

COPD: FROM BAD TO WORSE

DIFFERENTIAL GENE EXPRESSION IN COPD PROGRESSION

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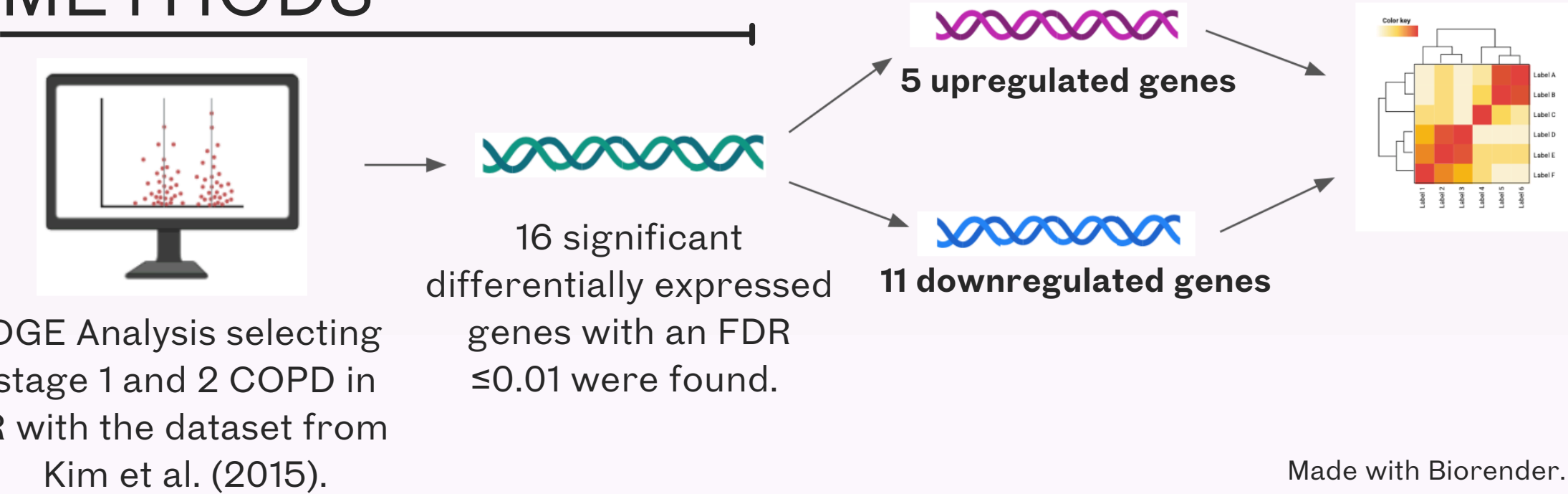


RESEARCH QUESTION: What gene expression differences distinguish moderate COPD from mild COPD, what are their biological functions and could they be used as progression markers?

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a persistent lung condition caused by damage to the lungs. The damage leads to **swelling and inflammation in the airways**, restricting the flow of air into and out of the lungs. COPD is usually caused by long-term exposure to cigarette smoke, dust, or chemicals [1]. This case study examines the difference in gene expression between mild and moderate COPD, using the dataset of Kim et al (2015). **Mild COPD** is characterized by mild airway obstruction, while **moderate COPD** is characterized with lung damage and functional decline [2].

