

多発性骨髄腫における シングルセル解析

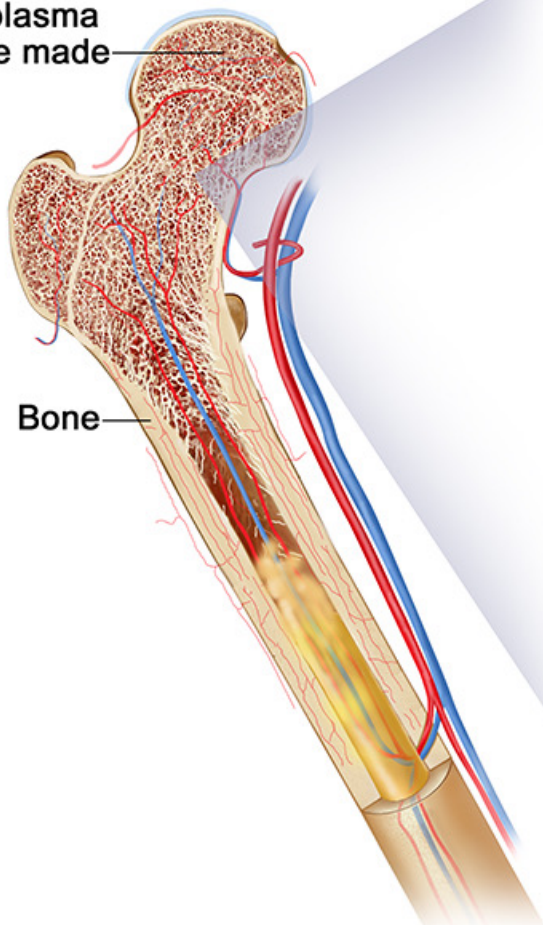
医歯薬学総合研究科

D2 小林 宏紀

多發性骨髓腫

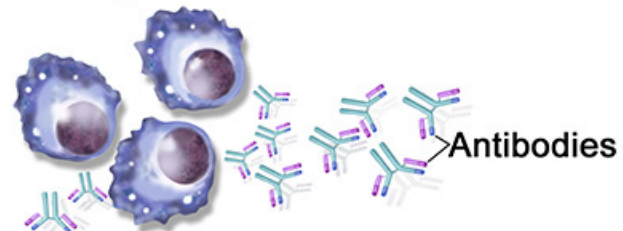
Multiple Myeloma

Red marrow
where plasma
cells are made



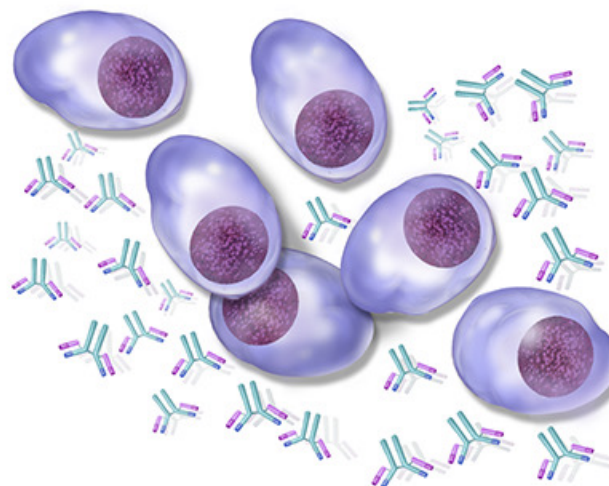
Bone

Normal plasma cells

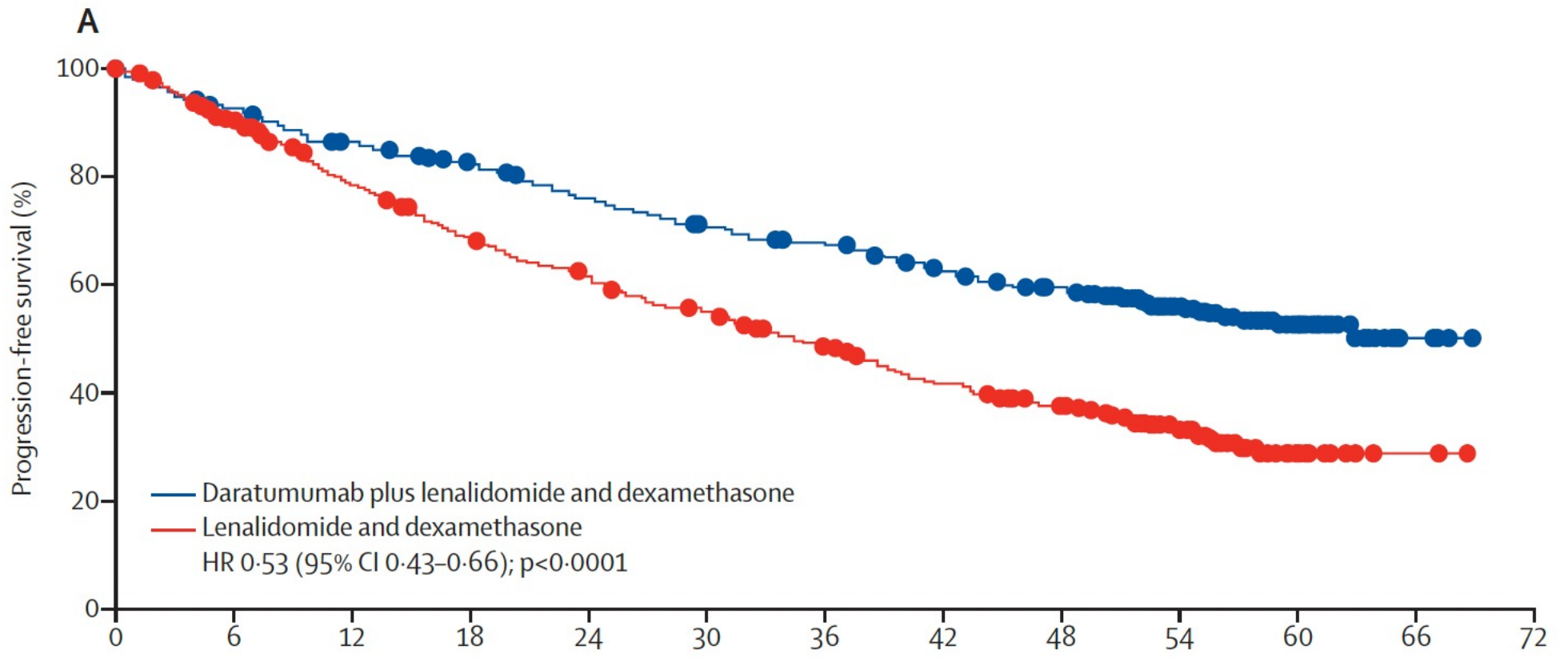


Antibodies

Multiple myeloma cells (abnormal plasma cells)



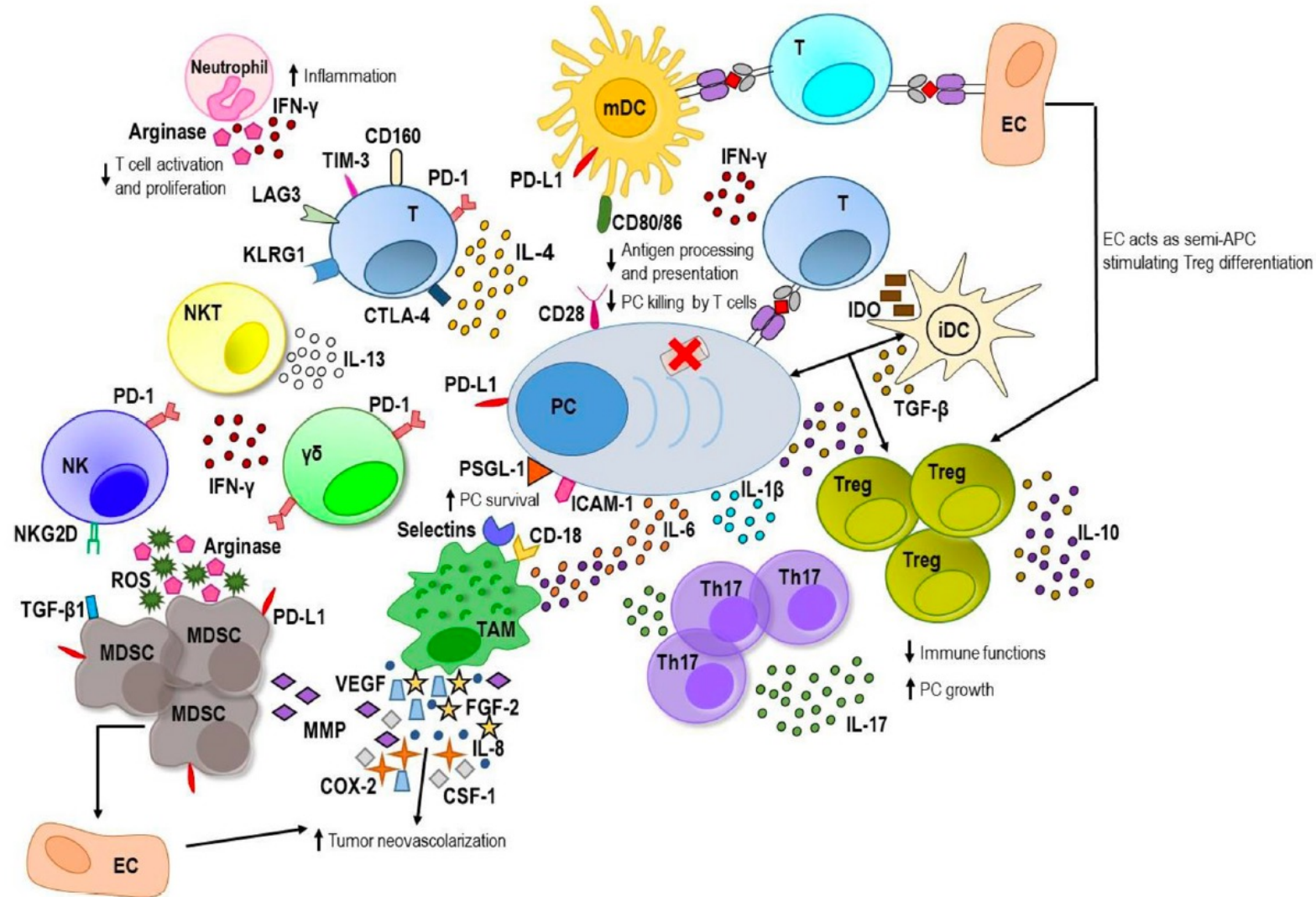
多発性骨髄腫の予後



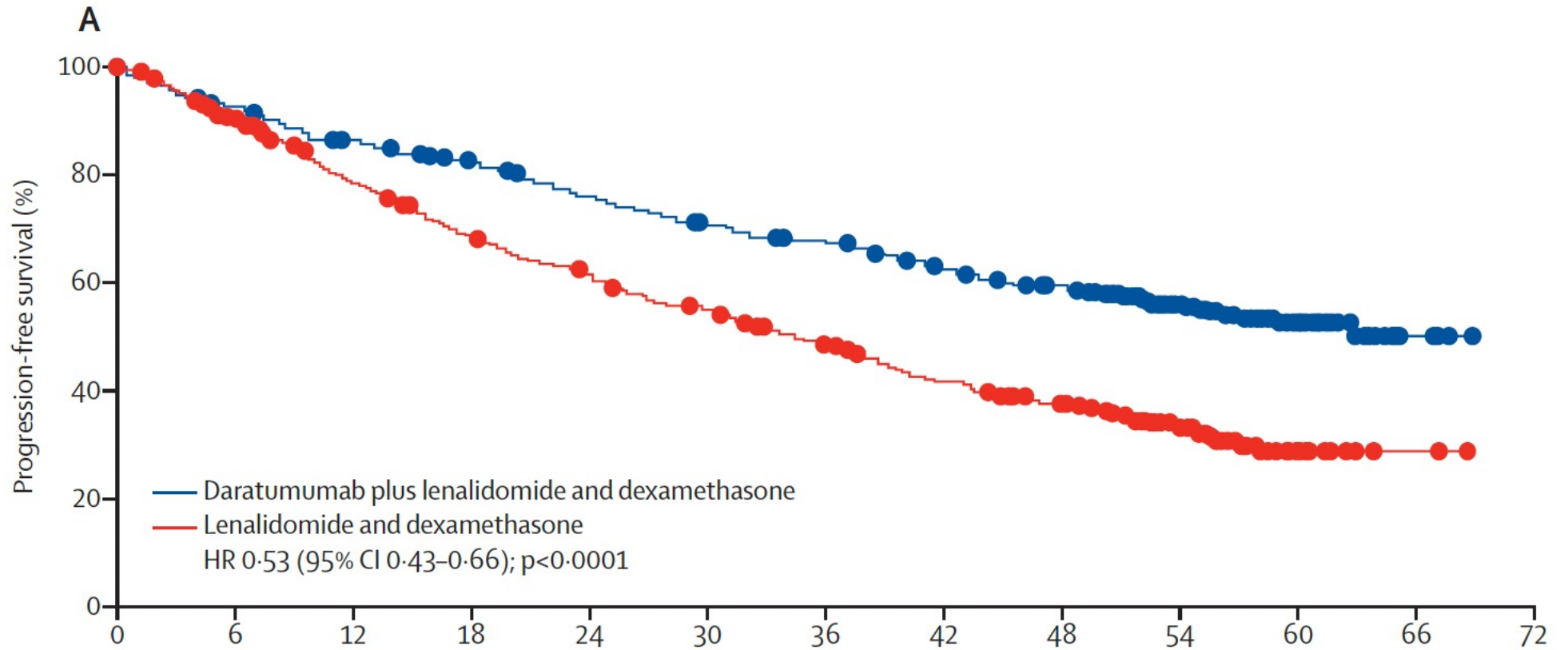
Number at risk (number censored)

