Crip2 | Hk2 | Mns1 | Rps6ka4 |
| Adam19 | Cstb | H2-K1 | Mrpl27 | Rsu1 |
| Agpat3 | Ctla4 | Hmgb2 | Mrps16 | S100a10 |
| Ahnak | Ctsa | Hopx | Msrp1 | S100a11 |
| Aip | Ctsd | Hoxd13 | Mt2 | S100a13 |
| Anxa1 | Cx3cr1 | Hsd11b1 | Myo1f | S100a4 |
| Anxa2 | Cxcr3 | Id2 | Ndufa8 | S100a6 |
| Anxa6 | Dap | Ifitm10 | Ndufb6 | Sf3b6 |
| Arf6 | Dapk2 | Ifng | Ndufb7 | Sgo1 |
| Arhgdib | Dbi | Il10ra | Ndufv3 | Sh2d1a |
| Asl | Dcps | Il18r1 | Nrp1 | Sh2d2a |
| Atpif1 | Dennd5a | Il18rap | P3h4 | Sirt2 |
| Atp6v0e | Dhrs1 | Itga4 | Padi2 | Smap1 |
| Aurkb | Dkk2 | Itgal | Pald1 | Smyd1 |
| Batf | Dlgap5 | Itgam | Pcyt1a | Snrnp27 |
| Bcl2a1b | Dock5 | Itgax | Pglyrp1 | Sntb2 |
| Bhlhe40 | Dtl | Itgb1 | Plscr1 | Snx10 |
| Birc5 | E2f8 | Jak1 | Ppib | Spdl1 |
| Bscl2 | Elovl1 | Kcnj8 | Pqlc3 | St3gal4 |
| Btf3 | Entpd1 | Kif22 | Prdx4 | Stab1 |
| Capn2 | Errfi1 | Klrc1 | Preld1 | Stard10 |
| Capns1 | Etfb | Klrg1 | Prf1 | Tcf19 |
| Carhsp1 | Fadd | Klrk1 | Prim2 | Tmem160 |
| Casp1 | Fam89b | Lamc1 | Prr13 | Tmem37 |
| Casp4 | Fasl | Lamtor5 | Prrc1 | Trappc1 |
| Casp7 | Fcgr2b | Lgals1 | Psma2 | Tspan31 |
| Ccl5 | Fcgrt | Lgals3 | Psmb10 | Tspo |
| Ccne1 | Fgl2 | Lig1 | Psmd8 | Ttk |
| Ccr2 | Frg1 | Litaf | Ptgr1 | Txndc5 |
| Ccr5 | Gabarapl1 | Lman2 | Ptpn13 | Unc119 |
| Cd160 | Gabarapl2 | Lpin1 | Pttg1 | Wnt3 |
| Cd48 | Galnt3 | Lrp10 | Rac2 | Xdh |
| Cd68 | Gem | Lsm1 | Racgap1 | Ybx3 |
| Cdc34 | Glrx | Lxn | Reep5 | Ykt6 |

| |
|-----------------|
| Cytolytic Score |
| Gzma |
| Gzmb |
| Prf1 |

Supplementary Table S3 Primer and oligo sequences used in this study.

