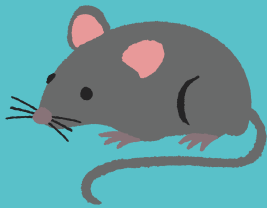


Comparative Transcriptomic Analysis of Aging in Rat Brain, Liver, and Kidney



Introduction

- **Yu et al. (2014)** profiled 11 rat organs across their lifespan
- We examined the **DEGs of the Brain, Liver, and Kidney between 21 weeks (adult) and 104 weeks (aged)**
- **Organ Purpose:** Kidney, brain and liver were selected because they differ in cellular composition, metabolic activity and tissue functions.
- **Age Purpose:** 21 and 104 week old rats were chosen to examine age-related changes in gene expression between young adult and older adults.
- **RQ:** How do age-related gene expression changes differ across the rat brain, liver, and kidney, and which organ shows the strongest transcriptomic signature of aging?

Methodology

1. **Data:** Gene expression in rats data from Yu et al.
2. **Filtering:** Lowly expressed genes removed using CPM thresholds
3. **Selection:** Samples filtered for the tissue of interest (brain, liver and kidneys) at age 21 and 104 weeks
4. **Analysis:** Normalization and DGA performed with edgeR
5. **Visualization:** Results placed in a volcano plot
6. **Analysis:** DEG overlap between organs shown in UpSet plot
7. Top significant genes roles identified via Ensembl.org



Volcano Plots By Organ

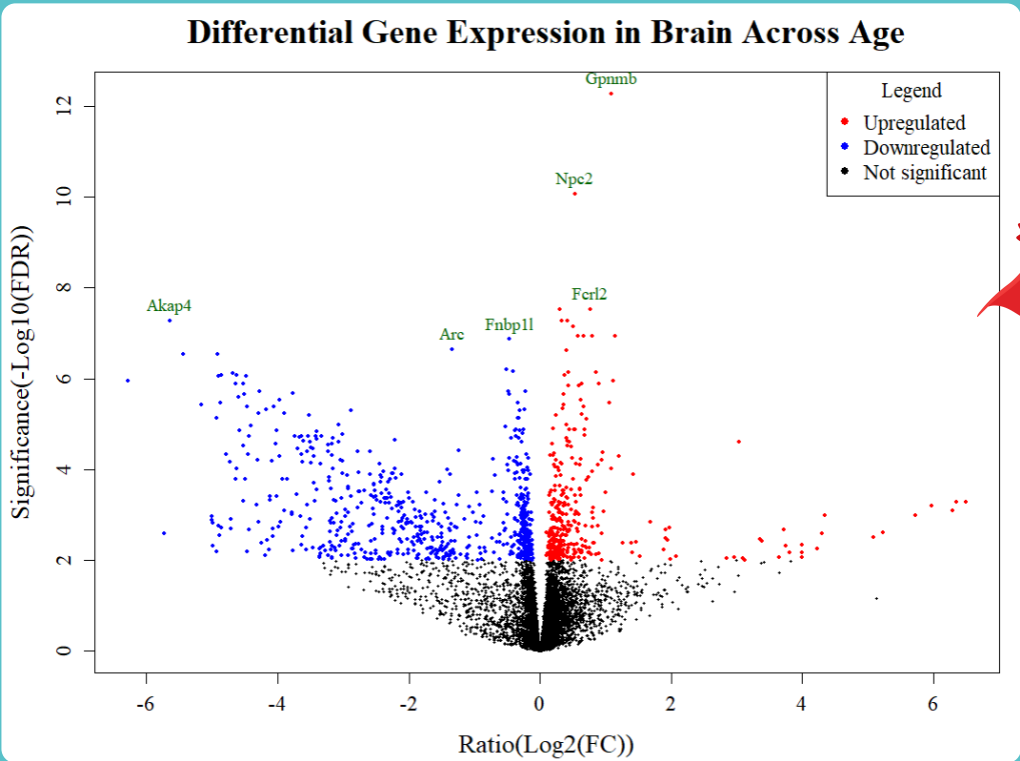


Figure 1: Volcano plot depicting differential gene expression in the Brain between 21 and 104 weeks. DGE was determined using edgeR in RStudio with the Benjamini-Hochberg FDR correction of the p-value. Each point on the graph represents a gene, with the False Discovery Rate in -Log10 on the y-axis and Fold change in Log2 on the x-axis. Significantly up and down regulated genes (FDR ≤ 0.01) are shown in red and blue, while non-significant genes are in black. The most significant genes are labeled.

