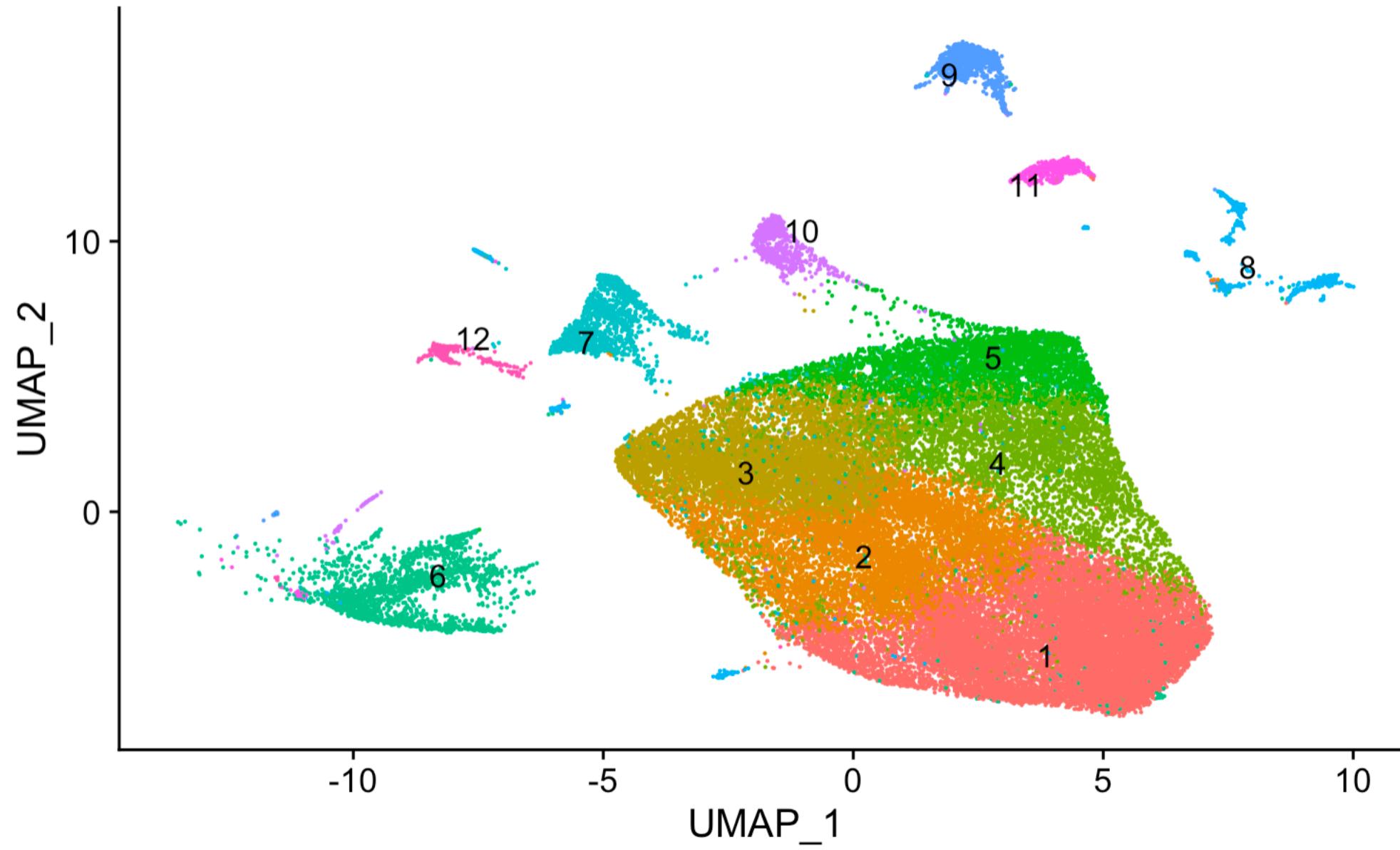
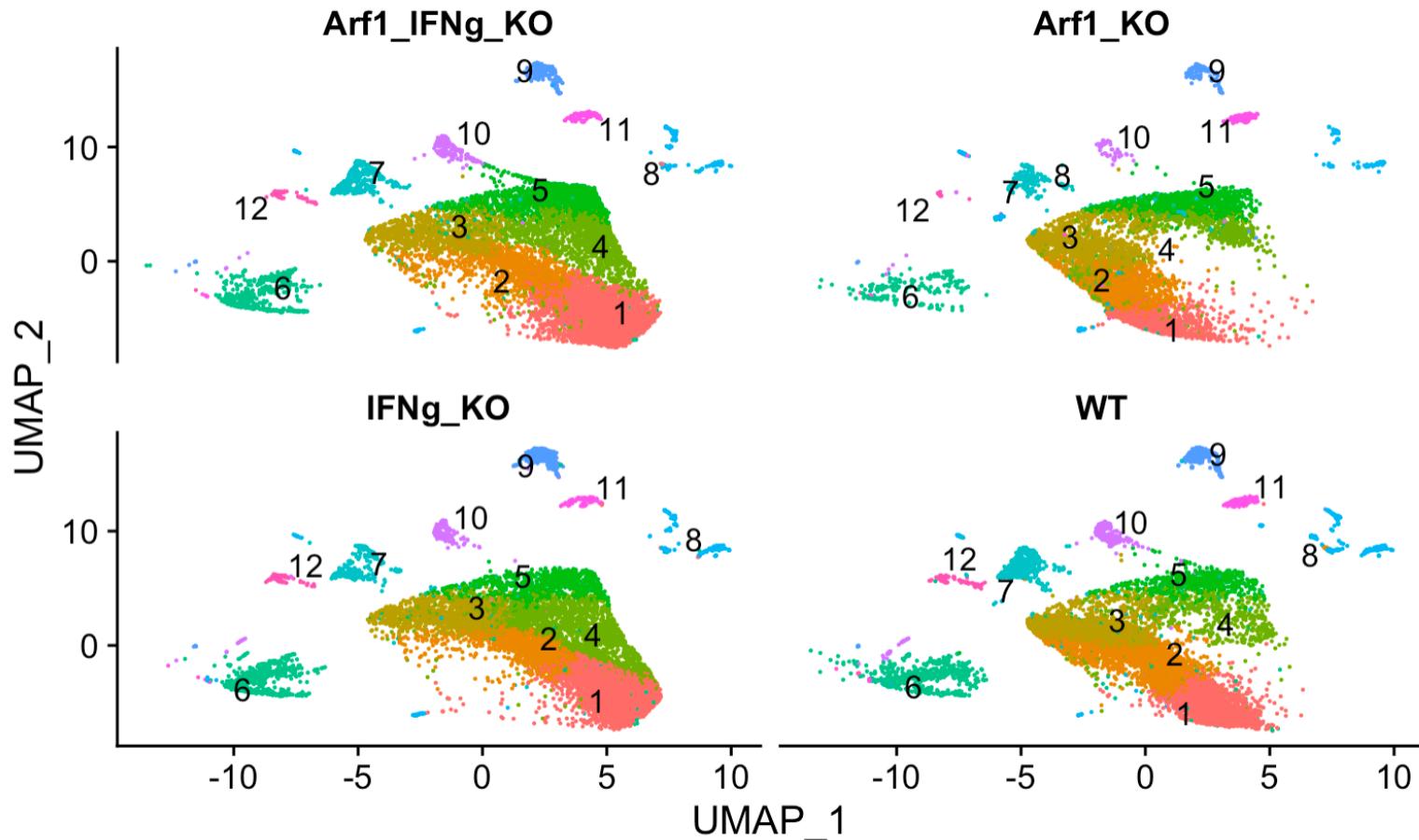


