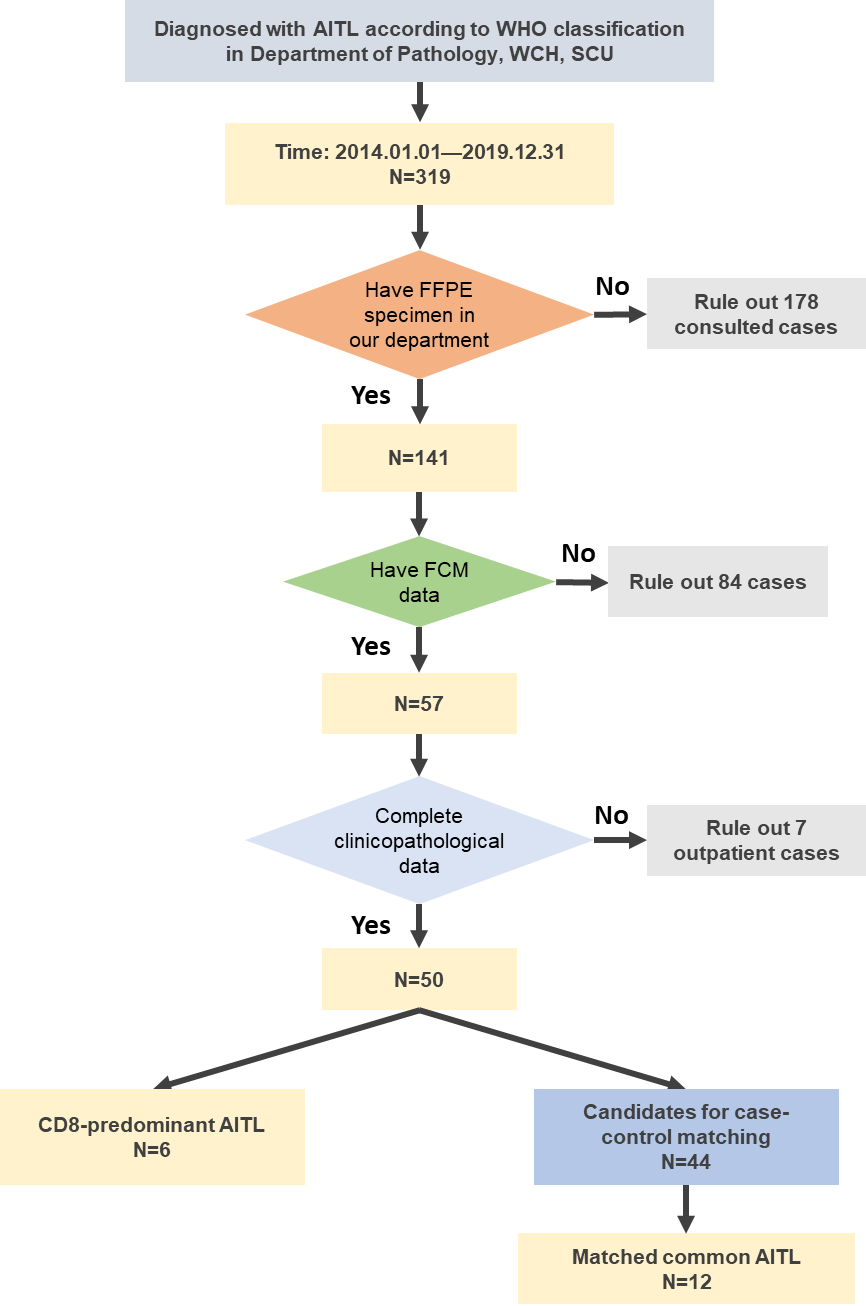
**Supplementary method**

***Case Selection***

Flowchart of case selection



***Histological, Immunohistochemical, and Epstein–Barr virus (EBV) Status Assessment***

Antibody reagents for immunohistochemical stating in this study

| **Antibody** | **Clonal** | **Manufacturer** | **Dilution** |
| --- | --- | --- | --- |
| CD20 | L26 | DAKO | 1:100 |
| CD2 | 2CO2 | Neomarkers | 1:100 |
| cCD3 | PS1 | DAKO | 1:100 |
| CD4 | 1F6 | Maixin | 1:50 |
| CD5 | 4C7 | Novocastra | 1:100 |
| CD8 | C8 | Maixin | 1:100 |
| CD10 | SP67 | ZhongShan | 1:150 |
| CD21 | EP64 | MaiXin | 1:100 |
| CD30 | Ber-H2 | Neomarkers | 1:50 |
| Bcl-6 | MX042 | MaiXin | 1:100 |
| CXCL13 | polyclonal | ZhongShan | 1:100 |
| PD1 | UMAB199 | ZhongShan | 1:50 |
| βF1 | TCR1151 | Endogen | 1:100 |
| Ki-67 | MIB1 | Neomarkers | 1:150 |

***Flow Cytometry***

Antibody reagents for flow cytometry in this study

|  |  |  |  |
| --- | --- | --- | --- |
| **Antibody** | **clonal** | **Fluorescence** | **Manufacturer** |
| CD2 | S5.2 | FITC | BD |
| CD3 | SK7 | PE/Percp-cy5-5 | BD |
| CD4 | SK3 | PE-cy7 | BD |
| CD5 | L17F12 | PerCP-cy5-5 | BD |
| CD7 | 4H9 | PE | BD |
| CD8 | SK1 | APC | BD |
| CD19 | SJ25C1 | AmCyam | BD |
| CD20 | L27 | APC-cy7 | BD |
| CD30 | Ber-H83 | FITC | BD |
| CD38 | HB7 | APC | BD |
| CD45 | 2D1 | APC-cy7 | BD |
| CD56 | NCAM16.2 | PE-cy7 | BD |
| Kappa | TB28-2 | FITC | BD |
| Lambda | 1-155-2 | PE | BD |

***TRB and IGH Sequencing***

According to the manufacturer’s instructions, TRB clonal rearrangement (monoclonal TRB rearrangement) was defined as follow and Top 1 clone in the case with monoclonal TRB rearrangement was regarded as lymphoma-derived clone

