

1-Revisiting data

BAI Qiang*

2021-09-29 09:21:39 +0200

Contents

| | |
|--|-----------|
| 1 Description | 2 |
| 2 Load data and packages | 2 |
| 3 Ploting with previous analysis (done by Arnaud) | 5 |
| 4 Try Merge instead of integrate | 11 |
| 4.1 Data processing | 11 |
| 4.2 Compare integrated and Merged | 12 |
| 5 Clustering after merge | 13 |
| 5.1 Find the marker of Cluster 1 | 14 |
| 5.2 KEGG enrichment | 15 |
| 6 Session information | 18 |
| 7 (References) | 20 |

*University Liege, mail qiang.bai@uliege.be

1 Description

Single-cell

2 Load data and packages

```
library(Seurat)
load(file="../../../../Data/Objects/Subset.integrated.rds")
```

1
2

An R object `Subset.integrated` obtained, containing the following information:

```
## An object of class Seurat
## 37418 features across 29678 samples within 4 assays
## Active assay: RNA (22597 features, 0 variable features)
## 3 other assays present: HTO, SCT, integrated
## 2 dimensional reductions calculated: pca, umap
```

1
2
3
4
5

Check metadata: in `Subset.integrated`, metadata contains the following data:

```
## [1] "orig.ident"                      "nCount_RNA"
## [3] "nFeature_RNA"                     "percent.mt"
## [5] "nCount_HTO"                       "nFeature_HTO"
## [7] "HTO_maxID"                        "HTO_secondID"
## [9] "HTO_margin"                        "HTO_classification"
## [11] "HTO_classification.global"        "hash.ID"
## [13] "nCount_SCT"                        "nFeature_SCT"
## [15] "SCT_snn_res.0.2"                  "seurat_clusters"
## [17] "Clustering"                       "Sample"
## [19] "Sample_Cluster"                  "Genotype"
## [21] "Treatment"                        "Global"
## [23] "RNA_snn_res.0.5"                 "RNA_snn_res.15"
## [25] "SingleR.labels"                  "Annotation"
```

1
2
3
4
5
6
7
8
9
10
11
12
13

Show some important data:

```
apply(Subset.integrated@meta.data [c("orig.ident", "hash.ID", "SCT_snn_res
.0.2", "seurat_clusters",
                               "Clustering", "Sample", "Sample_
Cluster", "Genotype",
                               "Treatment", "Global", "RNA_snn_res
.0.5", "RNA_snn_res.15",
                               "SingleR.labels", "Annotation")], 2,
table)
```

```
## $orig.ident
##
## SeuratProject
##               29678
##
## $hash.ID
##
## mouse-1 mouse-2 mouse-3 mouse-4 mouse-5
##      5821     6311     5989     6438     5119
```

1
2
3
4
5
6
7
8
9

```

##          10
## $SCT_snn_res.0.2          11
##          12
##          0   1   2   3   4   5          13
## 24531 2867 1211 601 342 126          14
##          15
## $seurat_clusters          16
##          17
##          0   1   10  100 101 102 103 104 105 106 107 108 109 11 110 111 112 113 18
##          114 115
## 491 477 364 151 151 150 150 139 137 136 131 129 128 363 128 127 123 123 19
##          117 111
## 116 117 118 119 12 120 121 122 123 124 125 126 127 128 129 13 130 131 20
##          132 133
## 110 109 105 101 358 99 98 97 84 79 63 63 54 53 45 358 41 41 21
##          39 33
## 134 136 14 15 16 17 18 19 2 20 21 22 23 24 25 26 27 28 22
##          29 3
## 20 4 357 347 346 344 340 323 411 322 319 316 313 312 312 312 311 308 23
##          304 398
## 30 31 32 33 34 35 36 37 38 39 4 40 41 42 43 44 45 46 24
##          47 48
## 302 298 297 295 294 292 281 281 280 278 394 266 264 263 263 260 258 256 25
##          256 252
## 49 5 50 51 52 53 54 55 56 57 58 59 6 60 61 62 63 64 26
##          65 66
## 252 392 250 247 246 244 243 238 238 238 237 236 378 235 233 231 227 219 27
##          217 215
## 67 68 69 7 70 71 72 73 74 75 76 77 78 79 8 80 81 82 28
##          83 84
## 215 209 208 373 208 205 203 202 202 198 198 197 194 189 370 187 187 187 29
##          185 184
## 85 86 87 88 89 9 90 91 92 93 94 95 96 97 98 99 30
## 180 179 176 175 173 365 173 172 162 160 159 158 158 156 155 155 31
##          32
## $Clustering          33
##          34
## Cluster1 Cluster2 Cluster3 Cluster4 Cluster5 Cluster6          35
## 23125      2730      1558      1531      520      214          36
##          37
## $Sample          38
##          39
## KO_Hp    KO_IL4C  KO_Naive      WT_Hp    WT_IL4C  WT_Naive          40
## 3735     4418     5260      4646     6284     5335          41
##          42
## $Sample_Cluster          43
##          44
## KO_Hp_Cluster1    KO_Hp_Cluster2    KO_Hp_Cluster3    KO_Hp_Cluster4          45
##          2835           405           194           130          46
## KO_Hp_Cluster5    KO_Hp_Cluster6    KO_IL4C_Cluster1  KO_IL4C_Cluster2          47
##          98            73            3122          510          48
## KO_IL4C_Cluster3  KO_IL4C_Cluster4  KO_IL4C_Cluster5  KO_Naive_Cluster1          49
##          200           312           274           4540          50
## KO_Naive_Cluster2  KO_Naive_Cluster3  KO_Naive_Cluster4  WT_Hp_Cluster1          51

```

```

##          354          321          45          3536 52
## WT_Hp_Cluster2 WT_Hp_Cluster3 WT_Hp_Cluster4 WT_IL4C_Cluster1 53
##          143          245          722          4570 54
## WT_IL4C_Cluster2 WT_IL4C_Cluster3 WT_IL4C_Cluster4 WT_IL4C_Cluster5 55
##          939          276          222          136 56
## WT_IL4C_Cluster6 WT_Naive_Cluster1 WT_Naive_Cluster2 WT_Naive_Cluster3 57
##          141         4522          379          322 58
## WT_Naive_Cluster4 WT_Naive_Cluster5
##          100          12
##
## $Genotype
##
##      KO      WT
## 13413 16265
##
## $Treatment
##
##      Hp      IL4C      Naive
## 8381 10702 10595
##
## $Global
##
## Cluster1 Cluster2 Cluster3 Cluster4 Cluster5 Cluster6
## 22831      781     1327     1849     1465     1425
##
## $RNA_snn_res.0.5
##
##      0      1     10     11     12     13     14     15     16      2      3      4      5      6
##      7      8
## 7922 3972 1138 986 733 722 348 255 70 2711 1847 1763 1706 1523
## 1441 1298
##      9
## 1243
##
## $RNA_snn_res.15
##
##      0      1     10    100    101    102    103    104    105    106    107    108    109    11    110    111    112    113
##     114    115
## 491 477 364 151 151 150 150 139 137 136 131 129 128 363 128 127 123 123
## 117 111
## 116 117 118 119 12 120 121 122 123 124 125 126 127 128 129 13 130 131
## 132 133
## 110 109 105 101 358 99 98 97 84 79 63 63 54 53 45 358 41 41
## 39 33
## 134 136 14 15 16 17 18 19 2 20 21 22 23 24 25 26 27 28
## 29 3
## 20 4 357 347 346 344 340 323 411 322 319 316 313 312 312 311 308
## 304 398
## 30 31 32 33 34 35 36 37 38 39 4 40 41 42 43 44 45 46
## 47 48
## 302 298 297 295 294 292 281 281 280 278 394 266 264 263 263 260 258 256
## 256 252
## 49 5 50 51 52 53 54 55 56 57 58 59 6 60 61 62 63 64
## 65 66

