FMF published-result reproduction

Generated: **2026-11-24 15:34**

Environment: R 4.5.0 / Bioconductor 3.21; DESeq2, limma, affy; Snakemake 8.30; Python 3.13.

What was reproduced

This run reproduces the open, patient-derived results that anchor the FMF signal work: the FMF-vs-healthy PBMC miRNA signature (GSE111311), the PFAPA/FMF flare whole-blood signature (GSE17732), the MEFV-knockdown miR-4520a result (GSE79954), the miR-204-3p/PI3K-gamma result (GSE98940), and the colchicine HUVEC response (GSE4090). The EGA monocyte RNA-seq anchor (EGAD00001010304) remains controlled-access and is not used here.

Scoreboard

dataset	reproduced	partial	not reproduced	not testable
GSE111311	8	0	0	0
GSE17732	32	0	0	0
GSE79954	1	0	0	0
GSE98940	3	1	0	0
GSE4090	1	0	0	0

GSE111311 — PBMC miRNA (NanoString)

Publication: PMID 29787577

Key run statistics:

- **de_p_0.01**: 8
- **de_padj_0.05**: 3
- **mirnas_tested**: 103
- **n_case**: 10
- **n_control**: 9
- **paired_pairs**: 9
- **pca_pc1_t_p**: 4.754e-05
- **pca_pc1_wilcox_p**: 4.33e-05
- **target_mirnas_expected**: 7
- **target_mirnas_reproduced**: 7
- **top_log2fc**: 2.747
- **top_p_value**: 5.439e-08
- **top_signal**: hsa-miR-4454+hsa-miR-7975

Published claims:

signal	comparison	expected_direction	status	observed_log2fc	p_value
hsa-let-7d-5p	FMF_vs_HC	down	reproduced	-0.602	0.0069
hsa-miR-107	FMF_vs_HC	down	reproduced	-0.751	0.0094
hsa-miR-144-3p	FMF_vs_HC	up	reproduced	2.84	4.84e-06
hsa-miR-148b-3p	FMF_vs_HC	down	reproduced	-0.437	0.0038
hsa-miR-21-5p	FMF_vs_HC	up	reproduced	0.571	0.0045
hsa-miR-4454+hsa-miR-7975	FMF_vs_HC	up	reproduced	2.75	5.44e-08
hsa-miR-451a	FMF_vs_HC	up	reproduced	1.52	7.02e-05
PC1_7miRNA	FMF_vs_HC	separated	reproduced	nan	4.75e-05

Top ranked signals from this dataset:

signal	comparison	direction	log2fc	p_value	adj_p	rank
hsa-miR-4454+hsa-miR-7975	FMF_vs_HC	up	2.75	5.44e-08	5.60e-06	28
hsa-miR-144-3p	FMF_vs_HC	up	2.84	4.84e-06	0.0002	66
hsa-miR-451a	FMF_vs_HC	up	1.52	7.02e-05	0.0024	649

hsa-miR-107	FMF_vs_HC	down	-0.751	0.0094	0.1209	6667
hsa-miR-21-5p	FMF_vs_HC	up	0.571	0.0045	0.0917	7293
hsa-let-7d-5p	FMF_vs_HC	down	-0.602	0.0069	0.1189	7454
hsa-miR-148a-3p	FMF_vs_HC	up	0.503	0.0496	0.5110	9364

GSE17732 — whole-blood mRNA (Affymetrix)

Publication: PMID 21478439

Key run statistics:
- **de_fmf_p_0.05**: 2260
- **de_hc_p_0.05**: 5629
- **de_paired_p_0.05**: 6334
- **genes_tested**: 13041
- **key_gene_hits**: PFAPA_flare_vs_nonflare=18 up/4 down at p<0.05;PFAPA_flare_vs_HC=18 up/4 down at p<0.05;FMF_flare_vs_HC=16 up/1 down at p<0.05
- **paired_pairs**: 6

Published claims:

signal	comparison	expected_direction	status	observed_log2fc	p_value
C1QB	PFAPA_flare_vs_HC	up	reproduced	3.08	8.00e-08
C1QB	PFAPA_flare_vs_nonflare_paired	up	reproduced	3.27	3.17e-07
C2	PFAPA_flare_vs_HC	up	reproduced	3.11	5.00e-08
C2	PFAPA_flare_vs_nonflare_paired	up	reproduced	2.94	2.20e-06
SERPING1	PFAPA_flare_vs_HC	up	reproduced	3.93	1.89e-08
SERPING1	PFAPA_flare_vs_nonflare_paired	up	reproduced	3.82	8.47e-07
IL1B	PFAPA_flare_vs_HC	up	reproduced	2.11	6.91e-08
IL1B	PFAPA_flare_vs_nonflare_paired	up	reproduced	2.01	1.03e-05
IL1RN	PFAPA_flare_vs_HC	up	reproduced	0.685	4.24e-05
IL1RN	PFAPA_flare_vs_nonflare_paired	up	reproduced	0.745	6.19e-05
CASP1	PFAPA_flare_vs_HC	up	reproduced	0.949	8.73e-07
CASP1	PFAPA_flare_vs_nonflare_paired	up	reproduced	1.16	2.07e-06
IL18RAP	PFAPA_flare_vs_HC	up	reproduced	1.37	0.0005
IL18RAP	PFAPA_flare_vs_nonflare_paired	up	reproduced	1.29	7.97e-06
AIM2	PFAPA_flare_vs_HC	up	reproduced	2.75	2.09e-09
AIM2	PFAPA_flare_vs_nonflare_paired	up	reproduced	3.01	2.10e-07
CXCL10	PFAPA_flare_vs_HC	up	reproduced	1.83	0.0064
CXCL10	PFAPA_flare_vs_nonflare_paired	up	reproduced	2.38	0.0003
CD3D	PFAPA_flare_vs_HC	down	reproduced	-1.06	5.77e-05
CD3D	PFAPA_flare_vs_nonflare_paired	down	reproduced	-0.906	7.50e-05
CD3E	PFAPA_flare_vs_HC	down	reproduced	-0.821	7.02e-05
CD3E	PFAPA_flare_vs_nonflare_paired	down	reproduced	-0.925	0.0002
CD8B	PFAPA_flare_vs_HC	down	reproduced	-1.18	7.17e-05
CD8B	PFAPA_flare_vs_nonflare_paired	down	reproduced	-1.28	9.75e-05
C1QB	FMF_flare_vs_HC	up	reproduced	2.01	0.0133
C2	FMF_flare_vs_HC	up	reproduced	1.57	0.0010
SERPING1	FMF_flare_vs_HC	up	reproduced	2.78	0.0039
IL1B	FMF_flare_vs_HC	up	reproduced	1.51	0.0005
IL1RN	FMF_flare_vs_HC	up	reproduced	0.453	0.0322
CASP1	FMF_flare_vs_HC	up	reproduced	0.621	0.0117
IL18RAP	FMF_flare_vs_HC	up	reproduced	1.2	0.0362
AIM2	FMF_flare_vs_HC	up	reproduced	1.89	0.0015

