Determining the biological mechanisms driving the association between COVID-19 and lung cancer in smokers and nonsmokers

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Introduction

Background: In spite of tremendous progress in the clinical management of COVID-19 as well as the development of vaccines to mitigate its effect and spread, the pandemic caused by SARS-Cov-2 continues to be a major public health issue. One major challenge caused by the pandemic is the clinical management of immunocompromised patients. In particular, lung cancer patients diagnosed with COVID-19 and specifically, smokers, have suffered an increased risk of death compared to other cancer patients. The biological mechanisms driving this disparity are still unknown.

Objective: Determine the different pathways responsible for driving the association between COVID-19 and lung cancer in smokers and nonsmokers.

Hypothesis: Molecular perturbations in the lung tissue affected by lung cancer patients could lead to measurable changes explaining the differences in the impact of COVID-19 on smoking and nonsmoking lung cancer patients.

Materials and Methods:
I. Obtain gene expression data for 555 lung cancer patients from TCGA
II. Differential gene expression analysis between 1) smokers and controls 2) nonsmokers and controls
III. Normalized RNA-seq data from COVID-19 lungs
IV. Differential gene expression analysis between COVID and nonsmoking controls from initial comparison
V. Determine genes associated with COVID in nonsmokers and COVID in smokers
VI. Differential gene expression analysis between COVID and nonsmokers/smokers using genes determined to be unique to each
VII. Pathway Analysis
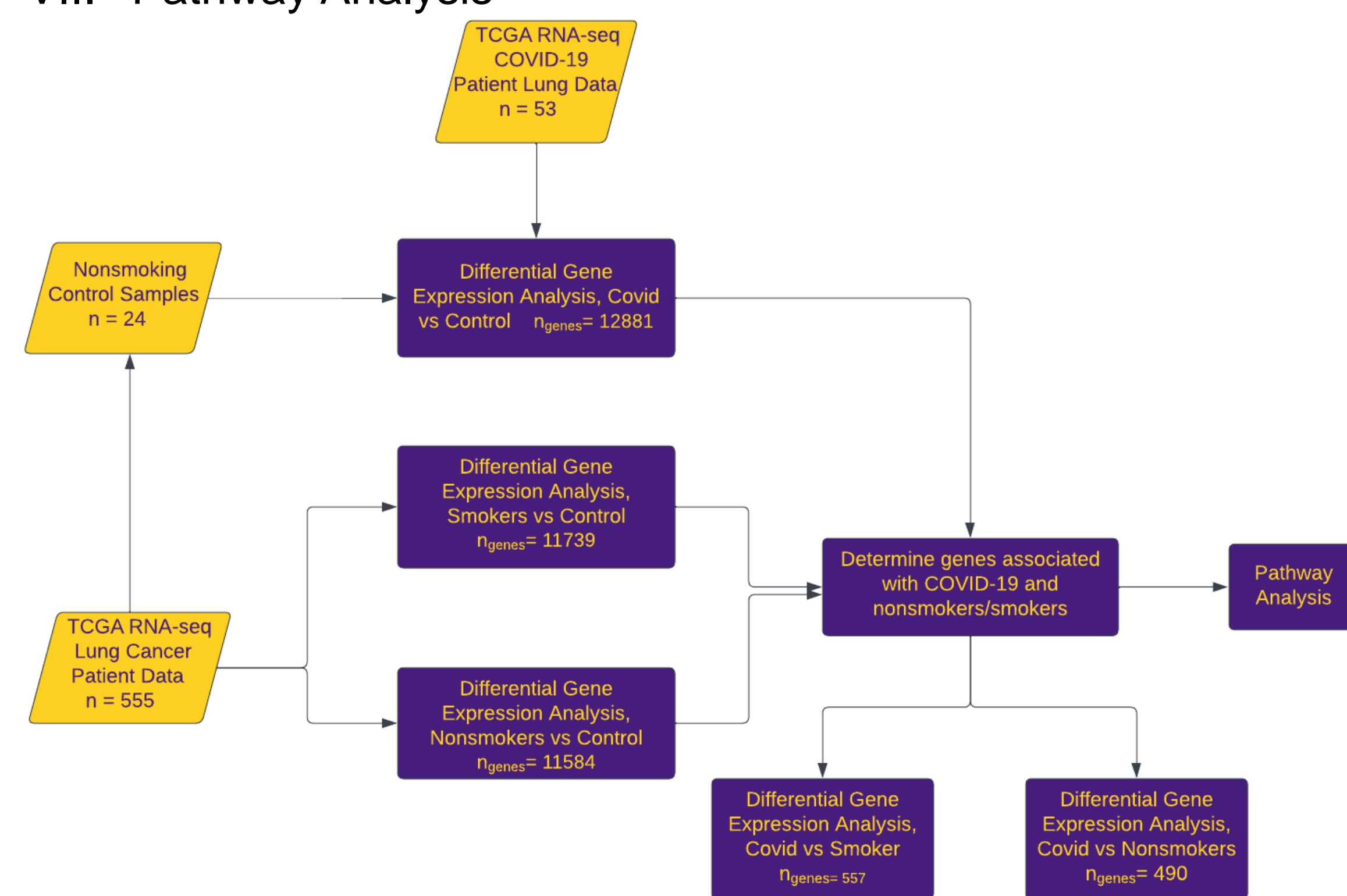
Figure 1: Flowchart depicting methods and materials. Only genes considered significant(adj. p < 0.05) carried over to the next step

