

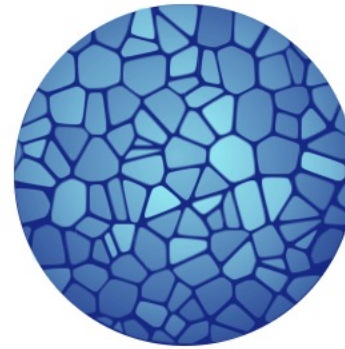
A single-cell transcriptomic atlas characterizes ageing tissues in the mouse

Coriell Journal Club 2021-03-30

Background

Single Cell Atlases

- “To create comprehensive reference maps of all human cells – the fundamental units of life – as a basis for both understanding human health and diagnosing, monitoring and treating disease”
- Founded 4-5 years ago
- Initially focused on young healthy adults as a baseline
- Now expanding to other populations, disease states



**HUMAN
CELL
ATLAS**



Tabula Muris

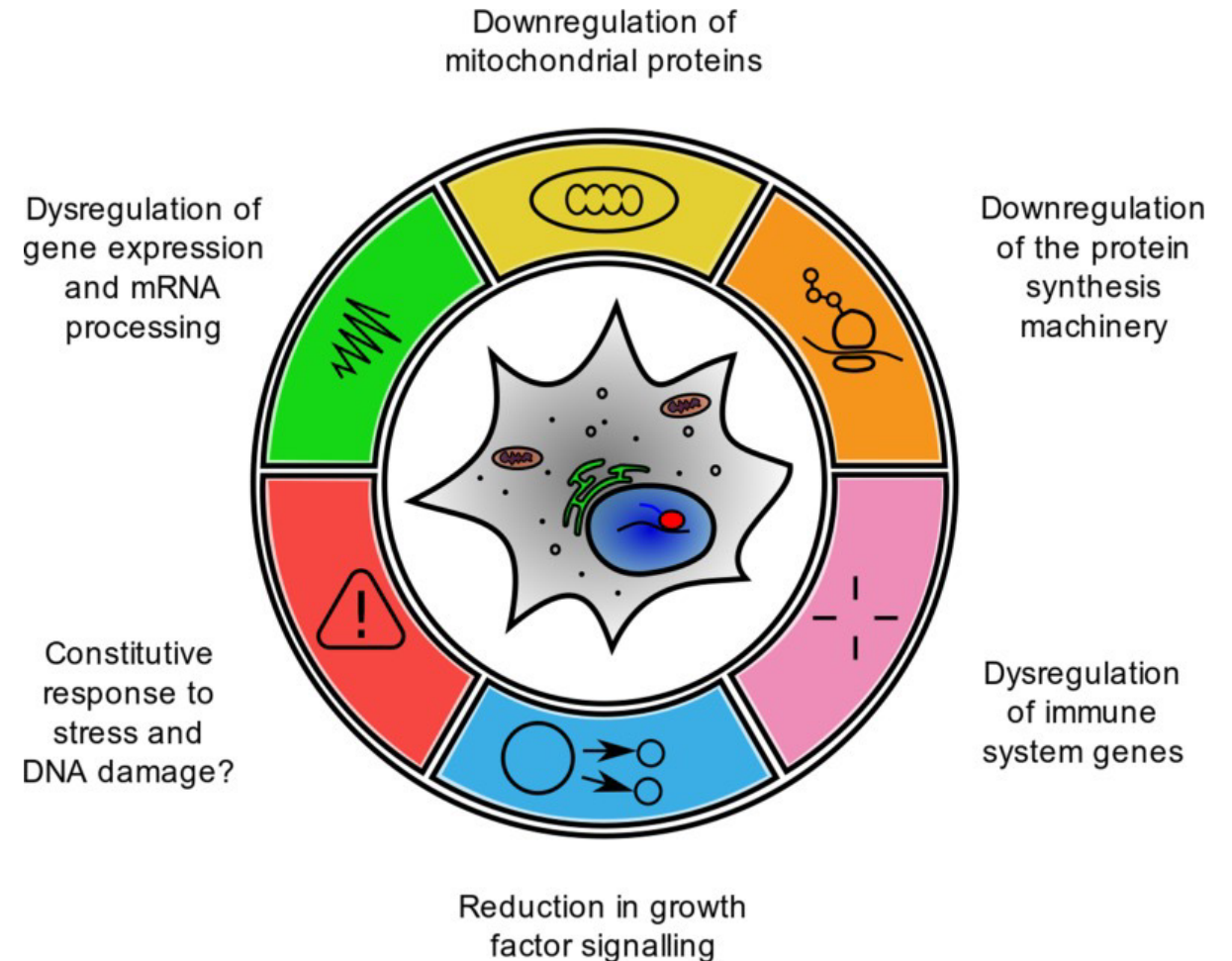
FACS, Droplet-based RNA-seq

- FACS
 - Have to know what to look for
 - Known that the stress of sorting changes cells gene expression
 - Can capture full length transcripts
- Droplet-based RNA-seq
 - Low read counts for only the 3' end of RNAs
 - Hard to impossible to capture rare cell populations
 - Hypothesis-free
 - Less stressful than FACS



Ageing and Gene Expression

- Known that gene expression changes with age
- However, cell composition changes too, for example, naïve T cells are replaced by memory T cells as you age
- Are changes in gene expression seen with age due to changes in the make up of the cell population or because the activity of aged cells changes?