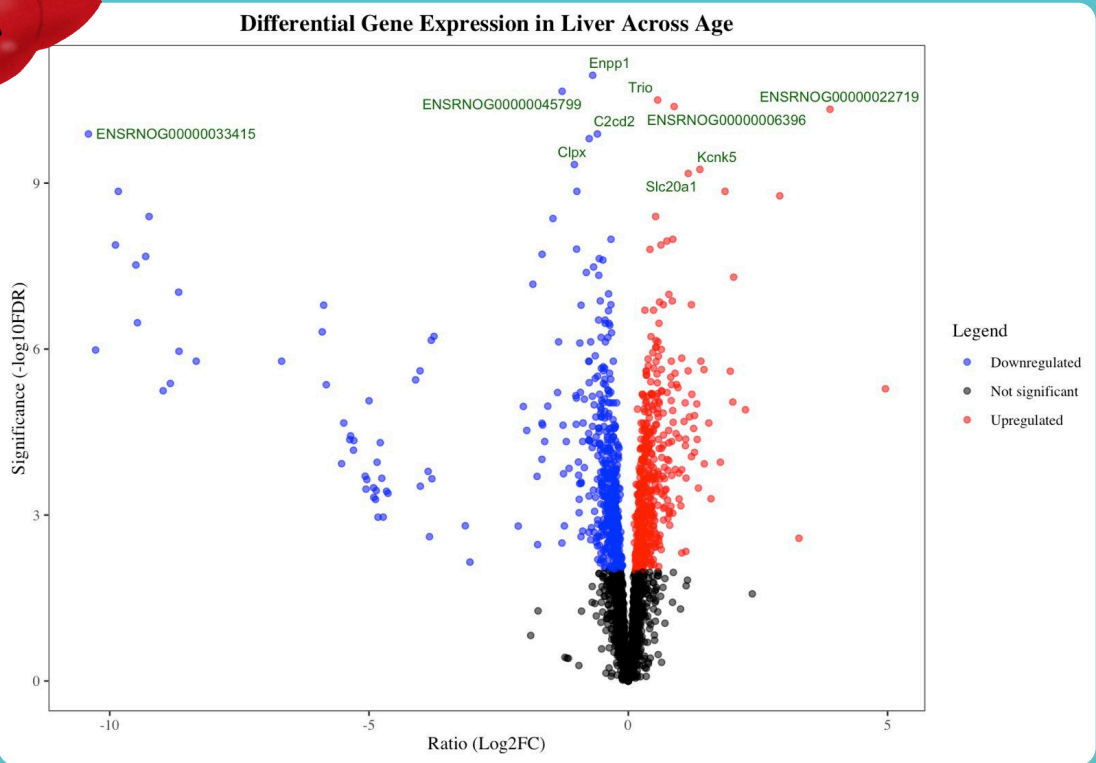


Figure 2: Volcano plot depicting differential gene expression in the Liver between 21 and 104 weeks. Axes and analysis methods are consistent with figure 1.