Results

Figure 2: Results from initial gene expression analysis. Venn diagram showing association in genes differentially expressed between each group and controls
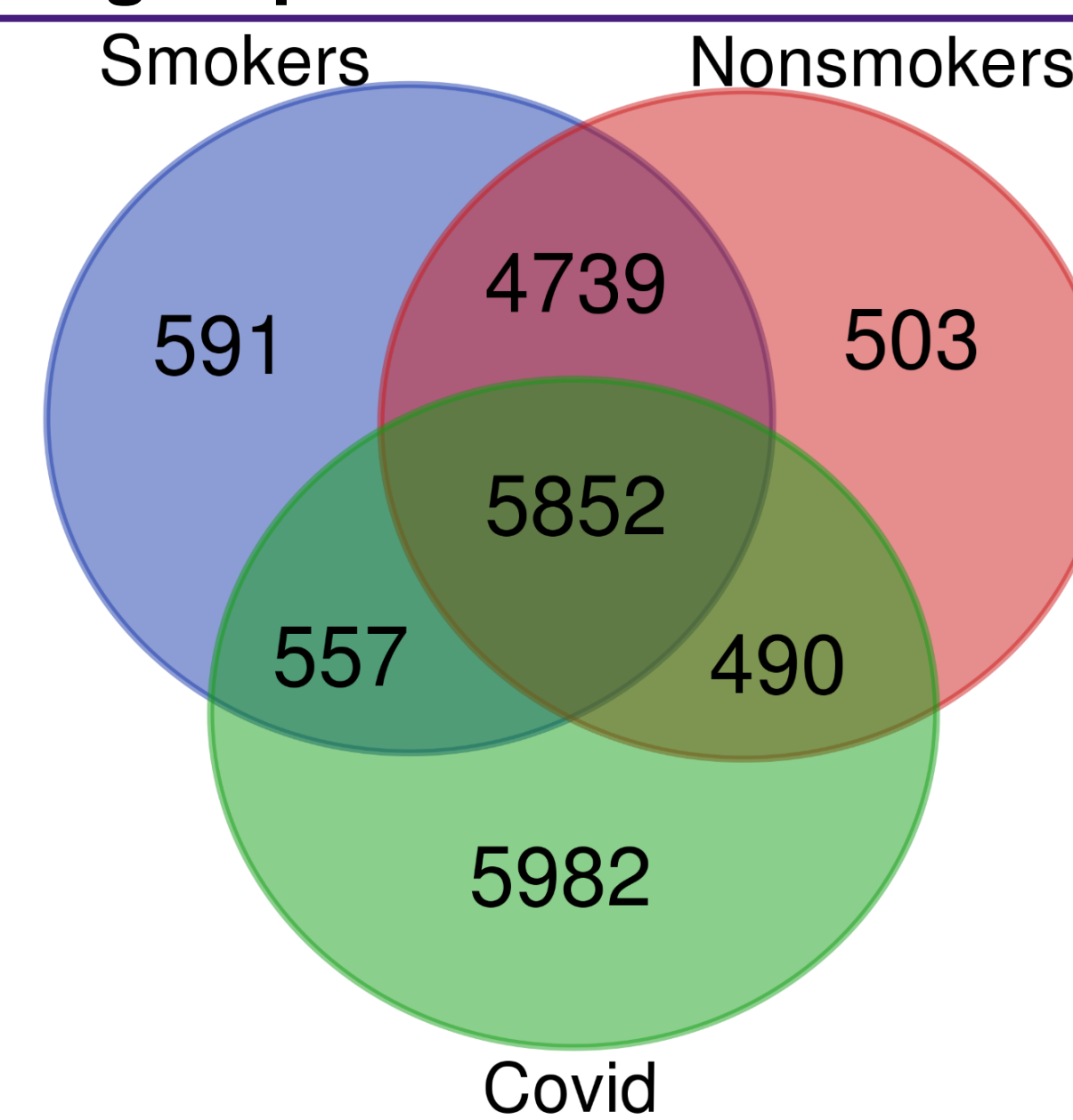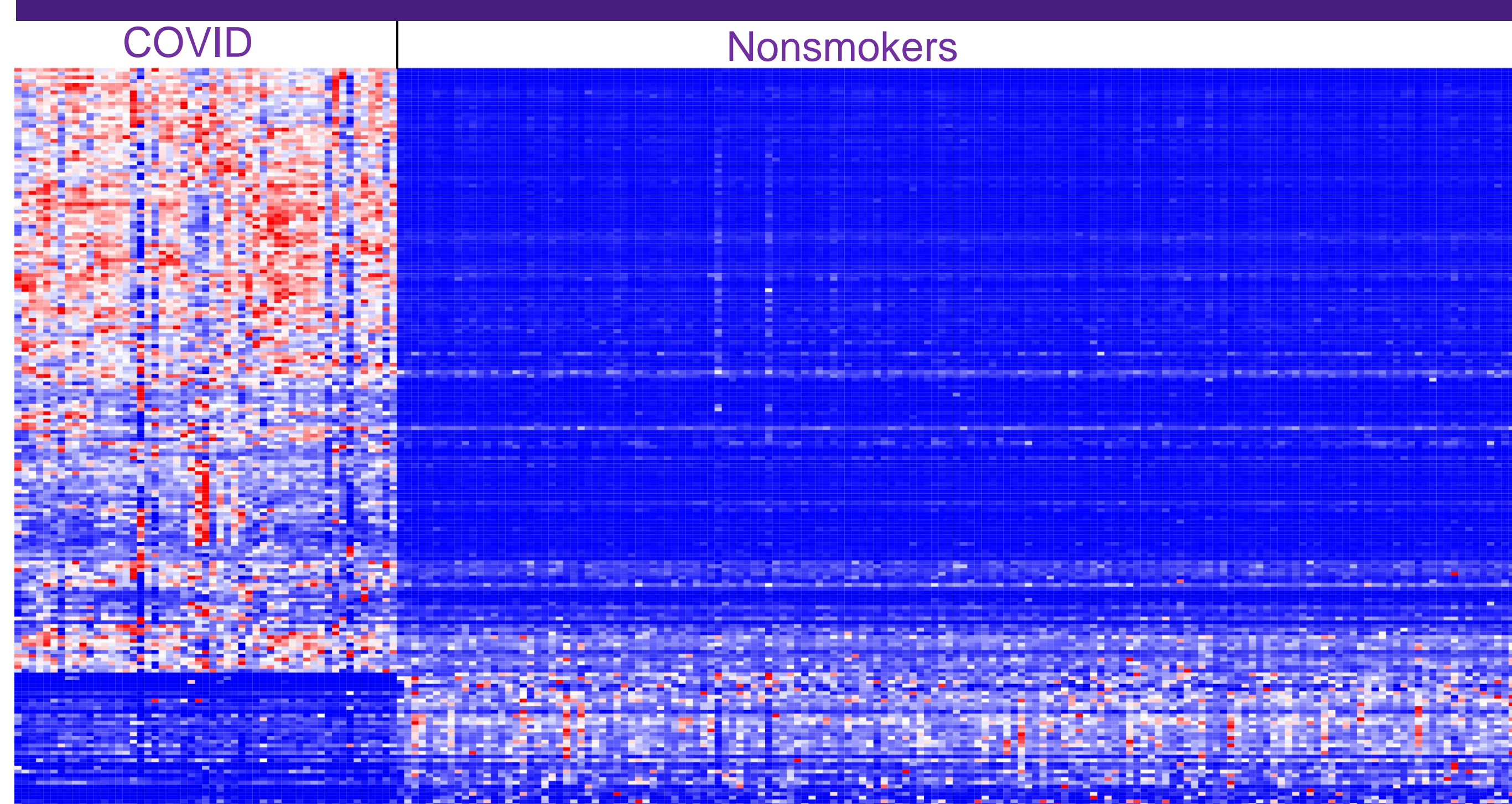

