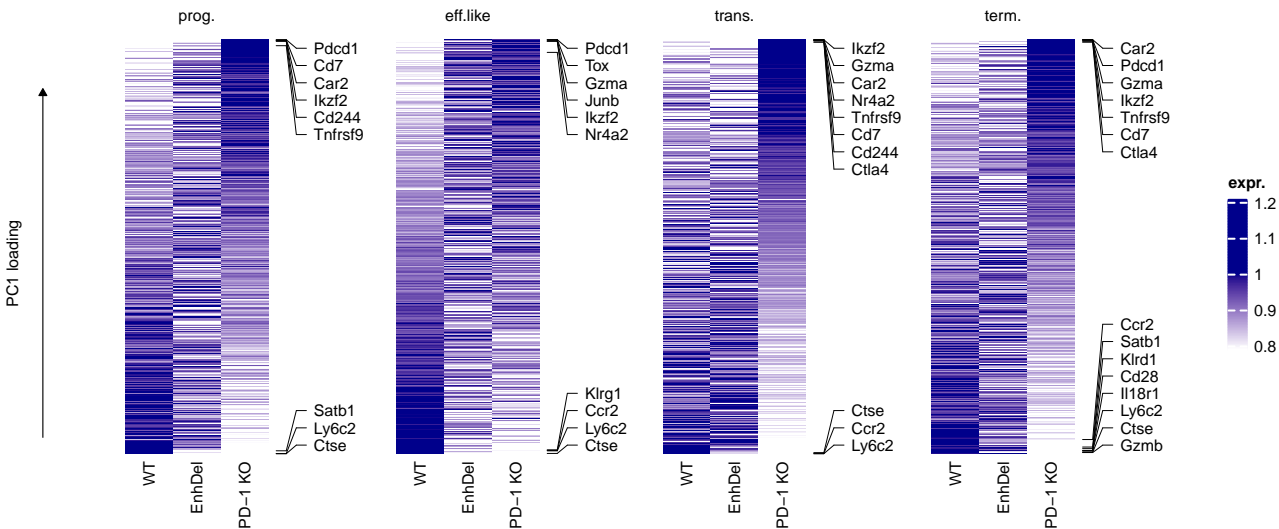


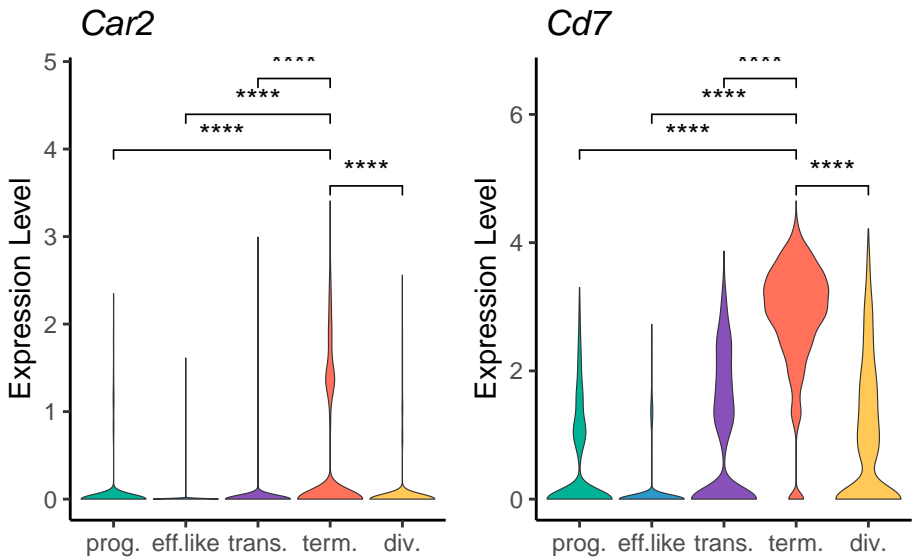
Supplementary Figures 4 Panels

Genetic perturbation of PD-1 expression does not alter formation of exhausted CD8+ T cell subsets.

