

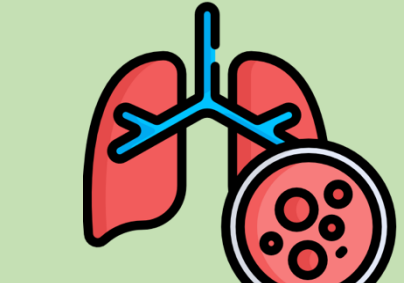
INTRODUCTION

COPD:

3rd

leading cause of death worldwide¹

3.4 million deaths globally in 2023¹



Elevates lung cancer risk 2-6x²

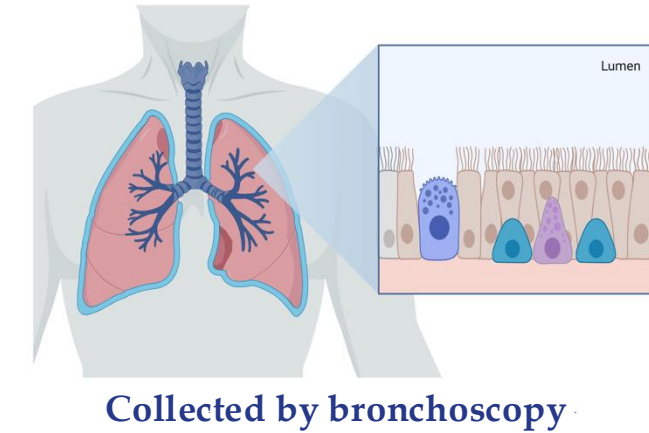
- COPD and lung cancer share **chronic airway inflammation**, but inflammation may not fully explain their molecular link³.
- COPD-associated airway changes may encompass additional **cancer-relevant transcriptional programs**.
- Conventional differential expression identifies individual dysregulated genes but may miss **coordinated biological programs** linking COPD and lung cancer⁴.

Hypothesis: We hypothesized that COPD-associated airway transcriptional programs provide insight into the molecular basis of lung cancer risk beyond inflammation.

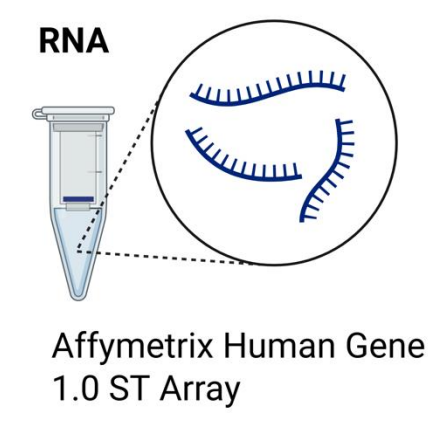
METHODS

1. Airway epithelium (AE) cohort and preprocessing

- Analyzed **232 AE transcriptomes**⁵.
- Clinical traits: **COPD status**, **FEV₁**, and **FEV₁/FVC**.



