Single-cell landscape of bronchoalveolar immune cells in patients with COVID-19

Mingfeng et al.

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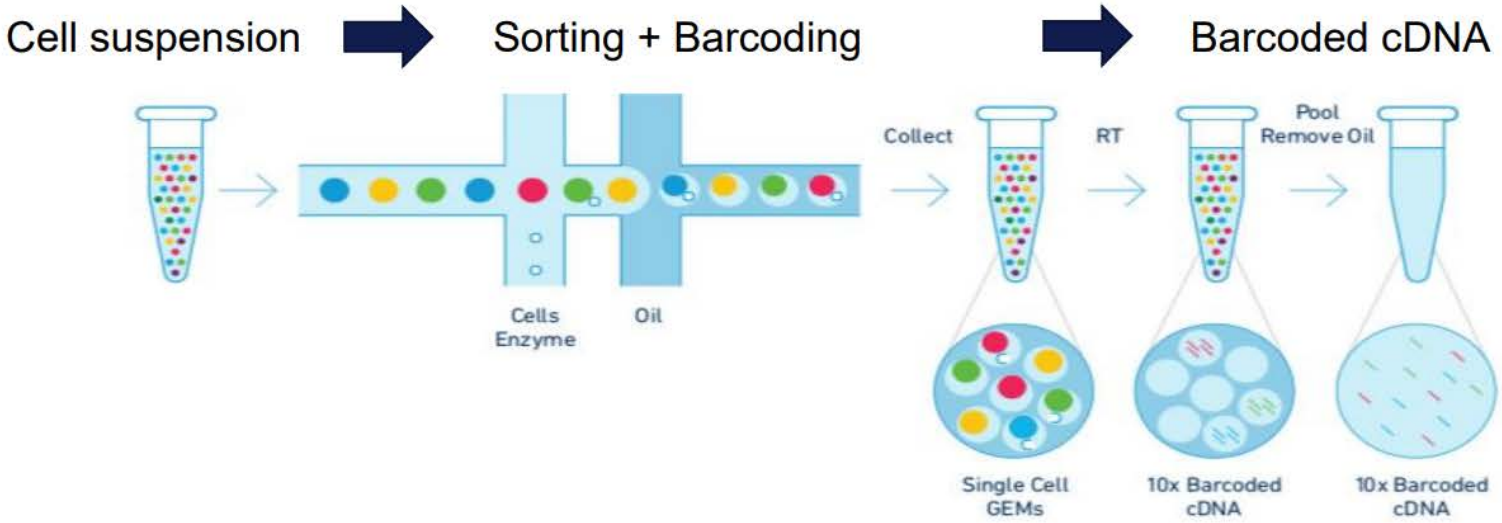
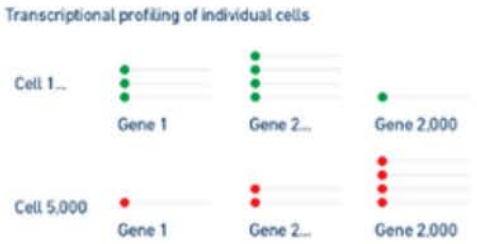
Single Cell RNA sequencing



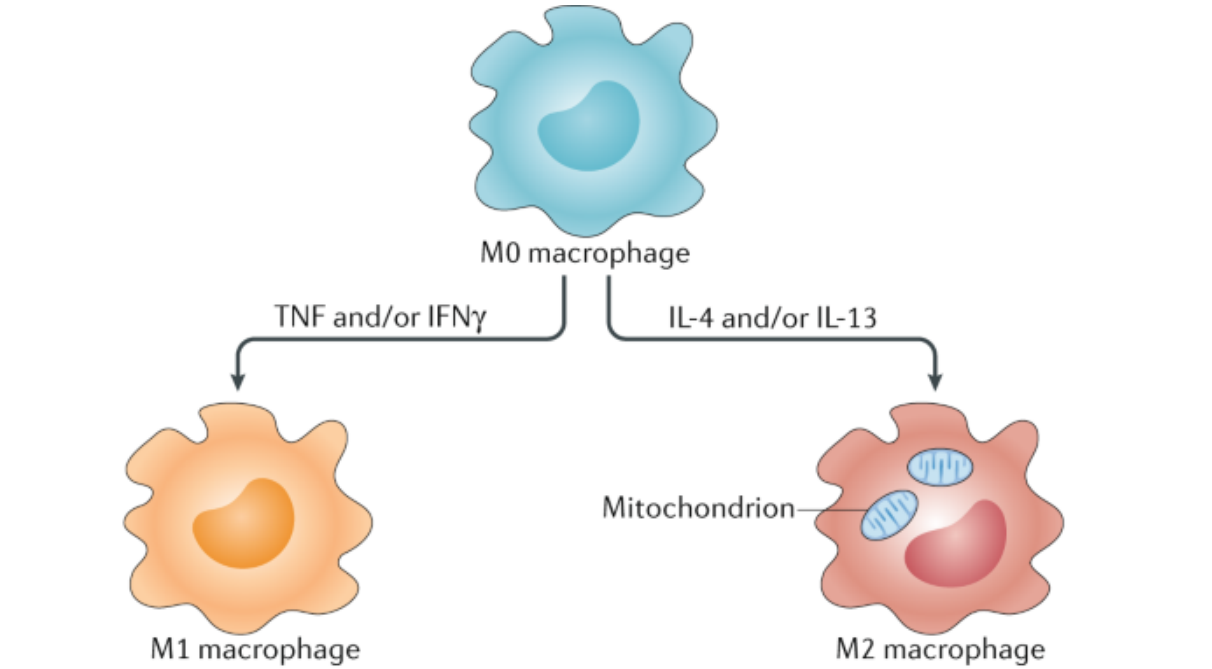
- Input: Single cells in suspension + 10x Gel Beads and Reagents
- Output: Digital gene expression profiles from every partitioned cell



→ max. 10.000/sample → ~15.000 genes /sample

10xgenomics.com

Macrophages



Abnormal immune responses in coronavirus animal models

IFN-1 and inflammatory monocyte-macrophages promote lethal SARS-CoV infection (Channappanavar et al. 2016)

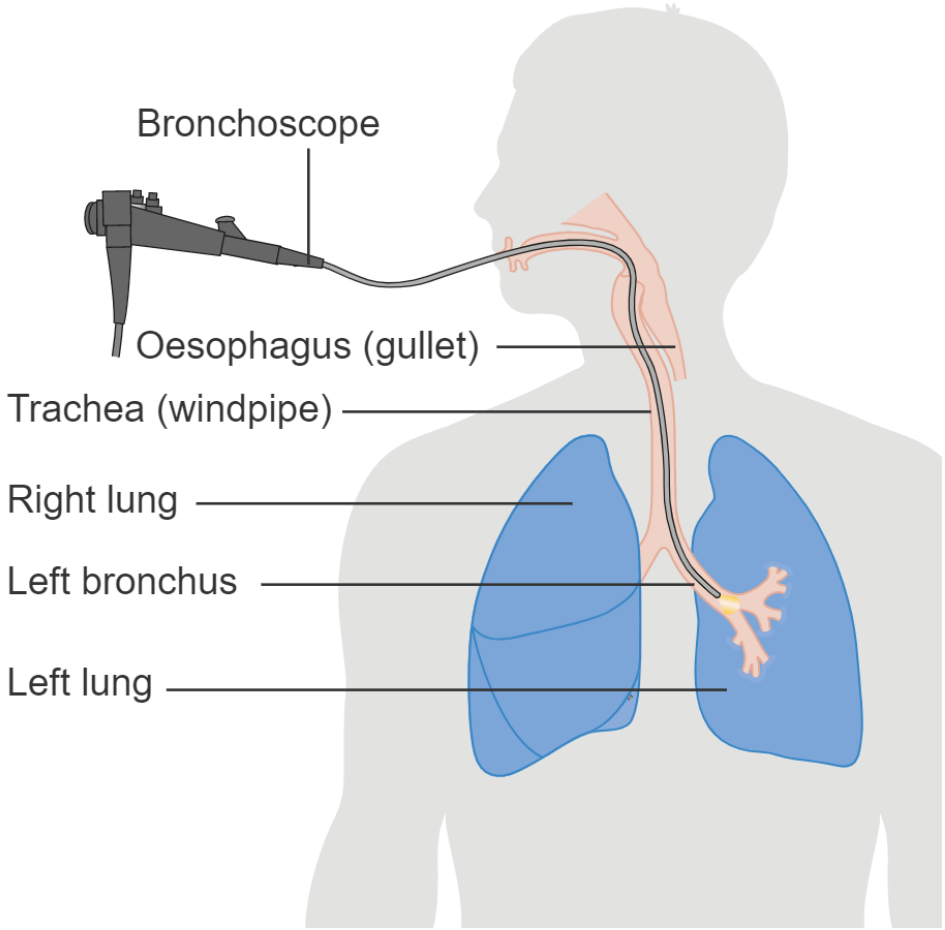
Alveolar macrophages undergo functional polarization in by COVID acutely infected macaques. (Liu et al. 2019)