Ccbr1045 update

2020.3.19



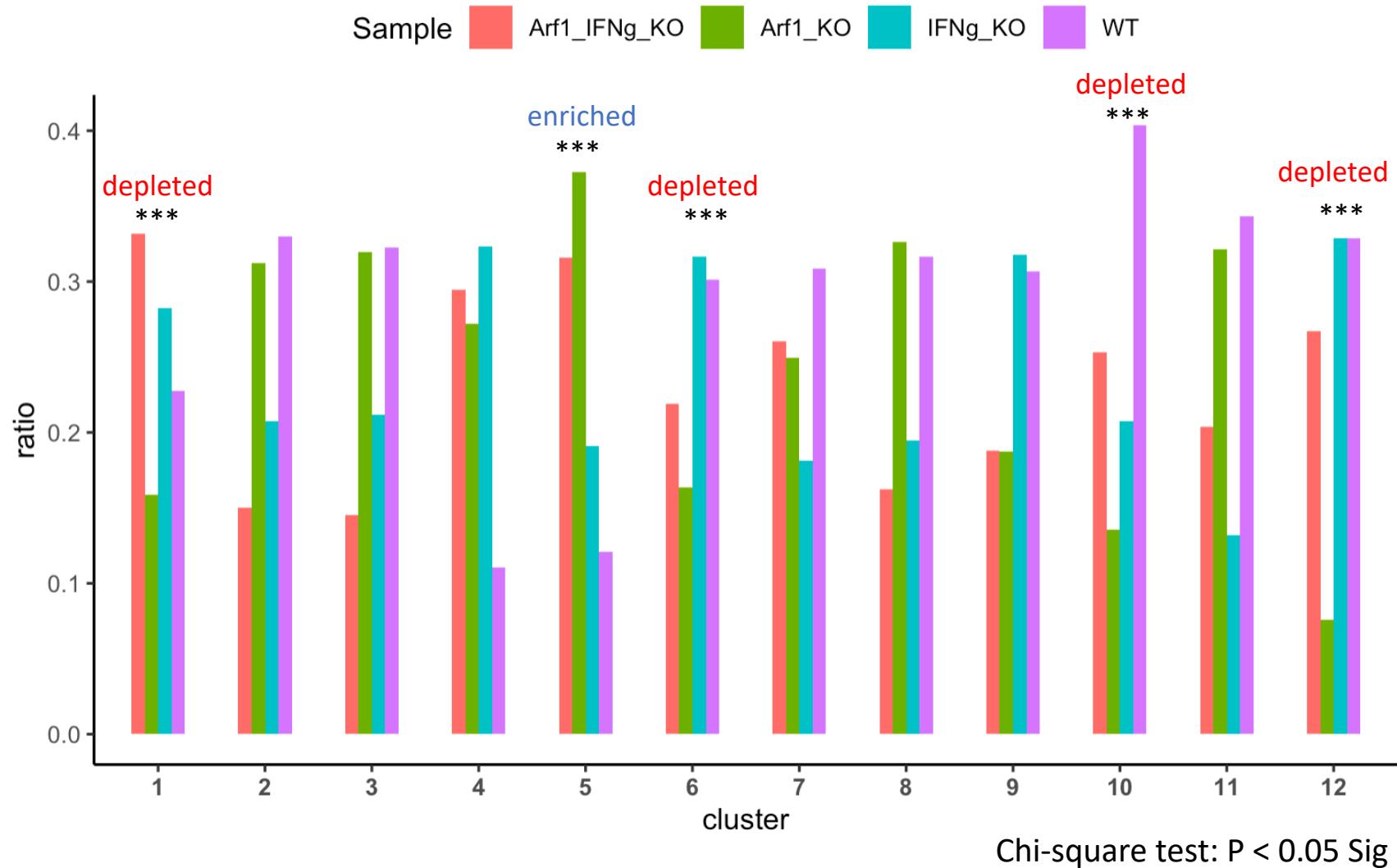
Only microglia cells – reshaped with 0.3 resolution into 12 microglia subclusters



Number of microglial cells for each cluster in each sample

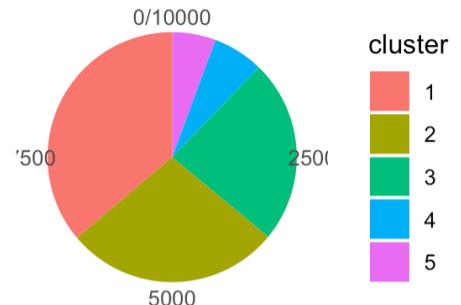
	Arf1_IFNg_KO	Arf1_KO	IFNg_KO	WT
1	4165	1990	3544	2855
2	1001	2080	1380	2198
3	844	1856	1230	1874
4	1392	1284	1527	522
5	1171	1380	707	447
6	412	308	596	567
7	317	304	221	376
8	169	340	203	330
9	171	170	289	279
10	172	92	141	274
11	111	175	72	187
12	74	21	91	91