METHODS



HEATMAP

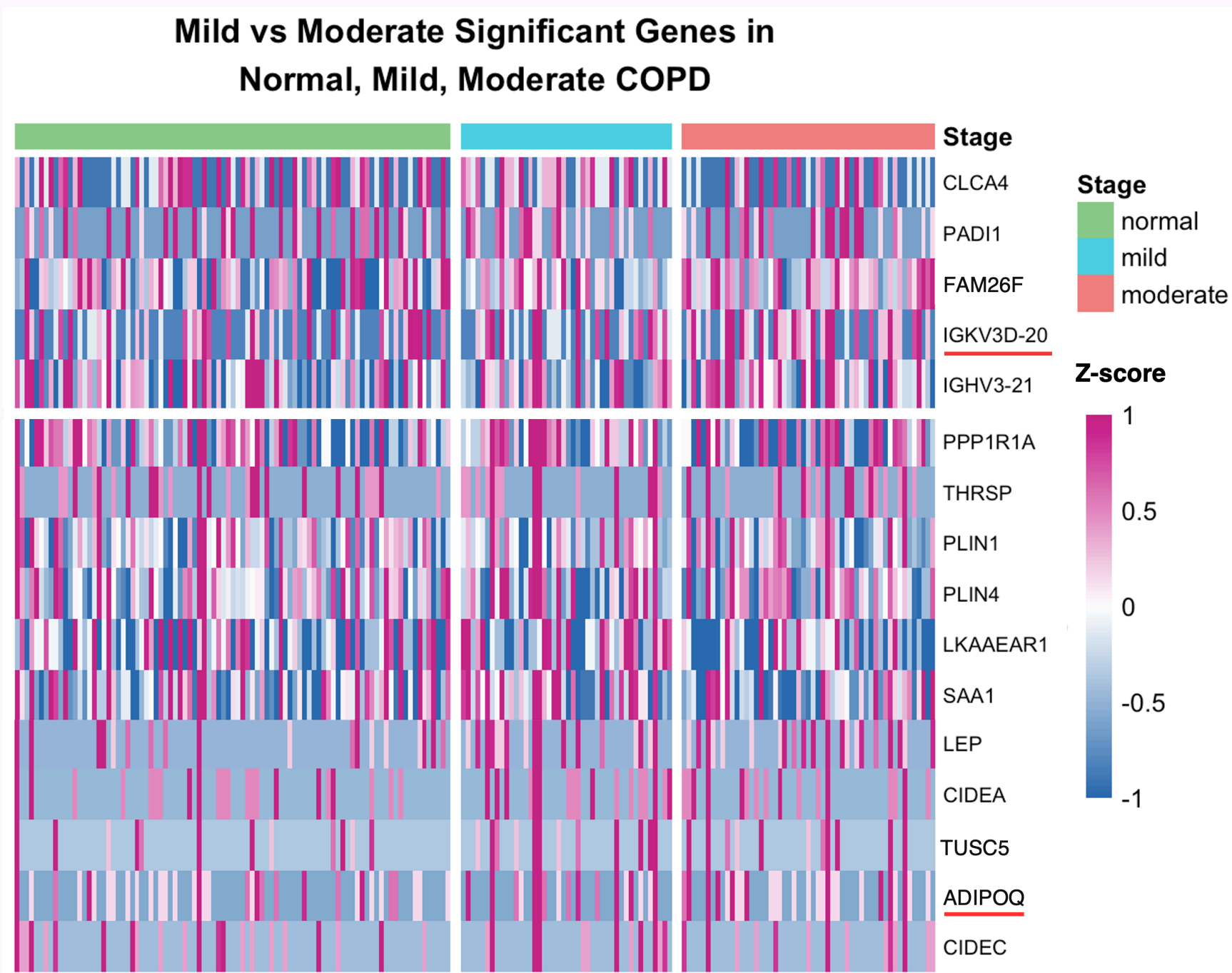


Figure 3: Heatmap showing gene expression differences between normal (green), mild (blue) and moderate (red) COPD. The figure above shows a heat map in which the y-axis displays a list of the 16 most significant genes with the different gene expression between mild and moderate COPD. In addition, a color scale is visible based on the z-score. On the right-hand side of the heat map showing high gene expressing (+1) in pink and low gene expression (-1) in blue. Two genes, which showed significant expressing on the vulcano and MA plot are underlined in red.