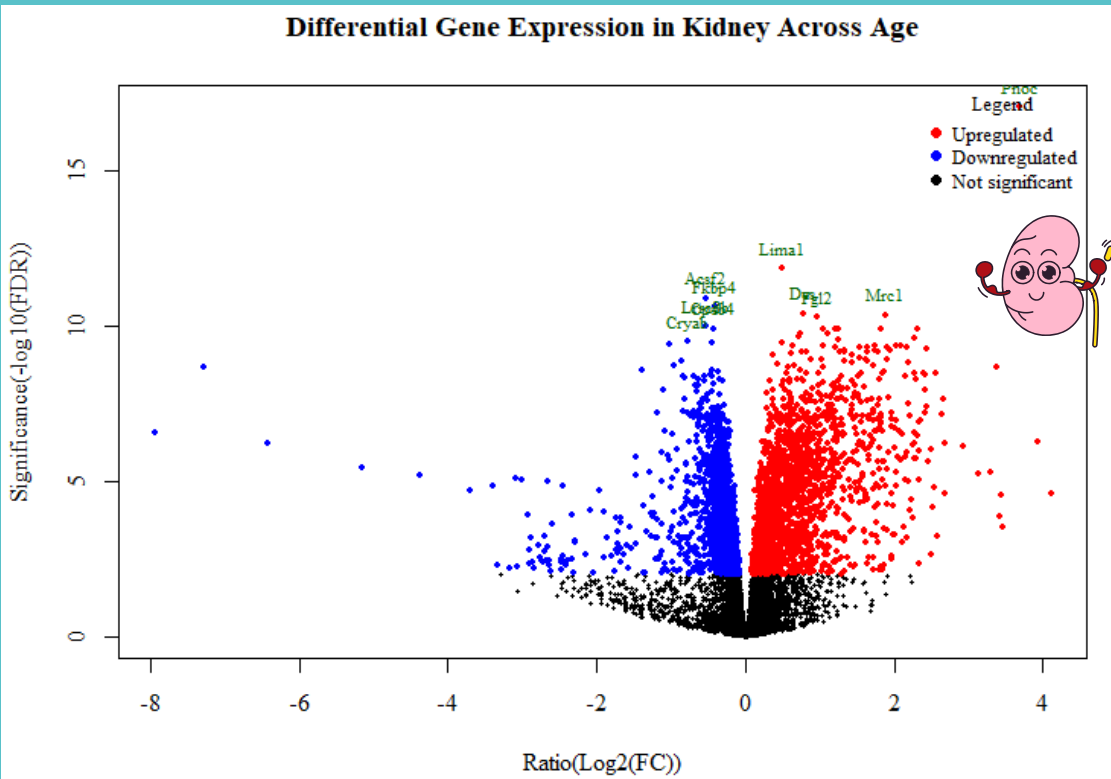


Figure 3: Volcano plot depicting differential gene expression in the Kidney between 21 and 104 weeks. Axes and analysis methods are consistent with figure 1 and 2.

References

g:Profiler – a web server for functional enrichment analysis and conversions of gene lists. (2025). Biit.cs.ut.ee. <https://biit.cs.ut.ee/gprofiler/gost>

Lui, J. C., Chen, W., Barnes, K. M., & Baron, J. (2010). Changes in gene expression associated with aging commonly originate during juvenile growth. *Mechanisms of Ageing and Development*, 131(10), 641–649. <https://doi.org/10.1016/j.mad.2010.08.010>

Rattus_norvegicus. Ensembl Genome Browser. (n.d.). https://mart.ensembl.org/Rattus_norvegicus/Info/Index

Rodríguez-Rodero, S., Fernández-Morera, J. L., Menéndez-Torre, E., Calvanese, V., Fernández, A. F., & Fraga, M. F. (2011). Aging genetics and aging. *Aging and disease*, 2(3), 186–195.

Yu, Y., Fuscoe, J. C., Zhao, C., Guo, C., Jia, M., Qing, T., Bannon, D. I., Lancashire, L., Bao, W., Du, T., Luo, H., Su, Z., Jones, W. D., Moland, C. L., Branham, W. S., Qian, F., Ning, B., Li, Y., Hong, H., Guo, L., ... Wang, C. (2014). A rat RNA-Seq transcriptomic BodyMap across 11 organs and 4 developmental stages. *Nature communications*, 5, 3230. <https://doi.org/10.1038/ncomms4230>