|  |  |
| --- | --- |
| **Condition** | **Criteria for monoclonal TRB rearrangement** |
| Total reads ≥20,000 | Reads of Top 1 clone > 2.5% total reads  Reads of Top 1 clone > twice of the reads of Top 3 clone |
| 10,000≤ Total reads <20,000 | Reads of Top 1 clone > 5% total reads  Reads of Top 1 clone > twice of the reads of Top 3 clone |

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The brief information of TRB sequencing data and identified lymphoma-derived clone of each case in this study were listed as follow:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Lymphoma derived clone** | | |
| **Case** | **Total reads** | **Reads** | **Frequency**  **(%)** | **CDR3** |
| C1 | 80960 | 9213 | 11.4 | CASSLGTGTNTEAFF |
| C2 | 81163 | 22837 | 25.1 | CASSRPQGEDTEAFF |
| C3 | 292931 | 101940 | 34.8 | CASSLLLGTEAFF |
| C4 | 270339 | 45417 | 16.8 | CATRYNYGYTF |
| C5 | 14544 | 2647 | 19.2 | CASSQETGRSDPLHF |
| N1 | 48638 | 12784 | 26.3 | CASSTANTEAFF |
| N2 | 145954 | 49008 | 33.8 | CASSFNQTPPLCYEQYF |
| N3 | 175029 | 50651 | 28.9 | CSAVGSYNEQFF |
| N4 | 248657 | 51822 | 18.3 | CSARYGTSGYNEQFF |
| N5 | 315572 | 163151 | 51.7 | CASSQEGWEGLNTEAFF |
| N6 | 173384 | 28790 | 16.6 | CASSLGRRVLEAFF |
| N7 | 117206 | 45876 | 39.1 | CASSATGDQPQHF |
| N8 | 222165 | 41545 | 18.7 | CASSQLETQYF |
| N9 | 96463 | 17074 | 17.7 | CASSRPGDYGYTF |
| N10 | 227583 | 36641 | 16.1 | CASSRQGTGDTQYF |
| N11 | 169391 | 11681 | 6.9 | CASSQVSTSGETQYF |
| N12 | 207255 | 95575 | 46.1 | CASSYSGGTYGYTF |

