

Supplementary Materials

Cell landscape of cerebrospinal fluid and neuroinflammatory signatures in the bacterial meningitis through high-throughput sequencing and meta-analysis

Haihan Xiao^{a, b, †}, Haijuan Xiao^{c, †}, Yun Zhang^a, Lingyun Guo^c, Zhenzhen Dou^c, Linlin Liu^c, Liang Zhu^c, Wenya Feng^c, Bing Liu^c, Bing Hu^c, Tianming Chen^c, Gang Liu^{c, *}, Tingyi Wen^{a, d, *}

^aCAS Key Laboratory of Pathogenic Microbiology and Immunology, Institute of Microbiology, Chinese Academy of Sciences, Beijing 100101, China

^bUniversity of Chinese Academy of Sciences, Beijing 100049, China

^cDepartment of Infectious Diseases, Beijing Children's Hospital, Capital Medical University, National Center for Children's Health, Beijing 100045, China

^dSavaid Medical School, University of Chinese Academy of Sciences, Beijing 100049, China

*Corresponding author. E-mail: wenty@im.ac.cn

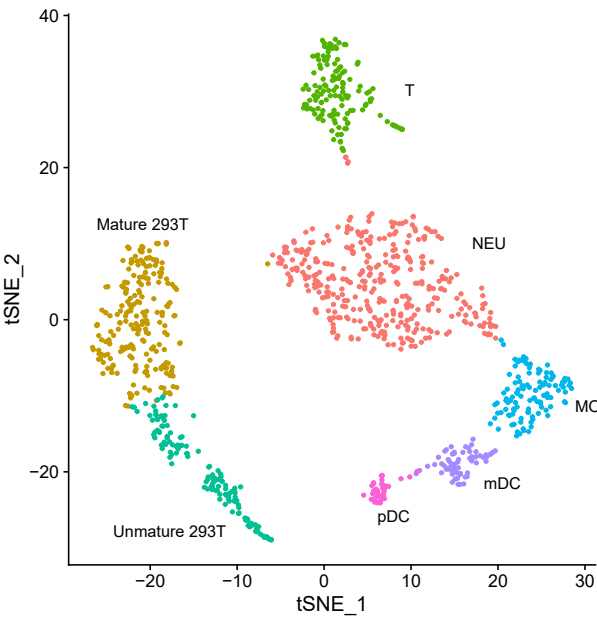
*Corresponding author. E-mail: liugangbch@sina.com

[†]These authors contributed equally to this work.

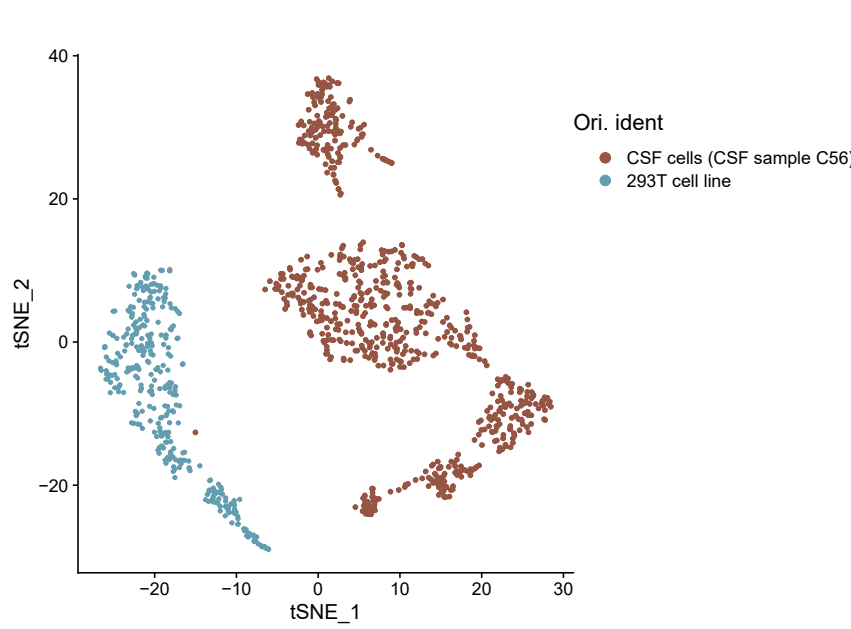
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A



