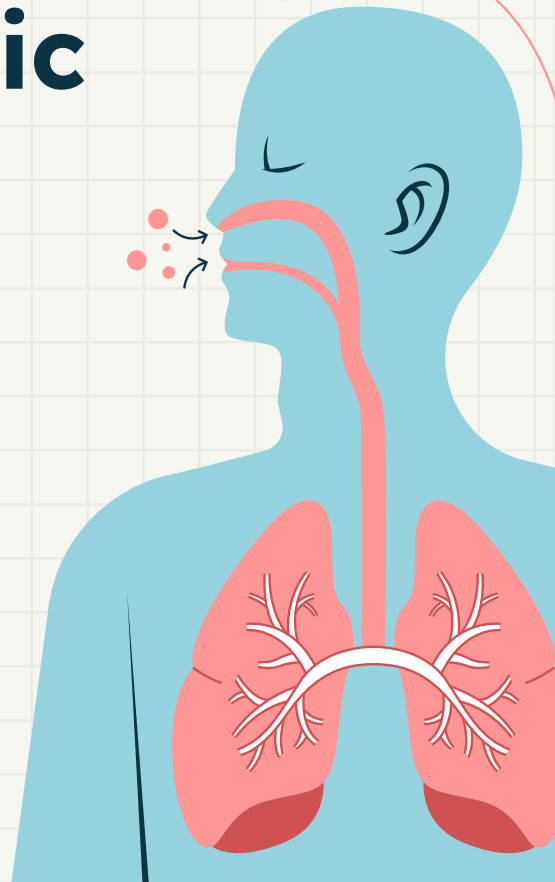
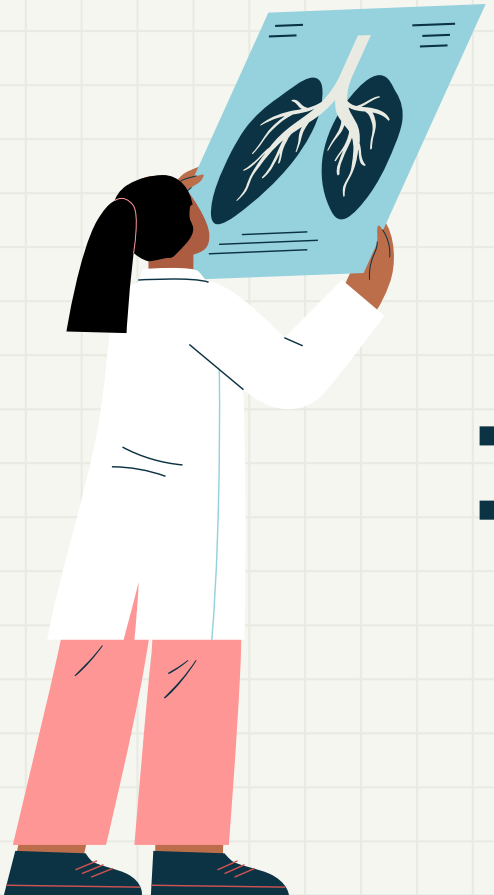
Evaluating the Multi-Omic Profile of Smoking and Non-Smoking Patients with Lung Adenocarcinoma

Joshua Lin, Ethen Chen, Changshen Chen



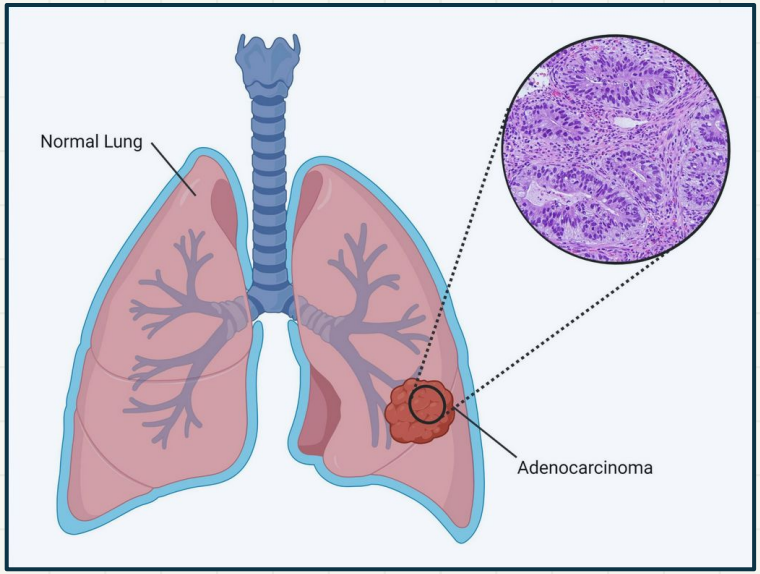


01

INTRODUCTION

Lung Adenocarcinoma LUAD

- A non-small cell lung cancer
- Accounting for about **40%** of all lung cancers
- The **leading cause** of cancer death in the United States