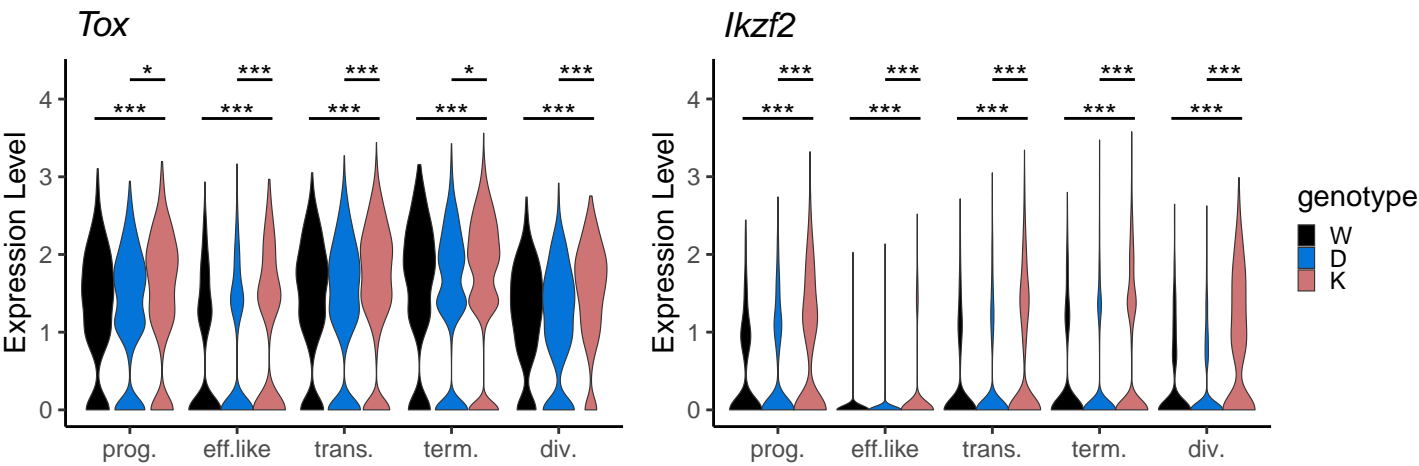
4a



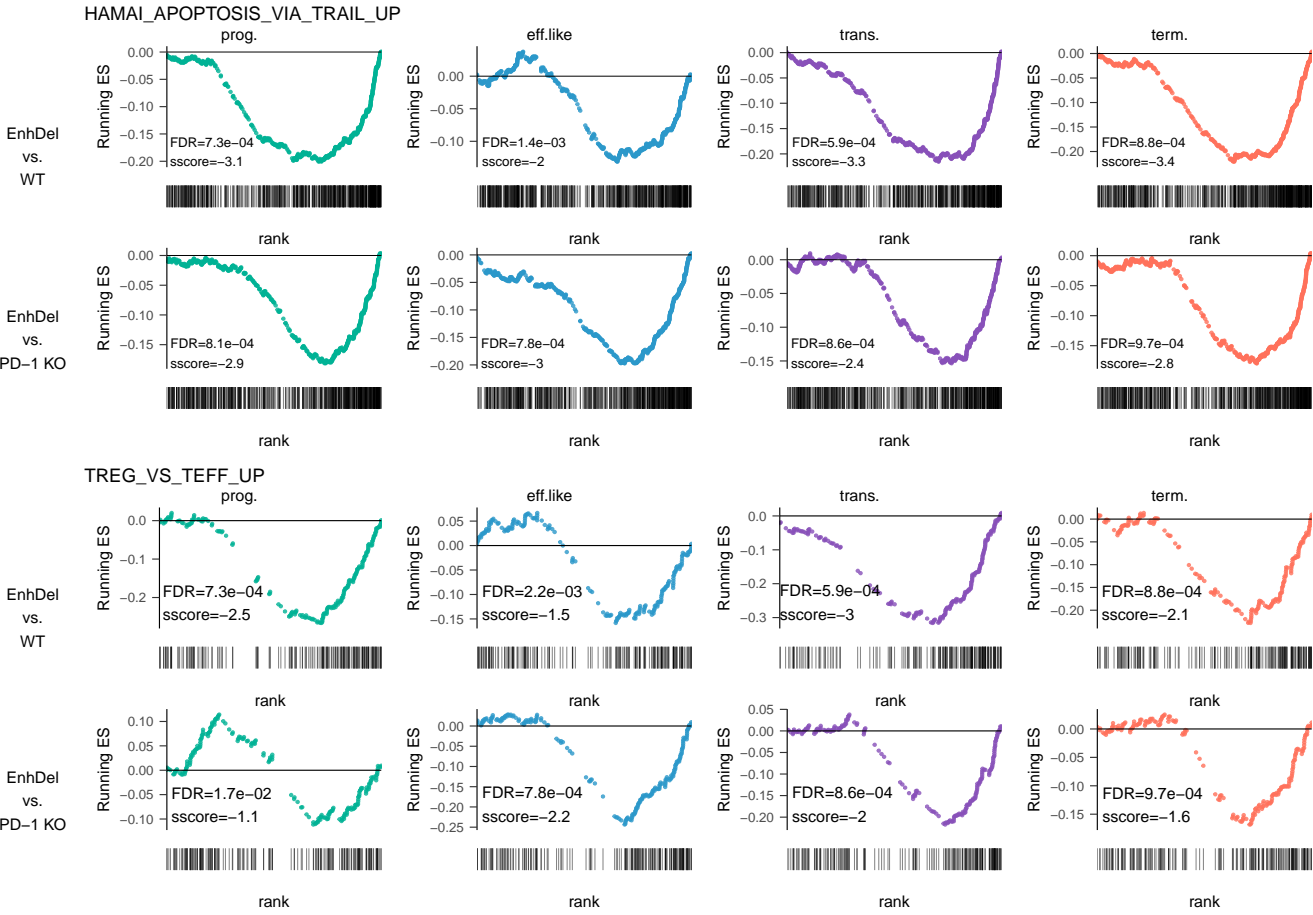
4b



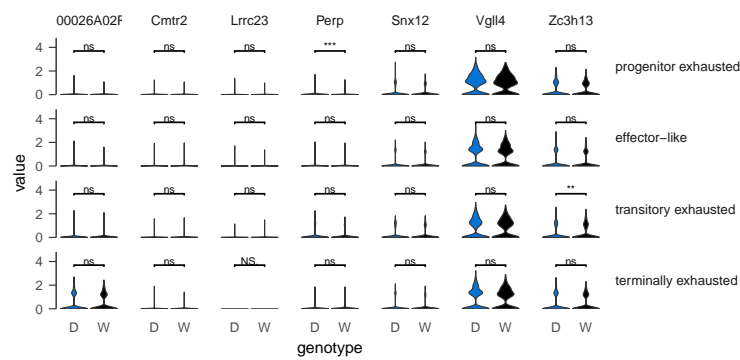
4c



