PM2.5 engages impairment of mucosal immunity, involving alteration of complement activation and cell junction assembly by regulated IL-17 levels pathological and proteomic approaches

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Abstract

PM2.5 is known for the induction of lung toxicity. However, the underlying mechanisms are yet to be characterized. BALB/c mice were intratracheally administered with concentrations of PM2.5 daily for 7 days. Histopathological analyses of lung tissue were performed. BALF proteomics were analyzed using QTOF LC-MS/MS. GO enrichment analysis, KEGG pathways, Reactome analysis, and STRING protein networking further assessed functional protein data. Specific proteins of interest were validated using multiplex ELISA. We found that PM2.5 induced marked neutrophilic inflammation in the lungs in a dose-dependent manner. Proteomics analysis identified 147 differentially expressed proteins (43 down-regulated and 104 up-regulated). GO analysis revealed that up-regulated proteins are mainly secretory and implicated in the inflammatory response, complement activation, and assembly of various cell junctions. Additionally, a decrease in serum IL-17A levels suggests its involvement in PM2.5-induced mucosal immunity impairment in the respiratory tract and potentially in non-exposed organs.

Background

This study aims to apply the proteomic analysis to identify PM2.5-induced changes of cellular protein expression and investigate the mechanisms of PM2.5-induced lung inflammation
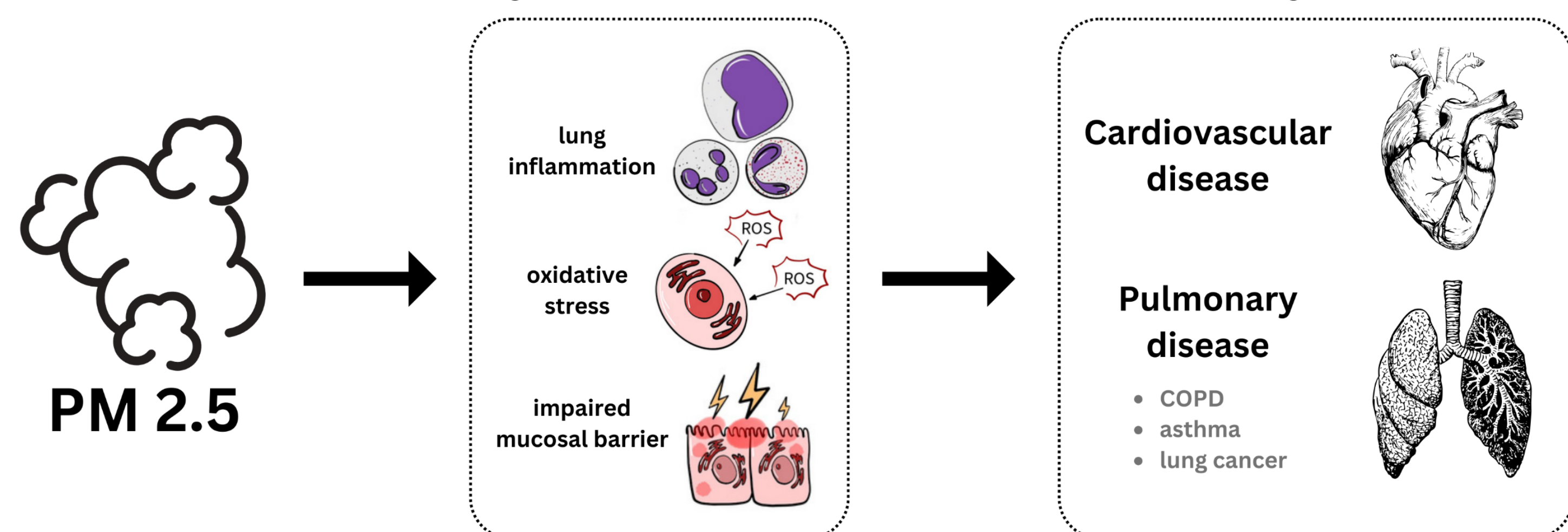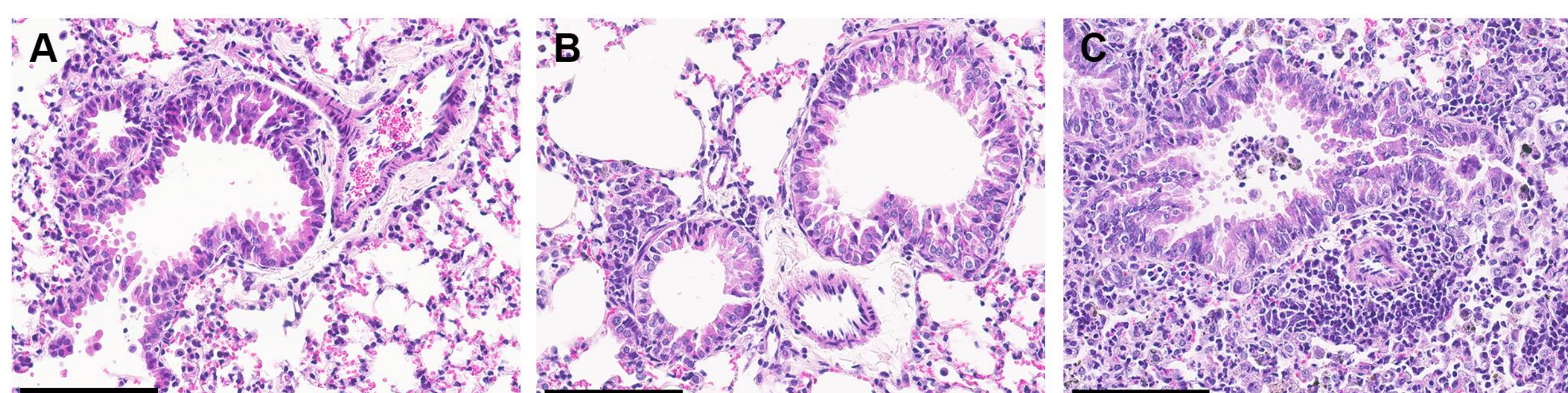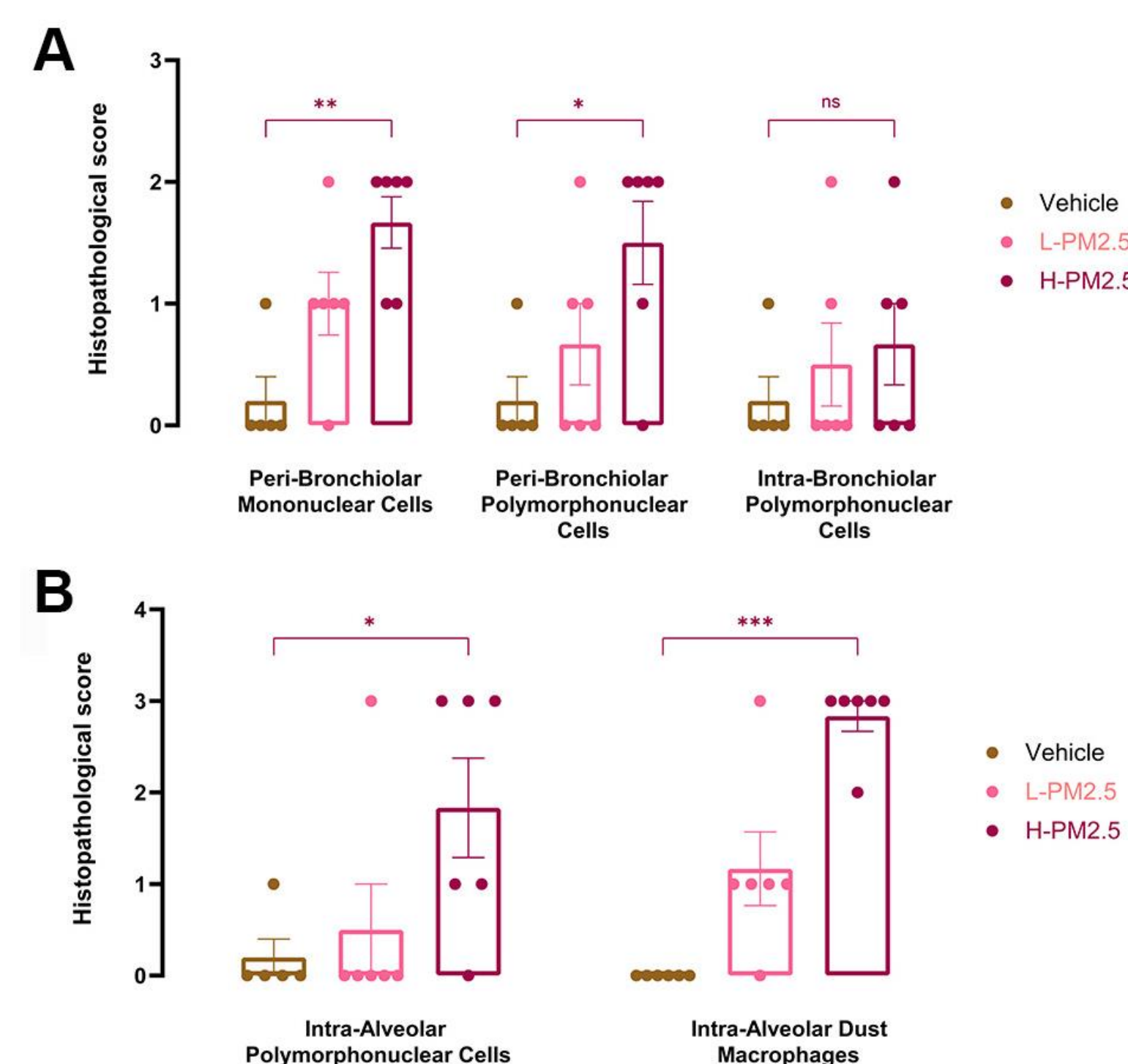