Top ranked signals from this dataset:

signal	comparison	direction	log2fc	p_value	adj_p	rank

CD177	PFAPA_flare_vs_HC	up	6.72	4.20e-11	3.49e-07	1
CD177	PFAPA_flare_vs_nonflare_paired	up	6.25	1.27e-07	0.0002	2
ANXA3	PFAPA_flare_vs_HC	up	3.83	6.27e-11	3.49e-07	3
CASP5	PFAPA_flare_vs_HC	up	3.85	5.76e-10	9.88e-07	4
SERPING1	PFAPA_flare_vs_HC	up	3.93	1.89e-08	6.02e-06	5
SEPTIN4	PFAPA_flare_vs_HC	up	3.38	2.80e-09	2.32e-06	6
HPR	PFAPA_flare_vs_HC	up	3.44	5.32e-09	3.15e-06	7
ANXA3	PFAPA_flare_vs_nonflare_paired	up	3.74	3.89e-08	0.0002	8
CASP5	PFAPA_flare_vs_nonflare_paired	up	4.12	2.05e-07	0.0002	9
HP	PFAPA_flare_vs_HC	up	3.37	7.83e-09	3.68e-06	10
GALNT14	PFAPA_flare_vs_HC	up	2.99	6.46e-09	3.51e-06	11
SEPTIN4	PFAPA_flare_vs_nonflare_paired	up	3.61	2.01e-07	0.0002	12

GSE79954 — THP-1 miRNA (Affymetrix)

Publication: PMID 27636101

Key run statistics:

- **de_p_0.01**: 424
- **de_padj_0.05**: 48
- **mir4520a_log2fc**: -2.427
- **mir4520a_p_value**: 9.567e-09
- **mir4520a_rank**: 1
- **n_case**: 4
- **n_control**: 5
- **probes_tested**: 25015
- **top_log2fc**: -2.427
- **top_p_value**: 9.567e-09
- **top_signal**: hsa-miR-4520a-3p_st

Published claims:

signal	comparison	expected_direction	status	observed_log2fc	p_value
hsa-miR-4520a-3p_st	MEFV_knockdown_vs_scramble	down	reproduced	-2.43	9.57e-09

Top ranked signals from this dataset:

signal	comparison	direction	log2fc	p_value	adj_p	rank
hsa-miR-4520a-3p_st	MEFV_knockdown_vs_scramble	down	-2.43	9.57e-09	0.0002	31
hsa-miR-19b-1-star_st	MEFV_knockdown_vs_scramble	down	-2.38	6.91e-07	0.0019	72
hsa-miR-4520b-3p_st	MEFV_knockdown_vs_scramble	down	-2.81	5.83e-05	0.0356	121
hsa-miR-4801_st	MEFV_knockdown_vs_scramble	down	-2.59	2.61e-05	0.0192	123
hsa-miR-3910_st	MEFV_knockdown_vs_scramble	down	-2.35	3.04e-05	0.0211	173
hsa-miR-378i_st	MEFV_knockdown_vs_scramble	down	-1.57	2.48e-07	0.0010	181
hsa-miR-4659a-5p_st	MEFV_knockdown_vs_scramble	down	-2.37	6.18e-05	0.0368	198
hsa-miR-335_st	MEFV_knockdown_vs_scramble	down	-2.29	7.88e-05	0.0427	243
hsa-miR-378c_st	MEFV_knockdown_vs_scramble	down	-1.4	6.47e-06	0.0074	476
hsa-miR-342-5p_st	MEFV_knockdown_vs_scramble	down	-1.64	4.51e-05	0.0294	492
hsa-miR-378_st	MEFV_knockdown_vs_scramble	down	-1.24	2.71e-06	0.0053	531
hsa-miR-378d_st	MEFV_knockdown_vs_scramble	down	-1.4	1.63e-05	0.0140	558

GSE98940 — THP-1 macrophage mRNA (Agilent)

Publication: PMID 29294109

FMF published-result reproduction

Key run statistics:
- **PIK3CG_log2fc**: -0.303
- **PIK3CG_p_value**: 0.02268
- **de_p_0.05**: 1448
- **de_padj_0.05**: 0
- **genes_tested**: 34755
- **n_case**: 2
- **n_control**: 2
- **top_log2fc**: -3.75
- **top_p_value**: 4.15e-06
- **top_signal**: lnc-ATMIN-3

Published claims:
signal	comparison	expected_direction	status	observed_log2fc	p_value
PIK3CG	miR-204-3p_vs_control	down	reproduced	-0.303	0.0227
IL12B	miR-204-3p_vs_control	down	reproduced	-0.591	0.0024
CXCL10	miR-204-3p_vs_control	down	reproduced	-0.474	0.0051
IL6	miR-204-3p_vs_control	down	partial	-0.442	0.0729