***RNA Sequencing***

The gene expression analysis was focus on the inflammation and immune response. The gene panel (772 genes) was designed based on the gene ontology biological process annotation. To reduce selection bias, all genes related to inflammation and immune response in the database of gene ontology biological process annotation (http://amigo.geneontology.org/amigo/search/annotation) were obtained and then the duplication, non-human genes, and gene products were removed. Then, in this designed gene panel, a comparative analysis was performed to identify the significantly differentially expressed genes. Finally, functional annotation was performed on the significantly differentially expressed genes.

Inflammation and immune response related gene panel

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| ***TAG*** | ***BCL3*** | ***EOMES*** | ***CYSLTR2*** | ***SASH3*** | ***CD3G*** | ***RAB27A*** | ***TNFRSF13B*** | ***CDH17*** | ***TBX21*** |
| ***FOXP3*** | ***IRAK3*** | ***PTK2B*** | ***IL6ST*** | ***SCTR*** | ***RIN3*** | ***PRKAR2B*** | ***SLIT2*** | ***TWSG1*** | ***DLG5*** |
| ***PAG1*** | ***LFNG*** | ***PRNP*** | ***TRIM27*** | ***RNF125*** | ***RUNX1*** | ***CBLB*** | ***IL1B*** | ***FAM3A*** | ***SOCS6*** |
| ***CD1C*** | ***POU2AF1*** | ***INHA*** | ***CLEC7A*** | ***TNF*** | ***GNG2*** | ***CD86*** | ***THOC1*** | ***CCL25*** | ***CD1D*** |
| ***CD226*** | ***IRF4*** | ***THY1*** | ***OTOP1*** | ***KLRK1*** | ***RAMP1*** | ***C3*** | ***DTX1*** | ***GPR27*** | ***RELB*** |
| ***CRH*** | ***P2RY11*** | ***HAVCR2*** | ***GPR116*** | ***IL4*** | ***SYK*** | ***ITFG2*** | ***PRKCQ*** | ***MERTK*** | ***ALOX15*** |
| ***TLR4*** | ***HMCES*** | ***SFTPD*** | ***HMGB1*** | ***ZBTB1*** | ***DPP4*** | ***FZD5*** | ***DUSP3*** | ***GNRH1*** | ***NFKBID*** |
| ***DOCK11*** | ***SAMHD1*** | ***OAS3*** | ***IL1RL1*** | ***HTRA1*** | ***NFKBIZ*** | ***CD163*** | ***IL18*** | ***IL13RA2*** | ***CD40LG*** |
| ***CORO1A*** | ***LEF1*** | ***PTPN6*** | ***NLRC3*** | ***ANGPT1*** | ***PDCD1LG2*** | ***JAK3*** | ***IFI16*** | ***MAFB*** | ***SRC*** |
| ***NR1D1*** | ***TRAFD1*** | ***TOB2*** | ***SERPINB9*** | ***RSAD2*** | ***RARA*** | ***IL1R1*** | ***ZBTB7B*** | ***WASL*** | ***FAM65B*** |
| ***CD1A*** | ***ADCY1*** | ***PIBF1*** | ***IL10*** | ***CLEC4G*** | ***SYT11*** | ***TMEM98*** | ***LGALS9C*** | ***LOXL3*** | ***PPP3CB*** |