COVID-19 is characterized by pneumonia, lymphopenia, exhausted lymphocytesa and a cytokine storm. (Xuetao Cao 2020)

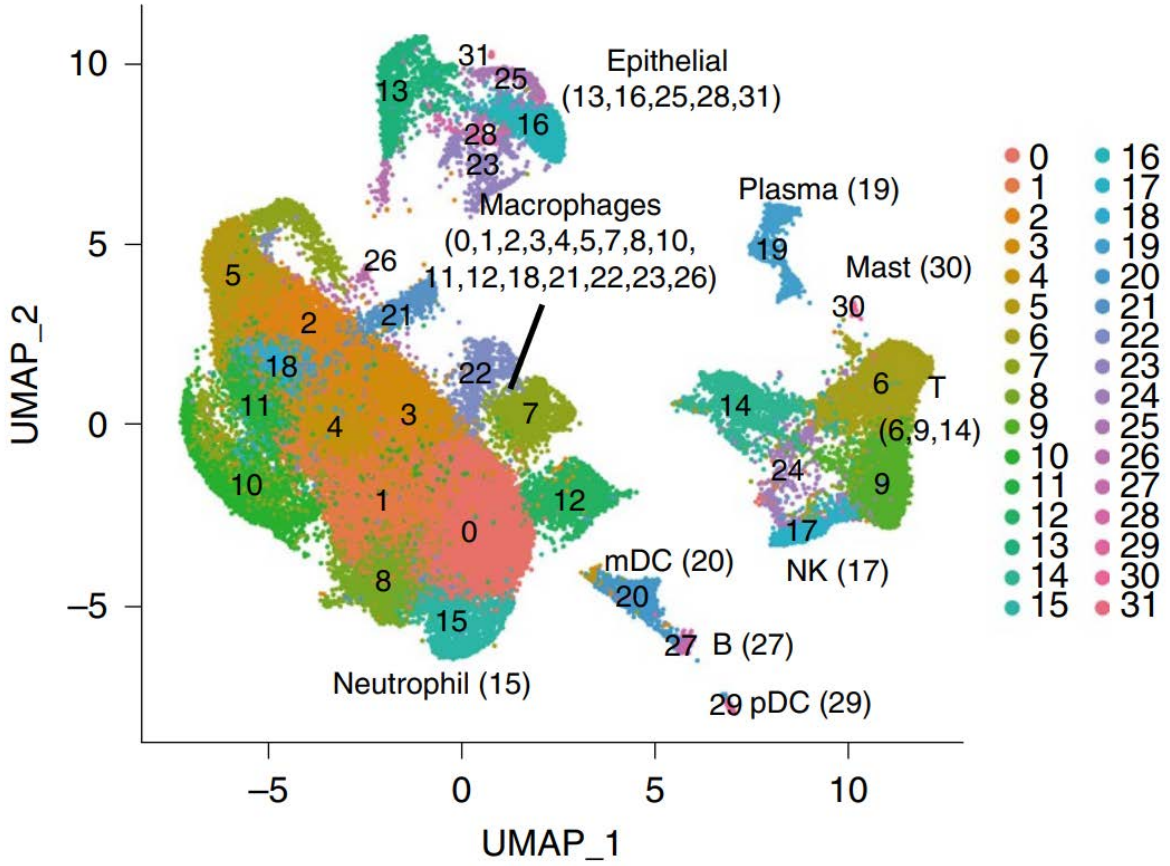
SCRNA seq on BALF cells

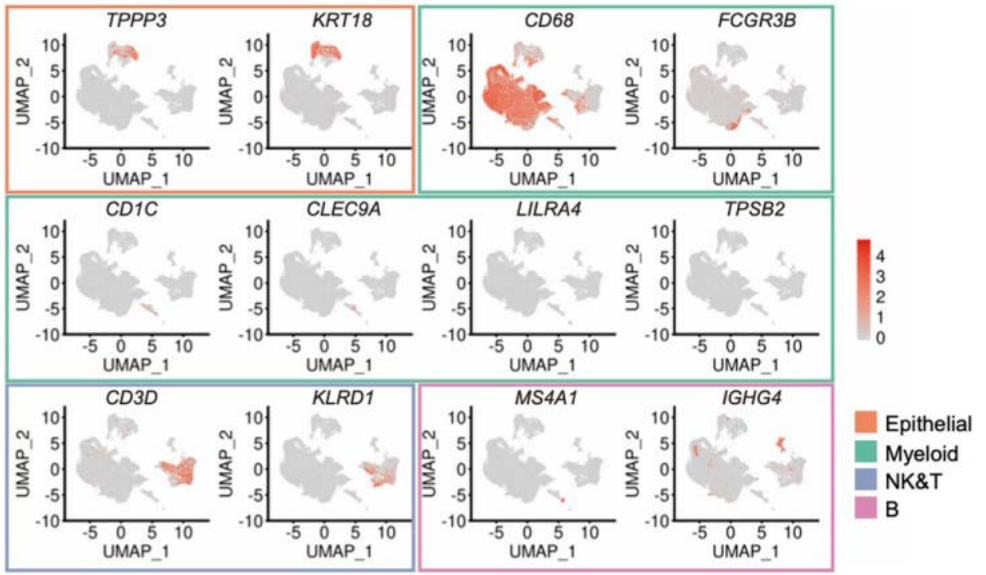
Conditions:

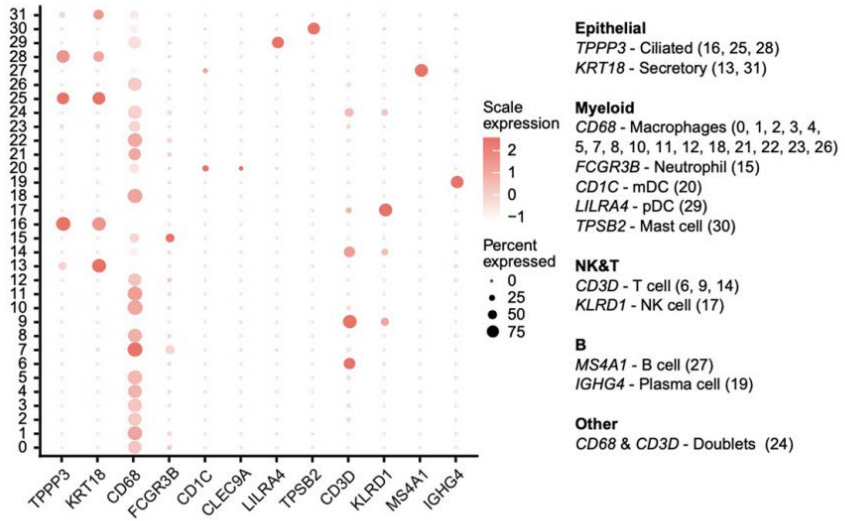
- 3 moderate COVID-19 +
- 1 severe/ 5 critical COVID-19 +
- 3 healthy controls
- 1 publicly available healthy control