4d and 4e

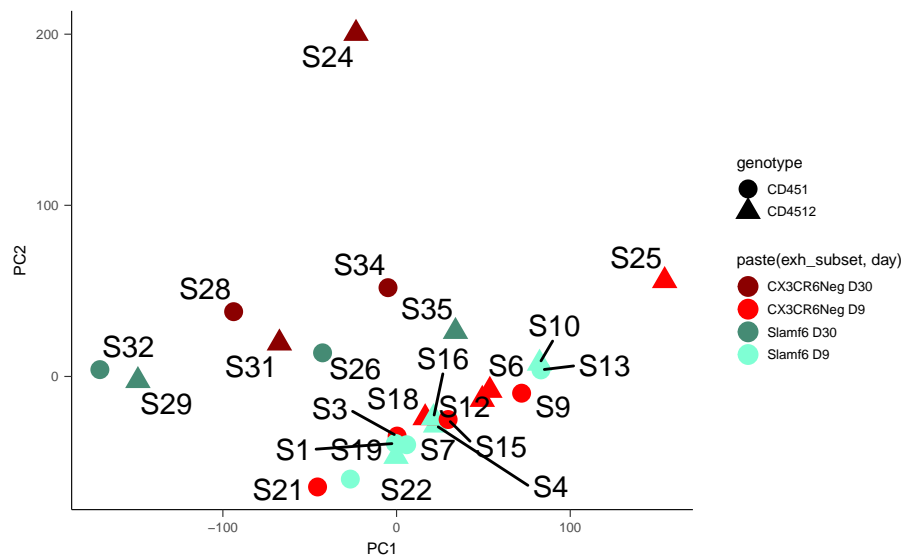


Off-target effects



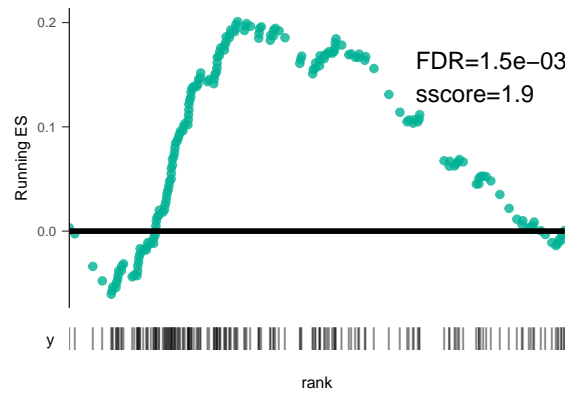
Early timepoint bulk RNAseq

