



# Gene Regulatory Network Analysis Reveals Transcription Factor Targets for Therapy of Aging Disorders

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# Gene Regulatory Network Based Transcriptional Analysis of Mammalian Heterochronic Parabiosis

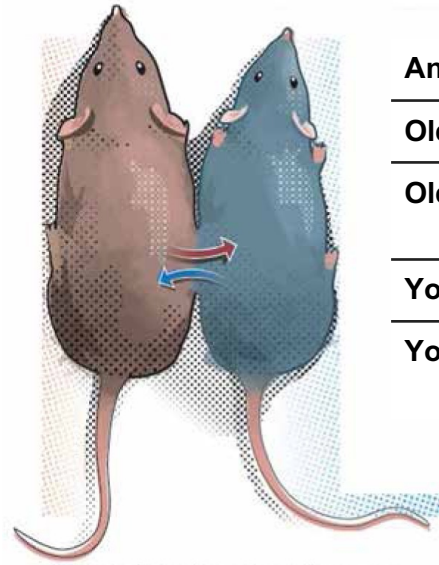
**Kavya M. Shah**

**PI: Lee Rubin, Ph.D.**

**Harvard Department of Stem Cell & Regenerative Biology**

# Background

- Parabiosis is a surgical process connecting the vascular system of a mouse to the blood of another
- Model system for studying tissue aging and regeneration
- **Research question:** *How are individual cell types affected by parabiosis?*



**Figure 1. Visual schematic for parabiosis.**

Animal Type	Biological Significance
Old-young (OY)	"Rejuvenated" state
Old-old (OO)	Control for normalizing OY expression values
Young-old (YO)	"Accelerated aging" state
Young-young (YY)	Control for normalizing YO expression values

**Table 1. Heterochronic and isochronic parabiosis animal types analyzed in study.**

# Methodology

1. Gene Regulatory Network construction (SCENIC)
2. Differential Gene Expression (DGE) analysis and post-processing (EdgeR)
3. Biomarker validation (*Tabula Muris Senis*)

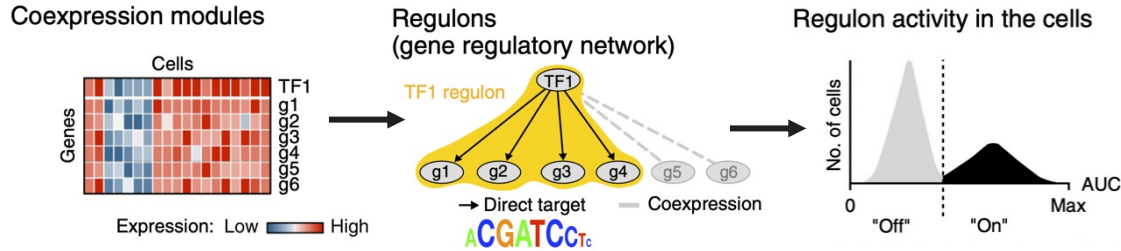


Figure 2. SCENIC workflow.