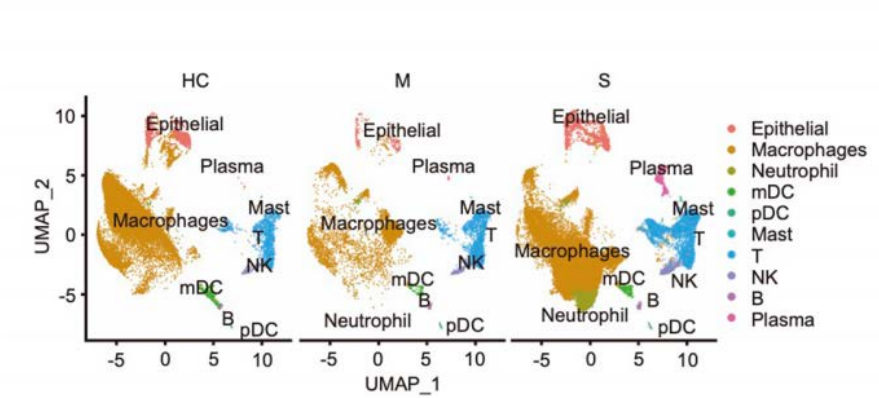
Clustering analysis and cell identification

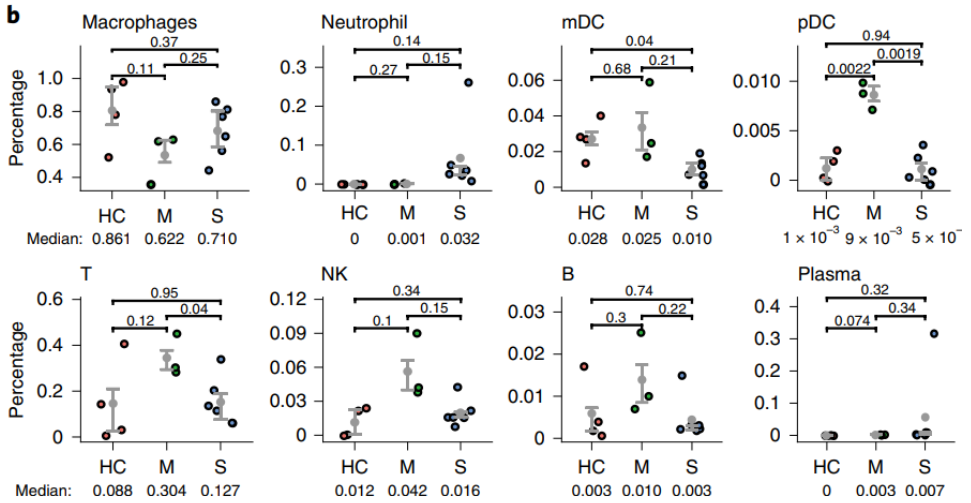


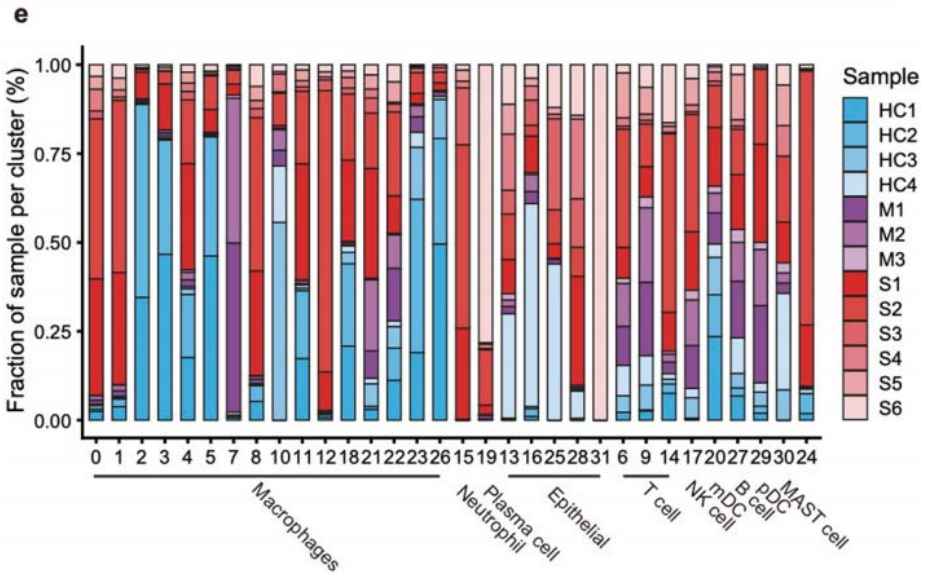




Specific macrophage in enrichment in different groups

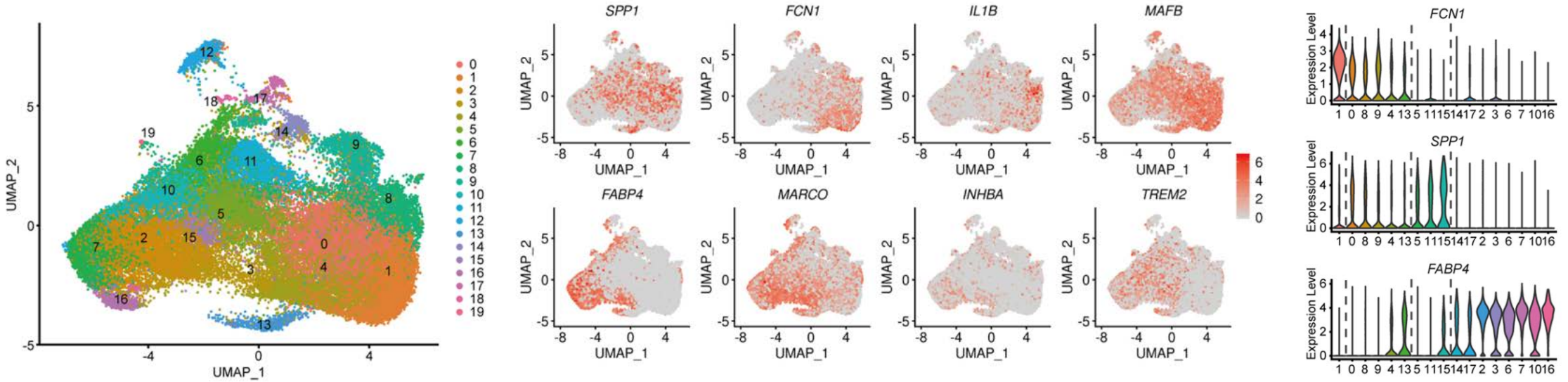


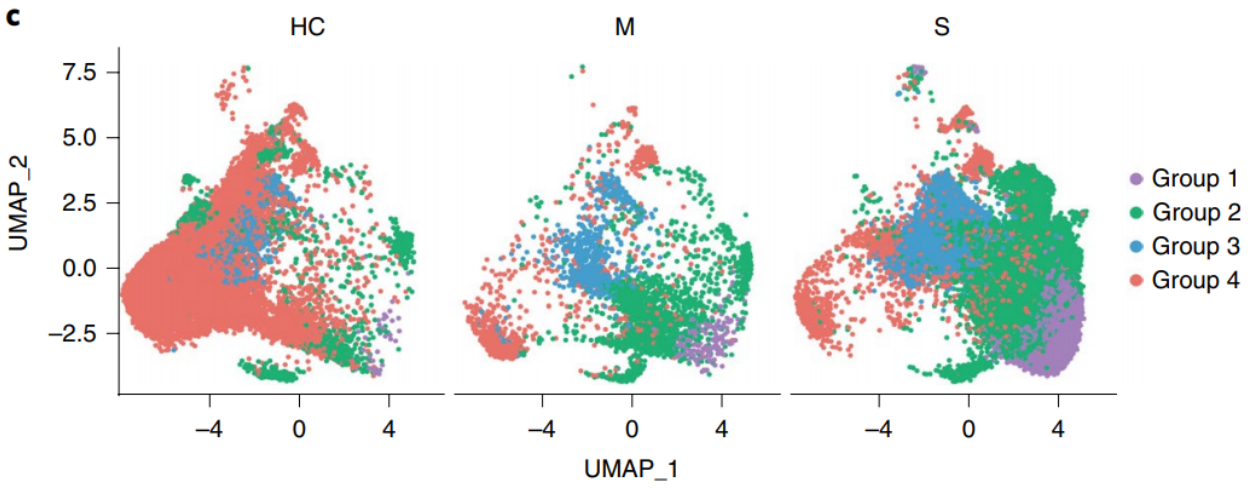


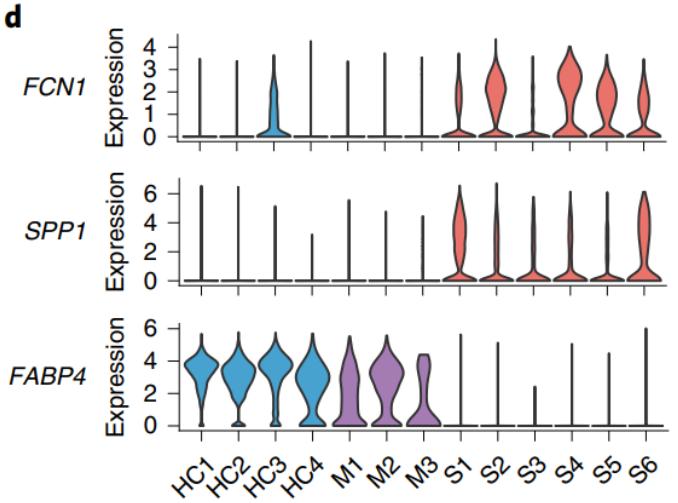


Group	MΦ(%)	NΦ(%)	mDC(%)	pDC(%)	T(%)	NK(%)	B(%)	Plasma(%)
HC	90.81	0	2.38	0.08	6.00	0.48	0.25	0.01
M	61.40	0.06	2.24	0.85	30.11	4.20	0.94	0.20
S	76.43	4.62	0.96	0.22	12.55	1.98	0.29	2.95

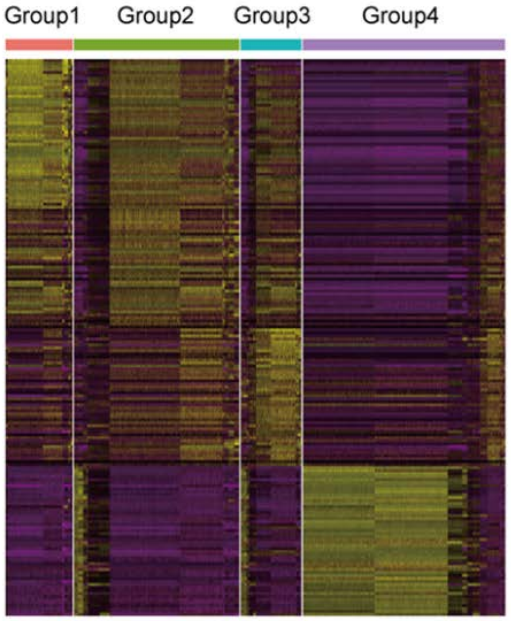
Macrophage subclustering revealed 4 major groups