Patterns of Gene Expression in COVID vs Smokers
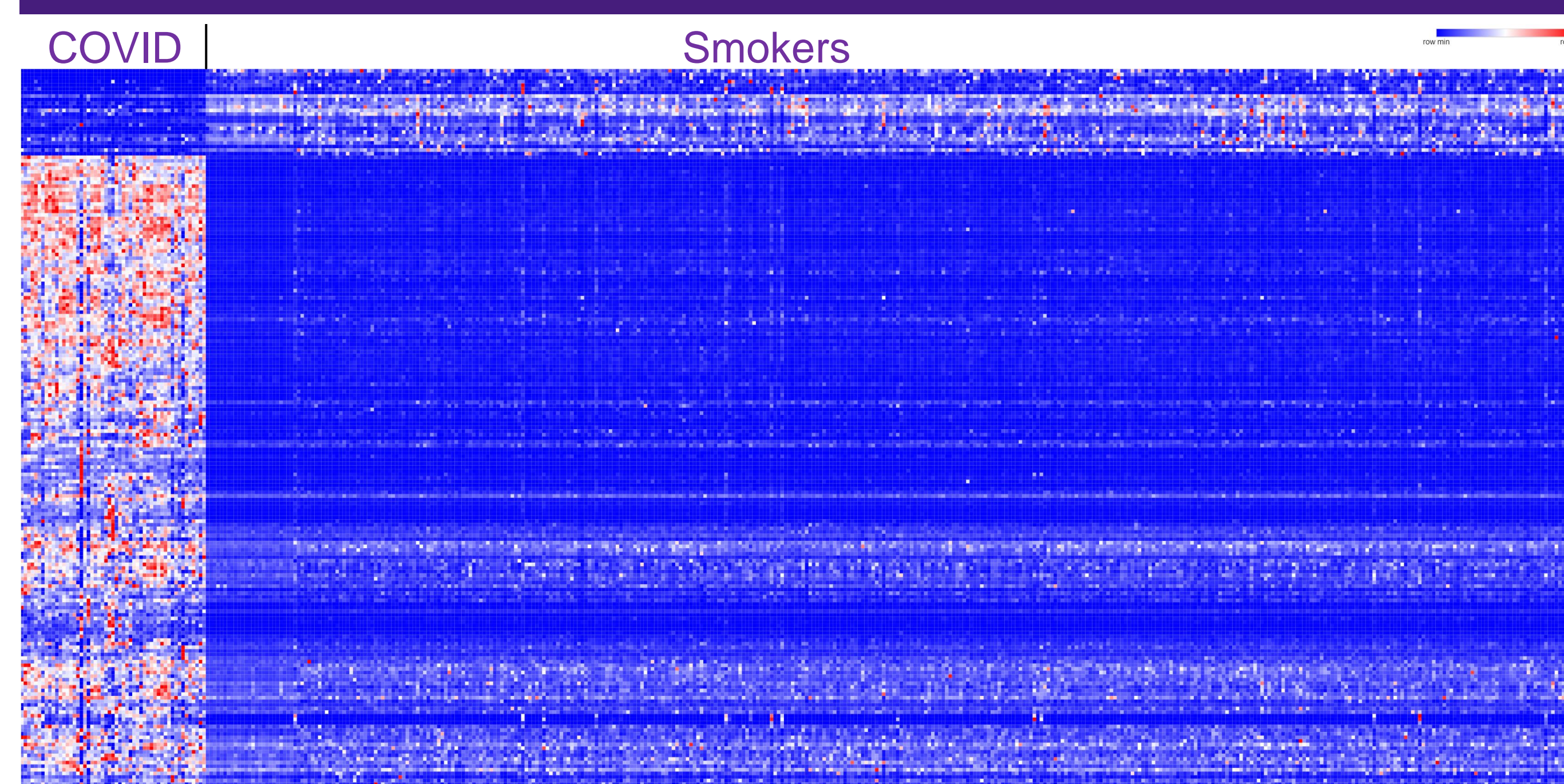
Figure 3: Heatmap from the 557 genes associated with COVID and smokers depicting