```

```

## 252 392 250 247 246 244 243 238 238 238 237 236 378 235 233 231 227 219 95
## 217 215
## 67 68 69 7 70 71 72 73 74 75 76 77 78 79 8 80 81 82 96
## 83 84
## 215 209 208 373 208 205 203 202 202 198 198 197 194 189 370 187 187 187 97
## 185 184
## 85 86 87 88 89 9 90 91 92 93 94 95 96 97 98 99 98
## 180 179 176 175 173 365 173 172 162 160 159 158 158 156 155 155 99
##
## $SingleR.labels
##
## T cells (T.8EFF.OT1.D10LIS) T cells (T.8EFF.OT1.D45VSV) 103
## 176 208 104
## T cells (T.8Mem) T cells (T.8NVE.OT1) 105
## 7735 21480 106
## T cells (T.8SP24-) 107
## 79 108
##
## $Annotation 109
##
## T-effector T-memory T-naive 112
## 384 7814 21480 113

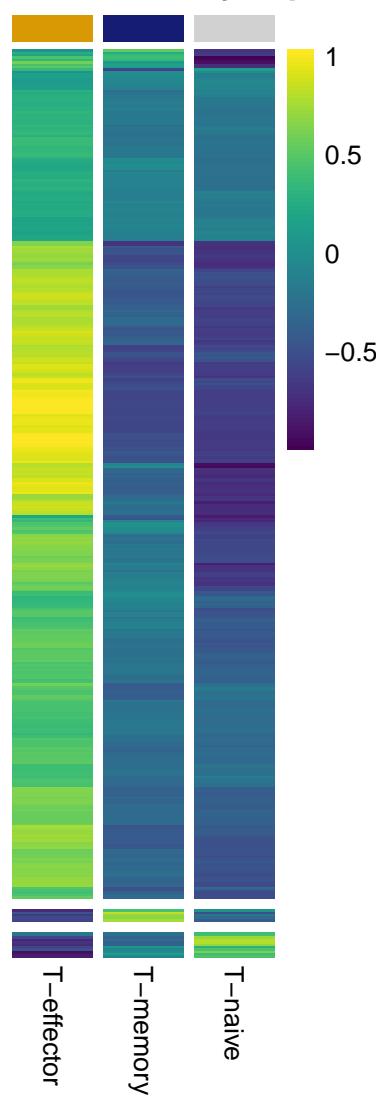
```

3 Ploting with previous analysis (done by Arnaud)

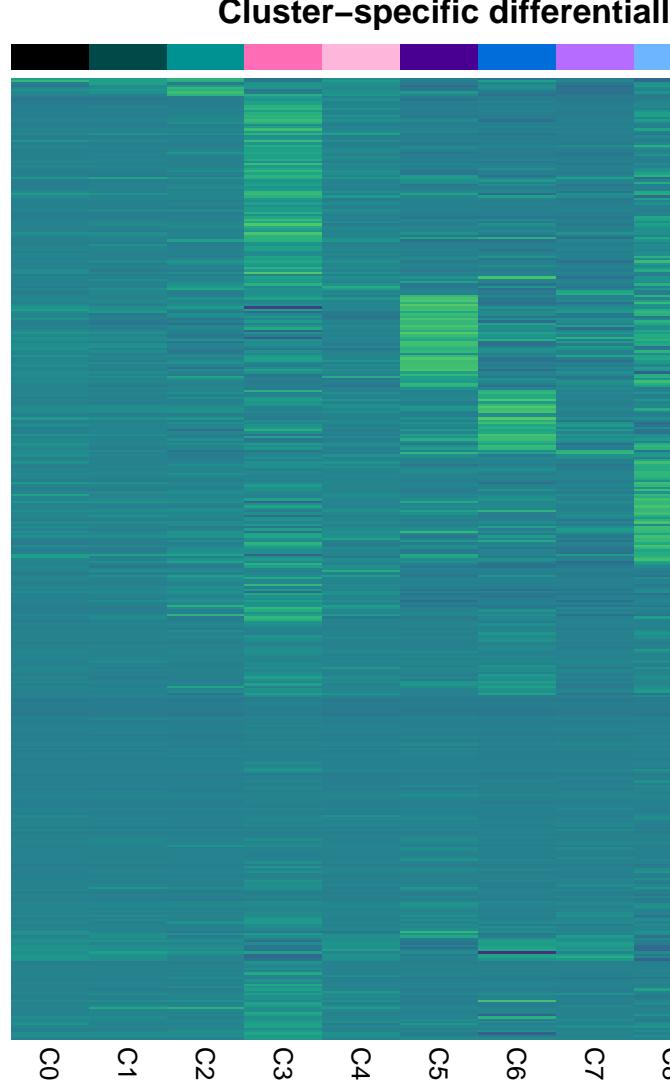
An analysis script can be found in “./Data/Objects/Main_Script.R”

```
source("../Data/Objects/Main_Script.R")
```

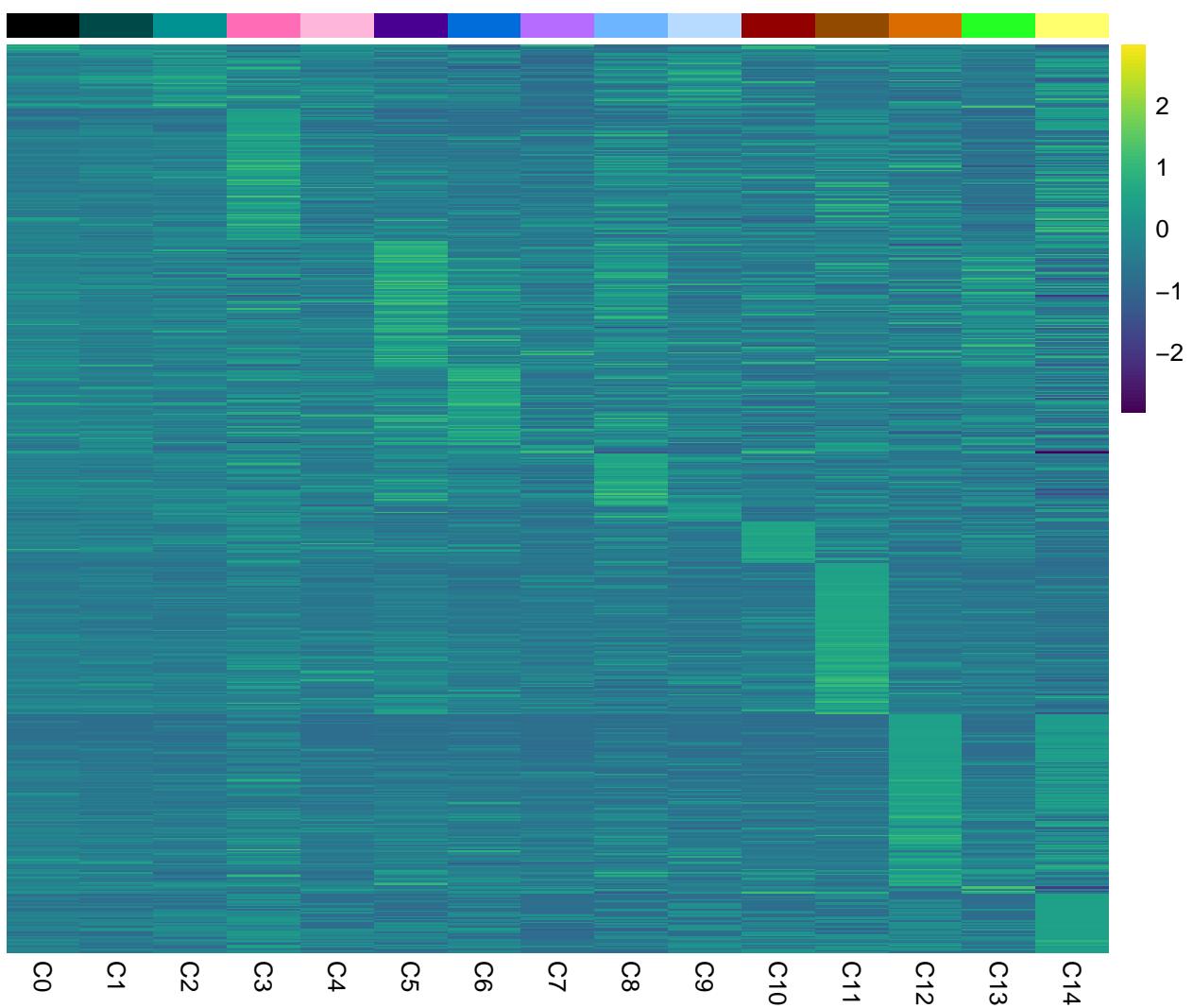
Cluster-specific differentially expressed genes