DEG, GO and GSEA analysis characterised Macrophages-subtypes



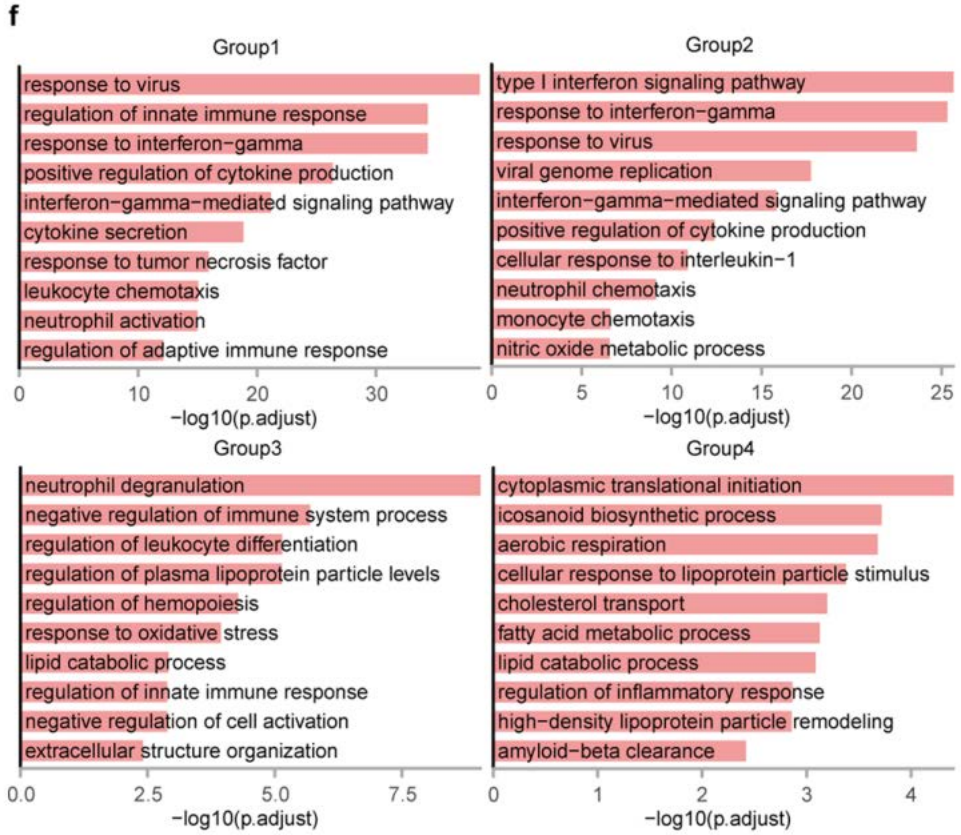
G1: *S100A9, S100A8, S100A12, VCAN, FCN1, CORO1A, SELL, CD14, CFP, RNASE2, SERPINB1, FPR1, COTL1, MPEG1, STAB1, MS4A6A*

G1&G2: *IL1RN, CCL7, IFITM2, IFIT2, IFIT3, IER2, MX1, NFKBIA, RSAD2, IFIT1, DUSP6*

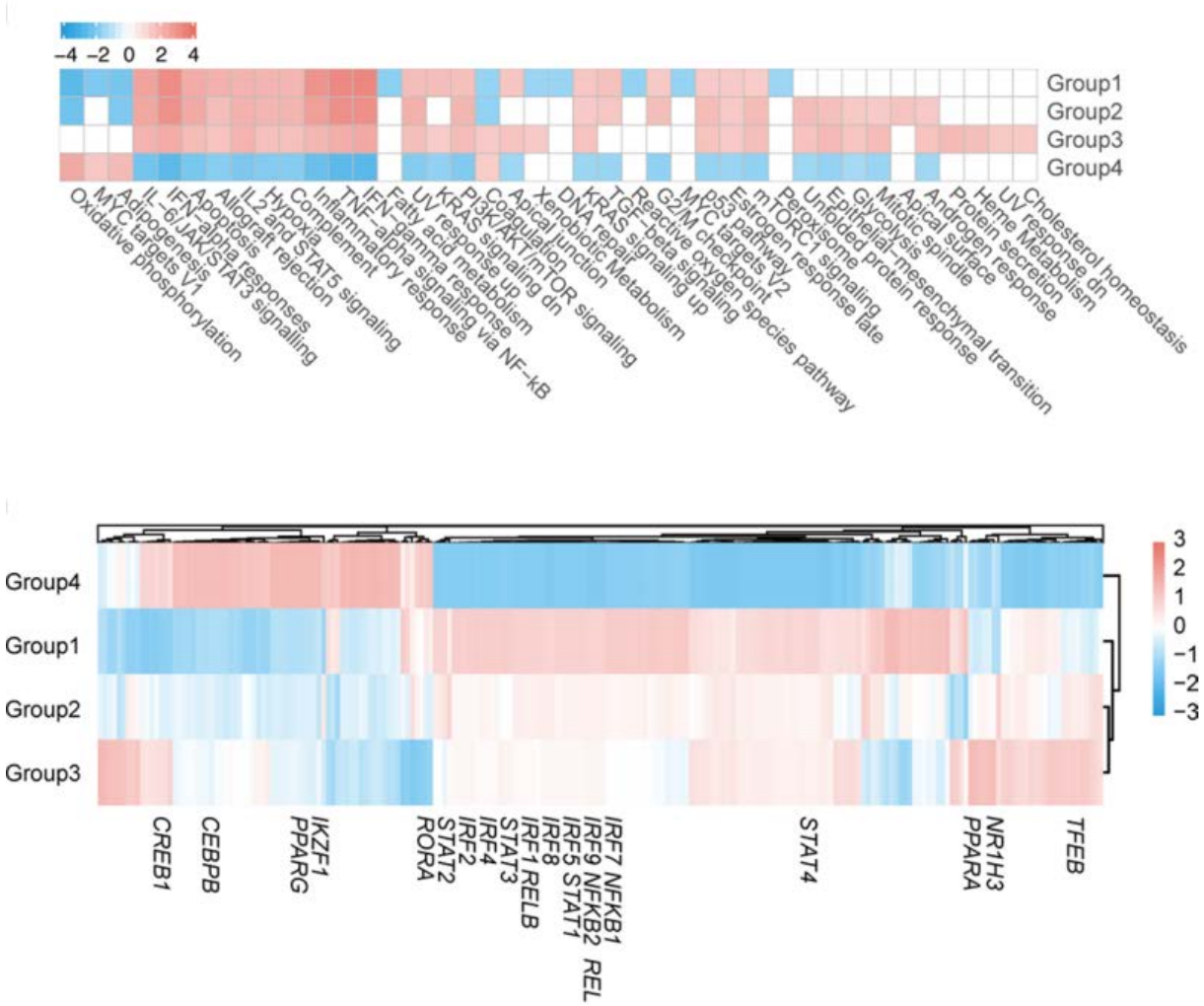
G2: *HSPA6, DNAJB1, HSPA1A, HSPA1B, CCL2, HSPB1, HSPH1, CCL8, BAG3, CCL3, TIMP1, HSP90AA1, CCL4, DEFB1, VAMP5, CCL4L2, CXCL10, NINJ1, SOD2, CCL3L1, BCL2A1, TYMP, SGK1, ISG15, CTSB, ANKRD22, CALHM6, GBP5, GBP1, ISG20, APOBEC3A, IDO1, TNFSF10, CLU, SLC25A37, PLEK, GCH1, CXCL11, PLA2G7, SLAMF7, CYP1B1*

