Fig. S1 Cohorts, statistical units, and analytical roles

Technical overview of complementary evidence layers; the arrangement does not imply a proven causal cascade.

1 Bulk lung cohorts

Statistical unit: sample / cohort

Source: GSE117261, GSE113439, GSE53408

2 Single-cell localization

Statistical unit: cell class / donor

Source: GSE169471

3 True-donor endothelial analysis

Statistical unit: donor pseudobulk

Source: GSE169471; 8 donors

4 External endothelial / PAEC

Statistical unit: donor / cohort

Source: GSE210248 + four PAEC cohorts

5 Vascular-state heterogeneity

Statistical unit: sample / cell state

Source: Feng et al. human PH

single-cell atlas

6 Spatial tissue context

Statistical unit: ROI / donor

Source: GSE256539; 217

ROIs

7 YAP/TAZ perturbation

Statistical unit: contrast / gene / signature

Source: GSE163456

8 Public HUVEC cistrome

Statistical unit: peak / motif / locus

Source: GSE163458

9 HPAEC experimental validation

Statistical unit: experimental replicate

Source: HPAEC

CHMH is a secondary descriptive analysis within the bulk evidence layer, not a central stage or independent subtype.

Fig. S2 Signature composition, detectable coverage, and gene-set overlap

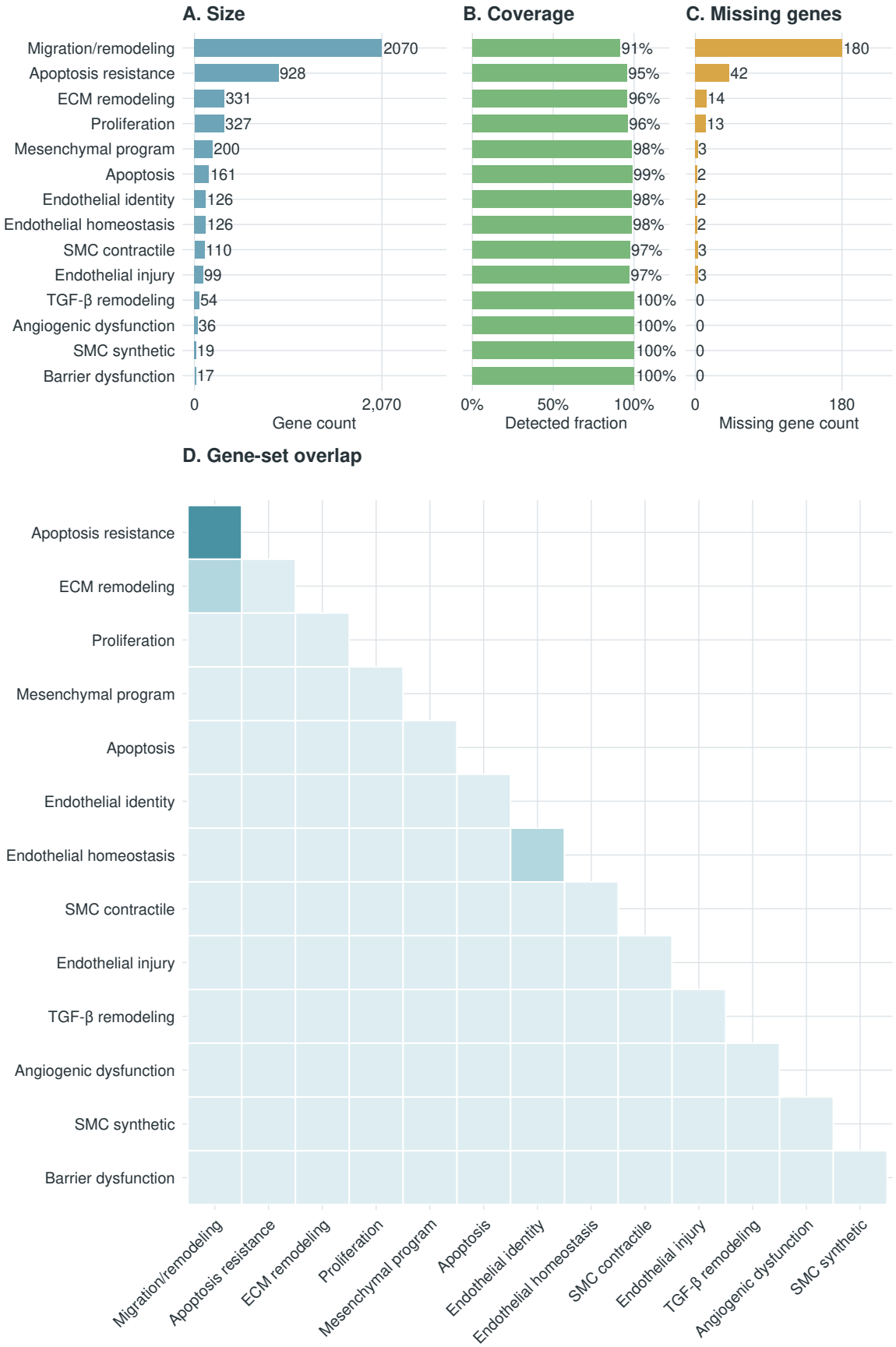


Fig. S3 Bulk coupling robustness across effect definitions

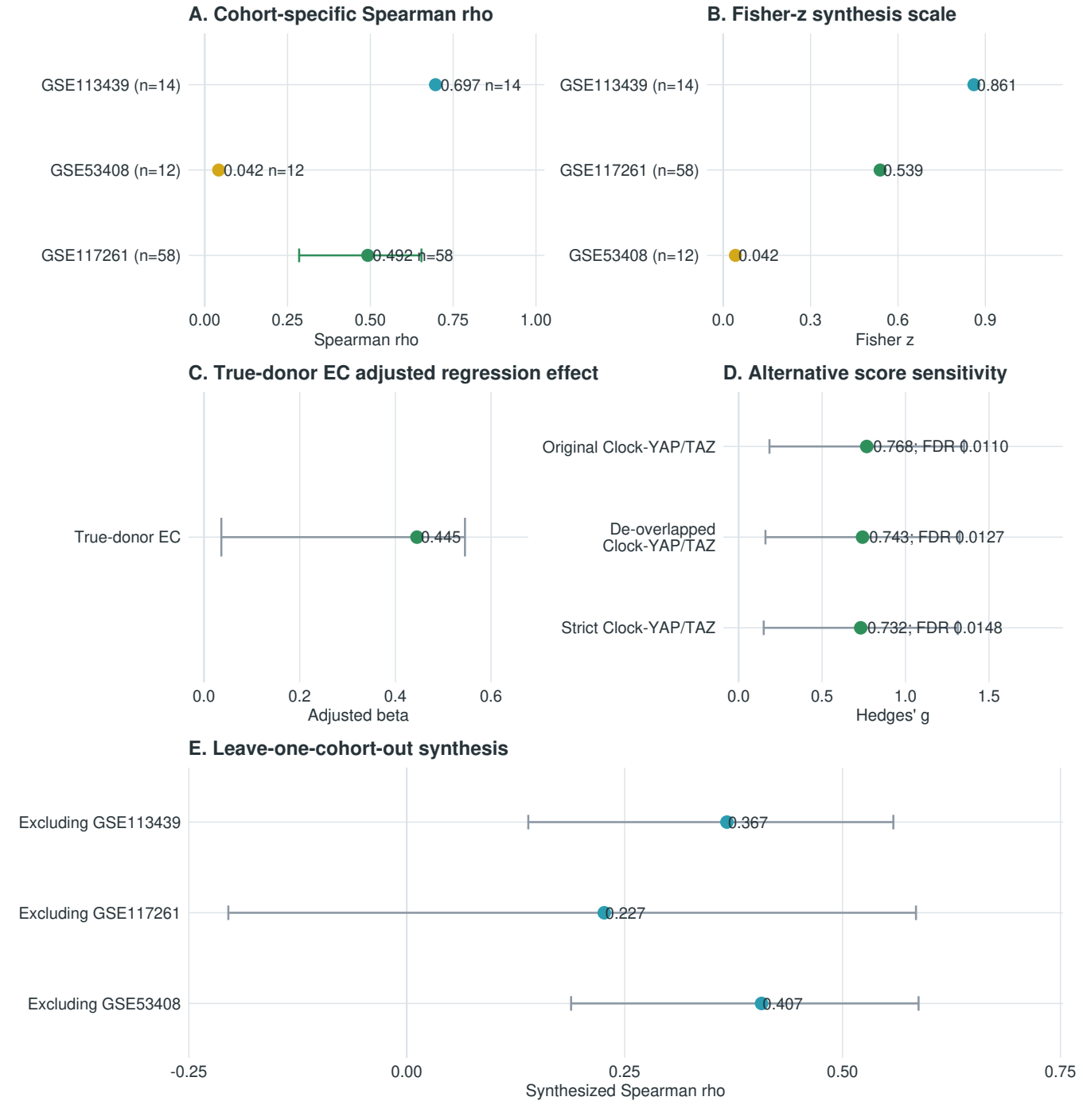
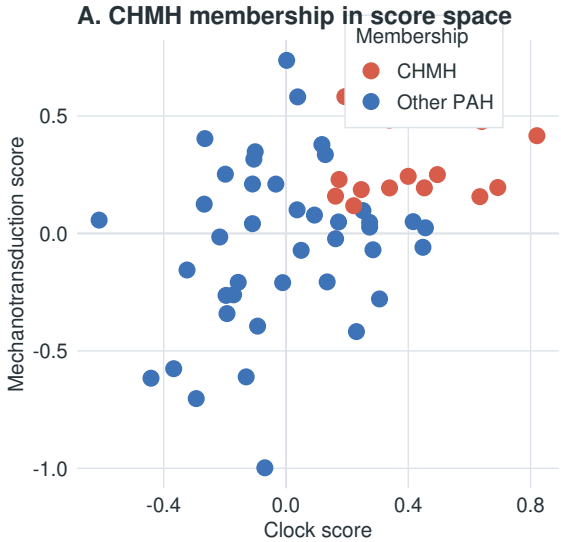
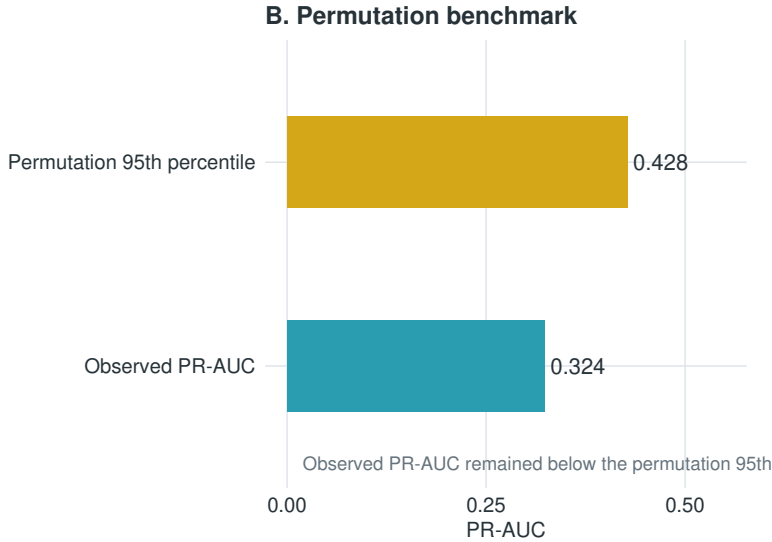
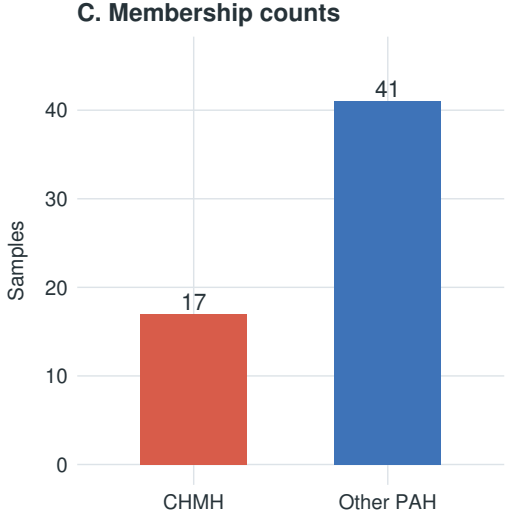