Lenalidomide and dexamethasone	369 (0)	307 (29)	255 (41)	220 (44)	196 (46)	172 (49)	146 (55)	123 (58)	105 (64)	63 (95)	12 (140)	2 (150)	0 (152)
Daratumumab plus lenalidomide and dexamethasone	368 (0)	335 (6)	309 (9)	290 (14)	266 (16)	246 (18)	232 (20)	210 (25)	195 (30)	123 (92)	51 (158)	5 (203)	0 (208)

多発性骨髄腫を構成する細胞

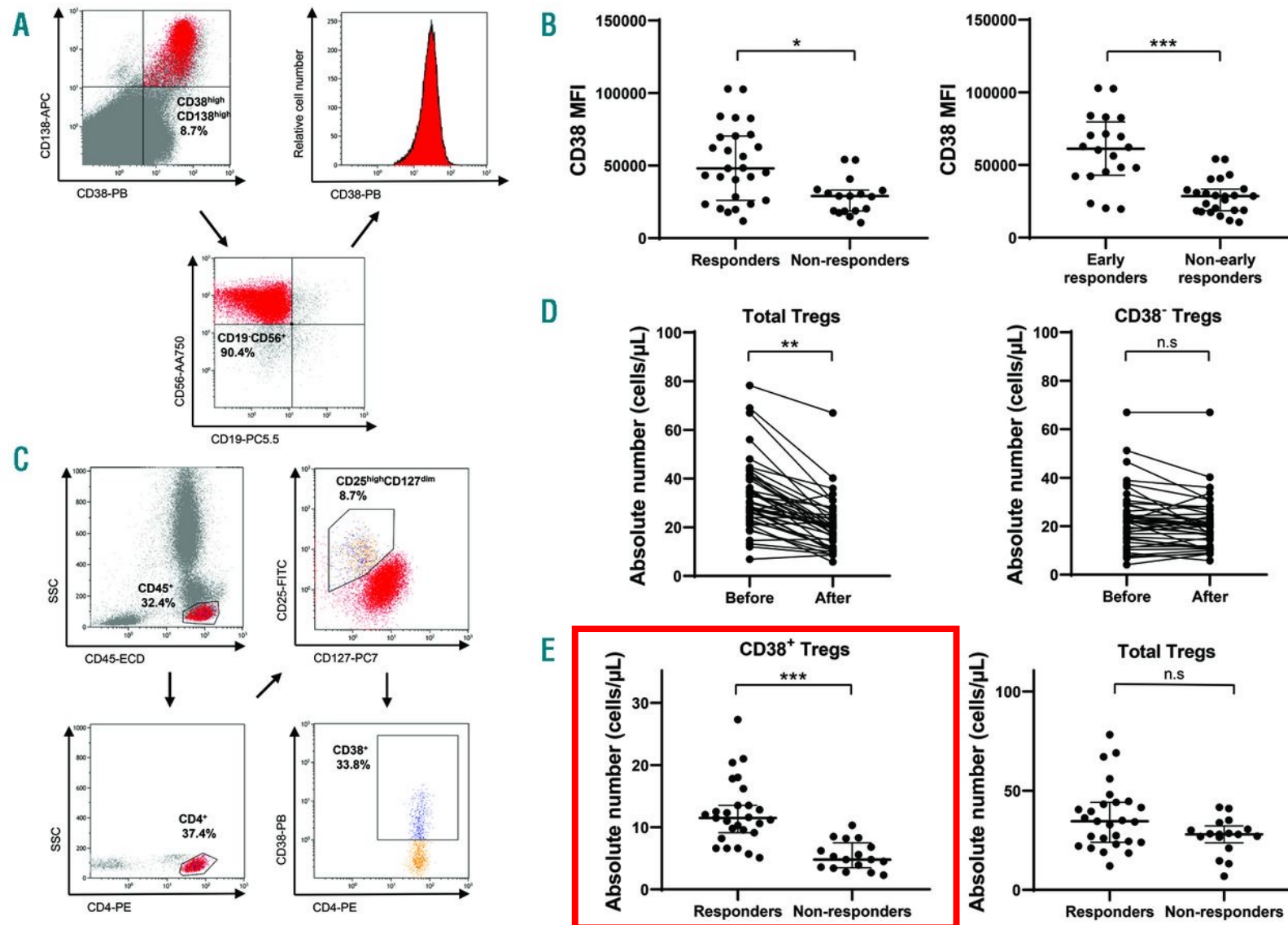


多発性骨髄腫の予後



	0	6	12	18	24	30	36	42	48	54	60	66	72
Number at risk (number censored)													
Lenalidomide and dexamethasone	369 (0)	307 (29)	255 (41)	220 (44)	196 (46)	172 (49)	146 (55)	123 (58)	105 (64)	63 (95)	12 (140)	2 (150)	0 (152)
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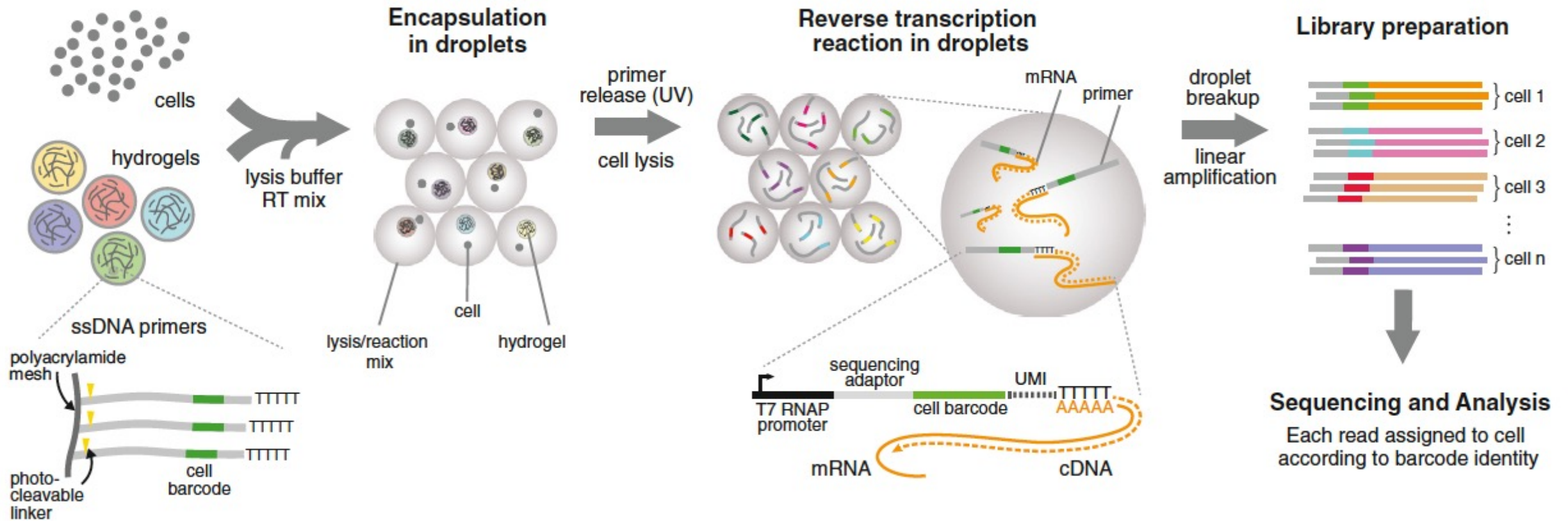
骨髓腫の微小環境と治療反応性

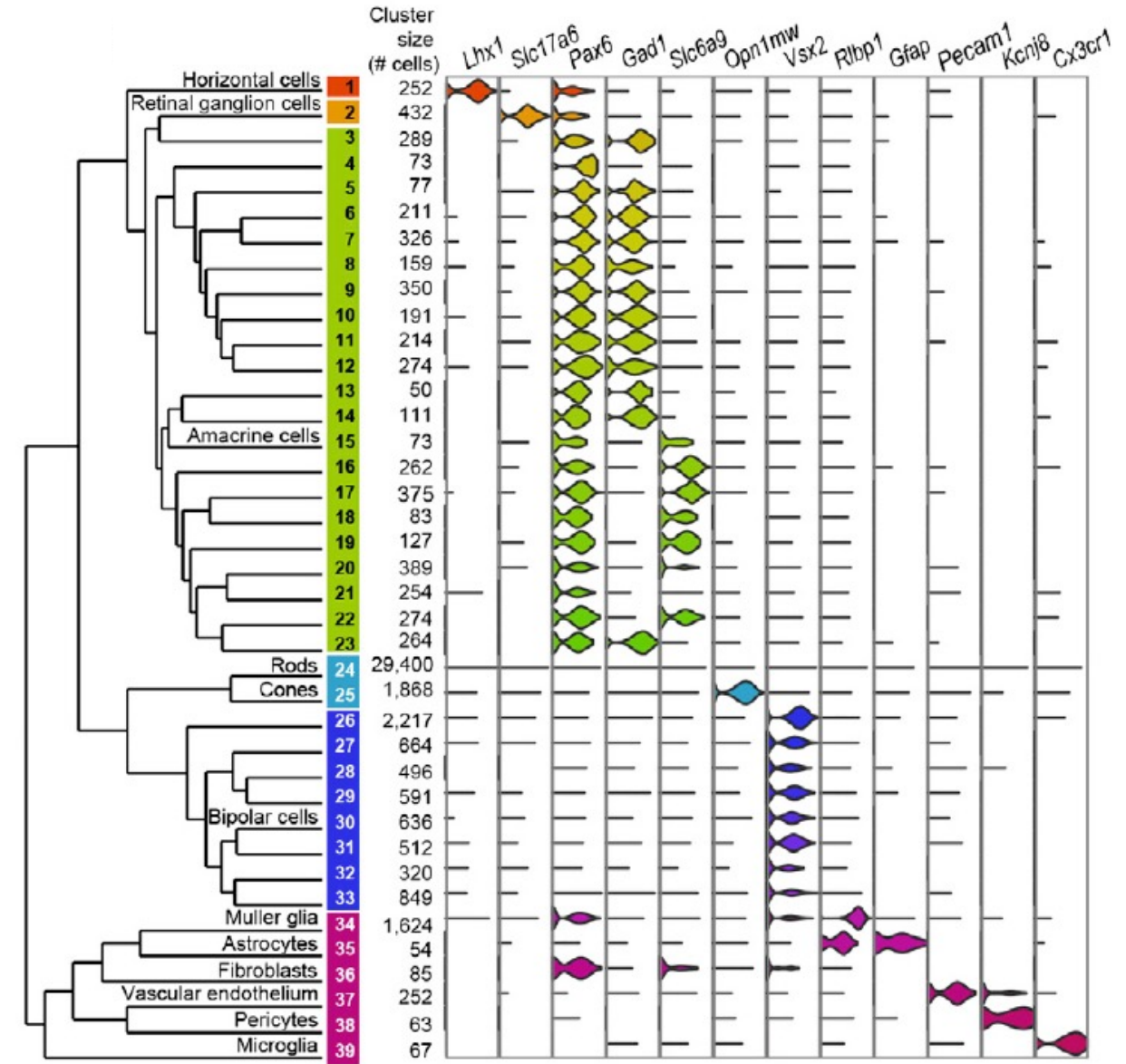
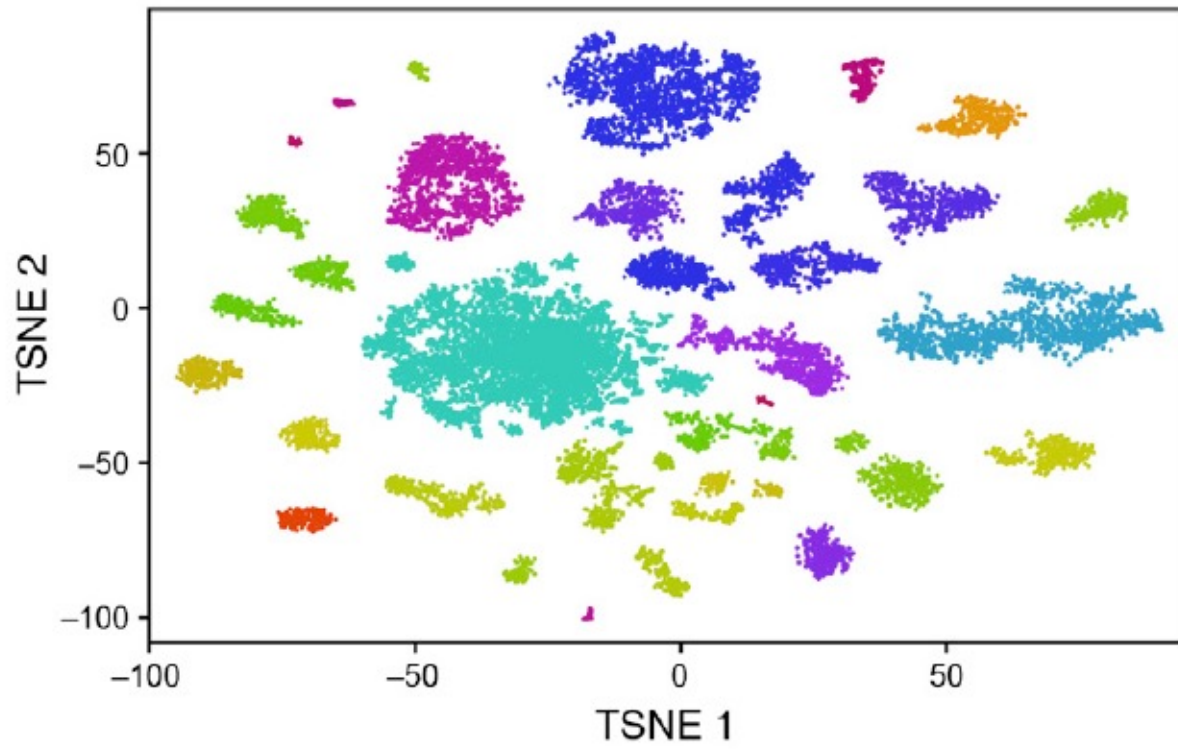