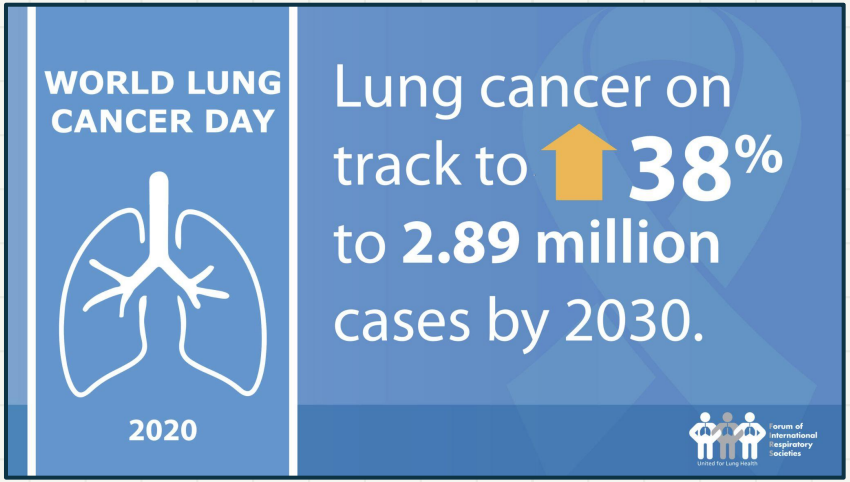


Lung Cancer Statistics

- **2.2** million new cases and **1.8** million related deaths occurred in 2020

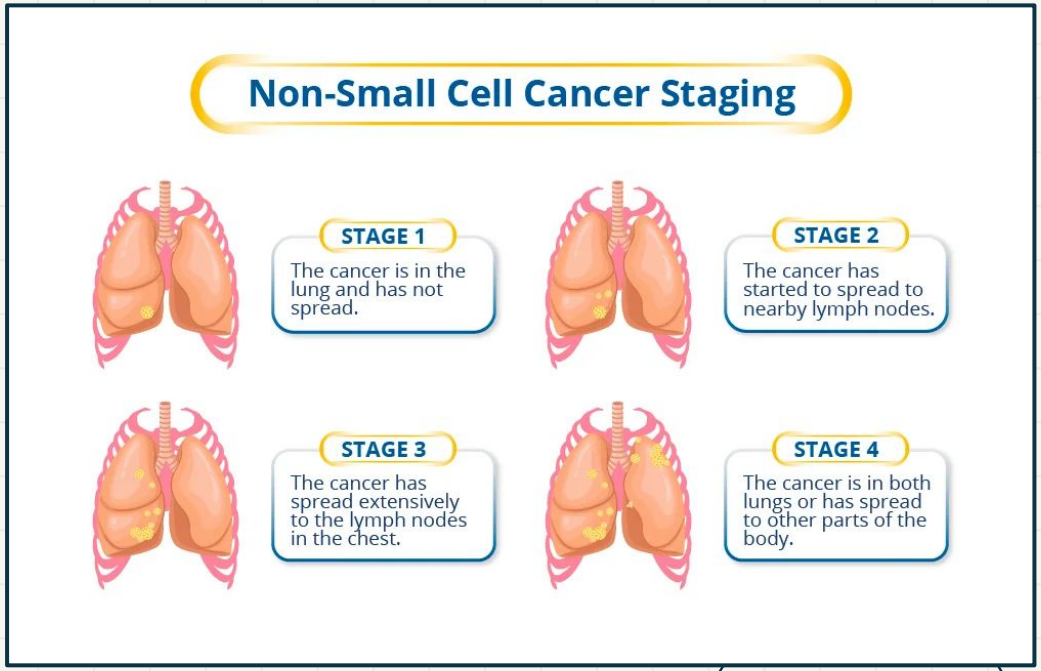
- **11.4%** of the total cancer cases and **18.0%** of the total cancer deaths

- For US, **229,000** new cases, accounting for **12.7%** of all cancer diagnoses



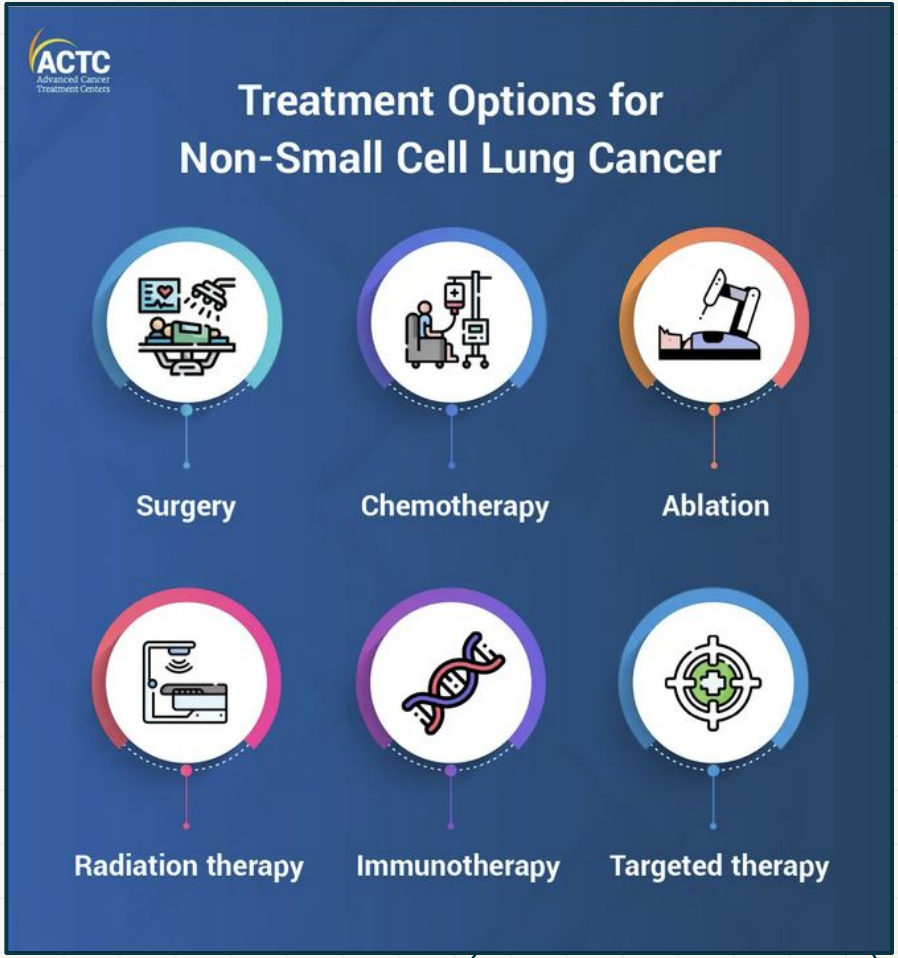
Prognosis

- Five-year survival rate at diagnosis:
  - **Stage 1:** 65%
  - **Stage 2:** 40%
  - **Stage 3:** 15%
  - **Stage 4:** 5%



Treatments

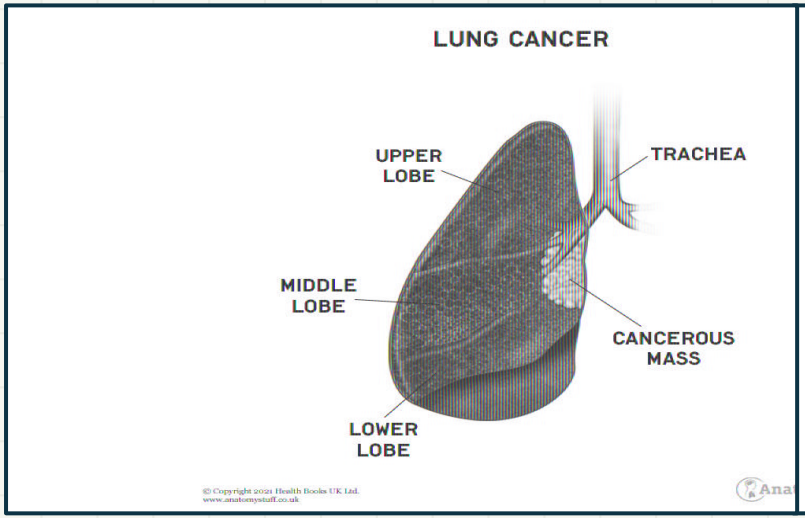
- Smoking versus Non-Smoking
- Based on specific genetic mutations