Top ranked signals from this dataset:
signal	comparison	direction	log2fc	p_value	adj_p	rank
lnc-ATMIN-3	miR-204-3p_vs_control	down	-3.75	4.15e-06	0.1442	25
lnc-SPTBN5-2	miR-204-3p_vs_control	down	-2.8	1.83e-05	0.3182	91
LOC102725316	miR-204-3p_vs_control	down	-3.17	0.0005	0.6151	175
lnc-SLC30A10-5	miR-204-3p_vs_control	down	-2.84	0.0003	0.5782	193
TTTY4C	miR-204-3p_vs_control	up	2.93	0.0011	0.6699	307
LOC286068	miR-204-3p_vs_control	up	2.46	0.0003	0.5782	314
COL16A1	miR-204-3p_vs_control	down	-2.66	0.0008	0.6151	347
CD5	miR-204-3p_vs_control	up	2.78	0.0013	0.6734	367
CER1	miR-204-3p_vs_control	up	2.01	0.0001	0.5782	393
NR1H4	miR-204-3p_vs_control	down	-1.91	8.01e-05	0.5782	394
lnc-C10orf40-1	miR-204-3p_vs_control	down	-2.98	0.0029	0.8664	420
LOC101928819	miR-204-3p_vs_control	down	-2.51	0.0010	0.6687	435

GSE4090 — HUVEC mRNA (two-colour cDNA)
Publication: PMID 16188942

Key run statistics:
- **cell_cycle_hits**: 8
- **de_late_p_0.05**: 1599
- **de_late_padj_0.05**: 211
- **genes_tested**: 12421
- **neutrophil_hits**: 2
- **samples**: 16
- **time_genes_p_0.05**: 3070
- **top_late_log2fc**: 3.456
- **top_late_p_value**: 1.313e-07
- **top_late_signal**: LCP1

Published claims:
signal	comparison	expected_direction	status	observed_log2fc	p_value
LCP1	colchicine_12_24h_vs_vehicle	changed	reproduced	3.46	1.31e-07

FMF published-result reproduction

Top ranked signals from this dataset:

signal	comparison	direction	log2fc	p_value	adj_p	rank
LCP1	colchicine_12_24h_vs_vehicle	up	3.46	1.31e-07	0.0014	15
GIMAP1-GIMAP5///GIMAP1///GIMAP5///LTBP4	colchicine_12_24h_vs_vehicle	down	-3.08	3.58e-07	0.0019	29
GIMAP1-GIMAP5///GIMAP1///GIMAP5	colchicine_12_24h_vs_vehicle	down	-2.67	1.32e-06	0.0028	58
STC2	colchicine_12_24h_vs_vehicle	up	2.38	9.92e-07	0.0028	74
PODXL	colchicine_12_24h_vs_vehicle	up	2.12	1.13e-06	0.0028	104
KITLG	colchicine_12_24h_vs_vehicle	up	2.48	8.95e-06	0.0057	109
LOC100126784///NAV2	colchicine_12_24h_vs_vehicle	up	2.15	2.98e-06	0.0045	122
MAF	colchicine_12_24h_vs_vehicle	up	2.14	5.54e-06	0.0057	146
SLC40A1	colchicine_12_24h_vs_vehicle	down	-2.54	4.70e-05	0.0122	157
MIR503HG	colchicine_12_24h_vs_vehicle	down	-2.04	9.30e-06	0.0057	183
KLHDC10	colchicine_12_24h_vs_vehicle	down	-3.09	0.0005	0.0366	188
MEOX2	colchicine_12_24h_vs_vehicle	down	-2.14	2.04e-05	0.0085	194

Cross-dataset reading for FMF

- The only direct FMF-vs-healthy patient comparison is the PBMC miRNA set (GSE111311). It reproduces the published seven-miRNA signature: miR-144-3p, miR-4454 and miR-451a up; let-7d-5p, miR-107 and miR-148b-3p down; miR-21-5p up.
- GSE79954 independently supports the miRNA layer: miR-4520a-3p is the top miRNA after MEFV knockdown, linking pyrin loss to miRNA regulation.
- GSE17732 shows the flare programme shared by FMF and PFAPA: complement (C1QB, C2, SERPING1), IL-1/IL-18 (IL1B, IL1RN, CASP1, IL18RAP), and IFN-induced (AIM2, CXCL10) genes up, with T-cell transcripts (CD3D, CD3E, CD8B) down. The FMF flare arm has only two samples.
- GSE98940 supports a PI3K-gamma brake: miR-204-3p overexpression lowers PIK3CG and TLR4-related cytokines, but n=2 per group makes this nominal.
- GSE4090 supplies a colchicine transcriptional response resource; it is context for confounding, not an FMF patient result.