Fig. S4 CHMH classification, permutation benchmark, and membership sensitivity







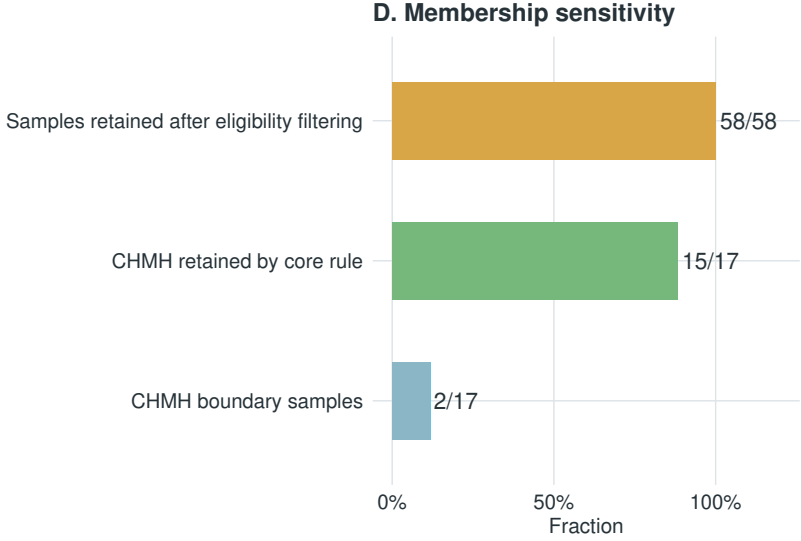
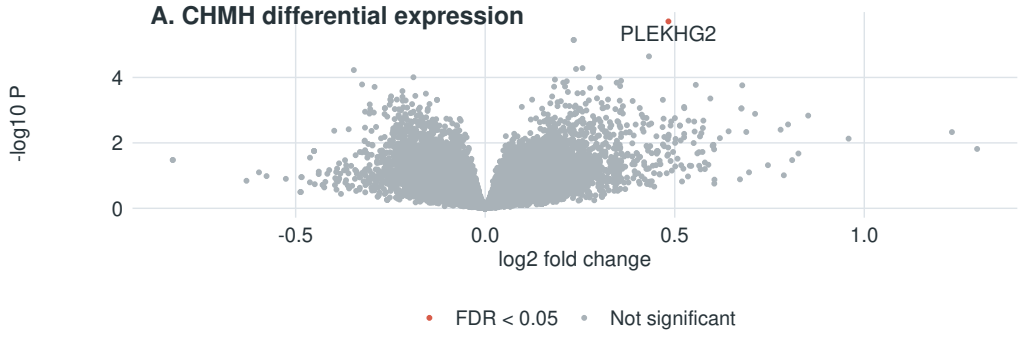
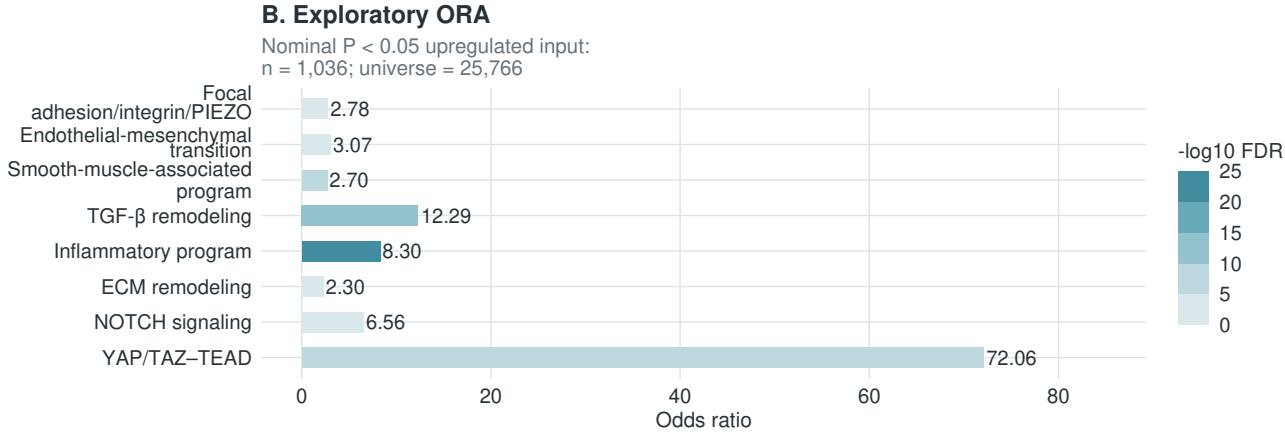
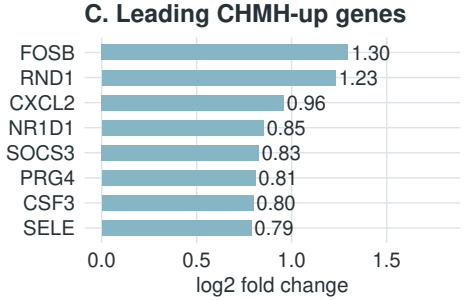
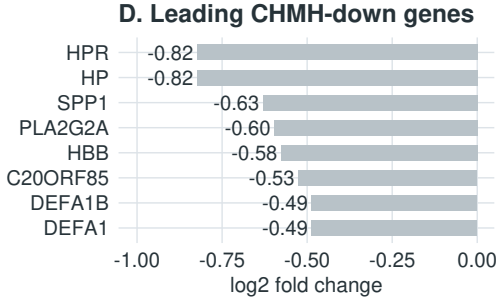


Fig. S5 CHMH expression, exploratory enrichment, and migration/remodeling response