B



C

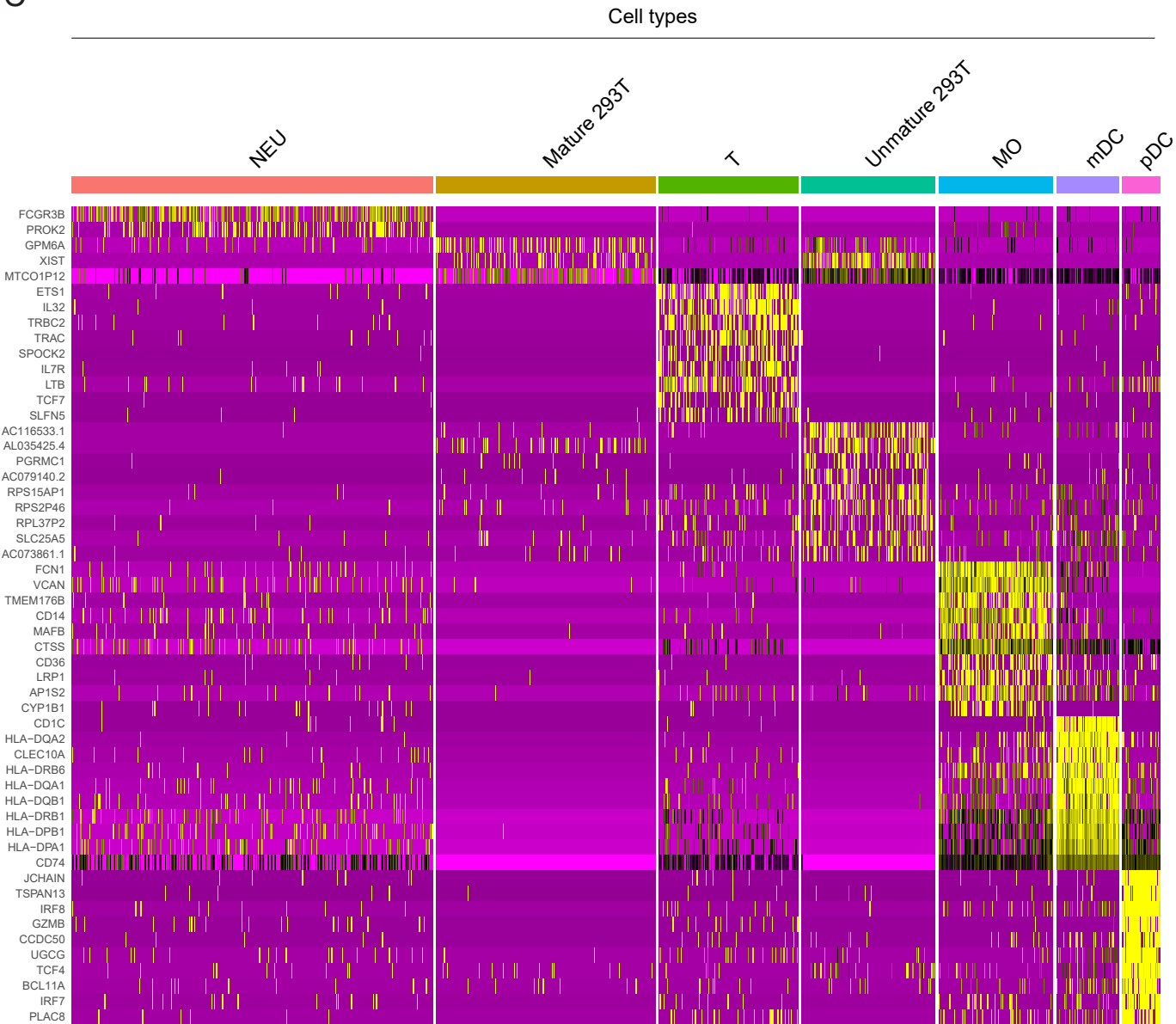


Fig. S1. scRNA-SEQ reveals cell subsets in the mixed clustering of CSF cells and 293T cells. (A) t-SNE shows the cell subsets after mixed clustering of CSF cells and 293T cells. CSF cells are the scRNA-SEQ data of sample C56. (B) t-SNE shows the origin identity of each cell. (C) Heatmap shows the marker genes of each cluster. The black to yellow gradient represents low to high logFC of each gene.

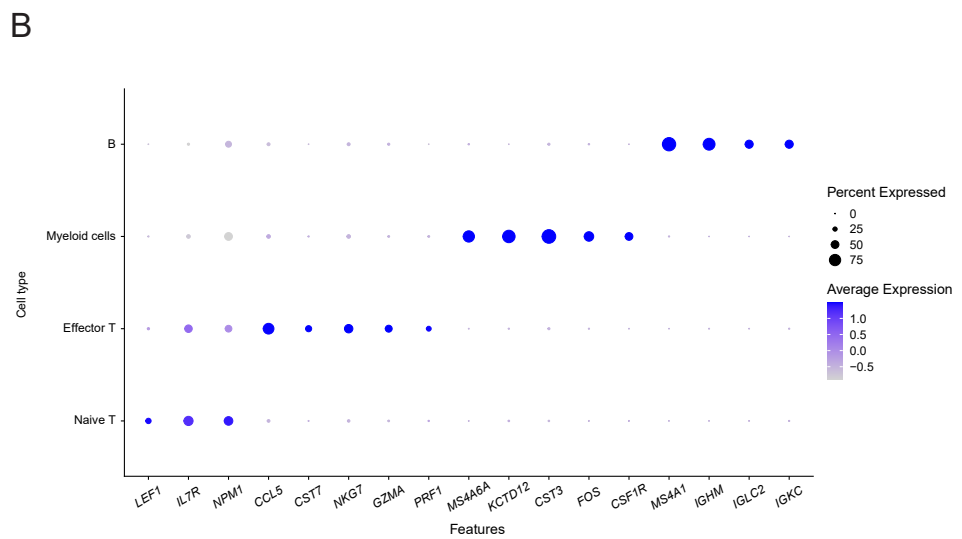
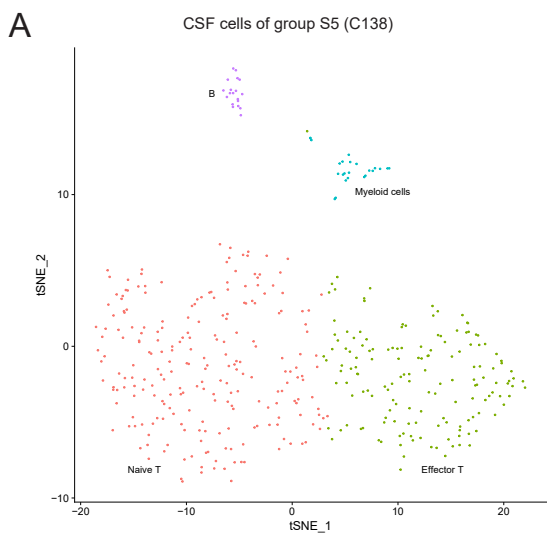


Fig. S2. scRNA-SEQ reveals the cell subsets of CSF cells in the recovery after unrafractory remission stage of BM. (A) t-SNE plot shows the cell subsets in CSF from sample C138. (B) Bubble plot shows the feature genes of each cluster. Shades of blue represent the relative abundance (the higher the abundance, the bluer the color), and bubble sizes represent the expression level (the higher the expression, the larger the size) of each gene.

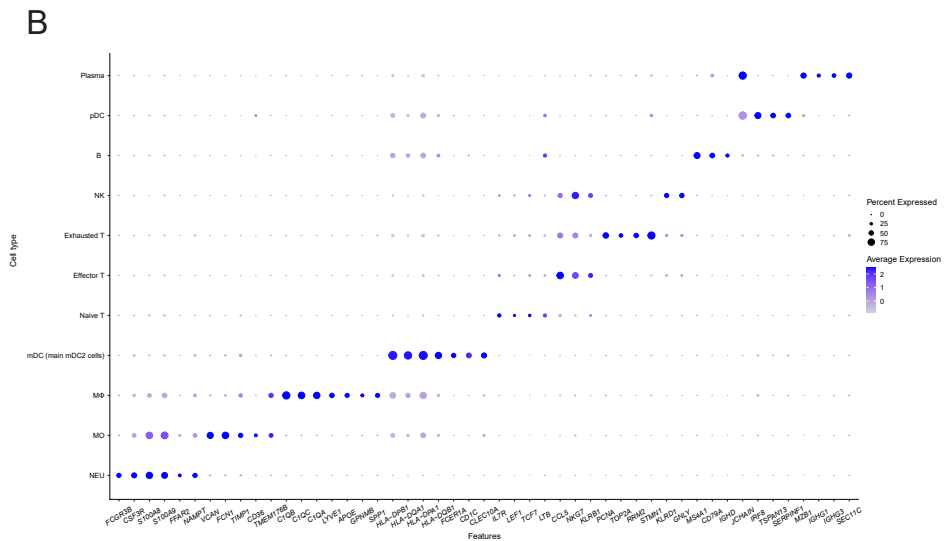
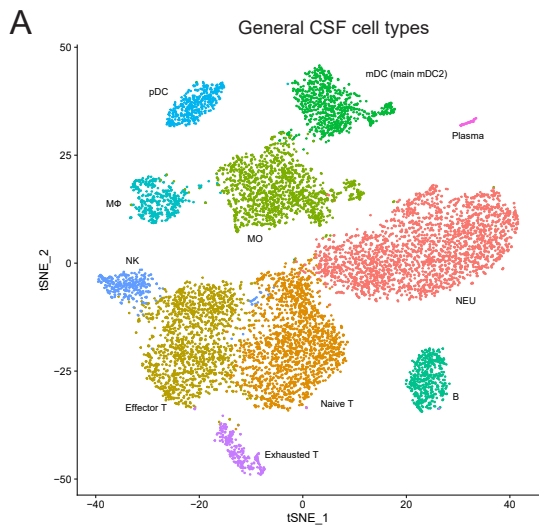


Fig. S3. scRNA-SEQ reveals the general cell subsets of CSF in BM. (A) t-SNE plot shows the cell subsets in CSF from BM patients. (B) Bubble plot shows the feature genes of each cluster. Shades of blue represent the relative abundance (the higher the abundance, the bluer the color), and bubble sizes represent the expression level (the higher the expression, the larger the size) of each gene.