G3: *LGMN, SPP1, RGS1, RNASE1, CCL18, HMOX1, C1QC, SDS, ARL4C, CTSL, GPR183, NR1H3, FPR3, ABCA1, TTYH3, CREG1, A2M, CTSZ, NRP2, PLTP, GPNMB, LHFPL2, SMPDL3A, PLD3, CD84, MARCKS, SDC3, TMEM176A, PMP22, MMP14, TMEM176B, MS4A4A, HSP90B1, CREM, CCL13, CD86, APOE, IL7R, TREM2, LIPA, TGFB1*

G4: *FABP4, CD52, APOC1, ALOX5AP, GCHFR, MARCO, HLA-DQB1, ALDH2, RBP4, TFRC, MCEMP1, FBP1, HLA-DQA1, INHBA, MSR1, ACP5, MRC1, PEBP1, LPL, AKR1C3, HPGD*



Macrophage microenvironment seems highly proinflammatory in severe COVID-19 cases

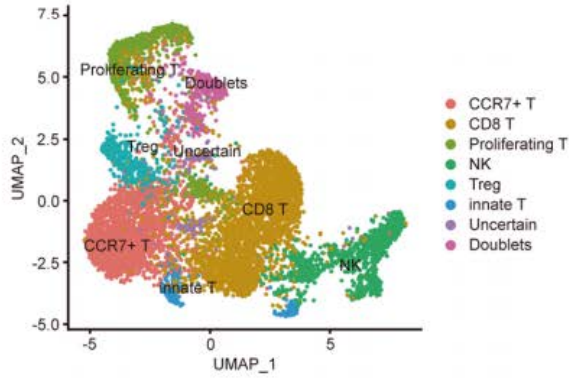


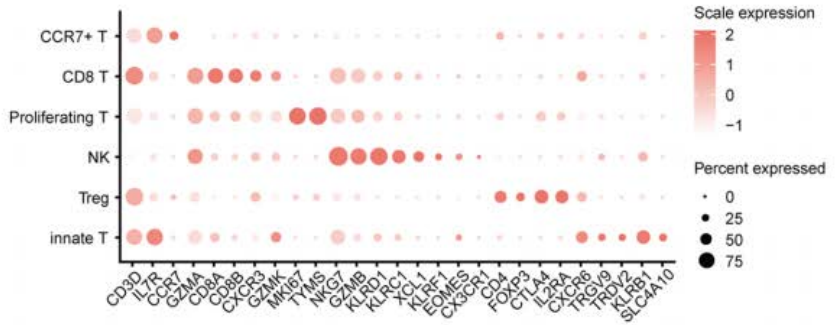
T-cell

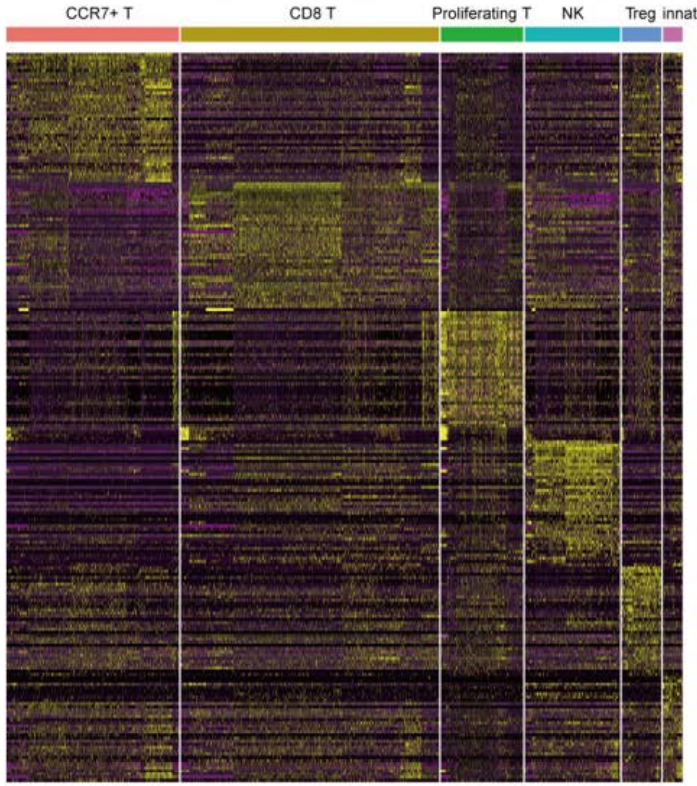
and

NK cell

Identification and Characterisation







CCR7+ T: *IL7R, LTB, RPS12, CCR7, RPL30, RPL34, EEF1A1, PABPC1, MAL, SARAF, FXYD5, LEF1, FLT3LG, JUNB, TSHZ2, S1PR1, TMEM123, KLF2, CMTM6, PDE4B, CMTM8, TRAT1, CXCR4, TNFRSF25, KDSR, SESN3, TNFRSF4, ICAM2, SOCS3, TMEM173, TCF7, NFKBIA, BIRC3, RIPOR2, PIM2, RGS1, FOS, SELL, DUSP1, CXCL10*

CD8 T: *CD8A, CD8B, CCL5, ZNF683, PTPRCAP, ITGA1, GZMH, CD52, GZMA, JAML, LINC02446, LAG3, CD2, GZMK, ABI3, CXCR6, CXCR3, FASLG, KLAA1551, PLEKHF1, PTPN22, GPP25, ITM2C, GRAP2, CD27, SCML4*