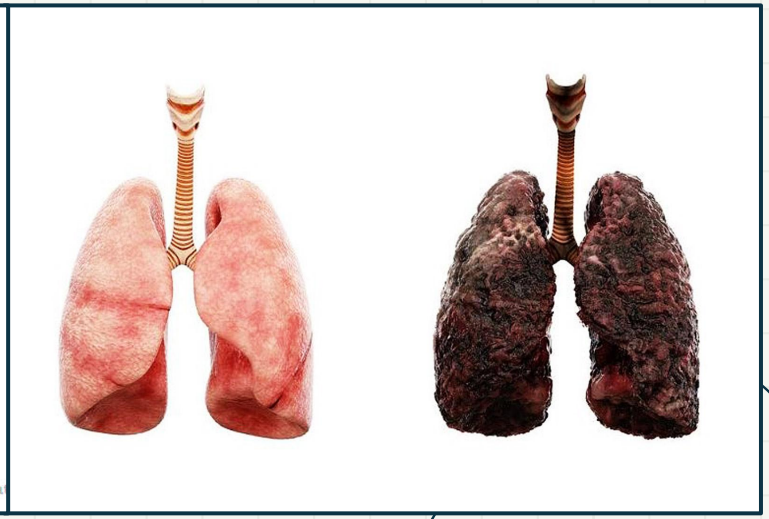


Correlation with Smoking

- In the United States, cigarette smoking is linked to about 80% to 90% of lung cancer deaths

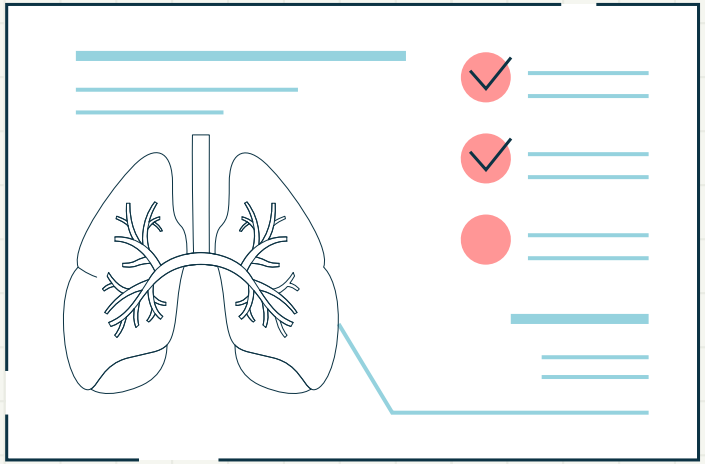
- 15 to 30 times more likely to get lung cancer or die from lung cancer

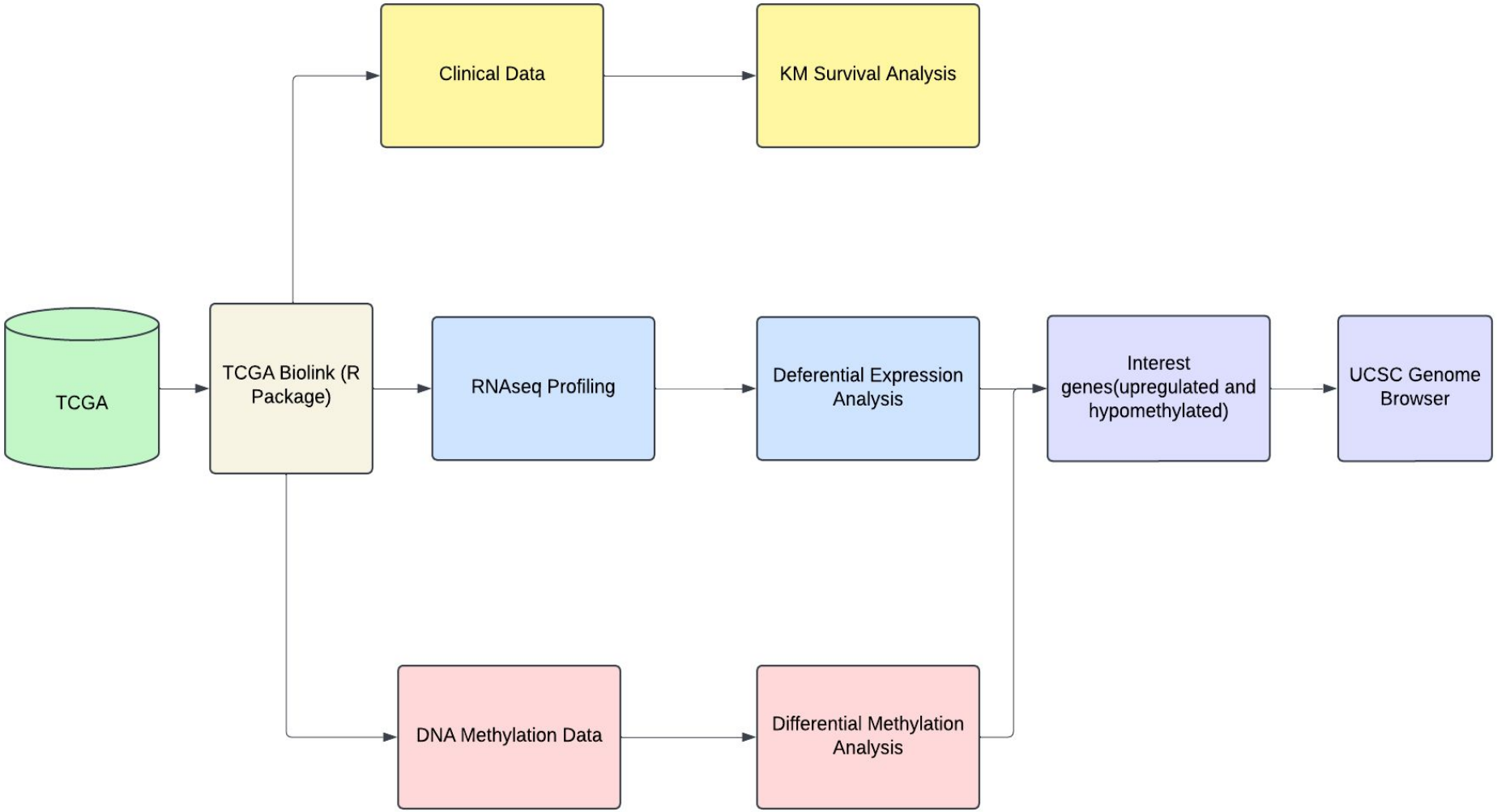




Does a prior history of smoking have correlations with distinct patterns in gene expression profiles, methylation signatures, and overall prognosis in patients with lung adenocarcinoma?