Results

Fig. 1a-b: Experimental Setup

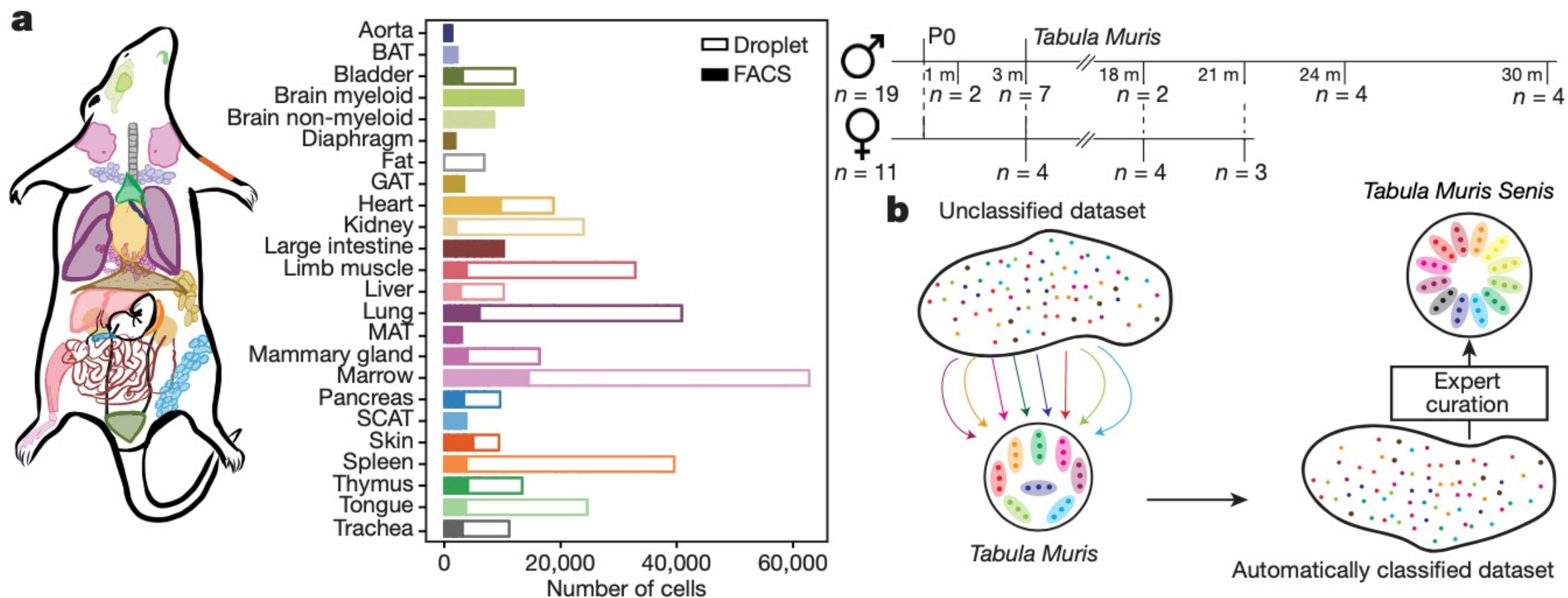


Fig. 1c-e: Cells Detected

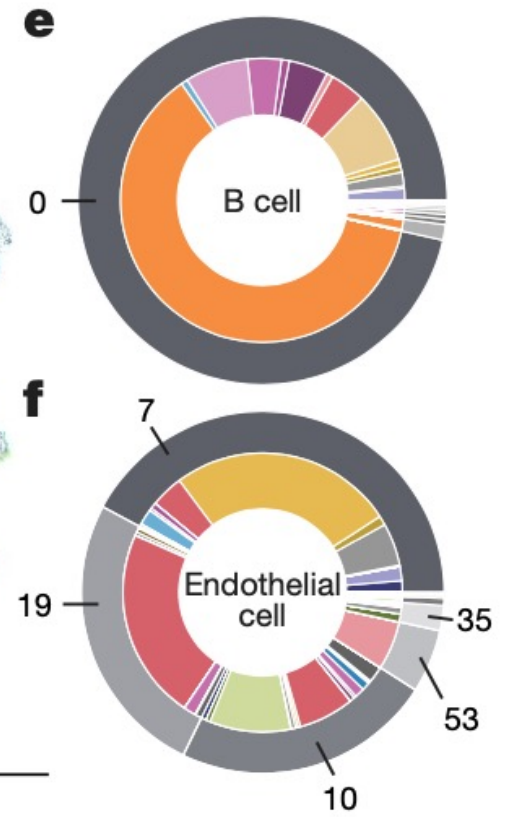
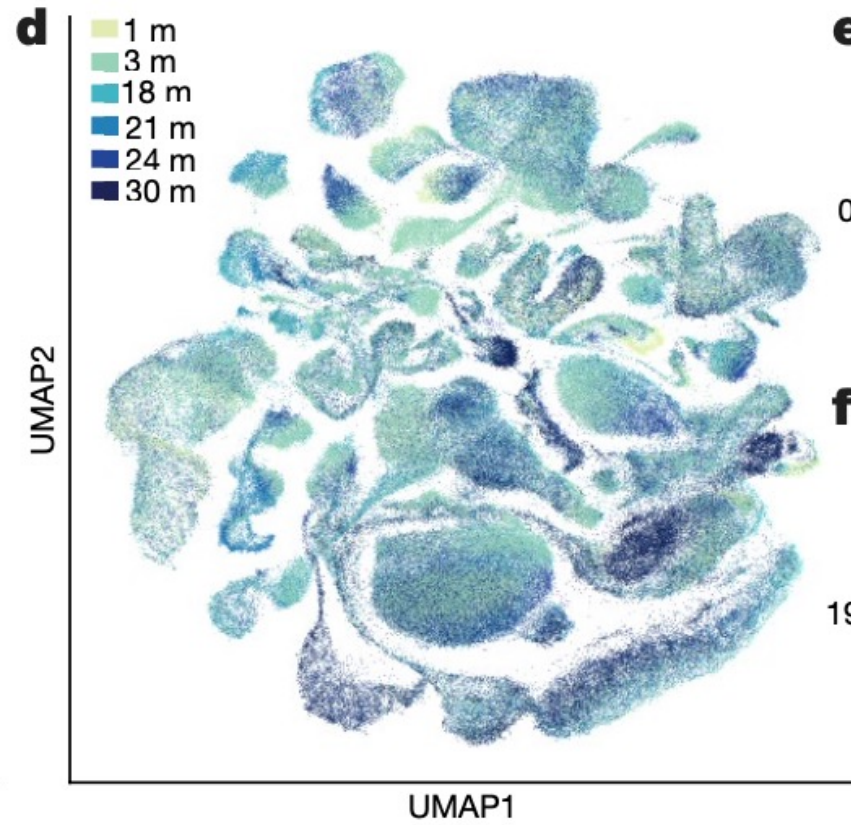
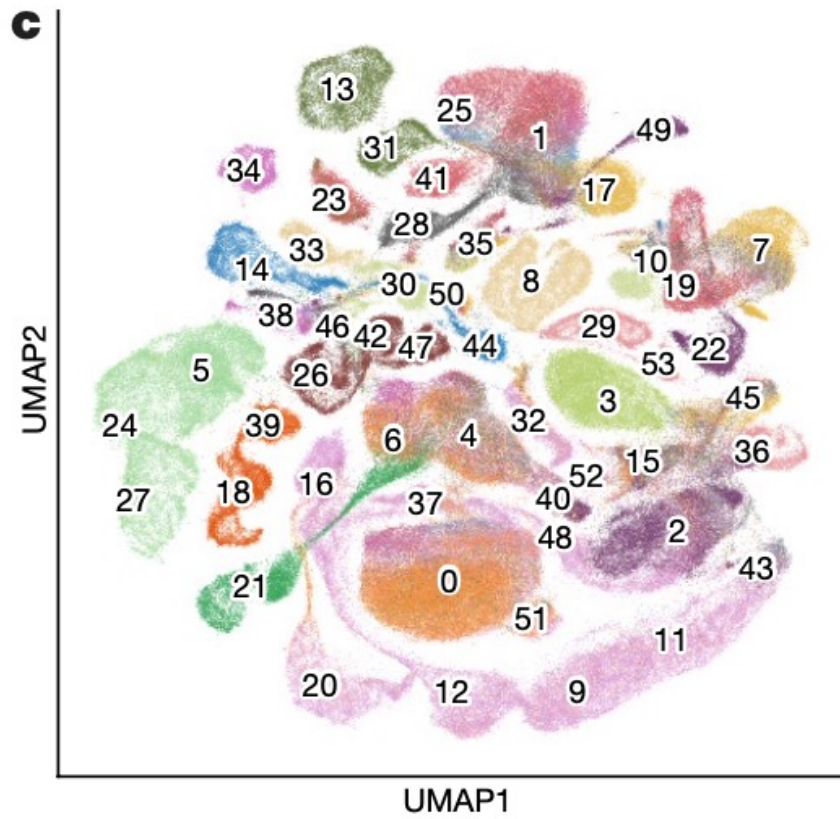