Methods
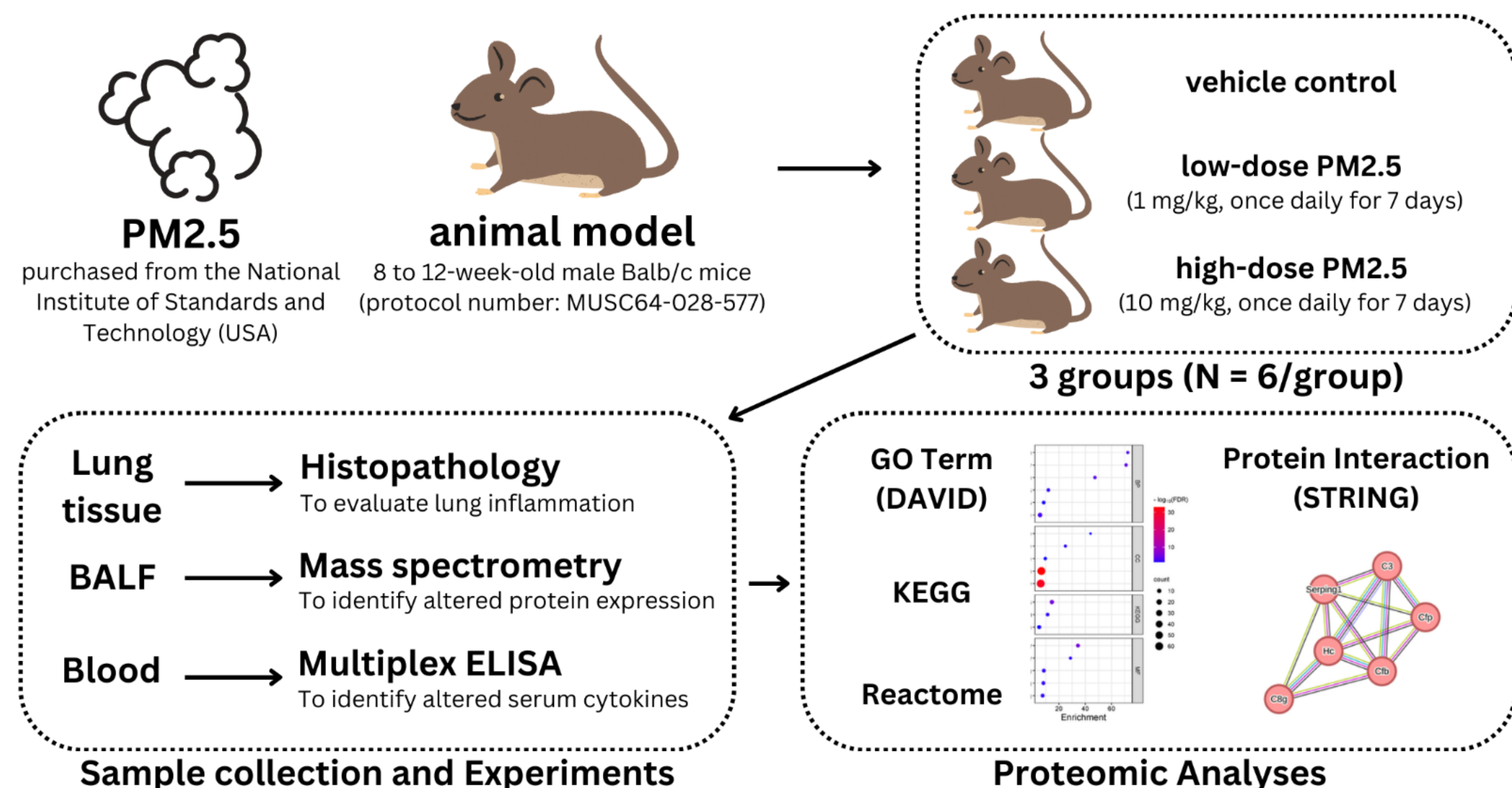
Result

1. PM 2.5 induces lung inflammation in mice.

Figure 1 H&E staining showing the infiltration of inflammatory cells such as neutrophils, macrophages, and lymphocytes, which are relatively increased in mice's lung section with control (A), low-dose (B), and high-dose(C) of PM2.5 exposure, respectively. (Scale bar = 200 μm)