02
Methods & Results

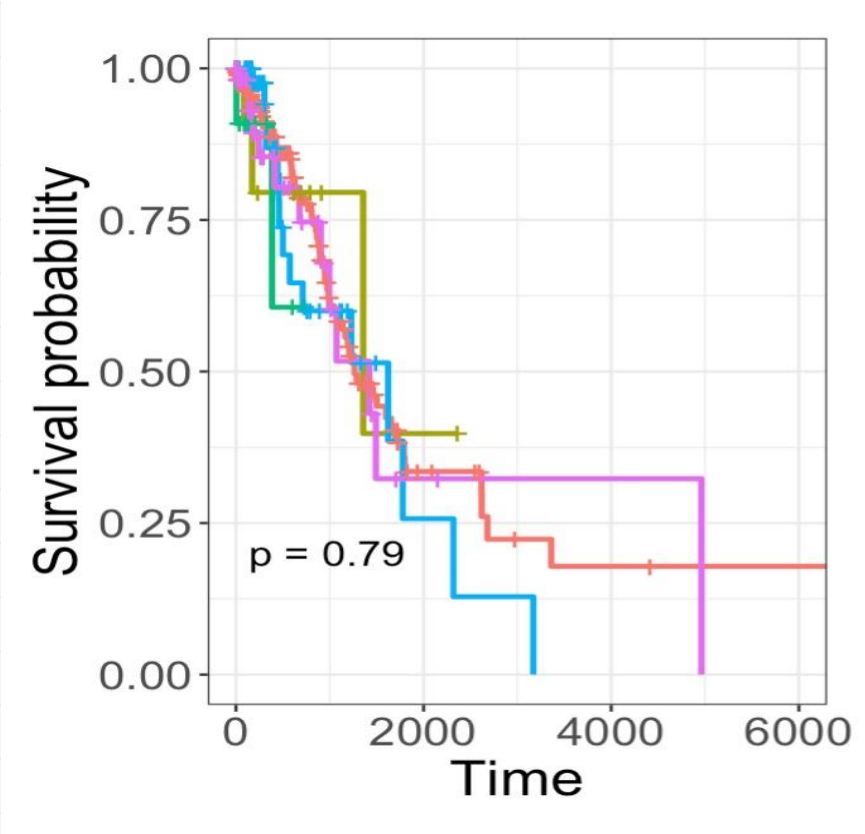



Clinical Data
KM Survival Analysis
TCGA
TCGA Biolink (R Package)
RNAseq Profiling
Deferential Expression Analysis
Interest genes(upregulated and hypomethylated)
UCSC Genome Browser
DNA Methylation Data
Differential Methylation Analysis

Patient Grouping by Smoking Exposure

Group	Smoking Pack Years	Number of Patients
Non-Smoker	0	70
Minimal Exposure	1-5	12
Mild Exposure	6-10	15
Moderate Exposure	11-20	56
Heavy Exposure	> 20	260