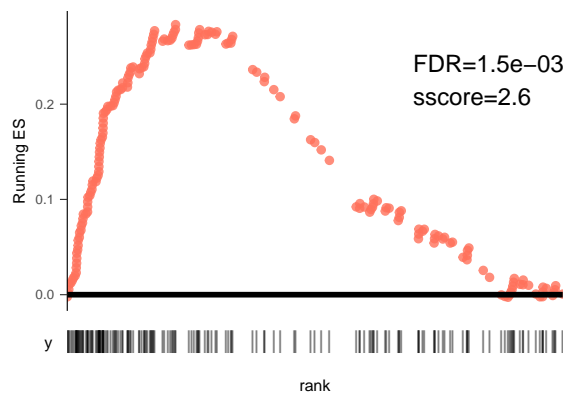
PCA



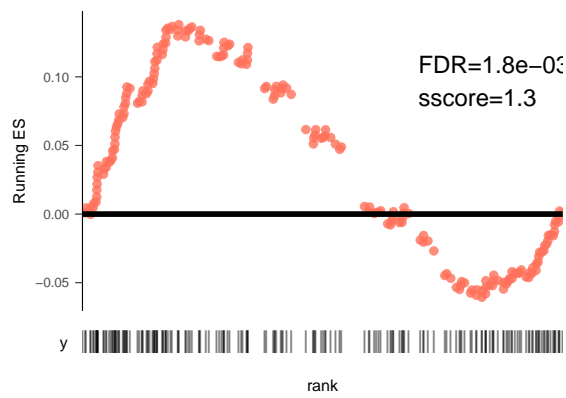
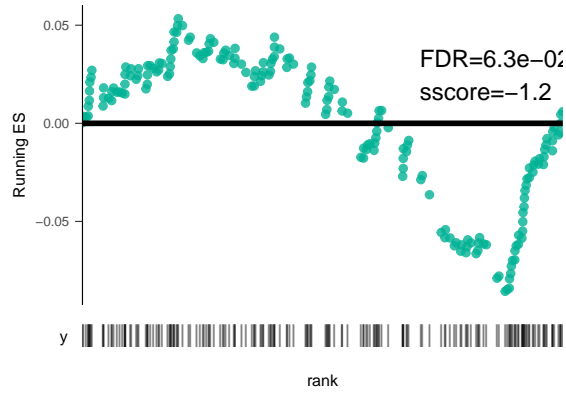
GSEA