Figure 2 Histopathology scores depicting the recruitment of inflammatory cells in the bronchi (A) and alveoli (B) in a dose-dependent manner

Result

2. PM2.5 alters proteomic characteristics in mice BALF.

Of the 478 proteins identified, 147 showed significant differences in expression (P<0.05). Among these, 43 were down-regulated, and 104 were up-regulated. Proteomic analyses indicated that the altered proteins were involved in complement activation, inflammatory response, and regulation of cell junction assembly.
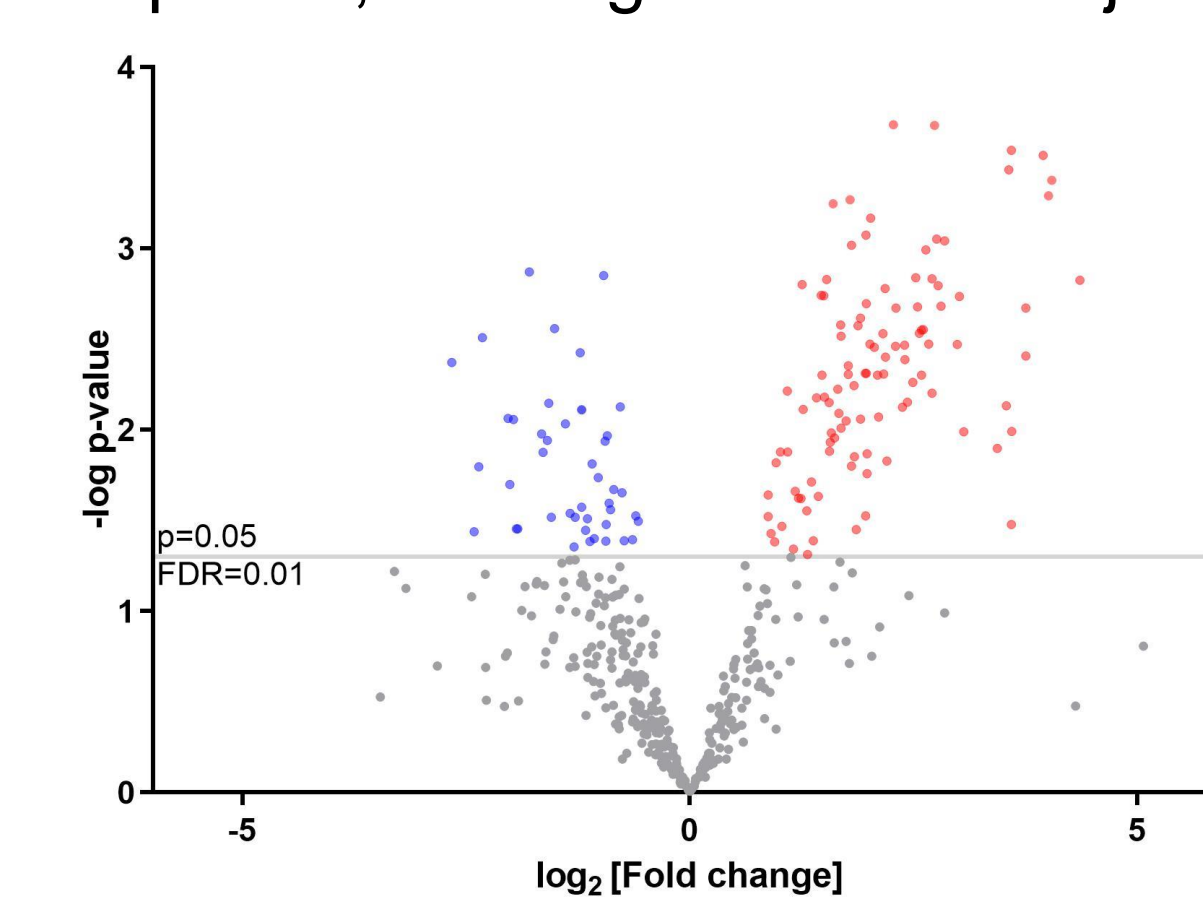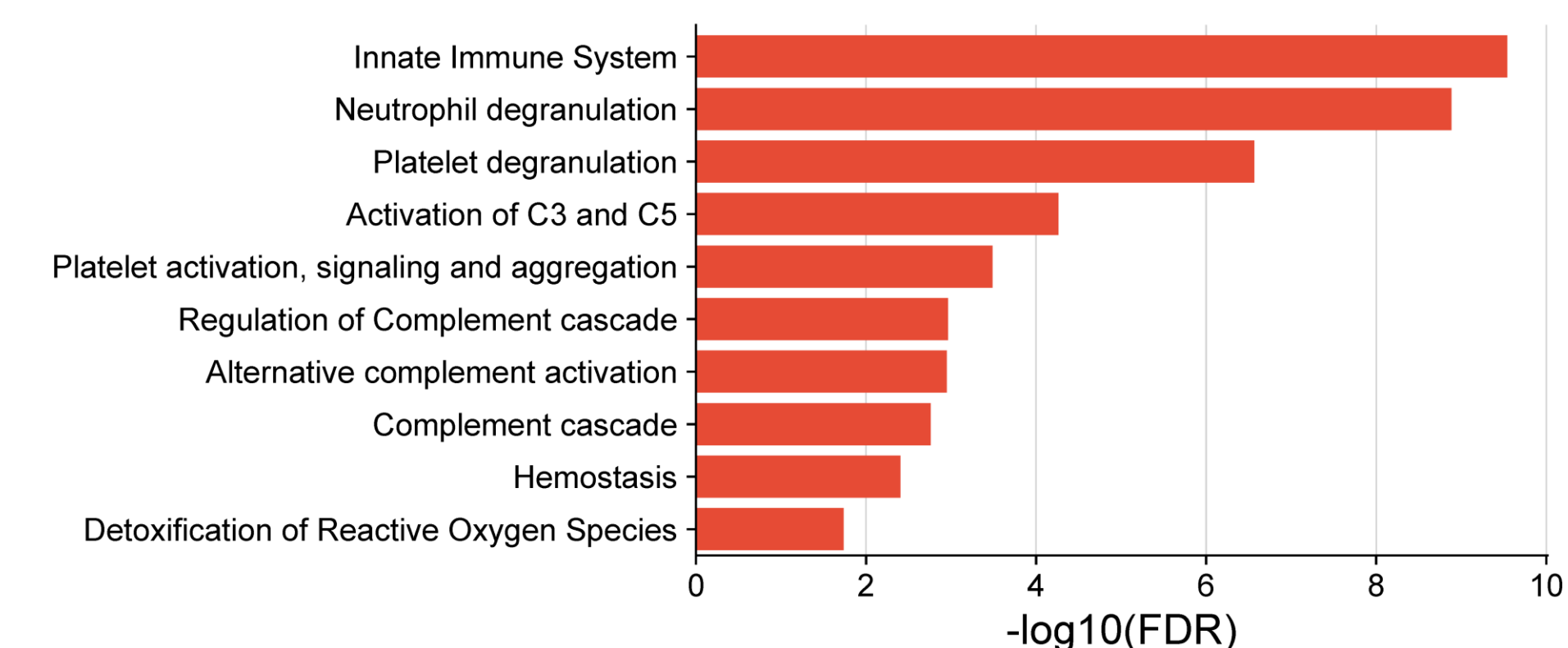