Arf1_KO is enriched in Cluster 5



Relative proportion cluster

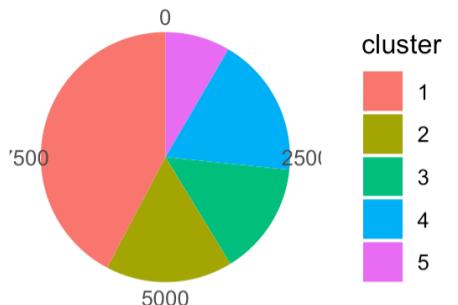
WT



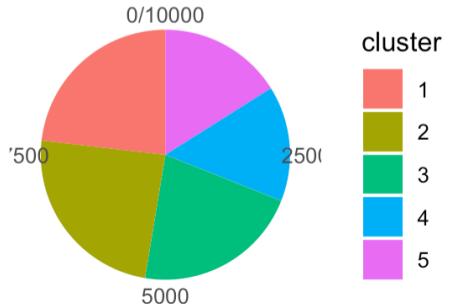
Arf1_IFNg_KO



IFNg_KO

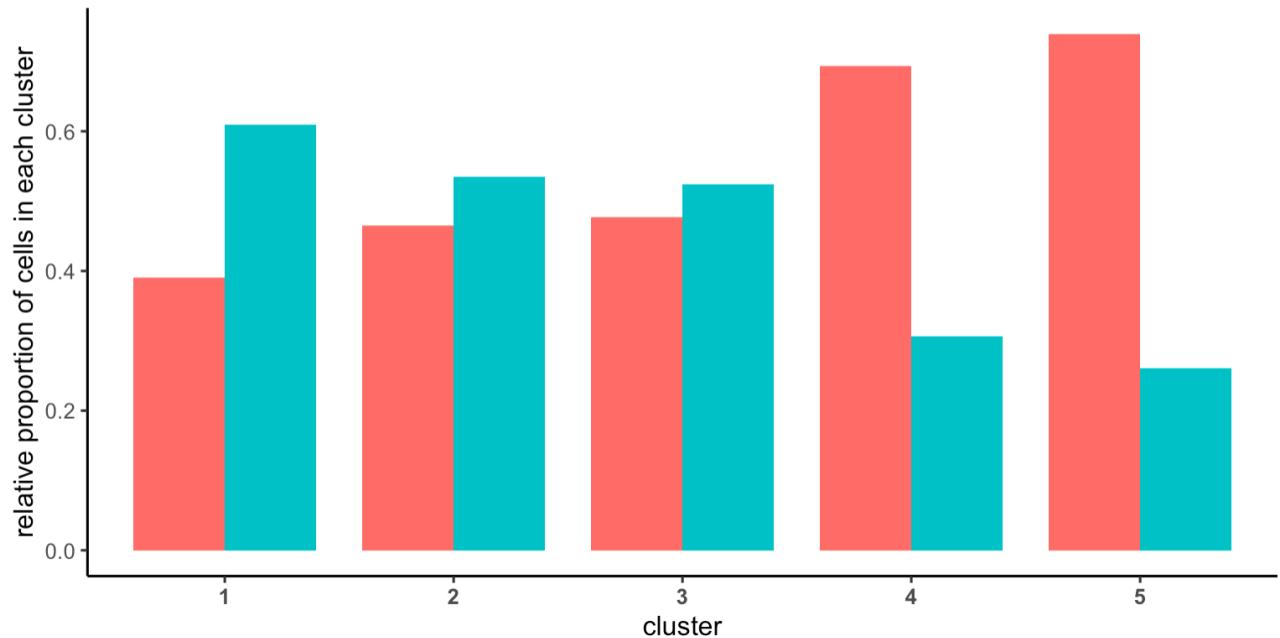


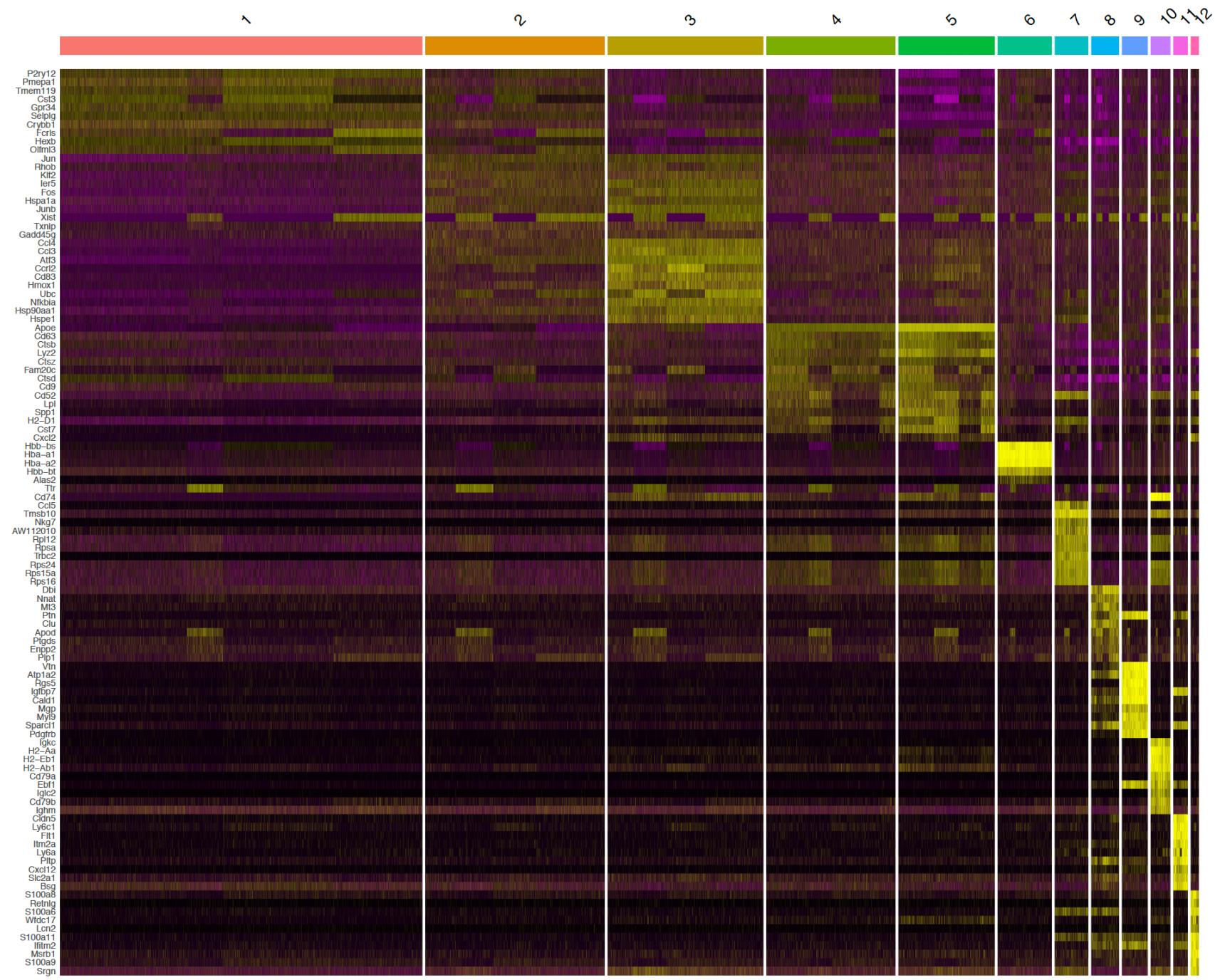
Arf1_KO



significantly higher proportion of cells in Arf1-KO cluster 5

SampleName Arf1_KO WT



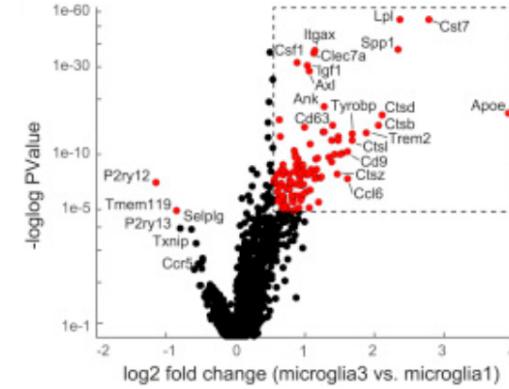


Markers (top 10 by average fold change)
for each microglia
subcluster

Article

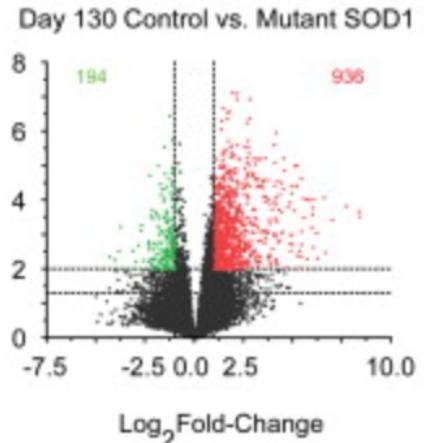
A Unique Microglia Type Associated with Restricting Development of Alzheimer's Disease

Hadas Keren-Shaul^{1, 6}, Amit Spinrad^{1, 2, 6}, Assaf Weiner^{1, 3, 6}✉, Orit Matcovitch-Natan^{1, 2, 6}, Raz Dvir-Szternfeld², Tyler K. Ulland⁴, Eyal David¹, Kuti Baruch², David Lara-Astaiso¹, Beata Toth⁵, Shalev Itzkovitz⁵, Marco Colonna⁴, Michal Schwartz^{2, 7}✉, Ido Amit^{1, 7, 8}✉



Alzheimer's disease (AD)

$$\text{Signed.value} = \text{sign(logFC)} * \log10(\text{Pvalue}) * \text{abs(logFC)}$$

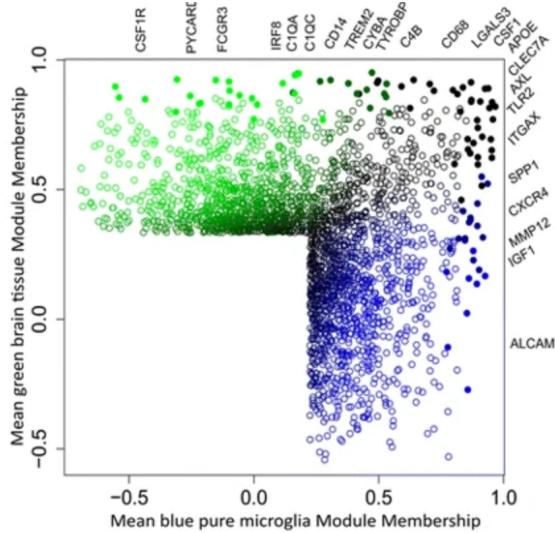


Amyotrophic lateral sclerosis (ALS)

Disease
-
normal

Induction of a common microglia gene expression signature by aging and neurodegenerative conditions: a co-expression meta-analysis