HALLMARK_OXIDATIVE_PHOSPHORYLATION

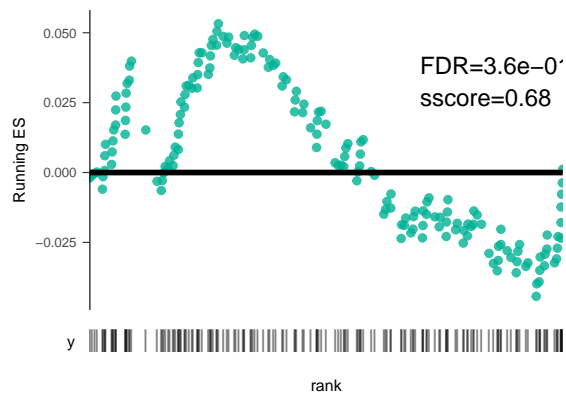


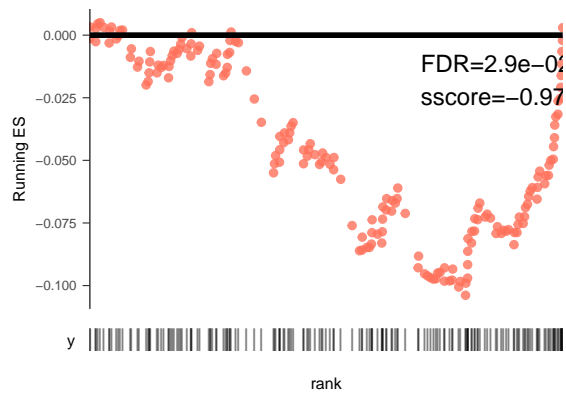


GSE9650_EFFECTOR_VS_EXHAUSTED_CD8_TCELL_UP

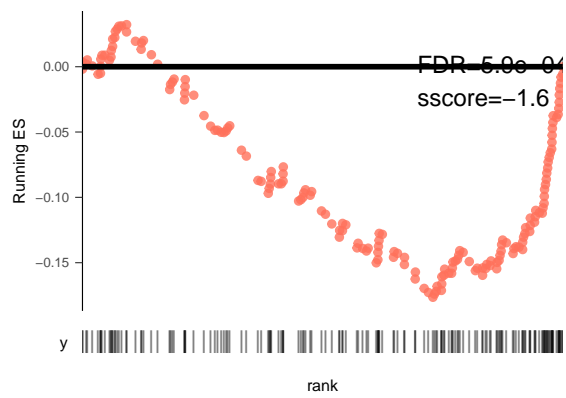
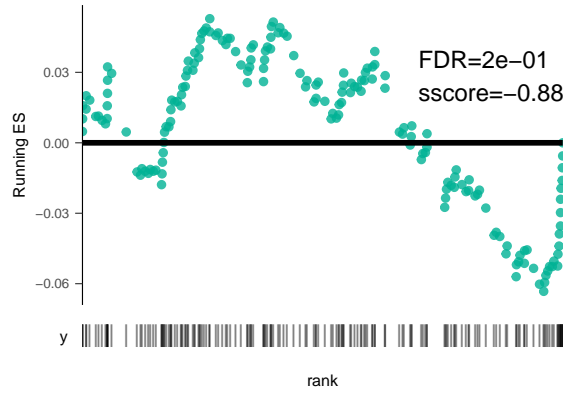