patterns of expression between the two groups among those genes. Top 200 genes shown
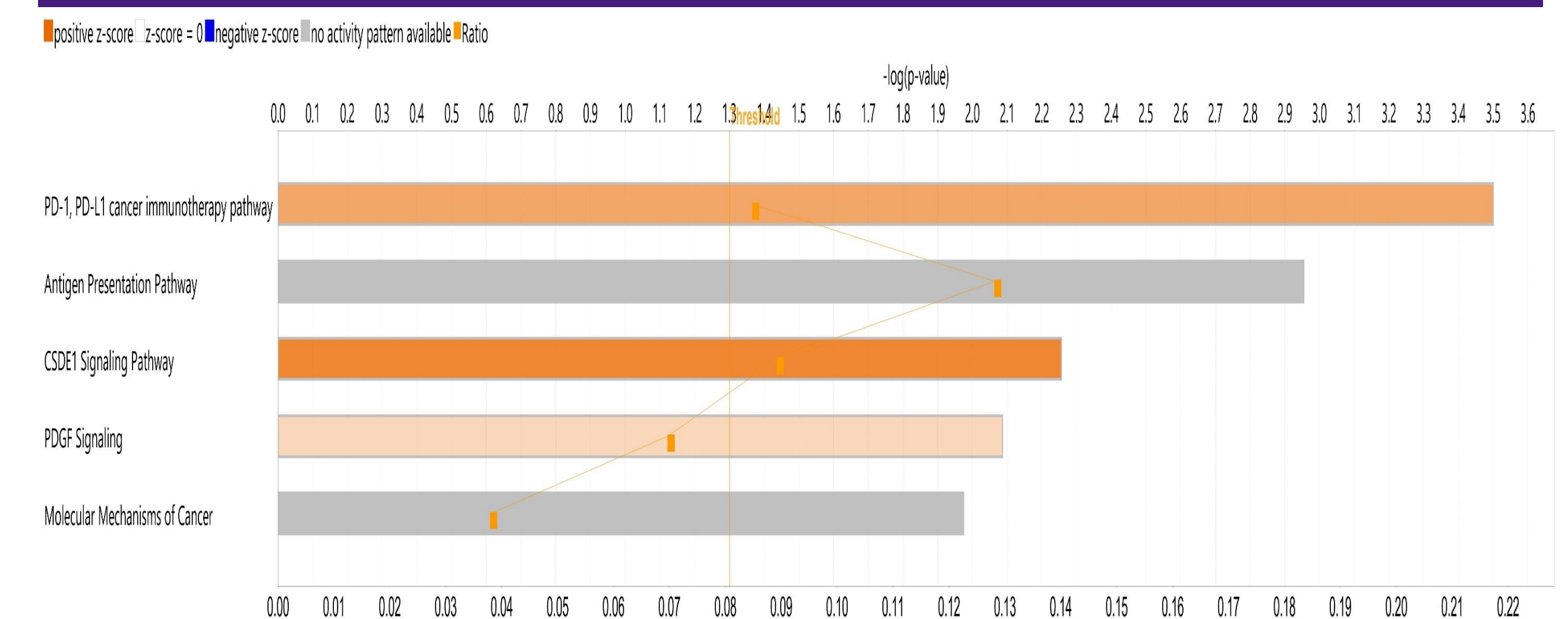
Patterns of Gene Expression in COVID vs Nonsmokers