Collected by bronchoscopy

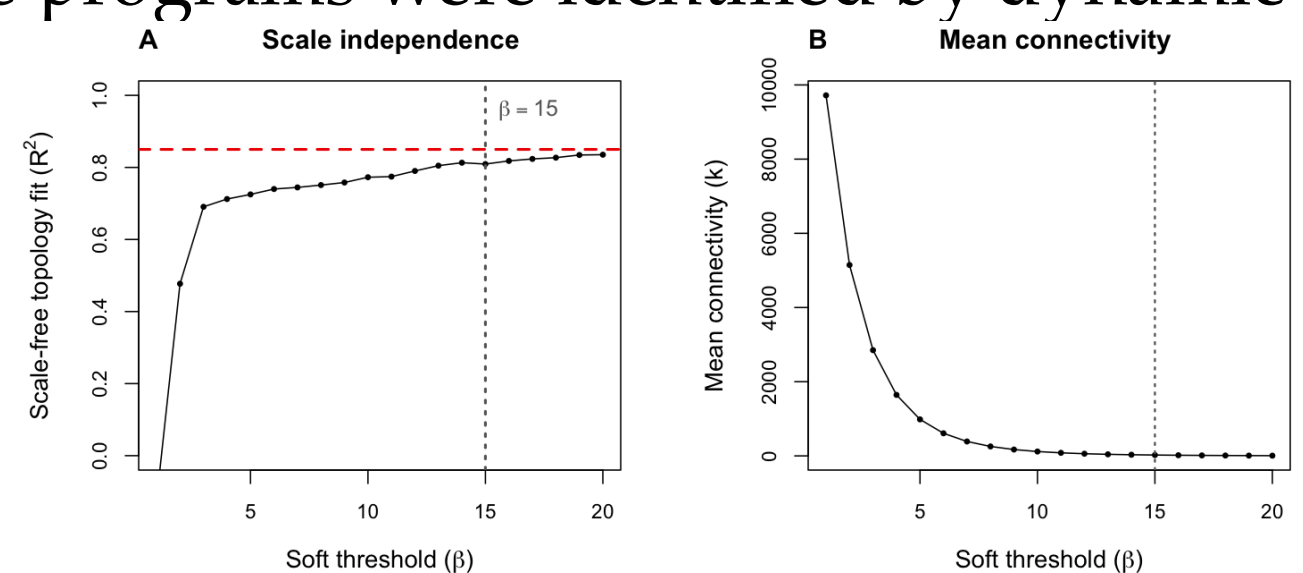


Affymetrix Human Gene 1.0 ST Array

COPD: *n*=85
non-COPD: *n*=147

2. Weighted gene co-expression network analysis (WGCNA) construction

- Co-expression networks were built using **WGCNA**^{4,6}.
- Soft-thresholding power = **15** ($R^2 > 0.85$).
- The programs were identified by dynamic tree cutting.



3. Program-trait association

- Program eigengenes were correlated with **COPD**, **FEV₁**, and **FEV₁/FVC** using **Spearman correlation**.
- kME values** were used to assess gene connectivity and COPD relevance.

4. Functional enrichment

- Pathway enrichment for GO Biological Process and Reactome terms performed with **gProfiler** (FDR-adjusted).

5. Preservation in NSCLC

- Preservation was tested in **TCGA-LUSC tumors** (*n* = 550) and **TCGA-LUAD** (*n* = 528) using **Zsummary** and **MedianRank**.

DISCUSSION AND CONCLUSION

- COPD airway biology extends beyond **inflammation**: proliferative and transcriptional programs were preserved across LUSC and LUAD.
- Network analysis reveals coordinated cancer-relevant biology** beyond individual-gene dysregulation.
- These conserved airway programs may represent **candidate molecular signals of lung cancer risk** warranting further investigation.

Future Direction for Research

- Determine **epithelial origin** of preserved programs using single-cell deconvolution to distinguish epithelial signals from immune and stromal contributions.
- Test program preservation in premalignant lung lesions** to determine whether these programs are present before invasive cancer.
- Validate preserved programs as biomarkers of lung cancer susceptibility** and their potential to improve risk stratification.
- Confirm findings in **additional cohorts**.

REFERENCES & ACKNOWLEDGEMENTS

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In accordance with the standards and guidance set forth by the Accreditation Council for Continuing Medical Education (ACCME), the authors disclose that AI was used in the preparation of this poster. Specifically, Claude Code (Anthropic) was used to regenerate and refine data visualizations from the authors' own analysis outputs. All underlying data, analyses, and scientific interpretations are those of the authors.

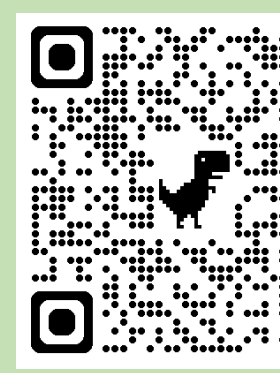
Acknowledgments

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RESULTS

1

Airway epithelium profiling identifies 33 gene co-expression programs, 13 of which are significantly and positively correlated with COPD.