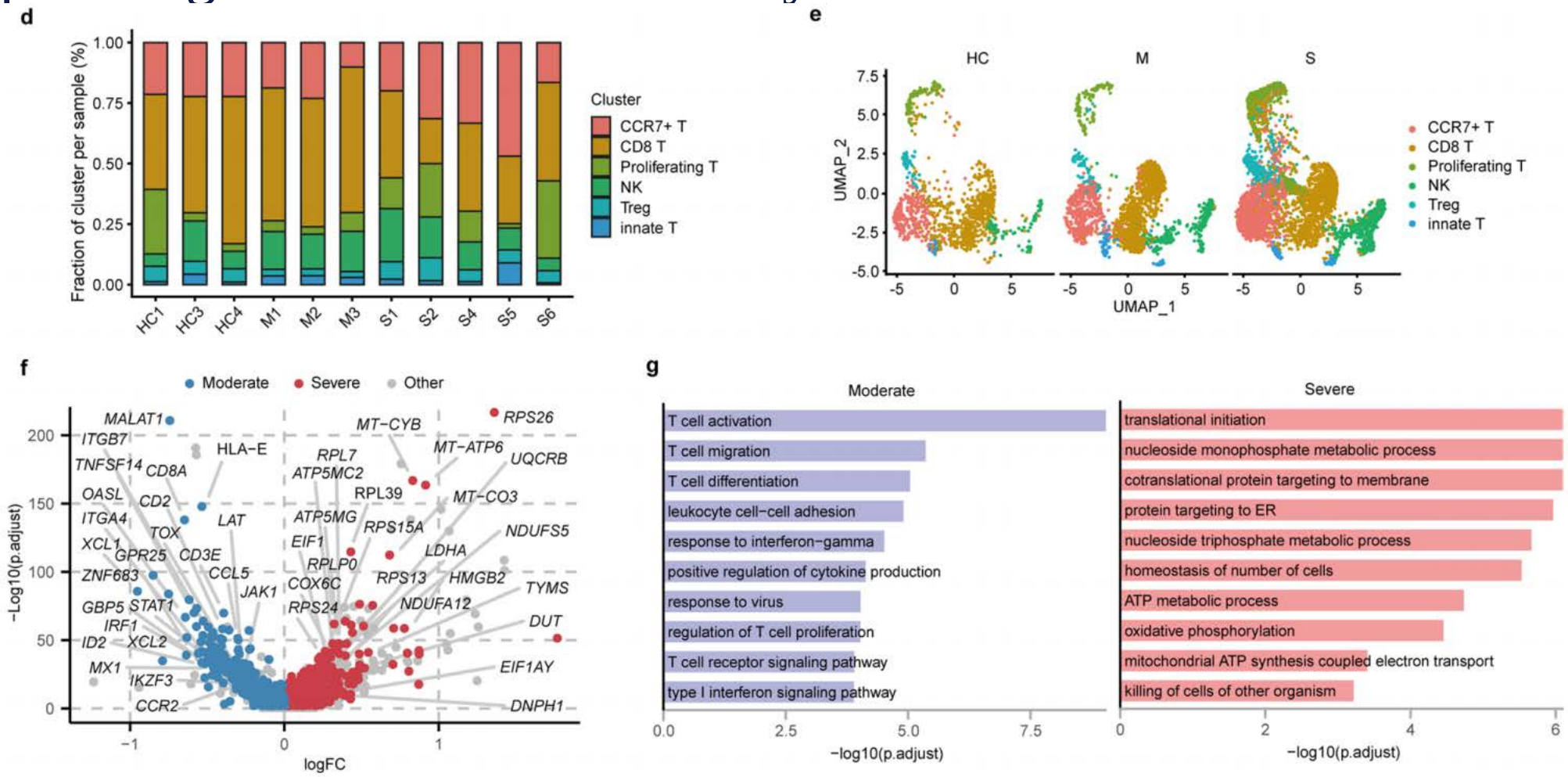
Proliferating T: *TUBA1B, HIST1H4C, HMGB2, TYMS, TUBB, UBE2C, H2AFZ, TOP2A, MKI67, DUT, CENPF, CKS1B, NUSAP1, CDK1, PCNA, H2AFV, SLC25A5, SMC4, CDT1, CENPM, BIRC5, TK1, DHFR, HMGB1, CLSPN, CENPU, RRM2, H2AFX, CKS2, HIST1H1B*

NK: *TYROBP, KLRD1, NKG7, FCER1G, GNLY, TRDC, PRF1, GZMB, KLRF1, XCL1, XCL2, SRGN, CCL3, CCL4, KLRC1, CST7, CD7, FCGR3A, CMC1, LAT2, IL2RB, MATK, IGFBP7, IFITM3, ADGRG3, FGFBP2, TNFRSF18, KLRC3, TXK, SLA, CCL4L2, KLRB1, GNPTAB, PLEK, MAP3K8, IFNG*

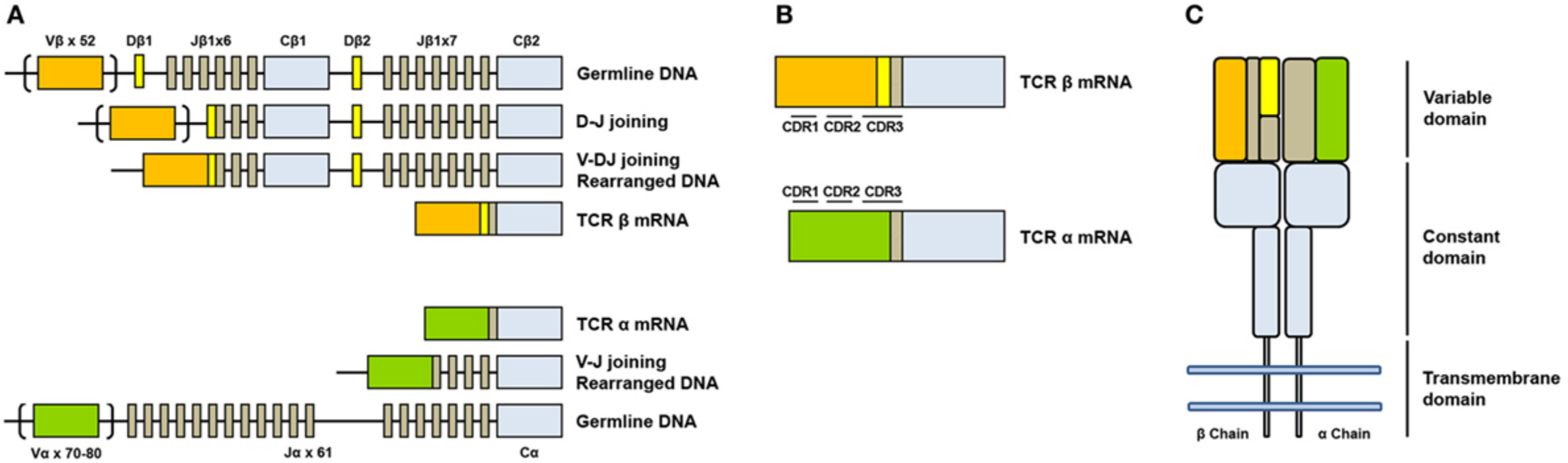
Treg: *CTLA4, MAF, FOXP3, TNFRSF1B, SLAMF1, LIMS1, IFI27, PBXIP1, PDCD1, SPOCK2, LAPTM5, ICOS, IL2RA, TYMP, LCK, CD5, GALM, DUSP4, BATF, CORO1B, UCP2, CREM, TIGIT*

innate T: *SLC4A10, TRDV2, KLRB1, IL7R, DUSP1, NCR3, TRAV1-2, TRGV9, TMIGD2, KLRG1, SPOCK2, CCR6, IL23R, CA2, RORC, ZFP36L1, RORA, JUN, CEBPD, CD69, DDX5, IL4I1, ADRB2, FYN, DUSP2, ZBTB16, CXCR6, ITM2B, GPR65, CCL20, SLAMF1*