Fig. S4. t-SNE plots show the distribution of myeloid cells (cNEUs, cytokine⁺ NEUs, cMOs, cytokine⁺ MOs, MΦs, mDC1s, mDC2s, SIGLEC6⁺AXL⁺ mDCs and CCR7⁺ mDCs) and lymphoid cells (naïve T cells, CD8⁺ T cells, CD4⁺ T cells, exhausted T cells, γδ T cells, NKs, B cells, pDCs and plasma cells), which identified by scRNA-SEQ, in the CSF at different BM stages. Each myeloid cell subtype are marked by multicolored hollow triangles, while each lymphoid cell subtype are marked by multicolored points.

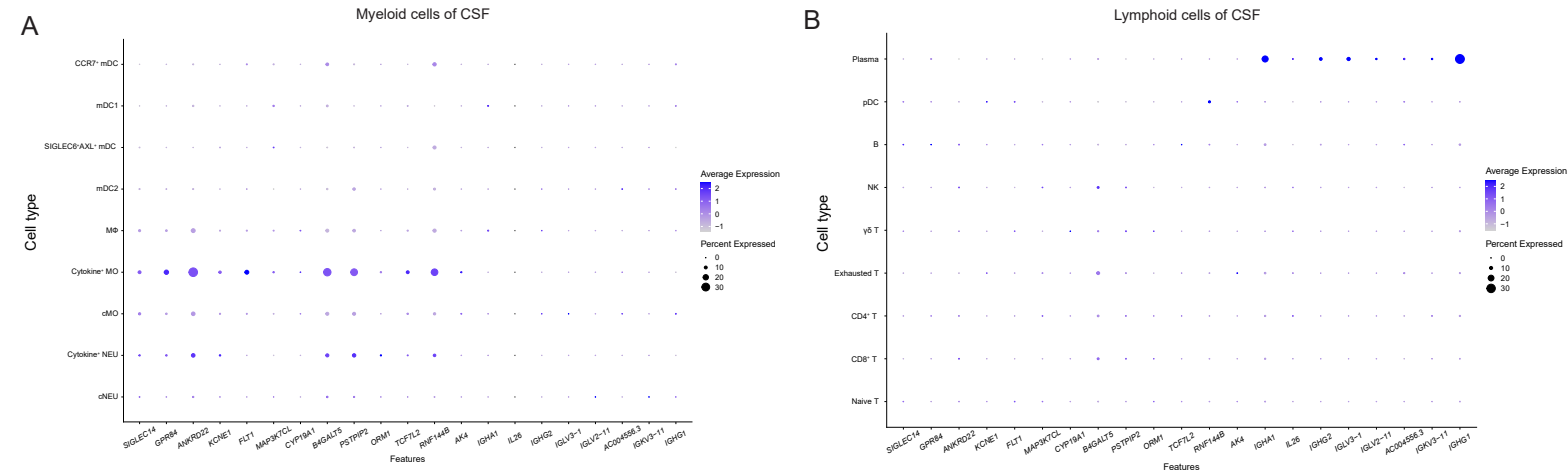


Fig. S5. Bubble plots show the expression of gene set (*SIGLEC14*, *GPR84*, *ANKRD22*, *KCNE1*, *FLT1*, *MAP3K7CL*, *CYP19A1*, *B4GALT5*, *PSTPIP2*, *ORM1*, *TCF7L2*, *RNF144B*, *AK4*, *IGHA1*, *IL26*, *IGHG2*, *IGLV3-1*, *IGLV2-11*, *AC004556.3*, *IGKV3-11* and *IGHG1*) on myeloid cell subsets (A) and lymphoid cell subsets (B) of CSF. Shades of blue represent the relative abundance (the higher the abundance, the bluer the color), and bubble sizes represent the expression level (the higher the expression, the larger the size) of each gene..

