



The Influence of Pack Years on COPD Genetics

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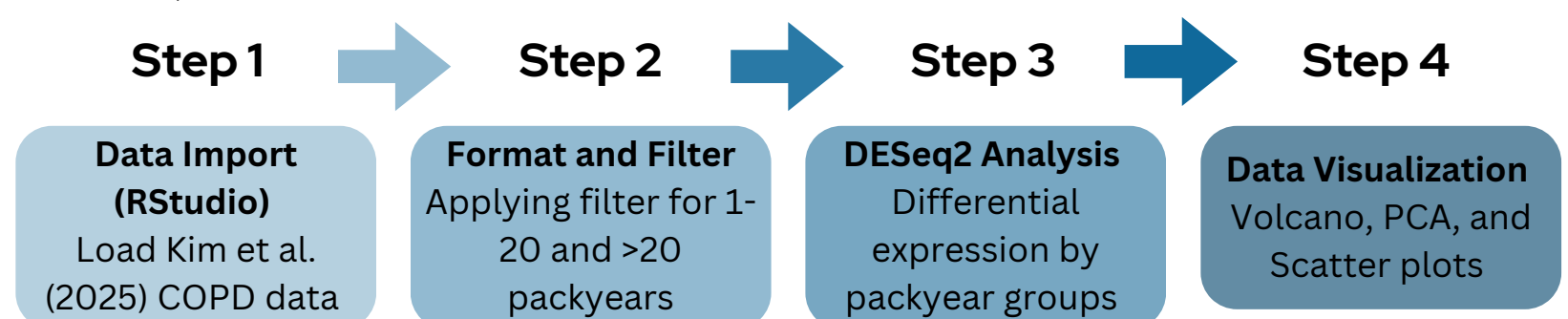
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Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a progressive lung disorder characterized by airflow limitation and chronic inflammation (Cosio et al., 2009; Vestbo et al., 2013). Smoking is the primary risk factor, but the severity and progression of COPD vary widely among individuals. Cumulative smoking exposure, often measured in pack-years, may influence molecular and genetic changes in the lungs, affecting which genes are dysregulated in COPD. **Therefore, this study examines whether the extent of smoking exposure modulates the genes most strongly associated with the disease.**

Methodology

The gene expression between patients with COPD and controls (smokers without COPD) was compared for light smokers and heavy smokers. Light smokers were defined by 1 to 20 packyears (smoking one pack per day for one year) and heavy smokers by more than 20 packyears (Mahmoudinezhad et al., 2022).