Patient Survival by Smoking Grouping



Heavy Exposure

Moderate Exposure

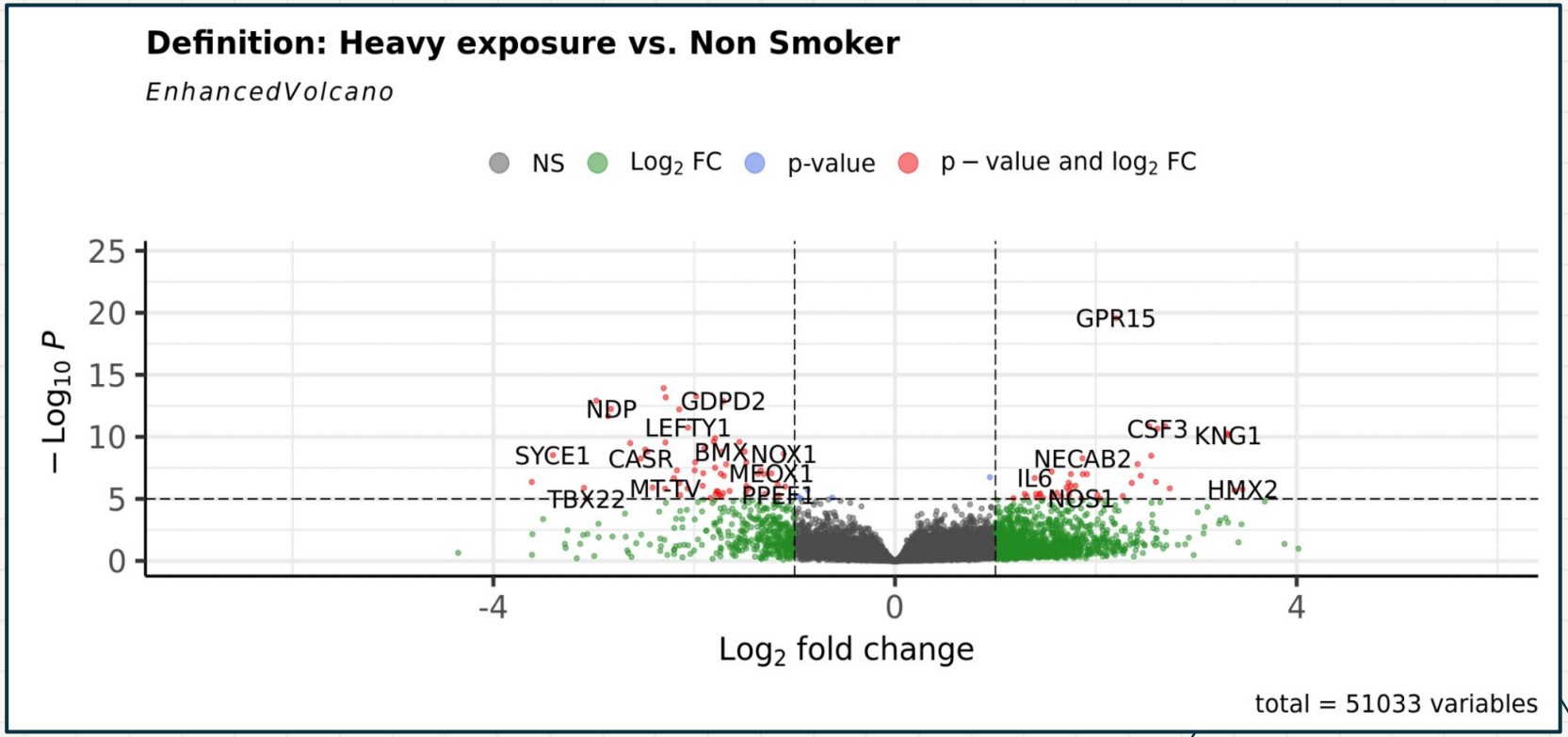
Mild Exposure

Minimal Exposure

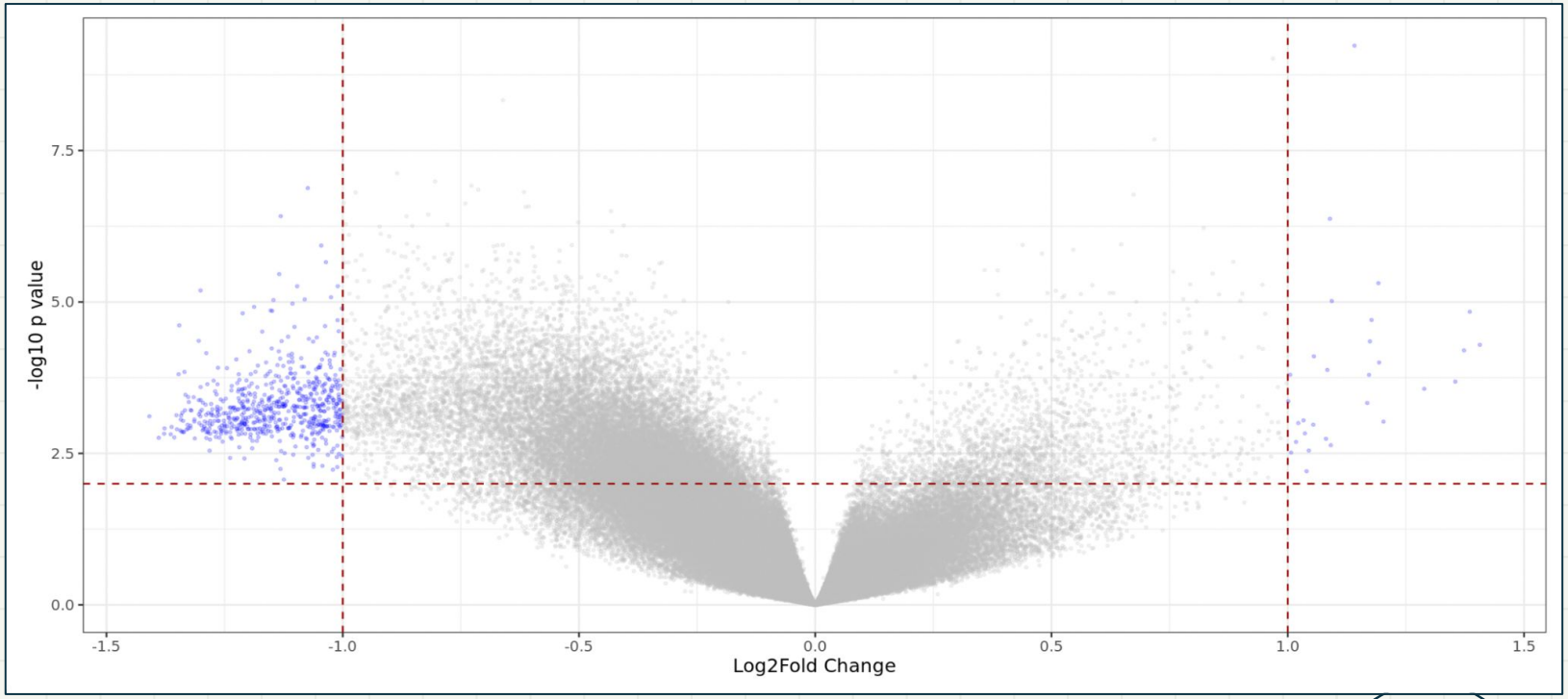
Non-Smoker

Volcano Plot on Differentially-Expressed Genes for Heavy-Exposure vs. Non Smoker groups

Covariates: Age and Gender



Volcano Plot on CpG Methylation Differences



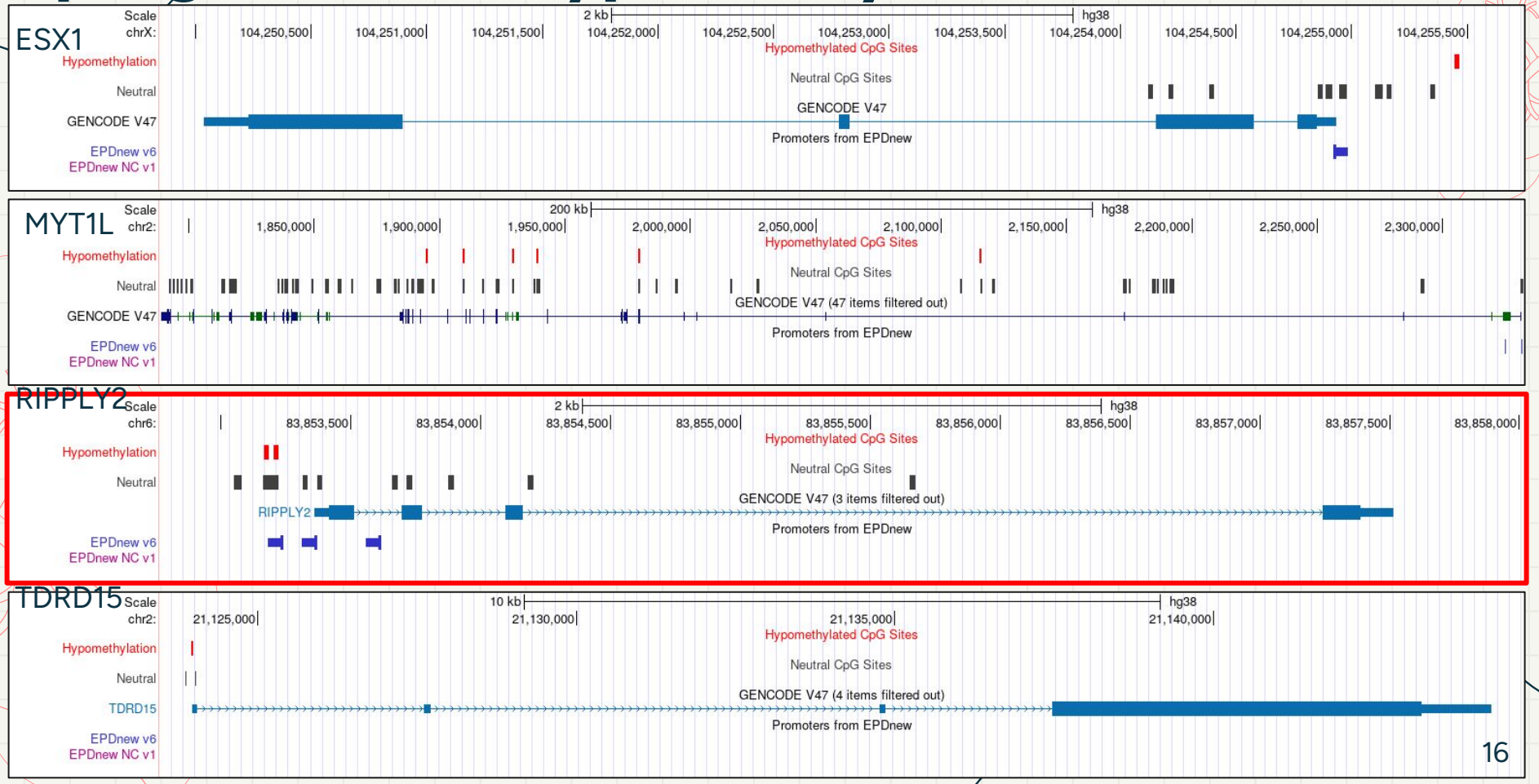
$-\log_{10}$(p-value)

