Re-analysis of Marin-Carli et al sMEC Data

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January 4, 2021

Contents

1 Purpose

To re-analyse cell populations from the Martin-Carli *et al*'s scRNAseq study of lactating mammary glands. This work is described in Martin Carli et al. (2020). This follows the analysis flow suggested for Seurat 3.2 seen at https://satijalab.org/seurat/v3.2/pbmc3k_tutorial.html

2 Data Input

Downloaded the data from GSE15889 and removed prefixes from filenames.
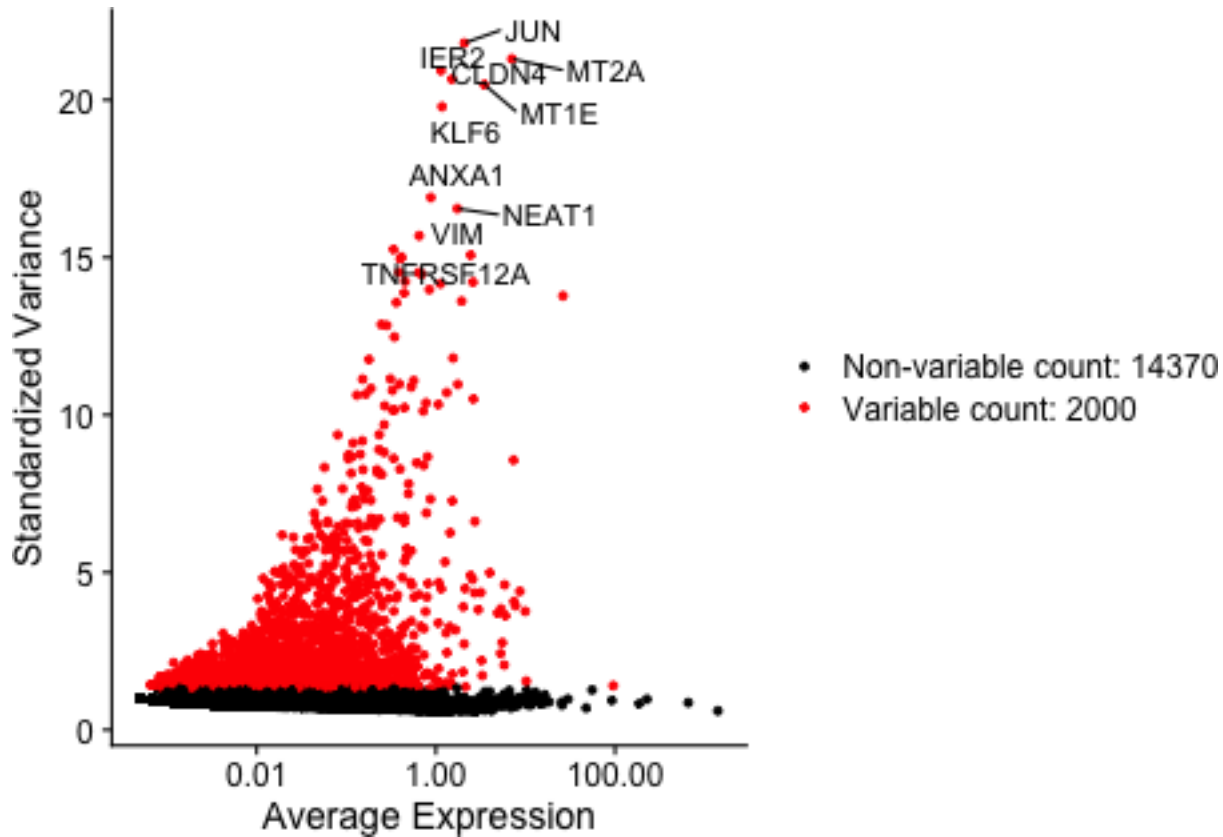
2.1 Preprocessing
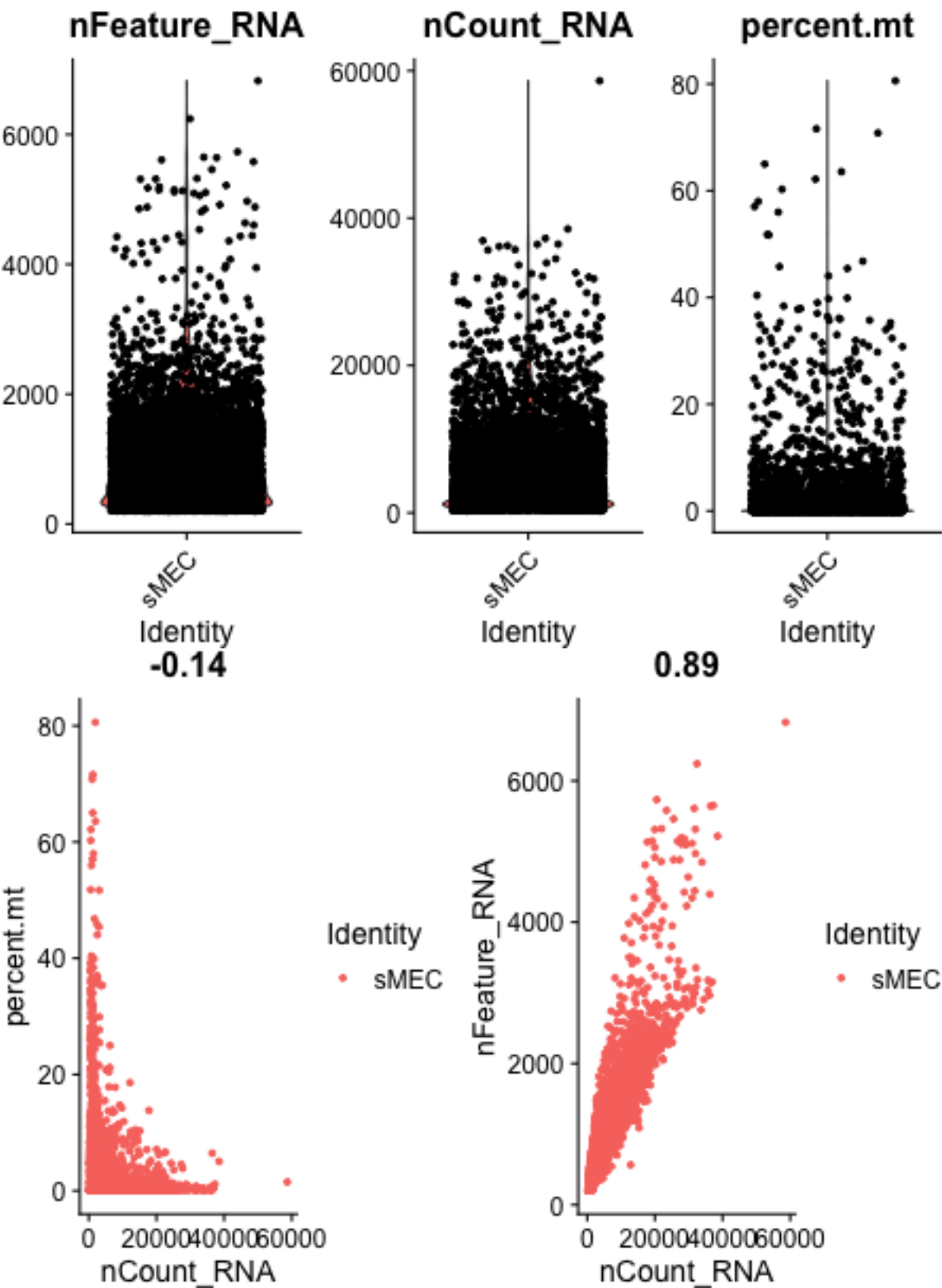
Normalizing Data

Normalizes the feature expression for each cell by the total expression x 1000, then log transforms

2.2 Highly Variable Features

Features with high cell to cell variability (highly expressed in some cells but not others)

2.3 Scaling

Shifts expression so that mean expression across cells is 0, and variance is 1. This reduces the impact of outliers on downstream analyses. We did not regress out specific sources of heterogeneity like mitochondrial contamination or cell cycle stage.

3 Dimensionality Reductions

```
## PC_ 1
## Positive:  SPP1, CLU, SCGB3A1, HPGD, MYBPC1
## Negative:  MALAT1, NEAT1, KLF6, JUNB, BTG1
## PC_ 2
## Positive:  CLDN4, TNFRSF12A, ELF3, MT1E, ATF3
## Negative:  SRGN, PTPRC, LAPTM5, CD52, CXCR4
## PC_ 3
## Positive:  TYROBP, FCER1G, SPI1, CD68, FABP5
## Negative:  ETS1, TRAC, CD3E, CD2, FYN
## PC_ 4
```

```
## Positive:  KIAA0101, TYMS, PTTG1, STMN1, CCNB1
## Negative:  NEAT1, MT-CO3, MT-CO1, MT-ND4, XIST
## PC_ 5
## Positive:  S100A10, S100A6, FTL, S100A4, HCST
## Negative:  KIAA0101, BIRC5, CCNB1, TYMS, TOP2A
```
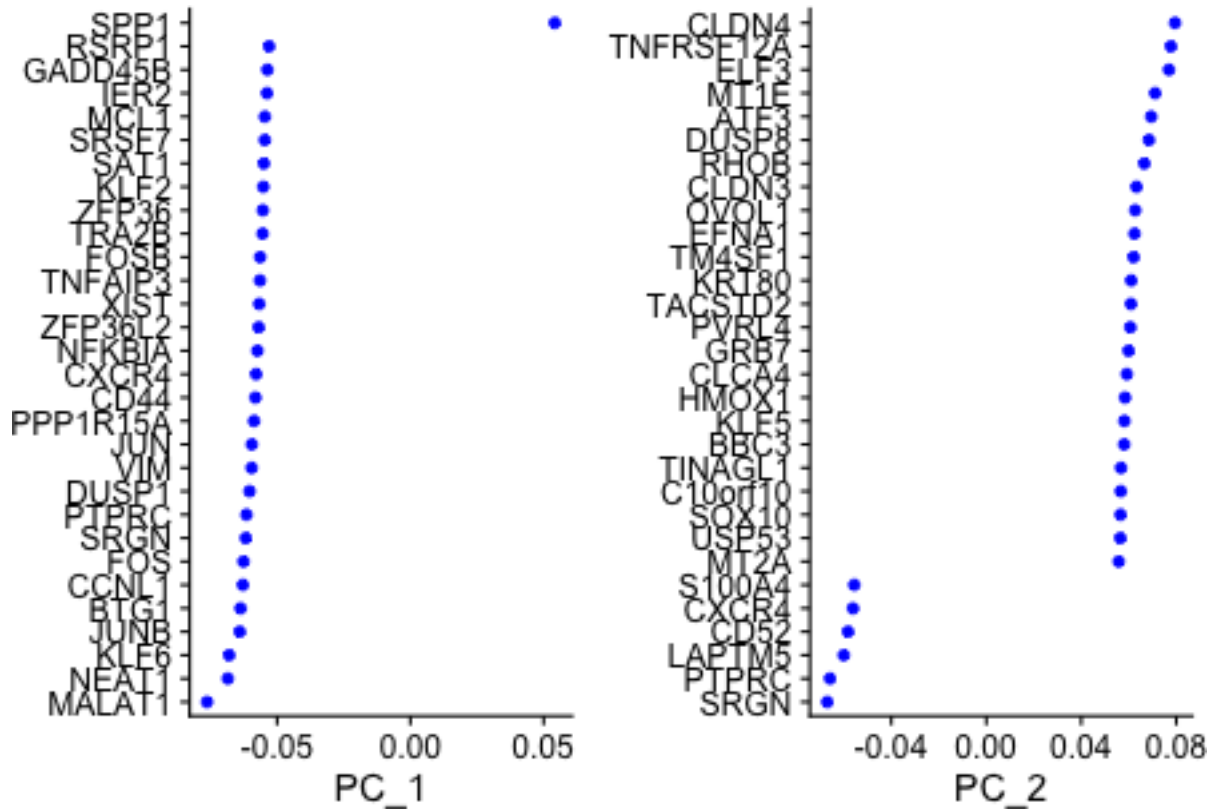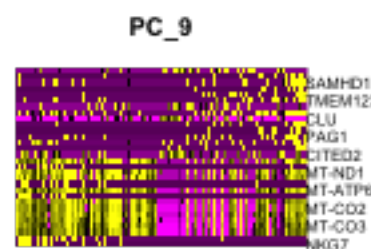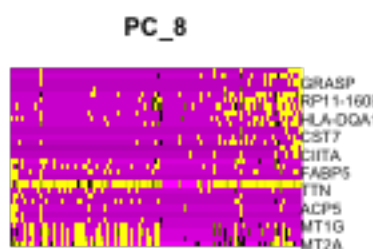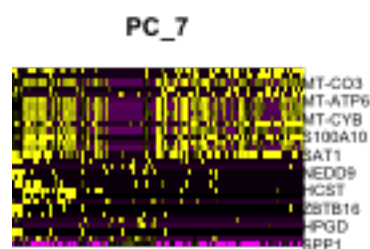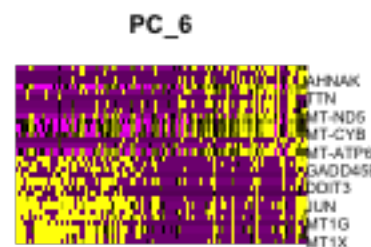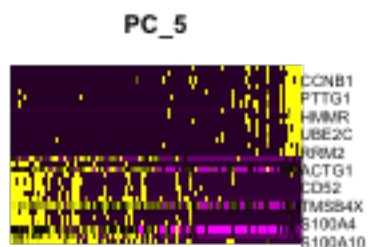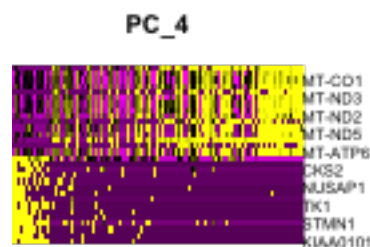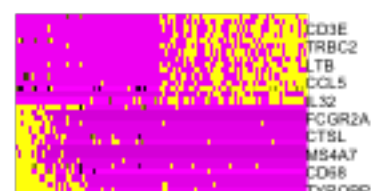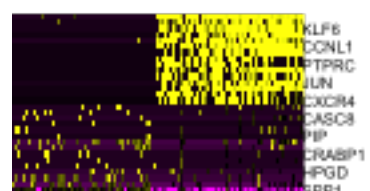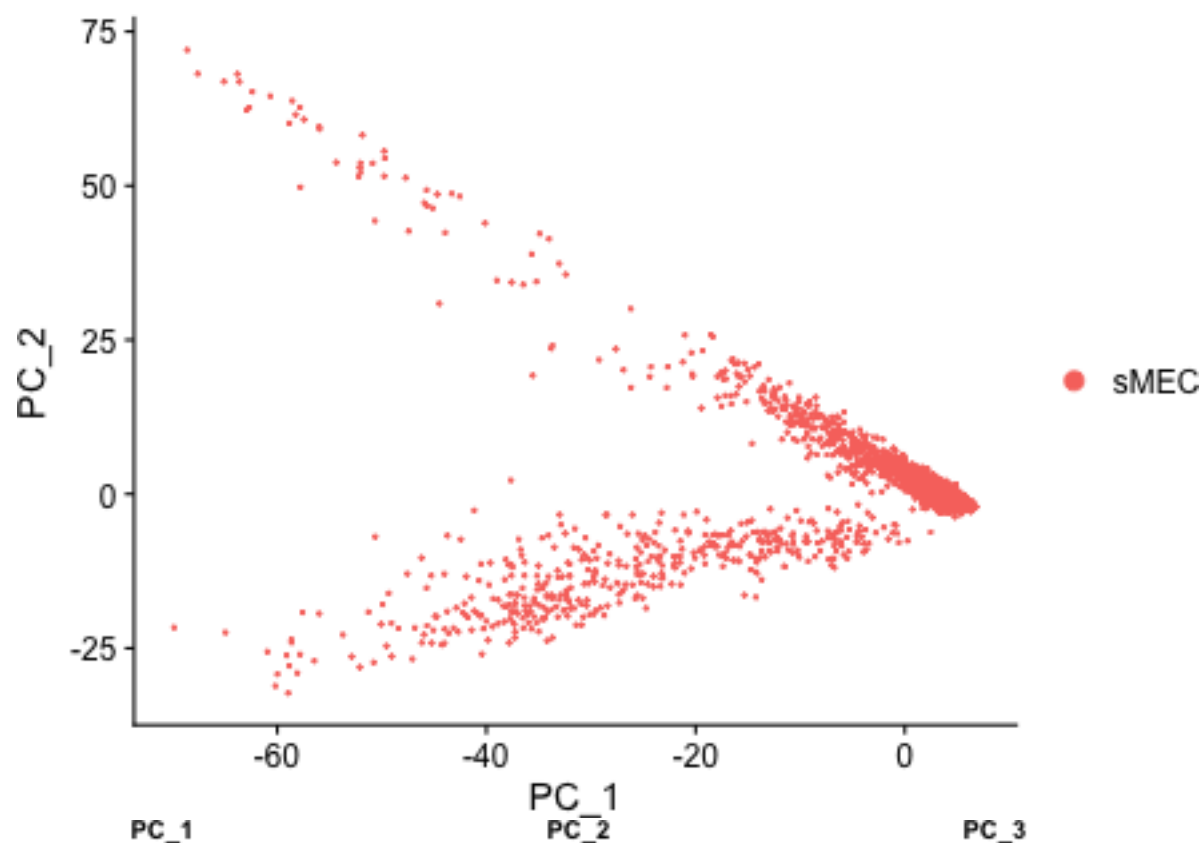
4   Determination of Number of Clusters