Results

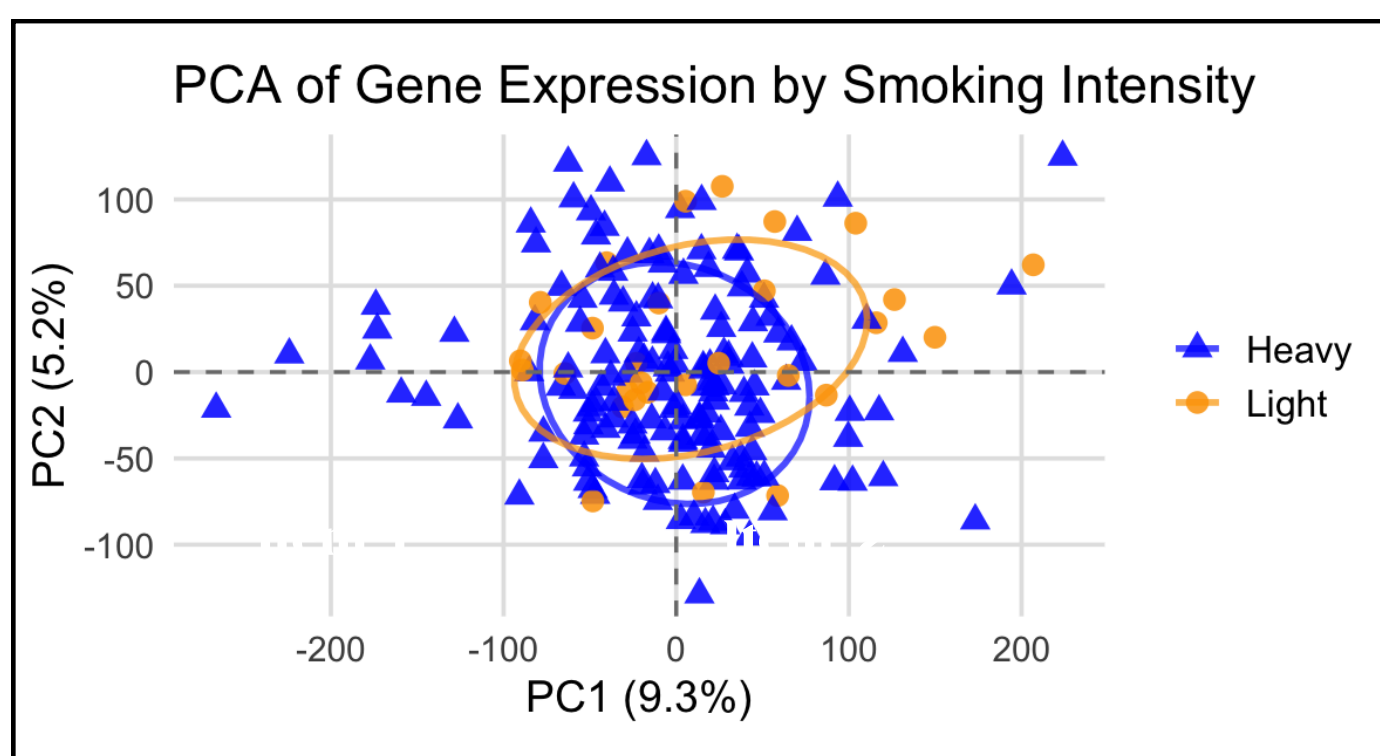


Figure 1. PCA plot showing the variation in gene expression between heavy (blue) and light (orange) smokers. The plot does not show clear clustering of the two different groups, indicating that the difference in gene expression between the two groups may not be big.