| ***ZFPM1*** | ***GNB1*** | ***C1QC*** | ***NME1*** | ***CD200R1*** | ***ADRB2*** | ***MC4R*** | ***ADORA2A*** | ***FBXO7*** | ***TSPAN32*** |
| ***KITLG*** | ***CACTIN*** | ***RHBDF2*** | ***GPATCH3*** | ***CD19*** | ***MFNG*** | ***PCBP2*** | ***LYAR*** | ***DHX58*** | ***PLA2G4A*** |
| ***PDCD1*** | ***SERPING1*** | ***TYROBP*** | ***CSDE1*** | ***PTGDR*** | ***PTPRJ*** | ***TRIB1*** | ***UBASH3B*** | ***GPR137*** | ***TGFB1*** |
| ***FGL2*** | ***ADCY7*** | ***CASP3*** | ***IL27RA*** | ***ADORA2B*** | ***VSIG4*** | ***FCGR1A*** | ***MME*** | ***IRF8*** | ***FCGR3A*** |
| ***HLA-DMB*** | ***ADRB1*** | ***CD274*** | ***TBC1D10C*** | ***MC1R*** | ***LRFN5*** | ***CX3CR1*** | ***RUNX3*** | ***IRF1*** | ***CD22*** |
| ***NDFIP1*** | ***HFE*** | ***FCRLB*** | ***LCP1*** | ***NBN*** | ***CALCRL*** | ***SMAD7*** | ***AVPR2*** | ***MAP3K7*** | ***BTN2A2*** |
| ***PRKCZ*** | ***PELI1*** | ***HRH2*** | ***TMEM176A*** | ***MSH2*** | ***GATA3*** | ***PGLYRP2*** | ***IL2*** | ***ERCC1*** | ***GPR20*** |
| ***TMBIM6*** | ***B2M*** | ***NMI*** | ***STAP1*** | ***RPS6*** | ***APPL1*** | ***CNR1*** | ***TREM2*** | ***TNFSF18*** | ***IL23A*** |
| ***TMEM176B*** | ***INPP5D*** | ***CLCF1*** | ***HLA-B*** | ***IL18R1*** | ***BMP4*** | ***BLK*** | ***CCR6*** | ***MALT1*** | ***APOD*** |
| ***CR1L*** | ***ITGAL*** | ***GGT5*** | ***SUSD4*** | ***FCGR2A*** | ***PAWR*** | ***TGFB3*** | ***GHRH*** | ***GPR15*** | ***IL12RB1*** |
| ***MUL1*** | ***PTH1R*** | ***TSPAN6*** | ***CCL19*** | ***ADAM17*** | ***CD96*** | ***C4BPB*** | ***PVR*** | ***CNOT7*** | ***DAK*** |
| ***DRD5*** | ***CD55*** | ***CD68*** | ***COL3A1*** | ***NOD2*** | ***PIK3R1*** | ***CD59*** | ***YTHDF2*** | ***SDC4*** | ***YTHDF3*** |
| ***IGKV1-39*** | ***SCGB1A1*** | ***PLCG2*** | ***IGKV2D-40*** | ***EZR*** | ***FBN1*** | ***ADIPOQ*** | ***IGHV3-48*** | ***TAPBPL*** | ***BANK1*** |
| ***NLRC5*** | ***NR1H2*** | ***UNC13D*** | ***IFNE*** | ***IGHV3-30*** | ***OAS1*** | ***ZC3H12A*** | ***IGLV3-1*** | ***GPR18*** | ***PTGER4*** |
| ***UBASH3A*** | ***IFNB1*** | ***IGKV3-20*** | ***PHPT1*** | ***GIPR*** | ***IGLV2-23*** | ***PTH2R*** | ***CD1B*** | ***GCSAM*** | ***TYRO3*** |
| ***MC2R*** | ***PLCG1*** | ***KIAA0922*** | ***TNFSF13*** | ***PKN1*** | ***MSH6*** | ***IGHG4*** | ***FAM49B*** | ***C1QBP*** | ***LPXN*** |
| ***APCS*** | ***TTLL12*** | ***RIPK2*** | ***HLA-DOA*** | ***TMEM178A*** | ***GPHA2*** | ***CUEDC2*** | ***MAPK14*** | ***LIG4*** | ***GPR25*** |