Fig. 2a-c: Expression of *Cdkn2*

- *Cdkn2a* codes for both p16 and p14arf
- Increased expression of *Cdkn2a* is associated with senescence
- Also, of the known senescence genes, it correlated most strongly with age in this data

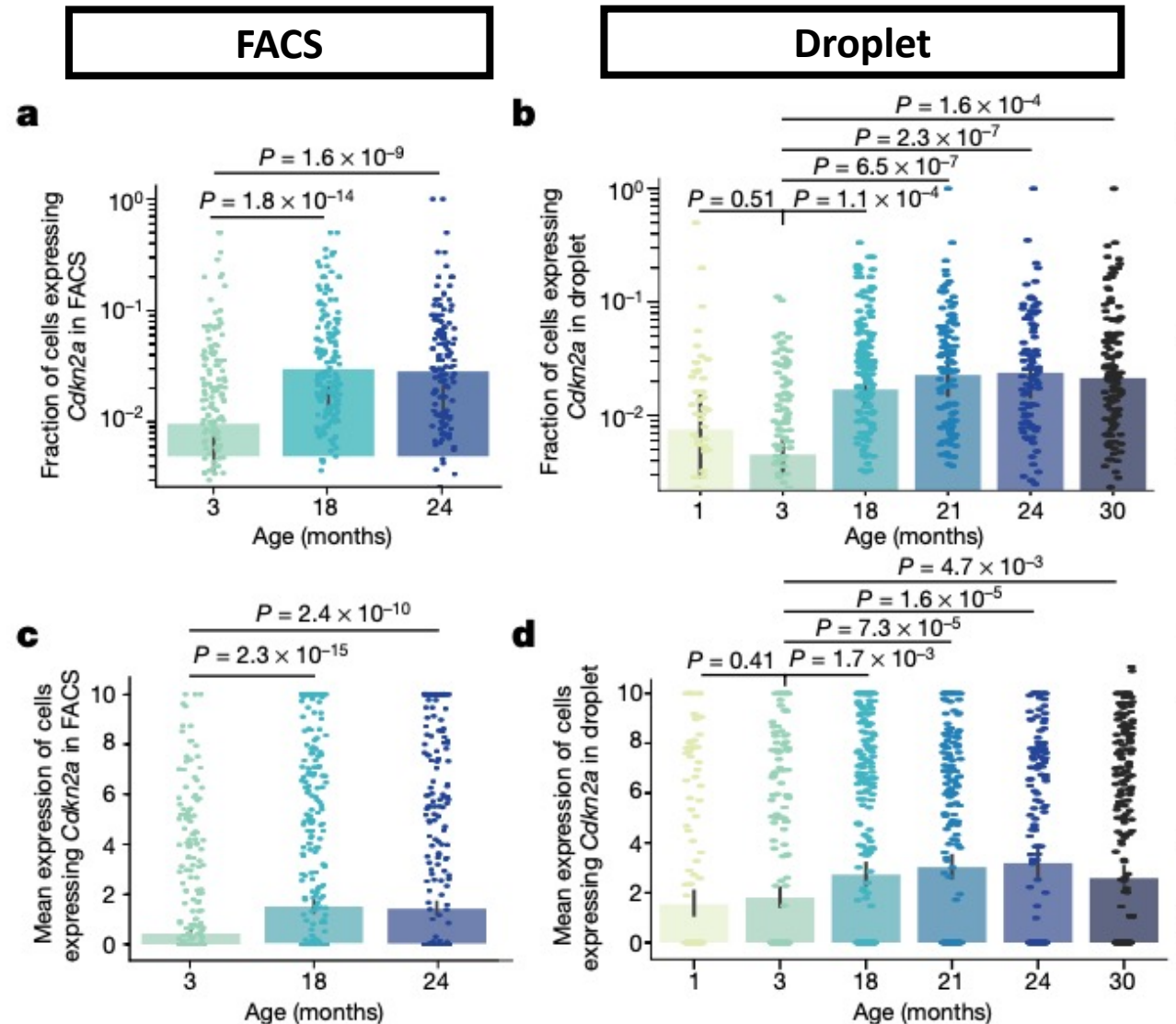


Fig. 2e-i: Cell Population Change w/ Age

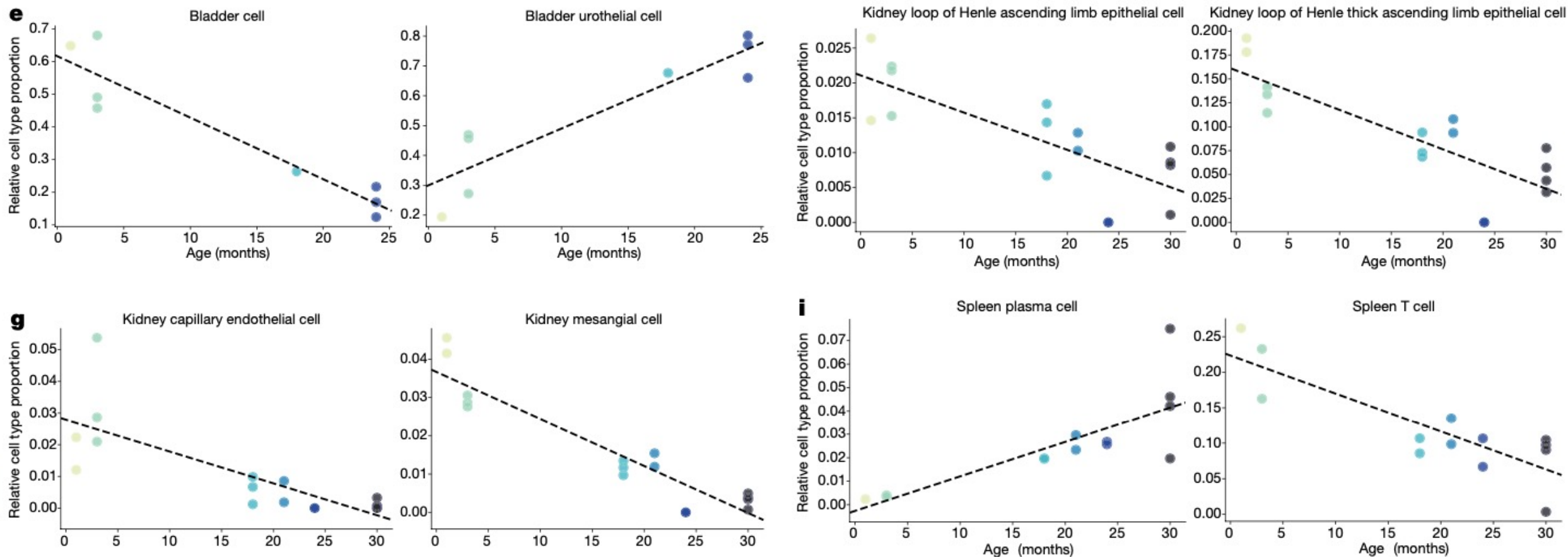


Fig. 2f-j: Differentially Expressed Genes w/ Age

- Top 10 up/down-regulated genes in each tissue
- 0.05 = 50% change = 1.5-fold change