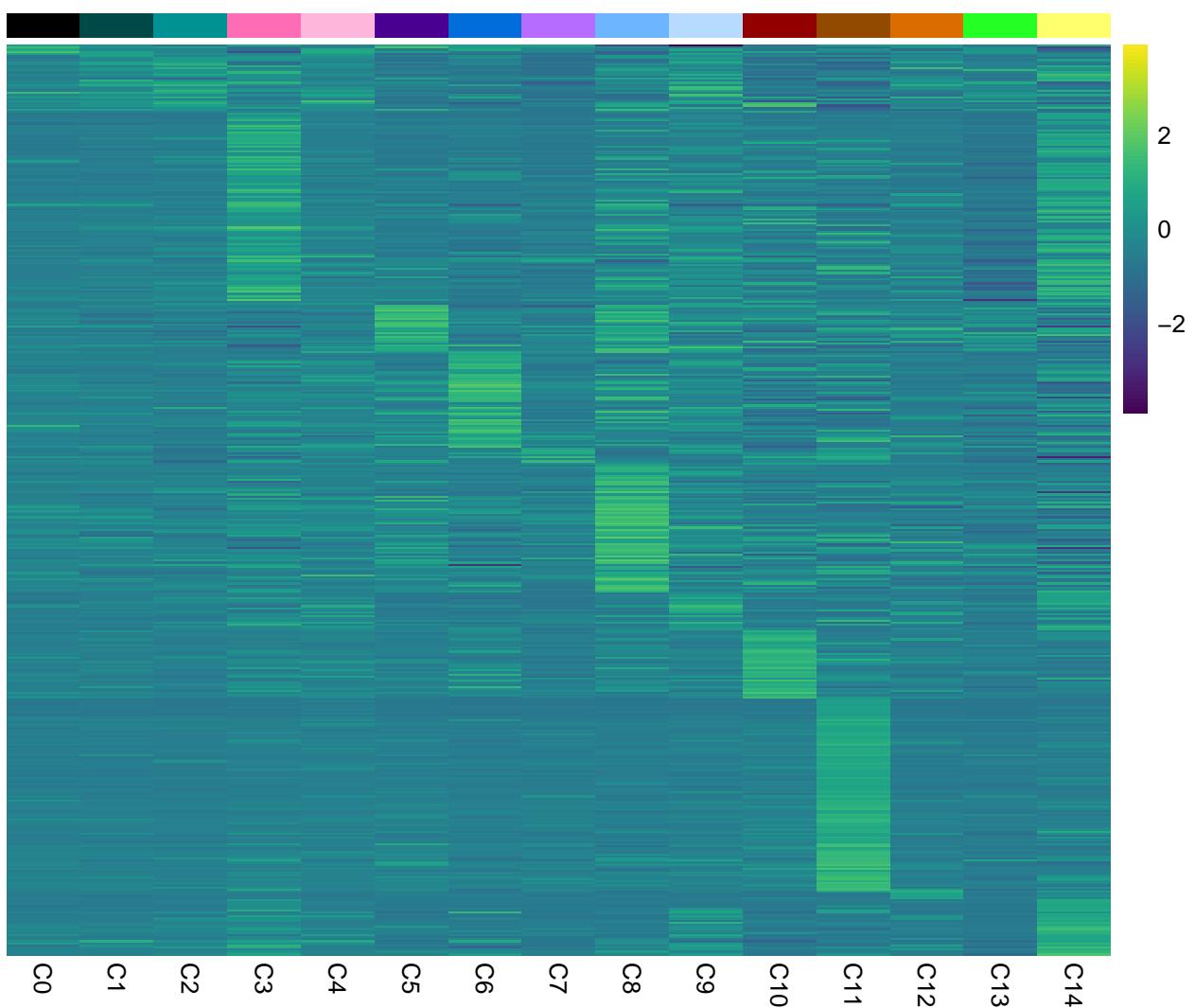
Cluster-specific differentiall



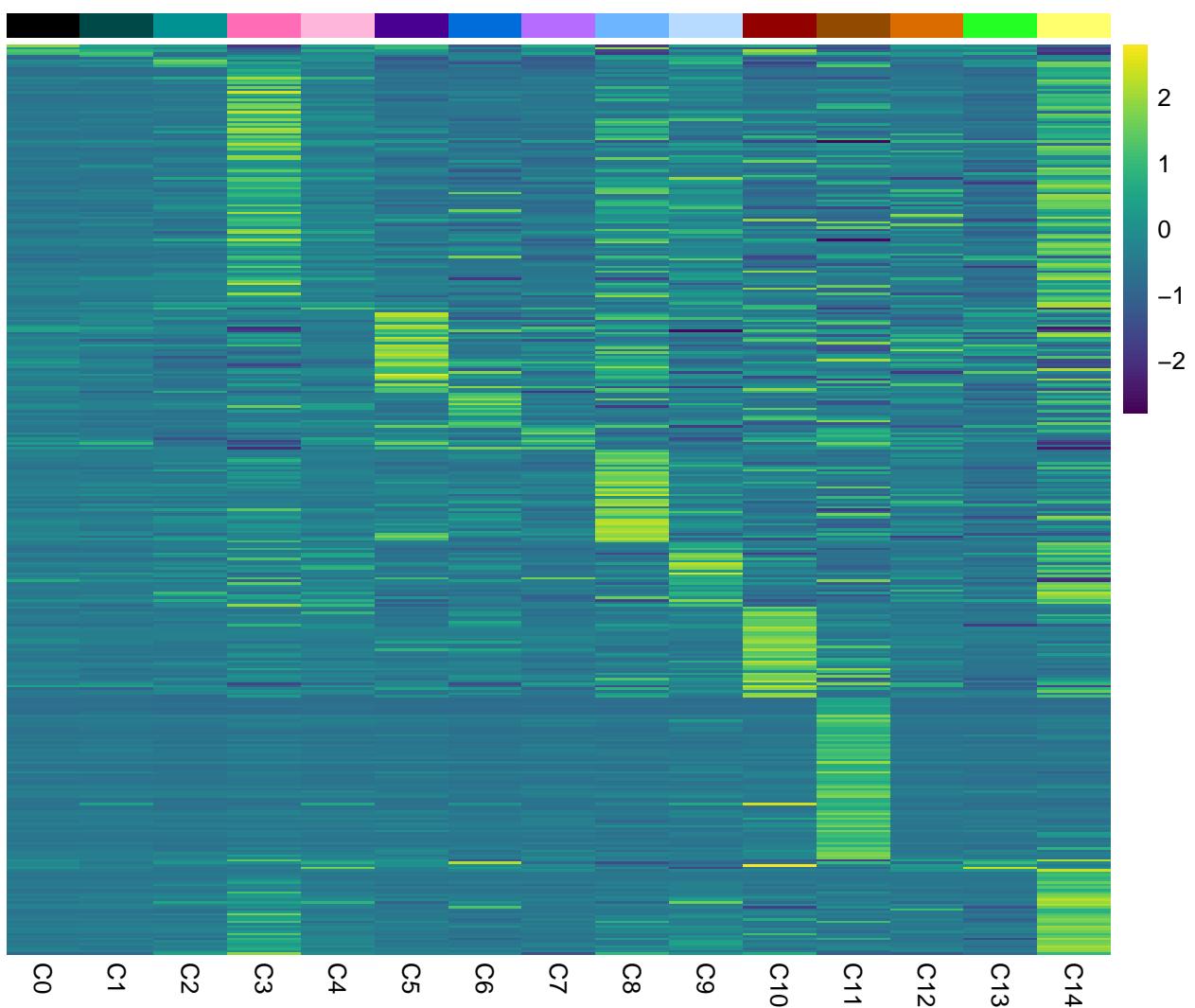
Cluster-specific differentially expressed genes