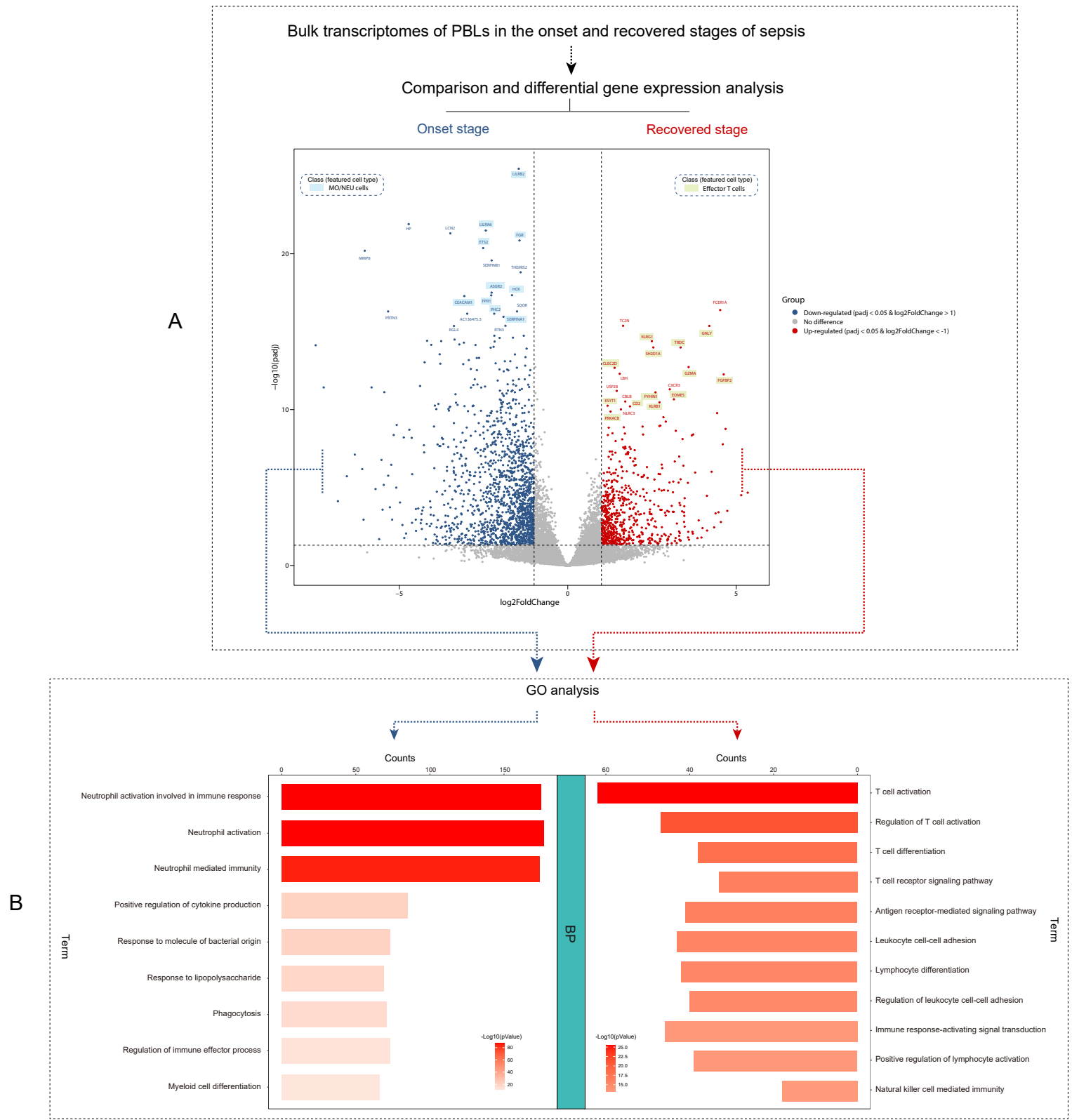


Fig. S8. Different molecular hallmarks between PBLs in sepsis onset and recovered stages. (A) Volcano plot shows the DEGs between PBLs in sepsis onset and recovered stages. The x-axis shows log2FC values, and the y-axis shows negative log ten padj values. Each gene is represented by a single spot. Significantly down-regulated ($\log_2FC \leq -2$ & $padj \leq 0.01$) and up-regulated ($\log_2FC \geq 2$ & $padj \leq 0.01$) genes are represented by blue and red spots, respectively. The thresholds of log2FC and padj are plotted with dashed lines. The names of down-regulated and up-regulated genes with top padj values are listed next to the corresponding spots. The background colors of down-regulated and up-regulated gene names represent the cell types of CSF and PBLs, respectively, which highly express the corresponding gene. (B) Bar charts show the terms of GO-BP enrichments targeting the down-regulated and up-regulated DEGs in the comparison. shades of red indicate the logarithmic P value of each GO-BP term from low to high (the more significant the P value is, the redder the color) (scaled). Bar lengths indicate the number of genes enriched for each GO-BP term.

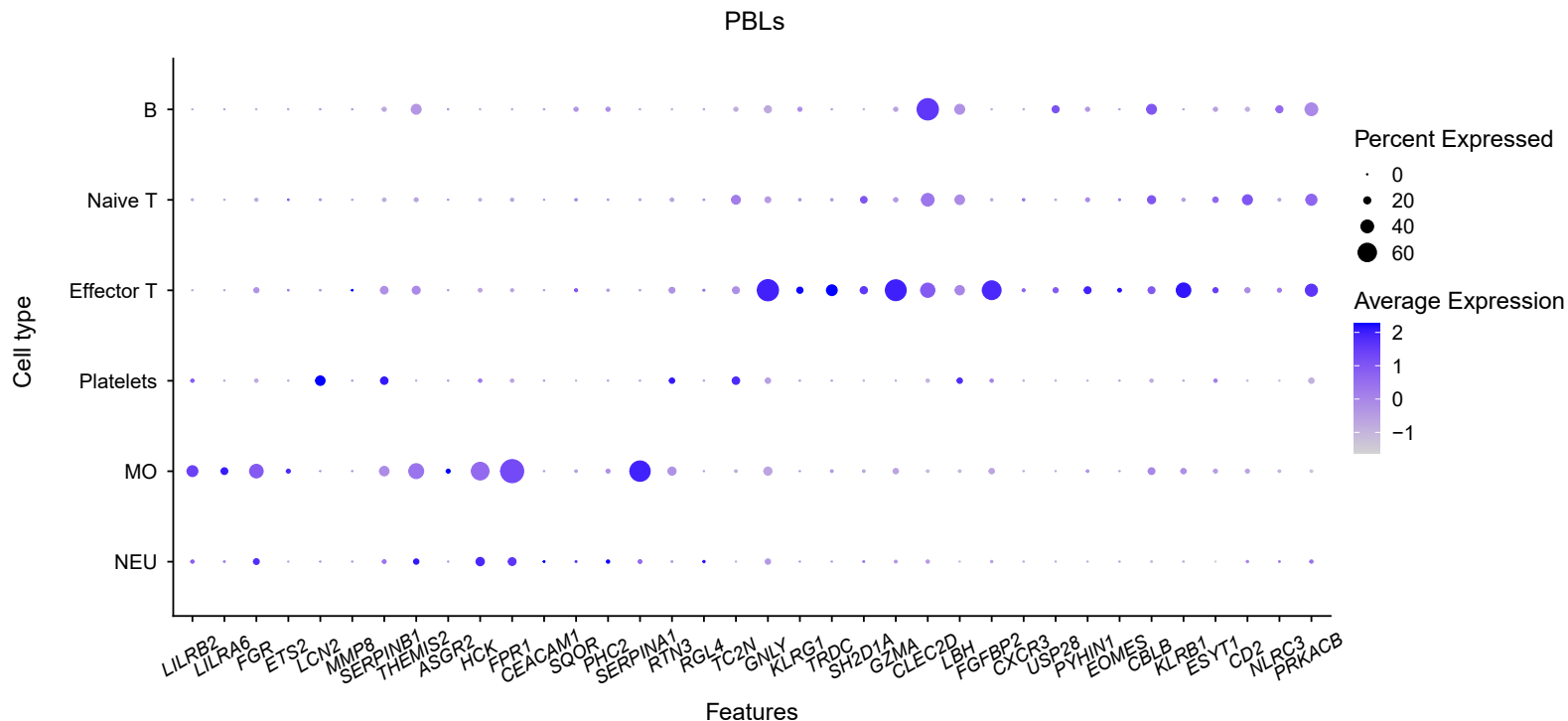
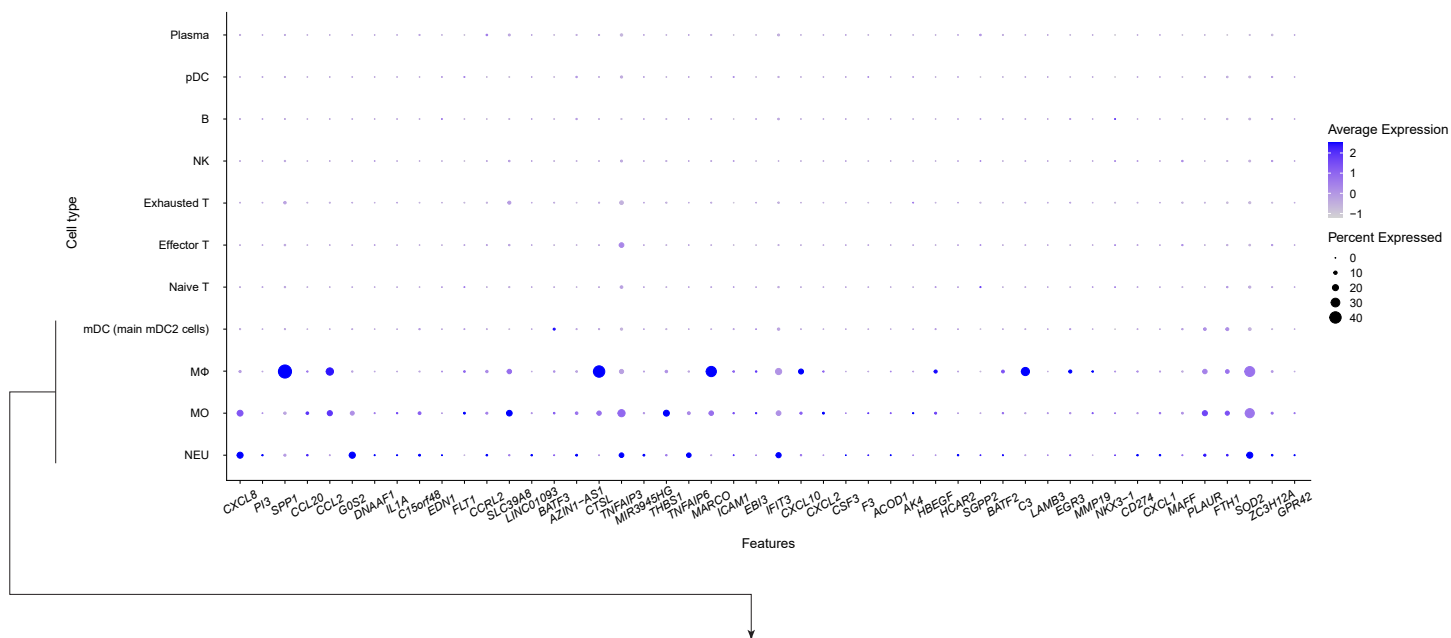