Figure 3 Volcano plot of differentially expressed (P<0.05) BALF proteins
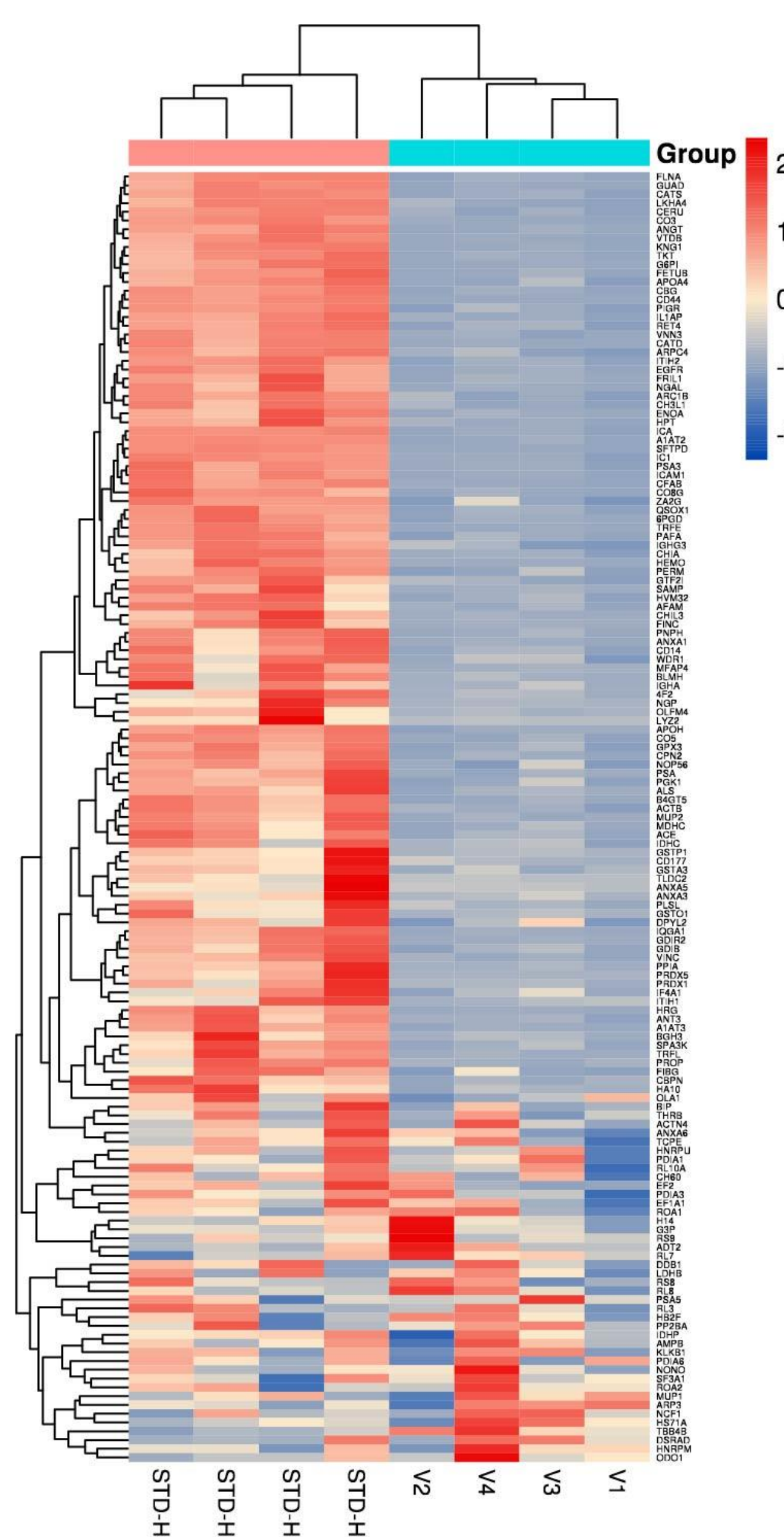
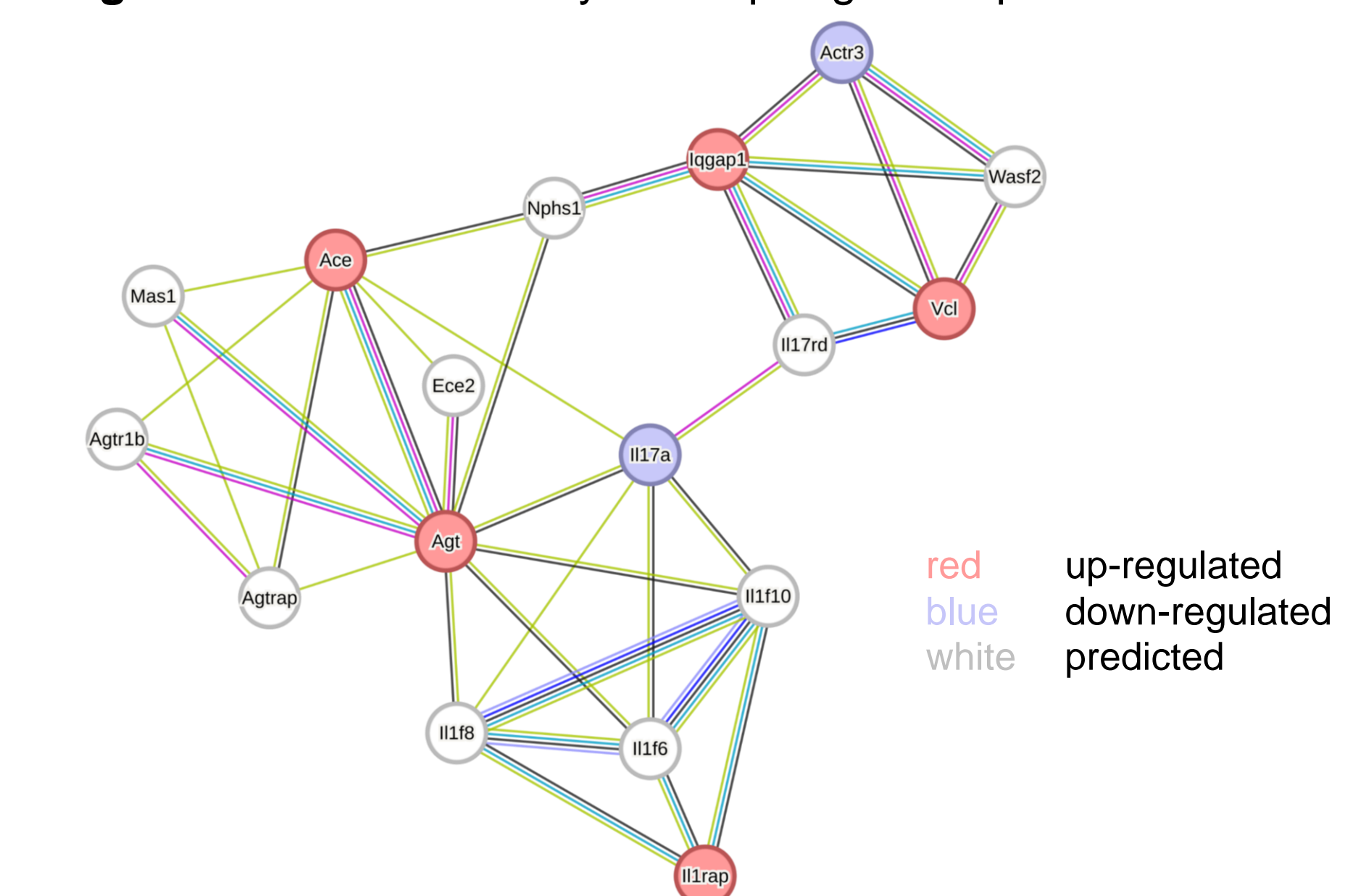Figure 4 