| sgRNA sequences | |
|----------------------------|-------------------------------|
| sgTet2 1F | CACCGCGATGGTTGAGGGATCTCGT |
| sgTet2 1R | aaacACGAGATCCCTCAACCATCGC |
| sgTet2 2F | CACCGCTGACGGCTGCTTTTACCG |
| sgTet2 2R | aaacCGGTAAAAGCAGCCGTCAGC |
| sglfng1 F | CACCGCGACTTCAGGGTAAAATACG |
| sglfng1 R | aaacCGTATTTACCCCTGAAGTCG |
| qPCR primers | |
| mlfng-F | CGGCACAGTCATTGAAAGCCTA |
| mlfng-R | GTTGCTGATGGCCTGATTGTC |
| mCxcl9-F | GAGCAGTGTGGAGTTCGAGG |
| mCxcl9-R | TCCGGATCTAGGCAGGTTTG |
| mCxcl10-F | AATGAGGGCCATAGGGAAGC |
| mCxcl10-R | AGCCATCCACTGGGTAAAGG |
| mTet2-F | AGAGAAGACAATCGAGAAGTCGG |
| mTet2-R | CCTTCCGTA CTCCCAA ACTCAT |
| m-Actb-F | CATTGCTGACAGGATGCAGAAGG |
| m-Actb-R | TGCTGGAAGGTGGACAGTGAGG |
| mCd80-F | GCAGGATACACCACTCCTCAA |
| mCd80-R | AAAGACGAATCAGCAGCACAA |
| mCd274-F | AGTATGGCAGCAACGTCACG |
| mCd274-R | TCCTTTTCCAGTACACCACTA |
| mlrf1-F | GGCCGATACAAAGCAGGAGAA |
| mlrf1-R | GGAGTTCATGGCACAACGGA |
| mlrf7-F | GAGACTGGCTATTGGGGGAG |
| mlrf7-R | GACCGAAATGCTTCCAGGG |
| mlfit3-F | GCTCAGGCTTACGTTGACAAGG |
| mlfit3-R | CTTTAGGCGTGTCCATCCTTCC |
| mCd74-F | AGTGCGACGAGAACGGTAAC |
| mCd74-R | CGTTGGGGAACACACACCA |
| mKrt19-F | GCCACCTACCTTGCTCGGATTG |
| mKrt19-R | GTCTCTGCCAGCGTGCCTTC |
| mKlf5-F | GGTTGCACAAAAGTTTATAC |
| mKlf5-R | GGCTTGGCGCCCGTGTGCTTCC |
| mKrt7-F | CGCCGCTGAGTGTGGACATCG |
| mKrt7-R | CTGGCTGCTCTTGGCTGACTTCTG |
| hCD274-F | TGCCGACTACAAGCGAATTACTG |
| hCD274-R | CTGCTTGTCCAGATGACTTCGG |
| hIRF1-F | GAGGAGGTGAAAGACCAGAGCA |
| hIRF1-R | TAGCATCTCGGCTGGACTTCGA |
| hIFIT3-F | CCTGGAATGCTTACGGCAAGCT |
| hIFIT3-R | GAGCATCTGAGAGTCTGCCCAA |
| hACTB-F | CACCATTGGCAATGAGCGGTTT |
| hACTB-R | AGGTCTTTGCGGATGTCCACGT |
| hMeDIP qPCR primers | |
| mCd274-F | AACACTAGATACCTAAACTGAAAGCTTCC |
| mCd274-R | GGCCCGGAGGCGG |
| mlrf1-F | CTCAATTTCCAGAGCAGCC |
| mlrf1-R | CCTCTTTCTGCAGACTCCCA |
| Genotyping primers | |
| gldh1F1 | GTCAAAGGCTGGCATGGTATAAT |
| gldh1R1 | TGGGCTCTATGGATAACTTCGTA |
| gldh1R2 | GAGGACCTGAGTAACTCCCTTTT |

| | |
|-------------------|-------------------------|
| gKras- 22907 | TGTCTTTCCCCAGCACAGT |
| gKras- 22908 | CTGCATAGTACGCTATACCCTGT |
| gKras- oIMR9592 | GCAGGTCGAGGGACCTAATA |
| gAlb-Cre- 20239 | TGCAAACATCACATGCACAC |
| gAlb-Cre- 20240 | TTGGCCCCTTACCATAACTG |
| gAlb-Cre-oIMR5374 | GAAGCAGAAGCTTAGGAAGATGG |

Supplementary Table S4 Cell type classification and labeling for calculating differentially expressed marker genes