Limitations

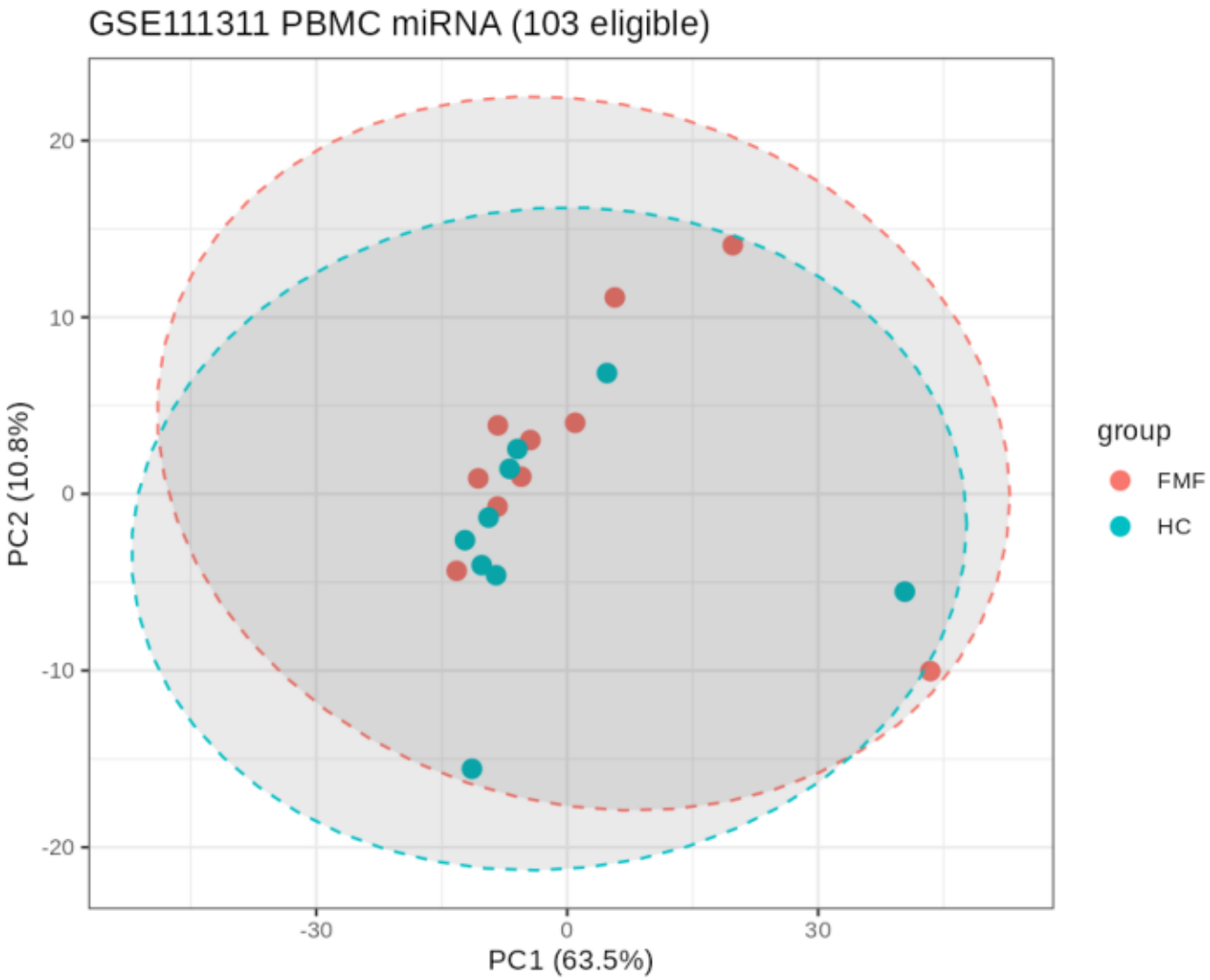
- No controlled-access EGA monocyte RNA-seq, genotype, severity, or colchicine-resistance labels are used in this run.
- GSE111311 has 9 healthy controls in GEO although the paper describes 10 matched pairs; one affected sample is unmatched. Fold changes therefore differ modestly from the publication even when directions and p-values agree.
- GSE17732 contains only two FMF flare samples; the FMF arm is exploratory.
- GSE98940 has two replicates per group and no BH-significant genes; only nominal directional evidence is claimed.
- GSE4090 is a two-colour HUVEC resource with sparse dose/time replication; it is used qualitatively.
- These results are research-only and are not a clinical classifier.

Reproduce

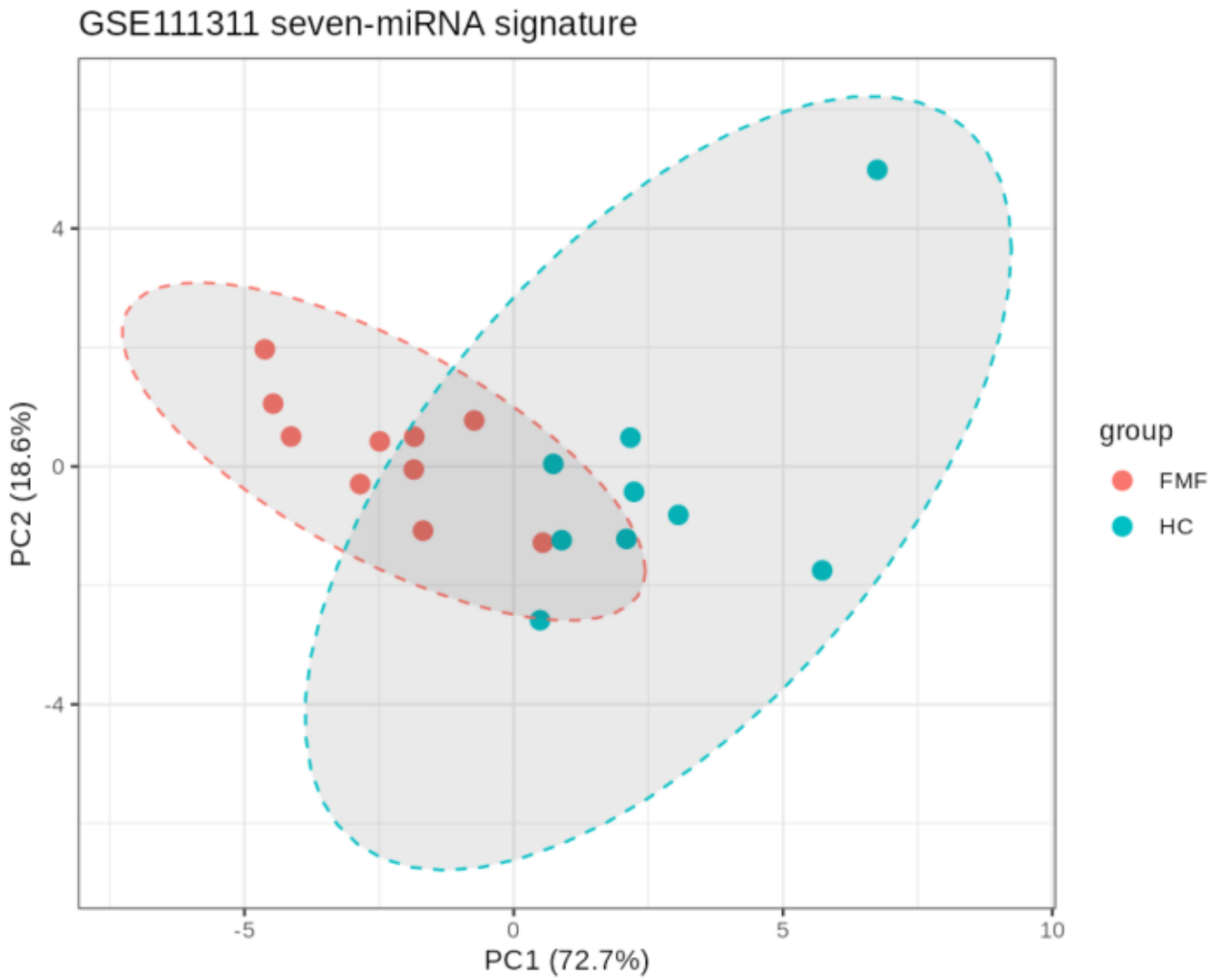
```
source scripts/setup_env.sh
.venv/bin/snakemake -s workflow/Snakefile -j 12 --rerun-incomplete
```

Artifacts: `results/reproduction/` (per-dataset tables and figures), `results/reproduction/signals.tsv`, `results/reproduction/verification.tsv`.