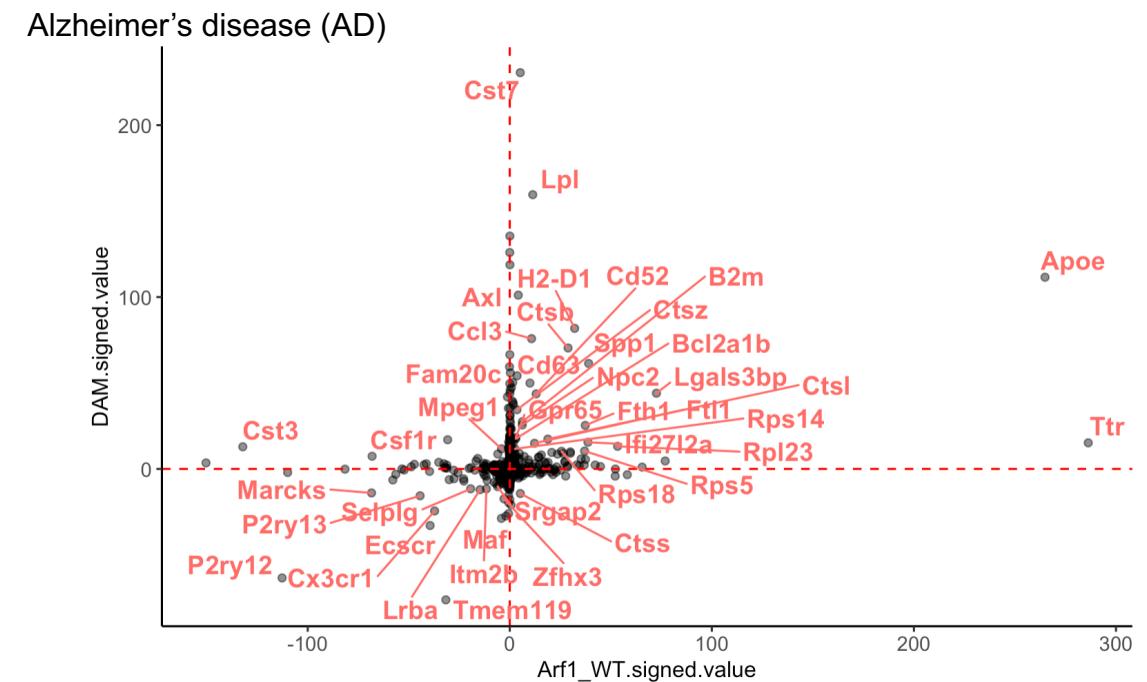
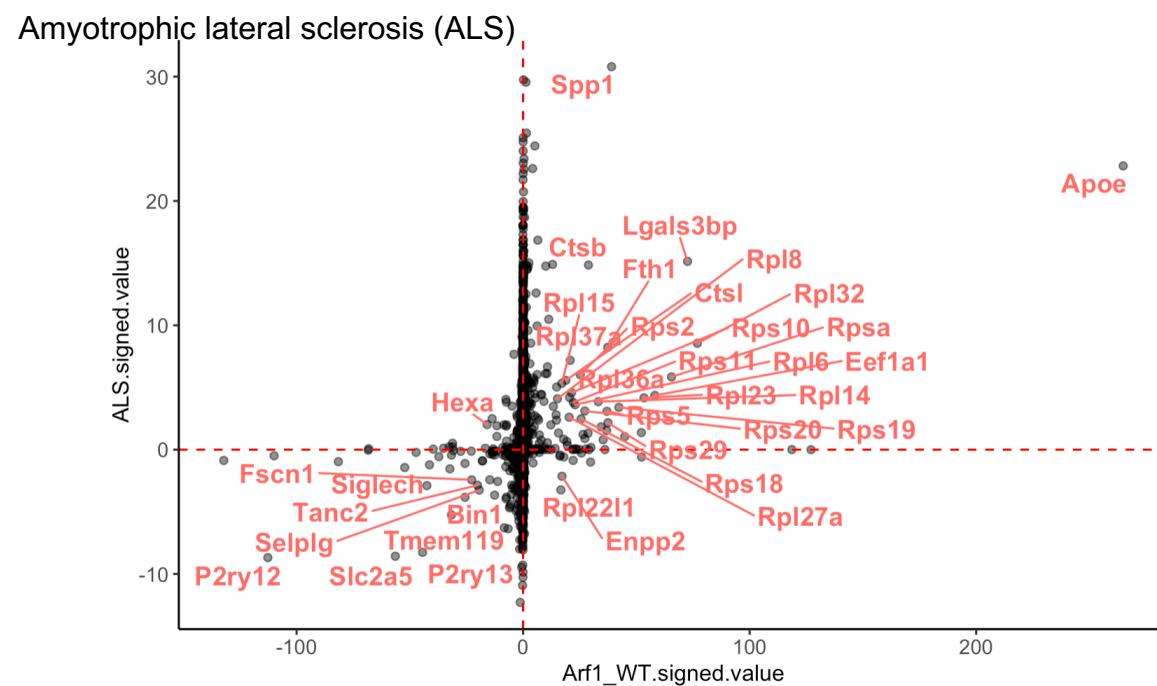
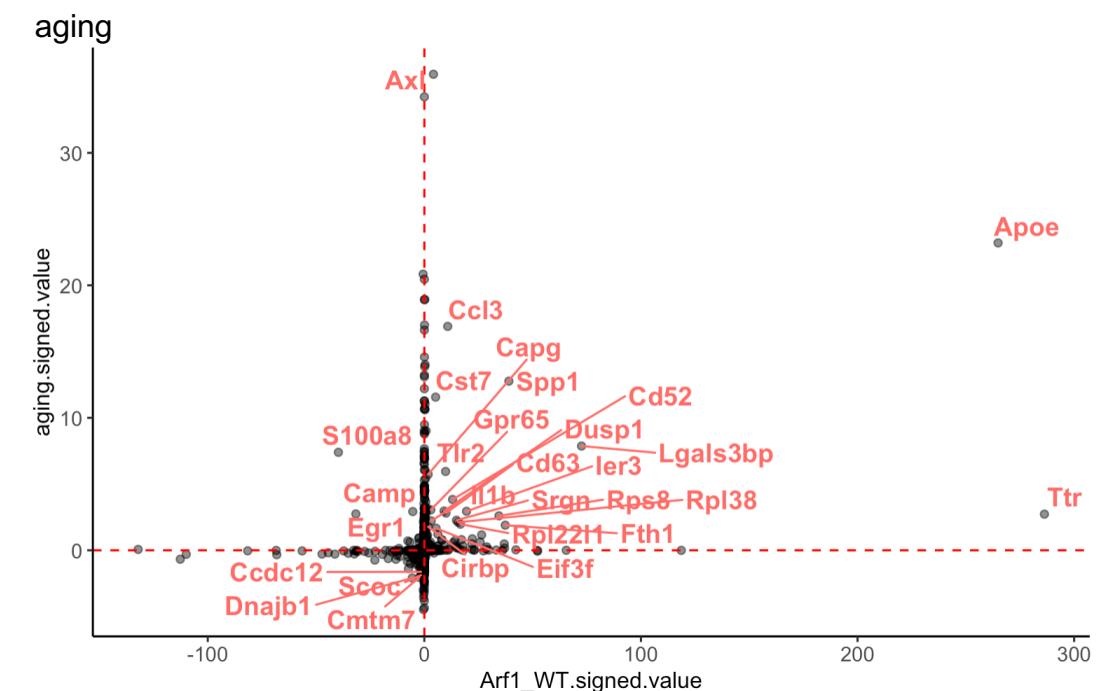
Inge R Holtman, Divya D Raj, Jeremy A Miller, Wandert Schaafsma, Zhuoran Yin, Nieske Brouwer, Paul D Wes, Thomas Möller, Marie Orre, Willem Kamphuis, Elly M Hol, Erik W G M Boddeke & Bart J L Eggen