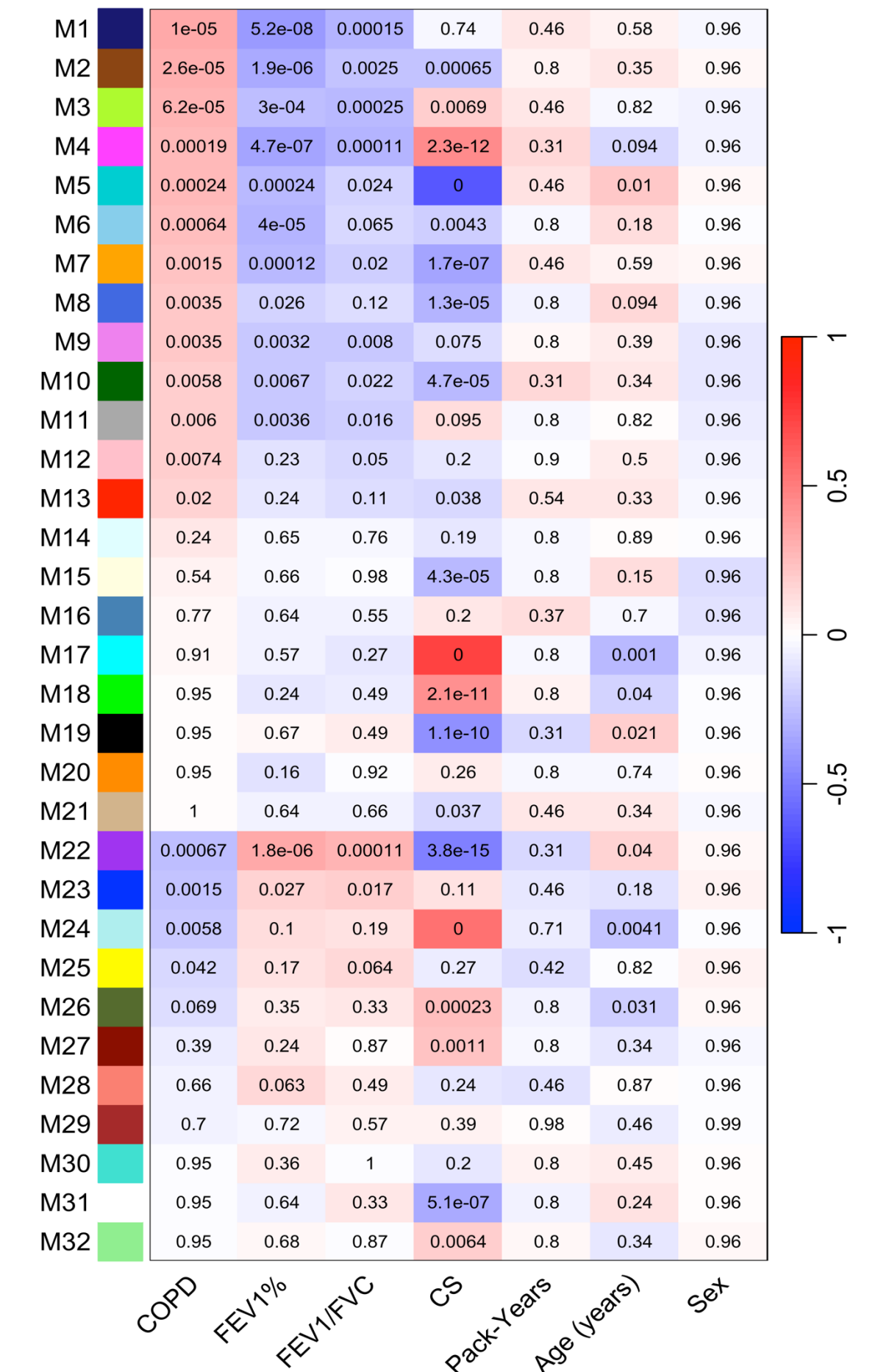
Table 1. AE cohort characteristics.

p-values: Wilcoxon rank-sum test for continuous variables (age, pack-years, FEV₁%, FEV₁/FVC); chi-squared test for categorical variables (sex, smoking status), COPD vs. non-COPD.