E. Program-response statistics

FDR	Permutation P	Welch P
0.0148	0.0115	0.00370

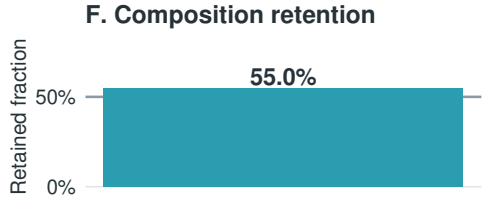


Fig. S6 True-donor EC coverage, eligibility, and influence diagnostics

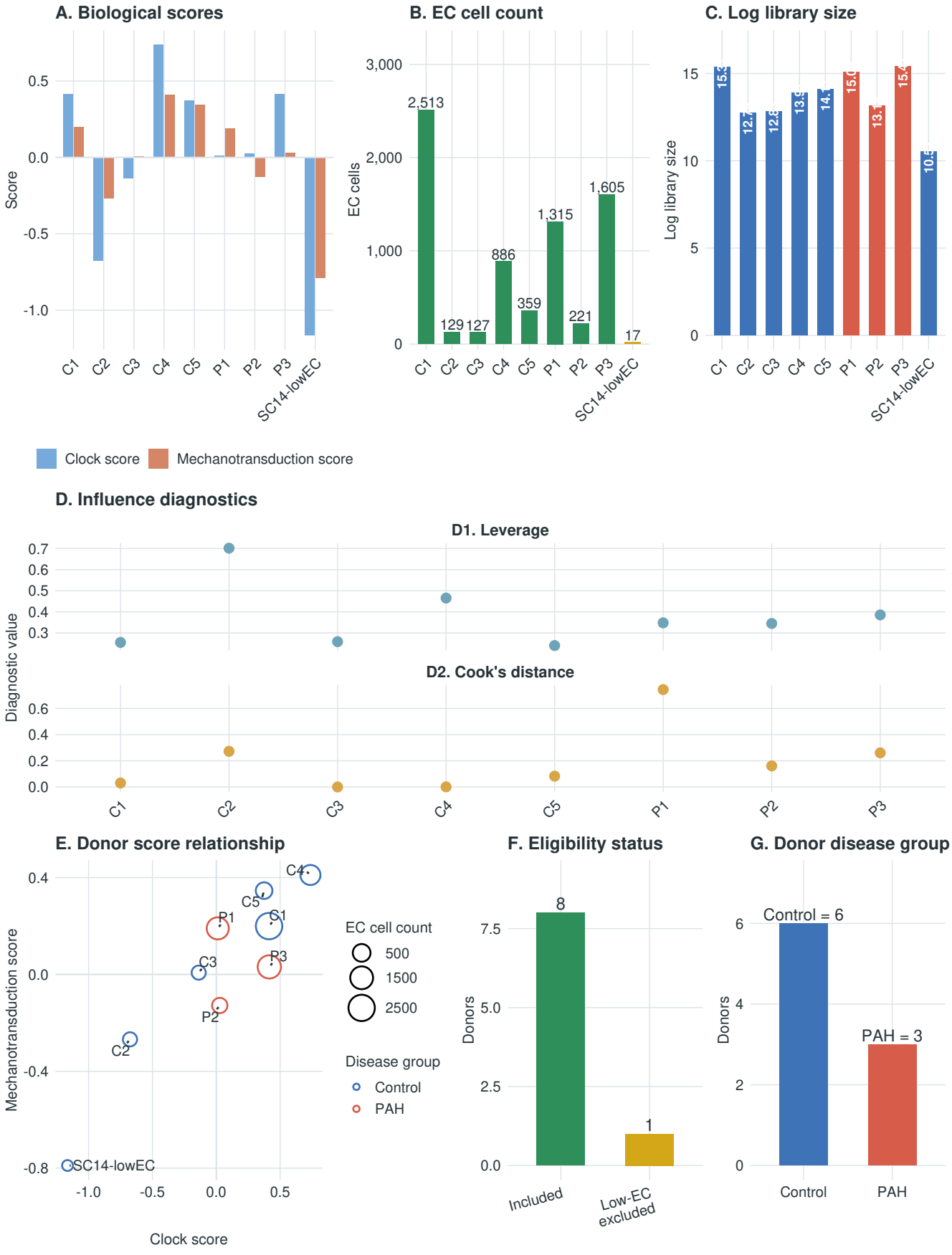


Fig. S7 Exploratory donor-aware evidence across non-endothelial cell classes

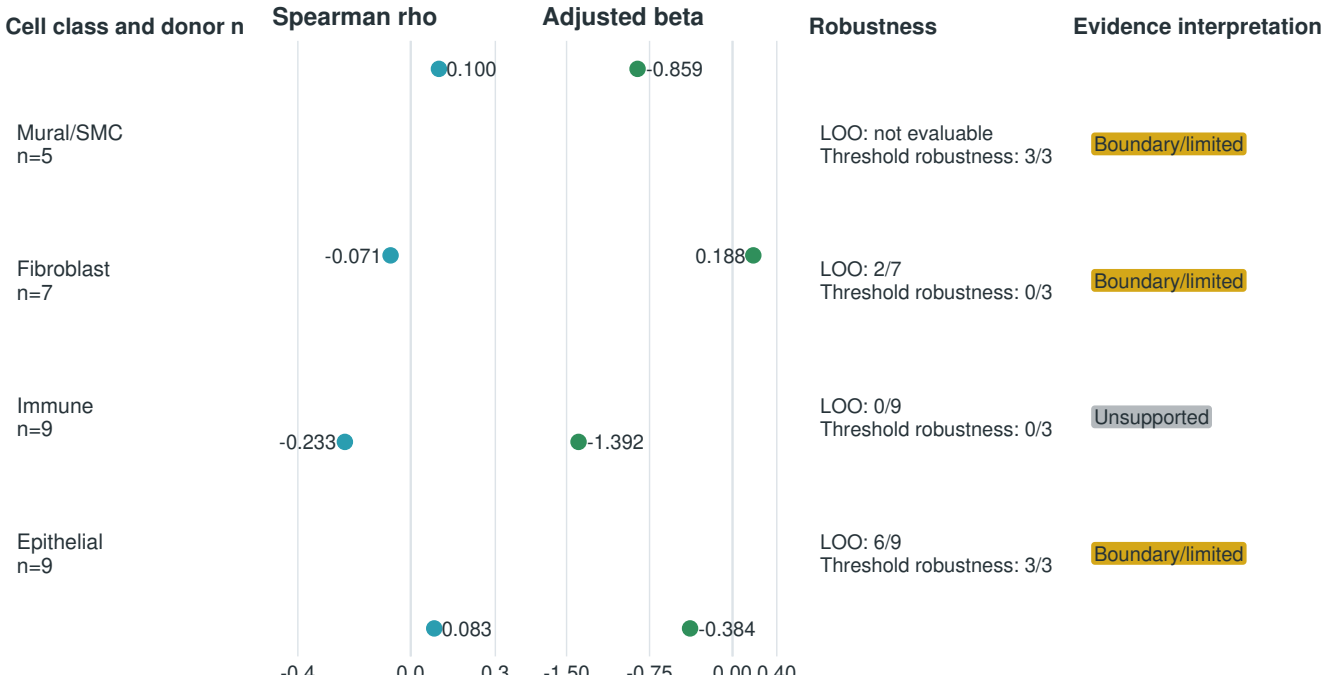


Fig. S8 True-donor endothelial coverage and sensitivity diagnostics

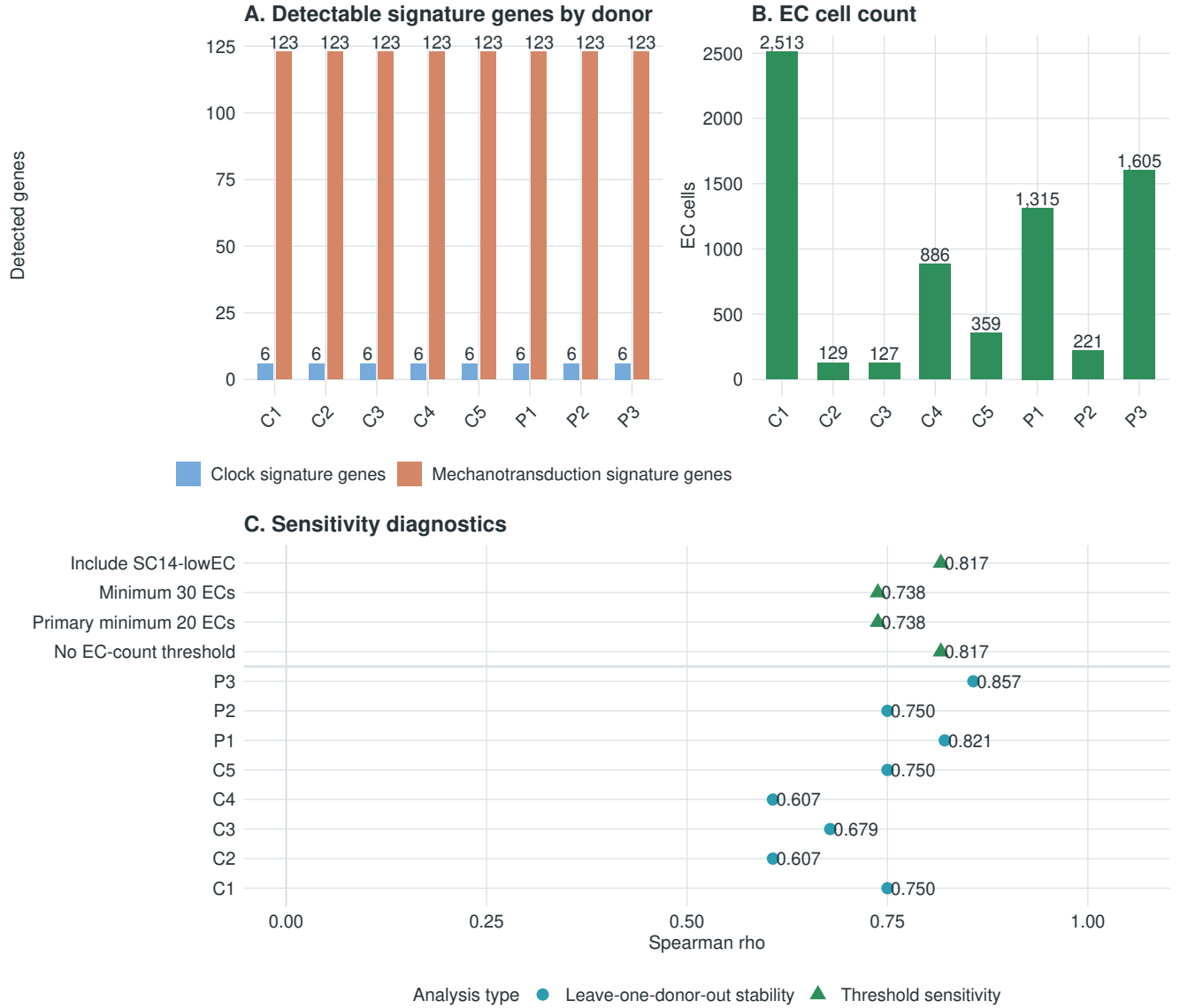