Overlap of Differentially Expressed Genes Between Organs

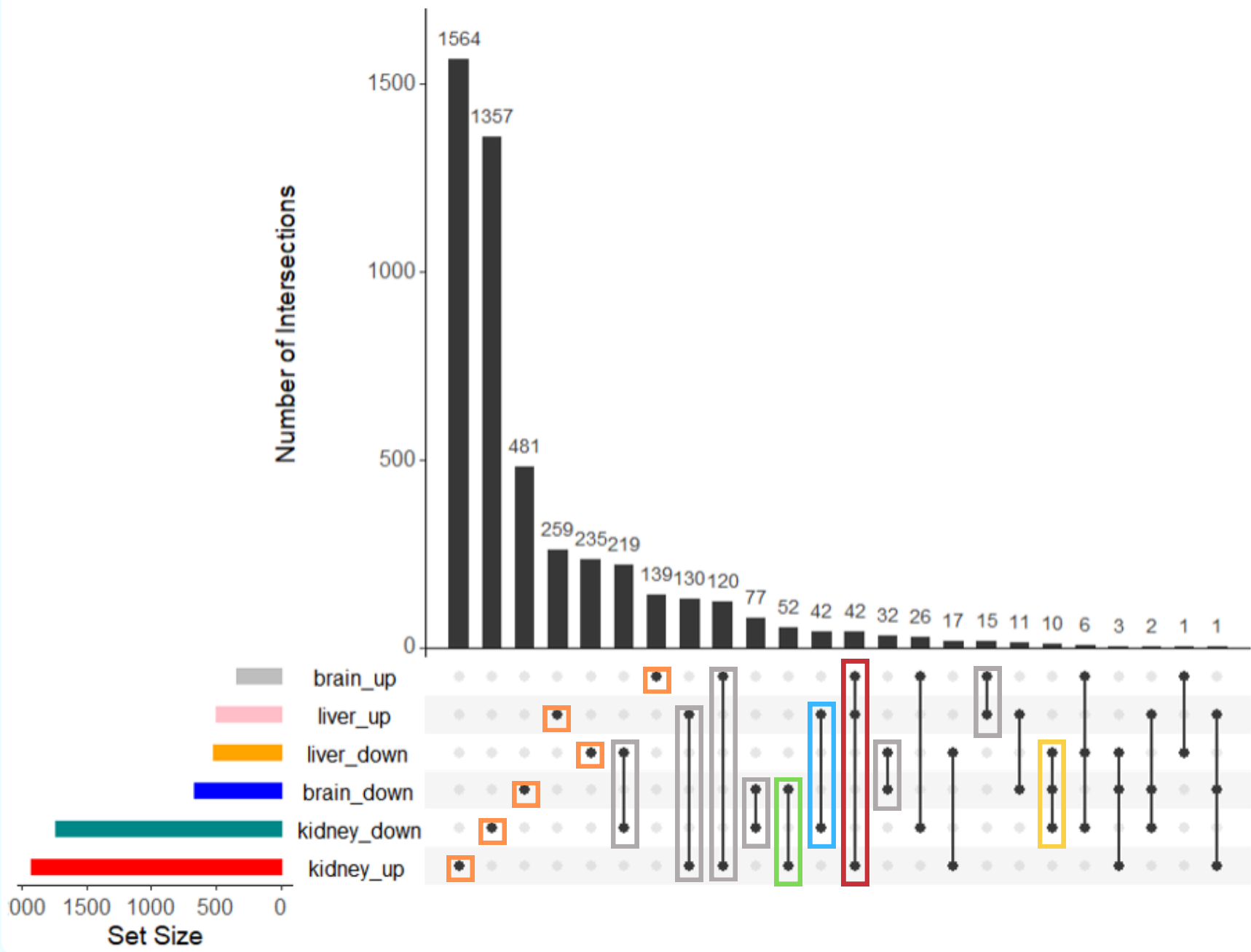


Figure 4: UpSet plot illustrating the overlap of differentially expressed genes (DEGs) across the brain, liver, and kidney between adult (21 weeks) and aged (104 weeks) rats. Set size bars (left) indicate the total number of up- or downregulated genes per organ, while intersection bars (top) show the number of genes shared across tissues. The kidney displayed the largest DEG set, indicating the strongest transcriptomic response to aging. A total of 42 genes were upregulated in all three tissues, and 10 genes were downregulated. Some intersections show opposing trends, where some genes are upregulated in one or two tissues and downregulated in another. This likely reflects tissue-specific adaptations to systemic aging signals. However, minor discrepancies could also arise from biological heterogeneity or limited sample size.

Results

- **42 genes upregulated in all tissues** (core aging genes) → Linked to systemic inflammation or immune activation.
- **10 genes downregulated in all tissues** → shared decline in metabolic function, stress resilience and cell proliferation with aging.
- **Kidney shows largest DGE count** → strongest transcriptomic response to aging.
- **Organ-specific responses** reflect age-related changes are tissue-specific, as significant DEGs in organ-specific volcano plots largely do not overlap with the core aging patterns identified in the UpSet plot.
 - **Brain** = Moderate alterations (mainly genes linked to neuronal signaling + synaptic function)
 - **Liver** = changes in metabolic + detoxification pathways
 - **Kidneys** = inflammation + tissue remodelling
- **Aging drives opposite gene expression across organs:**
 - Eg) **Agpat 3** (lipid metabolism) can be **downregulated in kidney** due to declining metabolic and transport function, while **upregulated in the liver** as a compensatory response to maintain metabolic and protective pathways.
 - Eg) **Fos/Nr4a1** (neuronal activity) can be **downregulated in the brain** due to reduced neuronal activity and cell loss, while **upregulated in the kidney** as a compensatory response to stress and metabolic demands.
- Patterns shared by **only two tissues** were often not significant in the third → focus on multi-gene overlaps to capture broader + stronger similarity patterns.

Conclusions

- Age-related gene expression changes: some shared core genes that are linked to inflammation and metabolic decline, but most changes are organ-specific.
- The kidneys exhibits the strongest transcriptomic response.
- Aging also drives opposite gene expression across different organs, reflecting tissue-specific compensatory mechanisms.