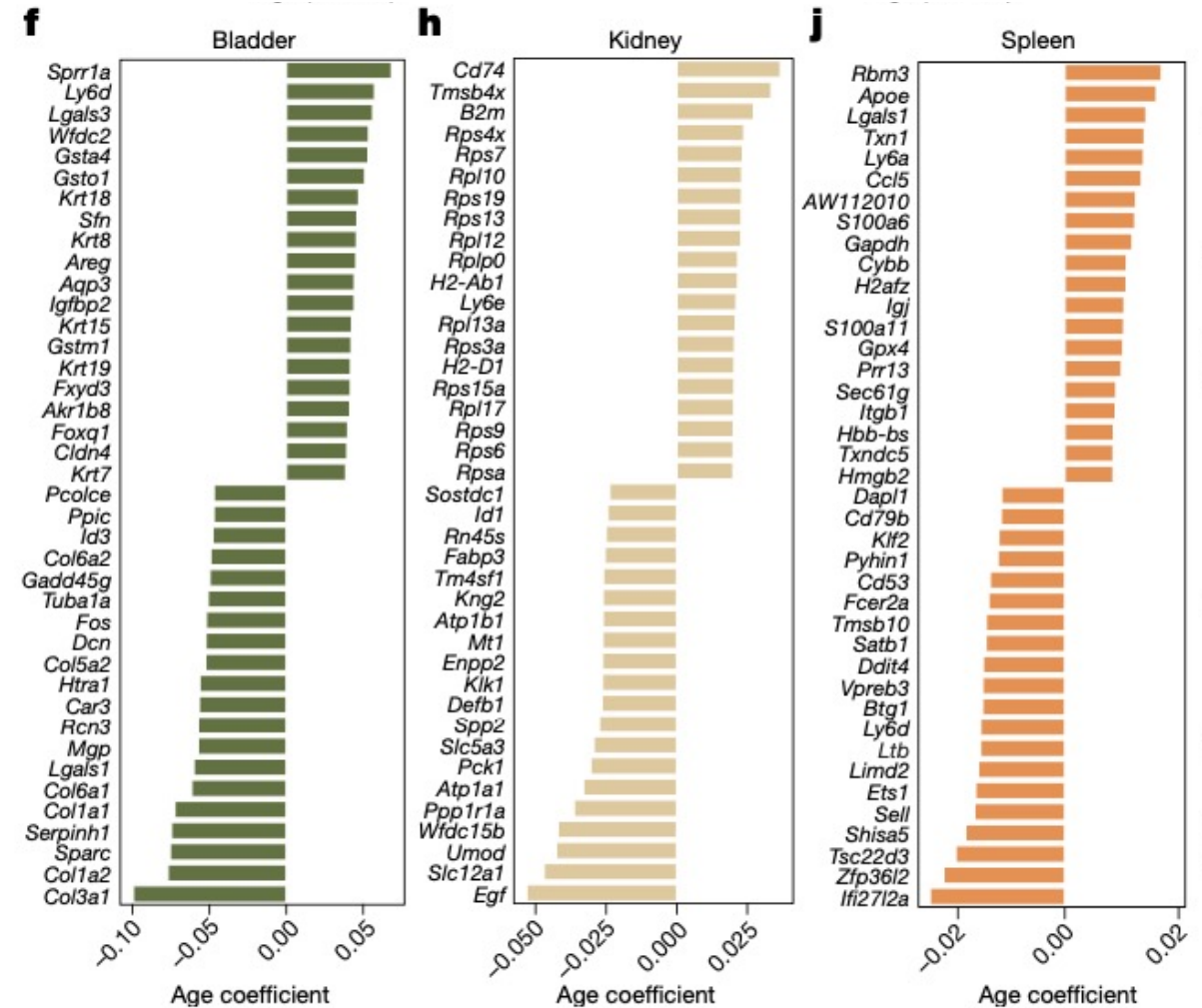


Fig. S6a-d: Liver Hepatocytes Decrease w/ Age

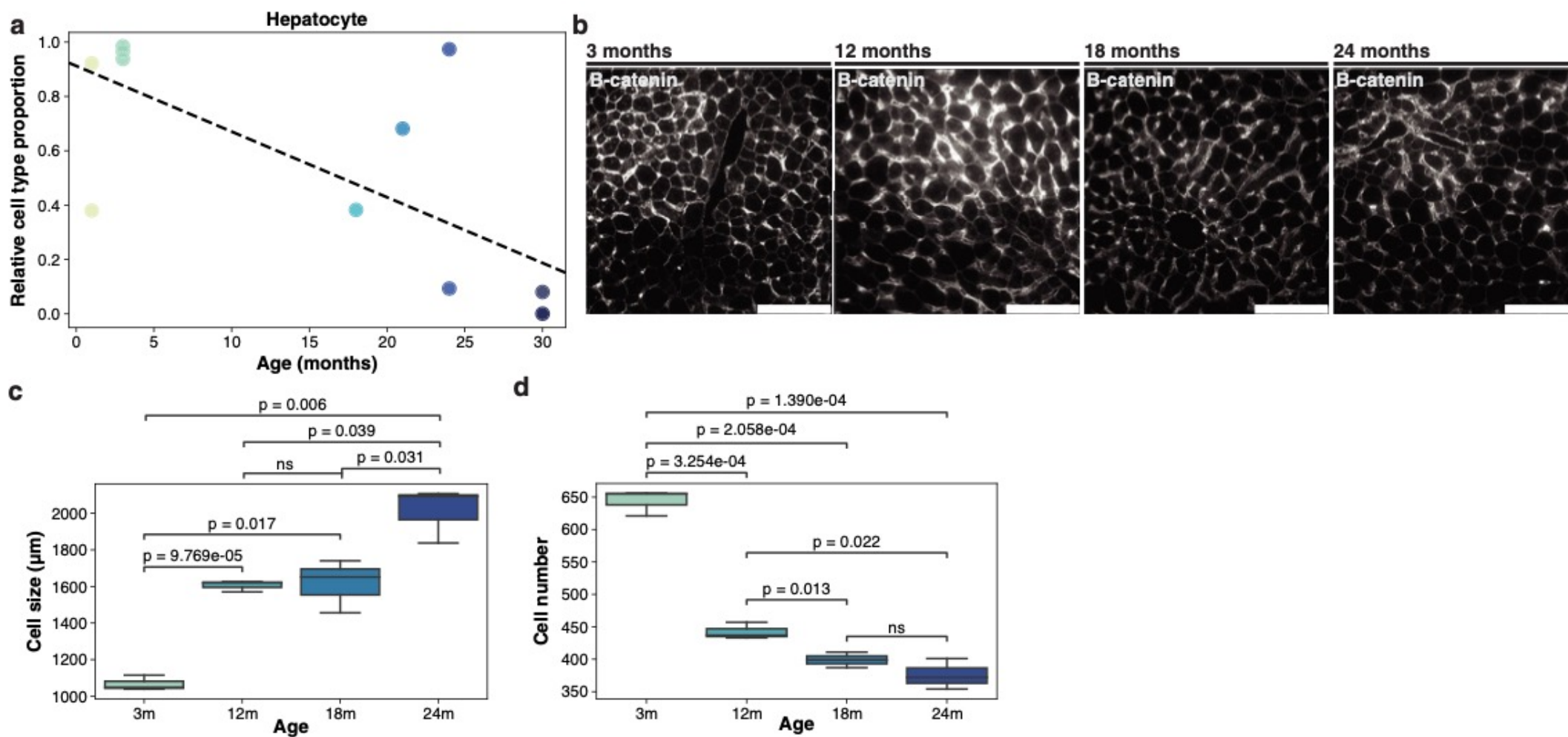