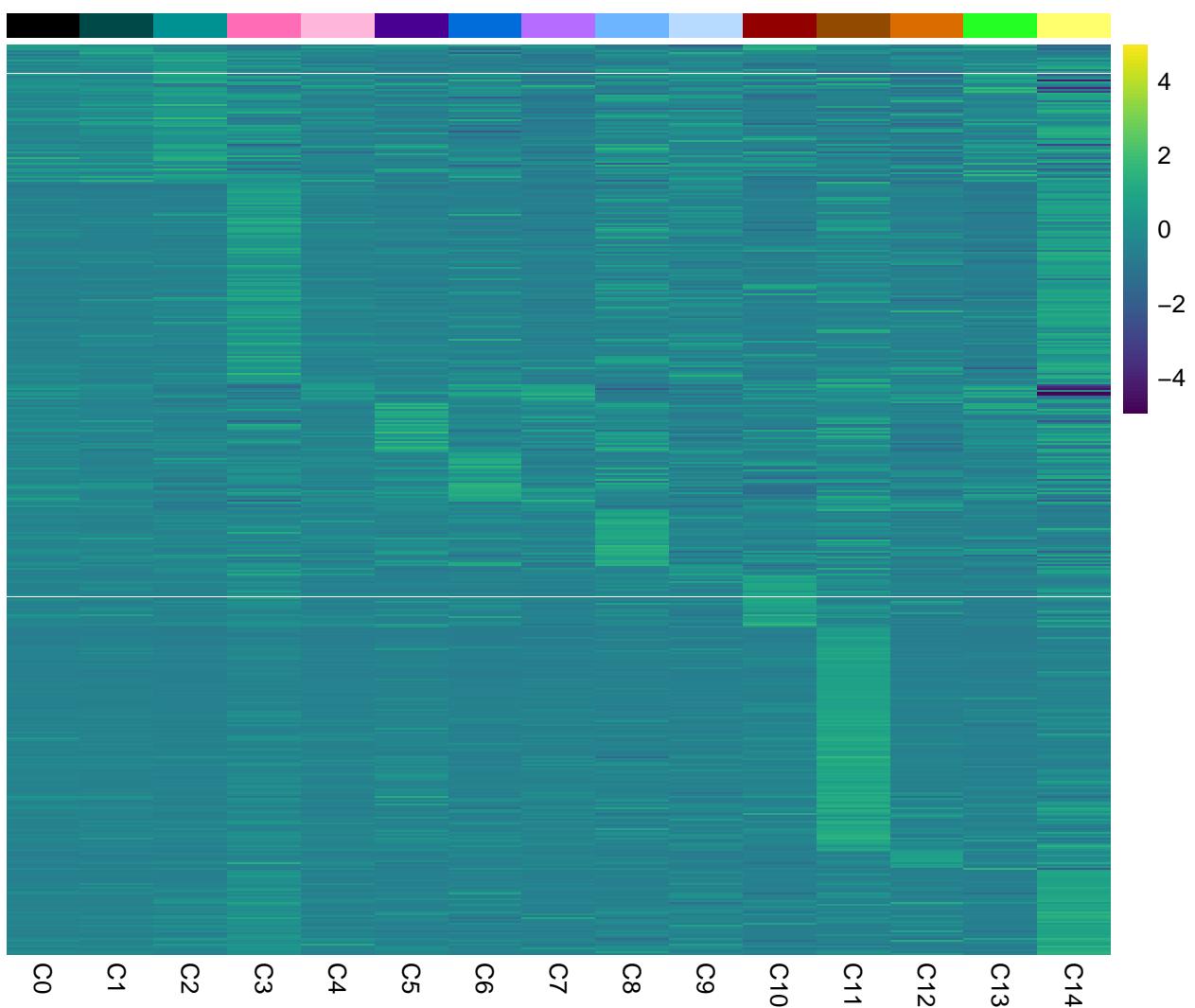
Cluster-specific differentially expressed genes

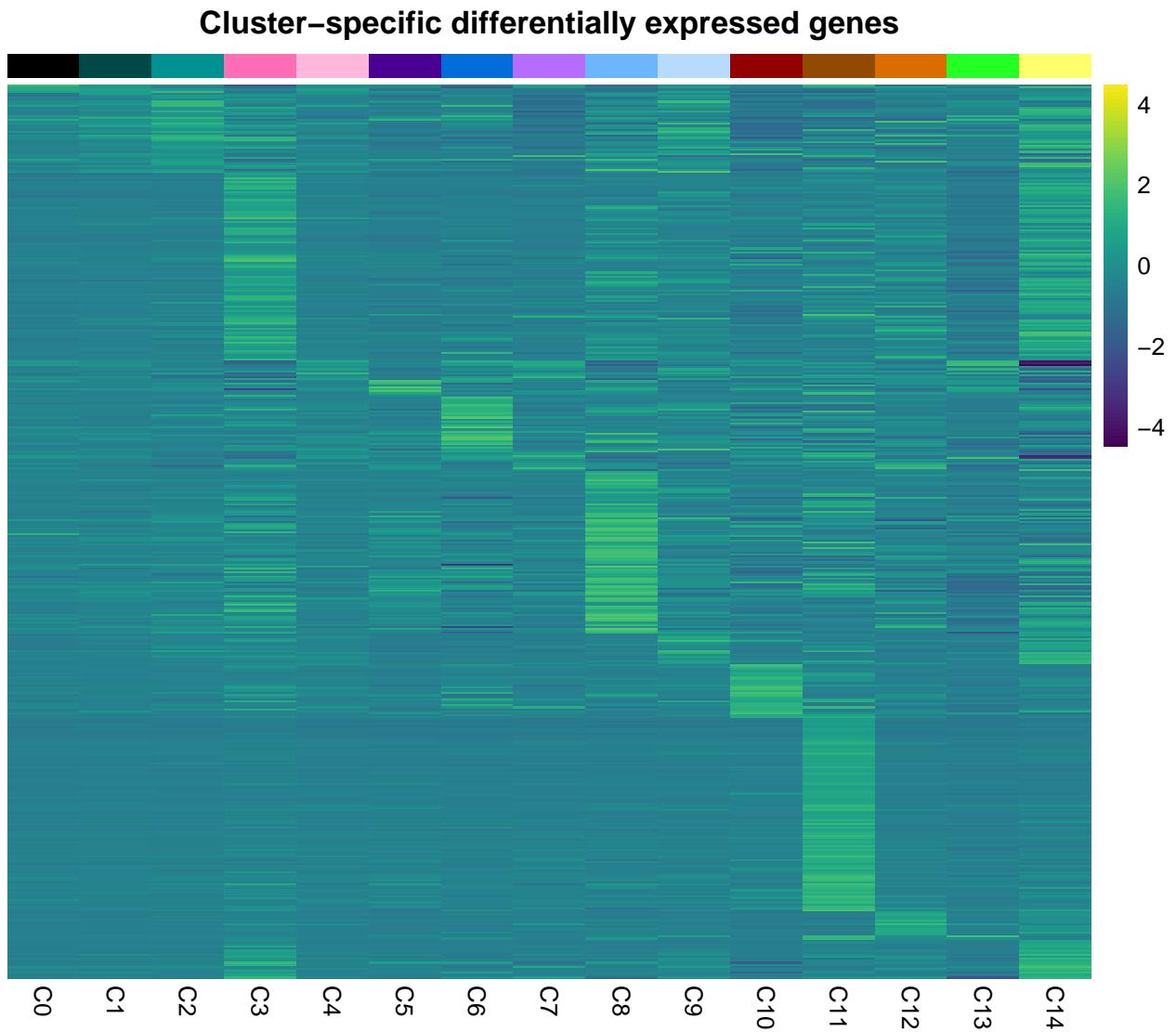


Cluster-specific differentially expressed genes



Cluster-specific differentially expressed genes





4 Try Merge instead of integrate

Merge all the samples of

```
## [1] "WT_Naive" "WT_IL4C"   "WT_Hp"      "KO_Naive" "KO_IL4C"   "KO_Hp"    1
```

Merge with Merge:

```
## An object of class Seurat
## 37418 features across 29678 samples within 4 assays
## Active assay: RNA (22597 features, 0 variable features)
## 3 other assays present: HTO, SCT, integrated 1
2
3
4
```