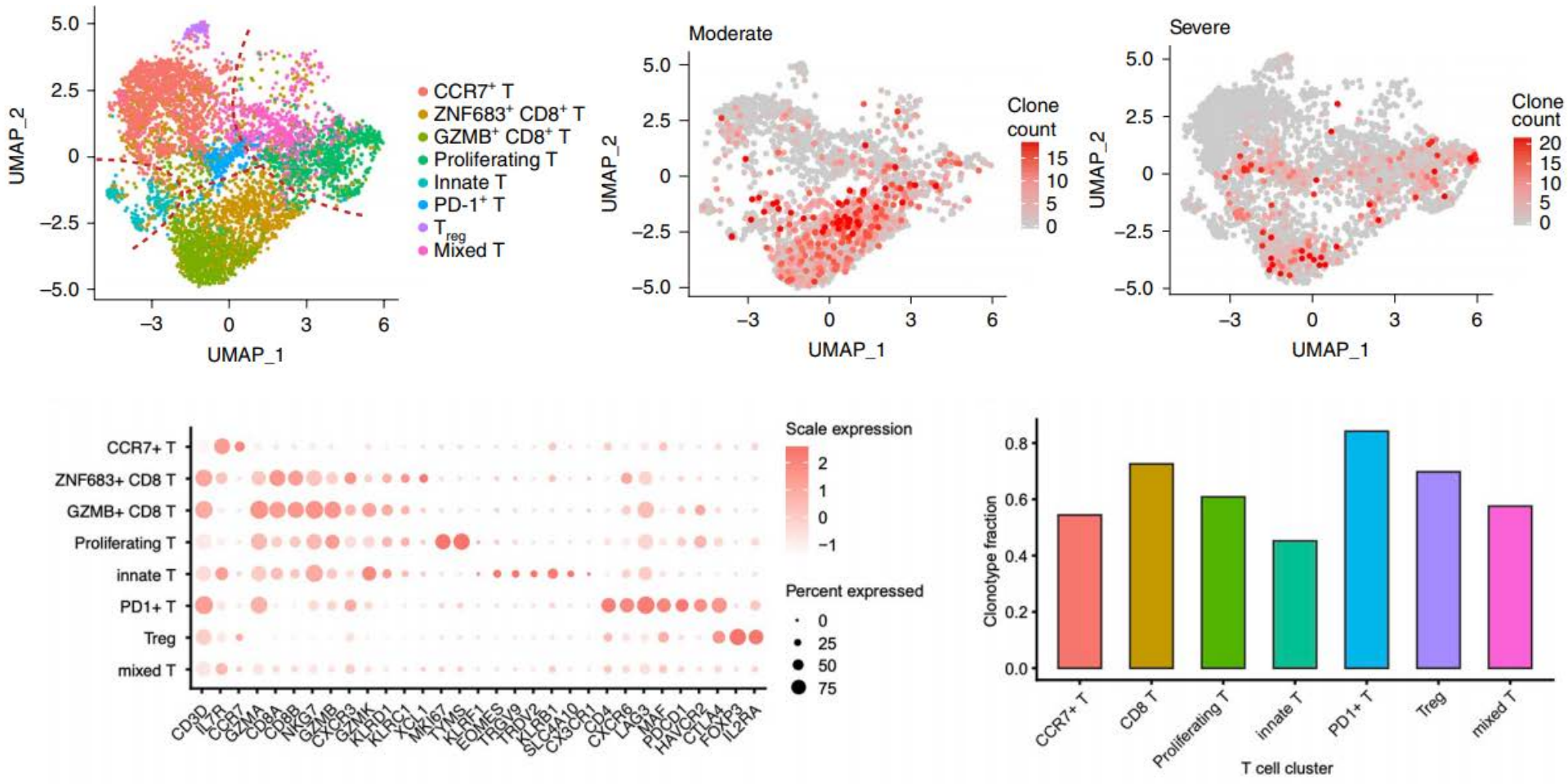
CD8+ T cells differ in mass and function depending on COVID-19 severity