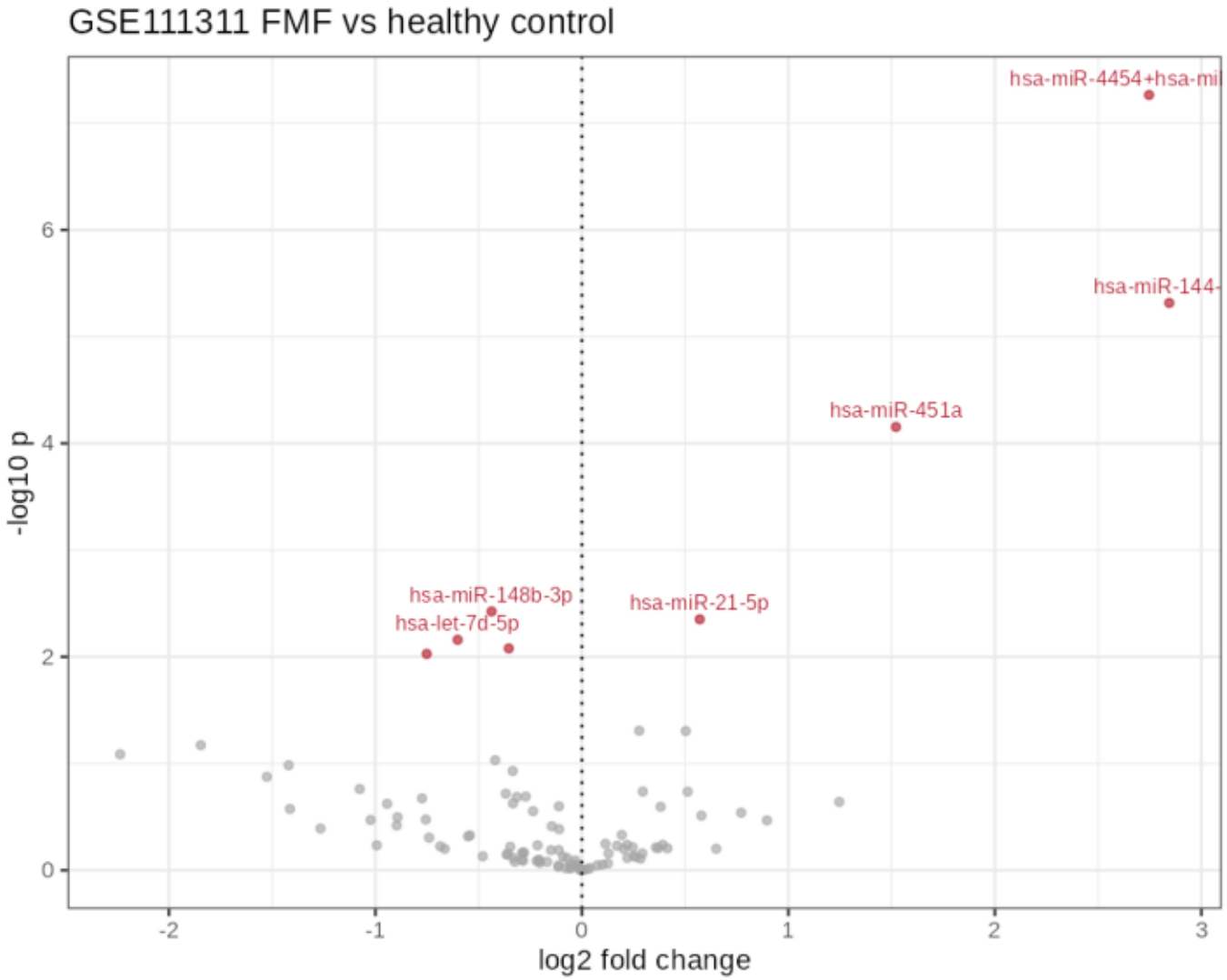
GSE111311 — pca.png



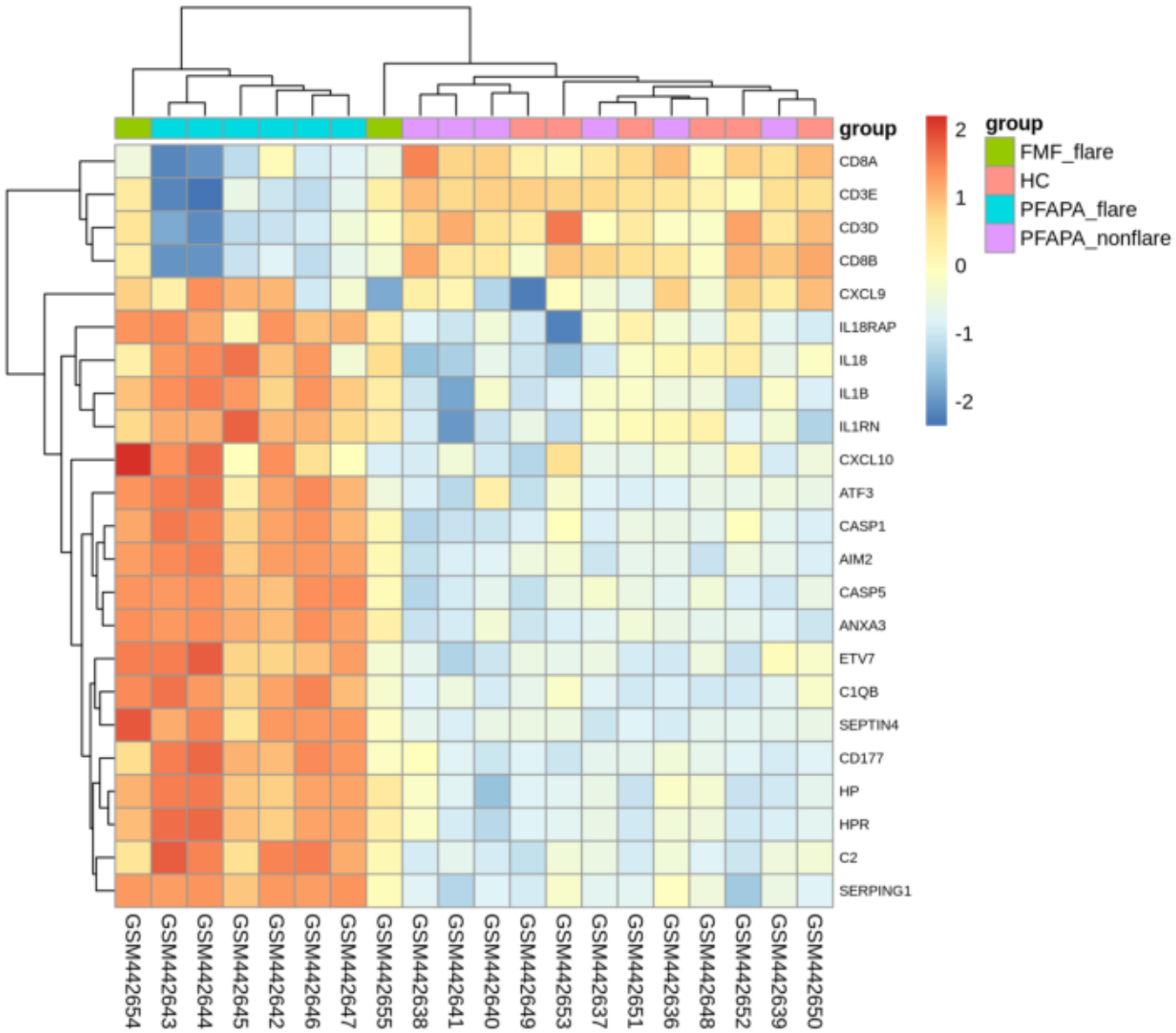