4.1 Data processing

```
subset.merge <- NormalizeData(subset.merge)
subset.merge <- ScaleData(subset.merge ,features = rownames(subset.merge))
subset.merge <- FindVariableFeatures(subset.merge) 1
2
3
```

```

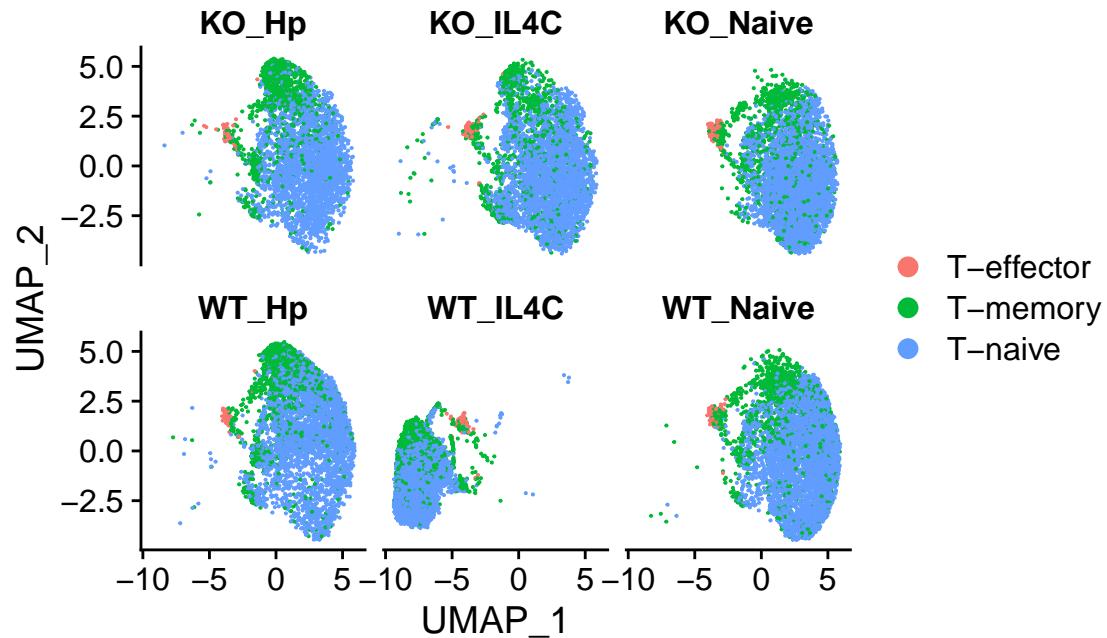
subset.merge <- RunPCA(subset.merge, features = VariableFeatures(subset.
  merge))
subset.merge <- FindNeighbors(subset.merge, reduction = "pca", dims =
  1:15)
subset.merge <- RunUMAP(subset.merge, dims = 1:15)