Fig. S9 True-donor EC robustness and sensitivity analyses

Fig. S10 External EC and PAEC cohort-specific evidence

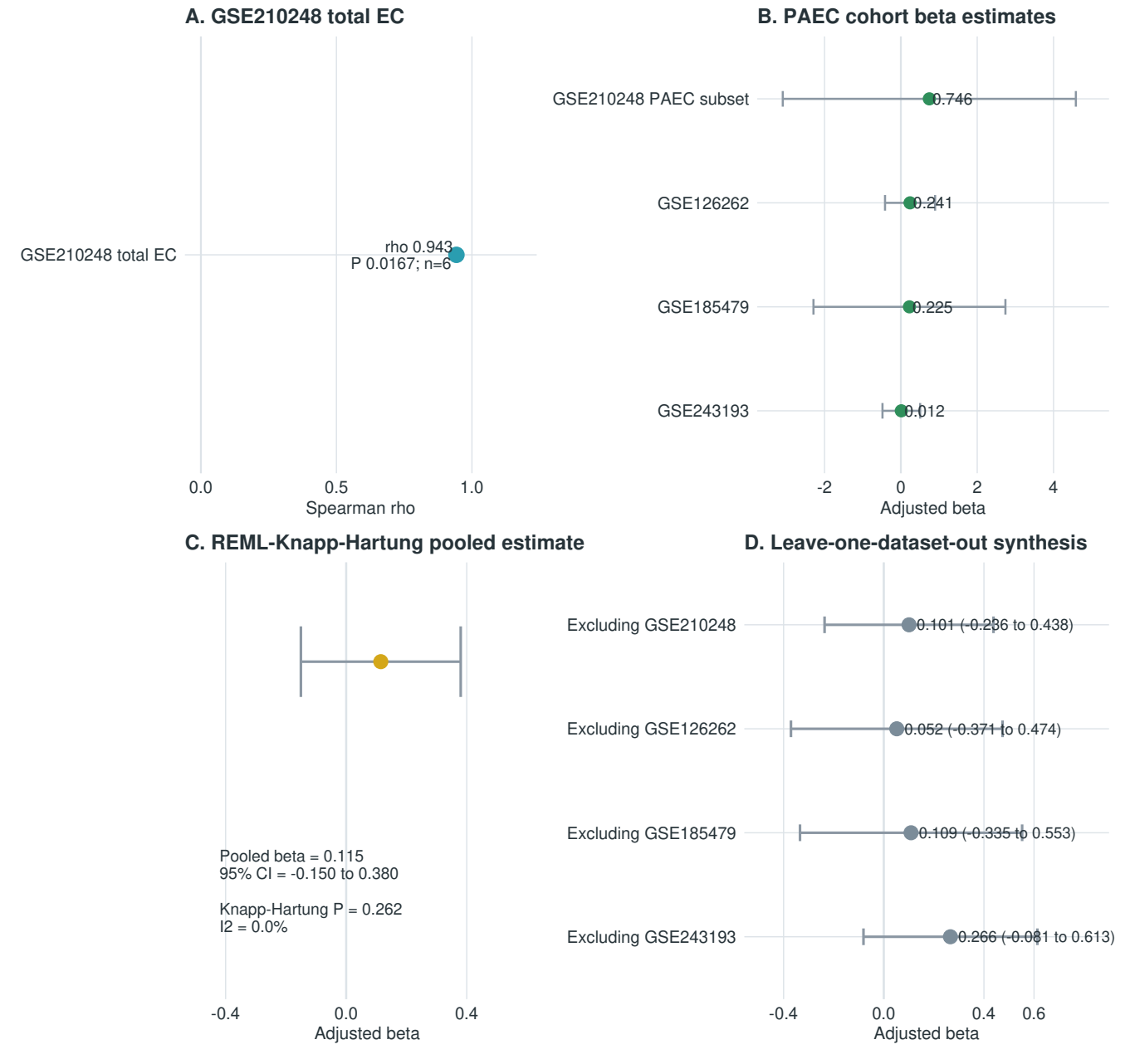


Fig. S11 Sample-level evidence for vascular cell-state-specific Clock-mechanotransduction coupling

Each point represents one sample-level unit; dashed lines are descriptive group-specific trends.

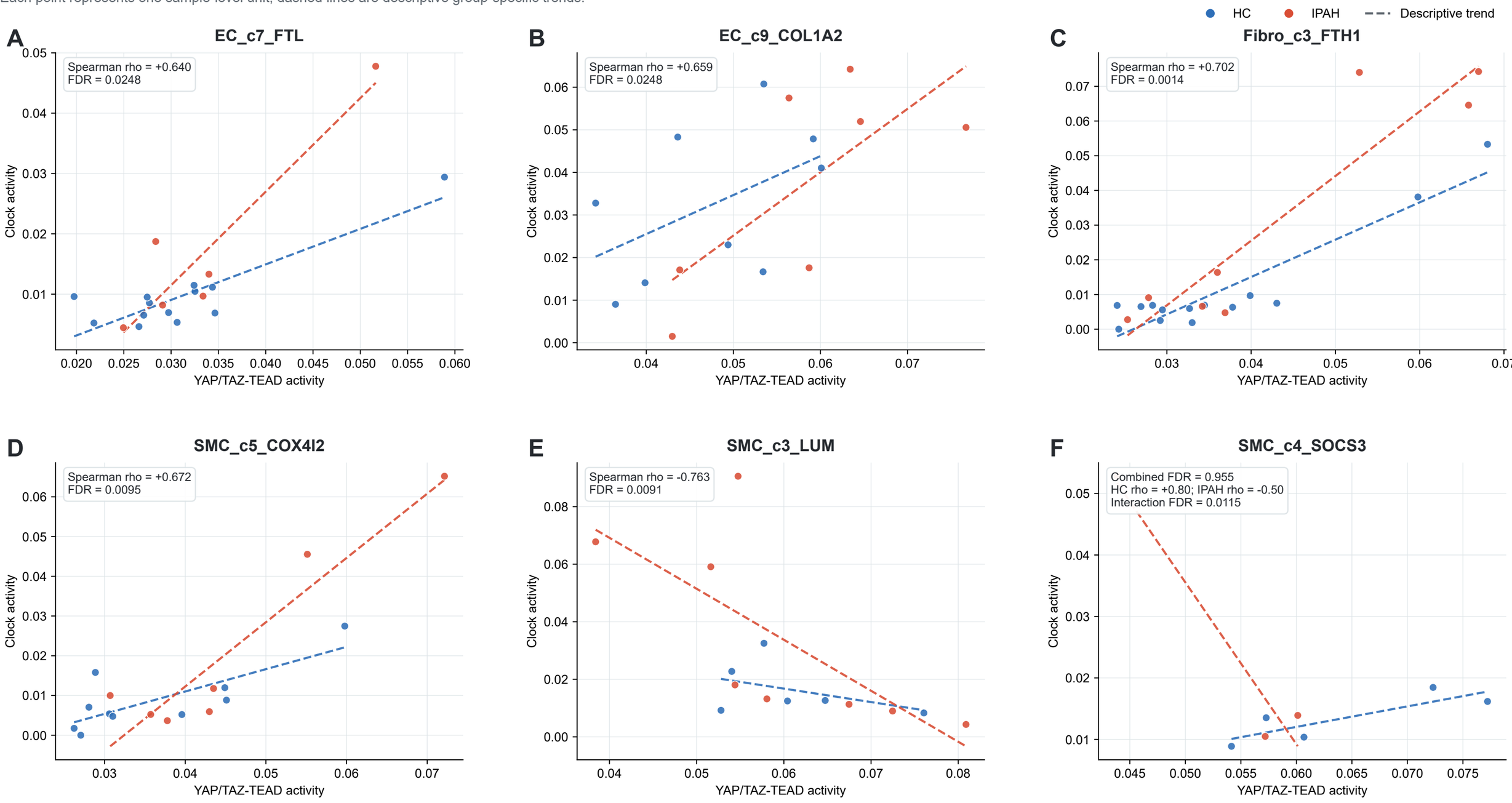
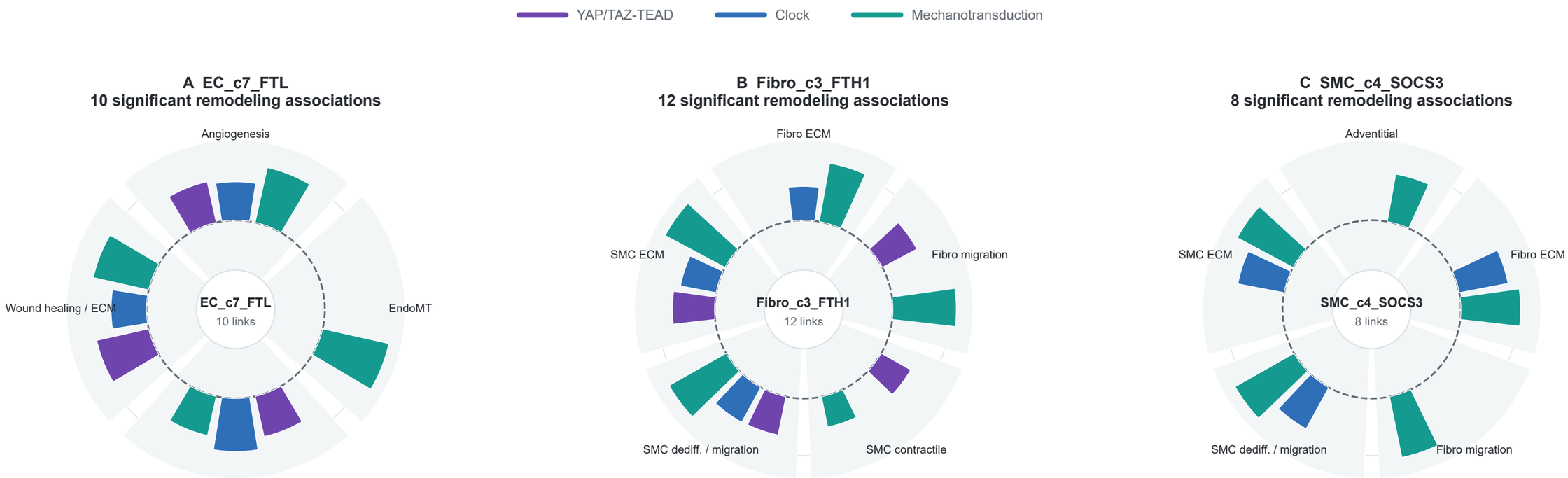