Fig. S9. Bubble plot shows the expression of gene set (*LILRB2, LILRA6, FGR, ETS2, LCN2, MMP8, SERPINB1, THEMIS2, ASGR2, HCK, FPR1, CEACAM1, SQOR, PHC2, SERPINA1, RTN3, RGL4, TC2N, GNLY, KLRG1, TRDC, SH2D1A, GZMA, CLEC2D, LBH, FGFBP2, CXCR3, USP28, PYHIN1, EOMES, CBLB, KLRB1, ESYT1, CD2, NLRC3* and *PRKACB*) on cell subsets of PBLs from BM patients. Shades of blue represent the relative abundance (the higher the abundance, the bluer the color), and bubble sizes represent the expression level (the higher the expression, the larger the size) of each gene.

A

General CSF cell types



B

Myeloid cells of CSF

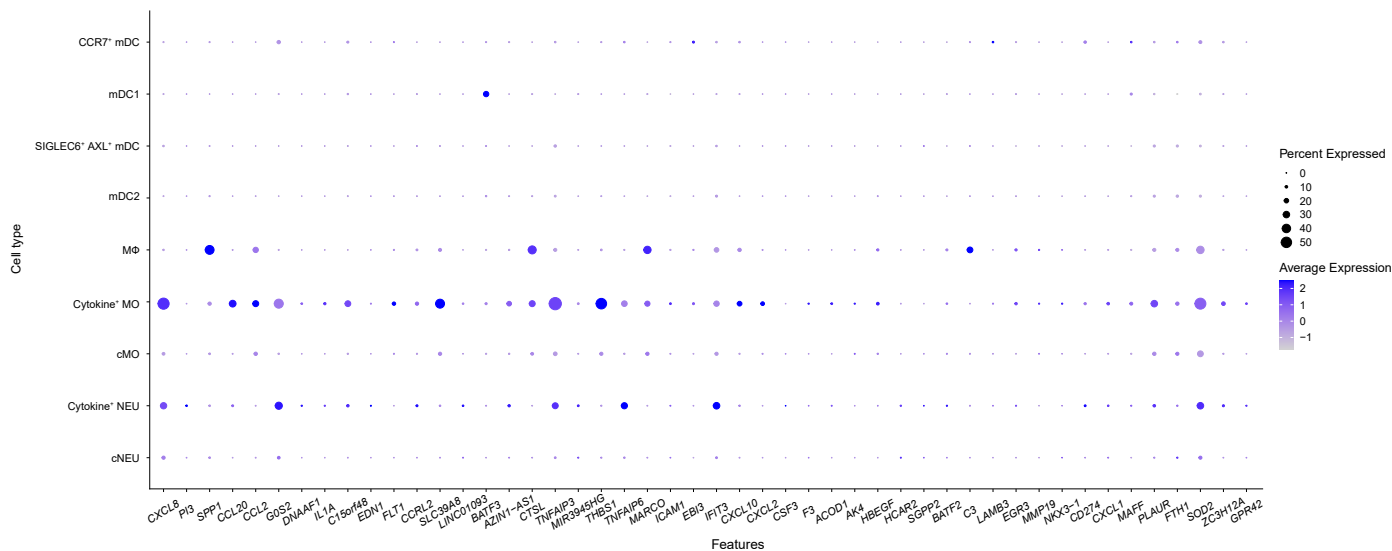


Fig. S10. Bubble plots show the expression of gene set (*CXCL8*, *PI3*, *SPP1*, *CCL20*, *CCL2*, *GOS2*, *DNAAF1*, *IL1A*, *C15orf48*, *EDN1*, *FLT1*, *CCRL2*, *SLC39A8*, *LINC01093*, *BATF3*, *AZIN1-AS1*, *CTSL*, *TNFAIP3*, *MIR3945HG*, *THBS1*, *TNFAIP6*, *MARCO*, *ICAM1*, *EBI3*, *IFIT3*, *CXCL10*, *CXCL2*, *CSF3*, *F3*, *ACOD1*, *AK4*, *HBEGF*, *HCAR2*, *SGPP2*, *BATF2*, *C3*, *LAMB3*, *EGR3*, *MMP19*, *NKX3-1*, *CD274*, *CXCL1*, *MAFF*, *PLAUR*, *FTH1*, *SOD2*, *ZC3H12A* and *GPR42*) on general cell subsets (A), and myeloid cell subsets (B), of CSF respectively. Shades of blue represent the relative abundance (the higher the abundance, the bluer the color), and bubble sizes represent the expression level (the higher the expression, the larger the size) of each gene.