Fig. S6e-f,k: Increase Immune Infiltration

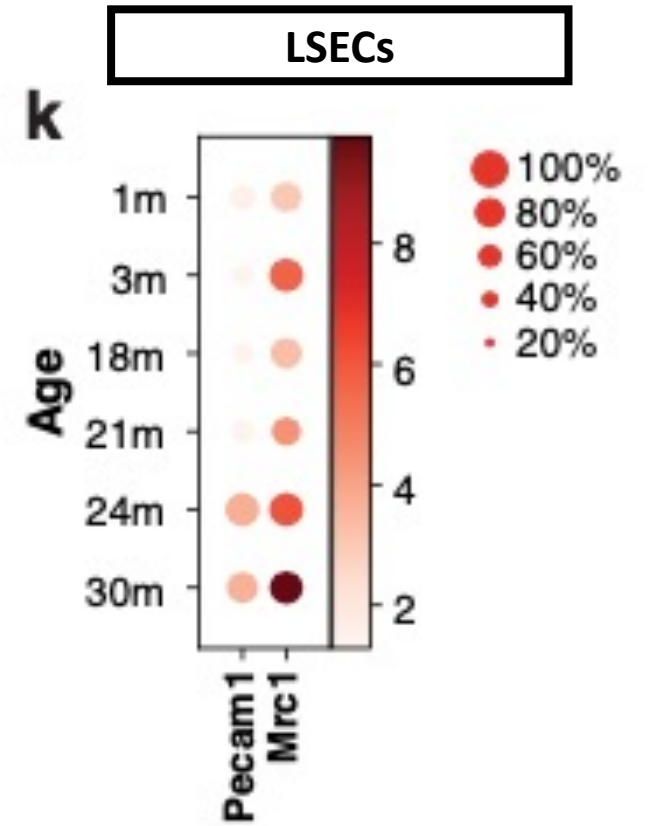
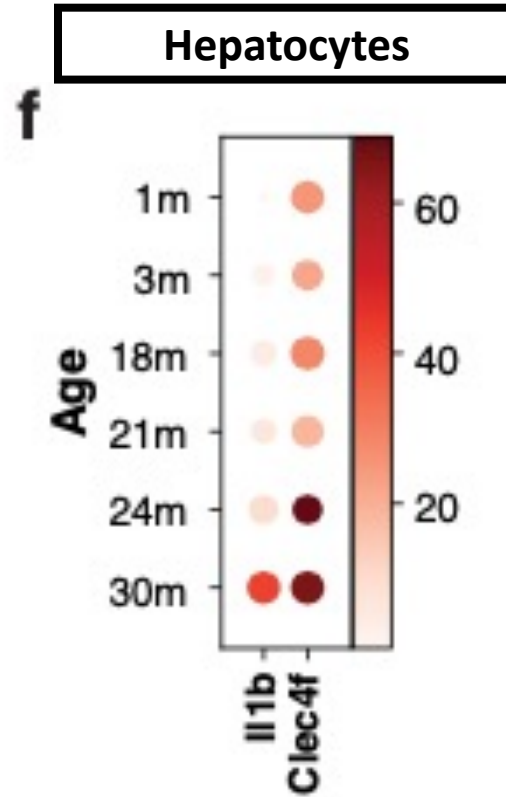
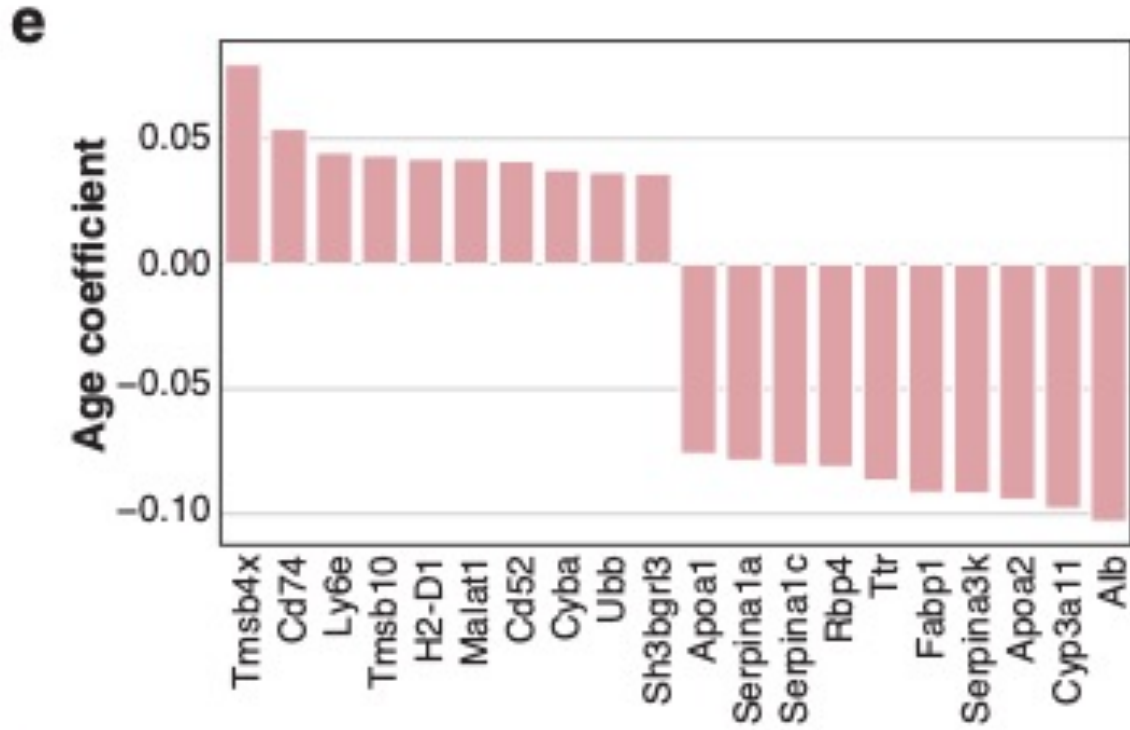