Log_2(Fold Change)

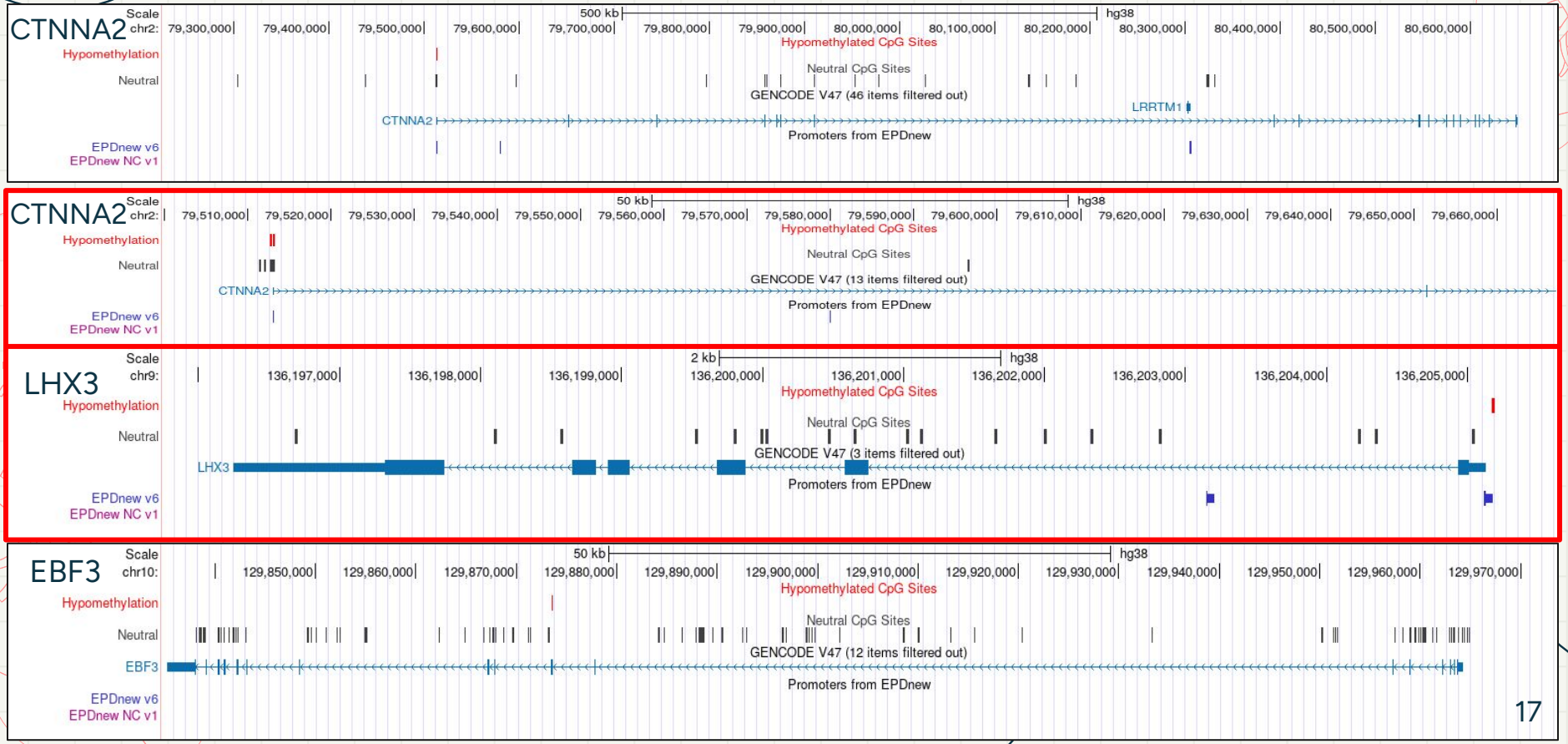
Interest Genes

	Significantly Upregulated	**Significantly Downregulated**
Significantly Hypermethylated	SHOX2	ASIC2
Significantly Hypomethylated	ESX1 MYT1L RIPPLY2 TDRD15	CTNNA2 LHX3 EBF3