研究目的

- シングルセルRNAデータ解析の標準的次元圧縮手法となっているt-SNEおよびUMAPを用いて治療感受性症例に特異的な発現パターンを示す“レスポンス細胞集団”と治療抵抗性症例に特異的な発現パターンを示す“抵抗性細胞集団”を抽出する

Single cell RNA sequence (scRNA-seq)

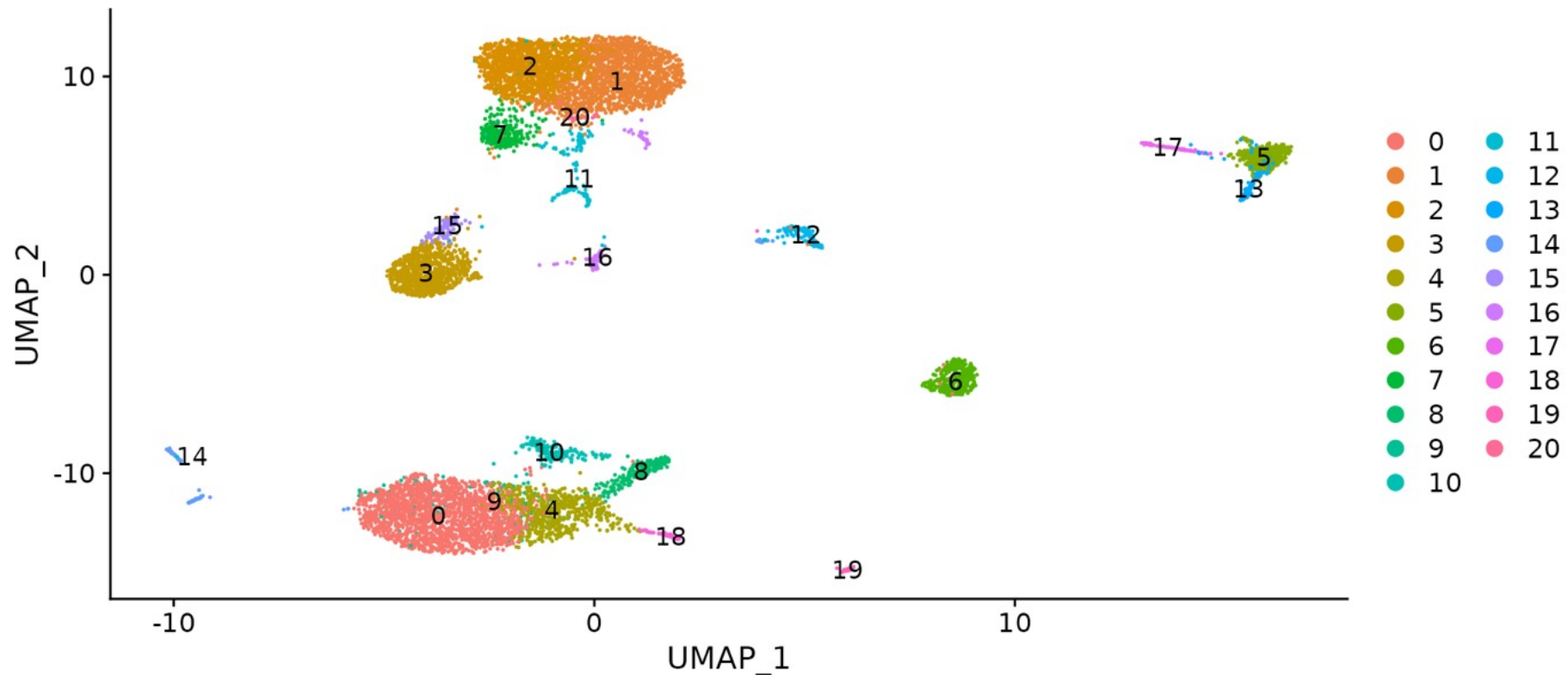




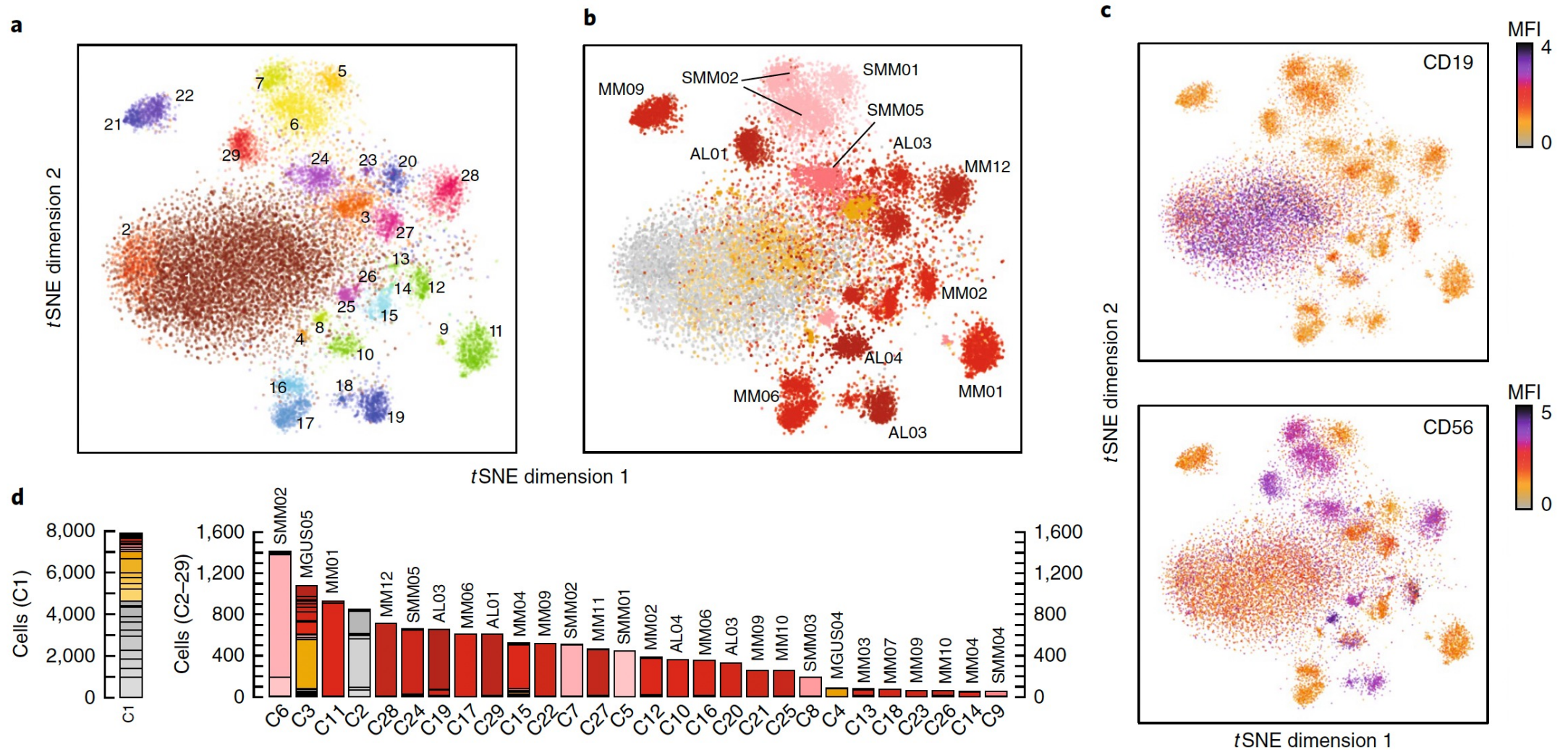
```

# perform visualization and clustering steps
cbmc <- NormalizeData(cbmc)
cbmc <- FindVariableFeatures(cbmc)
cbmc <- ScaleData(cbmc)
cbmc <- RunPCA(cbmc, verbose = FALSE)