| Cell type | Gene1 | Gene2 | Gene3 | Gene4 | Gene5 | Gene6 | Gene7 | Gene8 | Gene9 | Gene10 |
|---------------------------|----------------|----------------|---------------|---------------|---------------|---------------|---------------|-------------|------------|-------------|
| M1 | <i>Itgam</i> | <i>Ctsc</i> | <i>Cd74</i> | <i>C1qa</i> | <i>Cxcl9</i> | <i>Vcam1</i> | <i>Cd38</i> | | | |
| M2 | <i>Itgam</i> | <i>Lyz2</i> | <i>C1qb</i> | <i>Folr2</i> | <i>Mrc1</i> | <i>Arg1</i> | <i>Egr2</i> | <i>Lgmn</i> | <i>Il6</i> | <i>Cd74</i> |
| MDSC | <i>Itgam</i> | <i>Arg1</i> | <i>Fn1</i> | <i>Nos2</i> | <i>Pf4</i> | <i>Il1rn</i> | | | | |
| Neutrophils | <i>Itgam</i> | <i>S100a9</i> | <i>S100a8</i> | <i>Malat1</i> | <i>Ly6g</i> | | | | | |
| Neutrophil-like-monocytes | <i>Il1b</i> | <i>S100a9</i> | <i>S100a8</i> | <i>Ly6g</i> | <i>Ms4a4c</i> | <i>Ly6c2</i> | | | | |
| Monocyte | <i>Itgam</i> | <i>Ms4a6c</i> | <i>Lyz2</i> | <i>Il1b</i> | <i>Cxcl10</i> | <i>Ms4a4c</i> | <i>Ly6c2</i> | | | |
| DCs | <i>H2-Aa</i> | <i>Cd74</i> | <i>Flt3</i> | <i>Cd209a</i> | <i>Zbtb46</i> | <i>Batf3</i> | <i>H2-Ab1</i> | | | |
| pDCs | <i>Siglech</i> | <i>Bst2</i> | <i>Ccr9</i> | | | | | | | |
| Fibroblasts | <i>Sparc</i> | <i>Cd63</i> | <i>Dcn</i> | <i>Col3a1</i> | <i>Col1a2</i> | <i>Plaur</i> | | | | |
| Suppressive Stroma | <i>C1qb</i> | <i>H2-Eb1</i> | <i>ApoE</i> | <i>Arg1</i> | <i>C1qa</i> | | | | | |
| Adipocytes | <i>Cd5l</i> | <i>Ctsb</i> | <i>Il1b</i> | <i>Il6</i> | <i>Cd274</i> | | | | | |
| Endothelial | <i>Sparc</i> | <i>Selenop</i> | <i>Pecam1</i> | <i>Lyve1</i> | <i>Tek</i> | | | | | |
| MAST Cells | <i>Srgn</i> | <i>Lilr4b</i> | <i>Cpa3</i> | | | | | | | |
| Tcells | <i>Cd8a</i> | <i>Cd3d</i> | <i>Trbc2</i> | <i>Cd4</i> | <i>Pdcd1</i> | | | | | |
| Bcells | <i>Cd79a</i> | <i>Ighm</i> | <i>Cd79b</i> | <i>Cd19</i> | <i>Ms4a1</i> | <i>Cd22</i> | | | | |
| Plasma Cells | <i>Jchain</i> | <i>Igkc</i> | <i>Slamf7</i> | | | | | | | |
| Nk cells | <i>Ncr1</i> | <i>Gzma</i> | <i>Gzmb</i> | <i>Klra7</i> | <i>Klre1</i> | | | | | |
| Proliferating Tcells | <i>Stmn1</i> | <i>Hmgb2</i> | <i>Top2a</i> | <i>Cenpe</i> | <i>Mki67</i> | | | | | |

Supplementary Table S5 Gene list of HNF4 α target genes from TRANSFAC Predicted Transcription Factor Targets