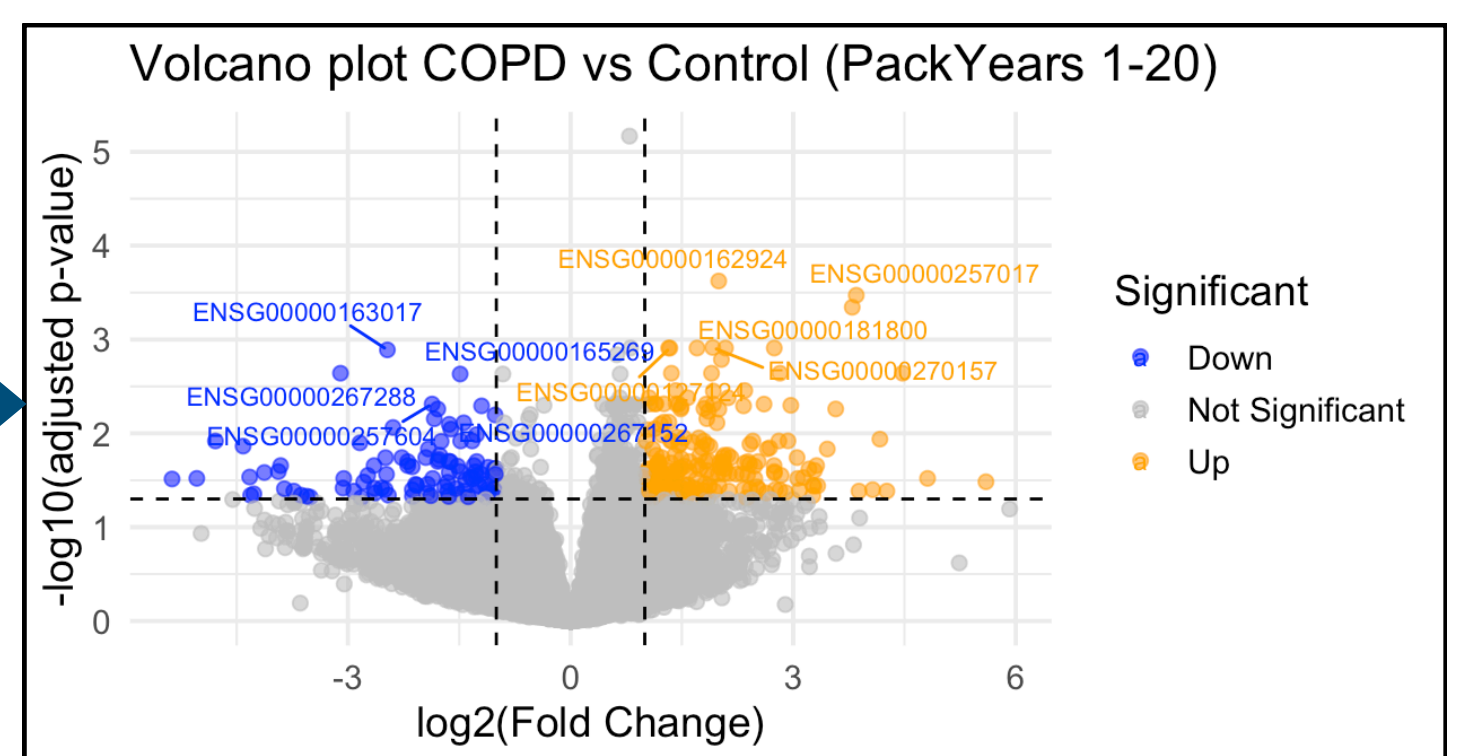


Figure 2. Volcano plot showing differential gene expression in COPD patients compared to control subjects with a smoking history of 1-20 pack-years. The 5 most significant genes that were upregulated are labeled, as well as those that were downregulated.

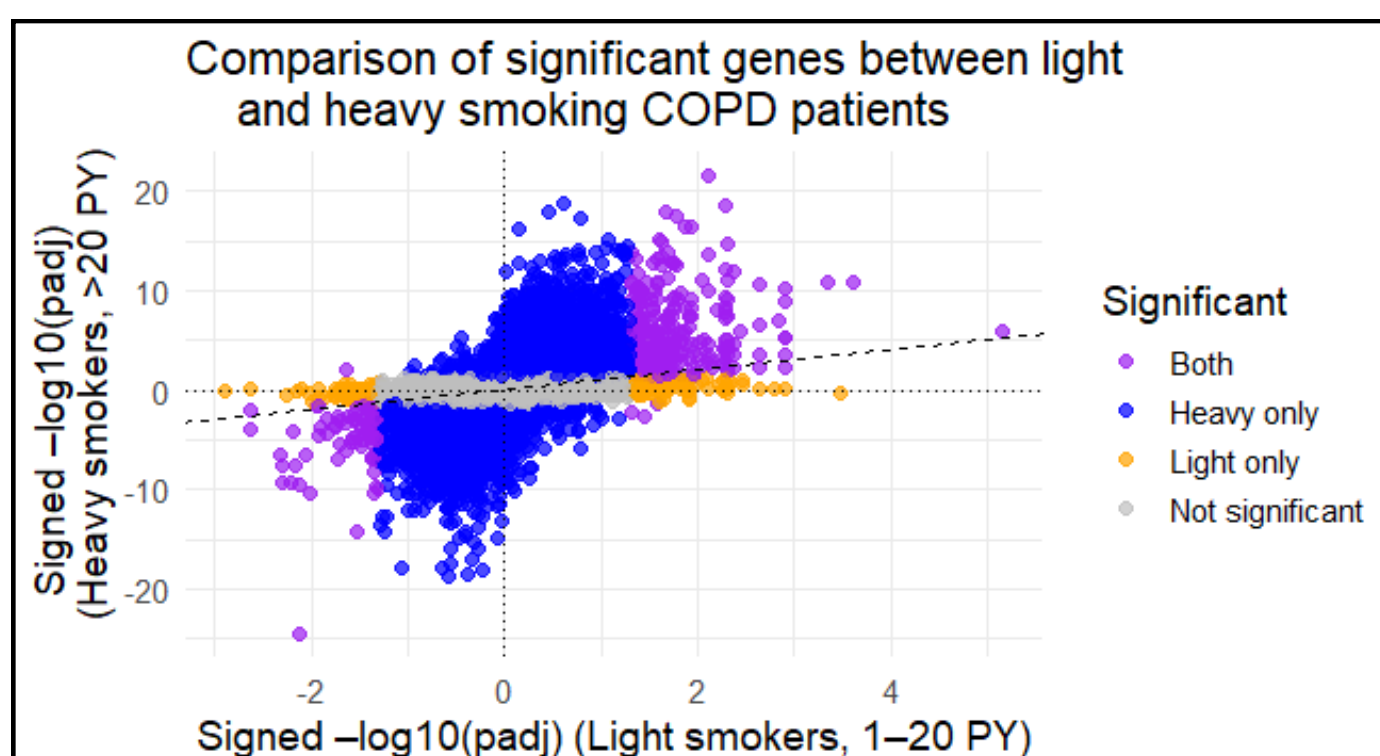


Figure 4. Scatterplot showing the signed $-\log_{10}$ (adjusted p-values) for differential gene expression in heavy vs light smoking COPD patients. A moderate positive correlation ($r = 0.50$) indicates that some genes are consistently regulated across both groups, while others are specific to smoking intensity.