cbmc <- FindNeighbors(cbmc, dims = 1:30)
cbmc <- FindClusters(cbmc, resolution = 0.8, verbose = FALSE)
cbmc <- RunUMAP(cbmc, dims = 1:30)
DimPlot(cbmc, label = TRUE)

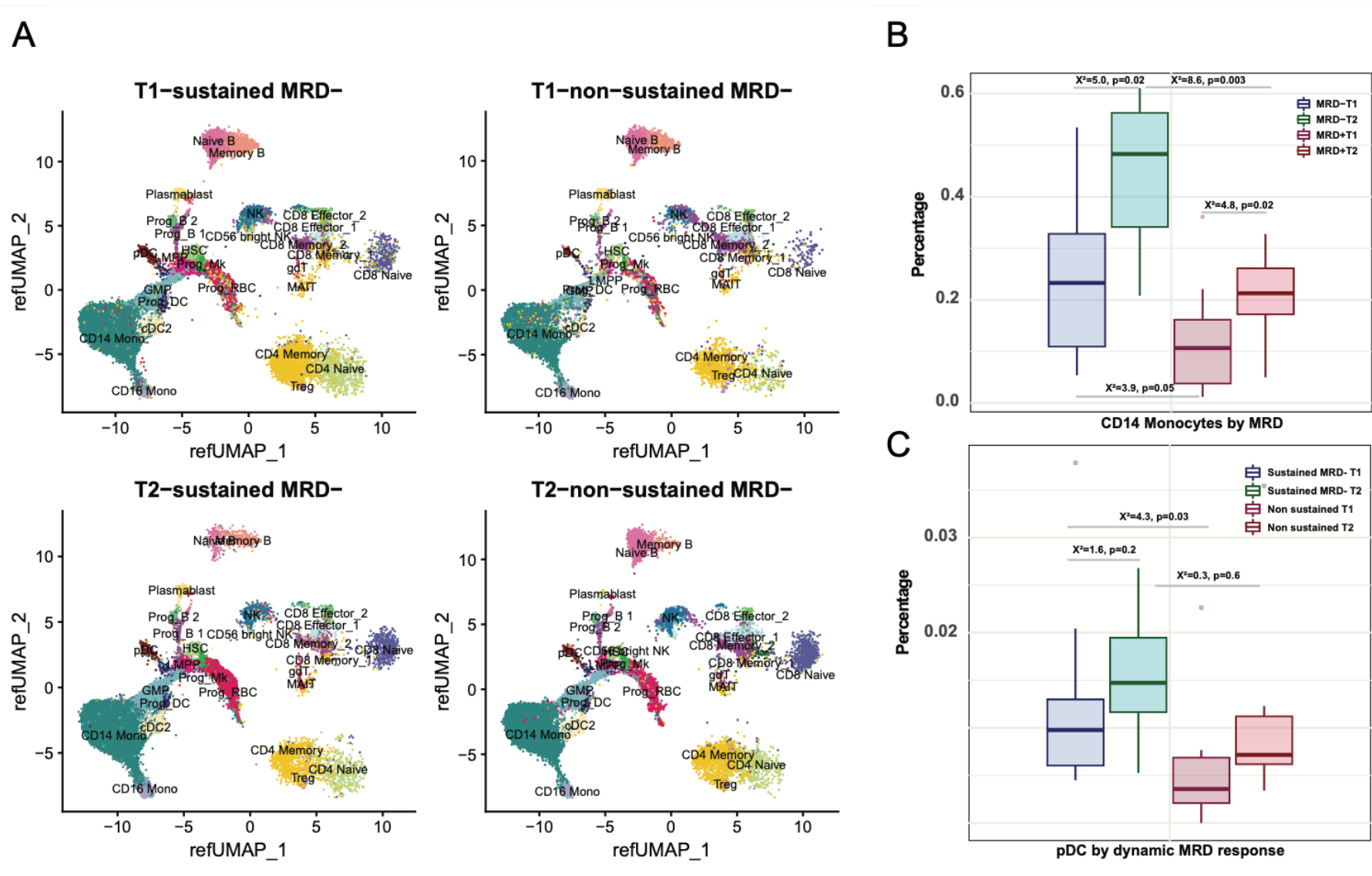
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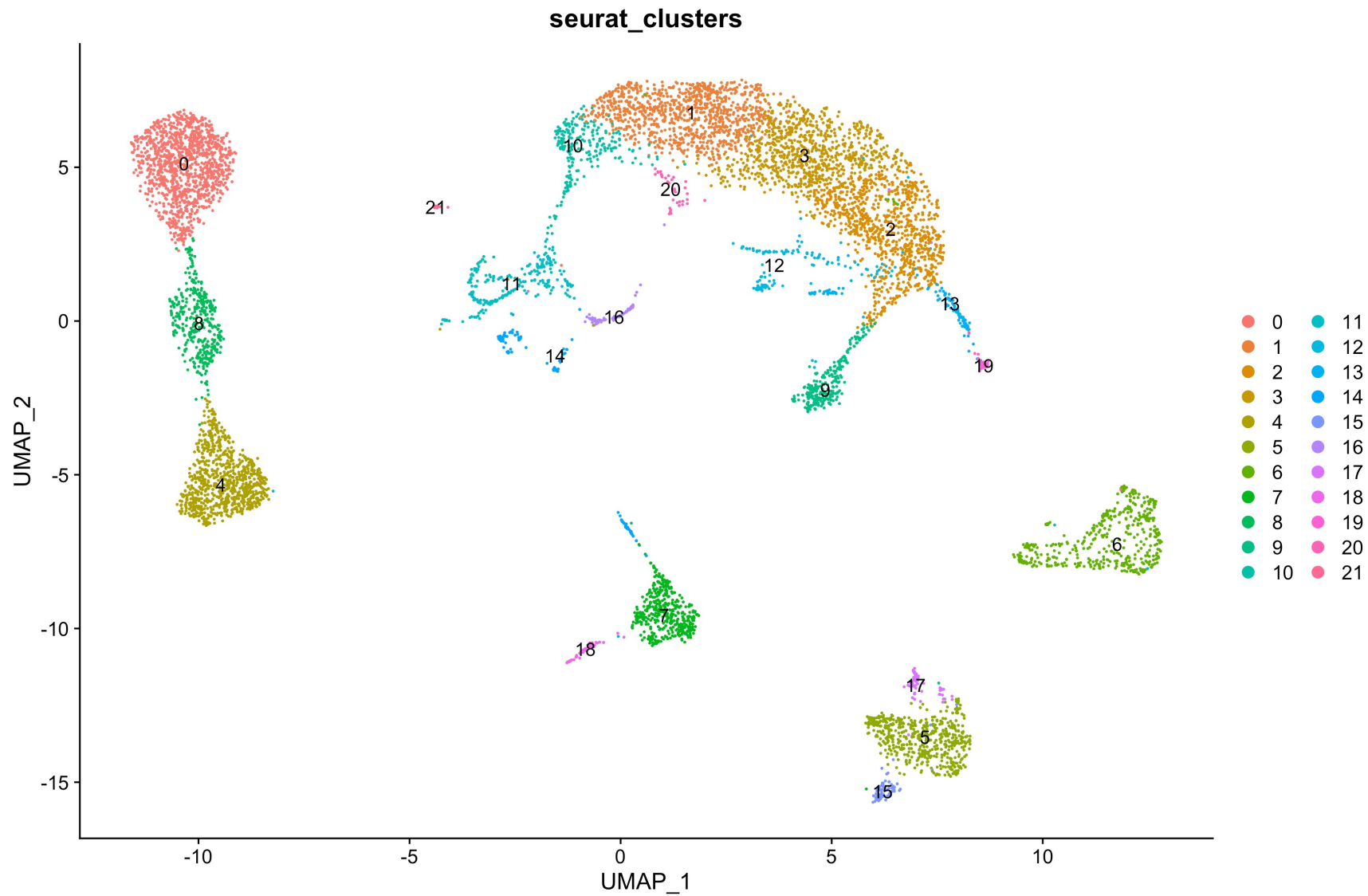
多発性骨髄腫のシングルセル解析

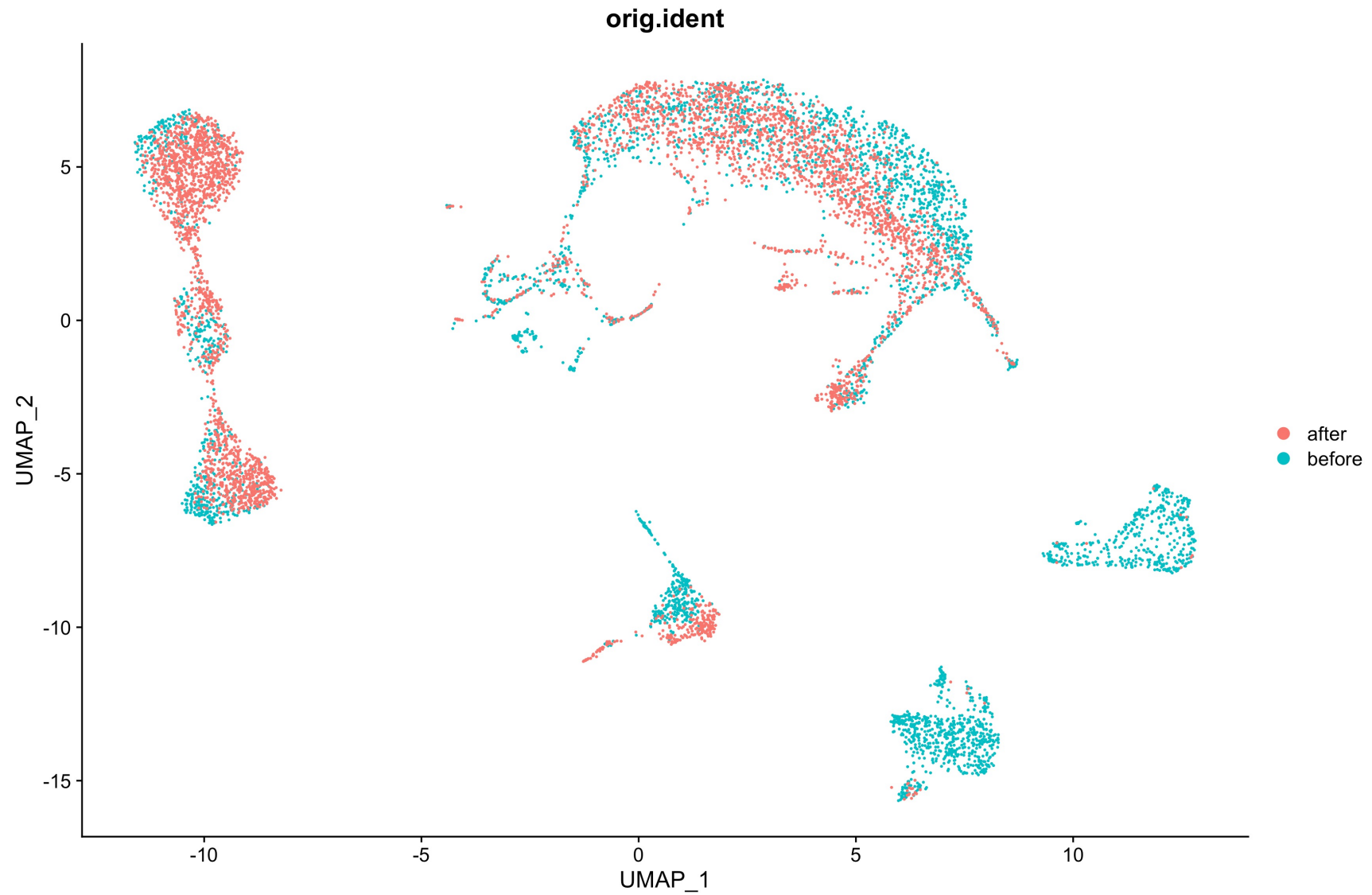


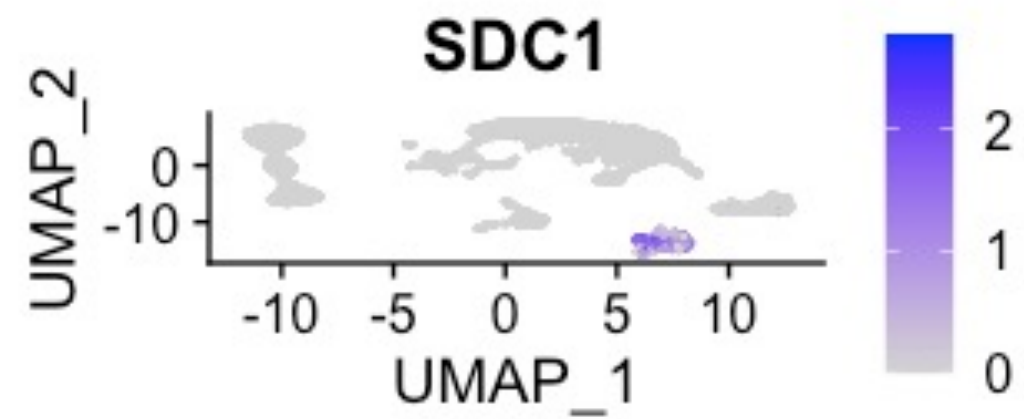
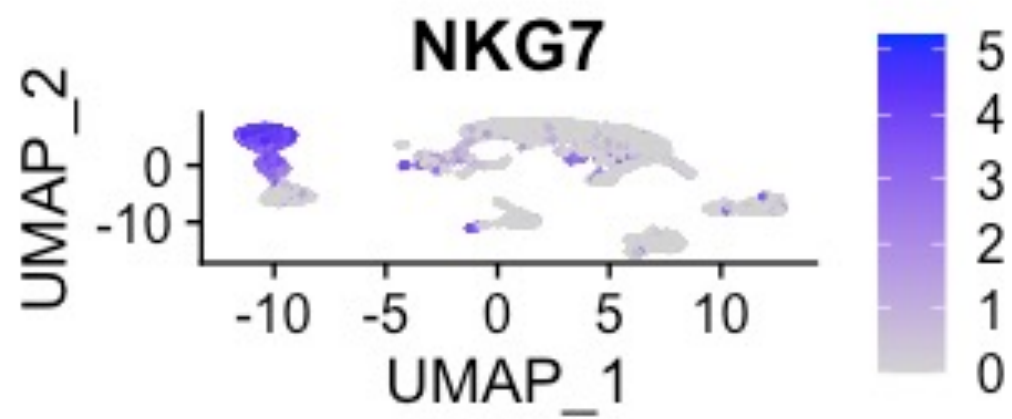