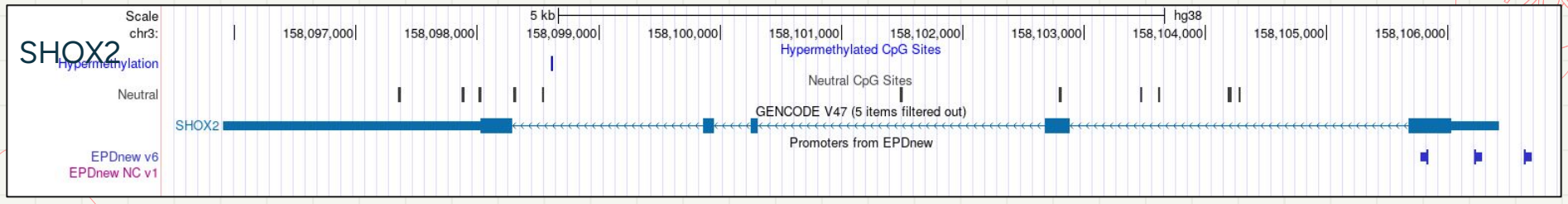
Upregulated & Hypomethylated



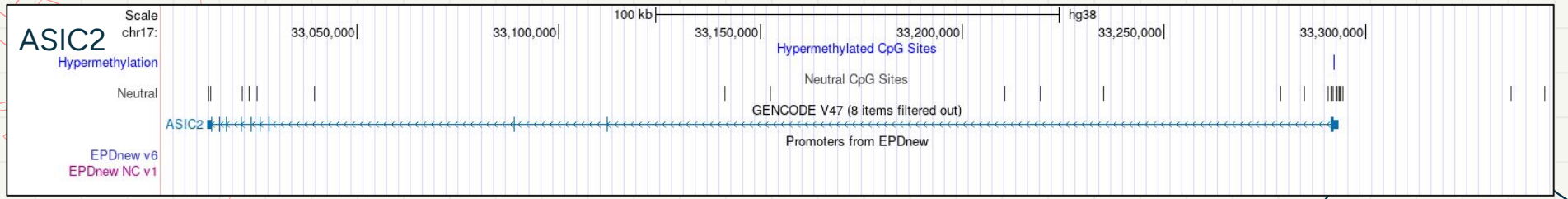
Downregulated & Hypomethylated



Upregulated & Hypermethylated

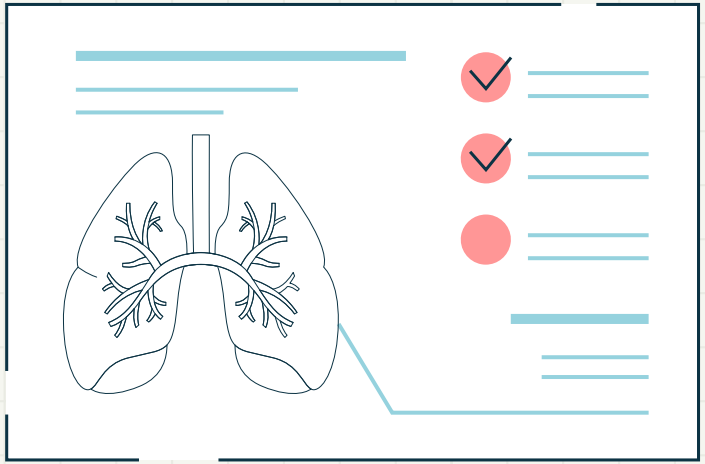


Downregulated & Hypermethylated

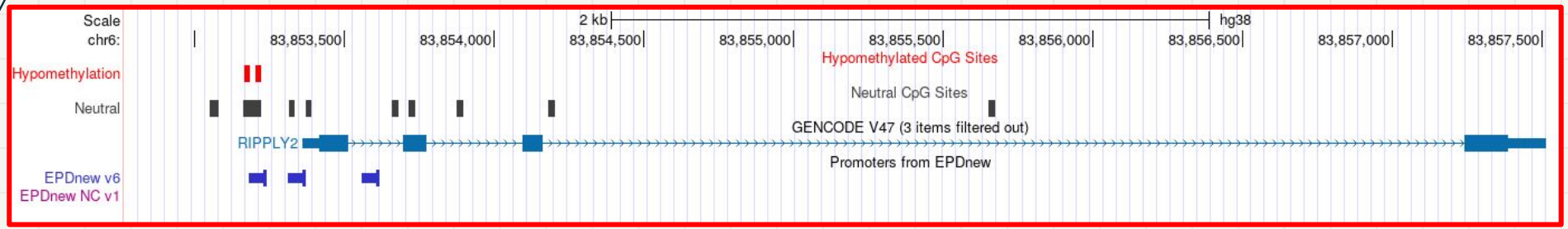


04

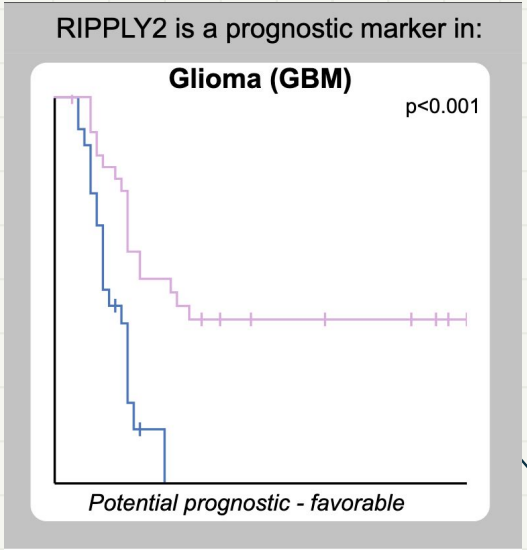
DISCUSSION



RIPPLY2 Upregulation & Hypomethylation

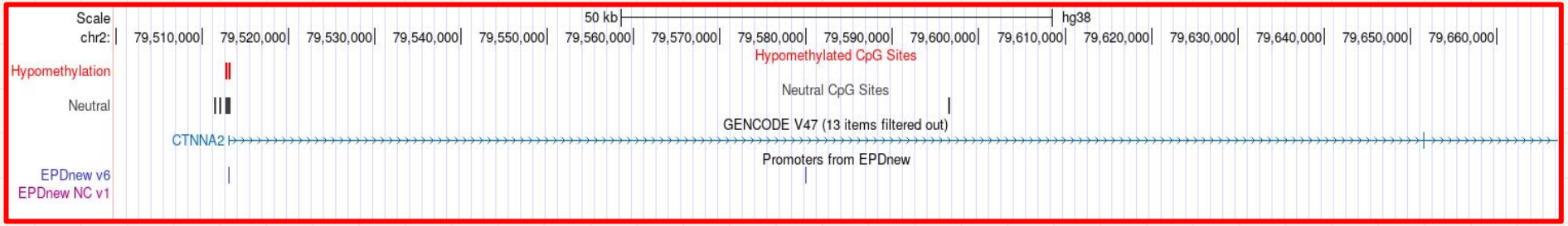


- Ripply Transcriptional Repressor 2 gene
- Human Protein Atlas - upregulation correlations with prognosis