Cluster heatmap of differentially expressed (P<0.05) BALF proteins
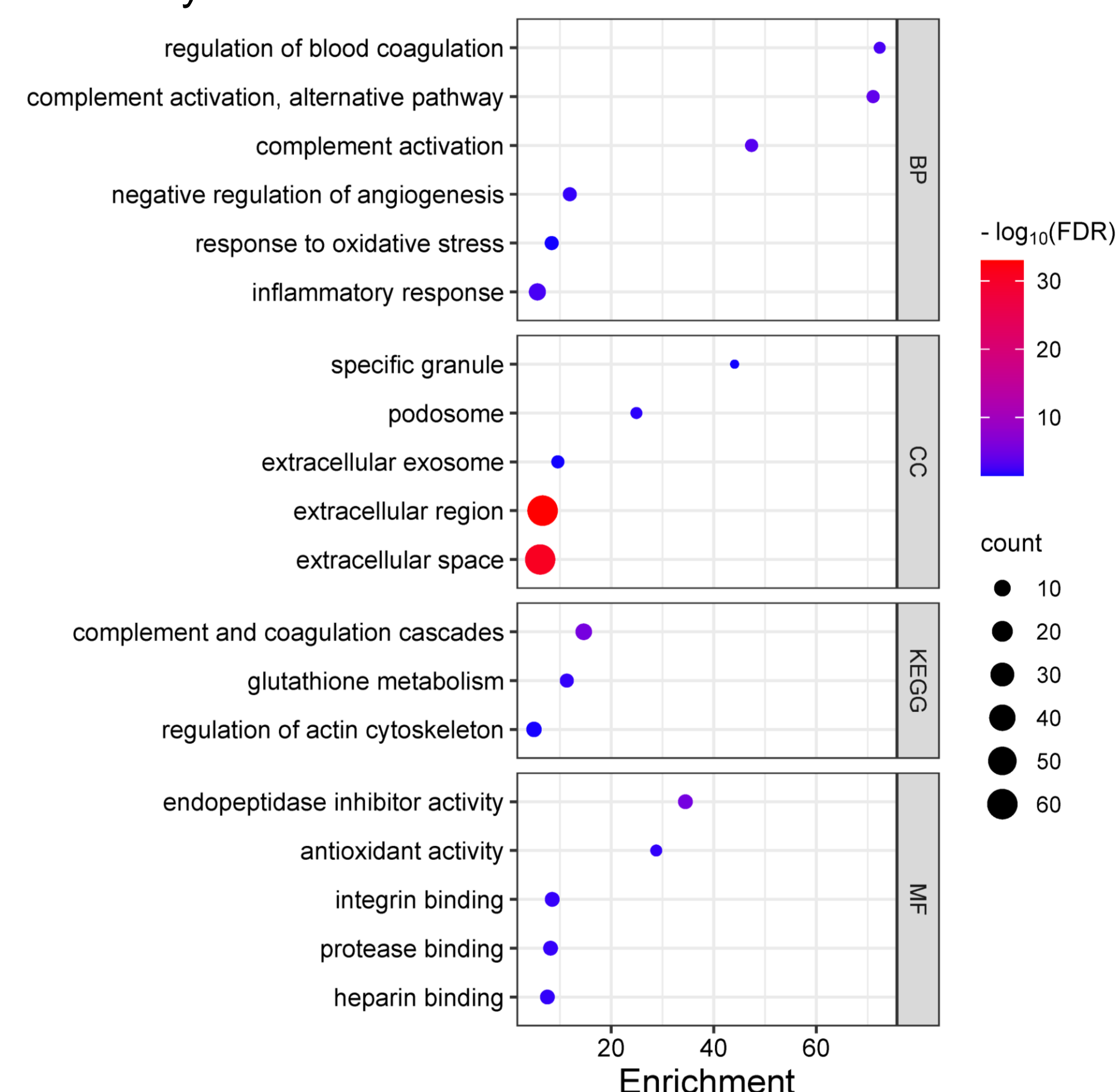
Figure 5 GO analysis using DAVID of up-regulated proteins