PBLs

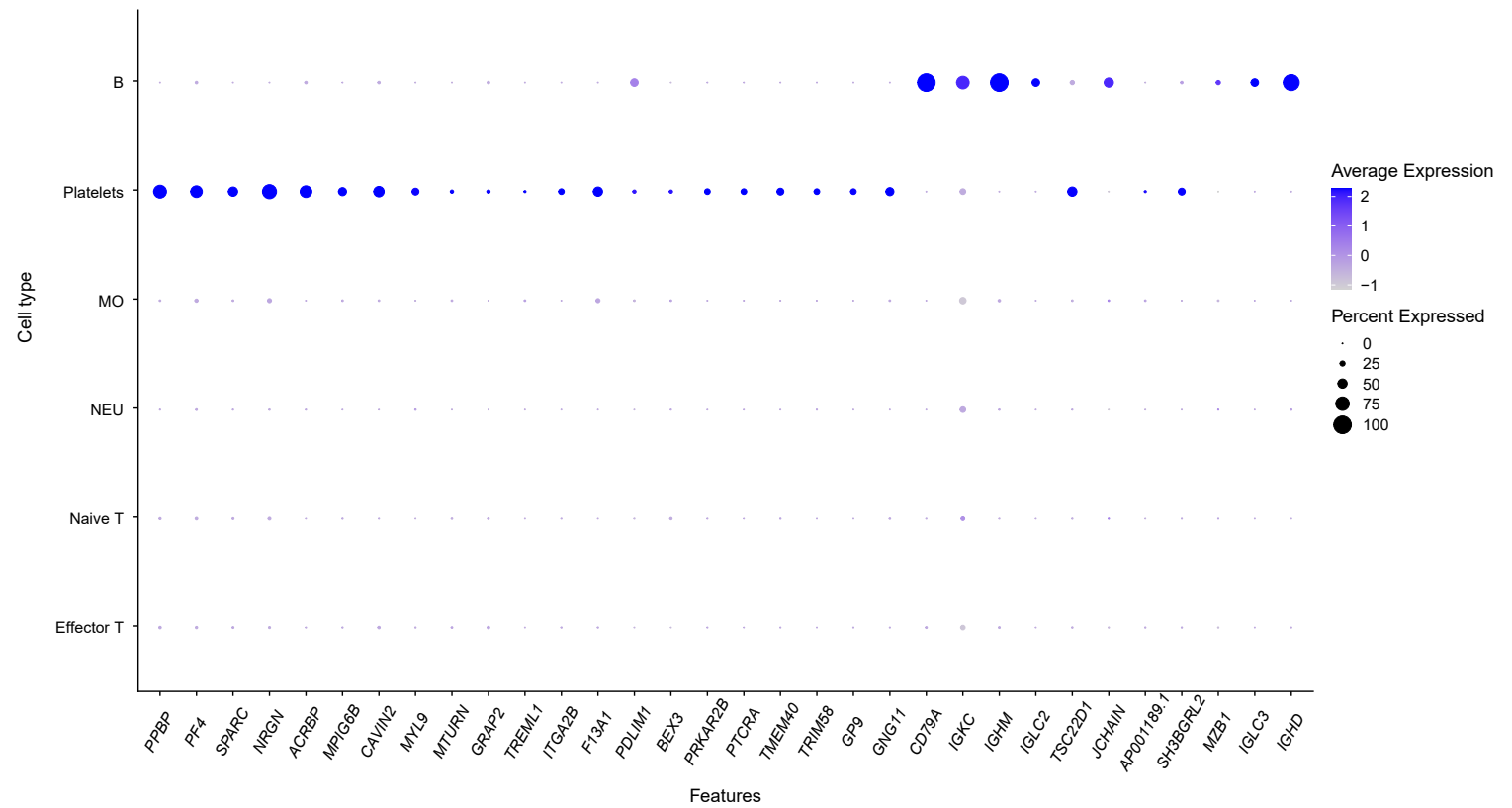


Fig. S11. Bubble plot show the expression of gene set (*PPBP*, *PF4*, *SPARC*, *NRGN*, *ACRBP*, *MPIG6B*, *CAVIN2*, *MYL9*, *MTURN*, *GRAP2*, *TREML1*, *ITGA2B*, *F13A1*, *PDLIM1*, *BEX3*, *PRKAR2B*, *PTCRA*, *TMEM40*, *TRIM58*, *GP9*, *GNG11*, *CD79A*, *IGKC*, *IGHM*, *IGLC2*, *TSC22D1*, *JCHAIN*, *AP001189.1*, *SH3BGRL2*, *MZB1*, *IGLC3*, and *IGHD*) on cell subsets of PBLs from BM patients. Shades of blue represent the relative abundance (the higher the abundance, the bluer the color), and bubble sizes represent the expression level (the higher the expression, the larger the size) of each gene.

General CSF cell types

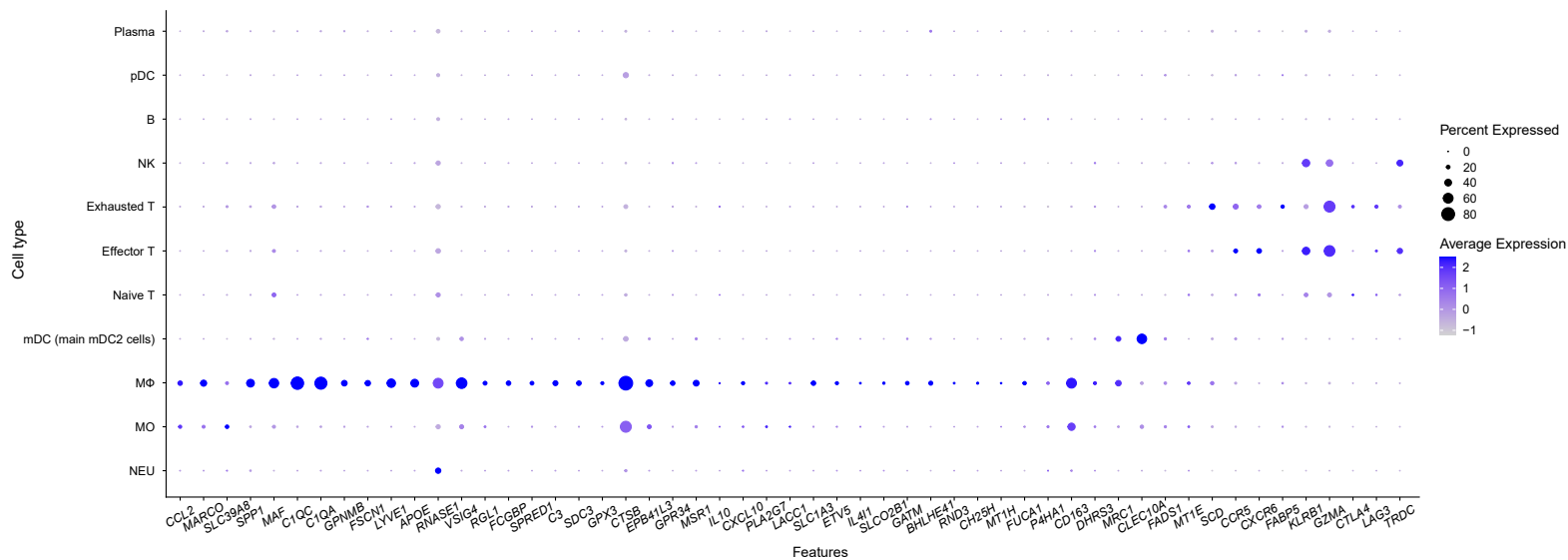


Fig. S12. Bubble plot show the expression of gene set (*CCL2*, *MARCO*, *SLC39A8*, *SPP1*, *MAF*, *C1QC*, *C1QA*, *GPNMB*, *FSCN1*, *LYVE1*, *APOE*, *RNASE1*, *VSIG4*, *RGL1*, *FCGBP*, *SPRED1*, *C3*, *SDC3*, *GPX3*, *CTSB*, *EPB41L3*, *GPR34*, *MSR1*, *IL10*, *CXCL10*, *PLA2G7*, *LACCI1*, *SLC1A3*, *ETV5*, *IL4I1*, *SLCO2B1*, *GATM*, *BHLHE41*, *RND3*, *CH25H*, *MT1H*, *FUCA1*, *P4HA1*, *CD163*, *DHRS3*, *MRC1*, *CLEC10A*, *FADS1*, *MT1E*, *SCD*, *CCR5*, *CXCR6*, *FABP5*, *KLRB1*, *GZMA*, *CTLA4*, *LAG3* and *GPR42*) on general cell subsets of CSF. Shades of blue represent the relative abundance (the higher the abundance, the bluer the color), and bubble sizes represent the expression level (the higher the expression, the larger the size) of each gene.