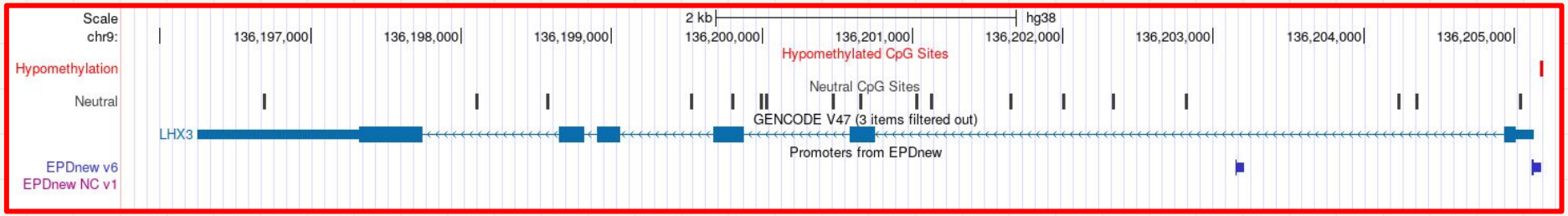
(*Expression of RIPPLY2 in Cancer - Summary*, 2014)

CTNNA2 Downregulation & Hypomethylation



- Catenin alpha-2
- Tumor suppressor gene

LHX3 Downregulation & Hypomethylation



- LIM Homeobox 3
- Potential oncogene for LUAD (*LHX3 LIM Homeobox 3 [Homo Sapiens (Human)] - Gene - NCBI*, 2024)
- "Early stage and radiosensitivity prognostic biomarker for LUAD" (Lin, X. et.al, 2017)

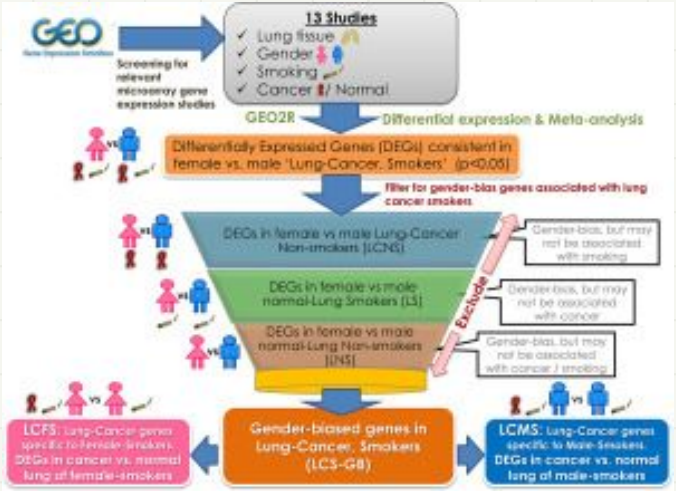
Therapeutic Implications

- Anti-EGFR targeted treatments
  - Higher prognosis for EGFR mutants (Kuśnierczyk, 2023)
  - 33% EGFR mutation differences btwn. non-smoking and heavy

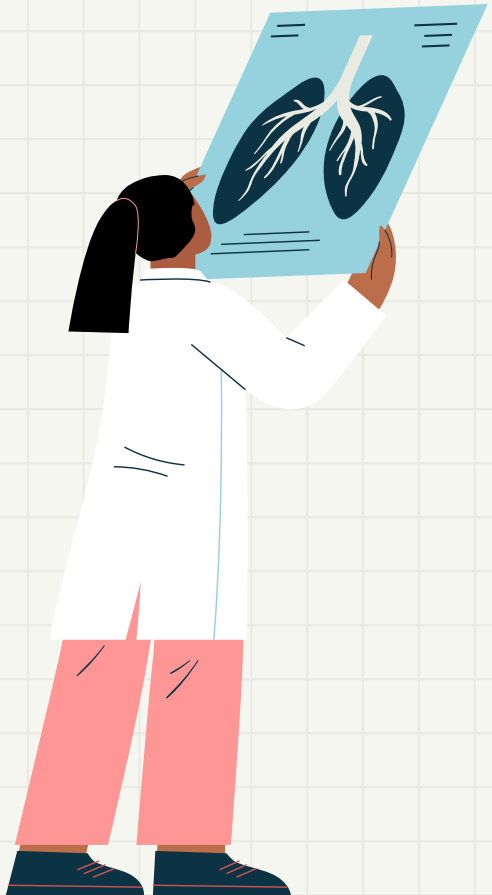
- Using hypomethylated gene targets for further research & treatments
  - Prognostic biomarkers for smoking groups

Future Research/Analysis

- Testing differences for LUAD subpopulations based on age at diagnosis ranges, gender, etc.
- Comparison of similar analysis to other NSCLC (squamous cell carcinoma - TCGA-LUSC)
- Using public databases other than/including TCGA to see how differences compare for LUAD patients
    - Gene Expression Omnibus (GEO) and Sequence Read Archive (SRA)



(Davuluri et al., 2021)



05

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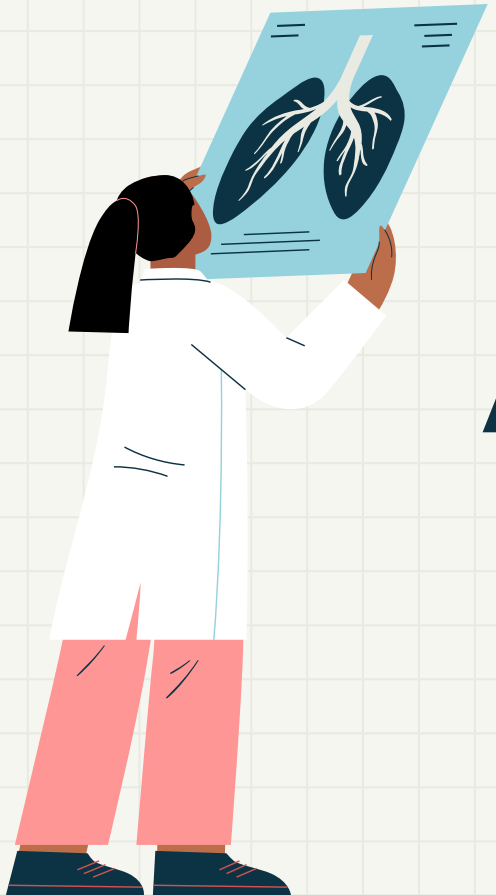

06

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THANKS!

DO YOU HAVE ANY QUESTIONS?

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