Used the JackStraw procedure in Macosko et al. (2015), sampling 1% of the data re-running the PCA and constructing a null distribution of feature scores, then repeating. This identified 'significant' PCs. We also did an elbow plot.
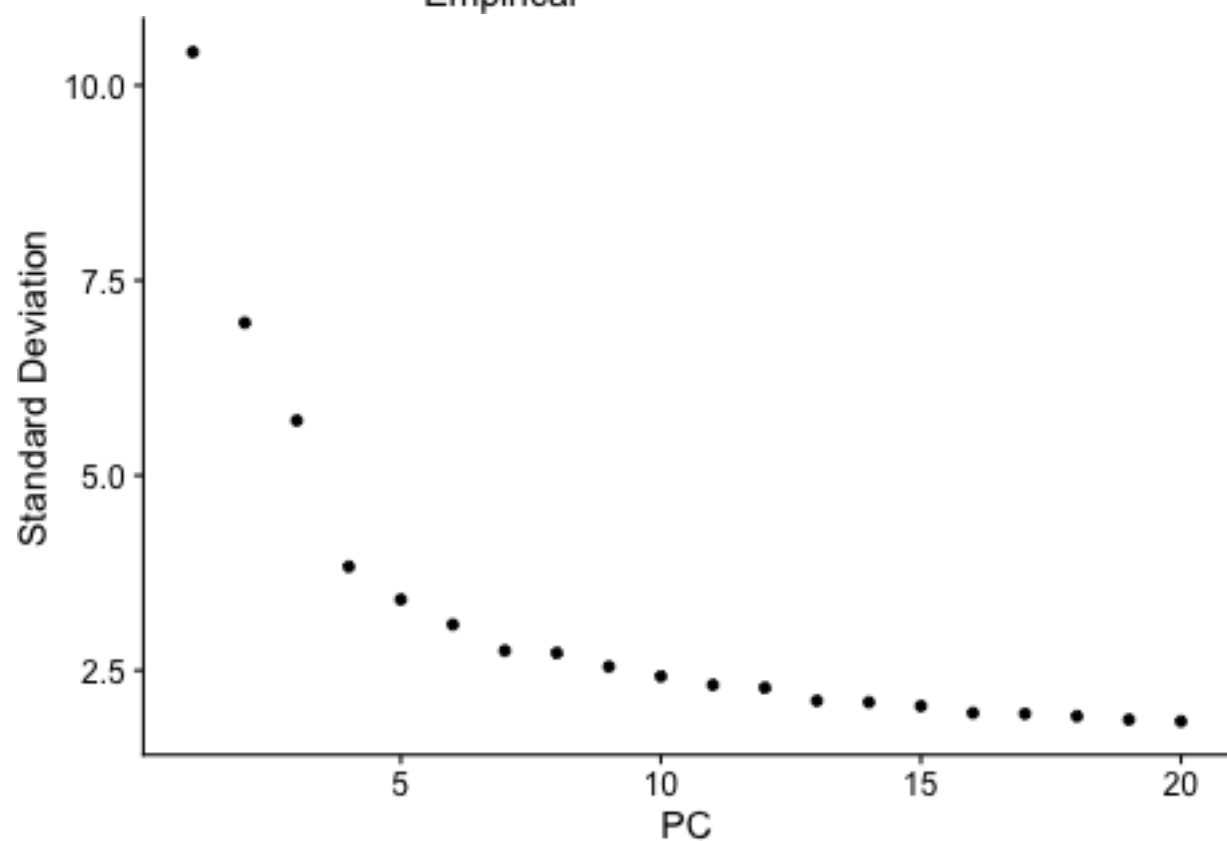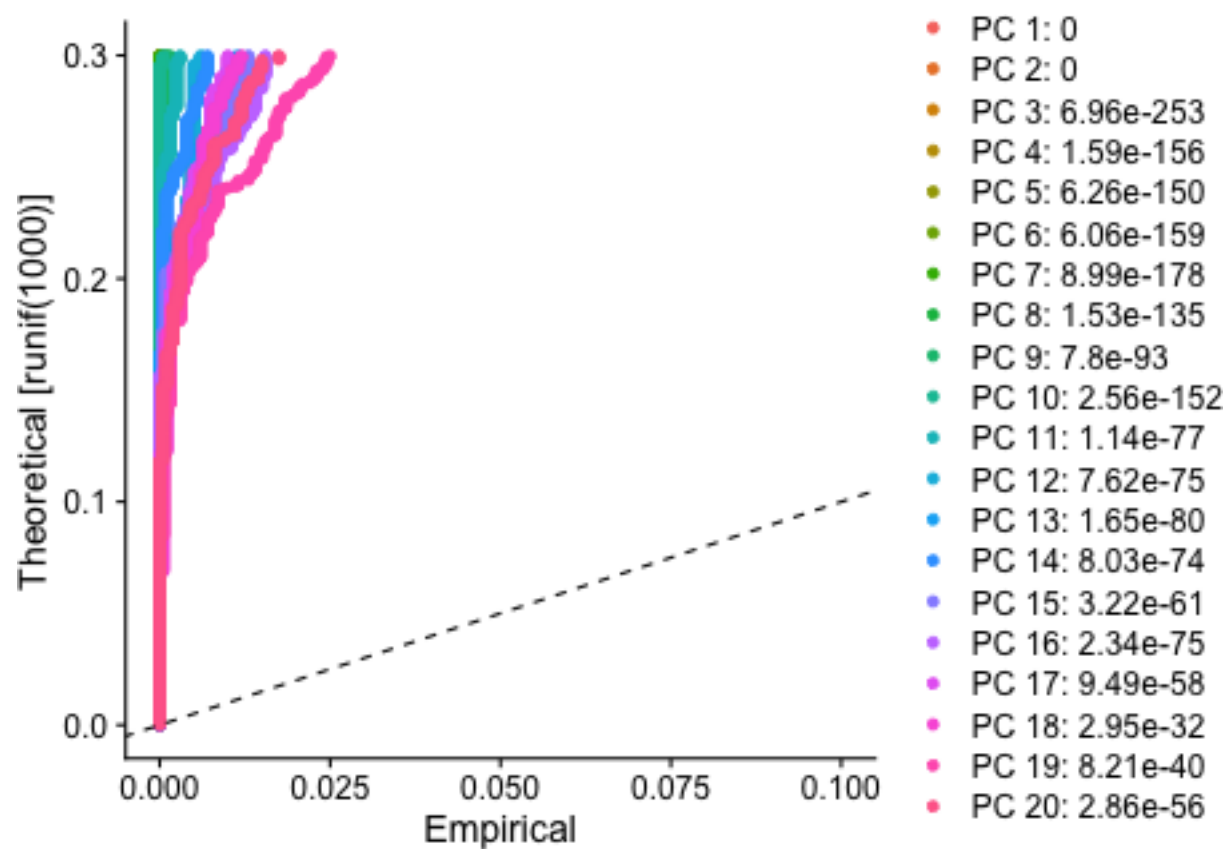
Based on this we decided to use 7 PCs to cluster the cells.

5 Clustering Cell Types

Seurat 3.2 uses a K-nearest neighbor approach then tries to partition this into commmunities of cell types.

5.1 Identification and Assignment of Clusters

```
## Modularity Optimizer version 1.3.0 by Ludo Waltman and Nees Jan van Eck
##
## Number of nodes: 5917
## Number of edges: 178451
##
## Running Louvain algorithm...
## Maximum modularity in 10 random starts: 0.7940
## Number of communities: 13
## Elapsed time: 0 seconds
```

5.2 Non-Linear Dimensionality Reduction

Did both UMAP and t-SNE plots using 7 clusters

5.2.1 t-SNE Plots
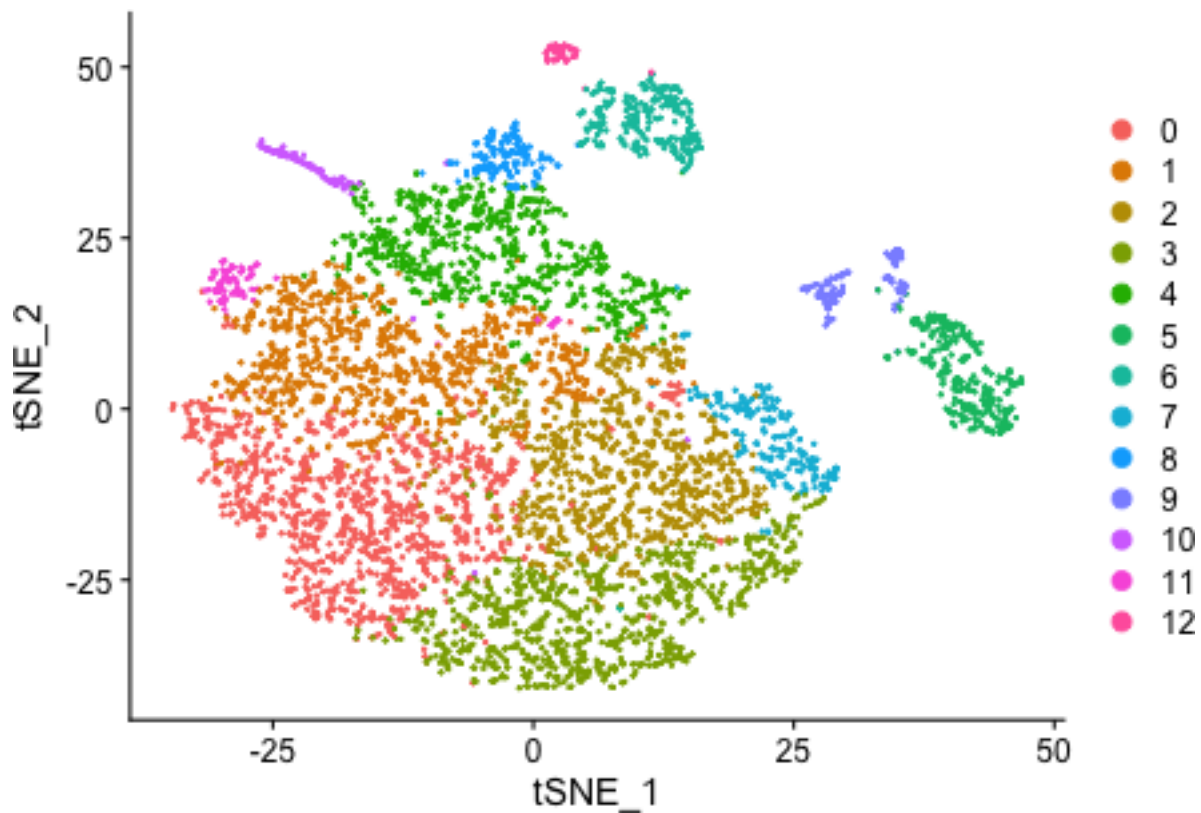
Figure 1: t-SNE plot of secreted MECs

