

AGING THROUGH ORGANS: *How Gene Expression Changes with Time*

Group 14: Anca Gorunescu, Bokke Bronswijk, Hielko Kasma, Esmée van Peer, Esmee Werkman, Kaj Mulder

To what extent does **gene expression** differ in certain organs depending on the **age of death**?

1. Data Grouping

- GTEx data for aorta, hippocampus and lung



2. Analysis

- Differential expression analysis with **DESeq2** (R library), **FDR-adjusted**.
- Functional enrichment of significant genes via **G:Profiler**.
- **PERMANOVA** on PCA distances to assess transcriptomic differences by age.

3. Visualization

- **Variance-stabilizing transformation**
- **PCA** to show age-dependent clustering
- Visualized with **volcano plots** highlighting significant genes.

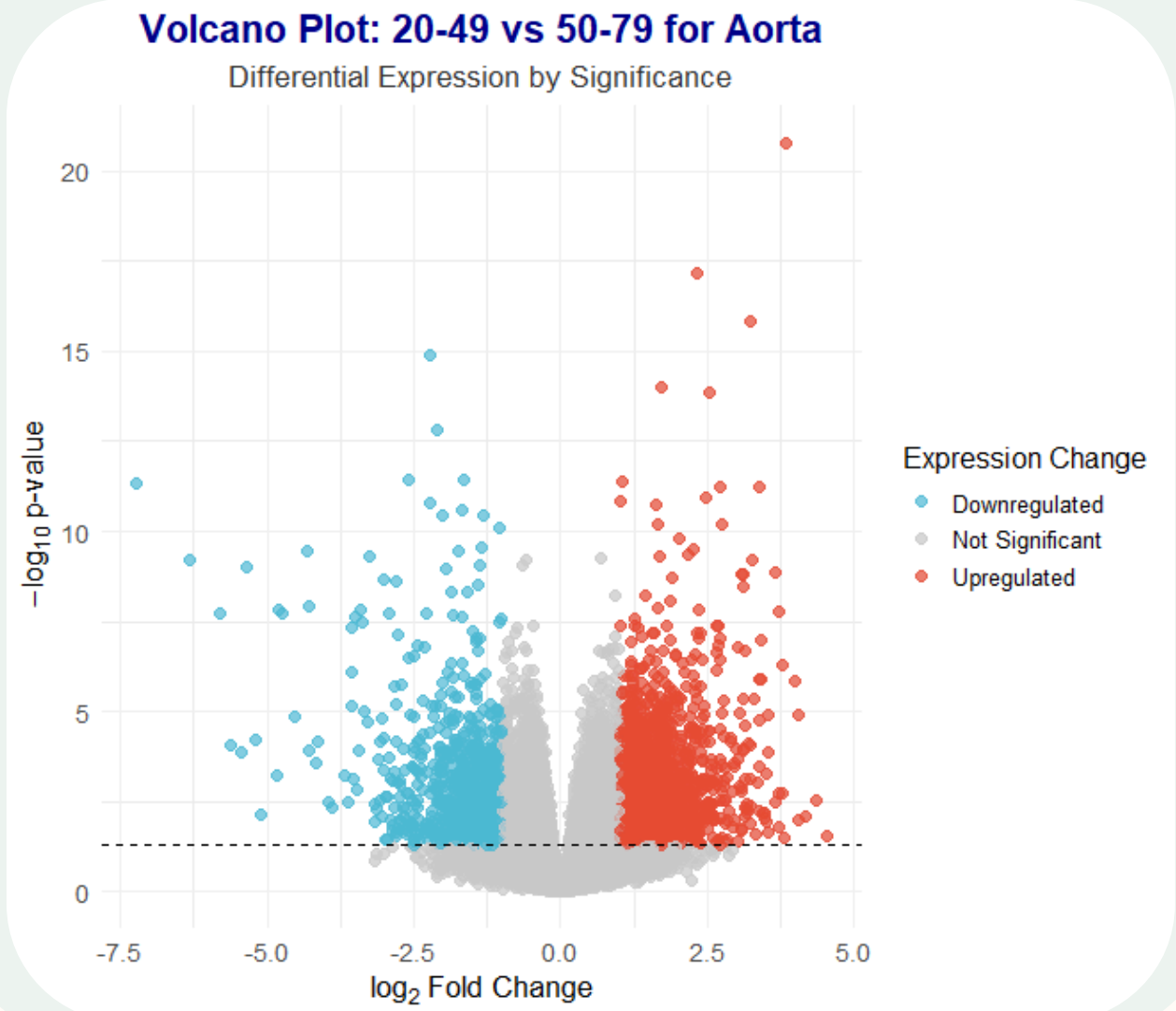
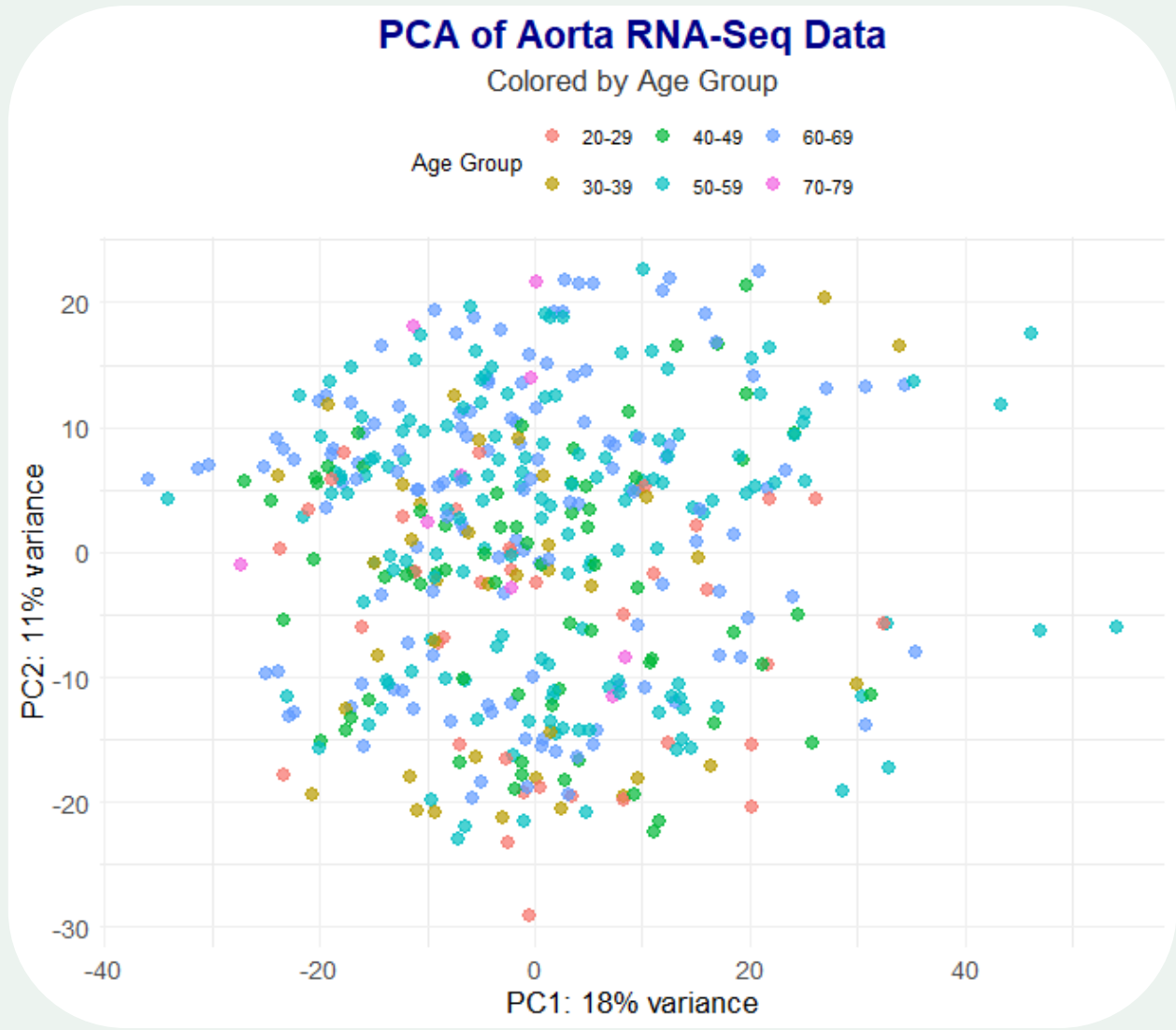
AORTA

- **Vascular aging** contributes to **age-related CVDs** (Gao et al., 2020).
- In mice, **aging** increases **immune/inflammatory activity** and reduces **ECM integrity** and **stress response** (Gao et al., 2020).
- In primates, **longevity-related genes** are **downregulated with age** (Zhang et al., 2020).