DGE VISUALISATION

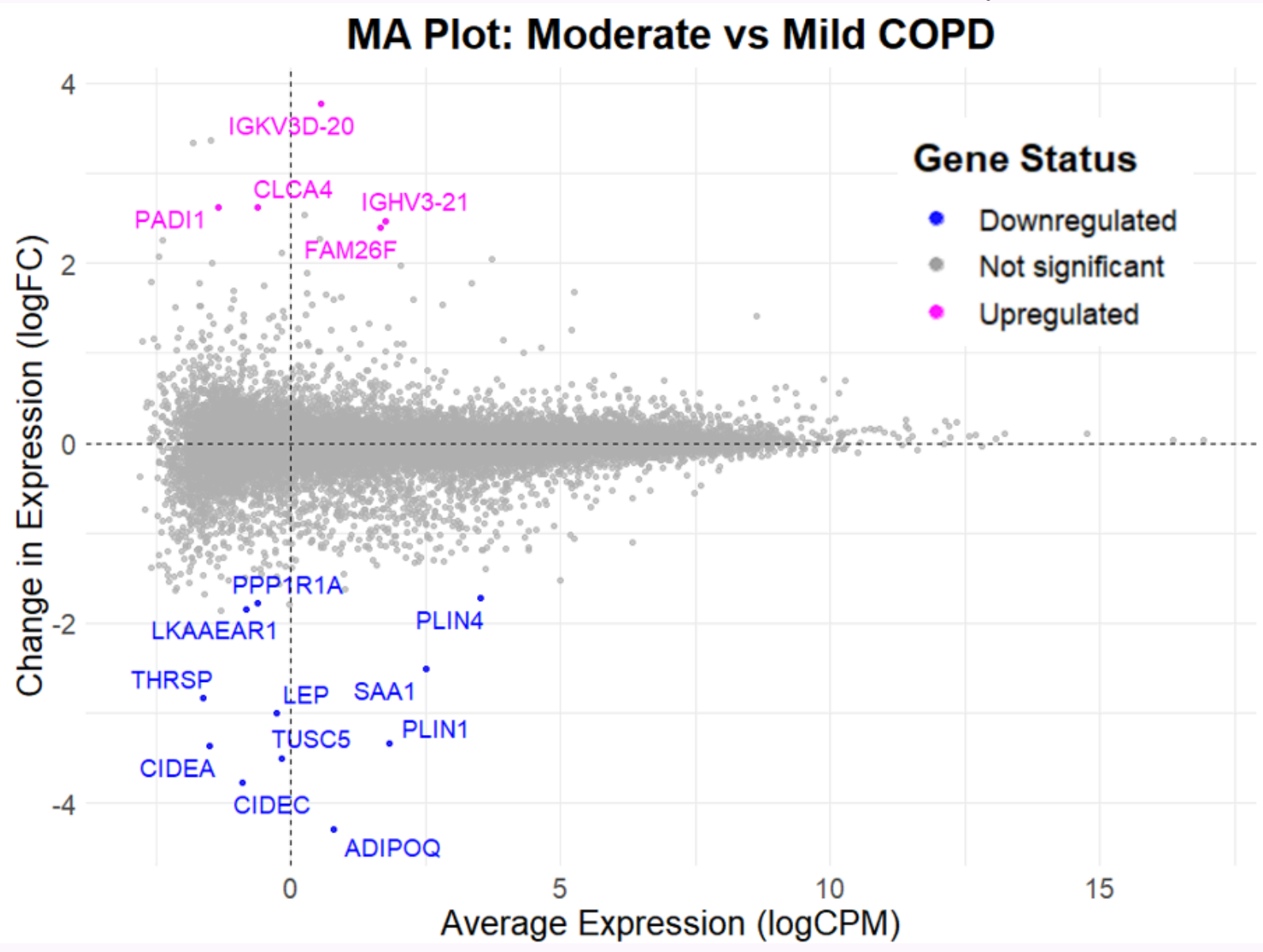


Figure 1: MA plot showing the change in gene expression for stage 2 COPD compared to stage 1 COPD on the y-axis against the average expression on the x-axis. Significantly up- and downregulated genes are highlighted in magenta and blue respectively. The vertical dashed line shows an average gene expression of 1 Count Per Million.