5.2.2 UMAP
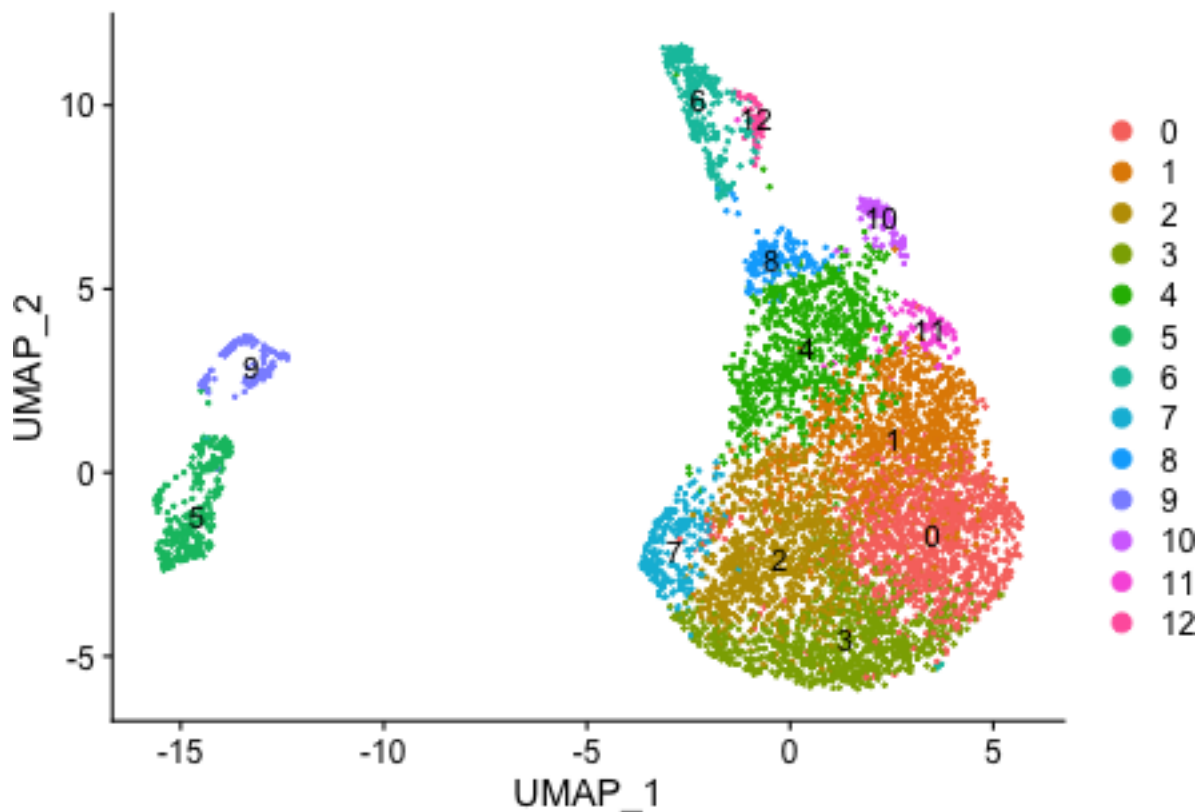
Figure 2: UMAP plot of secreted MECs

Table 1: Cell Specific Markers (All)

p_val	avg_logFC	pct.1	pct.2	p_val_adj	cluster	gene
0	0.916	0.611	0.176	0	4	LY6D
0	1.109	0.892	0.592	0	4	CLU
0	0.888	0.542	0.186	0	4	KRT15
0	3.261	0.997	0.137	0	5	MALAT1
0	2.638	0.772	0.012	0	5	PTPRC
0	2.774	0.994	0.545	0	5	MT-ATP6
0	2.964	0.846	0.085	0	6	JUN
0	3.724	0.643	0.050	0	6	MT1E
0	3.935	0.750	0.111	0	6	MT2A
0	1.590	1.000	0.664	0	7	MT-CO1
0	1.430	1.000	0.650	0	7	MT-CO3
0	1.373	0.860	0.358	0	7	MT-ND5
0	2.329	0.715	0.046	0	8	DEFB1
0	1.624	0.951	0.250	0	8	KRT7
0	2.003	0.812	0.215	0	8	KRT15
0	3.098	0.801	0.054	0	9	VIM
0	3.122	0.823	0.422	0	9	CD74
0	3.147	0.908	0.834	0	9	FTL
0	1.997	0.745	0.082	0	10	STMN1
0	1.974	0.816	0.319	0	10	H2AFZ

p_val	avg_logFC	pct.1	pct.2	p_val_adj	cluster	gene
0	1.914	0.857	0.474	0	10	TUBA1B
0	1.301	1.000	0.805	0	11	XDH
0	1.439	1.000	0.755	0	11	FASN
0	1.067	0.912	0.604	0	11	BTN1A1
0	3.137	0.882	0.070	0	12	MT1E
0	3.030	0.725	0.070	0	12	MT1X
0	3.073	0.922	0.133	0	12	MT2A

6   Feature Analysis

6.1   Annotation of clusters

Used for cell marker enrichment

Used CellMarker for enrichment analyses http://bio-bigdata.hrbmu.edu.cn/CellMarker/download/Human_cell_markers.txt. See Zhang et al. (2019) and http://bio-bigdata.hrbmu.edu.cn/CellMarker for details on this resource

6.1.1   Cluster 5
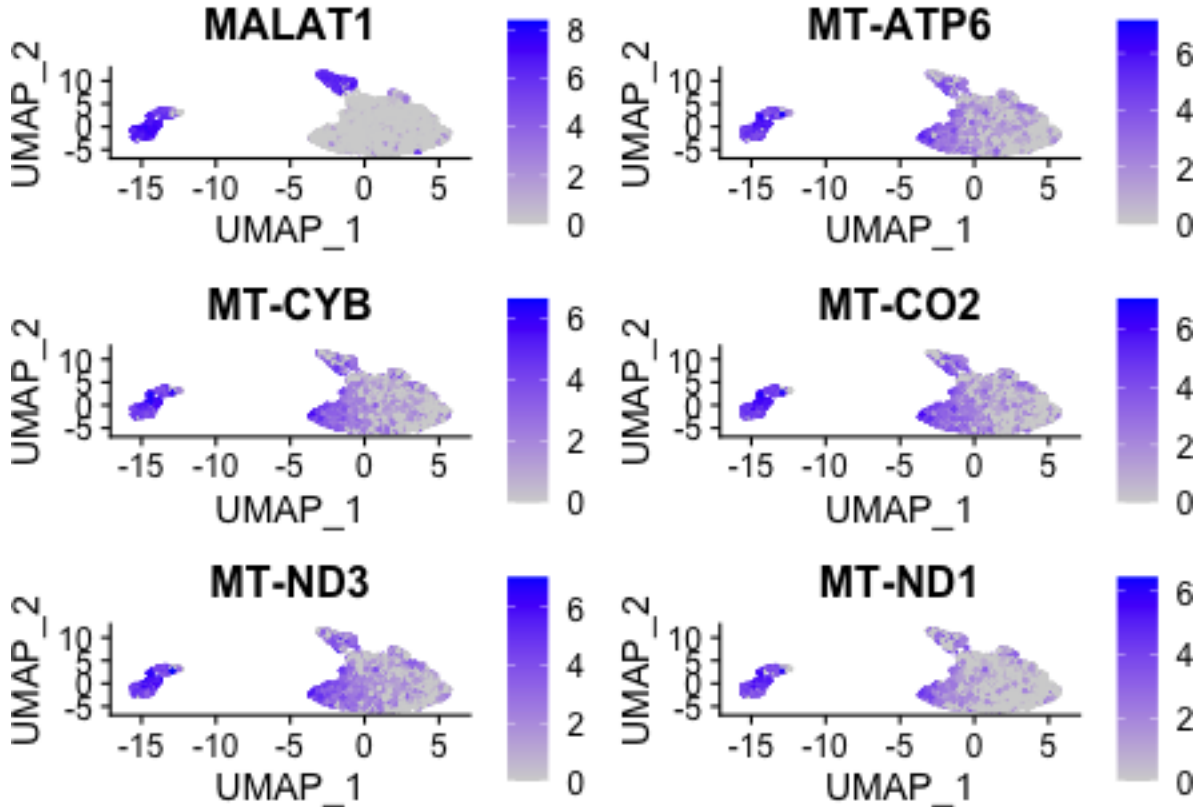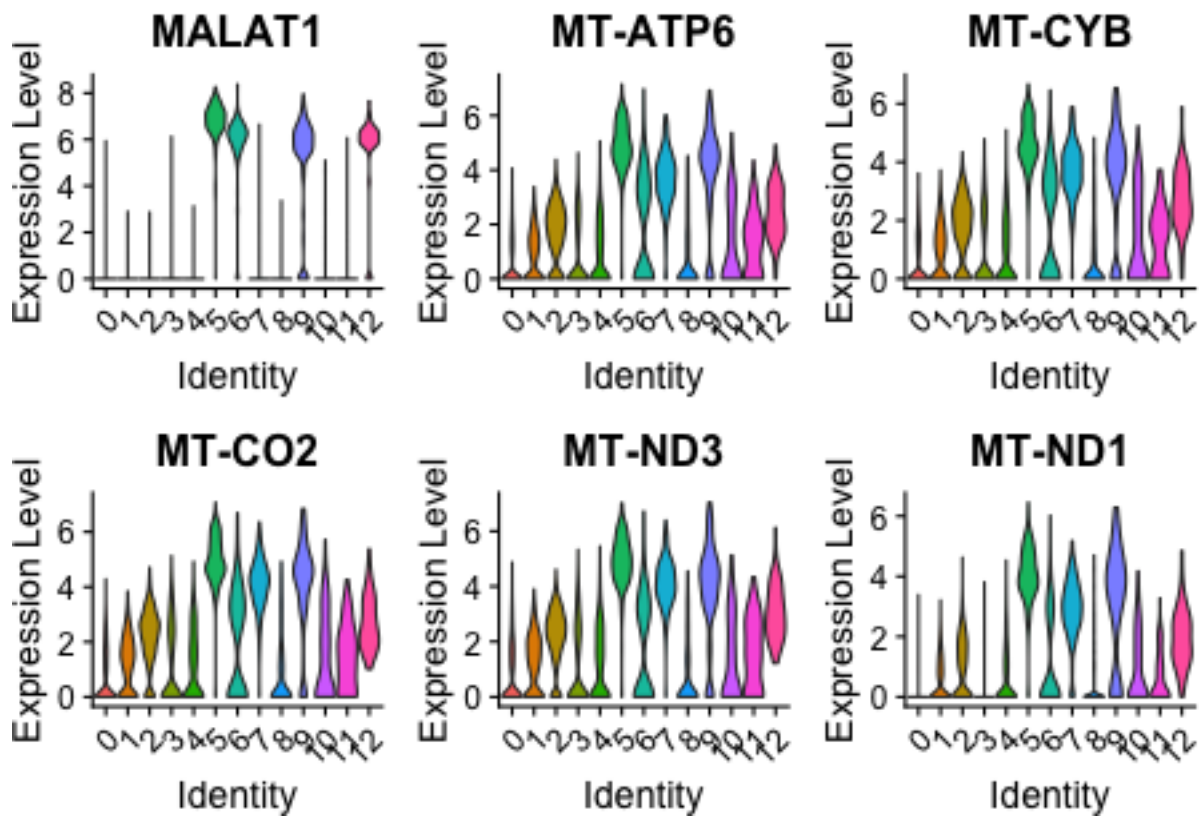
MALAT1

Expression Level

Identity

MT-ATP6

Expression Level

Identity

MT-CYB

Expression Level

Identity

MT-CO2

Expression Level

Identity

MT-ND3

Expression Level

Identity

MT-ND1

Expression Level

Identity

ID	Description	setSize	enrichmentScore	NES	pvalue	p.adjust	qvalues	rank	leading edge	core_enrichment
Fetal-kidney, Normal, Natural killer T (NK) cell	Fetal-kidney, Normal, Natural killer (N) cell	Fetal-kidney, Normal, Natural killer (N) cell	399	- 0.221	- 0.449	0.001	0.043	0.043	1276	tags=19%, list=6%, signal=30%	FOS/SYNE2/HLA-B/IL32/CXCR4/ZFP36L2/RNF213/SRGN/HLA-A/S100A4/LTB/CD44/TNFAIP3/NKTR/ETS1/IL7R/EML4/HLA-E/PRRC2C/CD52/FYN/S100A4/IRF1/B2M/ANKRD11/PIK3R1/ANKRD12/CCNL1/C/FUS/SRSF11/CORO1A/MACF1/AHNAK/EVL/ATRX/TXNIP/USP15/TNRC6B/F/RNF125/SP100/LCK/CD53/FMNL1/NCL/KMT2C/DUSP1/RNMT/PIM1/SMAP2/