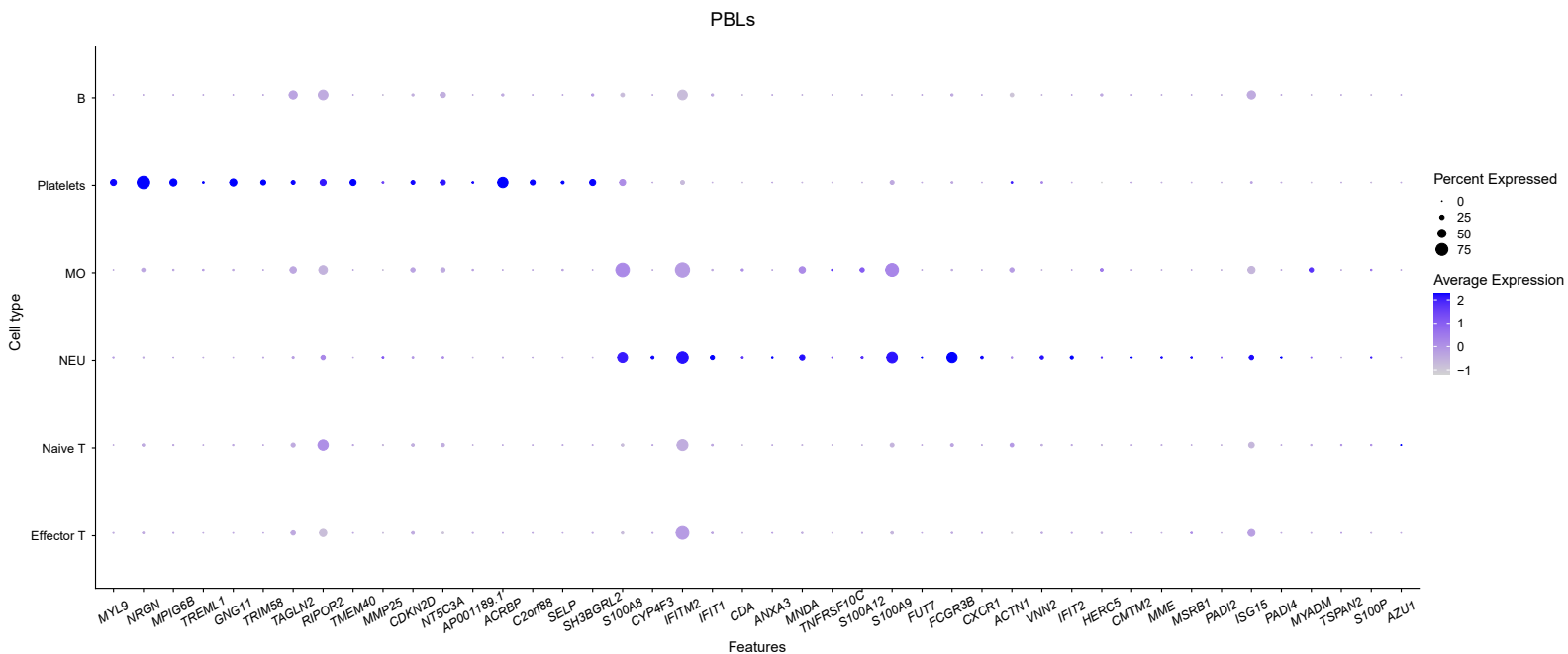


Fig. S13. Bubble plot show the expression of gene set (*MYL9, NRG1, MPIG6B, TREML1, GNG11, TRIM58, TAGLN2, RIPOR2, TMEM40, MMP25, CDKN2D, NT5C3A, AP001189.1, ACRBP, C2orf88, SELP, SH3BGR2, S100A8, CYP4F3, IFITM2, IFIT1, CDA, ANXA3, MNDA, TNFRSF10C, S100A12, S100A9, FUT7, FCGR3B, CXCR1, ACTN1, VNN2, IFIT2, HERC5, CMTM2, MME, MSRB1, PADI2, ISG15, PADI4, MYADM, TSPAN2, S100P* and *AZU1*) on cell subsets of PBLs from BM patients. Shades of blue represent the relative abundance (the higher the abundance, the bluer the color), and bubble sizes represent the expression level (the higher the expression, the larger the size) of each gene.