| ***HLA-A*** | ***CD180*** | ***LAPTM5*** | ***PTPRC*** | ***DLL1*** | ***LTF*** | ***PRKAR1B*** | ***DPEP1*** | ***IGLV3-27*** | ***PRDX2*** |
| ***PRKACB*** | ***ADRB3*** | ***IGLV1-51*** | ***LGALS1*** | ***GPER1*** | ***PRKAR1A*** | ***CBFB*** | ***CTC-534A2.2*** | ***ADCY4*** | ***IGKV2-30*** |
| ***LHCGR*** | ***TSC22D3*** | ***CD247*** | ***ITM2A*** | ***PYCARD*** | ***IGHG3*** | ***TLR3*** | ***AKT1*** | ***MDK*** | ***CRTAM*** |
| ***CD84*** | ***TRIM21*** | ***IGKV5-2*** | ***SOX9*** | ***GPR150*** | ***LRRC17*** | ***SUV420H1*** | ***CNR2*** | ***SCRIB*** | ***FAM19A3*** |
| ***APBB1IP*** | ***HTR7*** | ***HLA-H*** | ***TRAF6*** | ***VAMP7*** | ***ERBB2*** | ***CD40*** | ***IL2RA*** | ***ZNF683*** | ***FER*** |
| ***KLRF2*** | ***MNDA*** | ***DLG1*** | ***ADCY5*** | ***VIPR1*** | ***BATF*** | ***IGKV1D-12*** | ***HSPD1*** | ***TNFRSF14*** | ***MAPKBP1*** |
| ***DGKZ*** | ***SUV420H2*** | ***FCER1G*** | ***RAMP3*** | ***HLA-DRA*** | ***MAD2L2*** | ***FCRL3*** | ***FCGR2B*** | ***NOV*** | ***RORC*** |
| ***IL23R*** | ***ZNF675*** | ***TNFAIP3*** | ***NRARP*** | ***CLNK*** | ***GLMN*** | ***GBP1*** | ***HMOX1*** | ***SOX11*** | ***PELO*** |
| ***GAPT*** | ***HLA-F*** | ***ST3GAL1*** | ***IGLV3-19*** | ***A2M*** | ***HTR6*** | ***IL6R*** | ***NLRP3*** | ***PTHLH*** | ***NLRX1*** |
| ***NME2*** | ***IGKV1-33*** | ***TRAF2*** | ***IFNL1*** | ***IGHV1-2*** | ***IFNA7*** | ***CD46*** | ***STAT6*** | ***IGKV2D-28*** | ***GPBAR1*** |
| ***NBL1*** | ***IGHV2-5*** | ***ITCH*** | ***C5*** | ***F2RL1*** | ***IGHV2-70*** | ***TCTA*** | ***IL12A*** | ***IGKV2-28*** | ***PTPN2*** |
| ***IFNG*** | ***IL21*** | ***GPR137B*** | ***PADI2*** | ***CCL28*** | ***DENND1B*** | ***IGHV3-23*** | ***CD28*** | ***FURIN*** | ***IFNA10*** |
| ***PGLYRP1*** | ***AHR*** | ***IGKV1-17*** | ***C17orf99*** | ***IGKV3-15*** | ***IL6*** | ***ANXA1*** | ***PSMB4*** | ***CD1E*** | ***CDK6*** |
| ***RNF26*** | ***C4BPA*** | ***BTK*** | ***IL12B*** | ***TIGIT*** | ***SKAP1*** | ***ADM2*** | ***DOCK10*** | ***RIF1*** | ***LGALS9B*** |
| ***DRD2*** | ***IGLV6-57*** | ***TRAF3IP1*** | ***SEMA4A*** | ***IFNW1*** | ***CREB1*** | ***IGHV1-46*** | ***NPY5R*** | ***LAG3*** | ***RC3H2*** |
| ***GLI3*** | ***PRKACA*** | ***IGKV1-16*** | ***GLP2R*** | ***EXOSC6*** | ***FSHB*** | ***ZC3H8*** | ***NOTCH2*** | ***NPLOC4*** | ***NCKAP1L*** |