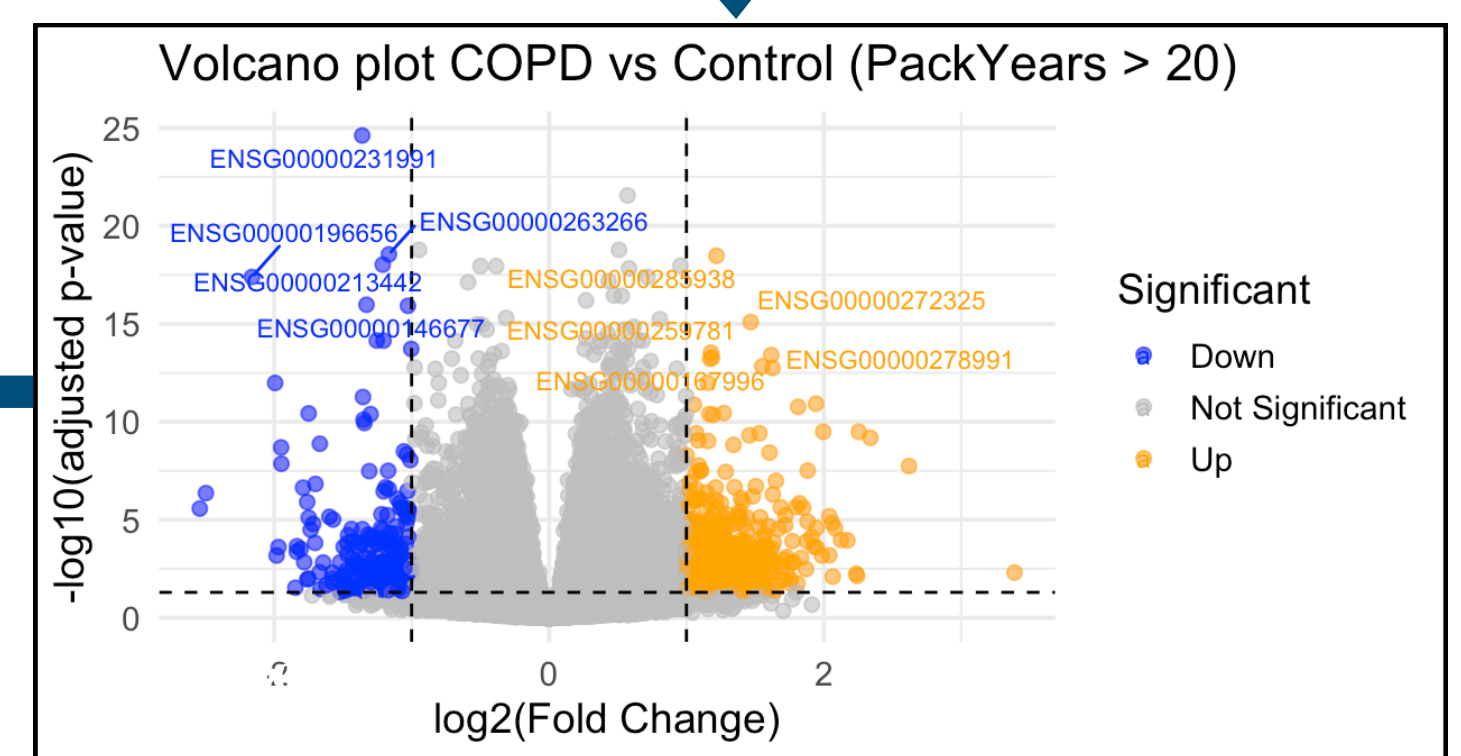


Figure 3. Volcano plot showing differential gene expression in COPD patients compared to control subjects with a smoking history of >20 pack-years. The 5 most significant genes that were upregulated are labeled, as well as those that were downregulated.

Conclusion

This study investigated whether smoking exposure, measured in pack-years, influences genes most strongly associated with COPD. DESeq2 indicated that packyears moderately affects gene expression. Comparison between light and heavy smokers revealed that the most significant genes differ between the two groups. Volcano plots suggest more COPD-associated genes in heavy smokers, but this likely reflects the larger sample size (160 vs. 28). Scatter plots show that some genes are significant in both groups, while others appear specific to heavy or light smokers. However, these observations are confounded by the unequal sample sizes. Overall, the higher number of genes significant in heavy smokers is likely influenced by sample size rather than a biological effect.

References