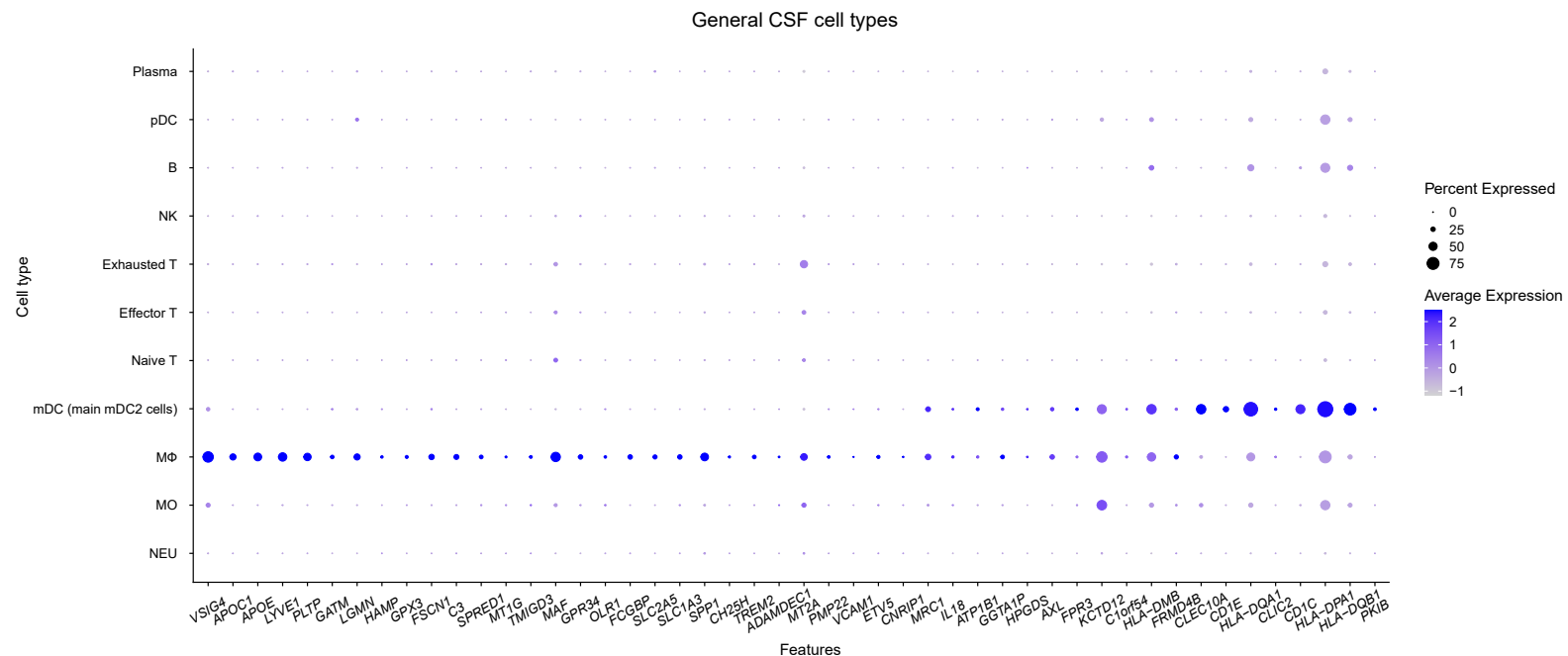


Fig. S14. Bubble plot show the expression of gene set (*VSIG4, APOC1, APOE, LYVE1, PLTP, GATM, LGMN, HAMP, GPX3, FSCN1, C3, SPRED1, MT1G, TMIGD3, MAF, GPR34, OLR1, FCGBP, SLC2A5, SLC1A3, SPP1, CH25H, TREM2, ADAMDEC1, MT2A, PMP22, VCAM1, ETV5, CNRIP1, MRC1, IL18, ATP1B1, GGT1P, HPGDS, AXL, FPR3, KCTD12, C1orf54, HLA-DMB, FRMD4B, CLEC10A, CD1E, HLA-DQA1, CLIC2, CD1C, HLA-DPA1, HLA-DQB1* and *PKIB*) on general cell subsets of CSF. Shades of blue represent the relative abundance (the higher the abundance, the bluer the color), and bubble sizes represent the expression level (the higher the expression, the larger the size) of each gene.

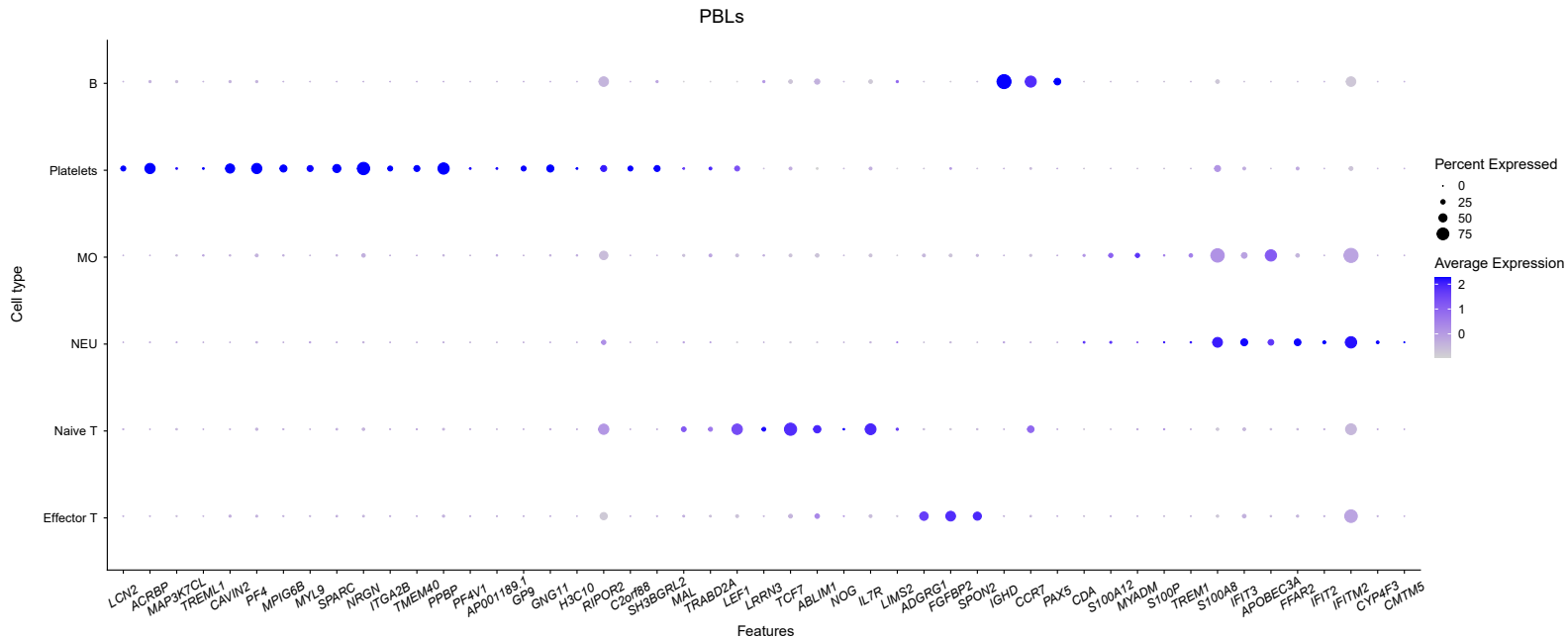


Figure S15. Bubble plot show the expression of gene set (*LCN2*, *ACRBP*, *MAP3K7CL*, *TREML1*, *CAVIN2*, *PF4*, *MPIG6B*, *MYL9*, *SPARC*, *NRGN*, *ITGA2B*, *TMEM40*, *PPBP*, *PF4V1*, *AP001189.1*, *GP9*, *GNG11*, *H3C10*, *RIPOR2*, *C2orf88*, *SH3BGR2*, *MAL*, *TRABD2A*, *LEF1*, *LRRN3*, *TCF7*, *ABLIM1*, *NOG*, *IL7R*, *LIMS2*, *ADGRG1*, *FGFBP2*, *SPON2*, *IGHD*, *CCR7*, *PAX5*, *CDA*, *S100A12*, *MYADM*, *S100P*, *TREM1*, *S100A8*, *IFIT3*, *APOBEC3A*, *FFAR2*, *IFIT2*, *IFITM2*, *CYP4F3* and *CMTM5*) on cell subsets of PBLs from BM patients. Shades of blue represent the relative abundance (the higher the abundance, the bluer the color), and bubble sizes represent the expression level (the higher the expression, the larger the size) of each gene.

Table legends

Table. S1. Characteristics of CSF and blood samples collected from BM patients in the study.

Table. S2. The sequences of the primers that are used in scRNA-SEQ and bulkRNA-SEQ.

Table. S3. The sequences of primers that are used in RT-qPCR for human *TREM2*, *SLCO2B1* and *β -actin*.

Table. S4. Ligand-receptor interactions of CSF cells that are identified with changed levels between in BM unrefractory and refractory remission stages.