GSE9650_EFFECTOR_VS_EXHAUSTED_CD8_TCELL_DN

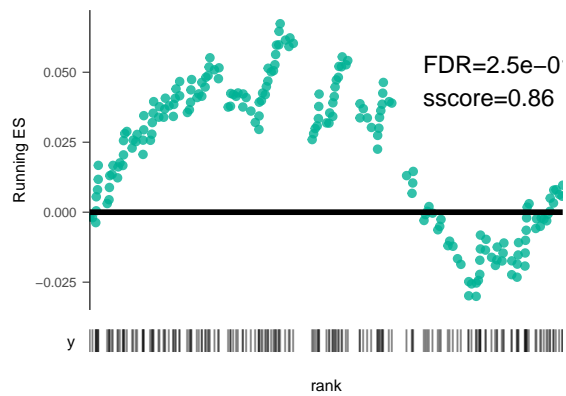


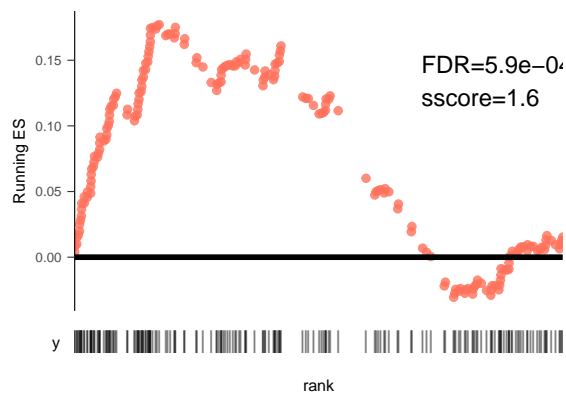


GSE9650_EXHAUSTED_VS_MEMORY_CD8_TCELL_UP



GSE9650_EXHAUSTED_VS_MEMORY_CD8_TCELL_DN





Overlap in significant genes enriched in enhancers

```
## [1] "Progenitor"
```

```
##               signif_up.sc30
## signif_up.bulk9 FALSE TRUE
##               FALSE 1786  506
##               TRUE  365  379
```

```
##
## Fisher's Exact Test for Count Data
##
## data:  signif_tbl
## p-value < 2.2e-16
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
##  3.065676 4.379506
## sample estimates:
## odds ratio
##  3.663205
```

```
## [1] "Terminal"
```

```
##               signif_up.sc30
## signif_up.bulk9 FALSE TRUE
##               FALSE 2096  500
##               TRUE  225  215
```

```
##
## Fisher's Exact Test for Count Data
##
## data:  signif_tbl
## p-value < 2.2e-16
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
##  3.224096 4.971956
## sample estimates:
## odds ratio
##  4.003384
```