Fig. S6g-j: Liver Hepatocytes Show Increase in Inflammatory Markers with Age

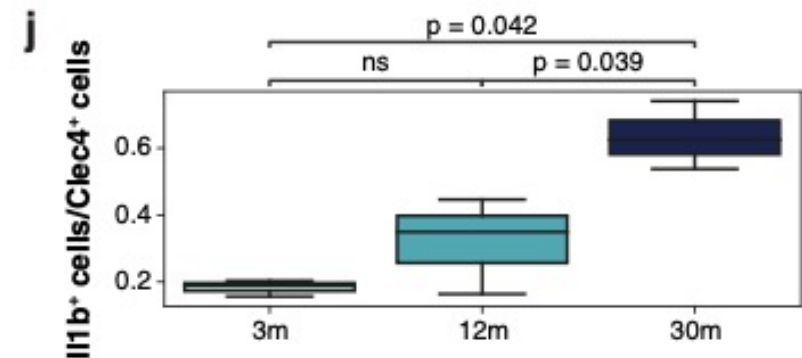
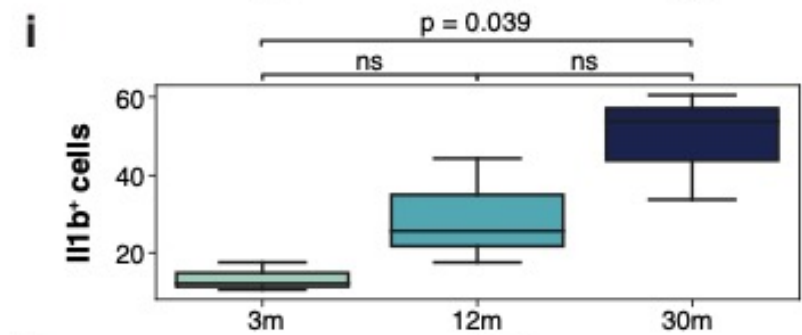
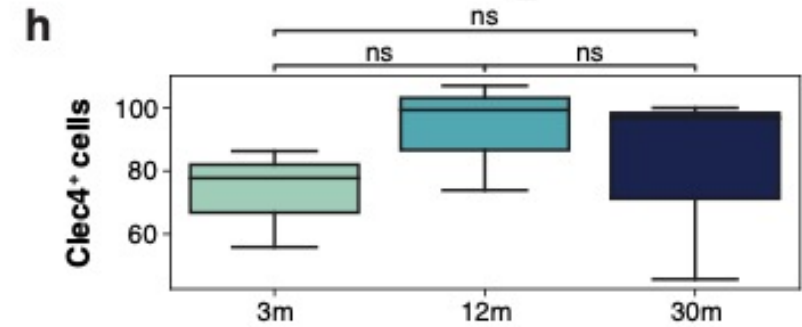
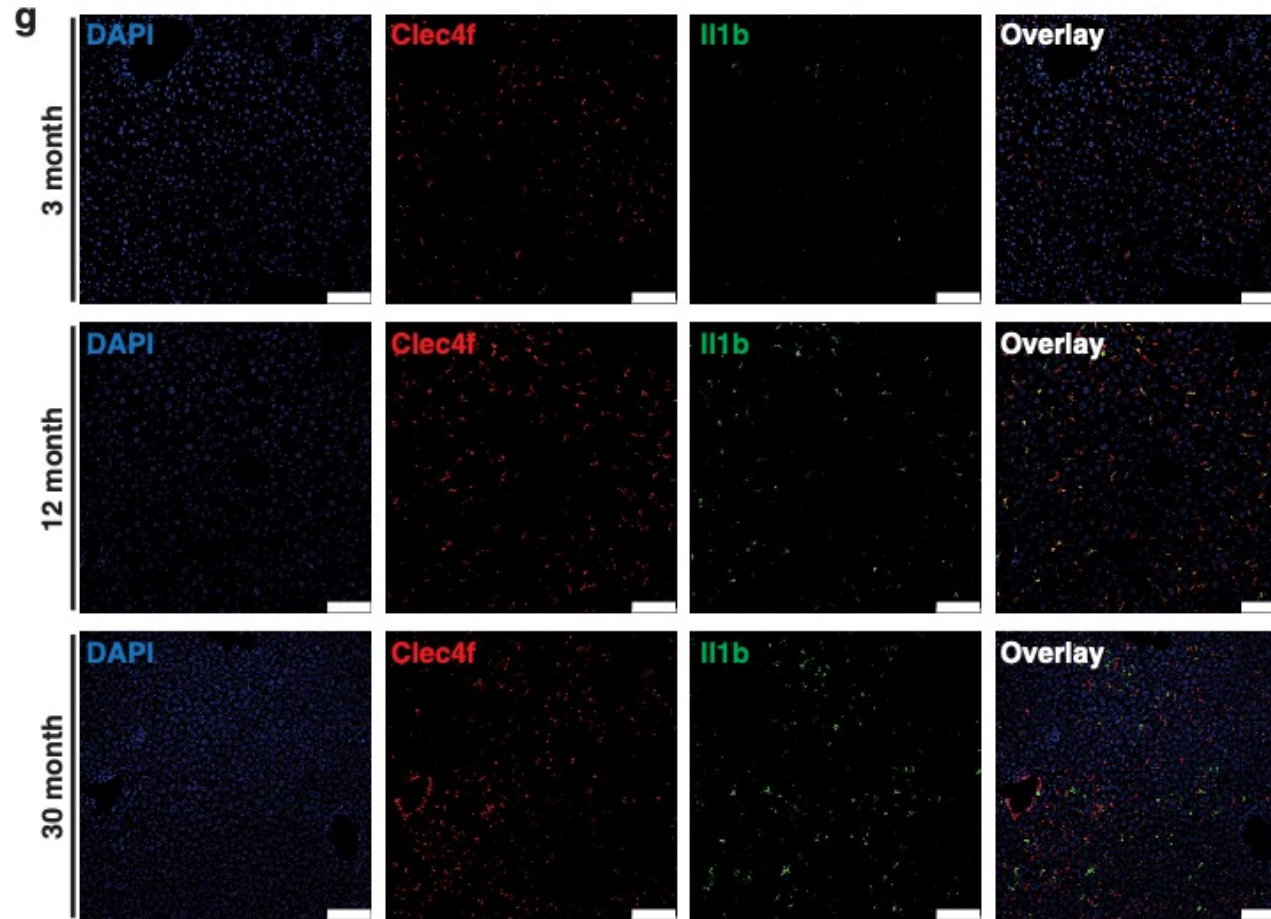