| | | | |
|----------------------------|-----------|---------|----------|
| HNF4 α target genes | TNFAIP8L2 | CMIP | SYAP1 |
| RSPO1 | ZBTB42 | NARS | SPSB2 |
| CILP | RNFT2 | GPN3 | PCSK7 |
| PLXDC2 | OSBPL5 | RAE1 | ESPL1 |
| DCN | RAB18 | SHANK2 | PQLC1 |
| LTF | HIST1H2BL | POLR2D | CLSTN2 |
| CRISP1 | COMMD7 | RDH11 | CSRP2 |
| COL6A5 | PROSER2 | PXDN | SMARCA5 |
| ACP5 | KBTBD6 | ALDH3B1 | PHF6 |
| ITGB8 | UBA7 | MARK2 | PLAT |
| ELN | BMP1 | ESYT1 | LAMC1 |
| CERS4 | LYN | MKL2 | RPS26 |
| FAIM2 | AFP | NDUFB4 | NR2F2 |
| MUC1 | TXNDC5 | SFXN2 | MRT04 |
| FAM83A | JUP | PIP5K1B | KDM5A |
| PI16 | INTU | TNFSF10 | MRPL20 |
| TMEM45A | ARHGEF3 | EXOSC10 | NLE1 |
| MDFI | EPB41L1 | PLRG1 | SF3B2 |
| IGSF9B | ENDOG | RANBP3 | LPAR2 |
| CNTLN | CLSTN1 | STK4 | RRBP1 |
| LAMC2 | RPS6KA4 | SSR4 | ERC1 |
| EMILIN1 | FAM216A | VEGFA | CTNBL1 |
| SLC36A4 | ADAMTS12 | EHBP1L1 | RAB4B |
| TMEM229B | MINPP1 | ARFIP1 | TOMM34 |
| ITIH2 | XKRX | CYB5B | RAB3IP |
| BLK | EXOSC9 | OXR1 | XRCC5 |
| PPP1R26 | ACMSD | DENR | TAB3 |
| CCRL2 | VPS26B | CHCHD1 | CBX4 |
| CDC42EP3 | CSNK1G2 | COX8A | RABGAP1 |
| MAN1C1 | PLEC | PTPRG | CISD3 |
| IKBKG | ATG4C | HSBP1 | BPTF |
| WNK2 | FIS1 | TCF20 | ENY2 |
| SLC7A7 | CYB5R3 | LYRM2 | FMN1 |
| SLC26A4 | ATXN1L | TBL1X | STIP1 |
| PTPRR | MAF1 | BAG4 | CUEDC2 |
| CRLF1 | GTPBP10 | RNF103 | POGZ |
| SH3TC2 | UBLCP1 | TOP2B | ARHGAP21 |
| ESRP2 | GNAI2 | NUDCD1 | BCL3 |
| SERPINA7 | FZD4 | LINGO1 | ERCC1 |
| KCTD21 | DMRTA2 | ZBTB38 | DGKA |
| TMEM185B | ALDH3A2 | SNX12 | GAS8 |
| CYTH4 | FAM89B | DLD | PITPNM1 |
| ELAC1 | ORAI2 | RUFY3 | NMI |
| HTR1B | HYAL1 | ERCC3 | FADS2 |
| ST8SIA4 | NCOA1 | CSAD | LIF |
| SCN5A | GEMIN7 | GPHN | SMCR8 |

| | | | |
|----------|----------|----------|---------|
| MALL | STK38L | TMEM175 | NFIA |
| COL18A1 | RPUSD1 | RCBTB2 | DCAF6 |
| NR1H3 | HMG3 | CREBRF | ZFP36L1 |
| CNTNAP2 | CLPB | TMEM183A | RPL10A |
| SLC13A2 | ME2 | SMIM11 | SMS |
| RBP1 | TRIM5 | PNO1 | THSD1 |
| HIST1H3H | N4BP3 | ECHS1 | KIF11 |
| CDA | CALCRL | MALT1 | FASTKD2 |
| AWAT2 | HSPA13 | MPC2 | CDR2L |
| PSKH1 | DNAL4 | SLC12A6 | ZHX3 |
| GNE | ARHGEF17 | SLC9A8 | COMP |
| MYLK | SEC61G | NOD1 | ANKRD17 |
| RHBDD2 | SNW1 | BCAT2 | RASD1 |
| RGS16 | AP2S1 | MCOLN1 | NTNG2 |
| CCDC8 | ABHD16B | NOL4 | STYXL1 |
| GPT | PTPN22 | CCDC114 | CD46 |
| KIFC2 | ODF2L | CHST1 | CRYBA1 |
| MAFK | SIRT1 | SLC10A1 | SLC23A1 |
| CIART | DTL | ARHGEF4 | CHRM4 |
| ARID3B | CHD5 | COL2A1 | MMRN2 |
| TMEM251 | COL20A1 | FKBP11 | IFNE |
| IFITM5 | EFCAB5 | TAS1R3 | VSIG2 |
| USP37 | NR1D2 | PLCD4 | ACRV1 |
| IRX3 | DNASE1 | ADRA2A | POU5F2 |
| COL6A2 | CUBN | CABP7 | PRR29 |