ID	Description	setSize	enrichmentScore	NES	pvalue	p.adjust	qvalue	rank	leading_edge	core_enrichment
Lung, Normal, Secretory cell	Lung, Normal, Secretory cell	15	0.71	2.27	0.000	0.000	0.000		tags=60%, list=..%, signal=55%	CD74/HLA-DPA1/HLA-DQA1/HLA-DRA/HLA-DRB1/HLA-DPB1/HLA-DQB1/HLA-DRB5/CXCL8/HLA-A
Embryonic prefrontal cortex, Normal, Microglia cell	Embryonic prefrontal cortex, Normal, Microglial cell	124	0.41	3.80	0.000	0.000	0.002		tags=60%, list=..%, signal=40%	CD74/TYROBP/FABP5/CTSD/FCER1G/SRGN/SAT1/CTSB/APOC1/B/GPX1/CYBA/AIF1/NPC2/RGS1/CCL3/GPR183/CTSS/ITGB2/FOSB/G.../IGSF6/MS4A7/ARRB2/LST1/APLP2/UCP2/CD86/RGS10/BRI3/JUNB/...E
Large intestine, Normal, Paneth cell	Large intestine, Normal, Paneth cell	81	0.46	2.97	0.000	0.000	0.004		tags=58%, list=..%, signal=43%	CD74/HLA-DPA1/HLA-DQA1/HLA-DRA/HLA-DRB1/TYROBP/HLA-DPB1/FCER1G/SRGN/HLA-DQB1/CTSL/CD68/LAPTM5/SOD2/CD83/AIF1/CTSZ/CXCL8/CCL3/ITG.../DMB/CD48/LCP1/LSP1/CEBPB/CXCL16/ITGAX/METRNL/GMFG/CD53...
Fetal kidney, Normal, Monocyte	Fetal kidney, Normal, Monocyte	212	0.36	7.60	0.000	0.000	0.269		tags=67%, list=..%, signal=55%	CD74/VIM/HLA-DRA/HLA-DRB1/TYROBP/CTSD/LGALS1/FCER1G/SRGN/SAT1/TIMP1/CTSB/C15.../SOD2/CD83/TYMP/HLA-B/GPX1/CYBA/AIF1/CXCL8/EMP3/CTSS/LGALS3/BTG1/HLA-A/ITGB2/BASP1/S100A10/CD52/FOSB/PLAUR/CAPG/S100A6/HCST/AS.../IGSF6/MS4A7/ARRB2/LST1/CST3/PKM/CTSH/APLP2/CD86/RGS10/...E/IFI30/JAML/RAB31/CFLAR/FMNL1/NAMPT/SLC16A3/EMILIN2/GLU.../DMA/CD63/RNASET2/QKI/VMP1/PFDN5/MTRNR2L8/RILPL2/RNH1/T...
Kidney, Renal Cell Carcinoma, B cell	Kidney, Renal Cell Carcinoma, B cell	23	0.57	2.04	0.000	0.000	0.054		tags=52%, list=..%, signal=48%	CD74/HLA-DPA1/HLA-DQA1/HLA-DRA/HLA-DRB1/HLA-DPB1/HLA-DQB1/HLA-DRB5/CD83/GPR183/CD52
Kidney, Normal, B cell	Kidney, Normal, B cell	38	0.47	2.41	0.000	0.000	0.061		tags=37%, list=..%, signal=35%	CD74/HLA-DPA1/HLA-DQA1/HLA-DRA/HLA-DRB1/HLA-DPB1/HLA-DQB1/LAPTM5/HLA-DRB5/CD83/GPR183/BASP1/CD52/CAPG

ID	Description	setSize	enrichmentScore	NES	pvalue	p.adjust	qvalues	rank	leading edge	core_enrichment
Kidney Renal Cell Carcinoma, Neutrophil	Kidney Renal Cell Carcinoma, Neutrophil	Kidney Renal Cell Carcinoma, Neutrophil	17	0.55	1.8	0.008	0.045	0.034	tags=71%, list=31%, signal=50%	FTL/TYROBP/SAT1/SOD2/FOS/CXCL8/RGS2/BCL2A1/S100A11/CEBPB

6.1.3 Cluster 6

MALAT1

JUN

MT2A

IER2

CLDN4

NEAT1

	ID	Description	setSize	enrichmentScore	NES	pvalue	p.adjust	qvalue	rank	leading_edge	core_enrichment
Brain, Normal, Astrocyte	Brain, Normal, Astrocyte	Brain, Normal, Astrocyte	16	0.722	2.130	0.000	0.00046			tags=94%, list=32%, signal=71%	MT2A/MT1X/JUN/IER2/ATF3/JUN...
Embryonic prefrontal cortex, Normal, Microglial cell	Embryonic prefrontal cortex, Normal, Microglial cell	Embryonic prefrontal cortex, Normal, Microglial cell	20	0.637	1.950	0.001	0.00146			tags=80%, list=32%, signal=63%	JUN/IER2/KLF6/DUSP1/IER3/FOS/...

6.1.4 Cluster 12

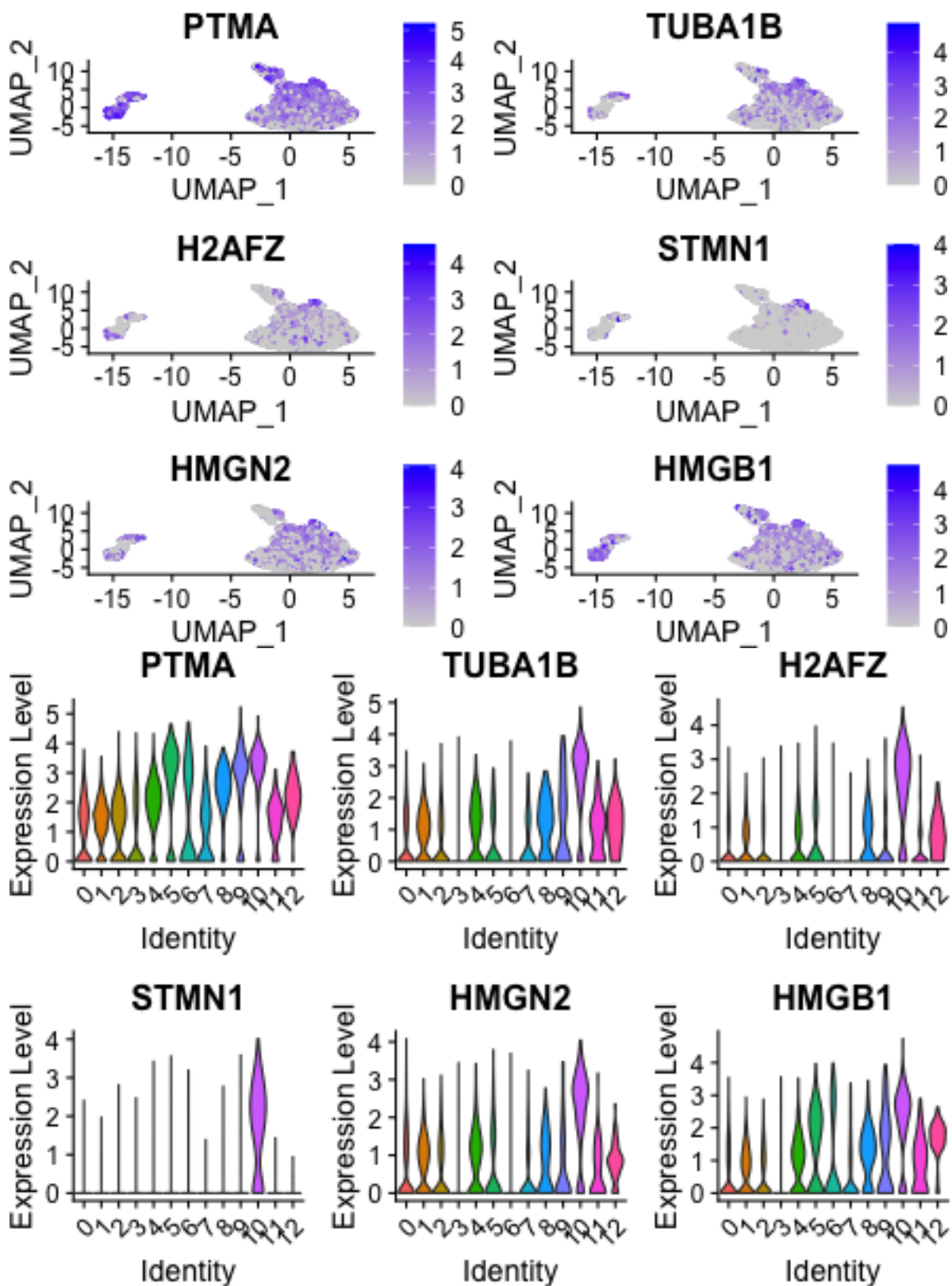|	ID	Description	setSize	enrichmentScore	NES	pvalue	p.adjust	qvalues	rank	leading_edge	core_enrichment
Brain, Normal, Astrocyte	Brain, Normal, Astrocyte	Brain, Normal, Astrocyte	29	0.723	2.85	0.00	0.00	0.00	91	tags=59%, list=9%, signal=55%	MT2A/MT1X/JUN/IER2/RHOB/JUND/FOS/ATF3/ZFP36
Embryonic pre-frontal cortex, Normal, Microglial cell	Embryonic pre-frontal cortex, Normal, Microglial cell	Embryonic pre-frontal cortex, Normal, Microglial cell	57	0.522	2.34	0.00	0.00	0.00	151	tags=44%, list=15%, signal=40%	N/IER2/KLF6/RHOB/DUSP1/FOS/ZFP36/JUNB/EGR1
Fetal kidney, Normal, Monocyte	Fetal kidney, Normal, Monocyte	Fetal kidney, Normal, Monocyte	129	0.407	1.99	0.00	0.00	0.00	274	tags=41%, list=27%, signal=39%	R2/KLF6/ANXA1/JUND/DUSP1/TNFRSF12A/ZFP36/M
Liver, Normal, Liver bud hepatic cell	Liver, Normal, Liver bud hepatic cell	Liver, Normal, Liver bud hepatic cell	27	0.593	2.31	0.00	0.00	0.00	155	tags=48%, list=15%, signal=42%	T1E/MT2A/MT1X/MT1G/RHOB/MT1M/MT1F/MCL1/
Liver, Hepatocellular Cancer, Regulatory T (Treg) cell	Liver, Hepatocellular Cancer, Regulatory T (Treg) cell	Liver, Hepatocellular Cancer, Regulatory T (Treg) cell	52	0.475	2.10	0.00	0.00	0.00	224	tags=50%, list=22%, signal=41%	SQSTM1/DDIT4/MCL1/PIM3/HSPB1/SLC3A2/SOX4/PHL
Blood, Normal, CD1C-CD141- dendritic cell	Blood, Normal, CD1C-CD141- dendritic cell	Blood, Normal, CD1C-CD141- dendritic cell	39	0.506	2.12	0.00	0.00	0.00	276	tags=62%, list=27%, signal=46%	T2A/DUSP1/HMOX1/TXNIP/S100A11/MAFB/WSB1/ZF

	ID	Description	setSize	enrichmentScore	NES	pvalue	p.adjust	qvalues	rank	leading_edge	core_enrichment
Kidney, Renal Cell Carcinoma, Neutrophil	Kidney, Renal Cell Carcinoma, Neutrophil	Kidney, Renal Cell Carcinoma, Neutrophil	10	0.722	2.13	0.00	0.00	0.001	50	tags=80%, list=15%, signal=69%	FOS/CEBPB/S100A11/SAT1/SLC25A37/ANXA3/NAMPT/...
Fetal gonad, Normal, Granulosa cell	Fetal gonad, Normal, Granulosa cell	Fetal gonad, Normal, Granulosa cell	20	0.542	1.96	0.003	0.01	0.008	97	tags=50%, list=20%, signal=41%	MT1E/MT2A/MT1F/NFKBIA/CEBPD/TAGLN2/ARHGAP...
Embryonic prefrontal cortex, Normal, Astrocyte	Embryonic prefrontal cortex, Normal, Astrocyte	Embryonic prefrontal cortex, Normal, Astrocyte	37	0.446	1.85	0.003	0.01	0.008	80	tags=38%, list=18%, signal=32%	MT1E/MT2A/JUN/HSPB1/SLC3A2/SOX4/ZFP36L1/ZFP3...
Embryo, Normal, Trophectoderm cell	Embryo, Normal, Trophectoderm cell	Embryo, Normal, Trophectoderm cell	25	0.497	1.90	0.004	0.017	0.010	46	tags=44%, list=15%, signal=39%	CLDN4/TACSTD2/CLDN3/PRSS8/S100A6/KRT18/CITED4...
Fetal gonad, Normal, Gonadal endothelial cell	Fetal gonad, Normal, Gonadal endothelial cell	Fetal gonad, Normal, Gonadal endothelial cell	63	0.375	1.72	0.005	0.017	0.013	63	tags=57%, list=36%, signal=39%	KLF6/TM4SF1/PIM3/HSPB1/MIDN/ANXA2/TLE1/S100A...
Umbilical cord blood, Normal, Multilymphoid progenitor cell	Umbilical cord blood, Normal, Multilymphoid progenitor cell	Umbilical cord blood, Normal, Multilymphoid progenitor cell	52	0.398	1.76	0.005	0.017	0.012	64	tags=46%, list=26%, signal=36%	...2/JUND/DUSP1/JUNB/PIM3/FOSB/MIDN/SOX4/TSC...