| ***HLA-DOB*** | ***EMILIN1*** | ***CD300A*** | ***FOXP1*** | ***LY9*** | ***RIOK3*** | ***IGLC3*** | ***GPR83*** | ***IGHV3-11*** | ***IGLV1-40*** |
| ***CUL4A*** | ***SEC14L1*** | ***PVRL2*** | ***VAMP2*** | ***SPINK5*** | ***LILRB1*** | ***SH2D1A*** | ***FYN*** | ***IGHV3-33*** | ***IGHV3-13*** |
| ***CXCL12*** | ***CD47*** | ***TNFRSF21*** | ***XCL1*** | ***FOXJ1*** | ***IL7R*** | ***IGKV1-5*** | ***IAPP*** | ***FCER2*** | ***VIPR2*** |
| ***SWAP70*** | ***BST2*** | ***EXO1*** | ***NLRP10*** | ***IGHV3-7*** | ***DUSP1*** | ***SHH*** | ***KLRD1*** | ***TP53BP1*** | ***TNFSF13B*** |
| ***DDT*** | ***CST7*** | ***IL31RA*** | ***CD300LF*** | ***GCG*** | ***PAXIP1*** | ***PRKAR2A*** | ***ADM*** | ***ARG1*** | ***PPM1B*** |
| ***IL4R*** | ***VTCN1*** | ***FOXF1*** | ***LILRB4*** | ***CAD*** | ***PLA2G2D*** | ***AXL*** | ***SLAMF8*** | ***GPNMB*** | ***CLEC12B*** |
| ***ICOS*** | ***RORA*** | ***ADORA1*** | ***ZBTB46*** | ***CR1*** | ***LAMP1*** | ***PLK2*** | ***MYC*** | ***THBS1*** | ***IGHG1*** |
| ***FADD*** | ***RLN2*** | ***SOCS5*** | ***C10orf54*** | ***IGHG2*** | ***CRHR2*** | ***HPX*** | ***GAL*** | ***VIMP*** | ***SAMSN1*** |
| ***SLC22A13*** | ***PRKACG*** | ***HOXA7*** | ***CLEC6A*** | ***CCR2*** | ***GREM1*** | ***SIRT2*** | ***EXOSC3*** | ***TGFB2*** | ***MYH9*** |
| ***ADCY2*** | ***ADA*** | ***ADCYAP1*** | ***PLA2G2F*** | ***SLC15A4*** | ***DCST1*** | ***TARM1*** | ***XBP1*** | ***ADCY9*** | ***SLC11A1*** |
| ***NR1H3*** | ***PLCB1*** | ***TSC1*** | ***CD160*** | ***KIR2DL4*** | ***CD81*** | ***SERPINB4*** | ***IGHV4-59*** | ***CR2*** | ***IGHV3-53*** |
| ***ZPBP2*** | ***IGLV2-14*** | ***ARRB2*** | ***RXFP1*** | ***STX7*** | ***CCL3*** | ***ATM*** | ***APOA2*** | ***SLAMF1*** | ***CRK*** |
| ***IGLC6*** | ***GHRHR*** | ***RNF8*** | ***IGHV4-34*** | ***AP1G1*** | ***ADCY3*** | ***PTGER2*** | ***IL20RB*** | ***ADTRP*** | ***PTGIR*** |
| ***MC5R*** | ***INHBA*** | ***VIP*** | ***IGKV1-12*** | ***CLDN18*** | ***LILRB3*** | ***C5AR2*** | ***LGALS3*** | ***SUPT6H*** | ***FSTL3*** |
| ***PTPN22*** | ***PARP3*** | ***FBXW7*** | ***KLRC1*** | ***ISG15*** | ***IGLV7-43*** | ***CX3CL1*** | ***HLA-E*** | ***TREX1*** | ***PRKDC*** |
| ***GPX1*** | ***DUSP10*** | ***AMBP*** | ***IGKV1D-39*** | ***RPS19*** | ***PARP14*** | ***SPI1*** | ***USP15*** | ***PSEN1*** | ***CD200*** |
| ***CARD9*** | ***IGKV4-1*** | ***CD74*** | ***HLX*** | ***LTA*** | ***ID2*** | ***CEACAM1*** | ***TNFSF4*** | ***CNOT6*** | ***IGKV3D-20*** |