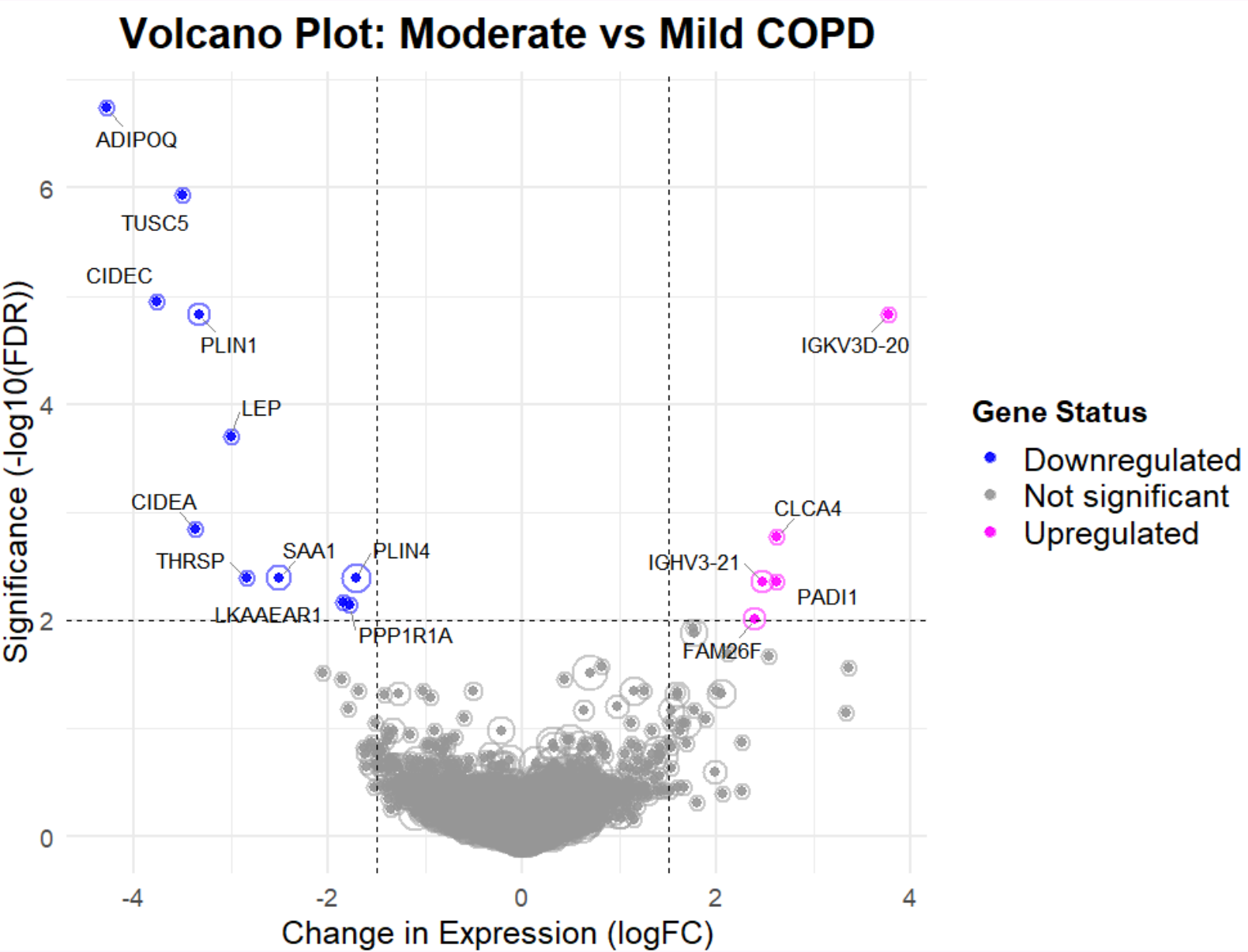


Figure 2: Volcano Plot showing the magnitude of fold change on the x-axis and the significance of the differences on the y-axis. The general expression of the genes is highlighted by the sphere surrounding the data points. The genes above the horizontal axis are significantly up- or down regulated between moderate compared to mild COPD. The genes inside the dotted lines show relatively low expressional differences between these two stages of the disease.

IGKV3D-20 (upregulated) and **ADIPOQ** (downregulated):

- Largest Fold Changes
- Highest significance
- Above threshold average gene expression of 1 CPM.