	ID	Description	setSize	enrichmentScore	NES	pvalue	p.adjust	qvalues	rank	leading_edge	core_enrichment
Fetal gonad, Normal, Mitotic fetal germ cell	Fetal gonad, Normal, Mitotic fetal germ cell	Fetal gonad, Normal, Mitotic fetal germ cell	61	0.380	1.73	0.006	0.018	0.012	229	tags=41%, list=23%, signal=34%	FLT3/DDIT4/MCL1/PIM3/SPTSSA/SLC3A2/SOX4/GABA...
Fetal gonad, Normal, Sertoli cell	Fetal gonad, Normal, Sertoli cell	Fetal gonad, Normal, Sertoli cell	62	0.371	1.69	0.006	0.018	0.013	368	tags=58%, list=37%, signal=39%	SAT.../CSTD2/SLC3A2/GADD45G/TUBB4B/SDC4/S100A10/Z...
Kidney, Normal, Mast cell	Kidney, Normal, Mast cell	Kidney, Normal, Mast cell	10	0.621	1.83	0.006	0.018	0.016	63	tags=50%, list=6%, signal=47%	...1F/EGR1/LMNA/TSC22D1/NFKBIA
Fetal gonad, Normal, Mitotic arrest phase fetal germ cell	Fetal gonad, Normal, Mitotic arrest phase fetal germ cell	Fetal gonad, Normal, Mitotic arrest phase fetal germ cell	110	0.325	1.58	0.009	0.024	0.014	469	tags=40%, list=27%, signal=33%	KLF6/RHOB/PNRC1/JMJD1C/HSPB1/TXNIP/ANXA2/TS...
Large intestine, Normal, Paneth cell	Large intestine, Normal, Paneth cell	Large intestine, Normal, Paneth cell	19	0.488	1.74	0.019	0.046	0.027	728	tags=68%, list=33%, signal=47%	HMOX1/CXCL2/CEBPB/MAFB/SGK1/SLC25A37/PPIF/N...

6.1.5 Cluster 10

	ID	Description	setSize	enrichmentScore	NES	pvalue	p.adjust	qvalues	rank	leading_edge	core_enrichment
Embryonic pre-frontal cortex, Normal, Neural progenitor cell	Embryonic pre-frontal cortex, Normal, Neural progenitor cell	Embryonic pre-frontal cortex, Normal, Neural progenitor cell	49	0.648	3.23	0.00	0.00	0.00	73	tags=69%, list=24%, signal=63%	H2AFZ/TUBA1B/CKS2/HMGN2/PTTG1/TOP2
Large intestine, Normal, MKI67+ progenitor cell	Large intestine, Normal, MKI67+ progenitor cell	Large intestine, Normal, MKI67+ progenitor cell	20	0.708	2.80	0.00	0.00	0.00	51	tags=75%, list=17%, signal=67%	PTTG1/TOP2A/HIST1H4C/TK1/CCNB1/CDC2
Fetal gonad, Normal, Endothelial cell	Fetal gonad, Normal, Endothelial cell	Fetal gonad, Normal, Endothelial cell	24	0.558	2.34	0.00	0.00	0.00	58	tags=54%, list=19%, signal=48%	STMN1/H2AFZ/TUBB/HMGN2/PTTG1/HMGB
Lung, Normal, FOXN4+ cell	Lung, Normal, FOXN4+ cell	Lung, Normal, FOXN4+ cell	16	0.496	1.80	0.01	0.04	0.029	23	tags=81%, list=40%, signal=51%	TYMS/PTMA/CDK1/PTGES3/RANBP1/UBE2
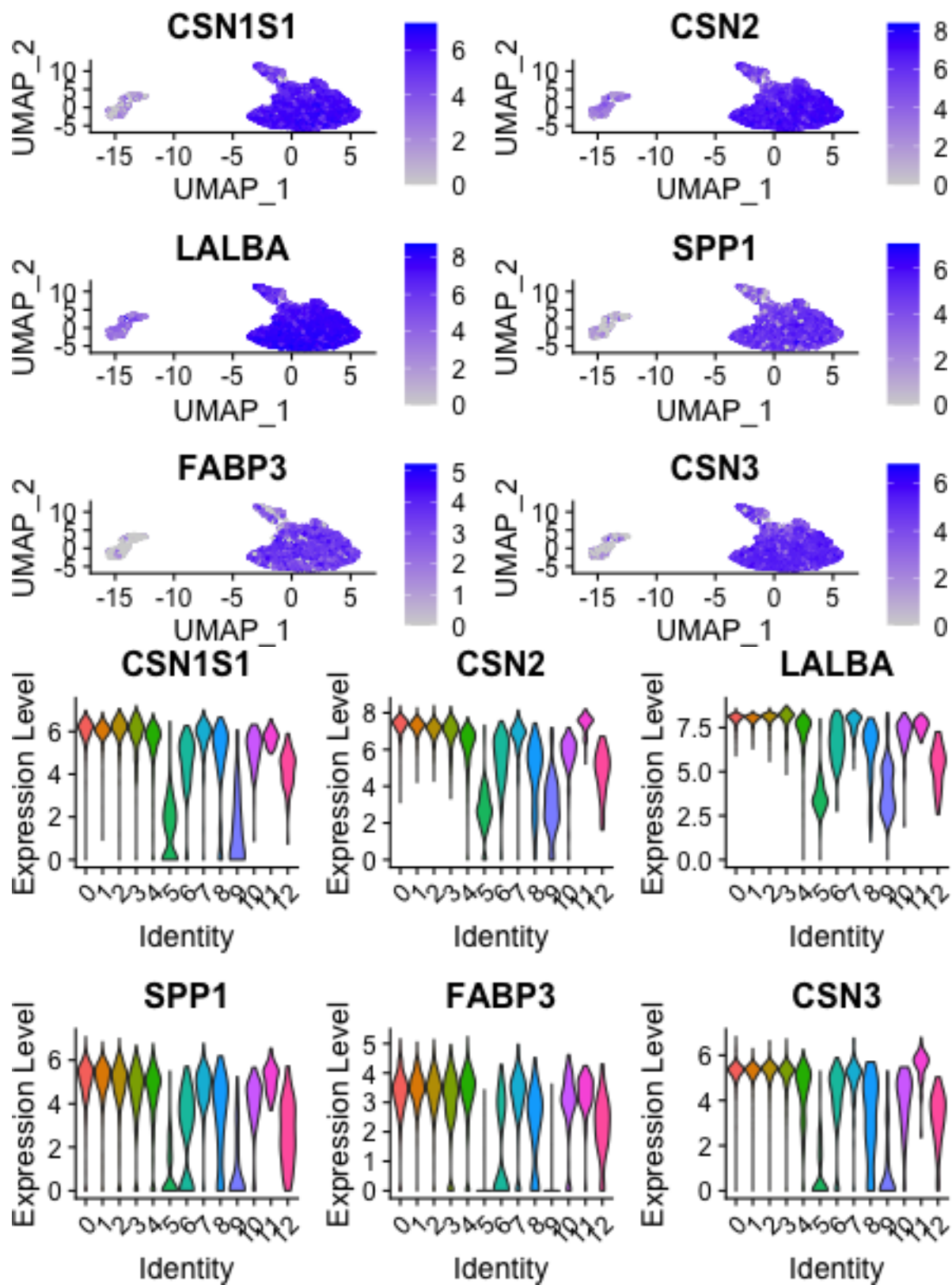
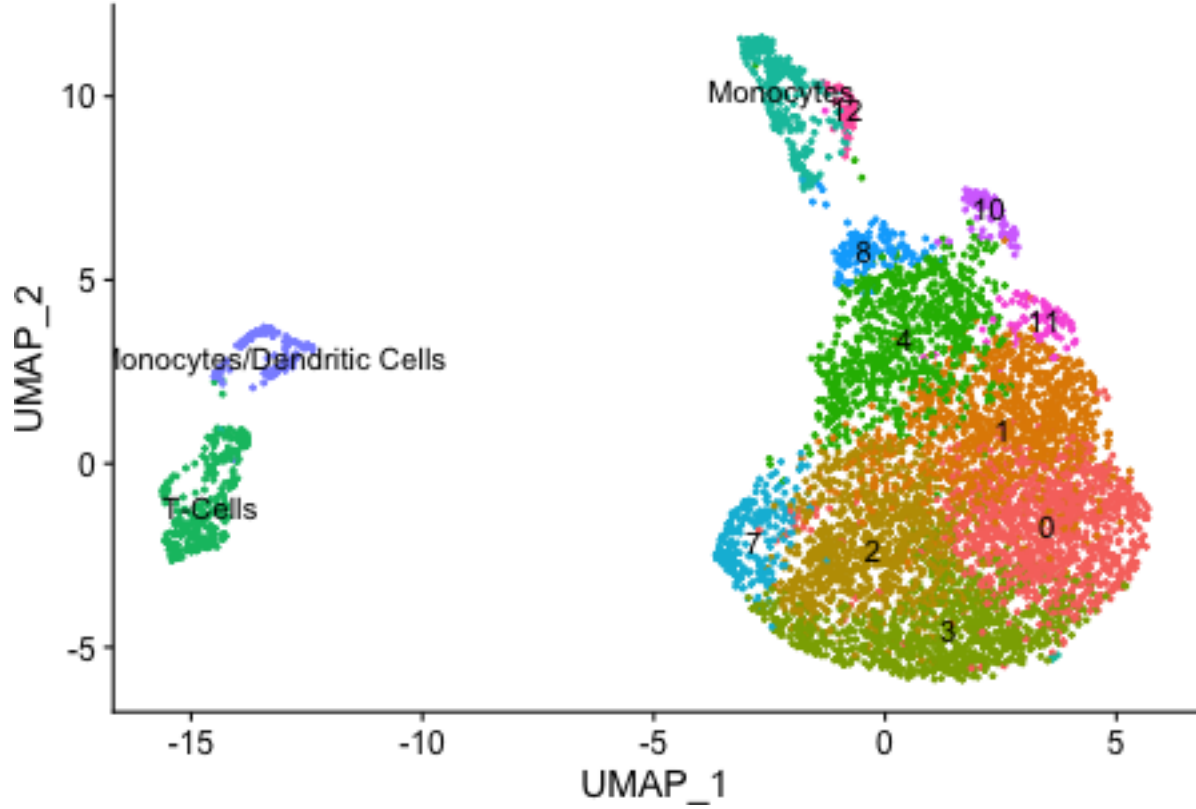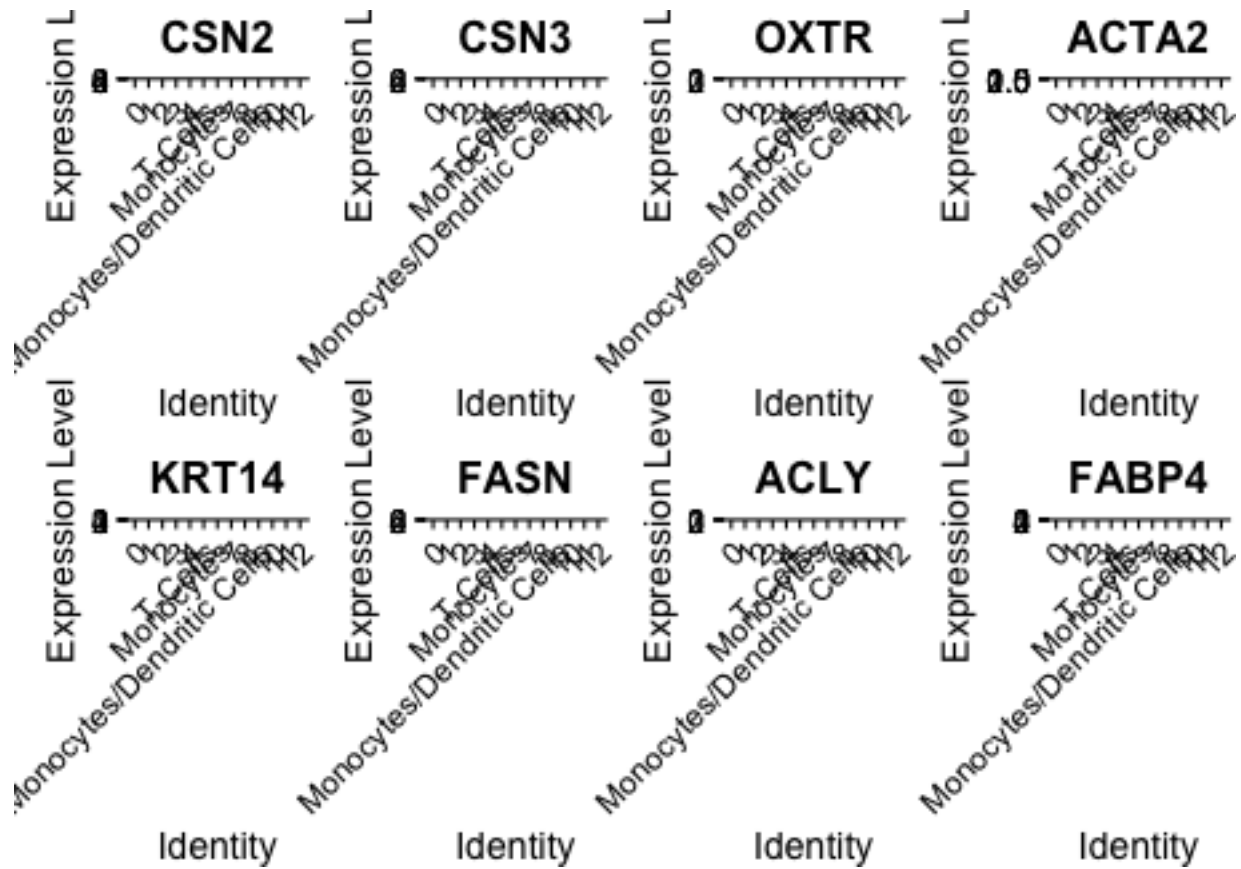| ID	Description	setSize	enrichmentScore	NES	pvalue	p.adjust	qvalues