Fig. S12 Extended remodeling fingerprints and subtype context

Signed radial associations are shown above; subtype effect summaries are shown below.



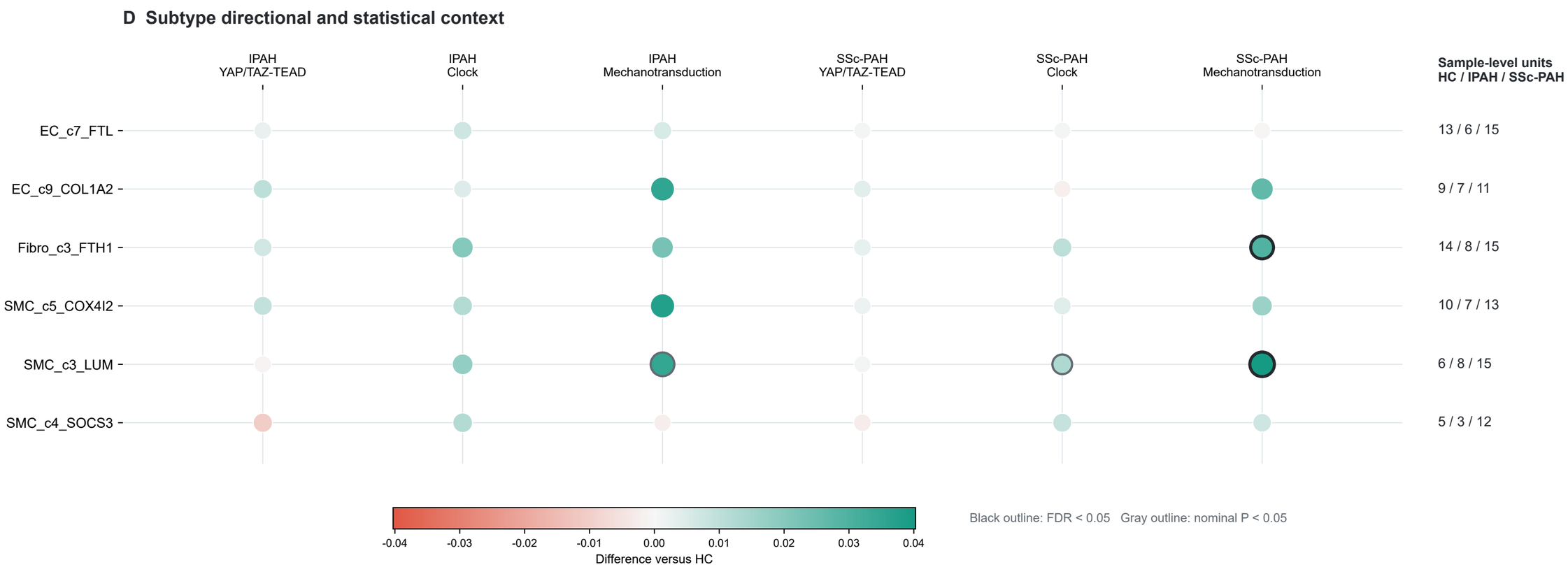


Fig. S13 NMF rank stability

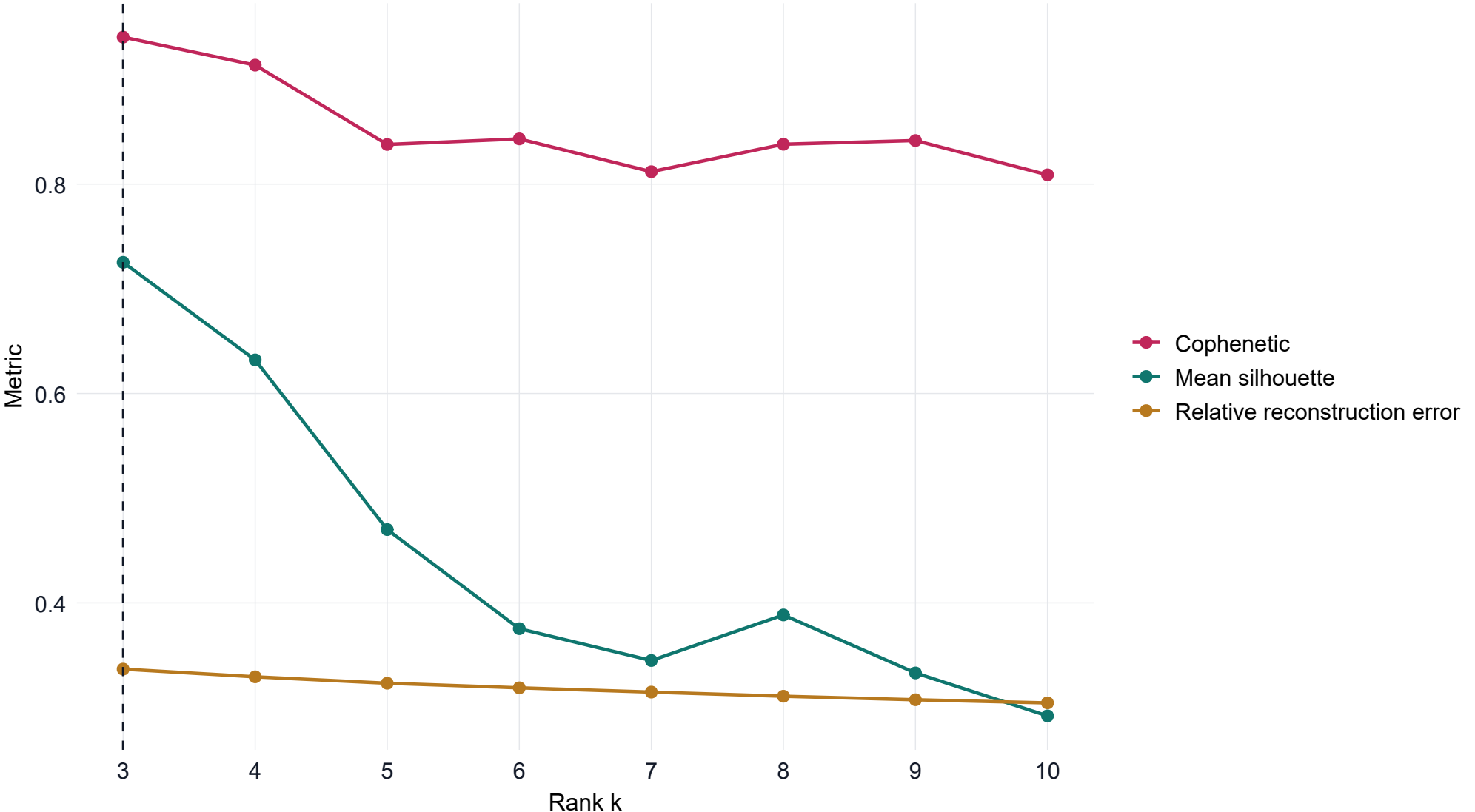


Fig. S14 NMF bootstrap program stability

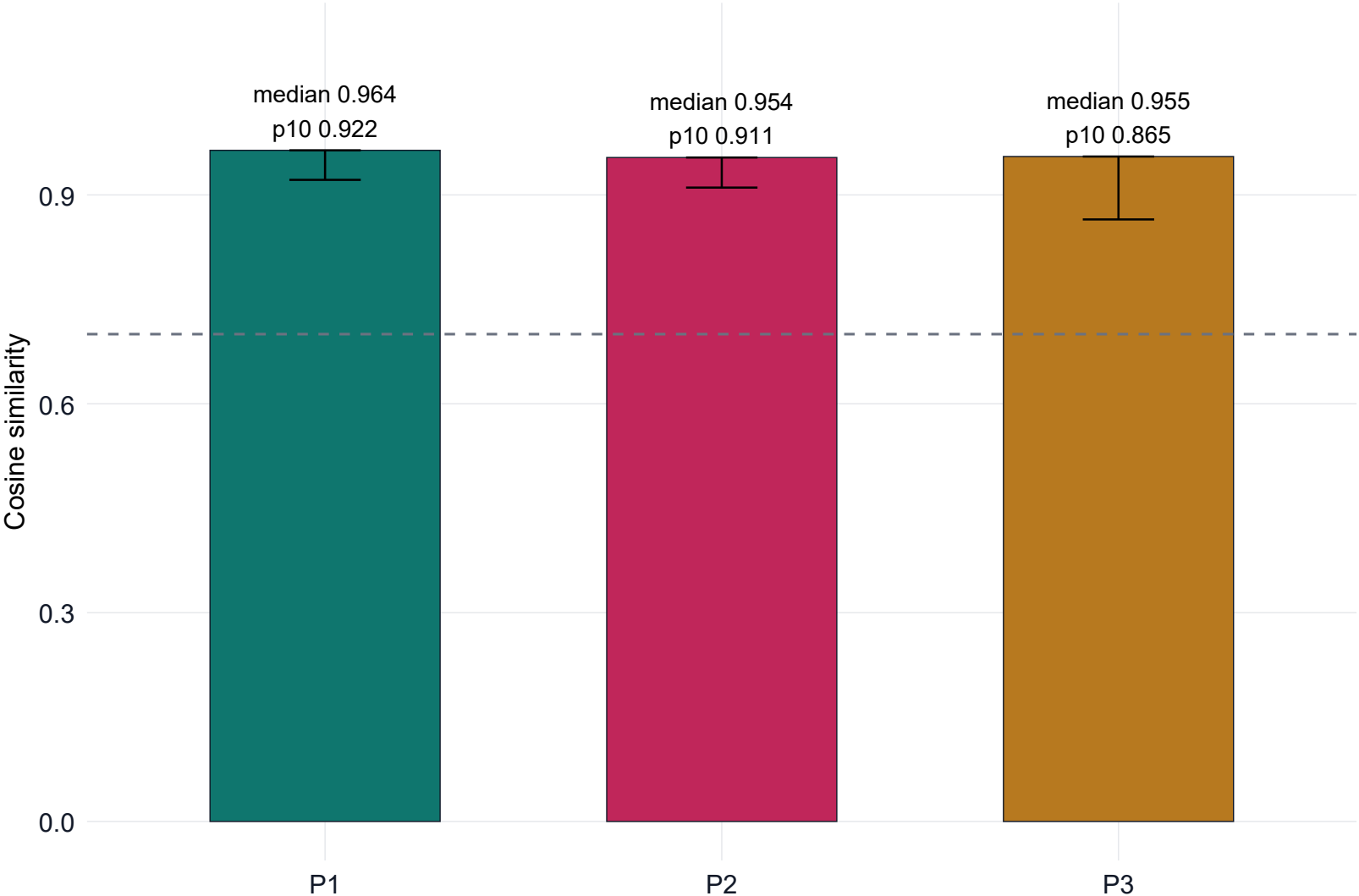


Fig. S15 ROI molecular-state manifold and technical covariates

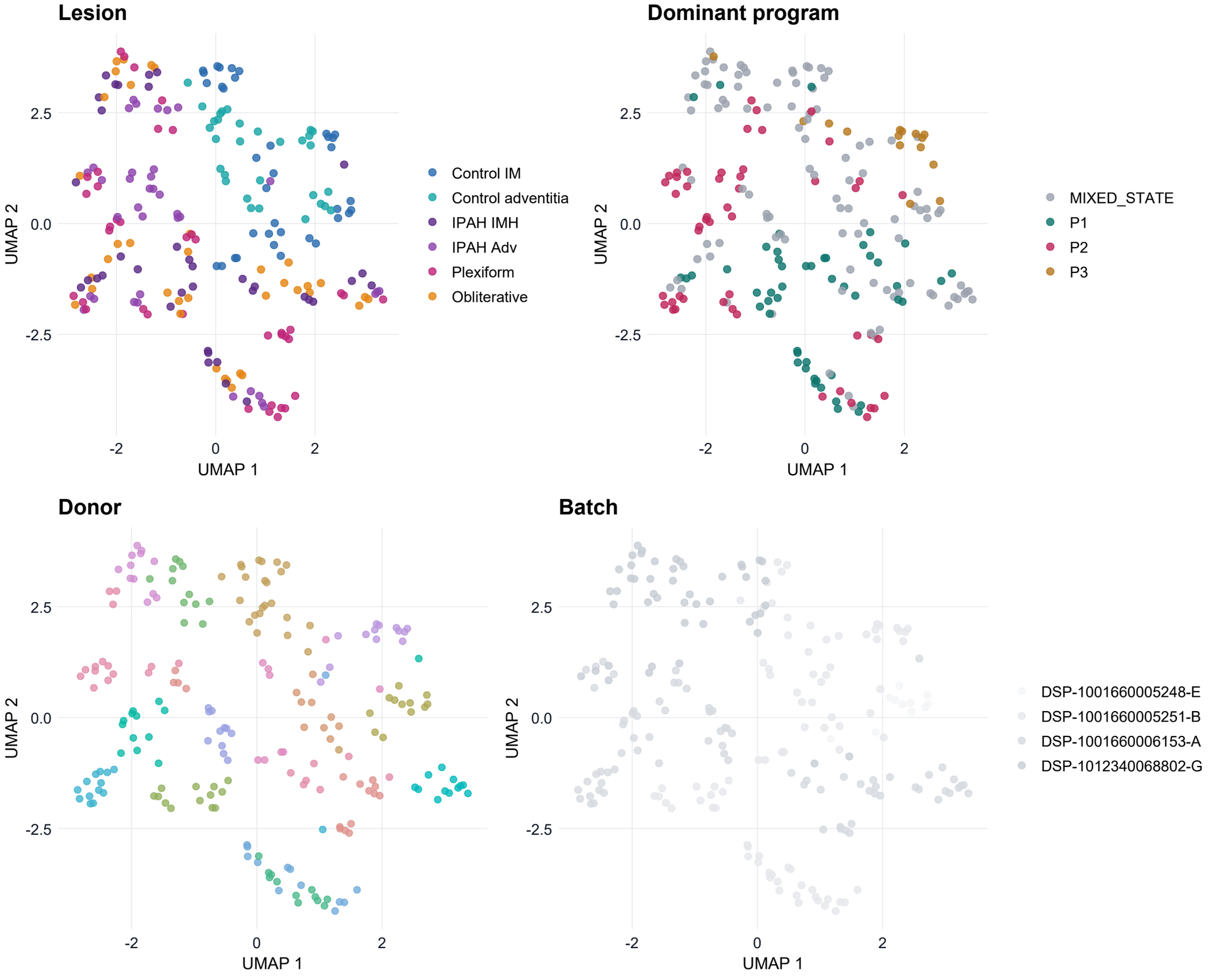


Fig. S16 Sampling architecture

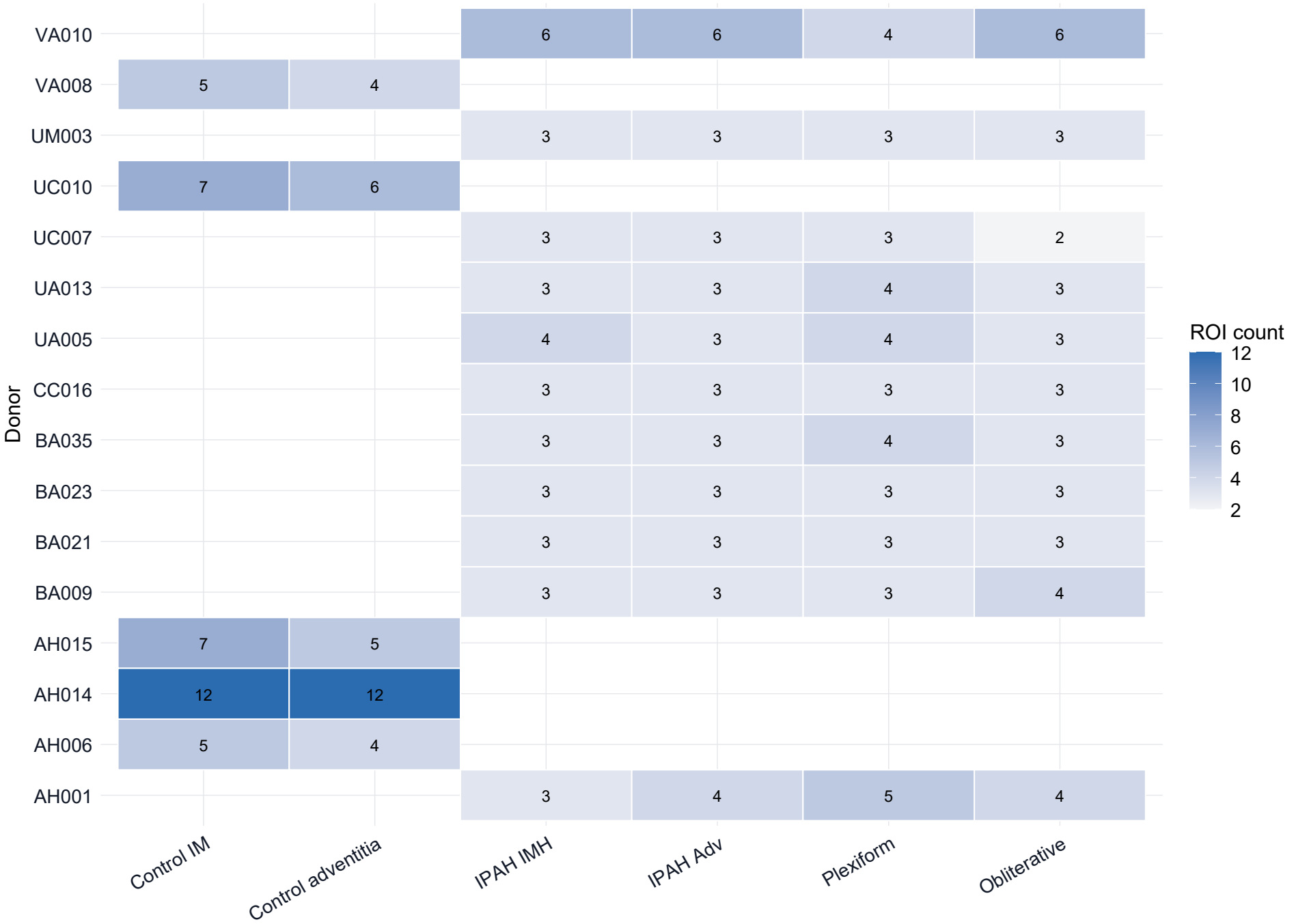


Fig. S17 Full program model contrasts

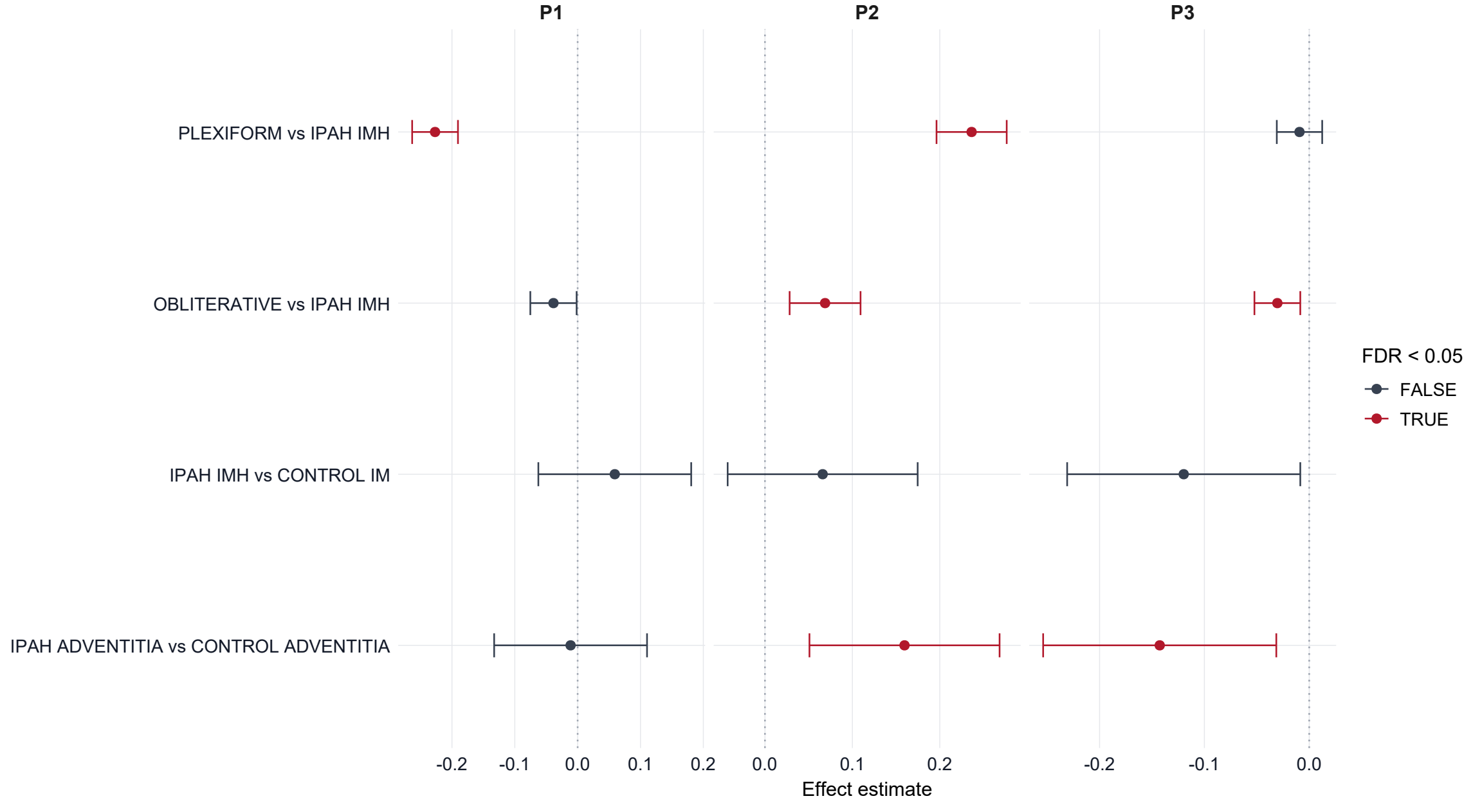
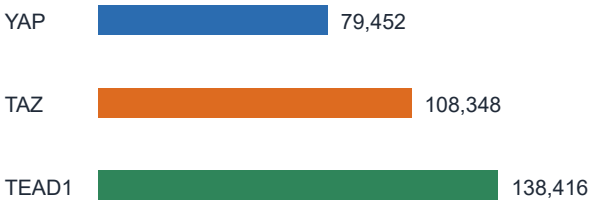


Fig. S18. Extended cistromic quality control and locus-level support for CRY1 and CLOCK

GSE163458 HUVEC YAP/TAZ/TEAD1 ChIP-seq with independent chromatin support at candidate CRY1 and CLOCK regulatory regions

A Peak-set and matched-input QC



Peak totals from source peak sets