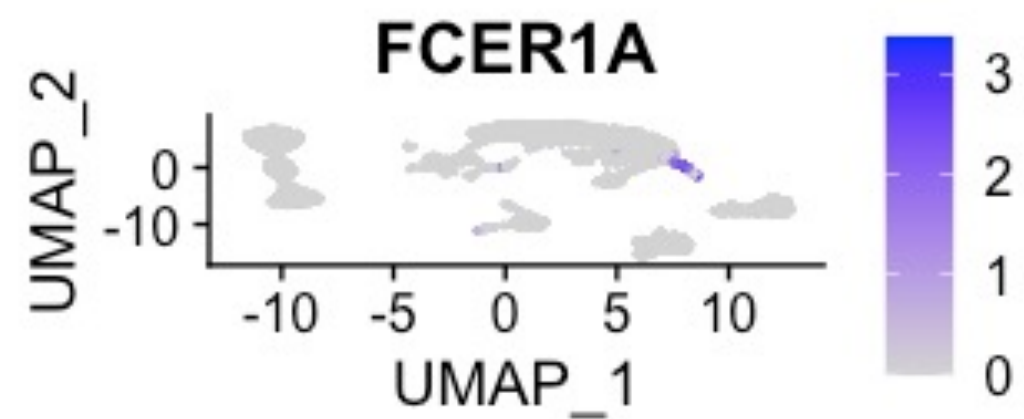
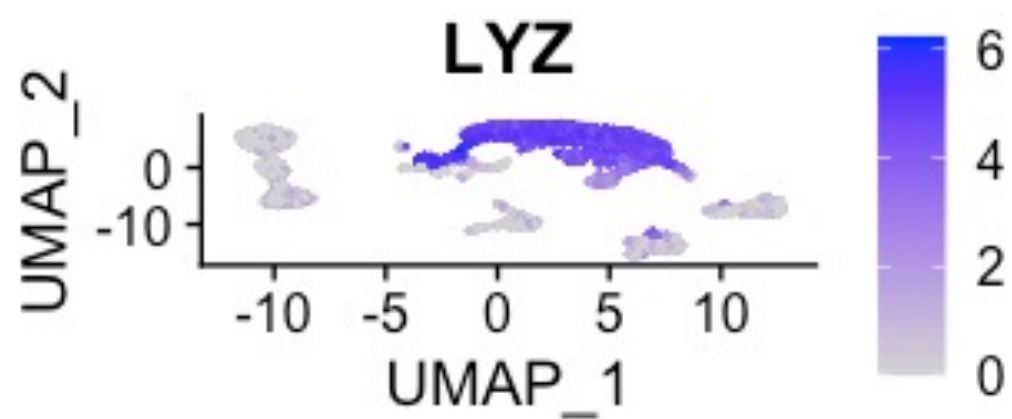
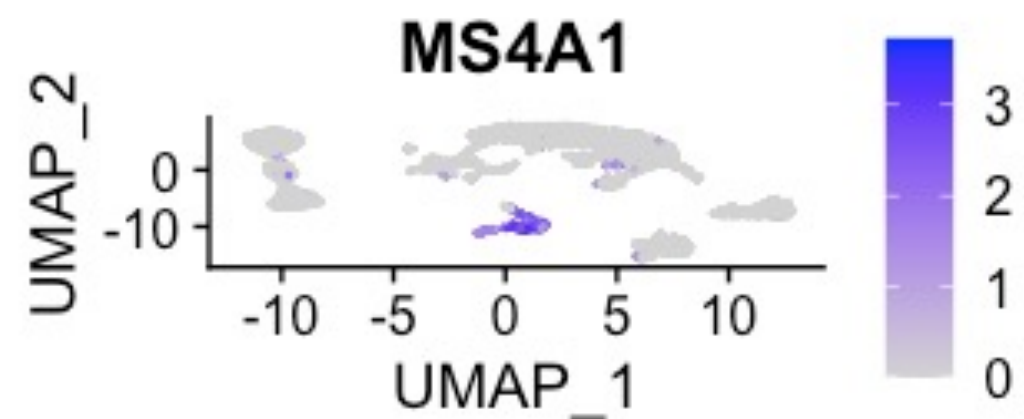
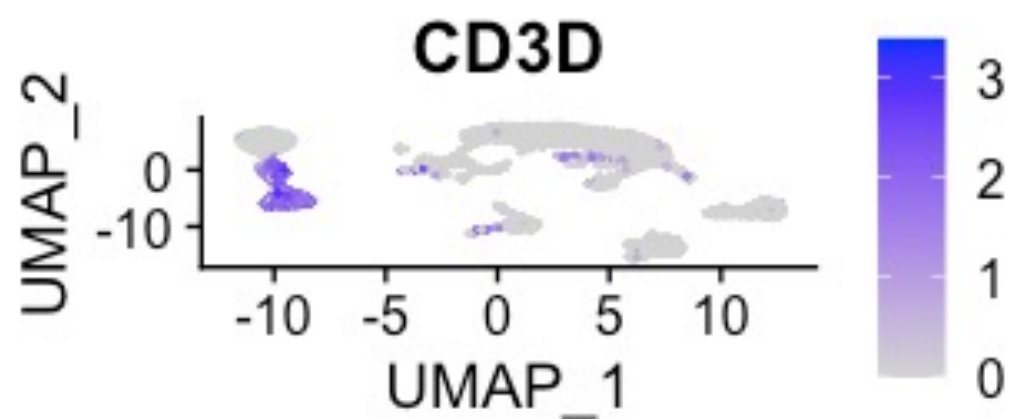
骨髓腫微小環境のシングルセル解析

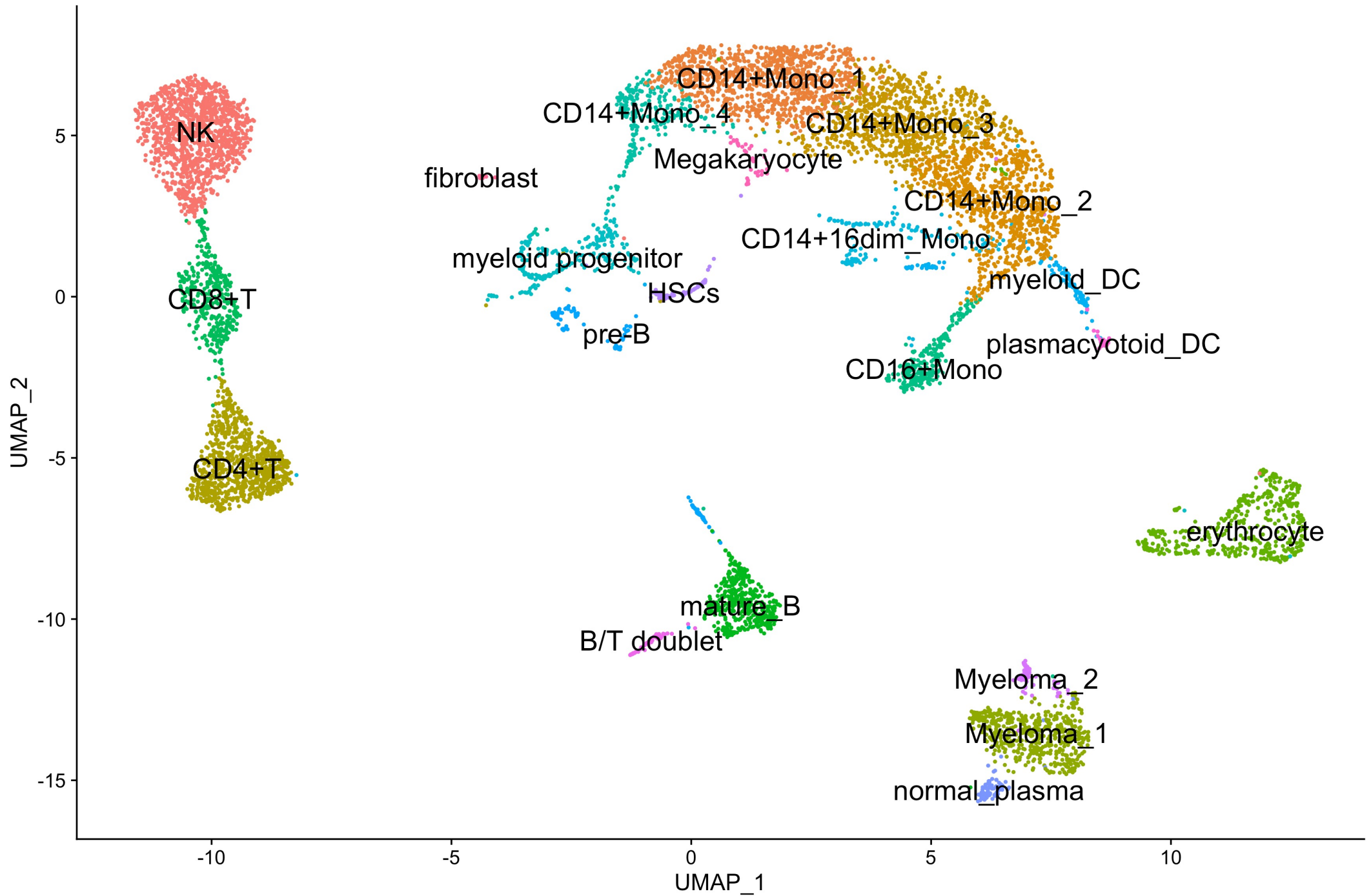


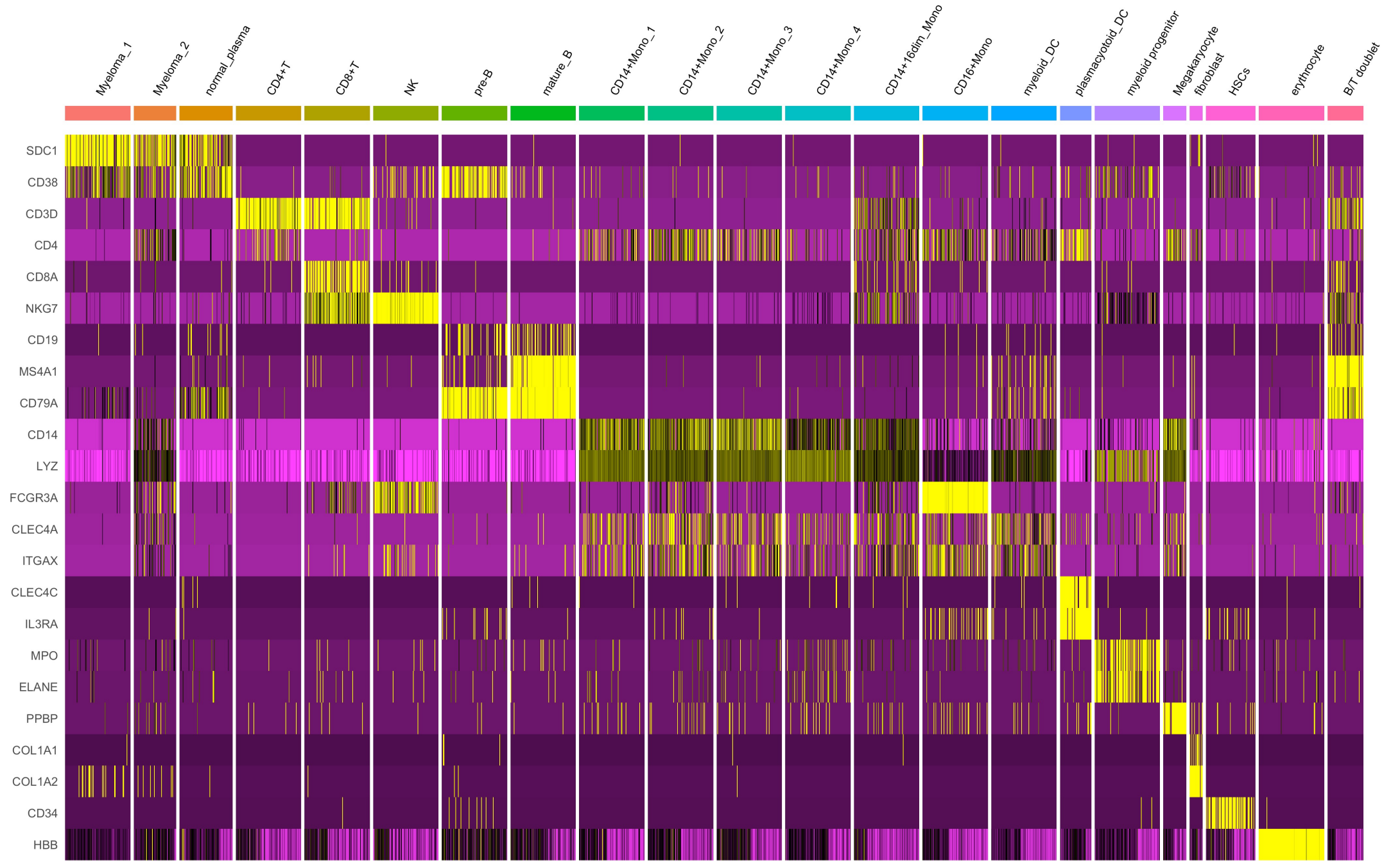
結果

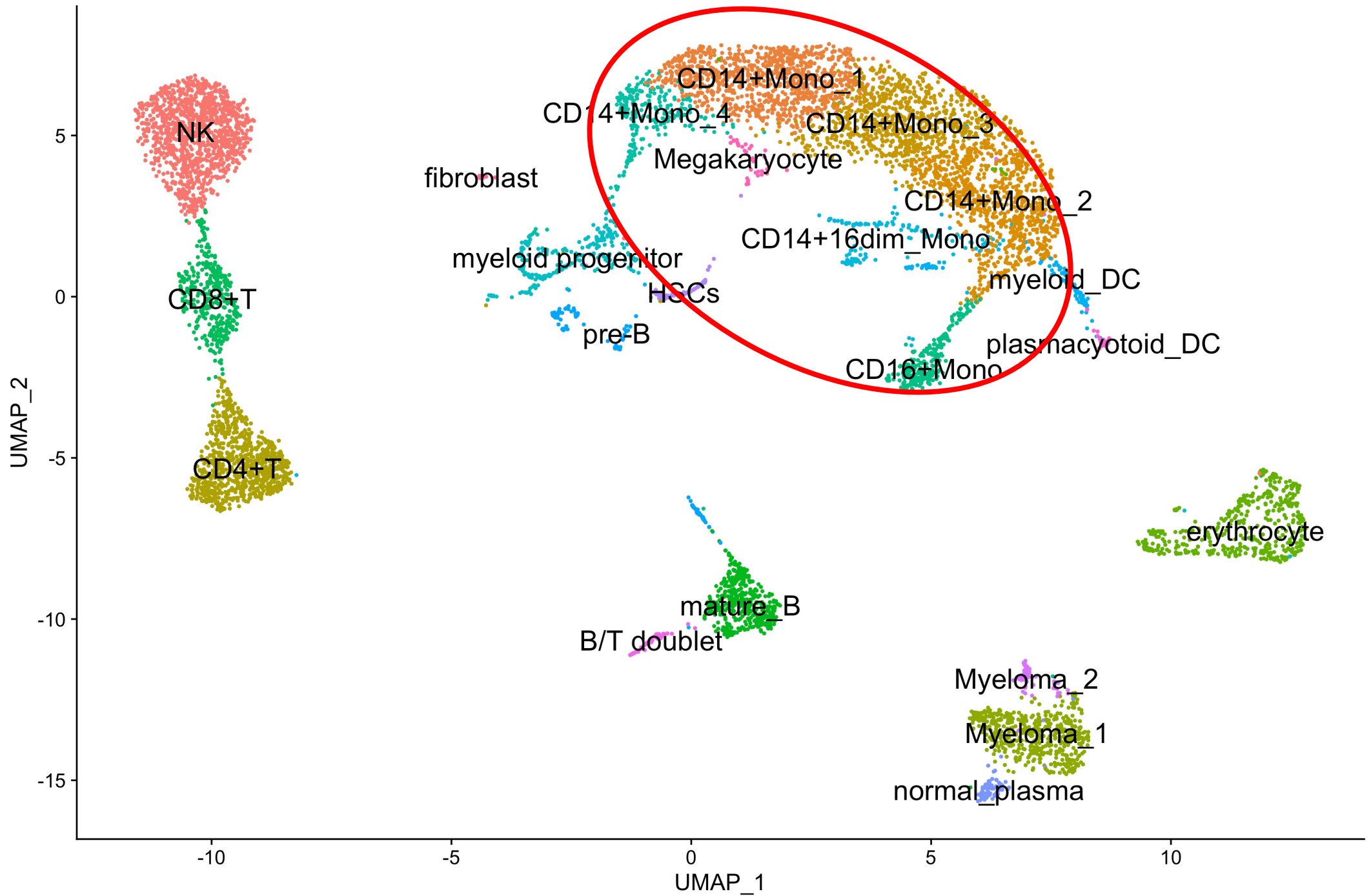


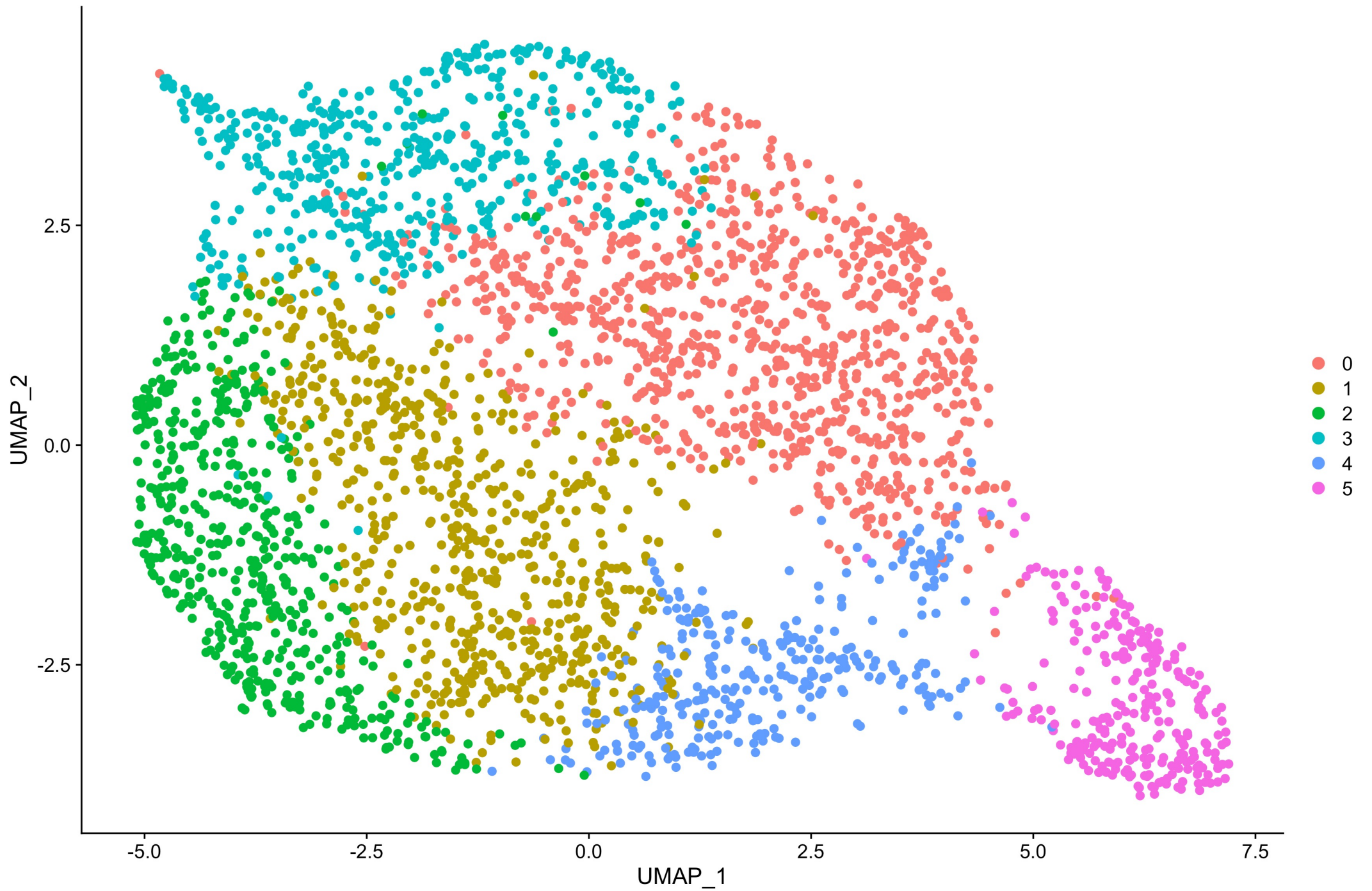












0

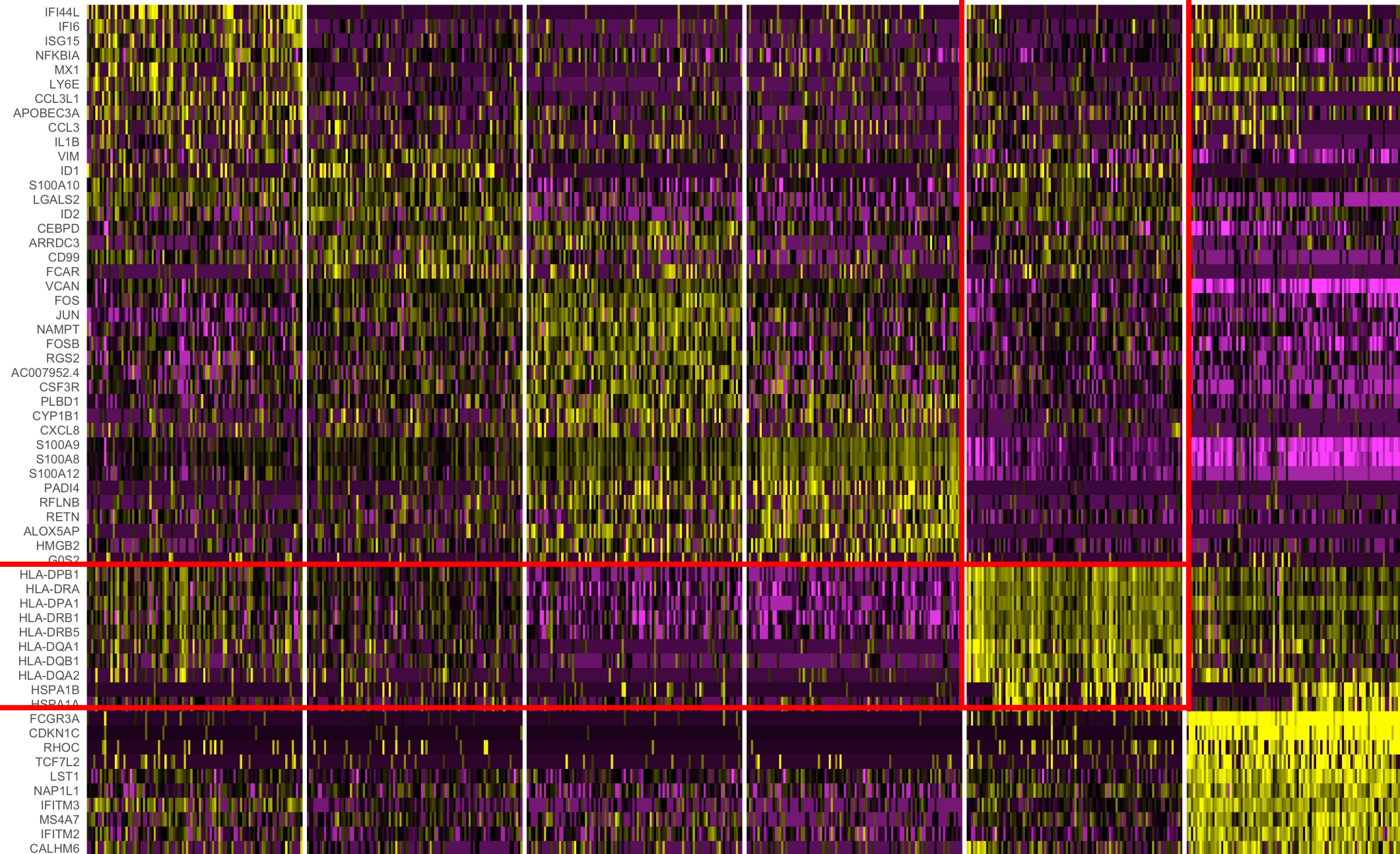