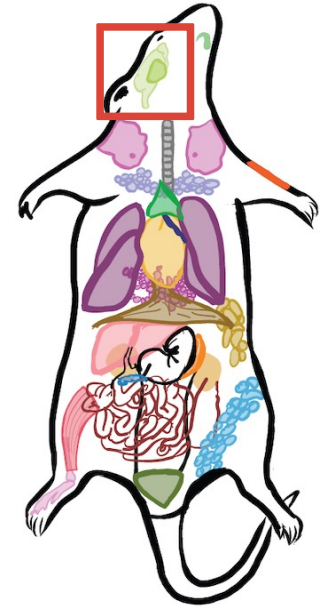
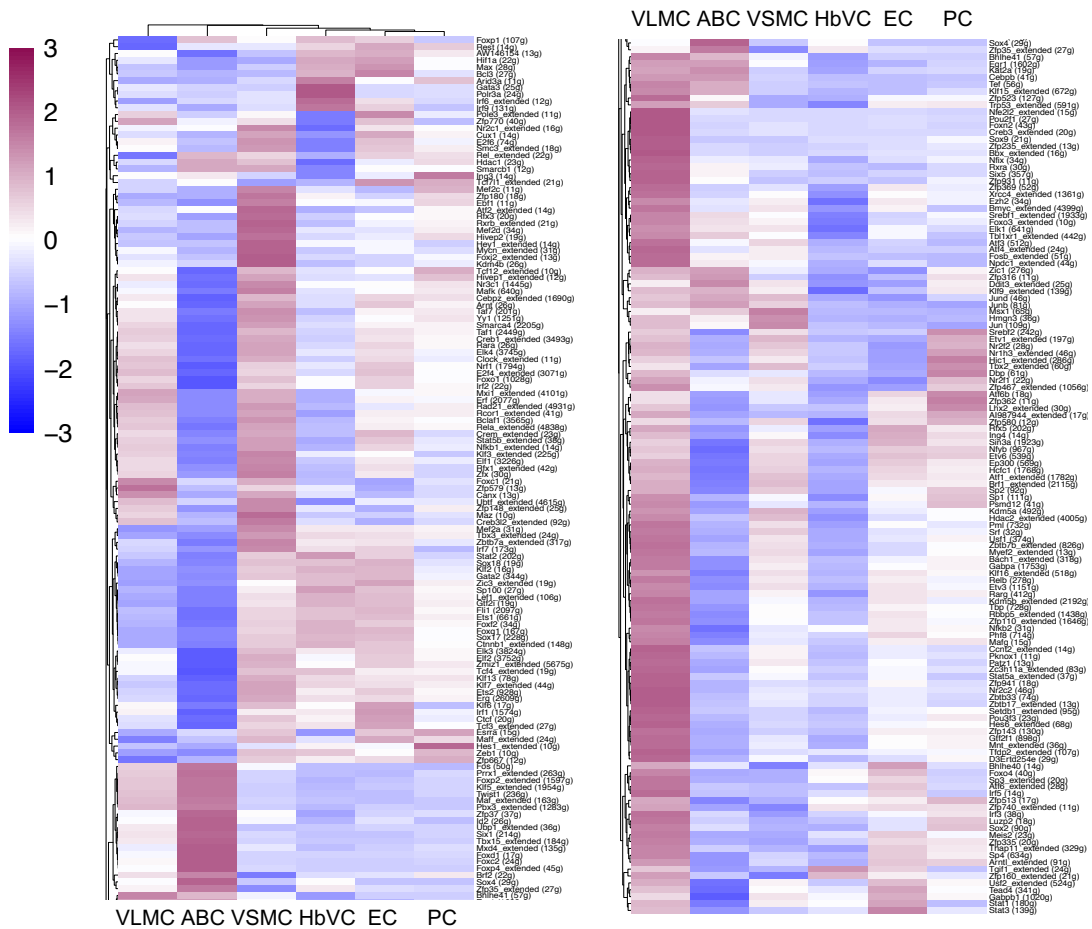
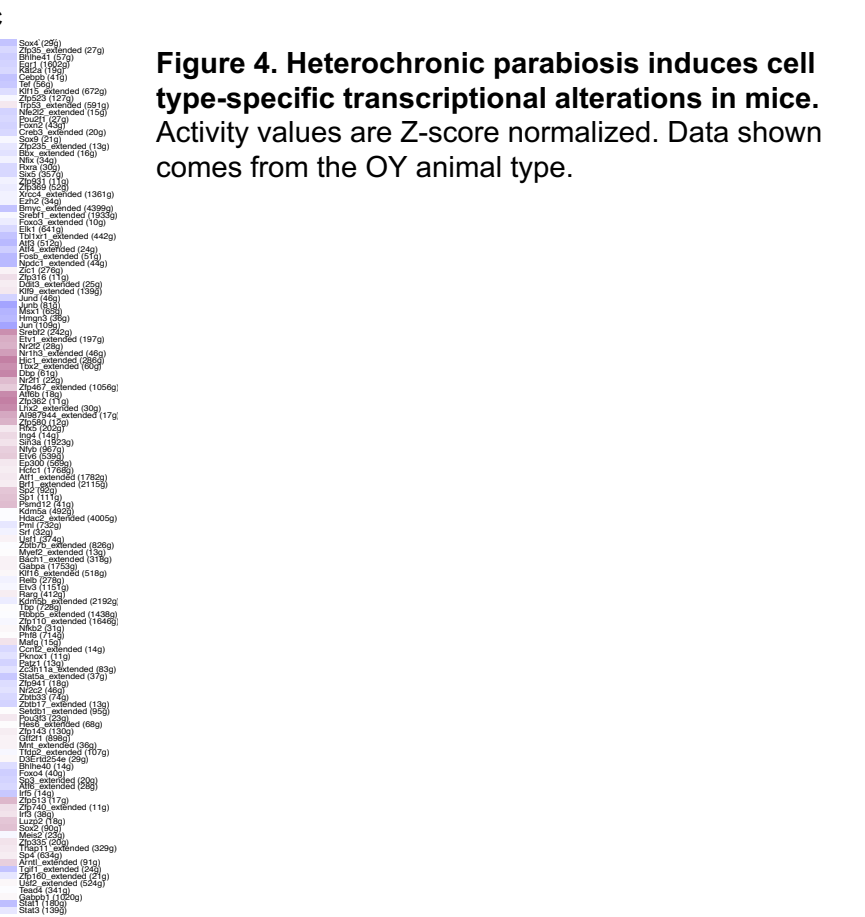