Matched input was included for each ChIP-seq factor

Peak-set sizes and input matching provide technical context

B Extended intersection structure

YAP: 29,778

TAZ: 49,714

TEAD1: 75,055

YAP+TAZ: 2,752

YAP+TEAD1: 8,504

TAZ+TEAD1: 18,127

YAP+TAZ+TEAD1: 31,475

Three-factor overlap: 31,475 regions

C TEAD motif-position detail

CRY1: 75 motif-bearing rows; 57 summit-near/proximal

CLOCK: 23 motif-bearing rows; 18 summit-near/proximal

Motif coordinates and distances are table-derived.

Candidate regions; no cis-element causality claimed.

CRY1 prioritized TEAD motif: +3 bp from TEAD1 summit

CLOCK prioritized TEAD motif: +47 bp from TEAD1 summit

D Extended CRY1 locus context

TEAD1: chr12:107,091,359-107,091,915; summit 107,091,490

YAP: chr12:107,092,075-107,092,786; summit 107,092,245

TEAD1: chr12:107,092,152-107,094,618; summit 107,094,299

YAP: chr12:107,093,891-107,094,547; summit 107,094,300

TAZ: chr12:107,092,291-107,094,653; summit 107,094,304

Prioritized CRY1 candidate region

TEAD motif: +3 bp from TEAD1 summit

Independent TEAD4 support: direct overlap

E Extended CLOCK locus context

TEAD1: chr4:55,545,040-55,545,460; summit 55,545,309

YAP: chr4:55,545,634-55,545,854; summit 55,545,705

TAZ: chr4:55,545,542-55,546,342; summit 55,545,958

TEAD1: chr4:55,545,770-55,546,122; summit 55,545,943

YAP: chr4:55,545,994-55,546,236; summit 55,546,091

Prioritized CLOCK candidate region

TEAD motif: +47 bp from TEAD1 summit

Independent TEAD4 HepG2 peak: not detected

F Independent open/active chromatin support

CRY1 HUVEC H3K27ac: overlap count = 1

CRY1 lung ATAC: overlap count = 4

CLOCK HUVEC H3K27ac: overlap count = 2

CLOCK lung ATAC: overlap count = 6

CRY1: H3K27ac and ATAC overlap observed

CLOCK: H3K27ac and ATAC overlap observed

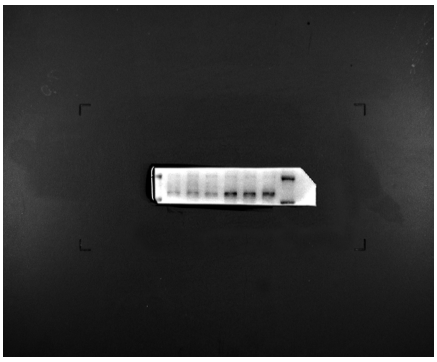
Primary cistromic dataset: GSE163458 (HUVEC). YAP 79,452 | TAZ 108,348 | TEAD1 138,416 | YAP/TAZ/TEAD1 triple overlap 31,475.