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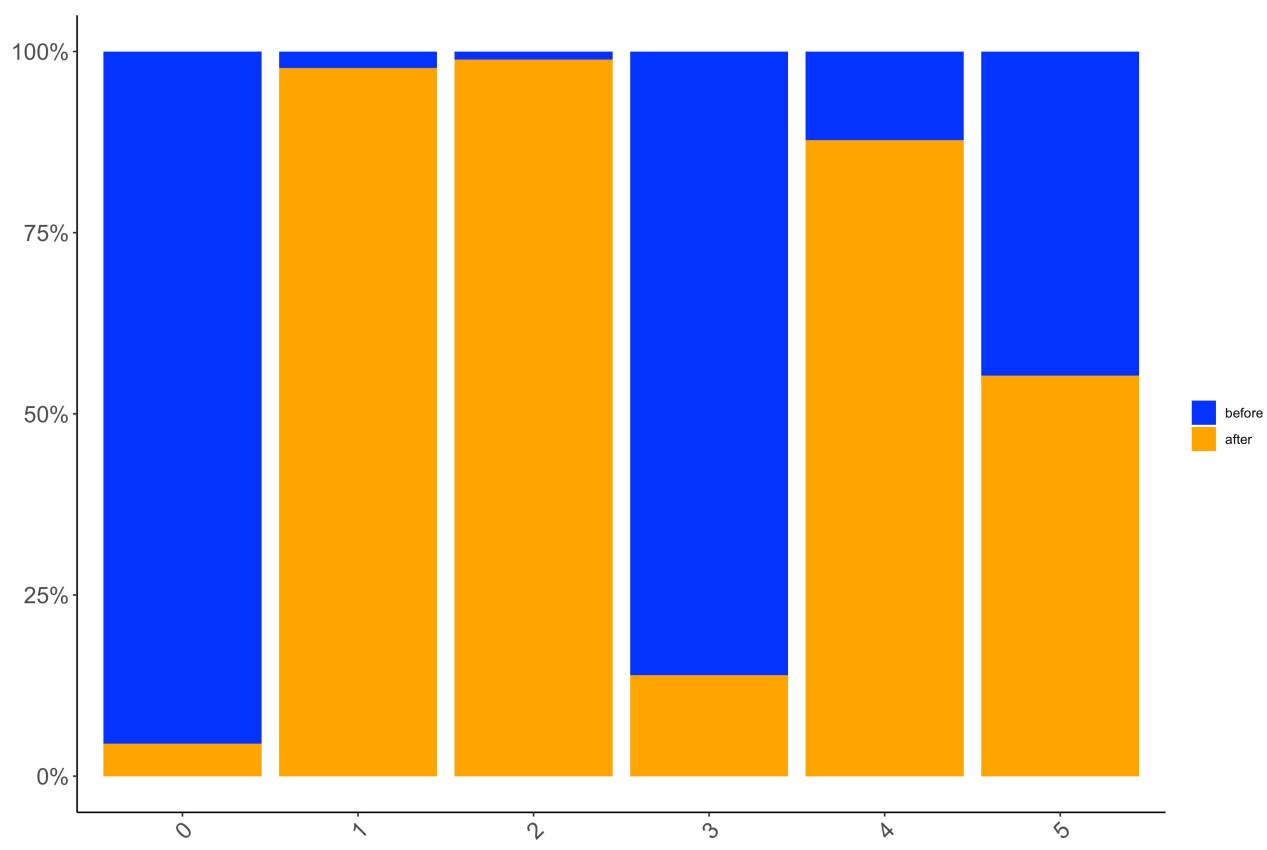
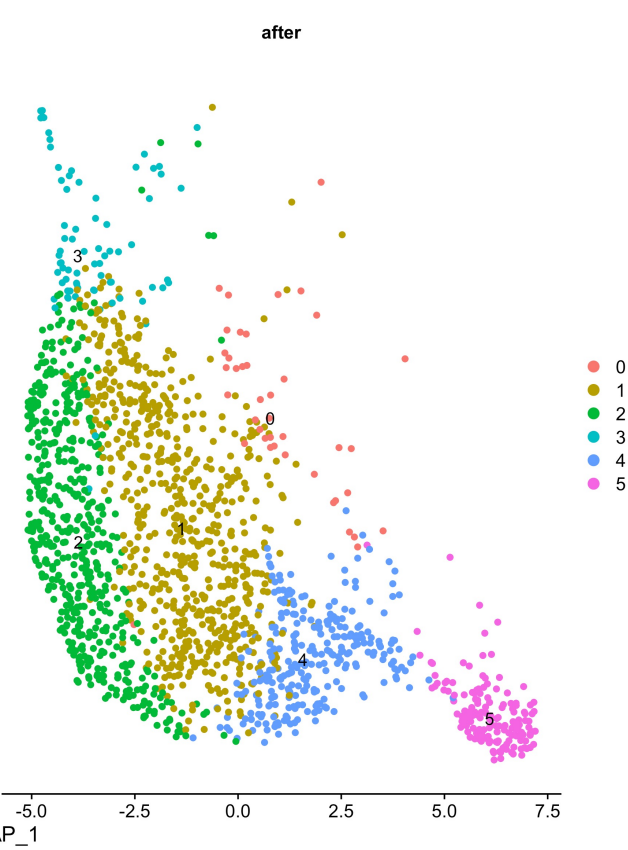
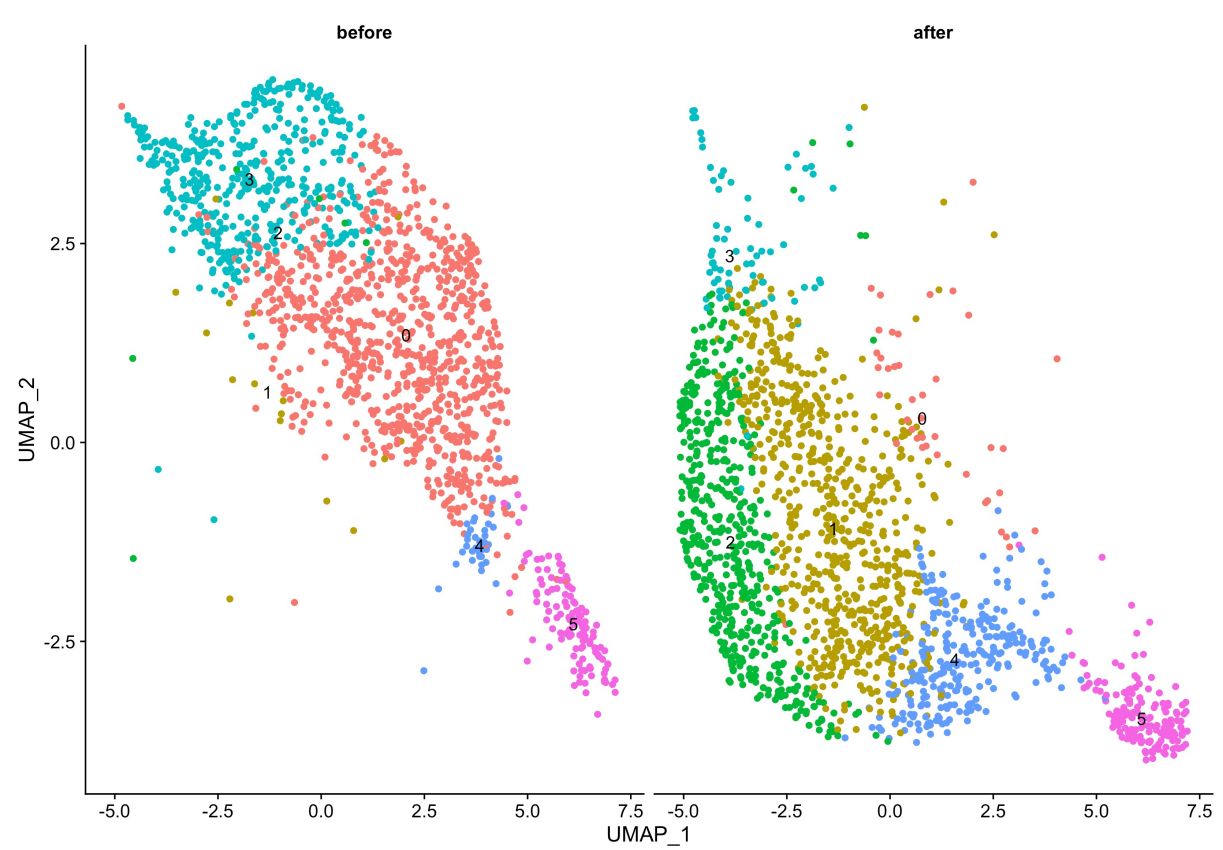
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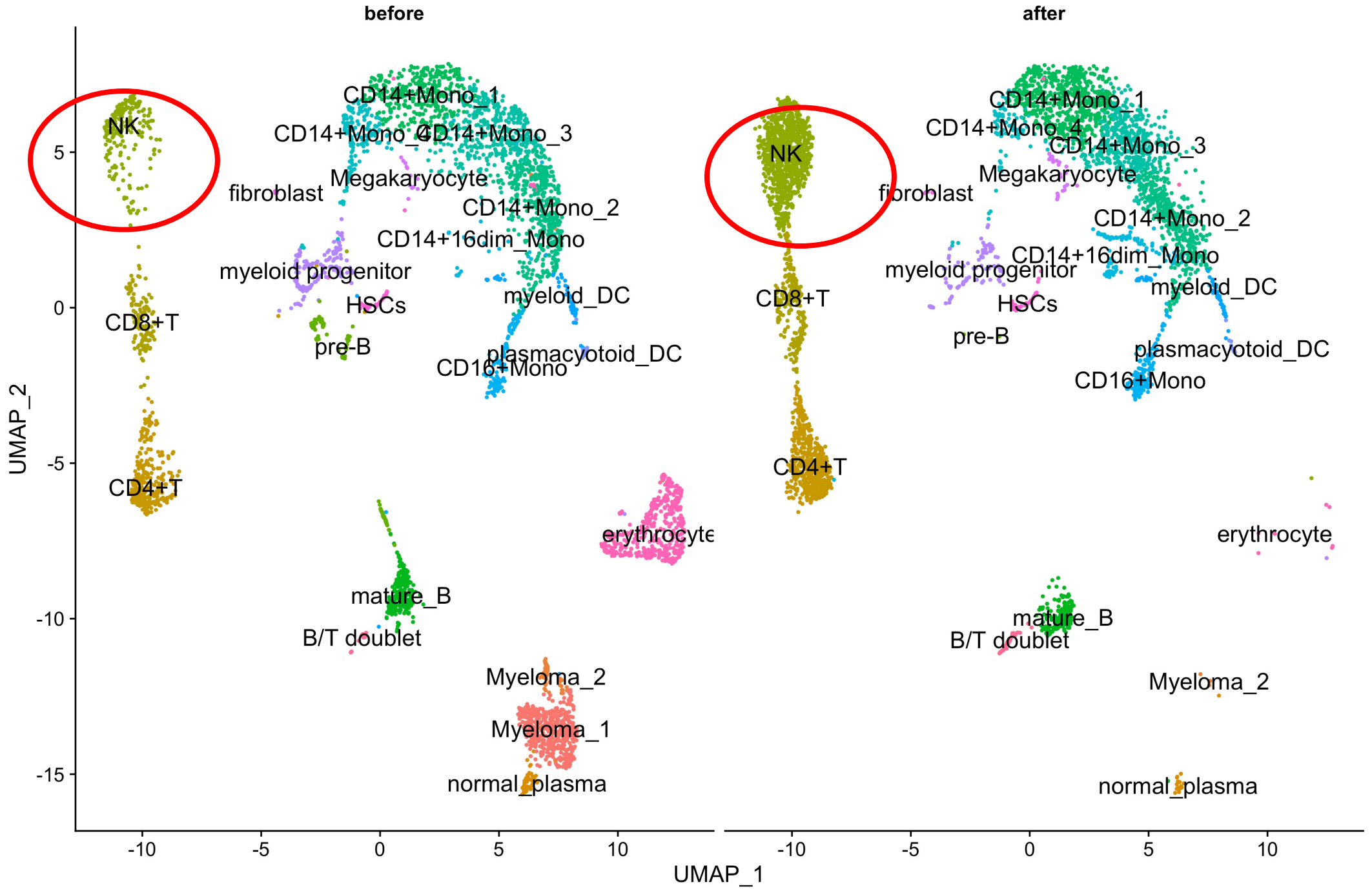
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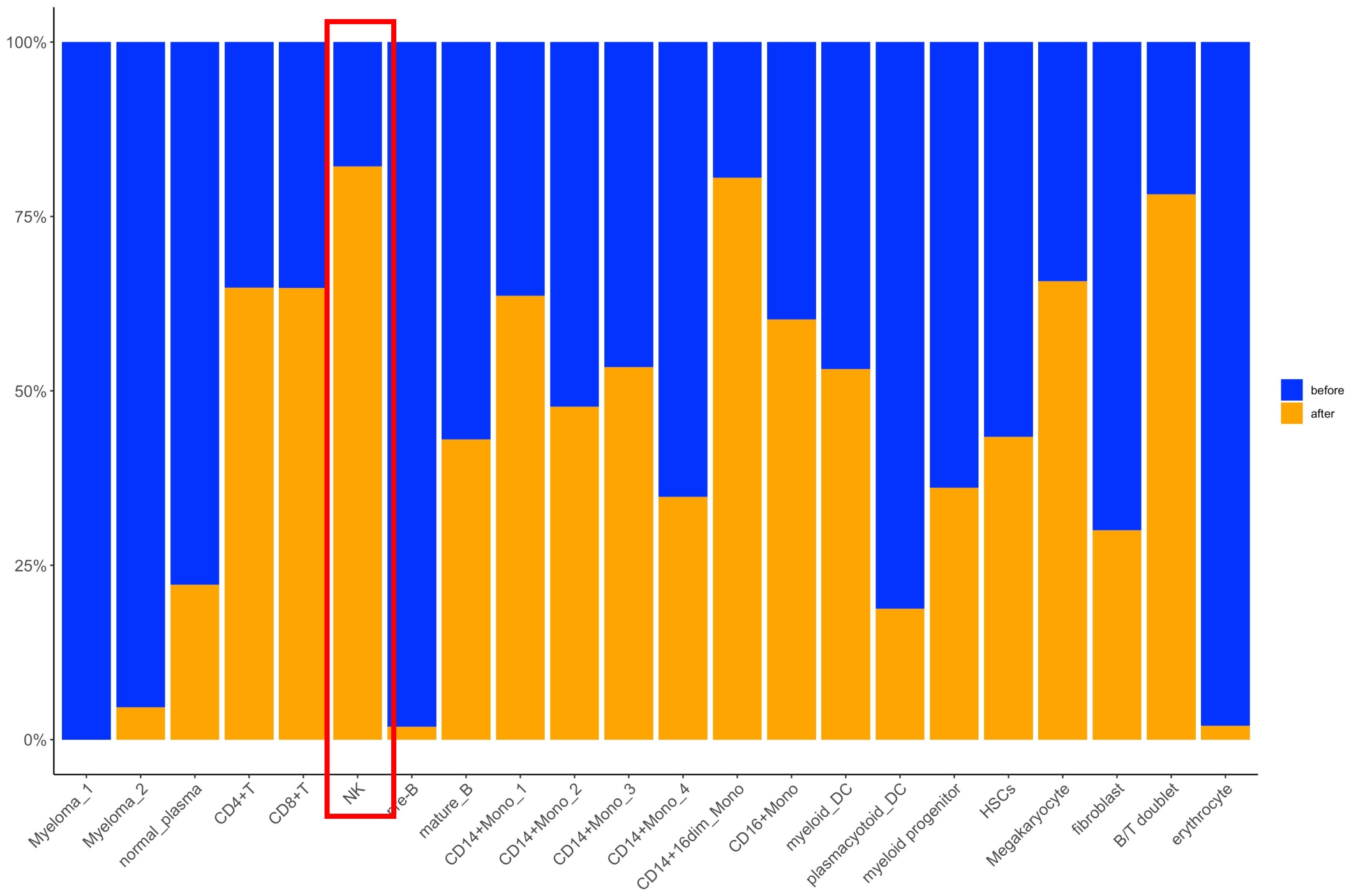
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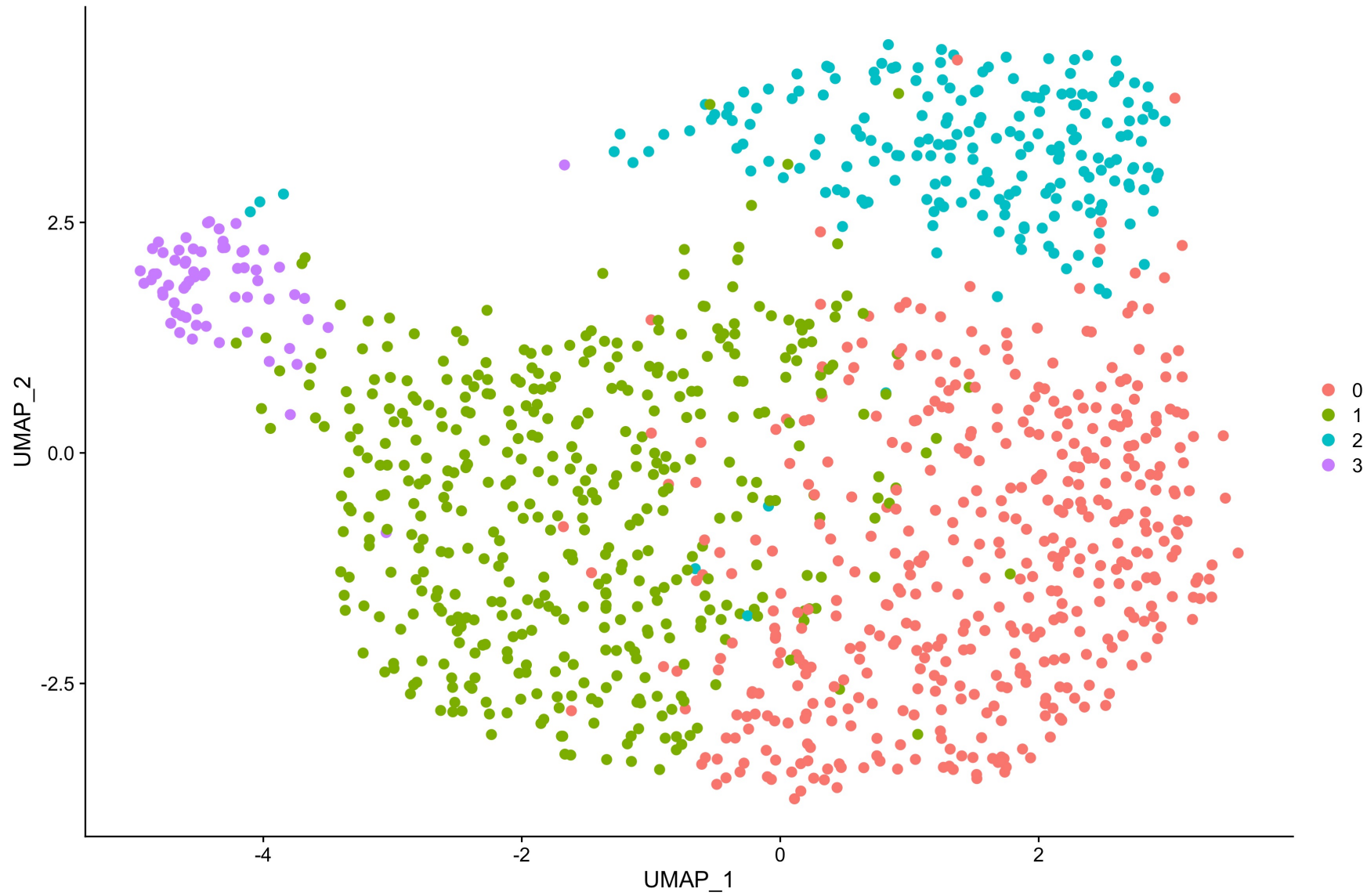