6.2 Summary of Clusters

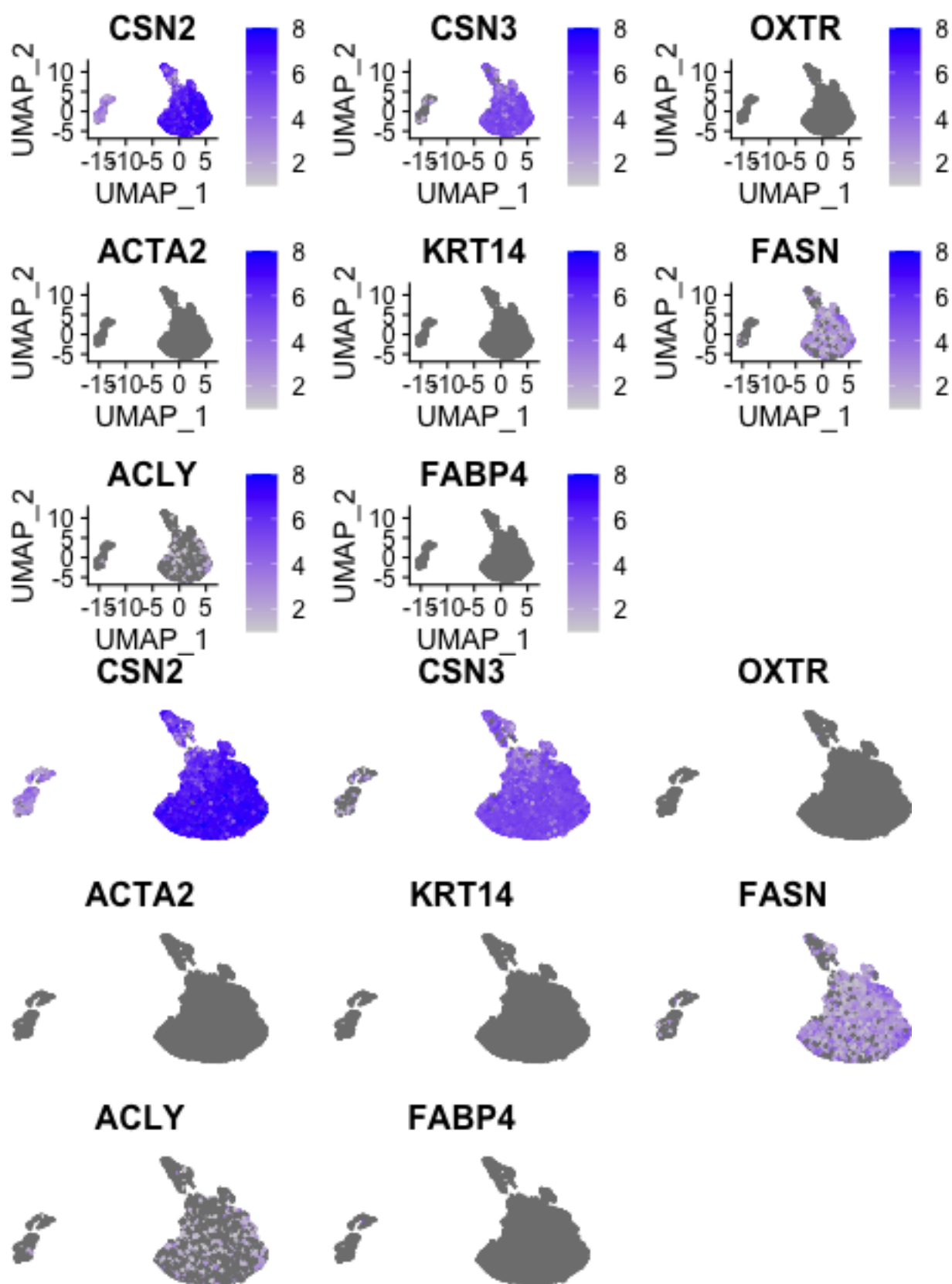Table 8: Cell proportions in each cluster

Var1	Freq
0	0.187
1	0.165
2	0.154
3	0.150
4	0.123
T-Cells	0.053
Monocytes	0.046
7	0.036
8	0.024
Monocytes/Dendritic Cells	0.024
10	0.017
11	0.014
12	0.009

, ## Analysis of clusters

Table 9: Clusters of genes of interest

	p_val	avg_logFC	pct.1	pct.2	p_val_adj	cluster	gene
FASN	0	0.660	0.855	0.755	0	7	FASN
FASN1	0	1.439	1.000	0.755	0	11	FASN
ACLY	0	0.845	0.713	0.286	0	11	ACLY
CSN3	0	0.577	1.000	0.935	0	11	CSN3