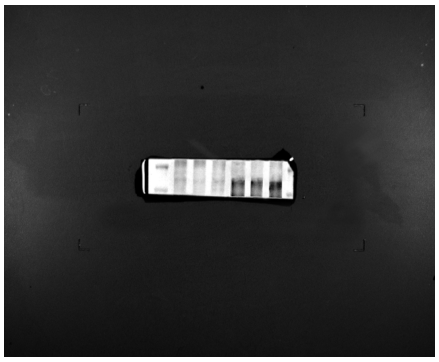
Fig. S19. Source Western blot images for CRY1 and CLOCK following constitutive YAP/TAZ activation in HPAECs

Grouping in this column: the first three samples belong to Con+EV, and the last three samples belong to YAP-S127A.

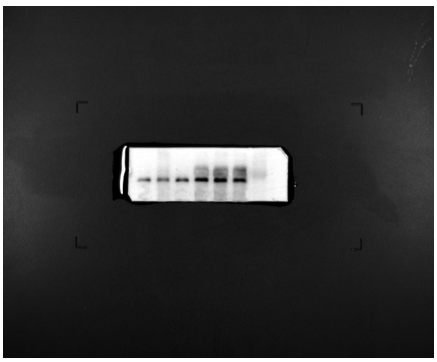
Grouping in this column: the first three samples belong to Con+EV, and the last three samples belong to TAZ-S89A.

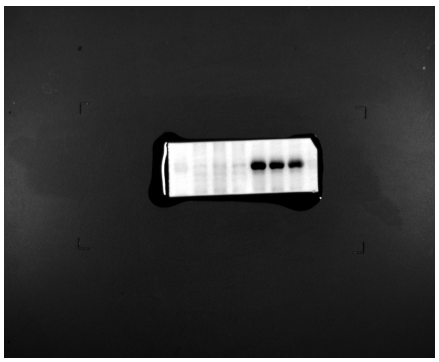
CLOCK



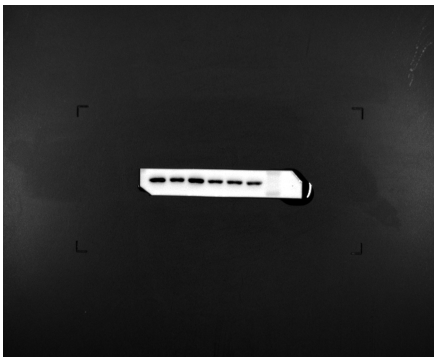


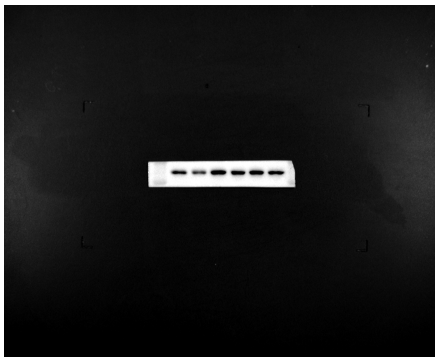
CRY1





β-actin





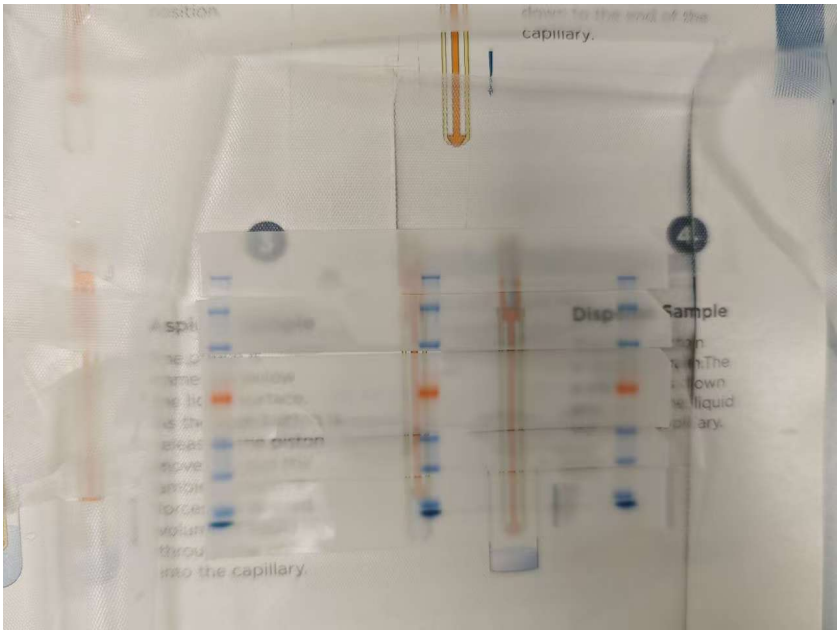
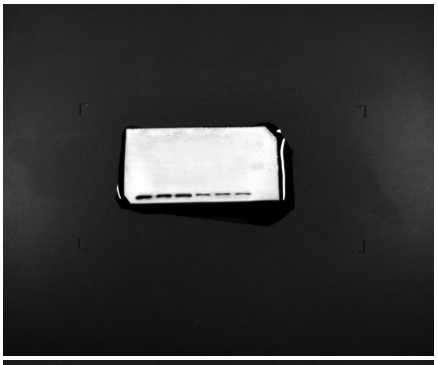


Fig. S20. Source Western blot images for CRY1 and CLOCK comparing constitutively active and TEAD-binding-deficient YAP/TAZ constructs in HPAECs

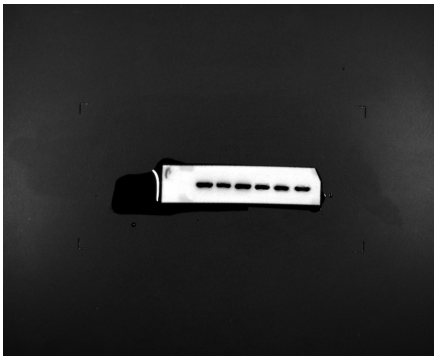
Grouping in this column: the first three samples belong to YAP-S127A, and the last three samples belong to YAP-S94A/S127A.

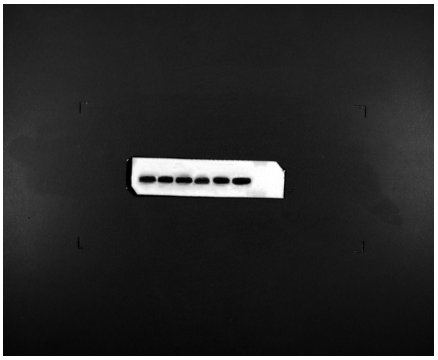
Grouping in this column: the first three samples belong to TAZ-S89A, and the last three samples belong to TAZ-S51A/S89A.

CLOCK

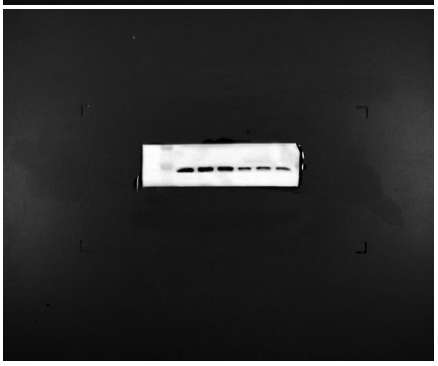


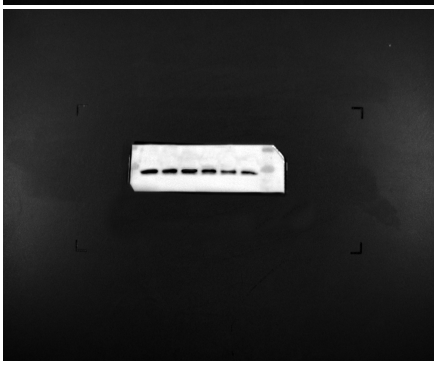
β-actin



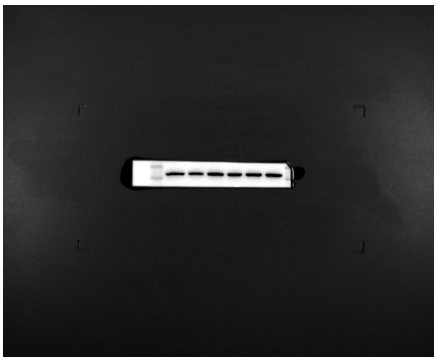


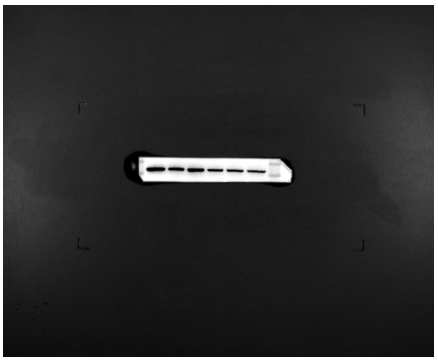
CRY1



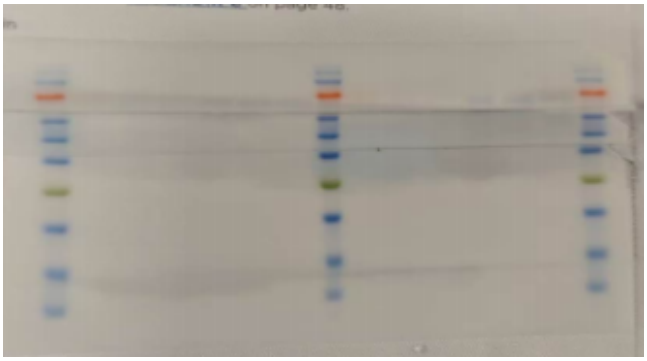


β-actin





CLOCK



CRY1