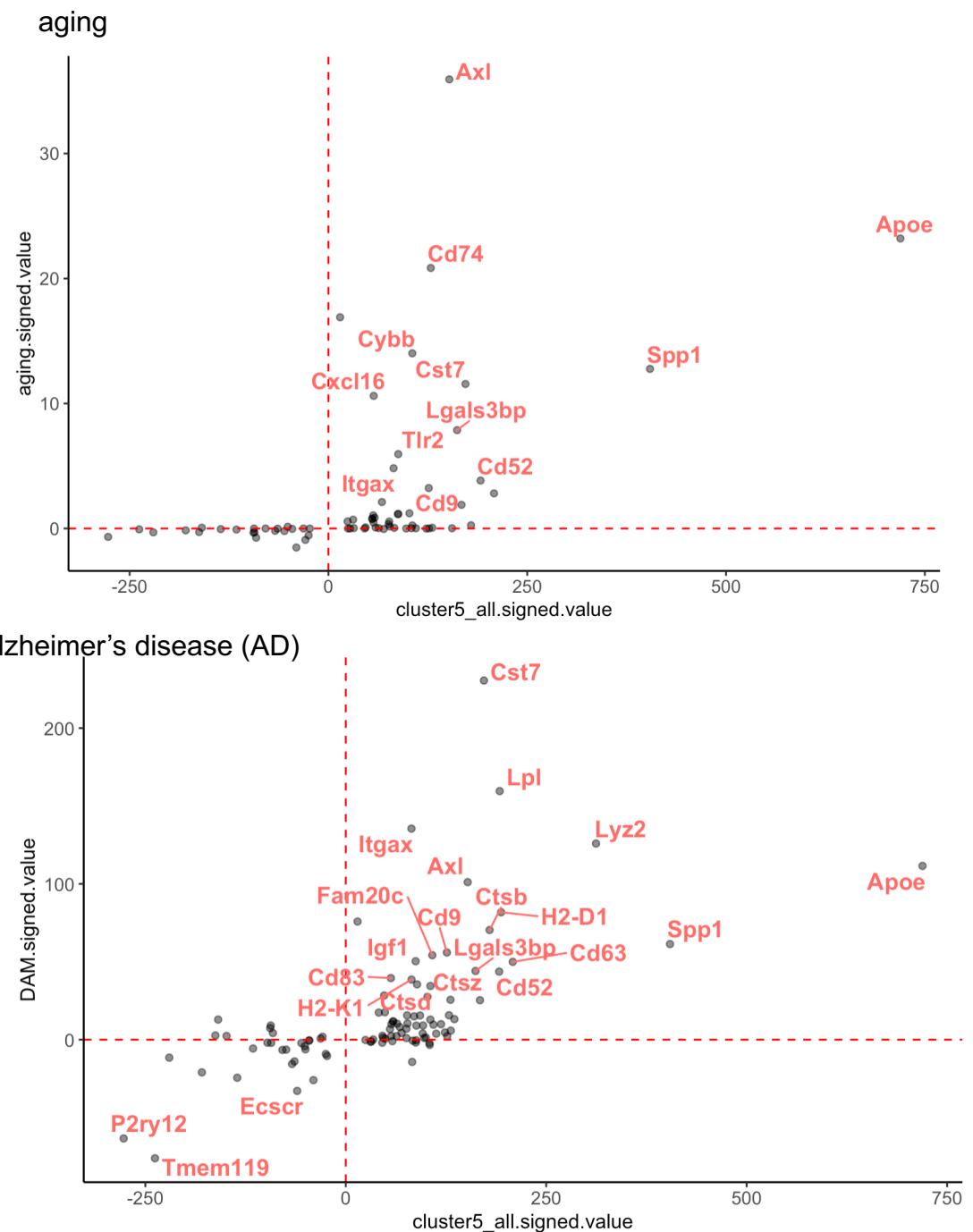
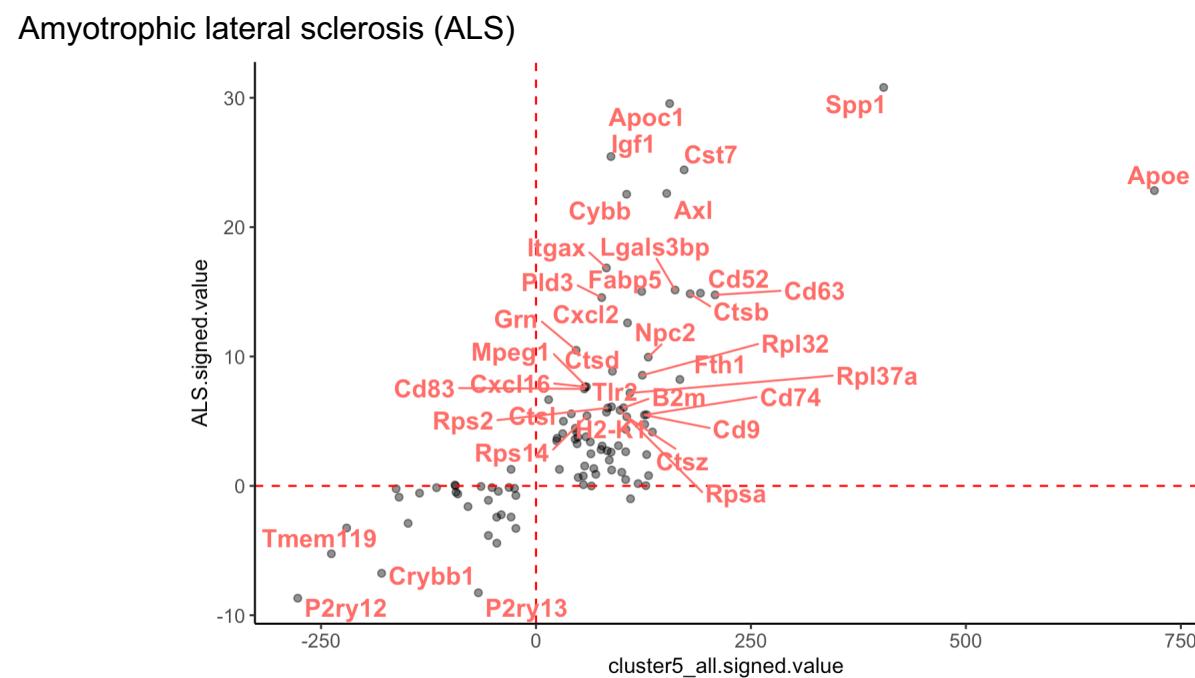
aging

Arf1 - WT

Top differentially expressed genes in Arf1-WT include some of the well-known neurodegenerative disease risk genes



Top markers in both Cluster 5 include some of the well-known neurodegenerative disease risk genes



WT cluster5-cluster1

	p_val	avg_logFC
Apoe	0.000000e+00	3.7682305
Lyz2	0.000000e+00	1.3760621
Cst3	0.000000e+00	-0.7037469
Selplg	0.000000e+00	-0.9091278
P2ry12	0.000000e+00	-1.1606572
Fth1	6.370845e-307	0.9107112
Tmem119	4.727361e-297	-1.0267639
H2-D1	3.978224e-273	0.9493257
Cd52	3.133708e-268	1.0109336
Axl	1.680051e-262	0.6358997
Cst7	3.482785e-230	0.7666977
Cd74	2.892335e-210	1.1384760
Lgmn	6.571348e-200	-0.5357838
Rpl23	3.901463e-198	0.6521820
Cd63	6.456380e-191	0.7937212
Spp1	1.070881e-181	1.1527889
Ftl1	2.521452e-177	0.7009952
Lpl	7.329135e-168	0.8418449
Rpl32	1.196618e-167	0.6132696
Olfml3	3.653158e-156	-0.6681941
H2-K1	1.246813e-154	0.6837535
Gpr34	1.748335e-153	-0.7532789
Cd83	3.106299e-152	0.8004666
Rpl10a	1.826243e-149	0.6075055
Rps16	4.019919e-148	0.5488351