GSE111311 — pca7.png



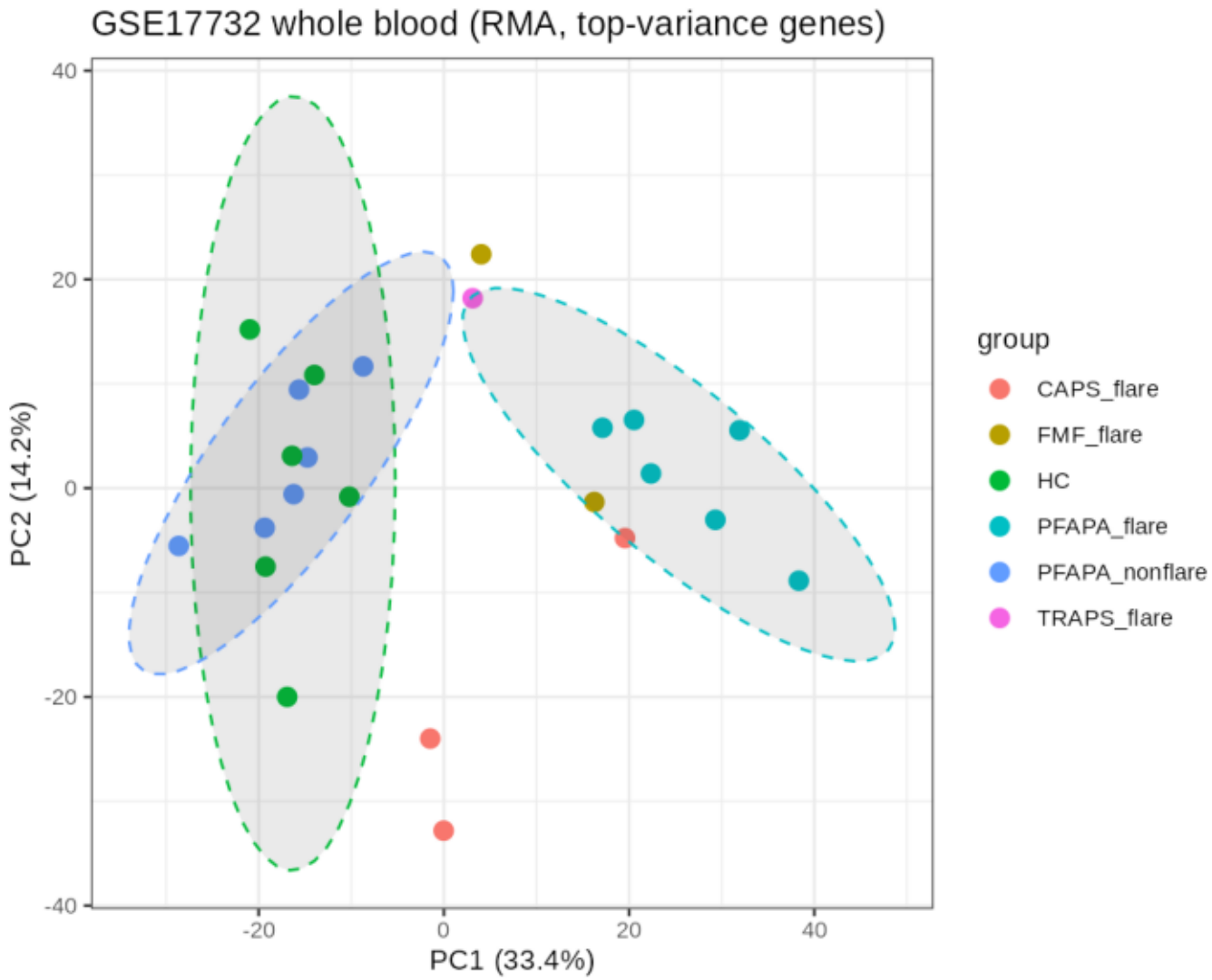
GSE111311 — volcano.png



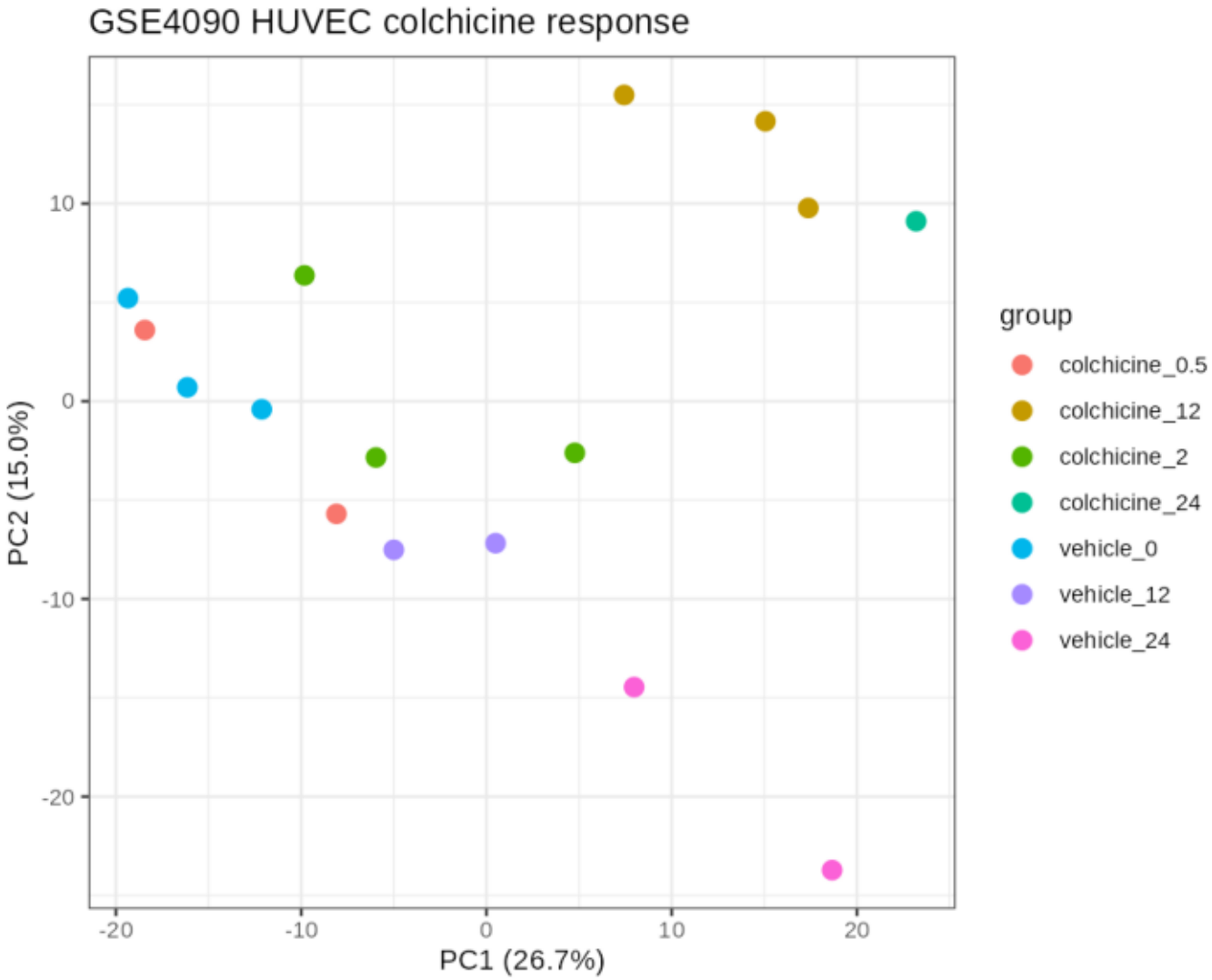