```

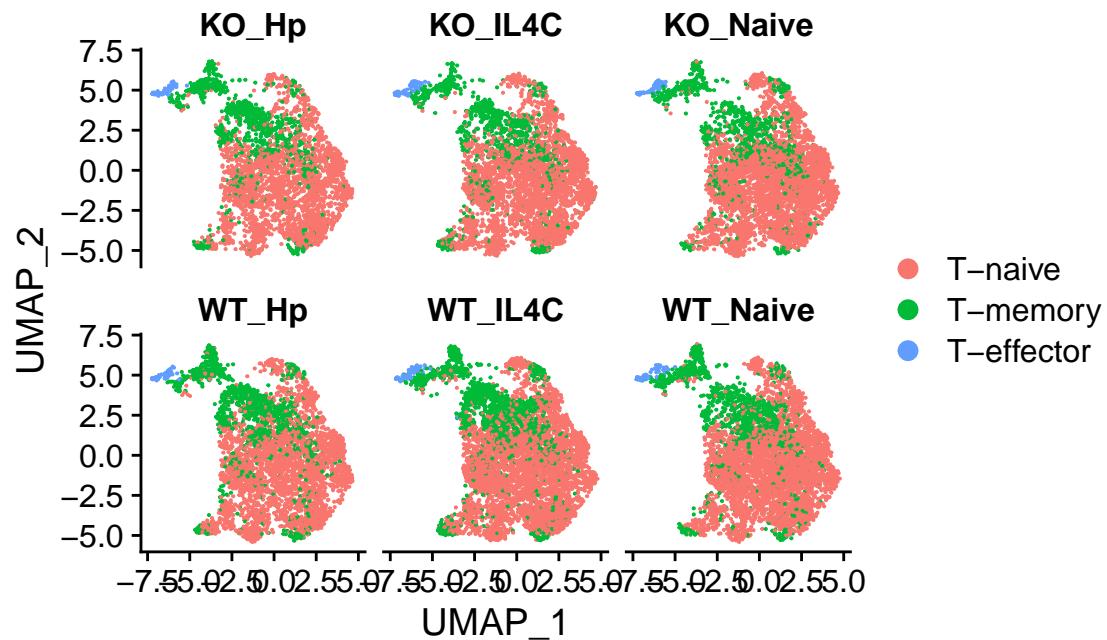
4
5
6

4.2 Compare integrated and Merged

Merged



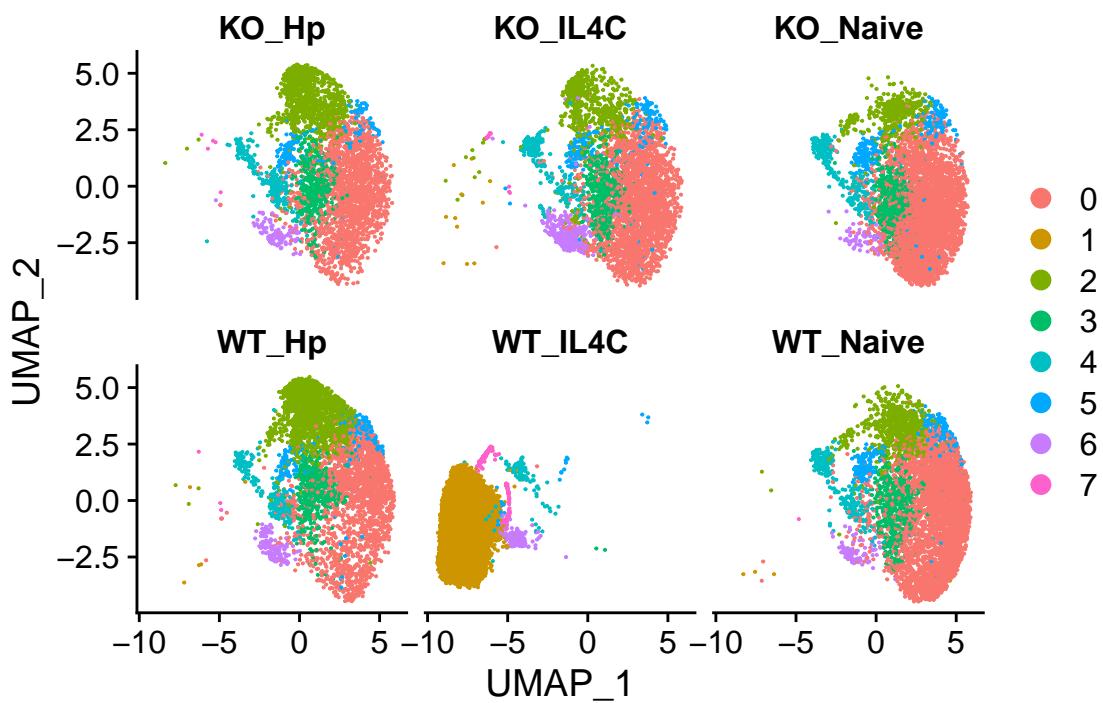
Integrated



5 Clustering after merge

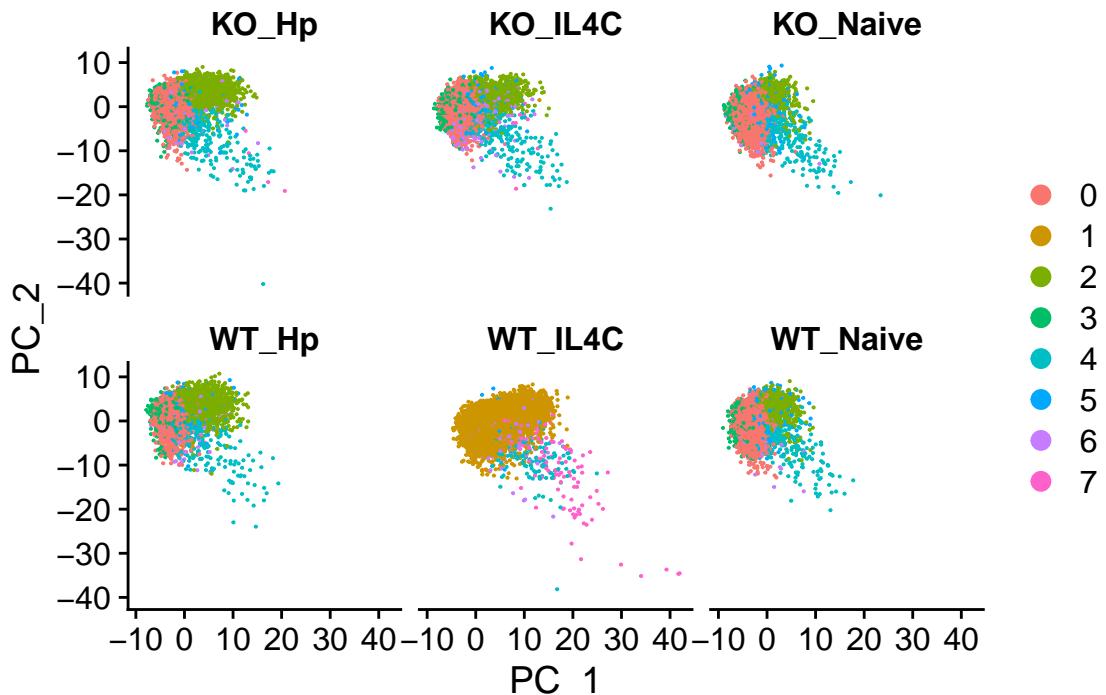
Give a resolution of 0.3:

```
## Modularity Optimizer version 1.3.0 by Ludo Waltman and Nees Jan van Eck 1
## 2
## Number of nodes: 29678 3
## Number of edges: 801718 4
## 5
## Running Louvain algorithm... 6
## Maximum modularity in 10 random starts: 0.8769 7
## Number of communities: 8 8
## Elapsed time: 7 seconds 9
```



IL4-treated WT has biggest difference. Cluster 1 is the difference.

Batch effect? Voici PCA plot:



It seems not to be a batch effect

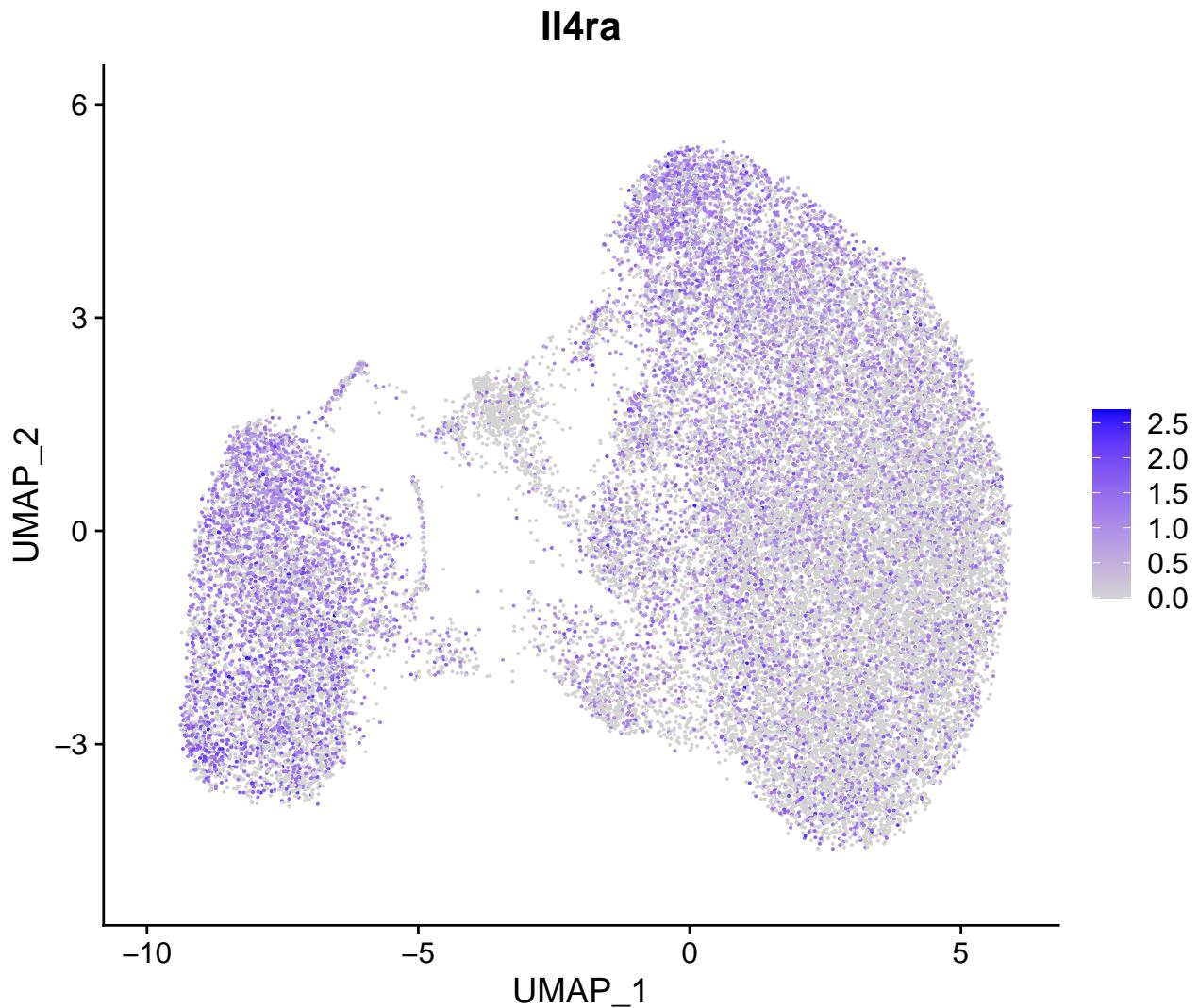
5.1 Find the marker of Cluster 1

```

## # A tibble: 133 x 5
##   p_val avg_log2FC pct.1 pct.2 p_val_adj
##   <dbl>     <dbl> <dbl> <dbl>      <dbl>
## 1     0       0.301  1     1        0
## 2     0       0.465  1     0.999    0
## 3     0       0.407  0.998 0.997    0
## 4     0       0.308  1     1        0
## 5     0       0.529  1     1        0
## 6     0       0.261  1     1        0
## 7     0       0.709  0.495 0.267    0
## 8     0       0.492  1     1        0
## 9     0       0.258  1     1        0
## 10    0       0.326  1     1        0
## # ... with 123 more rows

```

IL4ra is in the DE genes:



5.2 KEGG enrichment

```

library(clusterProfiler)

de_entrez.ident1 <- bitr( geneID = rownames(de.ident1), fromType = "SYMBOL"
  , toType = "ENTREZID", OrgDb = "org.Mm.eg.db", drop = TRUE ) $  

  ENTREZID
result.enrichKEGG.de_ident1 <- enrichKEGG(de_entrez.ident1, organism = "  

  mmu", keyType = "ncbi-geneid")
result.enrichKEGG.de_ident1@result$Description