Fig. S6l-o: LSEC Cell Counts, Not Expression, Increase with Age

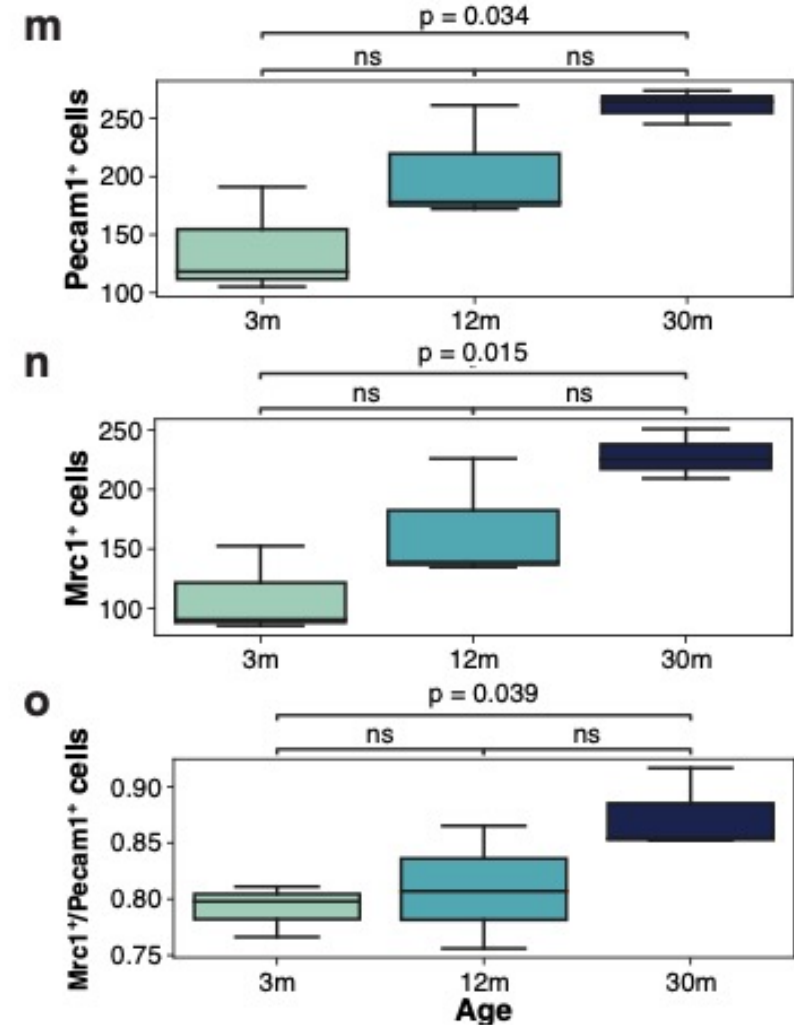
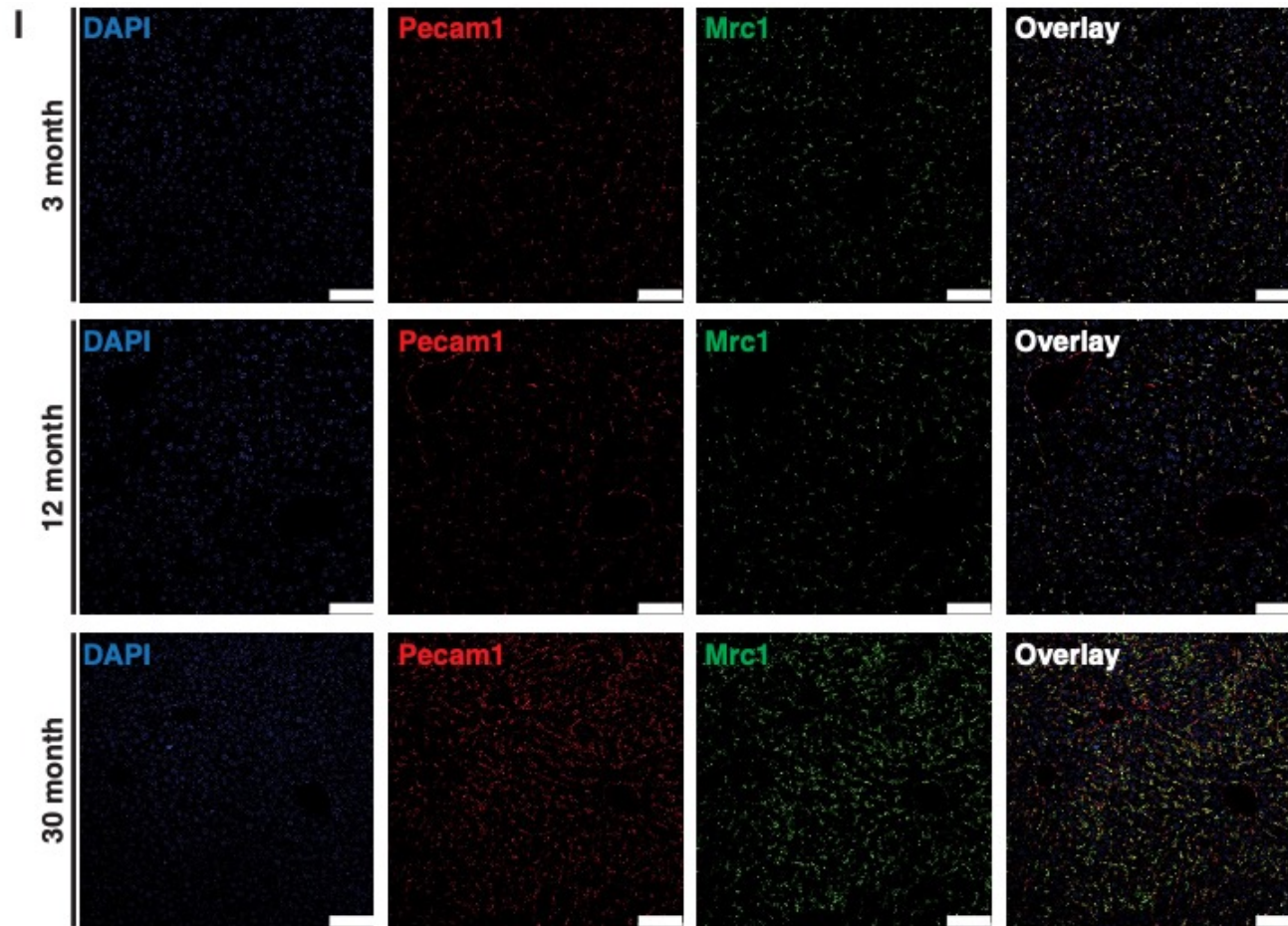