CSN2

CSN3

LTF

LALBA

CSN2

LALBA

CD14

KIT

SLC2A1

SLC35A2

SLC50A1

FABP3

CD36

AGPAT2

AGPAT3

CD4

CD7

CTLA4

CD27

CD38

CD24

IL10

RPTOR

MTOR
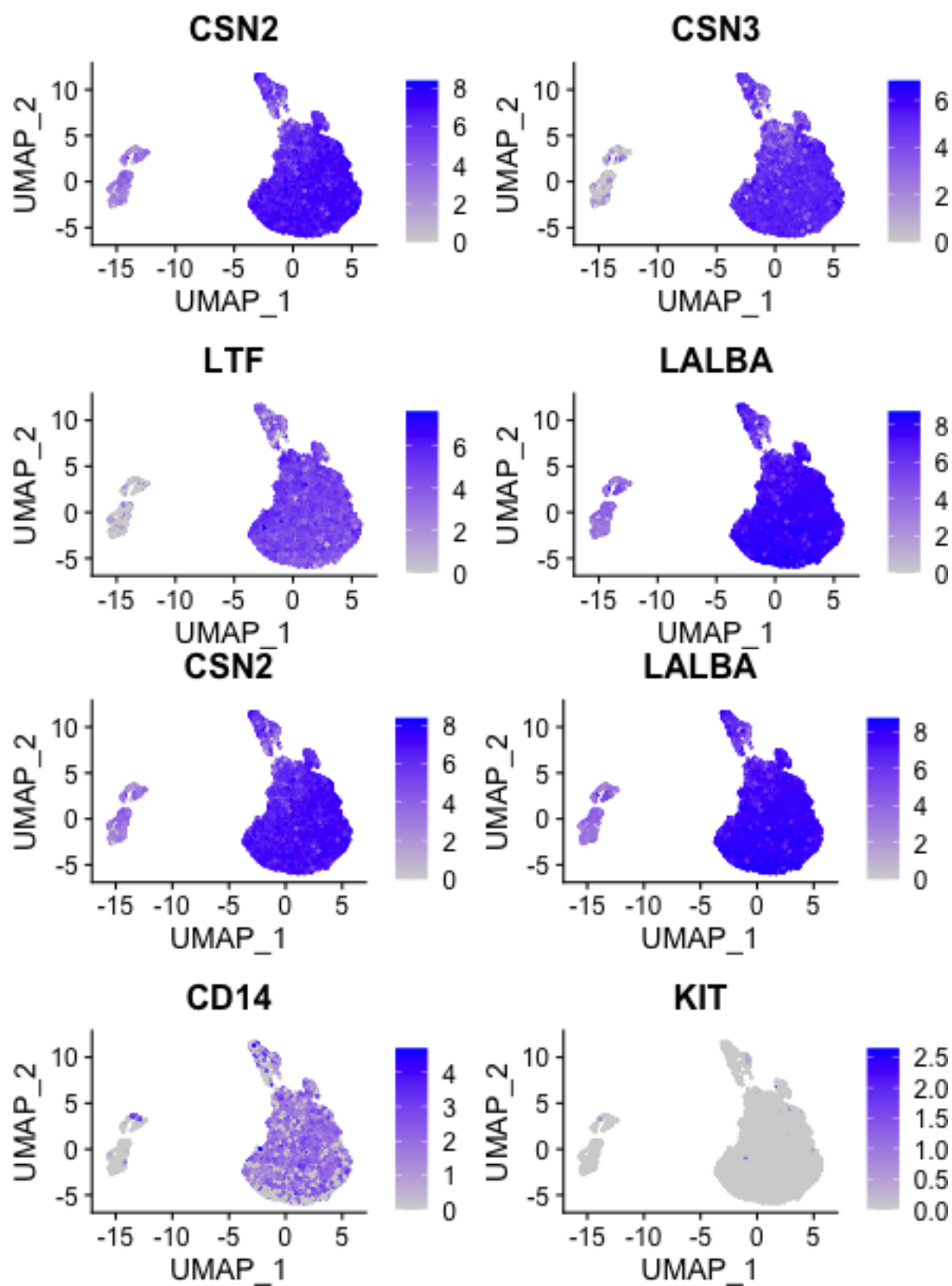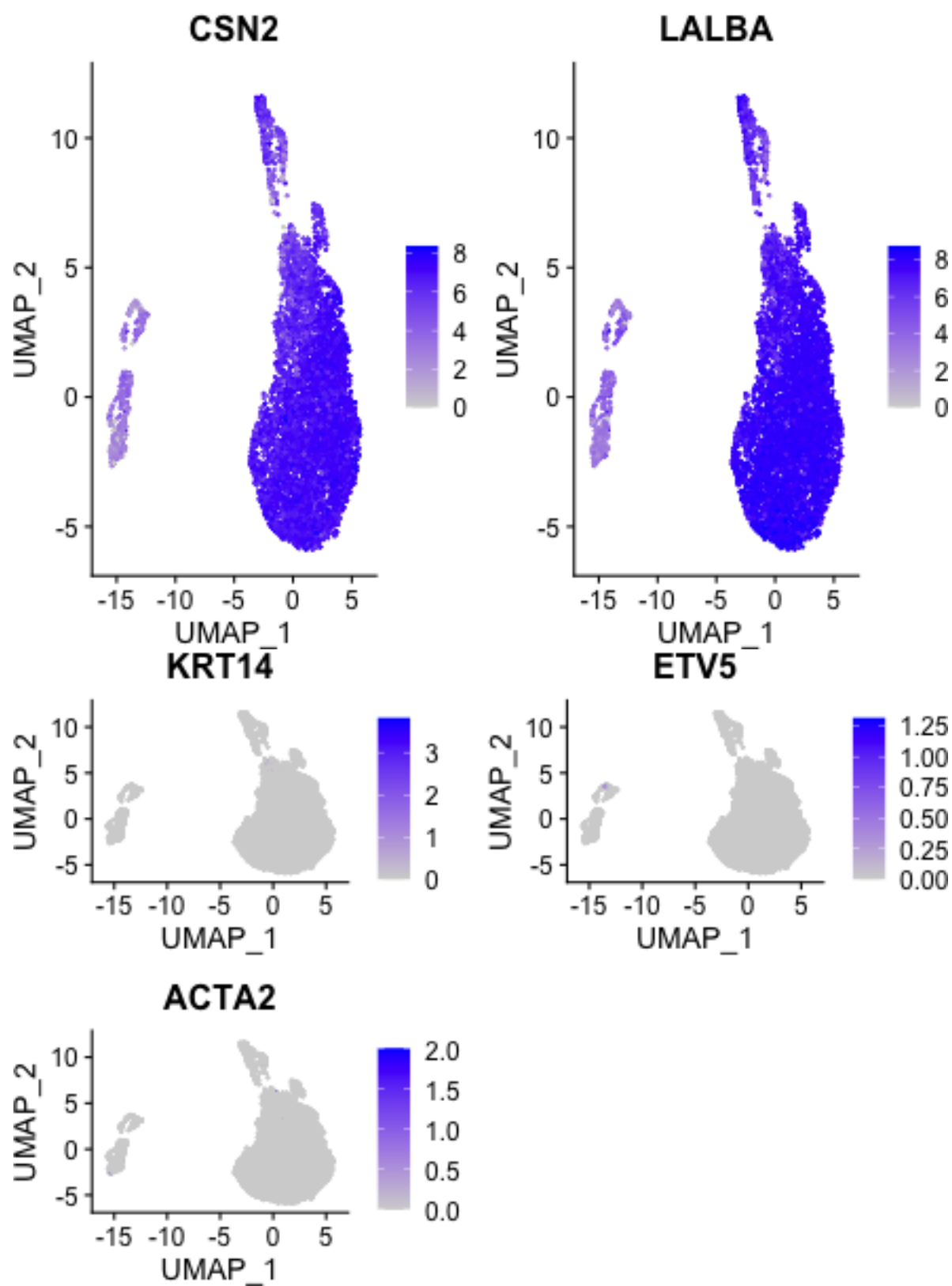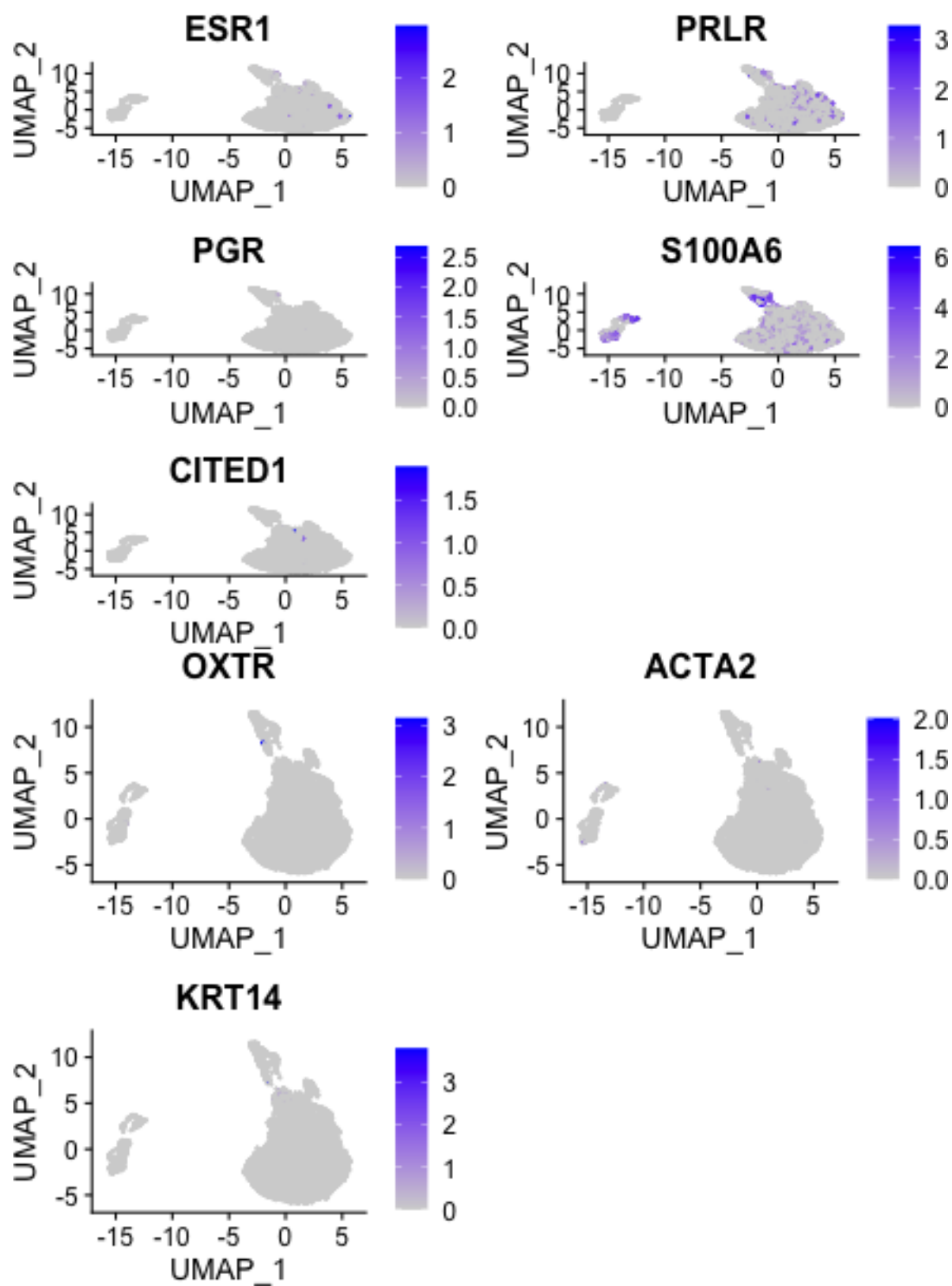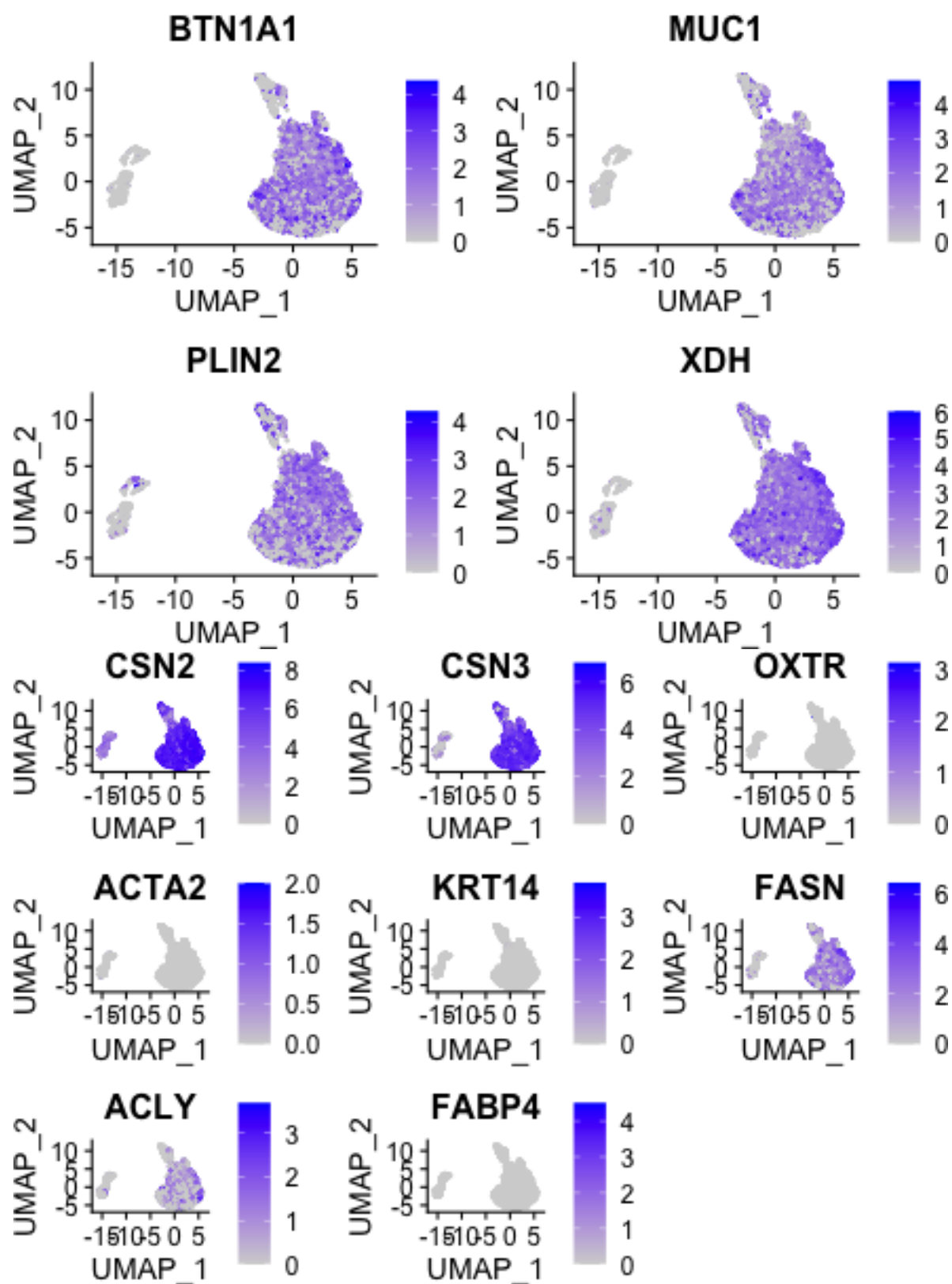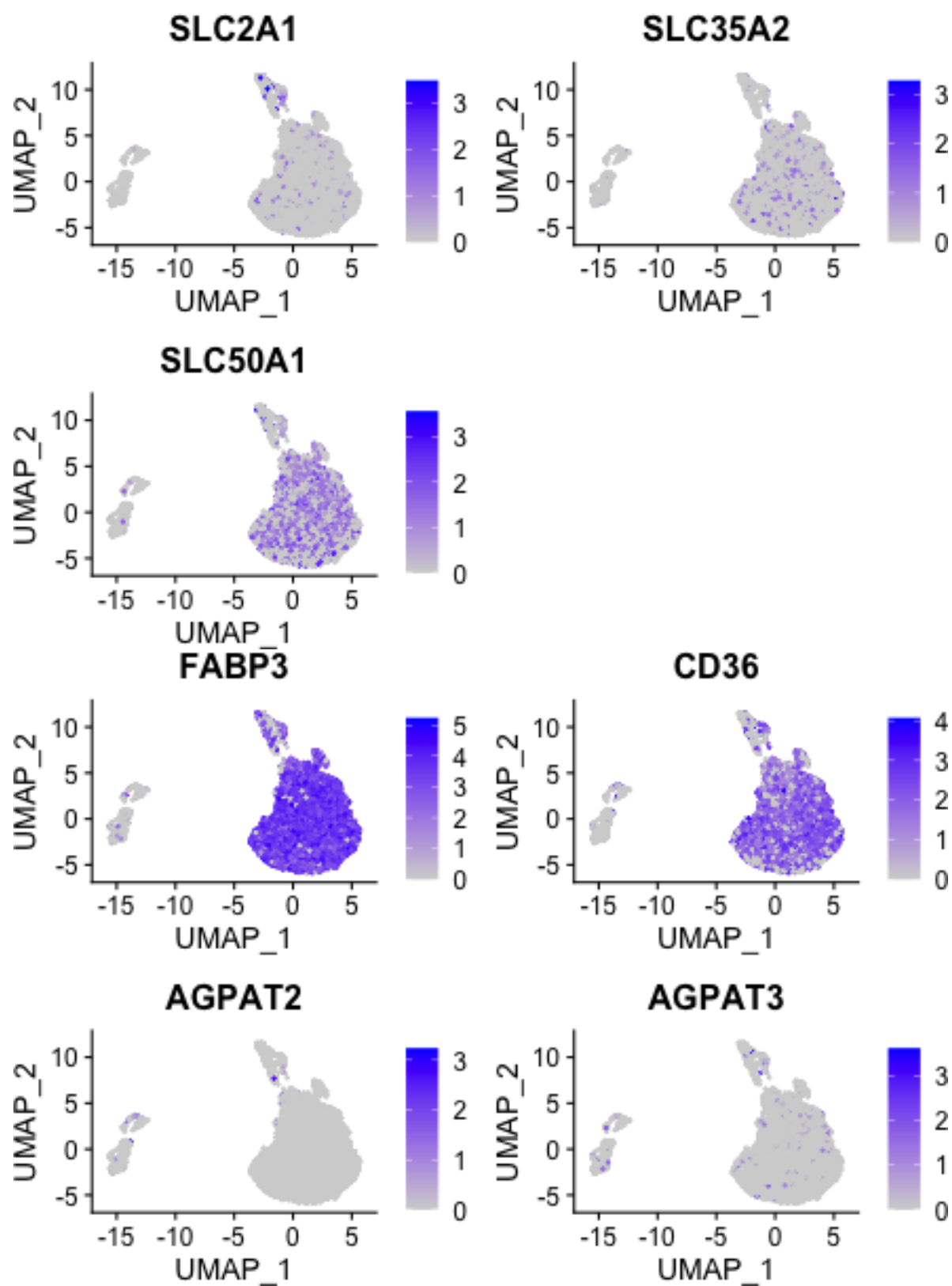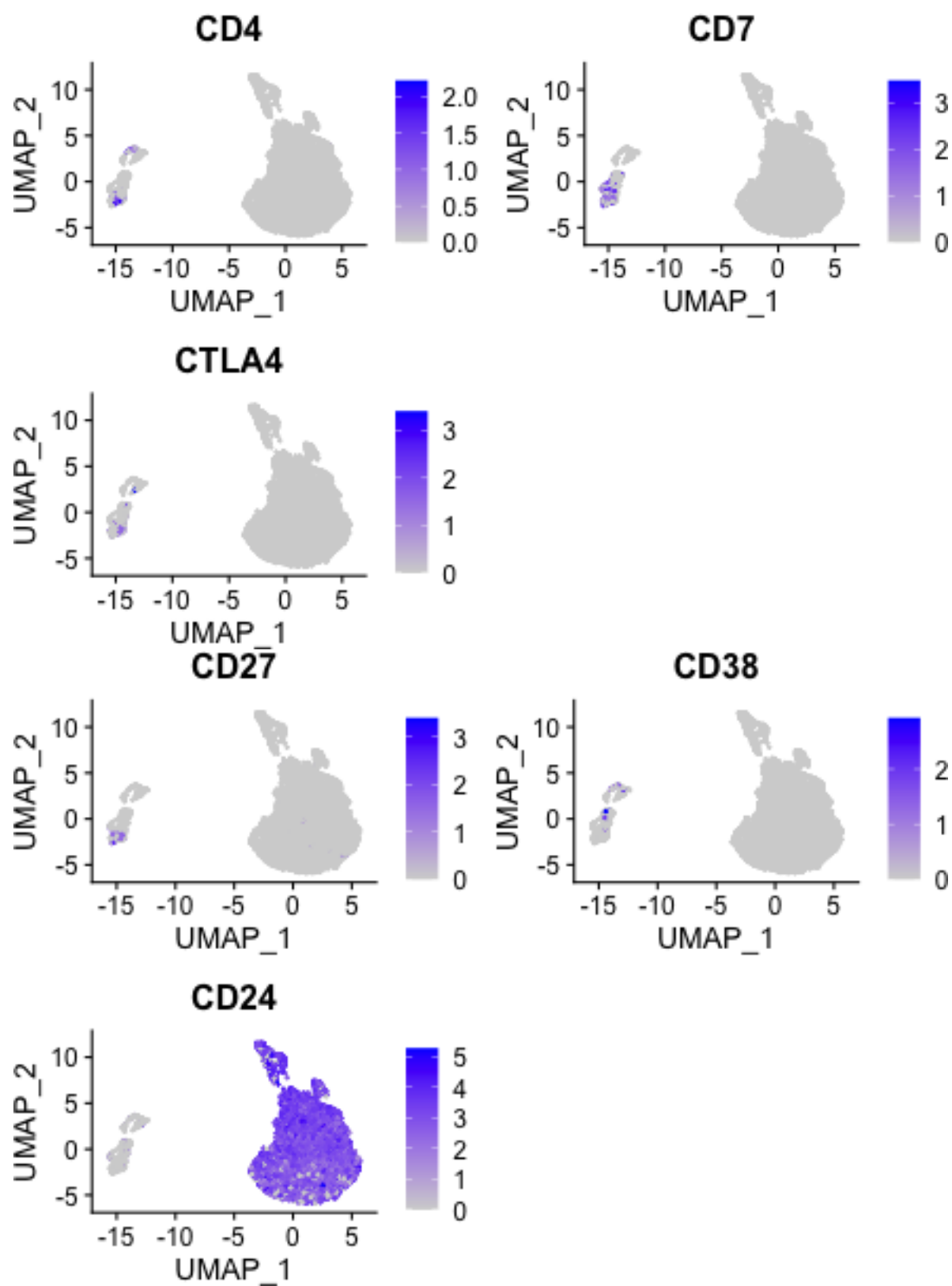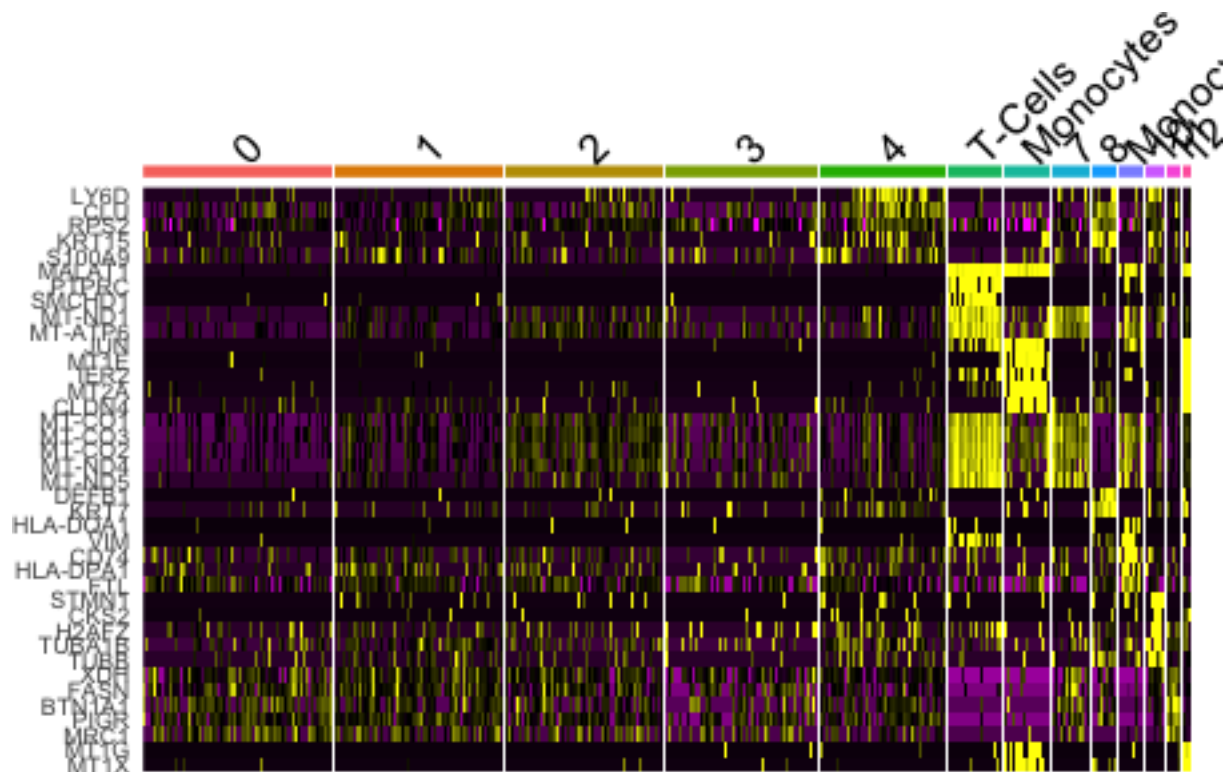
7 Session Information