Arf1 cluster5-cluster1

	p_val	avg_logFC
Apoe	0.000000e+00	3.2424778
Selplg	0.000000e+00	-0.9737924
P2ry12	0.000000e+00	-1.1450662
H2-D1	1.449769e-287	1.0642878
Cst3	4.395854e-274	-0.9229358
Hexb	3.450023e-260	-0.5577269
Tmem119	1.799193e-241	-0.9222702
Fth1	4.757204e-227	0.7932608
Axl	4.095194e-215	0.5549204
Lgals3bp	3.525993e-205	0.9354298
Cst7	1.400367e-203	0.7203935
Cx3cr1	4.560800e-196	-0.7035466
Cd52	2.210397e-189	0.8809517
Cd83	2.824432e-189	1.0923622
Ftl1	8.689610e-175	0.7143158
Lyz2	4.680859e-174	0.9053800
H2-K1	4.526141e-173	0.7549778
Ctsb	1.569723e-172	0.6936997
Ccrl2	2.748977e-171	0.9723916
Rpl23	3.438968e-171	0.5953459
Vsir	4.199635e-171	-0.6783073
Siglech	3.381944e-167	-0.7516767
Cd63	7.329389e-167	0.7462402
Spp1	6.742147e-166	1.6484115

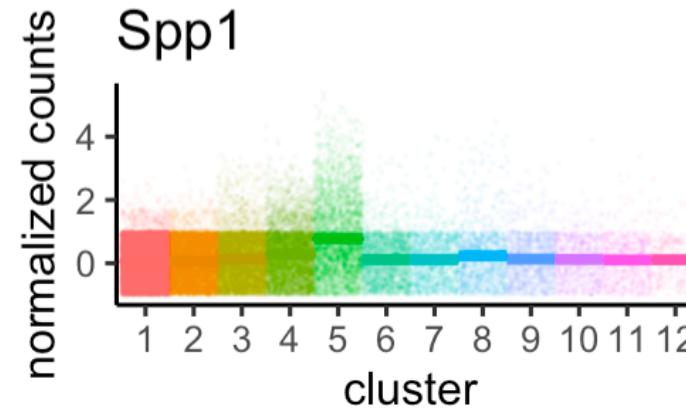
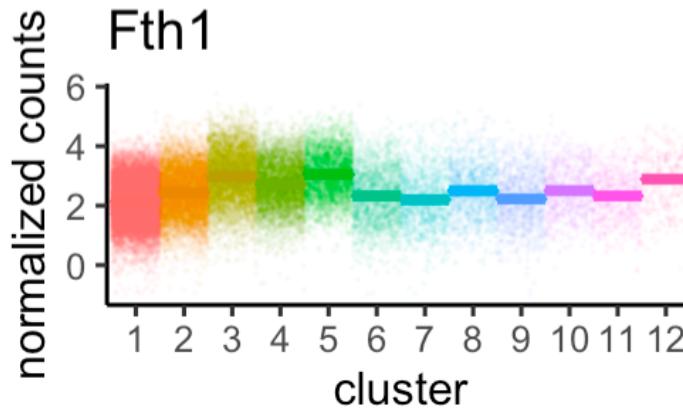
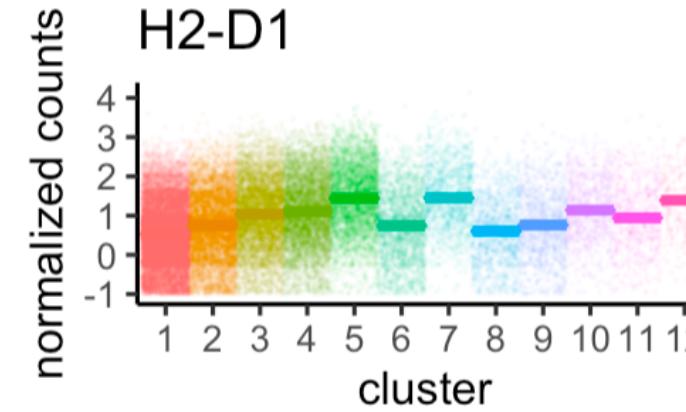
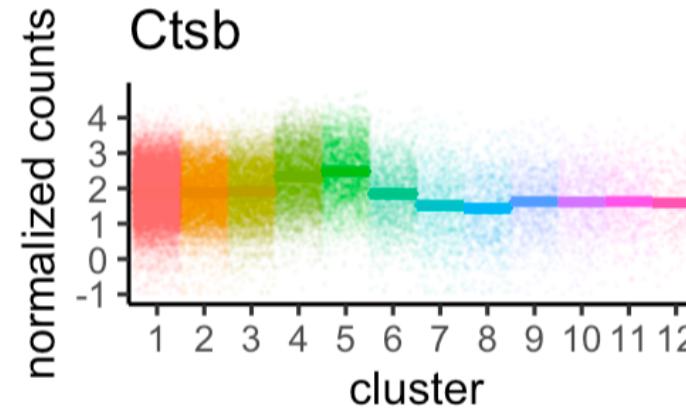
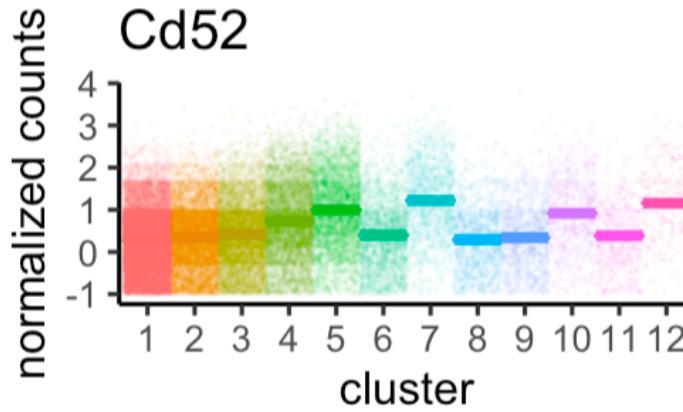
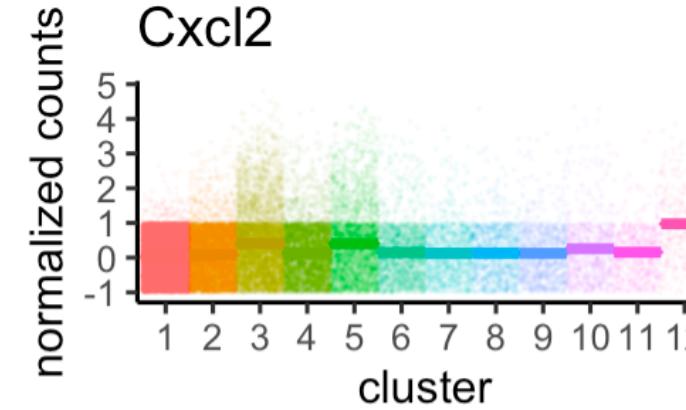
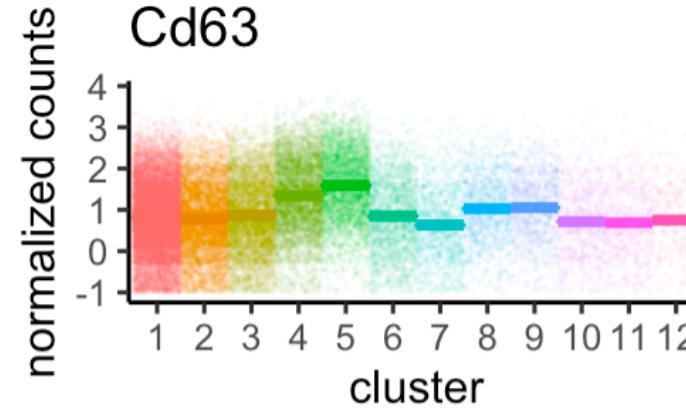
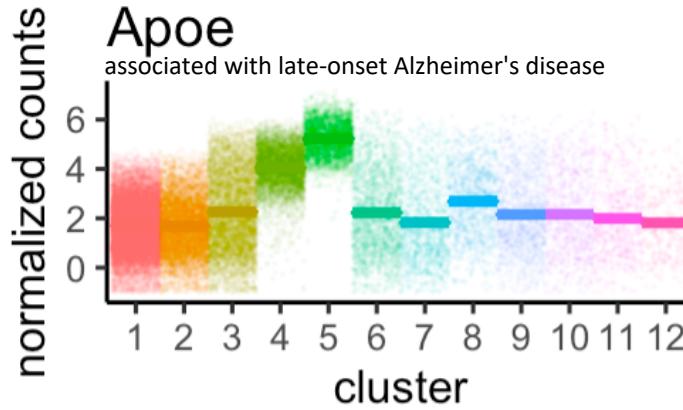
How similar are Arf1 cluster5 and WT cluster5 ?