Trait	COPD (<i>n</i> =85)	Non-COPD (<i>n</i> =147)	<i>p</i> -value
Age, years (mean +/- SD)	65.1 +/- 6.1	64.2 +/- 5.7	0.21
Sex, Male (<i>n</i> , %)	50 (59%)	81 (55%)	0.68
Smoking status, current (<i>n</i> , %)	29 (34%)	67 (46%)	0.12
Pack-years (mean +/- SD)	51.3 +/- 24.9	46.7 +/- 19.1	0.21
FEV ₁ % predicted (mean +/- SD)	61.1 +/- 12.7	92.9 +/- 13.1	<0.0001
FEV ₁ /FVC (mean +/- SD)	59.6 +/- 8.1	75.0 +/- 5.4	<0.0001

Figure 1. Program-trait heatmap.

Program-trait correlations, AE cohort (*n*=232). Programs ranked M1–M33 by COPD correlation, strongest positive to strongest negative. Cell text: FDR *q*-value.



2

COPD-associated airway programs are strongly preserved in both LUSC and LUAD tumor tissue.

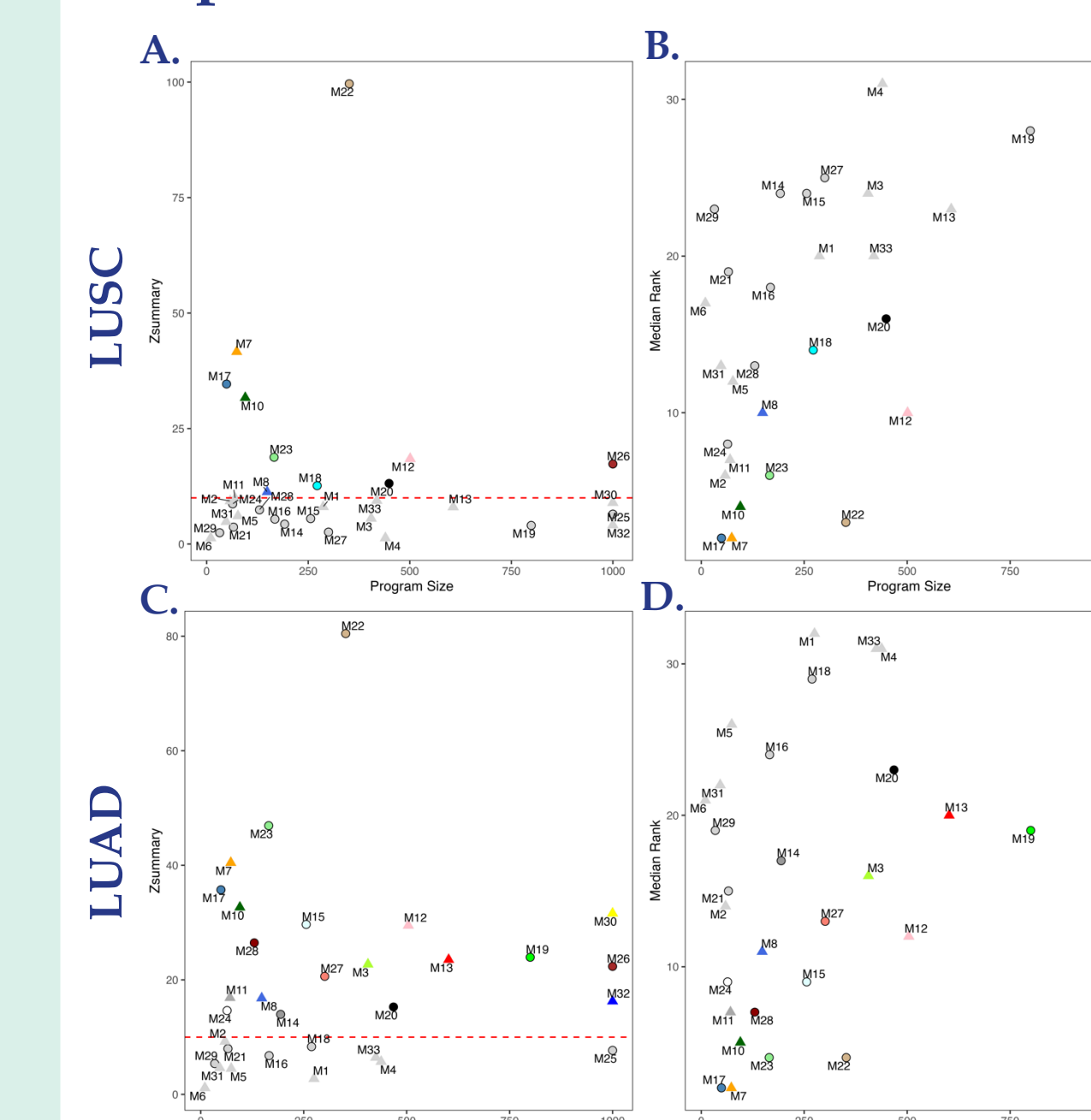


Figure 2. Preservation of AE co-expression programs in TCGA-LUSC and TCGA-LUAD. (A,C) Zsummary and (B,D) MedianRank vs. program size. Color denotes Zsummary ≥ 10 (strong preservation; red dashed line, A/C); triangles denote programs significantly associated with COPD ($q < 0.05$). M-numbers rank programs by COPD correlation strength.

4

The top COPD-preserved program reflects pro-mitotic transcriptional activity.