sessionInfo()

```
## R version 4.0.2 (2020-06-22)
## Platform: x86_64-apple-darwin17.0 (64-bit)
## Running under: macOS  10.16
##
## Matrix products: default
## BLAS:   /Library/Frameworks/R.framework/Versions/4.0/Resources/lib/libRblas.dylib
## LAPACK: /Library/Frameworks/R.framework/Versions/4.0/Resources/lib/libRlapack.dylib
##
## locale:
## [1] en_US.UTF-8/en_US.UTF-8/en_US.UTF-8/C/en_US.UTF-8/en_US.UTF-8
##
## attached base packages:
## [1] stats     graphics  grDevices utils     datasets  methods   base
##
## other attached packages:
## [1] ggplot2_3.3.3         clusterProfiler_3.16.1 Seurat_3.2.3
## [4] tibble_3.0.4          dplyr_1.0.2            tidyr_1.1.2
## [7] knitr_1.30
##
## loaded via a namespace (and not attached):
##   [1] fastmatch_1.1-0      plyr_1.8.6            igraph_1.2.6
##   [4] lazyeval_0.2.2       splines_4.0.2        BiocParallel_1.22.0
##   [7] listenv_0.8.0        scattermore_0.7      urltools_1.7.3
```
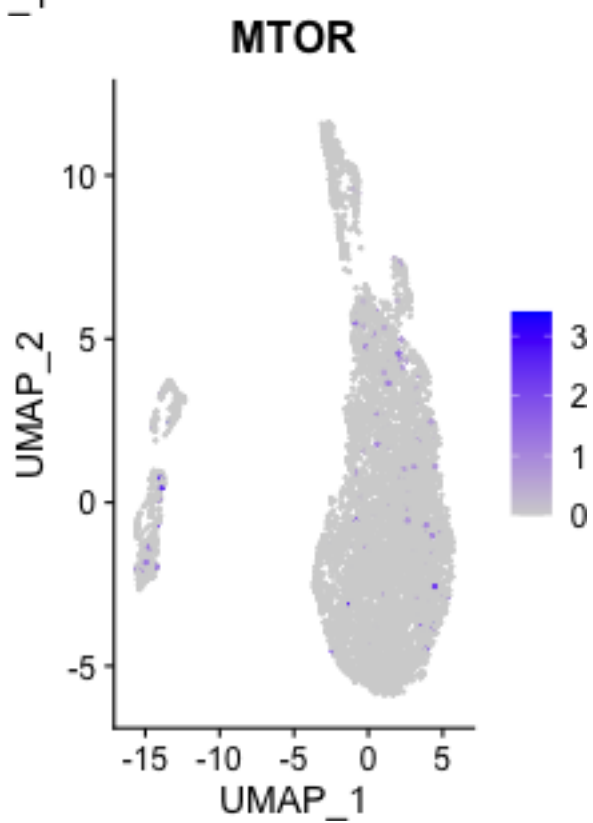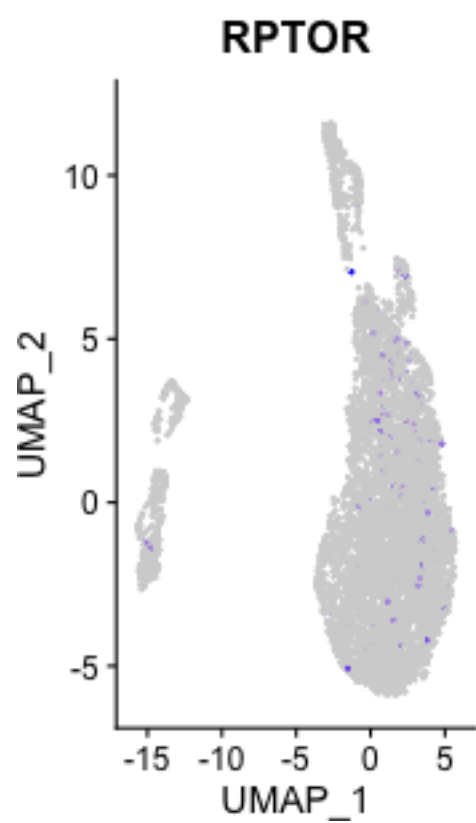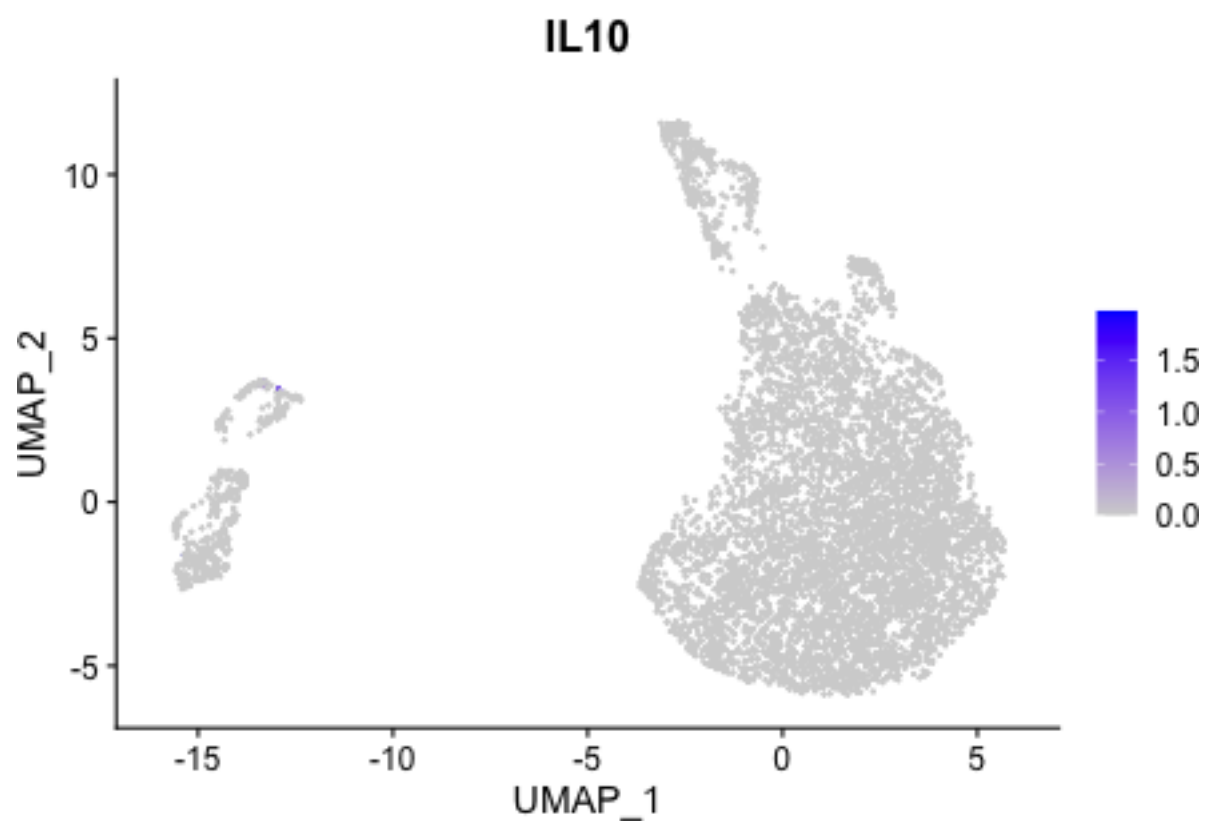
```
##  [10] digest_0.6.27          htmltools_0.5.0        GOSemSim_2.14.2
##  [13] viridis_0.5.1          magick_2.5.2           GO.db_3.11.4
##  [16] magrittr_2.0.1         memoise_1.1.0          tensor_1.5
##  [19] cluster_2.1.0          ROCR_1.0-11            limma_3.44.3
##  [22] globals_0.14.0         graphlayouts_0.7.1     matrixStats_0.57.0
##  [25] vroom_1.3.2            prettyunits_1.1.1      enrichplot_1.8.1
##  [28] colorspace_2.0-0       blob_1.2.1             ggrepel_0.9.0
##  [31] xfun_0.19              crayon_1.3.4           jsonlite_1.7.2
##  [34] scatterpie_0.1.5       spatstat_1.64-1        spatstat.data_1.7-0
##  [37] survival_3.2-7         zoo_1.8-8              glue_1.4.2
##  [40] polyclip_1.10-0        gtable_0.3.0           leiden_0.3.6
##  [43] future.apply_1.6.0     BiocGenerics_0.34.0    abind_1.4-5
##  [46] scales_1.1.1           DOSE_3.14.0            DBI_1.1.0
##  [49] miniUI_0.1.1.1         Rcpp_1.0.5             progress_1.2.2
##  [52] viridisLite_0.3.0      xtable_1.8-4           gridGraphics_0.5-1
##  [55] reticulate_1.18        europepmc_0.4          bit_4.0.4
##  [58] rsvd_1.0.3             stats4_4.0.2           htmlwidgets_1.5.3
##  [61] httr_1.4.2             fgsea_1.14.0           RColorBrewer_1.1-2
##  [64] ellipsis_0.3.1         ica_1.0-2              pkgconfig_2.0.3
##  [67] farver_2.0.3           uwot_0.1.10            deldir_0.2-3
##  [70] ggplotify_0.0.5        tidyselect_1.1.0       labeling_0.4.2
##  [73] rlang_0.4.10           reshape2_1.4.4         later_1.1.0.1
##  [76] AnnotationDbi_1.50.3   munsell_0.5.0          tools_4.0.2
##  [79] downloader_0.4         generics_0.1.0         RSQLite_2.2.1
##  [82] ggridges_0.5.2         evaluate_0.14          stringr_1.4.0
##  [85] fastmap_1.0.1          yaml_2.2.1             goftest_1.2-2
##  [88] bit64_4.0.5            fitdistrplus_1.1-3     tidygraph_1.2.0
##  [91] purrr_0.3.4            RANN_2.6.1             ggraph_2.0.4
##  [94] pbapply_1.4-3          future_1.21.0          nlme_3.1-151
##  [97] mime_0.9               xml2_1.3.2             DO.db_2.9
## [100] compiler_4.0.2         plotly_4.9.2.2         curl_4.3
## [103] png_0.1-7              spatstat.utils_1.17-0  tweenr_1.0.1
## [106] stringi_1.5.3          highr_0.8              RSpectra_0.16-0
## [109] lattice_0.20-41        Matrix_1.3-0           vctrs_0.3.6
## [112] pillar_1.4.7           lifecycle_0.2.0        BiocManager_1.30.10
## [115] triebeard_0.3.0        lmtest_0.9-38          RcppAnnoy_0.0.18
## [118] data.table_1.13.6      cowplot_1.1.1          irlba_2.3.3
## [121] httpuv_1.5.4           patchwork_1.1.1        qvalue_2.20.0
## [124] R6_2.5.0               promises_1.1.1         KernSmooth_2.23-18
## [127] gridExtra_2.3          IRanges_2.22.2         parallelly_1.22.0
## [130] codetools_0.2-18       MASS_7.3-53            withr_2.3.0
## [133] sctransform_0.3.2      S4Vectors_0.26.1       hms_0.5.3
## [136] mgcv_1.8-33            parallel_4.0.2         grid_4.0.2
## [139] rpart_4.1-15           rvcheck_0.1.8          rmarkdown_2.6
## [142] Rtsne_0.15             ggforce_0.3.2          Biobase_2.48.0
## [145] shiny_1.5.0
```

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