```

| | |
|---|---|
| ## [1] "Ribosome" | 1 |
| ## [2] "Coronavirus disease - COVID-19" | 2 |
| ## [3] "Diabetic cardiomyopathy" | 3 |
| ## [4] "Prion disease" | 4 |
| ## [5] "Huntington disease" | 5 |
| ## [6] "Parkinson disease" | 6 |
| ## [7] "Alzheimer disease" | 7 |
| ## [8] "Amyotrophic lateral sclerosis" | 8 |
| ## [9] "Bacterial invasion of epithelial cells" | 9 |

| | | |
|---------|---|----|
| ## [10] | "Pathways of neurodegeneration - multiple diseases" | 10 |
| ## [11] | "Chemical carcinogenesis - reactive oxygen species" | 11 |
| ## [12] | "Th1 and Th2 cell differentiation" | 12 |
| ## [13] | "Yersinia infection" | 13 |
| ## [14] | "Thermogenesis" | 14 |
| ## [15] | "Human T-cell leukemia virus 1 infection" | 15 |
| ## [16] | "Salmonella infection" | 16 |
| ## [17] | "Oxidative phosphorylation" | 17 |
| ## [18] | "Spinocerebellar ataxia" | 18 |
| ## [19] | "Fc gamma R-mediated phagocytosis" | 19 |
| ## [20] | "Measles" | 20 |
| ## [21] | "Th17 cell differentiation" | 21 |
| ## [22] | "VEGF signaling pathway" | 22 |
| ## [23] | "cGMP-PKG signaling pathway" | 23 |
| ## [24] | "Influenza A" | 24 |
| ## [25] | "Necroptosis" | 25 |
| ## [26] | "Carbon metabolism" | 26 |
| ## [27] | "Glycolysis / Gluconeogenesis" | 27 |
| ## [28] | "Endocytosis" | 28 |
| ## [29] | "Neutrophil extracellular trap formation" | 29 |
| ## [30] | "Regulation of actin cytoskeleton" | 30 |
| ## [31] | "PD-L1 expression and PD-1 checkpoint pathway in cancer" | 31 |
| ## [32] | "Viral myocarditis" | 32 |
| ## [33] | "Hematopoietic cell lineage" | 33 |
| ## [34] | "Calcium signaling pathway" | 34 |
| ## [35] | "Tight junction" | 35 |
| ## [36] | "T cell receptor signaling pathway" | 36 |
| ## [37] | "Proteasome" | 37 |
| ## [38] | "Cholesterol metabolism" | 38 |
| ## [39] | "Cellular senescence" | 39 |
| ## [40] | "HIF-1 signaling pathway" | 40 |
| ## [41] | "Natural killer cell mediated cytotoxicity" | 41 |
| ## [42] | "Legionellosis" | 42 |
| ## [43] | "Inflammatory bowel disease" | 43 |
| ## [44] | "Lysosome" | 44 |
| ## [45] | "Cytosolic DNA-sensing pathway" | 45 |
| ## [46] | "Autophagy - animal" | 46 |
| ## [47] | "Adherens junction" | 47 |
| ## [48] | "Fluid shear stress and atherosclerosis" | 48 |
| ## [49] | "Non-alcoholic fatty liver disease" | 49 |
| ## [50] | "Biosynthesis of amino acids" | 50 |
| ## [51] | "B cell receptor signaling pathway" | 51 |
| ## [52] | "JAK-STAT signaling pathway" | 52 |
| ## [53] | "Cardiac muscle contraction" | 53 |
| ## [54] | "Terpenoid backbone biosynthesis" | 54 |
| ## [55] | "Viral protein interaction with cytokine and cytokine receptor" | 55 |
| ## [56] | "Tuberculosis" | 56 |
| ## [57] | "Glycosphingolipid biosynthesis - lacto and neolacto series" | 57 |
| ## [58] | "Cytokine-cytokine receptor interaction" | 58 |
| ## [59] | "RNA polymerase" | 59 |
| ## [60] | "Parathyroid hormone synthesis, secretion and action" | 60 |
| ## [61] | "Autophagy - other" | 61 |
| ## [62] | "C-type lectin receptor signaling pathway" | 62 |
| ## [63] | "Pentose phosphate pathway" | 63 |

| | | |
|----------|---|-----|
| ## [64] | "Starch and sucrose metabolism" | 64 |
| ## [65] | "NOD-like receptor signaling pathway" | 65 |
| ## [66] | "Leukocyte transendothelial migration" | 66 |
| ## [67] | "Primary immunodeficiency" | 67 |
| ## [68] | "Sphingolipid signaling pathway" | 68 |
| ## [69] | "Platelet activation" | 69 |
| ## [70] | "Ferroptosis" | 70 |
| ## [71] | "Intestinal immune network for IgA production" | 71 |
| ## [72] | "Apoptosis" | 72 |
| ## [73] | "Apelin signaling pathway" | 73 |
| ## [74] | "Human immunodeficiency virus 1 infection" | 74 |
| ## [75] | "PI3K-Akt signaling pathway" | 75 |
| ## [76] | "Amino sugar and nucleotide sugar metabolism" | 76 |
| ## [77] | "Oxytocin signaling pathway" | 77 |
| ## [78] | "mTOR signaling pathway" | 78 |
| ## [79] | "Endocrine and other factor-regulated calcium reabsorption" | 79 |
| ## [80] | "Wnt signaling pathway" | 80 |
| ## [81] | "Allograft rejection" | 81 |
| ## [82] | "Graft-versus-host disease" | 82 |
| ## [83] | "Cell adhesion molecules" | 83 |
| ## [84] | "Fc epsilon RI signaling pathway" | 84 |
| ## [85] | "Long-term potentiation" | 85 |
| ## [86] | "Amphetamine addiction" | 86 |
| ## [87] | "MAPK signaling pathway" | 87 |
| ## [88] | "Axon guidance" | 88 |
| ## [89] | "Type I diabetes mellitus" | 89 |
| ## [90] | "Leishmaniasis" | 90 |
| ## [91] | "Phagosome" | 91 |
| ## [92] | "Gastric acid secretion" | 92 |
| ## [93] | "Renin secretion" | 93 |
| ## [94] | "Pancreatic cancer" | 94 |
| ## [95] | "Chemokine signaling pathway" | 95 |
| ## [96] | "Synaptic vesicle cycle" | 96 |
| ## [97] | "Pertussis" | 97 |
| ## [98] | "Arrhythmogenic right ventricular cardiomyopathy" | 98 |
| ## [99] | "EGFR tyrosine kinase inhibitor resistance" | 99 |
| ## [100] | "Autoimmune thyroid disease" | 100 |
| ## [101] | "Focal adhesion" | 101 |
| ## [102] | "RNA degradation" | 102 |
| ## [103] | "Proteoglycans in cancer" | 103 |
| ## [104] | "Rheumatoid arthritis" | 104 |
| ## [105] | "Colorectal cancer" | 105 |
| ## [106] | "Rap1 signaling pathway" | 106 |
| ## [107] | "Hypertrophic cardiomyopathy" | 107 |
| ## [108] | "Lipid and atherosclerosis" | 108 |
| ## [109] | "Dilated cardiomyopathy" | 109 |
| ## [110] | "Choline metabolism in cancer" | 110 |
| ## [111] | "Chagas disease" | 111 |
| ## [112] | "Glucagon signaling pathway" | 112 |
| ## [113] | "Glutamatergic synapse" | 113 |
| ## [114] | "Nucleocytoplasmic transport" | 114 |
| ## [115] | "Human cytomegalovirus infection" | 115 |
| ## [116] | "Thyroid hormone signaling pathway" | 116 |
| ## [117] | "Oocyte meiosis" | 117 |

| | |
|--|-----|
| ## [118] "Osteoclast differentiation" | 118 |
| ## [119] "Spliceosome" | 119 |
| ## [120] "Estrogen signaling pathway" | 120 |
| ## [121] "Dopaminergic synapse" | 121 |
| ## [122] "Insulin signaling pathway" | 122 |
| ## [123] "Retrograde endocannabinoid signaling" | 123 |
| ## [124] "Systemic lupus erythematosus" | 124 |
| ## [125] "Hippo signaling pathway" | 125 |
| ## [126] "Hepatitis B" | 126 |
| ## [127] "Hepatitis C" | 127 |
| ## [128] "Hepatocellular carcinoma" | 128 |
| ## [129] "Neuroactive ligand-receptor interaction" | 129 |
| ## [130] "cAMP signaling pathway" | 130 |
| ## [131] "Transcriptional misregulation in cancer" | 131 |
| ## [132] "Kaposi sarcoma-associated herpesvirus infection" | 132 |
| ## [133] "Epstein-Barr virus infection" | 133 |
| ## [134] "Ras signaling pathway" | 134 |
| ## [135] "MicroRNAs in cancer" | 135 |