Venn diagram here...

FC heatmap here...

Does cluster5 have an over-representation of neurodegenerative disease-associated genes?

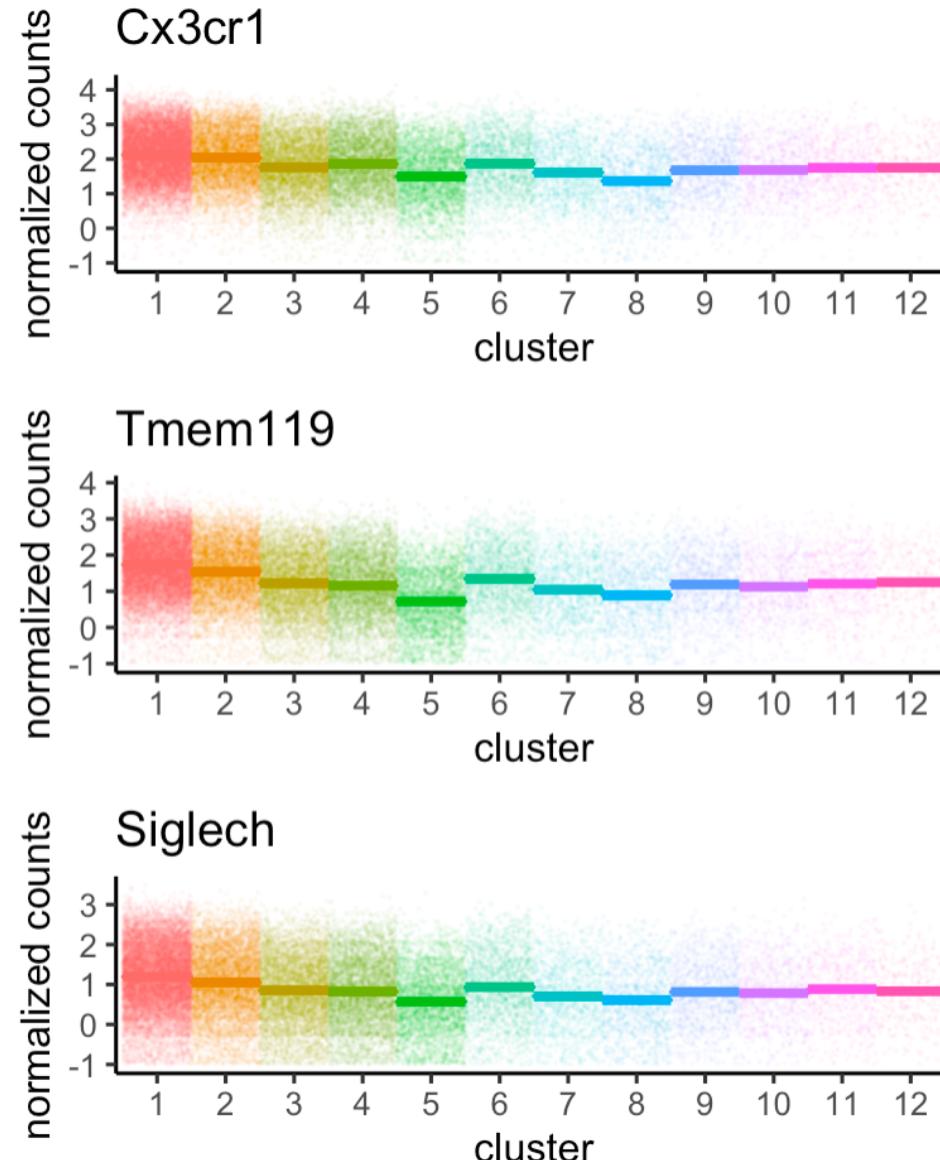
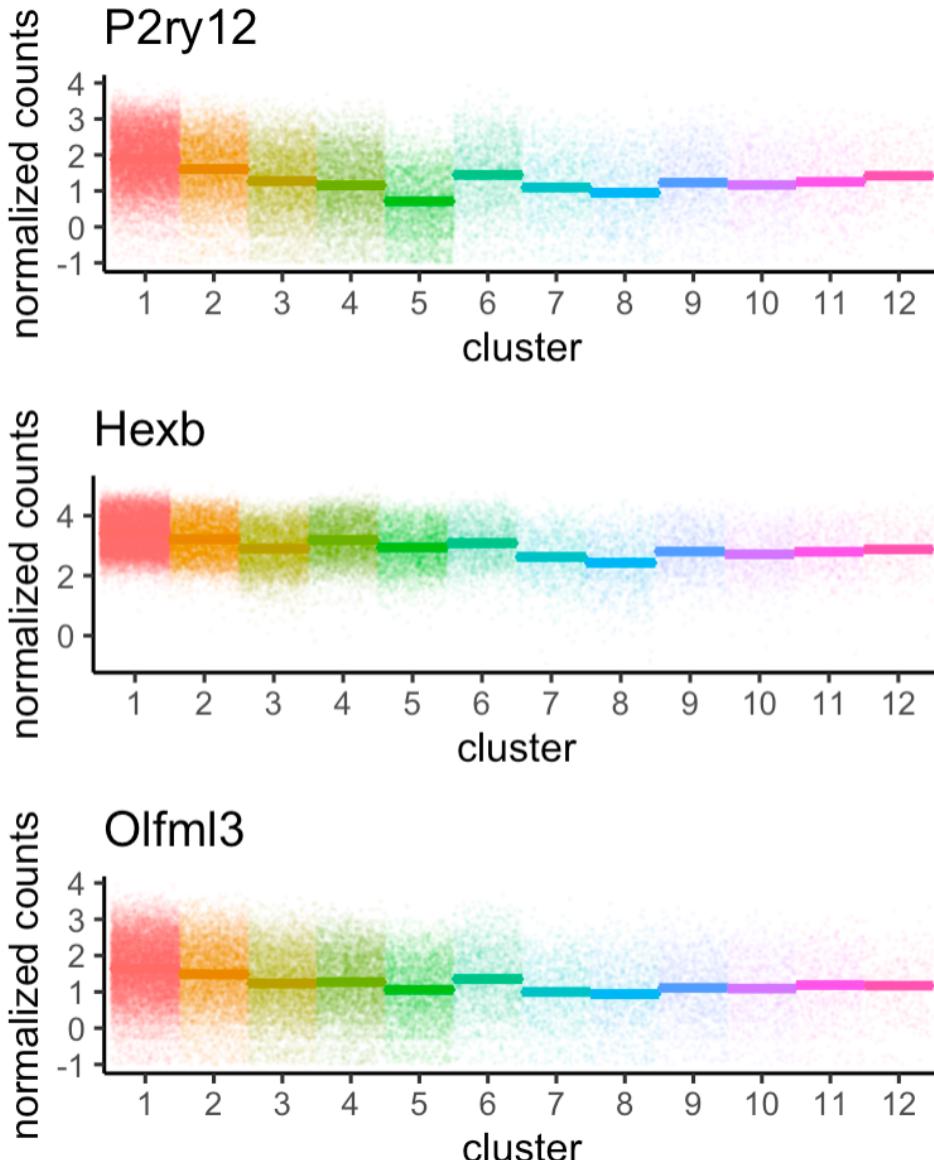
Proportion of disease-associated genes in the top markers of each cluster here...