Figure 3. FACS-sorted tissues identified in TMS dataset. Relevant tissue (Brain non-myeloid) is boxed.

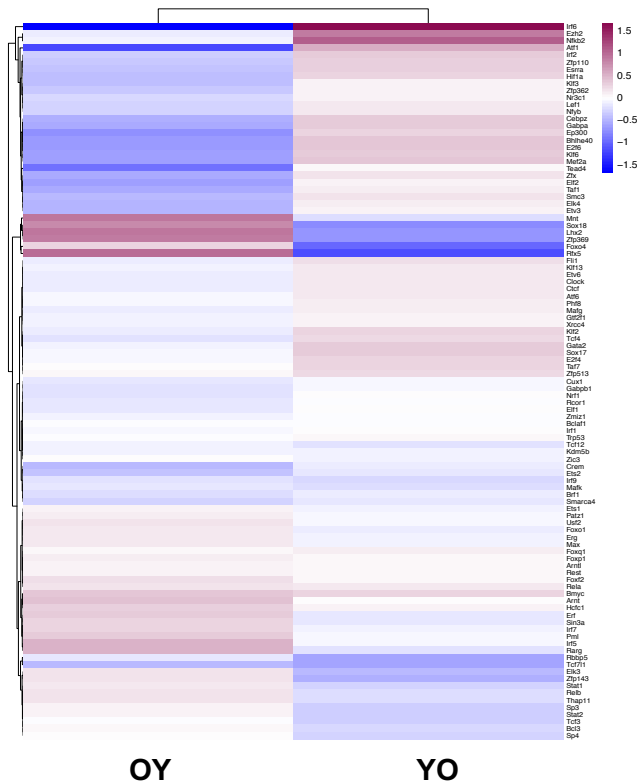
# Results



**Figure 4. Heterochronic parabiosis induces cell type-specific transcriptional alterations in mice.** Activity values are Z-score normalized. Data shown comes from the OY animal type.