6 Session information

| | |
|--|----|
| ## R version 4.0.3 (2020-10-10) | 1 |
| ## Platform: x86_64-pc-linux-gnu (64-bit) | 2 |
| ## Running under: Ubuntu 20.04.3 LTS | 3 |
| ## | 4 |
| ## Matrix products: default | 5 |
| ## BLAS: /usr/lib/x86_64-linux-gnu/openblas-pthread/libblas.so.3 | 6 |
| ## LAPACK: /usr/lib/x86_64-linux-gnu/openblas-pthread/liblapack.so.3 | 7 |
| ## | 8 |
| ## locale: | 9 |
| ## [1] LC_CTYPE=en_US.UTF-8 LC_NUMERIC=C | 10 |
| ## [3] LC_TIME=en_GB.UTF-8 LC_COLLATE=en_US.UTF-8 | 11 |
| ## [5] LC_MONETARY=en_GB.UTF-8 LC_MESSAGES=en_US.UTF-8 | 12 |
| ## [7] LC_PAPER=en_GB.UTF-8 LC_NAME=C | 13 |
| ## [9] LC_ADDRESS=C LC_TELEPHONE=C | 14 |
| ## [11] LC_MEASUREMENT=en_GB.UTF-8 LC_IDENTIFICATION=C | 15 |
| ## | 16 |
| ## attached base packages: | 17 |
| ## [1] grid parallel stats4 stats graphics grDevices utils | 18 |
| ## [8] datasets methods base | 19 |
| ## | 20 |
| ## other attached packages: | 21 |
| ## [1] org.Mm.eg.db_3.12.0 AnnotationDbi_1.52.0 | 22 |
| ## [3] clusterProfiler_3.18.1 ggrepel_0.9.1 | 23 |
| ## [5] RColorBrewer_1.1-2 cowplot_1.1.1 | 24 |
| ## [7] viridis_0.6.1 viridisLite_0.4.0 | 25 |
| ## [9] ggplot2_3.3.5 dplyr_1.0.7 | 26 |
| ## [11] tidyverse_1.1.3 scales_1.1.1 | 27 |
| ## [13] pheatmap_1.0.12 SingleR_1.4.1 | 28 |
| ## [15] SummarizedExperiment_1.20.0 Biobase_2.50.0 | 29 |
| ## [17] GenomicRanges_1.42.0 GenomeInfoDb_1.26.7 | 30 |
| ## [19] IRanges_2.24.1 S4Vectors_0.28.1 | 31 |
| ## [21] BiocGenerics_0.36.1 MatrixGenerics_1.2.1 | 32 |

| | | |
|---|----------------------|----|
| ## [23] matrixStats_0.60.0 | SeuratObject_4.0.2 | 33 |
| ## [25] Seurat_4.0.3 | | 34 |
| ## | | 35 |
| ## loaded via a namespace (and not attached): | | 36 |
| ## [1] utf8_1.2.2 | reticulate_1.20 | 37 |
| ## [3] tidyselect_1.1.1 | RSSQLite_2.2.7 | 38 |
| ## [5] htmlwidgets_1.5.3 | BiocParallel_1.24.1 | 39 |
| ## [7] Rtsne_0.15 | scatterpie_0.1.6 | 40 |
| ## [9] munsell_0.5.0 | codetools_0.2-18 | 41 |
| ## [11] ica_1.0-2 | future_1.21.0 | 42 |
| ## [13] miniUI_0.1.1.1 | withr_2.4.2 | 43 |
| ## [15] colorspace_2.0-2 | GOSemSim_2.16.1 | 44 |
| ## [17] highr_0.9 | knitr_1.33 | 45 |
| ## [19] rstudioapi_0.13 | ROCR_1.0-11 | 46 |
| ## [21] tensor_1.5 | DOSE_3.16.0 | 47 |
| ## [23] listenv_0.8.0 | labeling_0.4.2 | 48 |
| ## [25] GenomeInfoDbData_1.2.4 | polyclip_1.10-0 | 49 |
| ## [27] bit64_4.0.5 | farver_2.1.0 | 50 |
| ## [29] downloader_0.4 | parallelly_1.27.0 | 51 |
| ## [31] vctrs_0.3.8 | generics_0.1.0 | 52 |
| ## [33] xfun_0.24 | R6_2.5.0 | 53 |
| ## [35] graphlayouts_0.7.1 | rsvd_1.0.5 | 54 |
| ## [37] bitops_1.0-7 | spatstat.utils_2.2-0 | 55 |
| ## [39] cachem_1.0.5 | fgsea_1.16.0 | 56 |
| ## [41] DelayedArray_0.16.3 | assertthat_0.2.1 | 57 |
| ## [43] promises_1.2.0.1 | ggraph_2.0.5 | 58 |
| ## [45] enrichplot_1.10.2 | gtable_0.3.0 | 59 |
| ## [47] beachmat_2.6.4 | globals_0.14.0 | 60 |
| ## [49] goftest_1.2-2 | tidygraph_1.2.0 | 61 |
| ## [51] rlang_0.4.11 | splines_4.0.3 | 62 |
| ## [53] lazyeval_0.2.2 | spatstat.geom_2.2-2 | 63 |
| ## [55] BiocManager_1.30.16 | yaml_2.2.1 | 64 |
| ## [57] reshape2_1.4.4 | abind_1.4-5 | 65 |
| ## [59] httpuv_1.6.1 | qvalue_2.22.0 | 66 |
| ## [61] tools_4.0.3 | ellipsis_0.3.2 | 67 |
| ## [63] spatstat.core_2.3-0 | ggridges_0.5.3 | 68 |
| ## [65] Rcpp_1.0.7 | plyr_1.8.6 | 69 |
| ## [67] sparseMatrixStats_1.2.1 | zlibbioc_1.36.0 | 70 |
| ## [69] purrr_0.3.4 | RCurl_1.98-1.3 | 71 |
| ## [71] rpart_4.1-15 | deldir_0.2-10 | 72 |
| ## [73] pbapply_1.4-3 | zoo_1.8-9 | 73 |
| ## [75] cluster_2.1.0 | magrittr_2.0.1 | 74 |
| ## [77] data.table_1.14.0 | RSpectra_0.16-0 | 75 |
| ## [79] scattermore_0.7 | D0.db_2.9 | 76 |
| ## [81] lmtest_0.9-38 | RANN_2.6.1 | 77 |
| ## [83] fitdistrplus_1.1-5 | patchwork_1.1.1 | 78 |
| ## [85] mime_0.11 | evaluate_0.14 | 79 |
| ## [87] xtable_1.8-4 | gridExtra_2.3 | 80 |
| ## [89] compiler_4.0.3 | tibble_3.1.3 | 81 |
| ## [91] shadowtext_0.0.8 | KernSmooth_2.23-20 | 82 |
| ## [93] crayon_1.4.1 | htmltools_0.5.1.1 | 83 |
| ## [95] mgcv_1.8-33 | later_1.2.0 | 84 |
| ## [97] DBI_1.1.1 | tweenr_1.0.2 | 85 |
| ## [99] MASS_7.3-53 | Matrix_1.3-4 | 86 |

| | | |
|------------------------------------|-----------------------|-----|
| ## [101] cli_3.0.1 | igraph_1.2.6 | 87 |
| ## [103] pkgconfig_2.0.3 | rvcheck_0.1.8 | 88 |
| ## [105] plotly_4.9.4.1 | spatstat.sparse_2.0-0 | 89 |
| ## [107] XVector_0.30.0 | stringr_1.4.0 | 90 |
| ## [109] digest_0.6.27 | sctransform_0.3.2 | 91 |
| ## [111] RcppAnnoy_0.0.19 | spatstat.data_2.1-0 | 92 |
| ## [113] rmarkdown_2.9 | leiden_0.3.9 | 93 |
| ## [115] fastmatch_1.1-3 | uwot_0.1.10.9000 | 94 |
| ## [117] DelayedMatrixStats_1.12.3 | shiny_1.6.0 | 95 |
| ## [119] lifecycle_1.0.0 | nlme_3.1-152 | 96 |
| ## [121] jsonlite_1.7.2 | BiocNeighbors_1.8.2 | 97 |
| ## [123] limma_3.46.0 | fansi_0.5.0 | 98 |
| ## [125] pillar_1.6.2 | lattice_0.20-41 | 99 |
| ## [127] fastmap_1.1.0 | httr_1.4.2 | 100 |
| ## [129] survival_3.2-7 | G0.db_3.12.1 | 101 |
| ## [131] glue_1.4.2 | png_0.1-7 | 102 |
| ## [133] bit_4.0.4 | ggforce_0.3.3 | 103 |
| ## [135] stringi_1.7.3 | blob_1.2.2 | 104 |
| ## [137] BiocSingular_1.6.0 | memoise_2.0.0 | 105 |
| ## [139] irlba_2.3.3 | future.apply_1.7.0 | 106 |

7 (References)