DIFFERENCES IN BIOLOGICAL FUNCTION

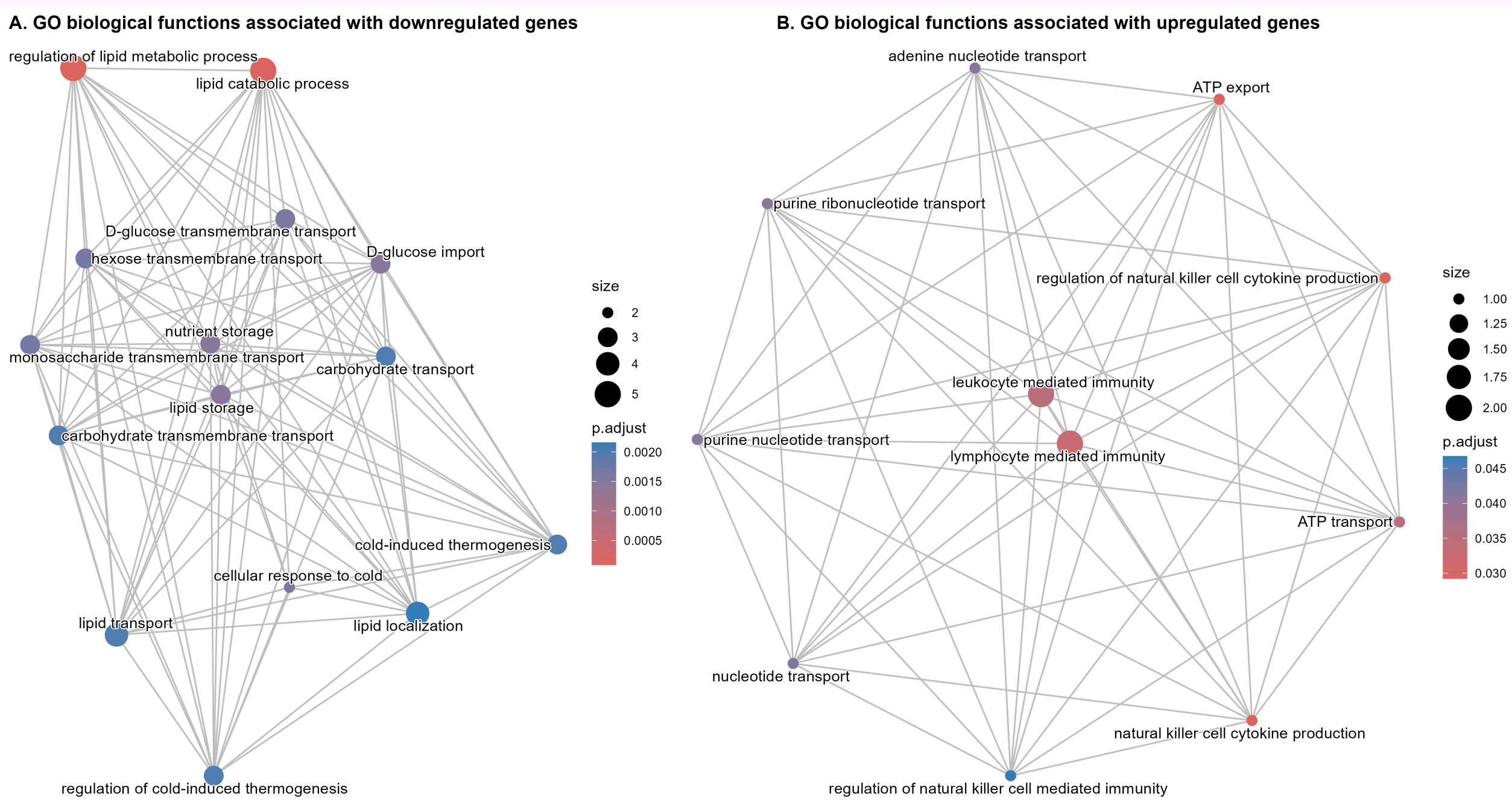


Figure 4: Gene ontology term enrichment analysis performed on the A: 11 found significantly downregulated genes and B: 5 significantly upregulated genes between moderate compared to mild COPD patients. The sizing showcases the number of genes associated with the biological process. Graph A showcases downregulated regulation of lipid metabolic processes, lipid catabolic processes amongst other metabolic processes while graph B shows upregulation within immunological pathways.

CONCLUSION

- 16 differentially expressed genes were found
 - 5 were **upregulated** in moderate COPD
 - 11 were **downregulated** in moderate COPD
 - Most interesting genes → **IGKV3D** and **ADIPOQ**
- Important functions of genes
 - **Immune response** upregulated
 - **Lipid metabolism** downregulated
- High **inter-patient variability**
 - No progression markers

FUTURE PERSPECTIVES

- Single cell RNA sequencing
- Study all COPD stages (incl. stage 3 (severe) COPD)
- Larger sample size

REFERENCES AND SUPPLEMENTARY DATA