| ***SLA2*** | ***WHSC1*** | ***RC3H1*** | ***GATA2*** | ***CALCA*** | ***MICA*** | ***INSL3*** | ***TP53*** | ***CTNNB1*** | ***IGLV1-44*** |
| ***CCL2*** | ***LST1*** | ***AZGP1*** | ***IGHV4-39*** | ***PLCL2*** | ***IL17D*** | ***STAT3*** | ***MYB*** | ***HLA-DPB1*** | ***MAD1L1*** |
| ***IGKC*** | ***ATP7A*** | ***TFRC*** | ***CD80*** | ***FBXO38*** | ***IGKV1D-16*** | ***RAMP2*** | ***IGKV3-11*** | ***IL4I1*** | ***PIAS3*** |
| ***GPR55*** | ***IGLC2*** | ***IGLC1*** | ***SFRP1*** | ***ENTPD7*** | ***ADCY6*** | ***C20orf196*** | ***MICB*** | ***FAM35A*** | ***PPARG*** |
| ***IGLV3-21*** | ***CD244*** | ***APOA1*** | ***MTOR*** | ***METTL3*** | ***LYN*** | ***MR1*** | ***STAT2*** | ***KLRC2*** | ***DRD4*** |
| ***DRD3*** | ***USP18*** | ***HLA-DRB1*** | ***CD4*** | ***IGLV3-25*** | ***GLP1R*** | ***SLAMF6*** | ***BCL6*** | ***HCK*** | ***IGKV2-29*** |
| ***LGALS9*** | ***HTR4*** | ***IGLV1-47*** | ***PVRIG*** | ***CALCB*** | ***GPR176*** | ***MMP28*** | ***ZP3*** | ***IGHV3-9*** | ***ARG2*** |
| ***RLN3*** | ***UNG*** | ***IGHV1-69*** | ***LRCH1*** | ***GGT1*** | ***IL27*** | ***GPR39*** | ***IFNK*** | ***GPR68*** | ***CEBPB*** |
| ***ICAM1*** | ***GPR45*** | ***GRN*** | ***IGLV2-8*** | ***DRD1*** | ***CTLA4*** | ***TARBP2*** | ***CCL21*** | ***SOCS1*** | ***ADAR*** |
| ***SPN*** | ***TNFAIP8L2*** | ***IGKV2D-30*** | ***BPI*** | ***FGR*** | ***MLH1*** | ***HSPA9*** | ***MIA3*** | ***ABL1*** | ***LRRC32*** |
| ***IHH*** | ***YES1*** | ***NPSR1*** | ***LDLR*** | ***UFD1L*** | ***GPR183*** | ***EIF2AK4*** | ***ADCYAP1R1*** | ***LHB*** | ***HLA-G*** |
| ***RXFP2*** | ***CALCR*** | ***GPS2*** | ***LILRB2*** | ***PCK1*** | ***NLRP6*** | ***MIF*** | ***LAX1*** | ***CRHR1*** | ***TSHR*** |
| ***RNF168*** | ***SIRT1*** | ***SCT*** | ***MILR1*** | ***BMP5*** | ***FSHR*** | ***C6orf106*** | ***POMC*** | ***GPR84*** | ***IGLV2-11*** |
| ***ENPP3*** | ***GPR32*** | ***RHBDD3*** | ***IGLC7*** | ***CYSLTR1*** | ***GPAM*** | ***LGALS7*** | ***CARTPT*** | ***GIP*** | ***PTH2*** |
| ***NPS*** | ***ADCY8*** | ***INS*** | ***PTH*** | ***TSHB*** | ***IGKV1D-33*** | ***CGA*** | ***AVP*** | ***MC3R*** | ***IFNA2*** |
| ***FGL1*** | ***TAAR1*** | ***IFNA8*** | ***IFNA16*** | ***IFNA4*** | ***IFNA6*** | ***IFNA14*** | ***IFNA1*** | ***NKX2-3*** | ***IFNA21*** |
| ***IFNA5*** | ***IFNA17*** |  |  |  |  |  |  |  |  |