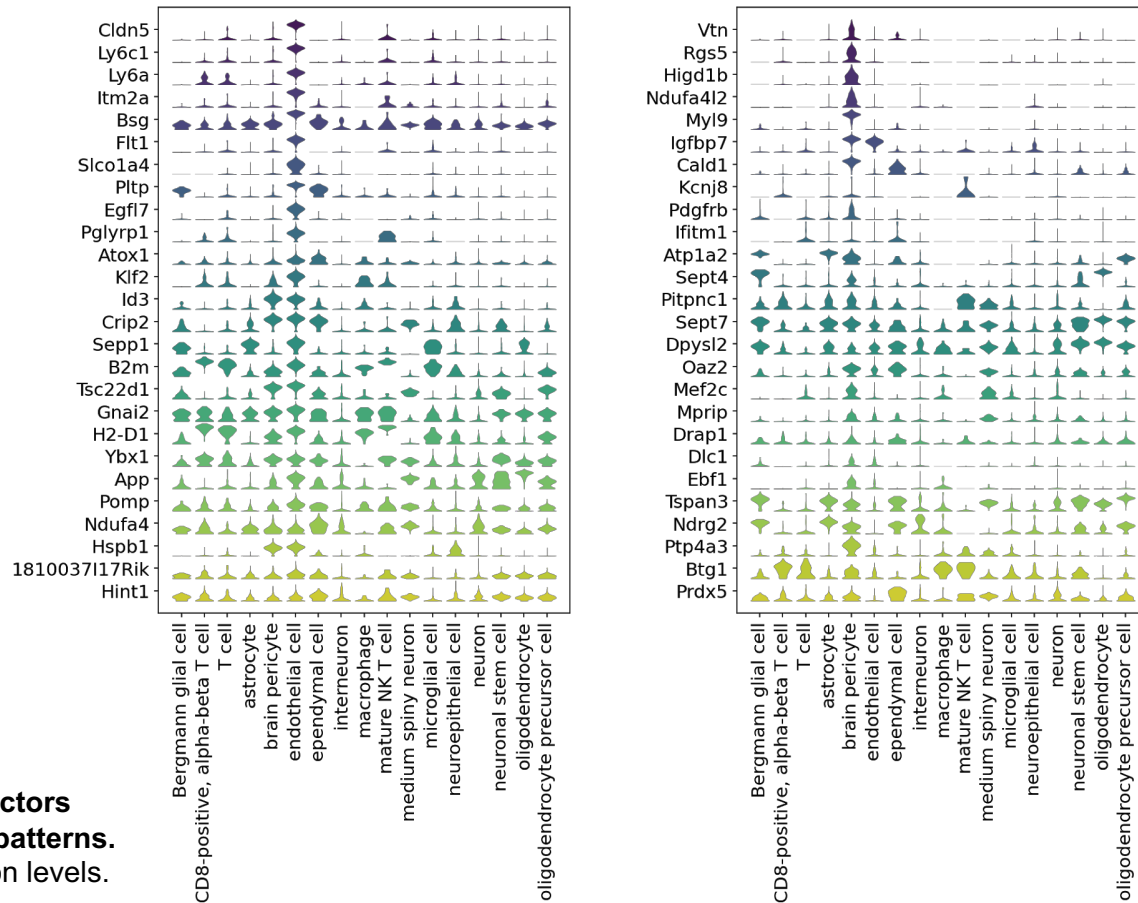


# Results



**Figure 5. SCENIC-significant transcription factors display bidirectional differential expression patterns.** Heatmap displays log fold-changes in expression levels.

**Figure 6. Biomarkers used for cell type identification show strong reliability in *Tabula Muris Senis* dataset.** Endothelial and pericyte cell markers shown in left and right panels, respectively.



# Next Steps

- Continue validation of differential expression and gene regulatory network analysis data via *Tabula Muris Senis* dataset
- Perform immunohistochemical assays to determine *in vivo* effects of most promising "rejuvenation" transcription factor candidates

# Acknowledgements

- PI: Lee Rubin
- Mentors: Methodios Ximerakis and Kristina Holton
- (Virtual) PRISE and HCRP



*My PRISE entryway!*