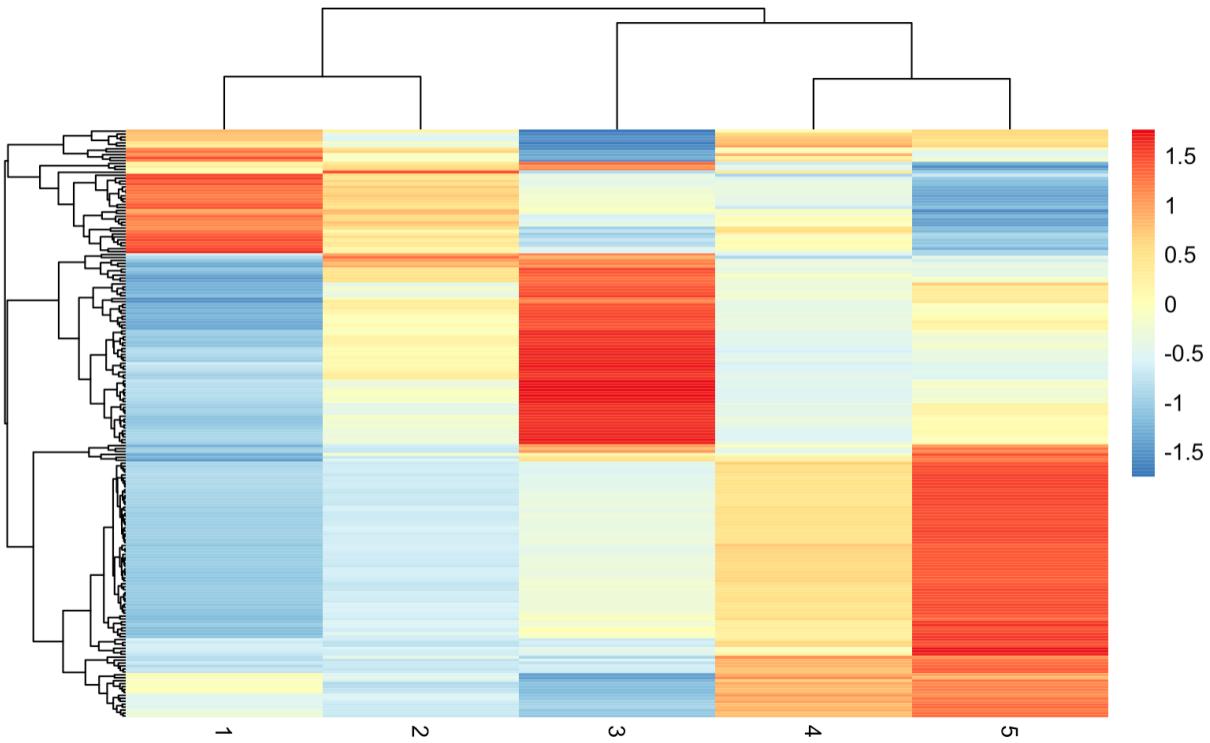
Top markers for Cluster 5 include many known disease risk factors

An increase in expression from Cluster 1 to Cluster 5

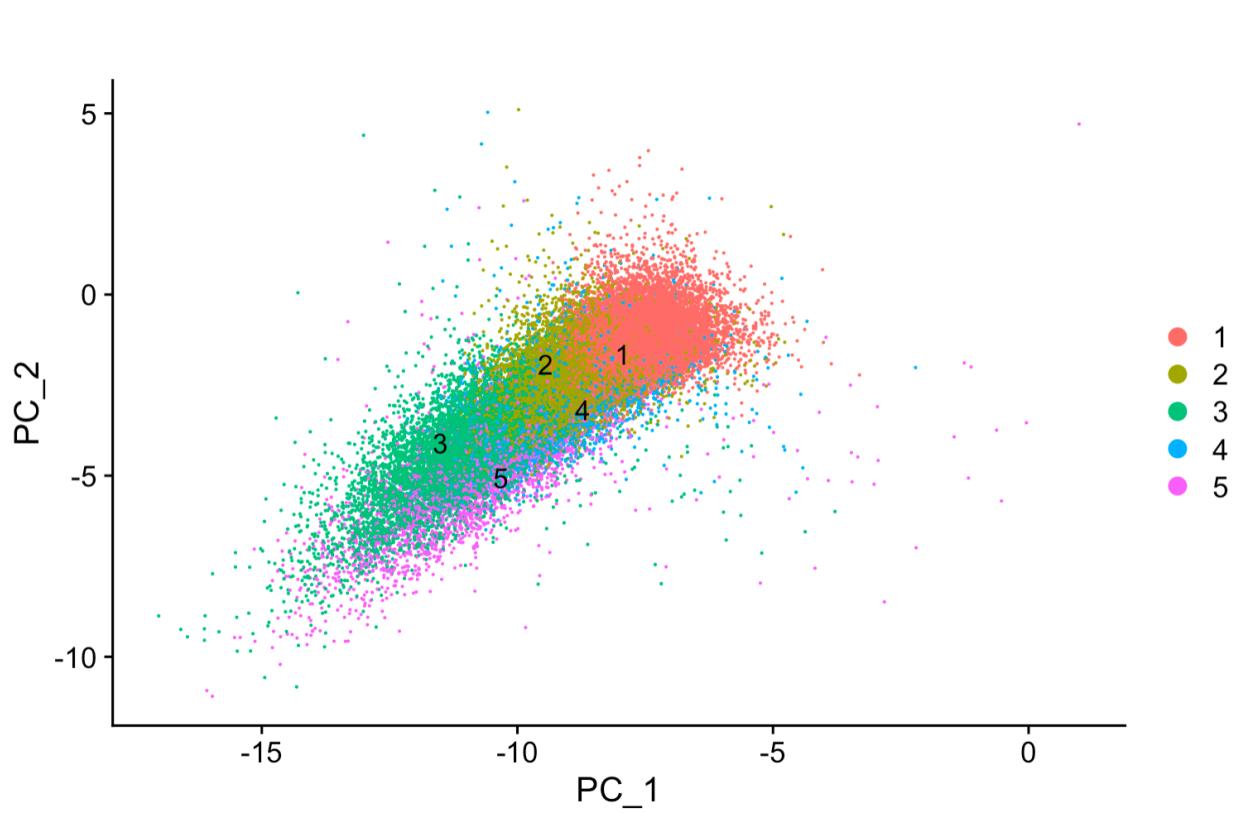
Top marker of Cluster 1 include mostly “microglial marker genes”



Top 500 most variable genes (mean expression) cluster1 - 5



PCA cluster1 - 5



- Plot that shows shift of cluster 1-5 for Arf1 and WT(density plot doesn't look good, so will stick with bar plot)
- Transfer microgliaReshape to Biowulf and FindAllMarker for each cluster(biowulf) and Doheatmap
- Plot that shows Arf1 and WT cluster 5-1 degs are very similar (also INFg and Arf1_INFg)
- Total of three to make: 1. Arf1-WT, Arf1-IFNg, Arf1-Arf1_IFNg, IFNg-WT, Arf1_IFNg-WT (venn diagram, find key genes). (biowulf swarm job) 2. FindAllMarkers 3. Cluster5 – Cluster1
- Heatmap(up and down-regulated genes for Cluster5 – Cluster1, and Arf1-WT degs),
- Heatmap of cluster1-5 to show clustering(most variable genes or all genes)
- ORA for Arf1-WT

To do for Guohao

- Look into myCluster5_cluster1_deg_ORA and decide which pathways to do dotplot, which ones to show network

Cluster5 - enriched pathways

From file: myCluster5_cluster1_deg_ORA