GSE17732 — key_gene_heatmap.png



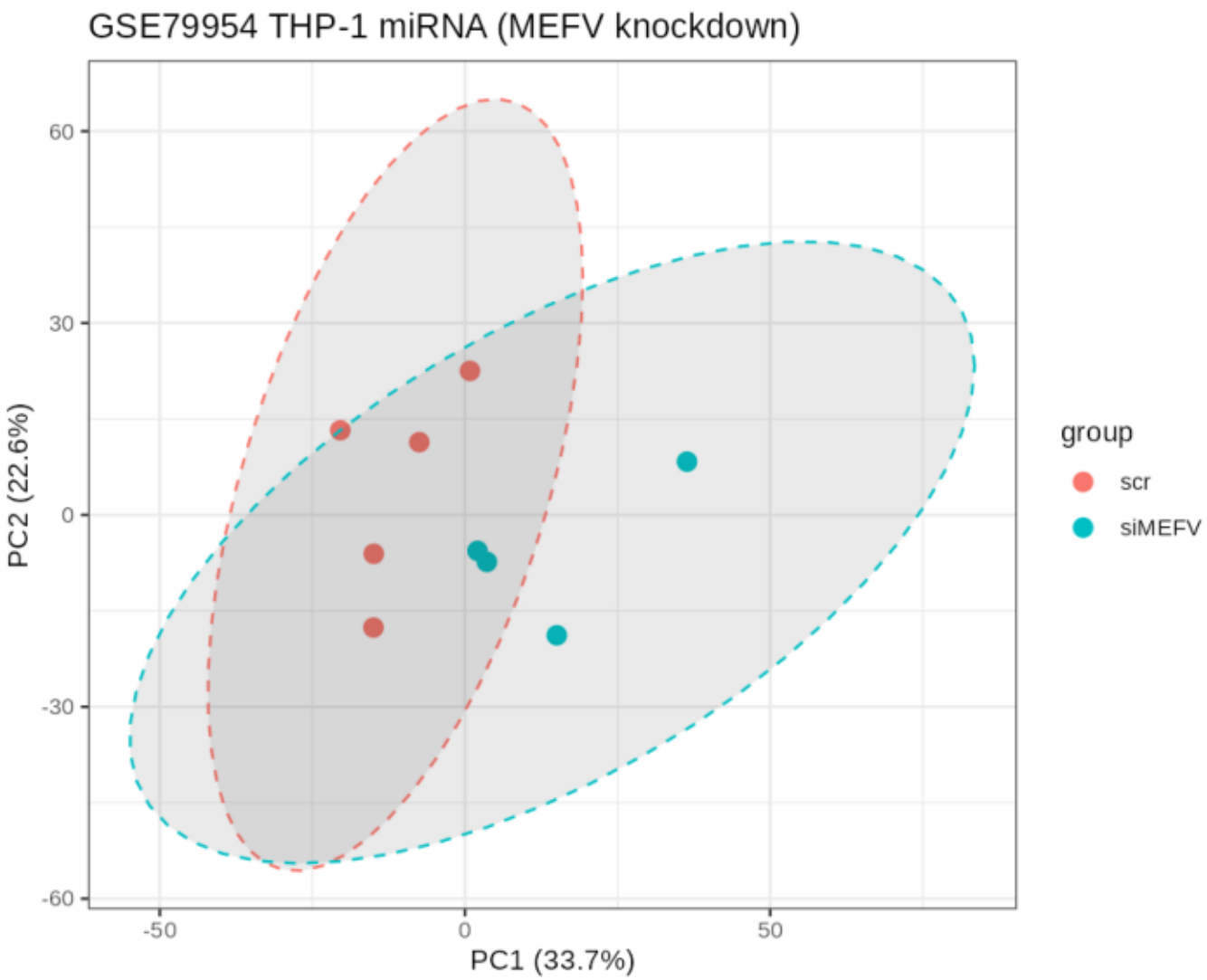
GSE17732 — pca.png