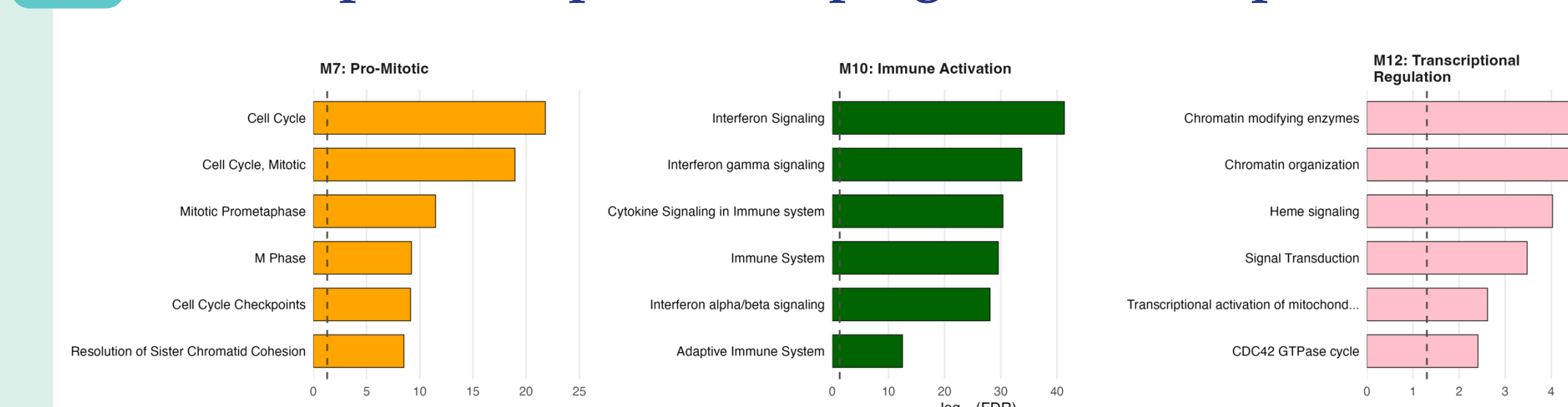


Figure 3. Representative pathways for the top three COPD-preserved programs. M7: Cell Cycle/Mitotic, $p = 1.6 \times 10^{-22}$; M10: Interferon Signaling, $p = 4.8 \times 10^{-42}$; M12: Chromatin organization, $p = 9.3 \times 10^{-6}$; dashed line = FDR 0.05.

3

Table 2. Summary table.

Transcriptional programs, size, COPD correlation (AE), and Zsummary (LUSC, LUAD) for the top three COPD-associated programs preserved in both tumor cohorts, with representative pathways.

Transcriptional Program	Genes	COPD <i>r</i>	LUSC Zsum	LUAD Zsum	Representative Pathways