Are the same differences present in humans?

PCA: No clear age-group clustering → major variance not age-driven (3.7%, $p=0.001$).

Volcano plot: Comparing Young (20–49) vs Old (50–79) shows significant up- (2049) and downregulated (889) genes.



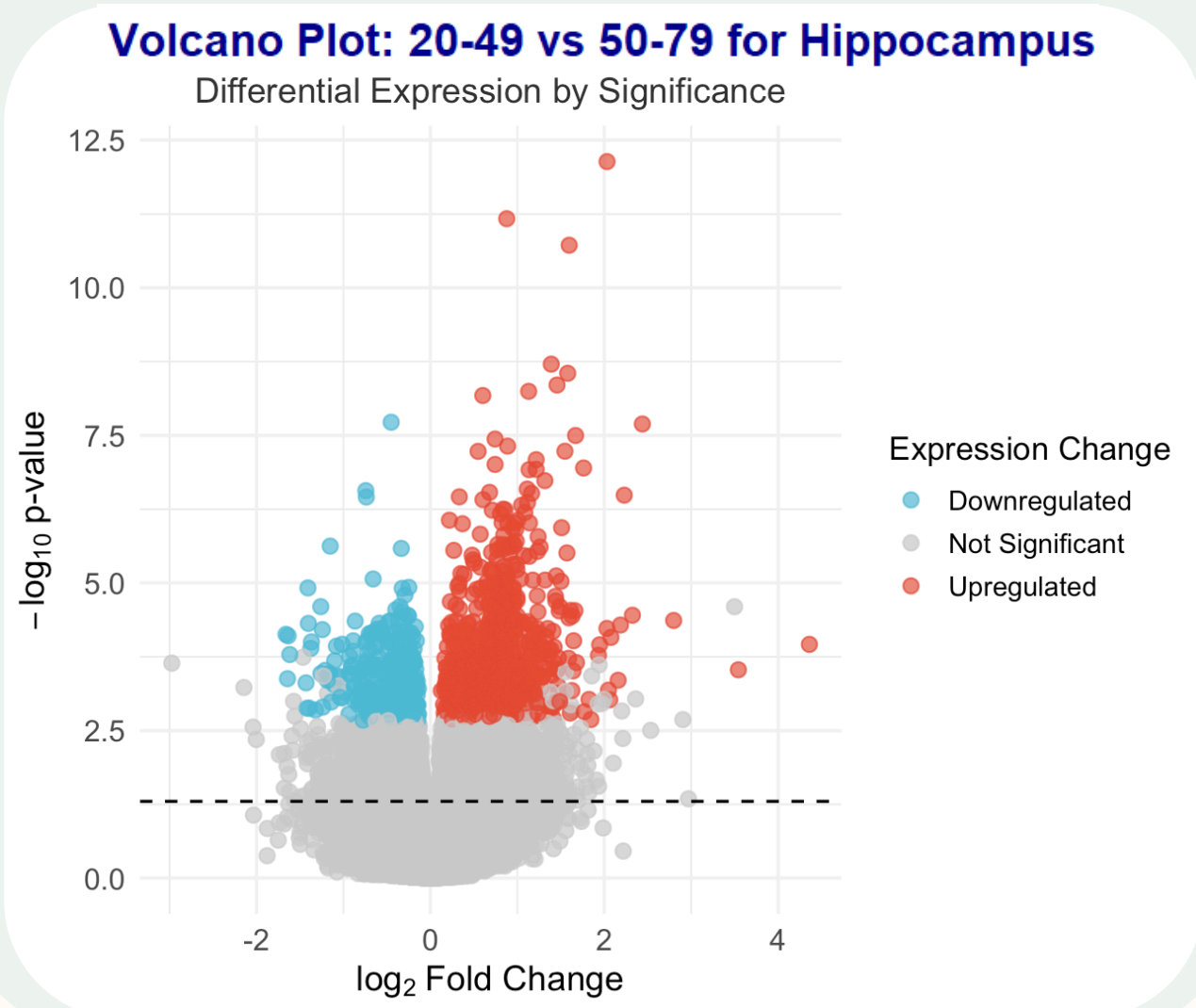
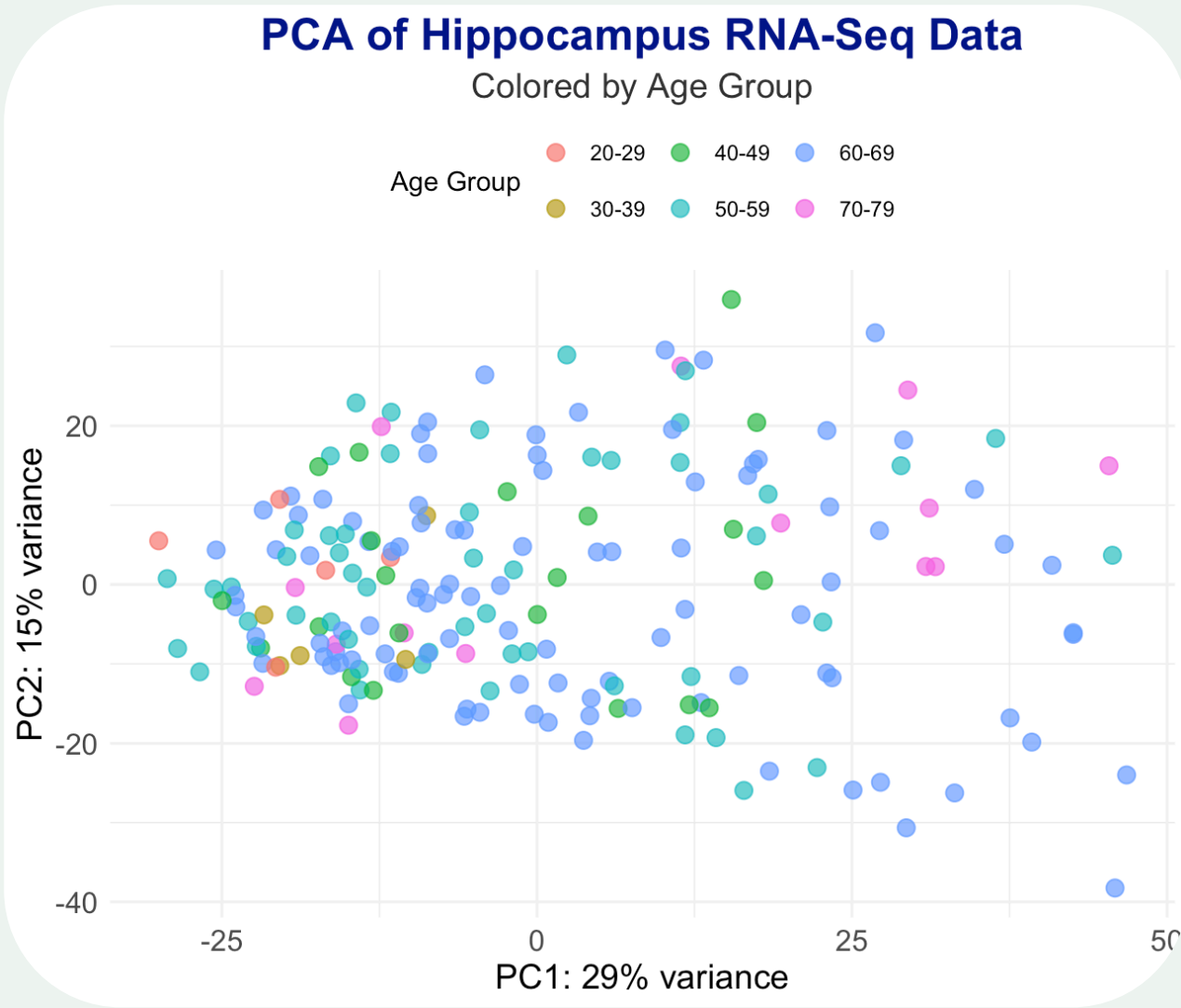
HIPPOCAMPUS