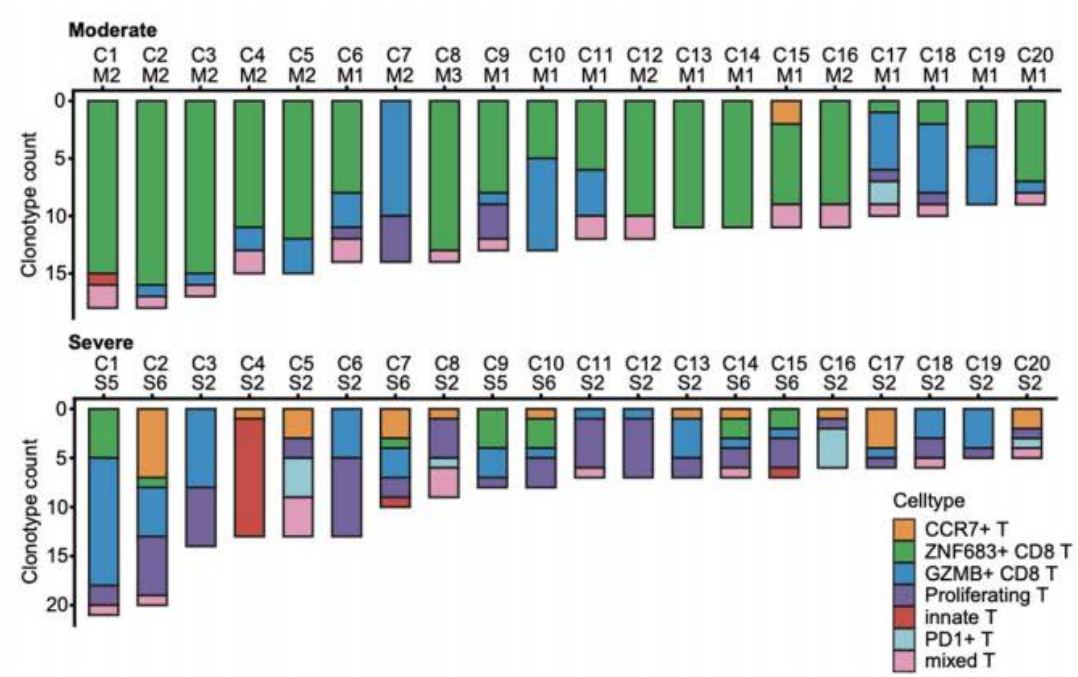
Single-cell T cell receptor sequencing

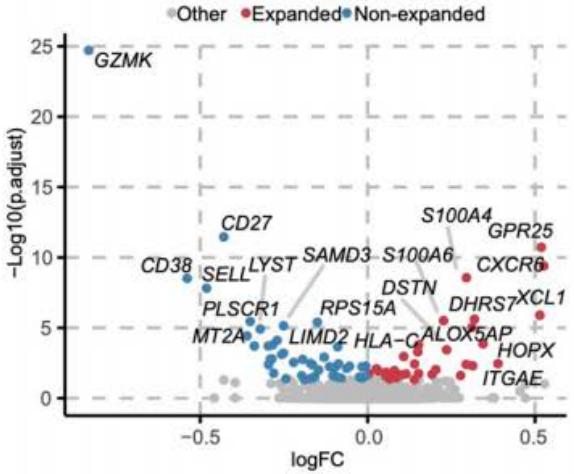


scTCR-seq of BALF from patients with COVID-19

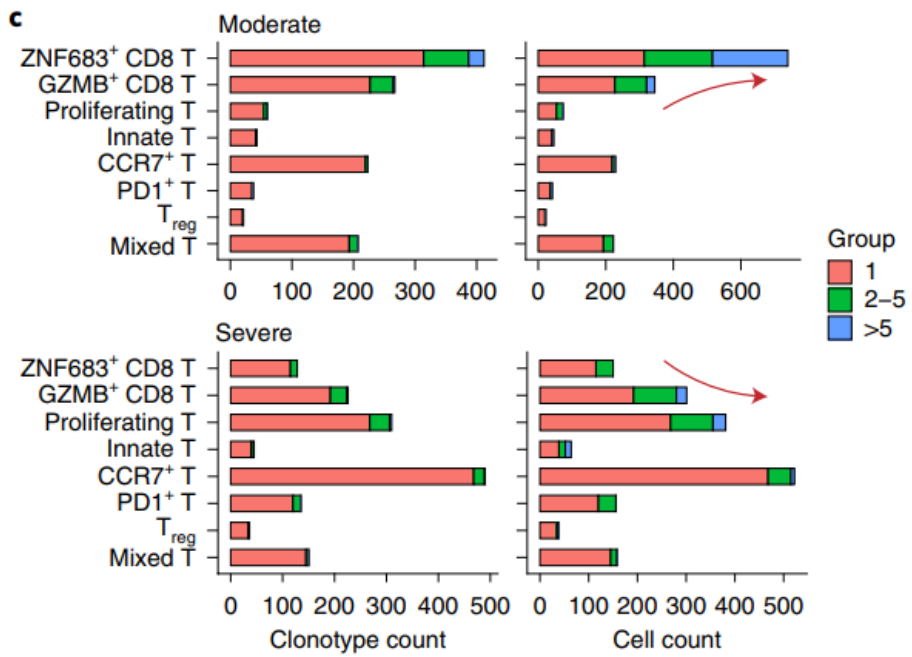


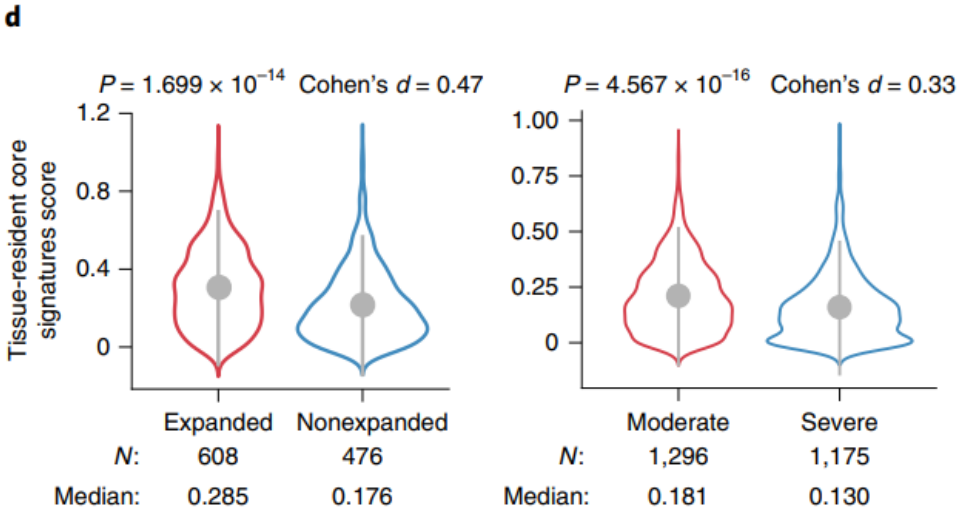
ZNF683+ cluster enriched in moderate infections express tissue-residence genes



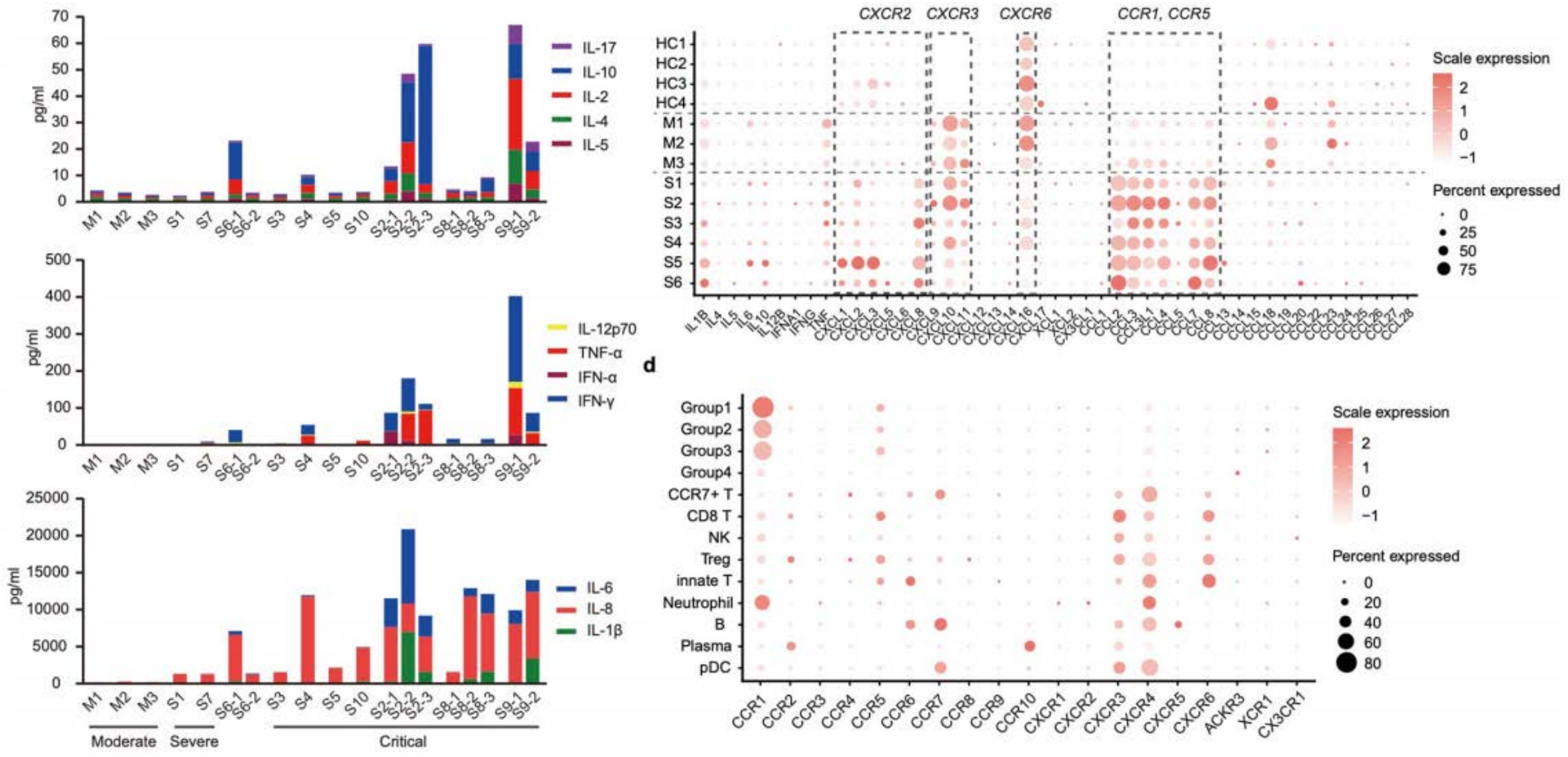


CD8+ T cells are less expanded, more proliferative and more phenotypically heterogeneous in severe/critical infected patients

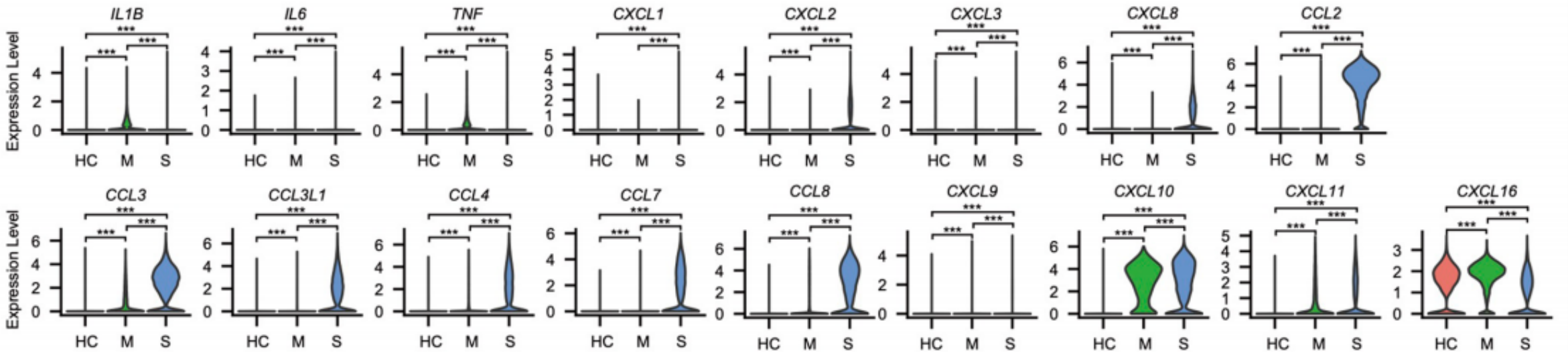




Lung macrophages in patients with severe COVID-19 infection contribute to local inflammation



Lung macrophages in patients with moderate COVID-19 infection attract T cells



Conclusion

Text einfügen

Macrophagen einteilung