Figure 4: Heatmap from the 490 genes unique to COVID and nonsmokers depicting differential gene expression between the two groups among those genes. Top 200 genes shown
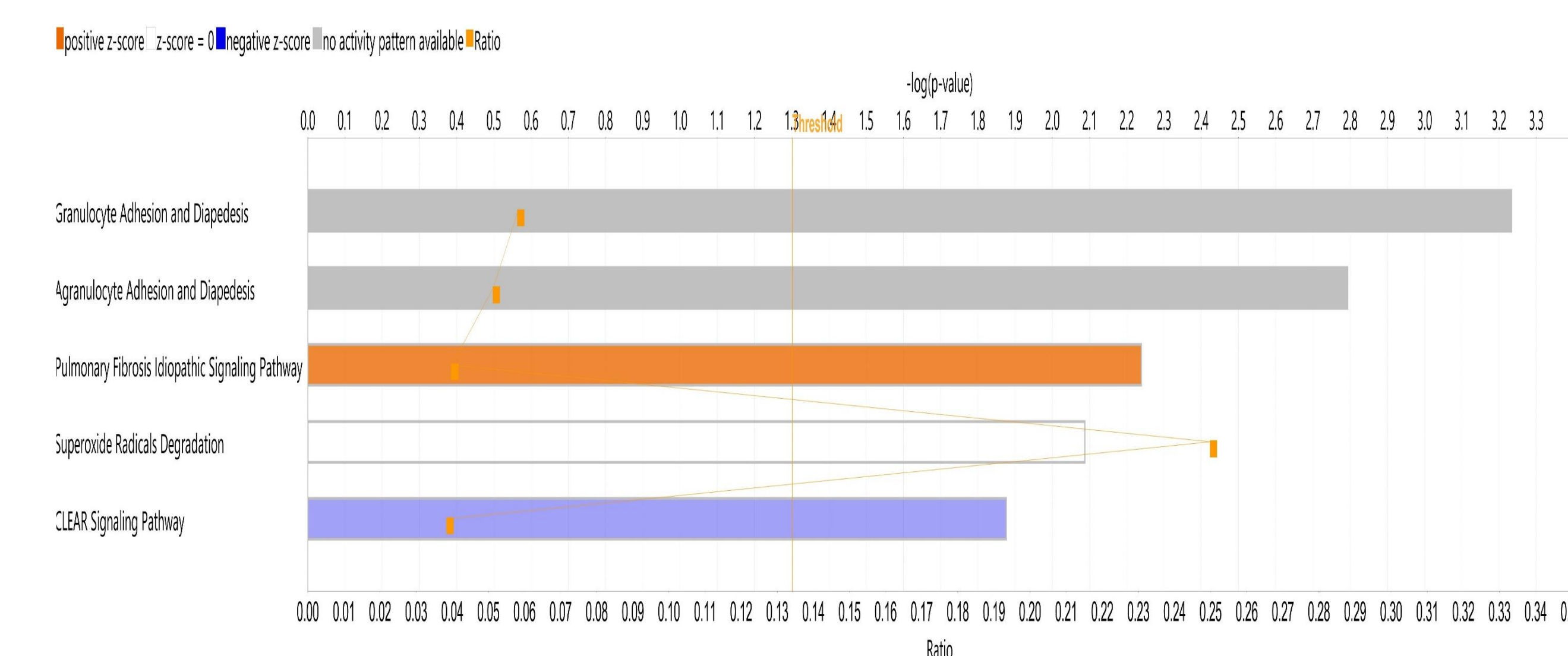
Pathway Analysis

Pathways Involved in COVID and Smokers

Figure 5: Graph showing top pathways driving the association between COVID-19 and lung cancer in smokers.

Pathways Involved in COVID and Nonsmokers

Figure 6: Graph showing top pathways driving the association between COVID-19 and lung cancer in nonsmokers.

Conclusion

- Discovered genes uniquely associated with COVID-19 in smoking lung cancer patients
- Discovered genes uniquely associated with COVID-19 in nonsmoking lung cancer patients
- Different pathways driving the association between COVID-19 and lung cancer in smokers vs nonsmokers.

- Further study is recommended using data from lung cancer patients who also have COVID.