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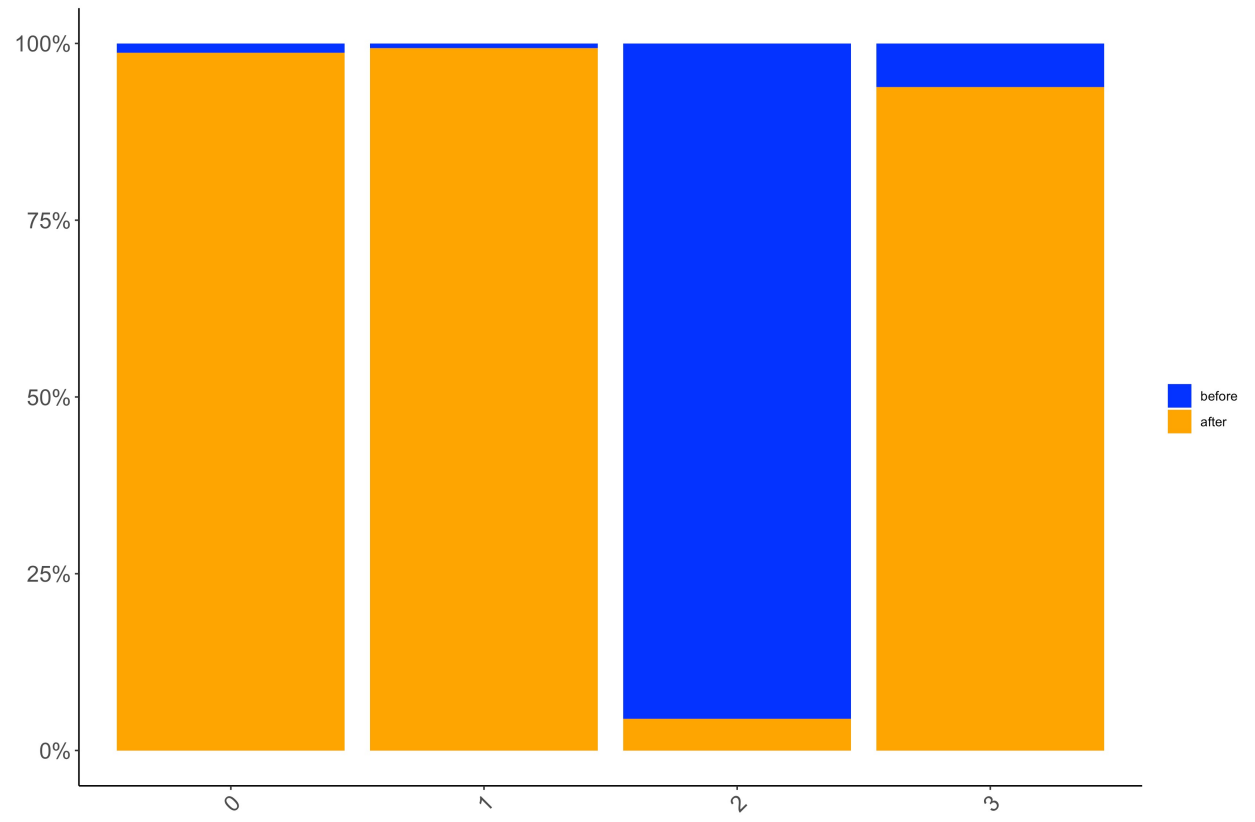
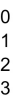
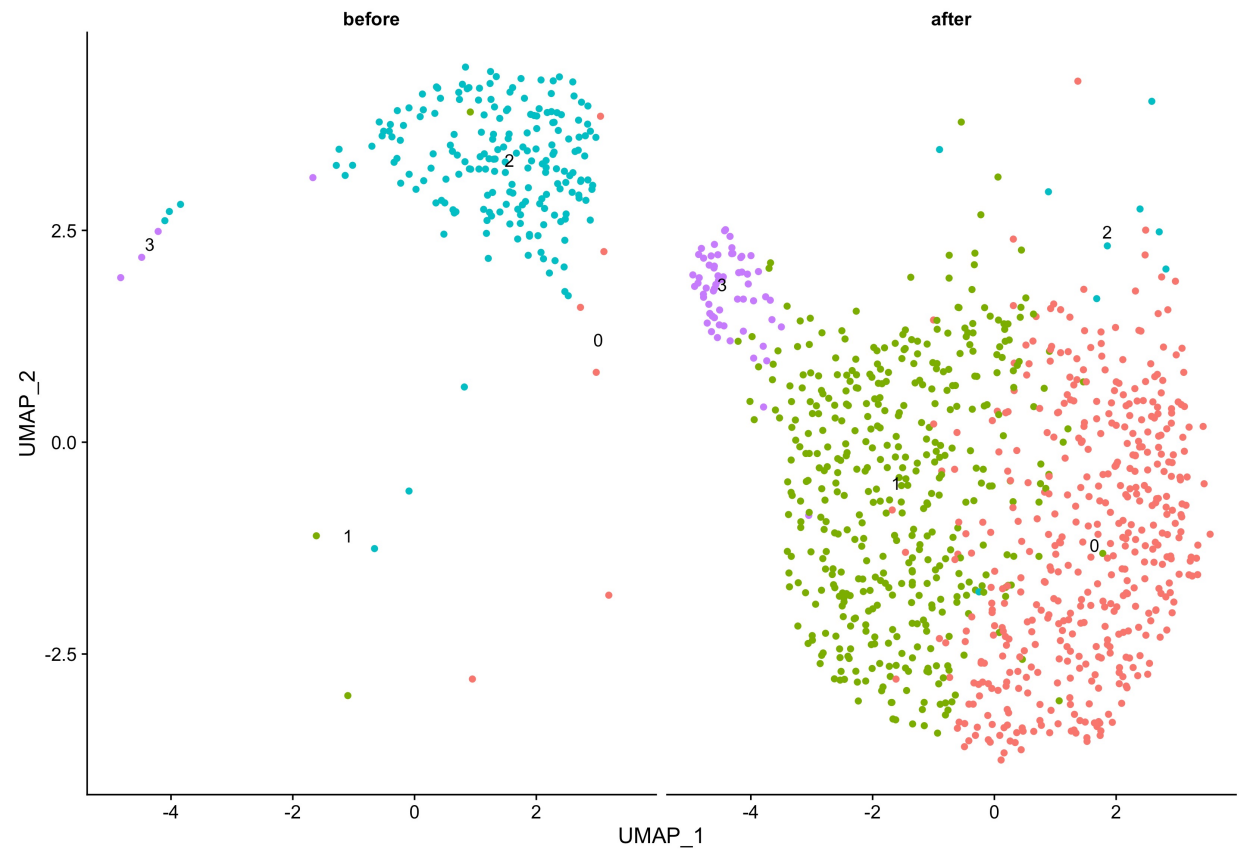










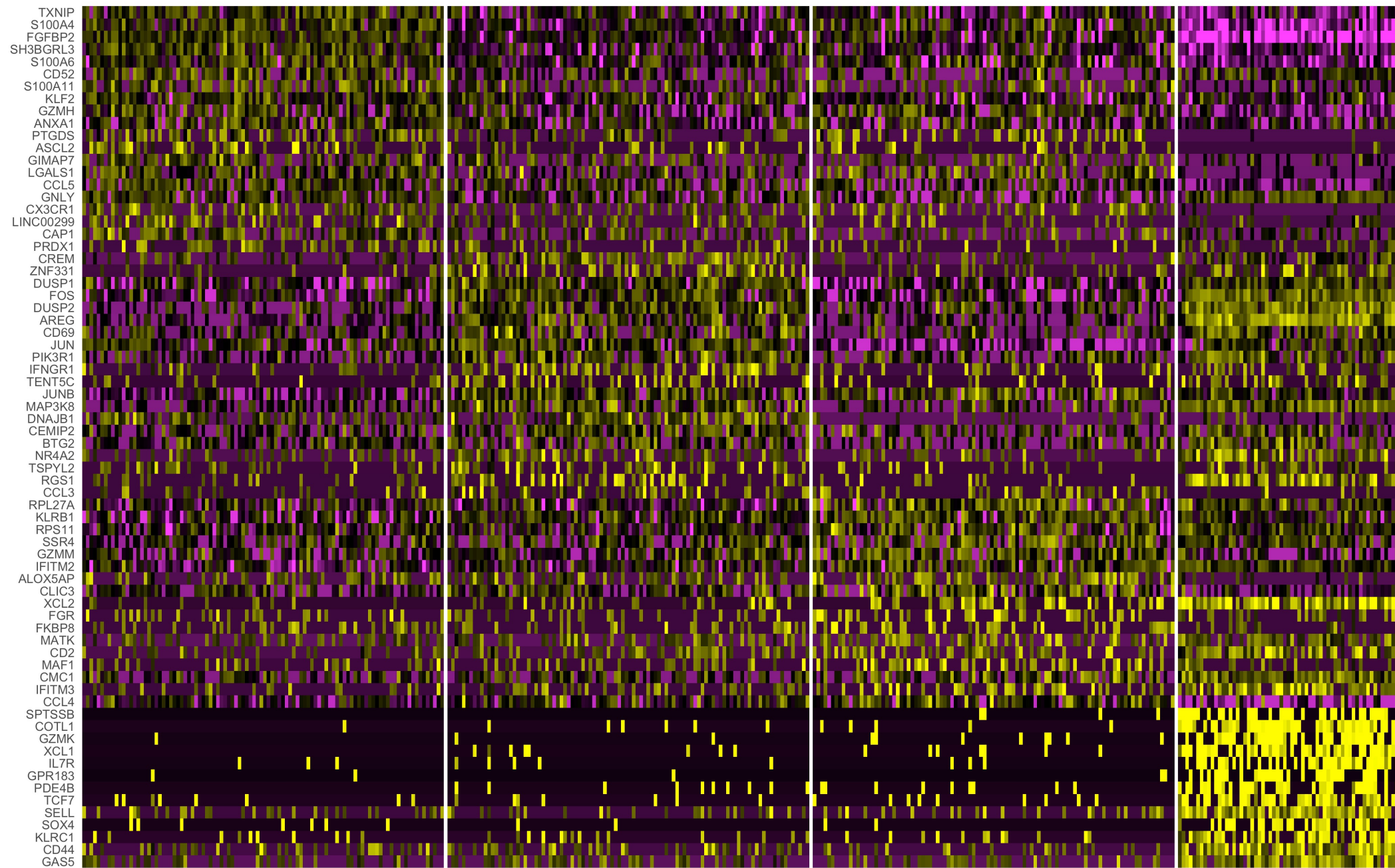


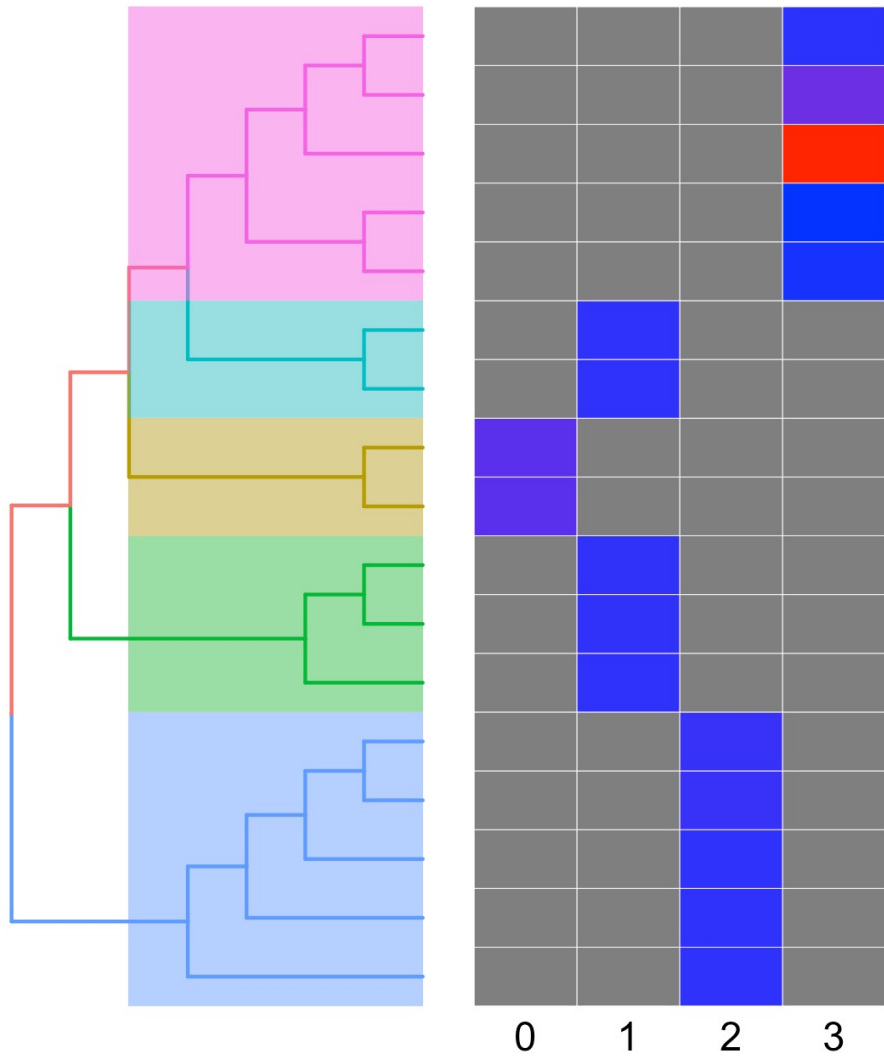
0

1

2

3





- mRNA 5'-UTR binding
- rRNA binding
- structural constituent of ribosome
- T cell receptor binding
- MHC protein complex binding
- R-SMAD binding
- DNA-binding transcription activator activity, RNA polymerase II-specific
- S100 protein binding
- calcium-dependent protein binding
- MAP kinase tyrosine/serine/threonine phosphatase activity
- protein tyrosine/threonine phosphatase activity
- MAP kinase phosphatase activity
- oxygen carrier activity
- haptoglobin binding
- oxygen binding
- peroxidase activity
- oxidoreductase activity, acting on peroxide as acceptor

今後の方向

- 多発性骨髄腫の臨床検体解析数を増やす。
- 治療感受性に関わる遺伝子発現パターンを抽出する。