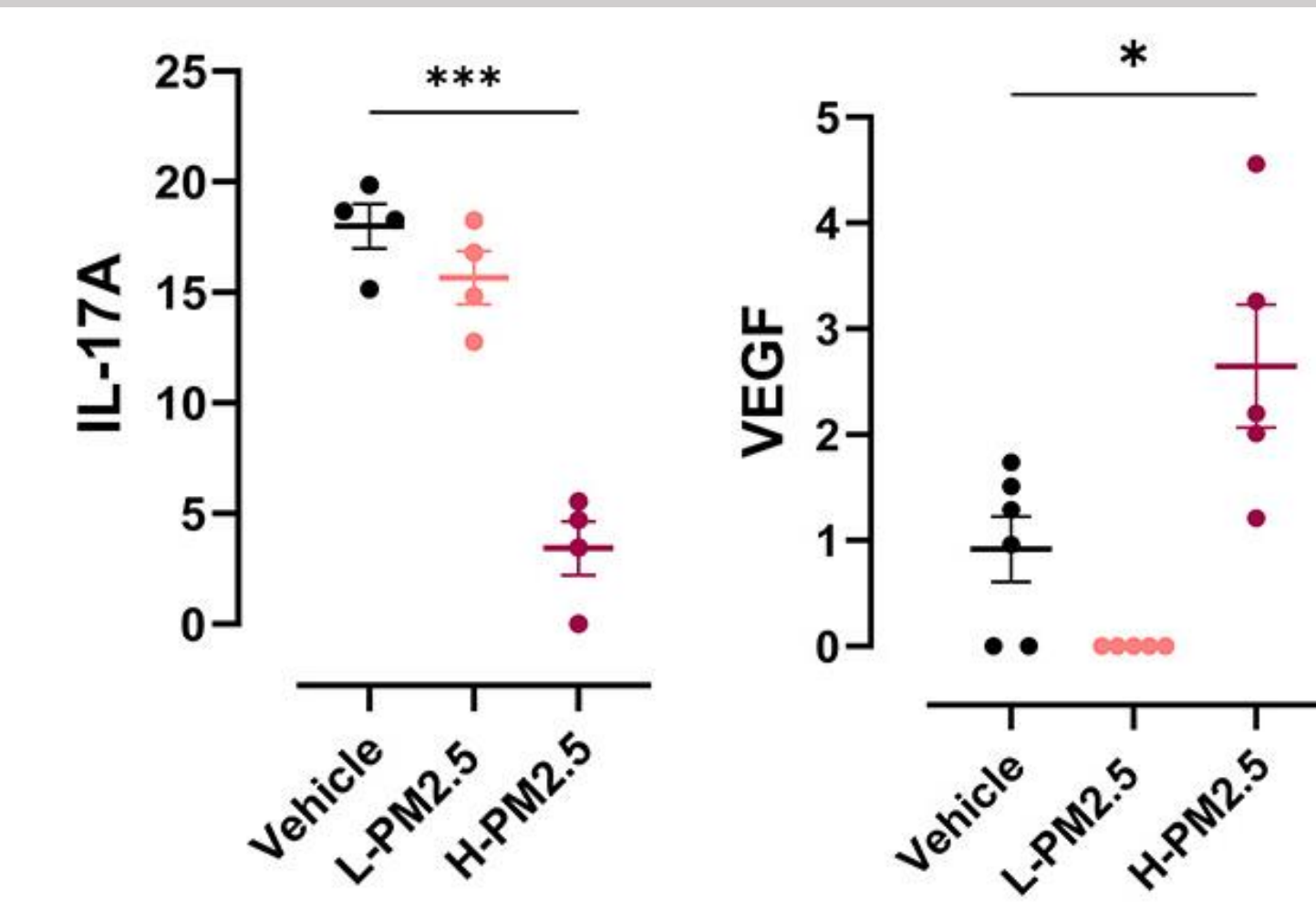Figure 6 Reactome analysis of up-regulated proteins

red — up-regulated
blue — down-regulated
white — predicted

Figure 7 STRING protein interaction network

3. PM2.5 alters the IL-17 and VEGF levels in mice serum.

Figure 8 Combined bar graphs and scatter plots illustrating results from Multiplex ELISA showing IL-17 and VEGF levels after exposure to different amounts of PM2.5

Acknowledgment

Conclusion

Our findings provide evidence of the mechanistic involvement of IL-17 in PM2.5-induced inflammation. This insight facilitates the development of biomarkers for PM2.5 exposure and targeted therapies for PM2.5-related lung diseases.