- The hippocampus is **particularly vulnerable** to the aging process (Bettio et al., 2017).
- Hippocampal volume peaks in the fourth decade and **declines progressively with age** (Gohel et al., 2025).
- Brain aging involved expression of **genes** linked to **mitochondrial dysfunction, inflammation, and stress responses** (Zeier et al., 2011).

Are these declines visible in gene expression?

PCA: No clear clustering → after PERMANOVA: significant effect (p -value : 0.001***), 4.7% of variance explained by age.

Volcano plot: Comparing Young (20-49) vs. Old (50-79) shows significant up- (1572) and downregulated (753) genes.



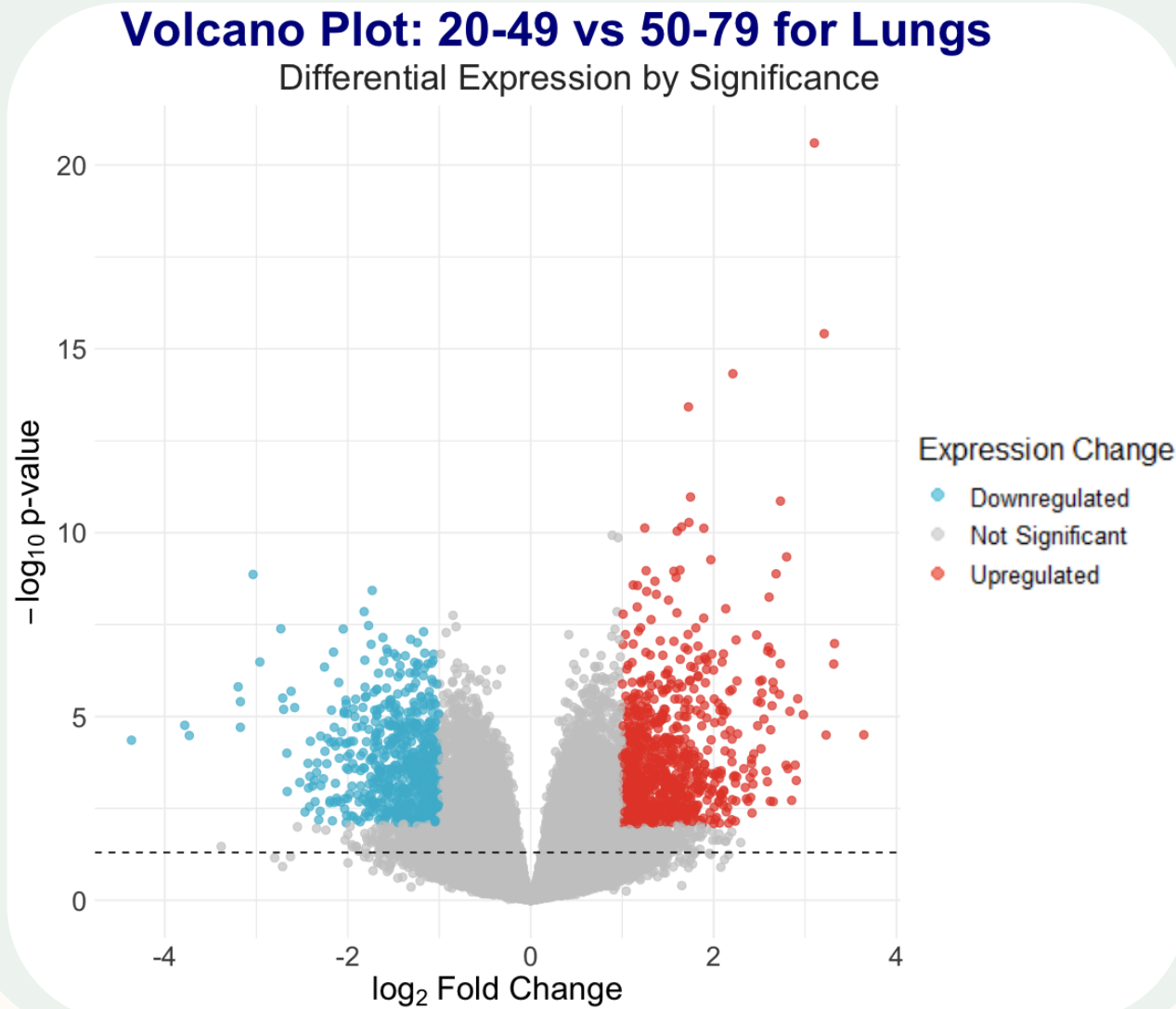
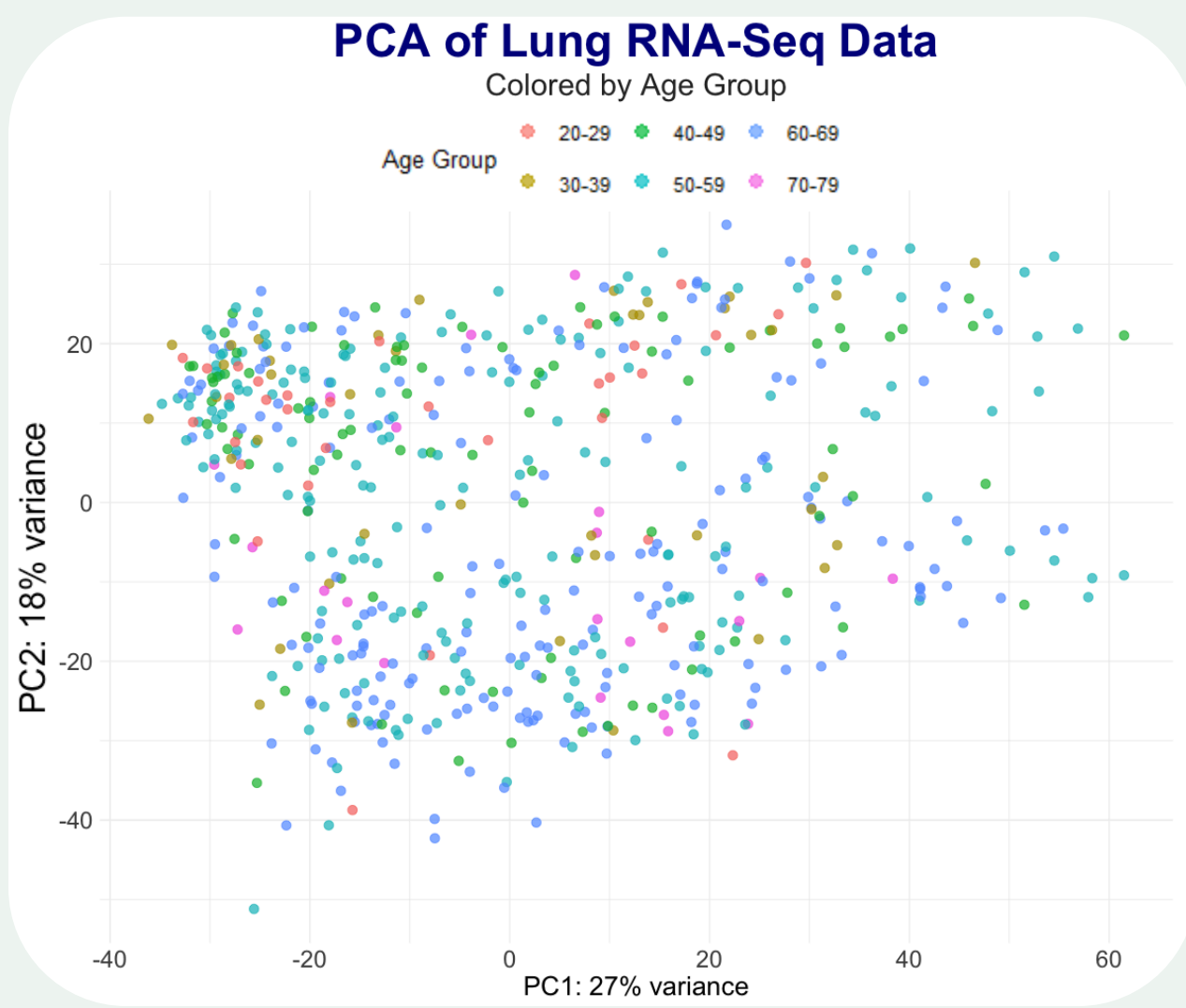
LUNG

- Aging **impairs lung elasticity**, reduces immune defenses, and increases susceptibility to **respiratory diseases** like pneumonia and COPD (Berger et al., 2010)
- Some genes are more **up/downregulated in the lungs** when we have compared different age groups in **previous RNAseq research** (Jeong et al., 2020)

Are these declines visible in gene expression?

PCA: No clear age-group clustering → After PERMANOVA: Significant clustering, 23.83% of variance explained by age with p -value = 0.001

Volcano plot: Comparing Young (20–49) vs Old (50–79) shows significant up- (836) and downregulated (632) genes.



CONCLUSION

Gene expression changes with age are organ-specific:

- **Metabolic and stress response genes** upregulated and **structural and oxidative stress-related genes** downregulated in the **aorta**
- **Immune activation and RNA editing genes** upregulated and **neuronal structure genes** downregulated in the **hippocampus**
- **Tissue repair and inflammation genes** upregulated and **airway defense and regeneration** downregulated in the **lung**

Overall, very little overlap in age-related gene changes was observed across organs, with statistical analysis confirming no significant shared changes, highlighting that aging drives distinct molecular processes in different tissues.

REFERENCES