M7: Pro-Mitotic	78	0.23	41.6	40.5	Cell Cycle, Mitotic Prometaphase, M Phase
M10: Immune Activation	98	0.20	31.7	32.7	Interferon Signaling, Cytokine Signaling, Immune System
M12: Transcriptional Regulation	514	0.19	18.5	29.5	Chromatin Modifying Enzymes, Chromatin Organization

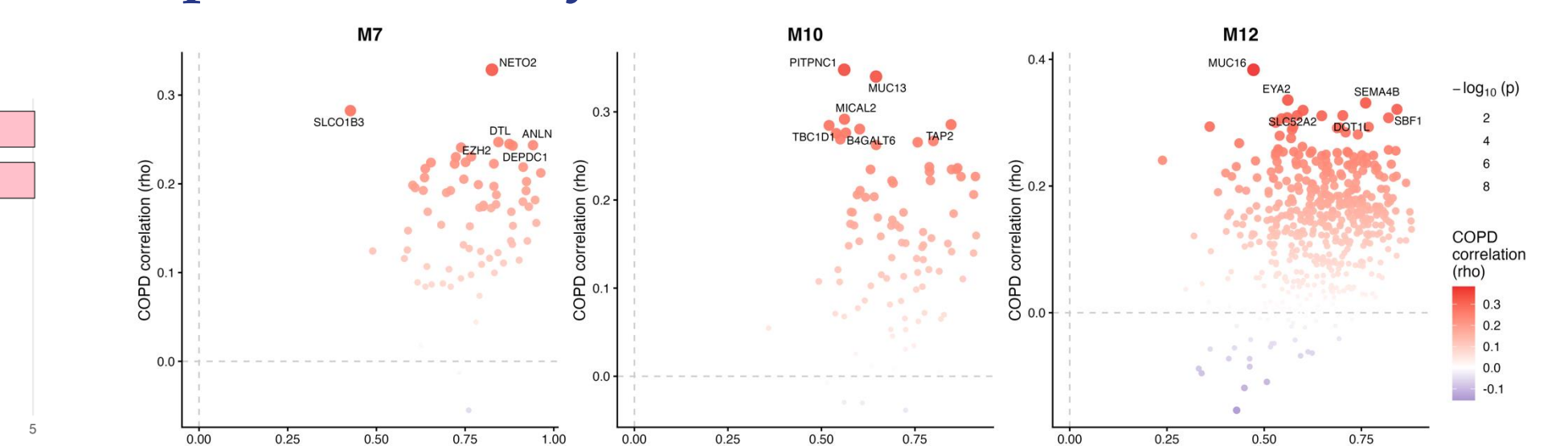


Figure 4. Hub genes for the top three COPD-preserved programs: program membership (kME) vs. gene-level COPD Spearman correlation. Fill = COPD correlation (ρ); point size = $-\log_{10}(p)$; top 6 genes by $|\rho|$ labeled per program.