END

```
## R version 4.0.3 (2020-10-10)
## Platform: x86_64-apple-darwin17.0 (64-bit)
## Running under: macOS Big Sur 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] grid parallel stats4 stats graphics grDevices utils
## [8] datasets methods base
##
## other attached packages:
## [1] SeuratObject_4.0.4 Seurat_3.1.1
## [3] ggrastr_1.0.1 scattermore_0.8
## [5] ggforce_0.3.3 ggrepel_0.9.1
## [7] circlize_0.4.14 ComplexHeatmap_2.4.3
## [9] ggridges_0.5.3 gridExtra_2.3
## [11] viridis_0.6.2 viridisLite_0.4.0
## [13] ggpubr_0.4.0 cowplot_1.1.1
## [15] readr_2.1.2 tibble_3.1.6
## [17] purrr_0.3.4 tidyr_1.2.0
## [19] stringr_1.4.0 ggplot2_3.3.6
## [21] dplyr_1.0.9 DESeq2_1.28.1
## [23] SummarizedExperiment_1.18.2 DelayedArray_0.14.1
## [25] matrixStats_0.61.0 Biobase_2.48.0
## [27] GenomicRanges_1.40.0 GenomeInfoDb_1.24.2
## [29] IRanges_2.22.2 S4Vectors_0.26.1
## [31] BiocGenerics_0.34.0 here_1.0.1
##
## loaded via a namespace (and not attached):
## [1] utf8_1.2.2 reticulate_1.24 R.utils_2.11.0
## [4] tidyselect_1.1.2 RSQLite_2.2.12 AnnotationDbi_1.50.3
## [7] htmlwidgets_1.5.4 BiocParallel_1.22.0 Rtsne_0.15
## [10] munsell_0.5.0 codetools_0.2-18 mutoss_0.1-12
## [13] ica_1.0-2 future_1.25.0 withr_2.5.0
## [16] colorspace_2.0-3 knitr_1.39 rstudioapi_0.13
## [19] ROCR_1.0-11 ggsignif_0.6.3 listenv_0.8.0
## [22] Rsc_0.0.0.9000 labeling_0.4.2 Rdpack_2.3
## [25] GenomeInfoDbData_1.2.3 mnormt_2.0.2 polyclip_1.10-0
## [28] bit64_4.0.5 farver_2.1.0 rprojroot_2.0.3
## [31] parallelly_1.31.1 vctrs_0.4.1 generics_0.1.2
## [34] TH.data_1.1-1 xfun_0.30 R6_2.5.1
## [37] ggbeeswarm_0.6.0 clue_0.3-60 rsvd_1.0.5
## [40] locfit_1.5-9.4 bitops_1.0-7 cachem_1.0.6
## [43] assertthat_0.2.1 vroom_1.5.7 SDMTTools_1.1-221
## [46] scales_1.2.0 multcomp_1.4-19 beeswarm_0.4.0
## [49] gtable_0.3.0 globals_0.14.0 sandwich_3.0-1
## [52] rlang_1.0.6 genefilter_1.70.0 GlobalOptions_0.1.2
## [55] splines_4.0.3 rstatix_0.7.0 lazyeval_0.2.2
## [58] broom_0.8.0 reshape2_1.4.4 yaml_2.3.5
## [61] abind_1.4-5 backports_1.4.1 tools_4.0.3
## [64] ellipsis_0.3.2 RColorBrewer_1.1-3 TFisher_0.2.0
## [67] Rcpp_1.0.9 plyr_1.8.7 zlibbioc_1.34.0
## [70] RCurl_1.98-1.6 pbapply_1.5-0 GetoptLong_1.0.5
## [73] zoo_1.8-9 cluster_2.1.3 magrittr_2.0.3
## [76] data.table_1.14.2 lmtest_0.9-40 RANN_2.6.1
## [79] tmvnsim_1.0-2 mvtnorm_1.1-3 fitdistrplus_1.1-8
```

## [82]	hms_1.1.1	evaluate_0.15	xtable_1.8-4
## [85]	XML_3.99-0.9	shape_1.4.6	compiler_4.0.3
## [88]	KernSmooth_2.23-20	crayon_1.5.1	R.oo_1.24.0
## [91]	htmltools_0.5.2	tzdb_0.3.0	geneplotter_1.66.0
## [94]	DBI_1.1.2	tweenr_1.0.2	MASS_7.3-56
## [97]	Matrix_1.4-1	car_3.0-13	cli_3.4.1
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## [103]	qqconf_1.2.3	igraph_1.3.0	pkgconfig_2.0.3
## [106]	sn_2.0.2	numDeriv_2016.8-1.1	plotly_4.10.0
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## [115]	sctransform_0.3.3	RcppAnnoy_0.0.19	rmarkdown_2.14
## [118]	leiden_0.3.10	uwot_0.1.11	rjson_0.2.21
## [121]	lifecycle_1.0.1	nlme_3.1-157	jsonlite_1.8.0
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## [130]	plotrix_3.8-2	survival_3.3-1	glue_1.6.2
## [133]	png_0.1-7	bit_4.0.4	stringi_1.7.6
## [136]	blob_1.2.3	memoise_2.0.1	mathjaxr_1.6-0
## [139]	irlba_2.3.5	future.apply_1.9.0	ape_5.6-2