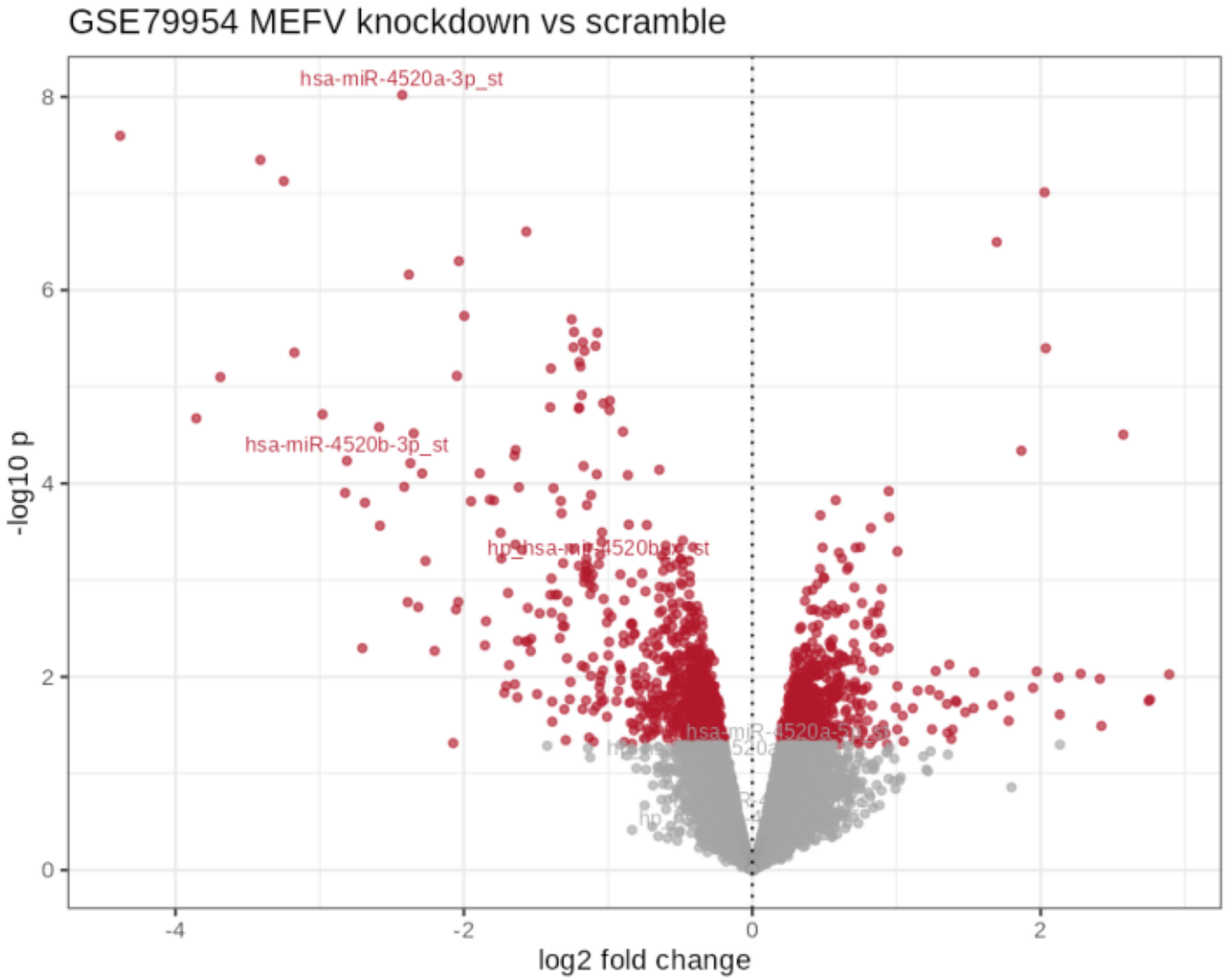
GSE4090 — pca.png



GSE79954 — pca.png



GSE79954 — volcano.png



GSE98940 — pca.png