Fig. 3: Mutational burden with age

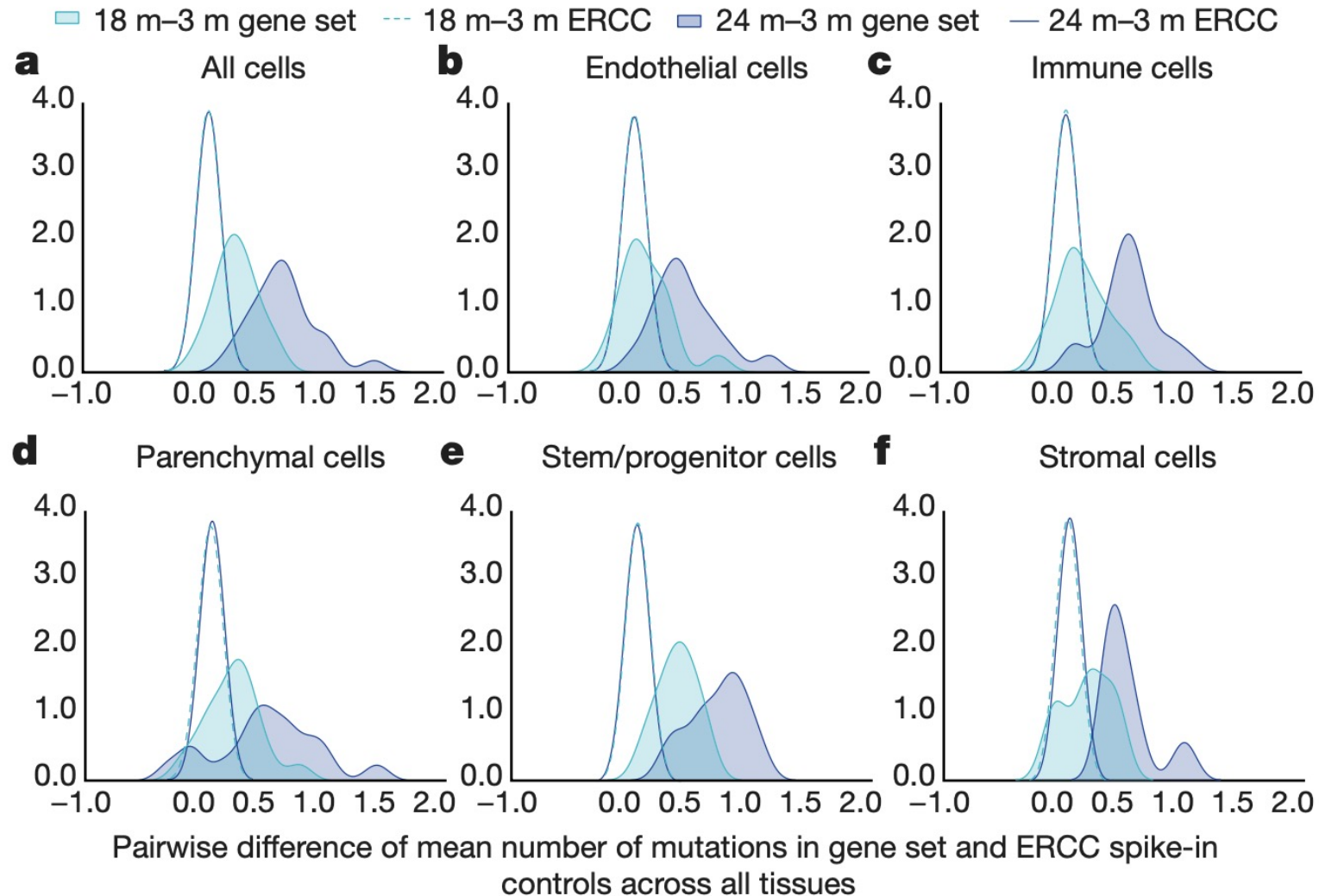


Fig 4: Immune System Changes with Age

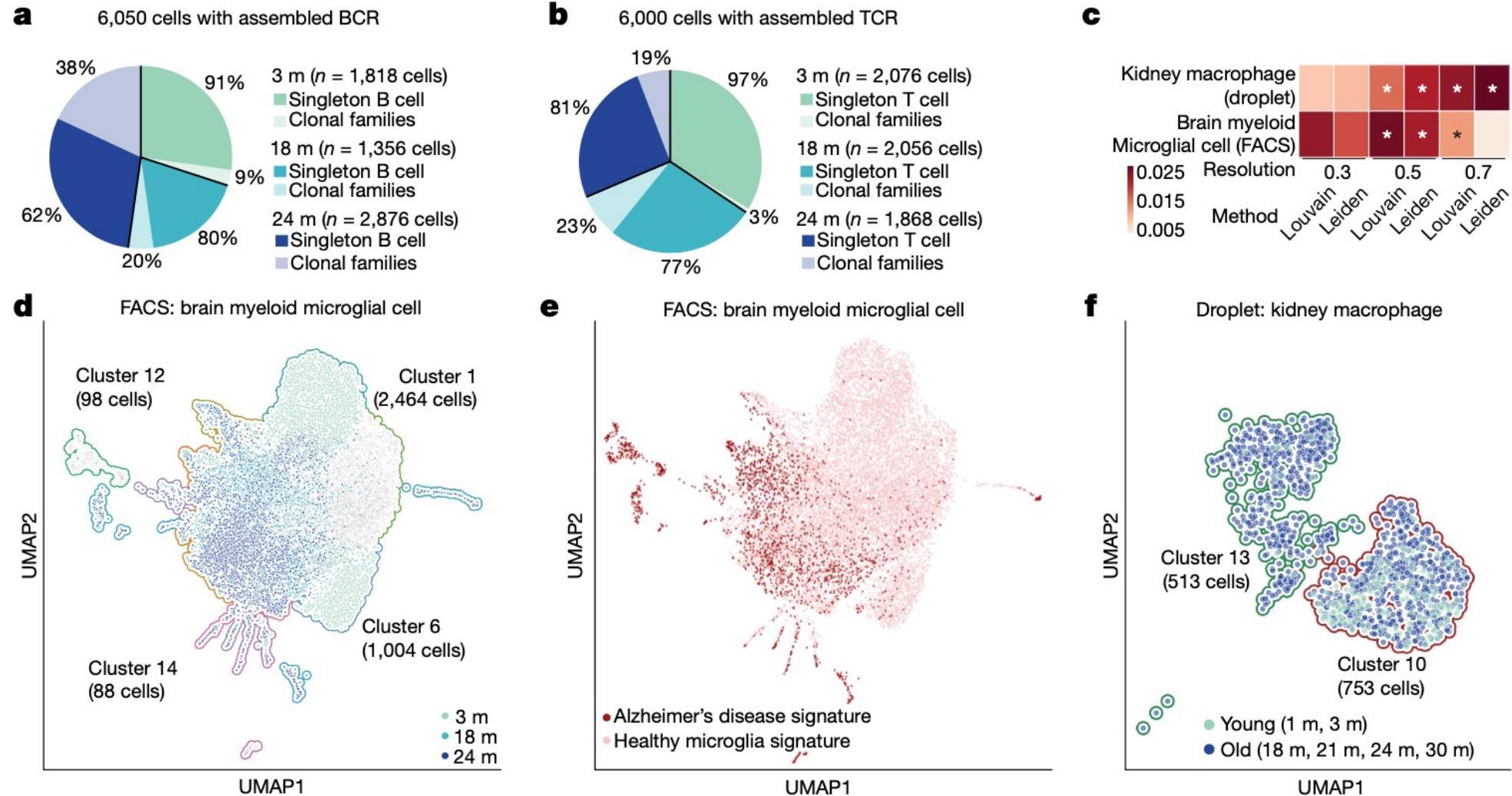


Fig. S5a,b: Gene Expression Changes with Age are a Combination of Cell Population Changes and Expression Changes?

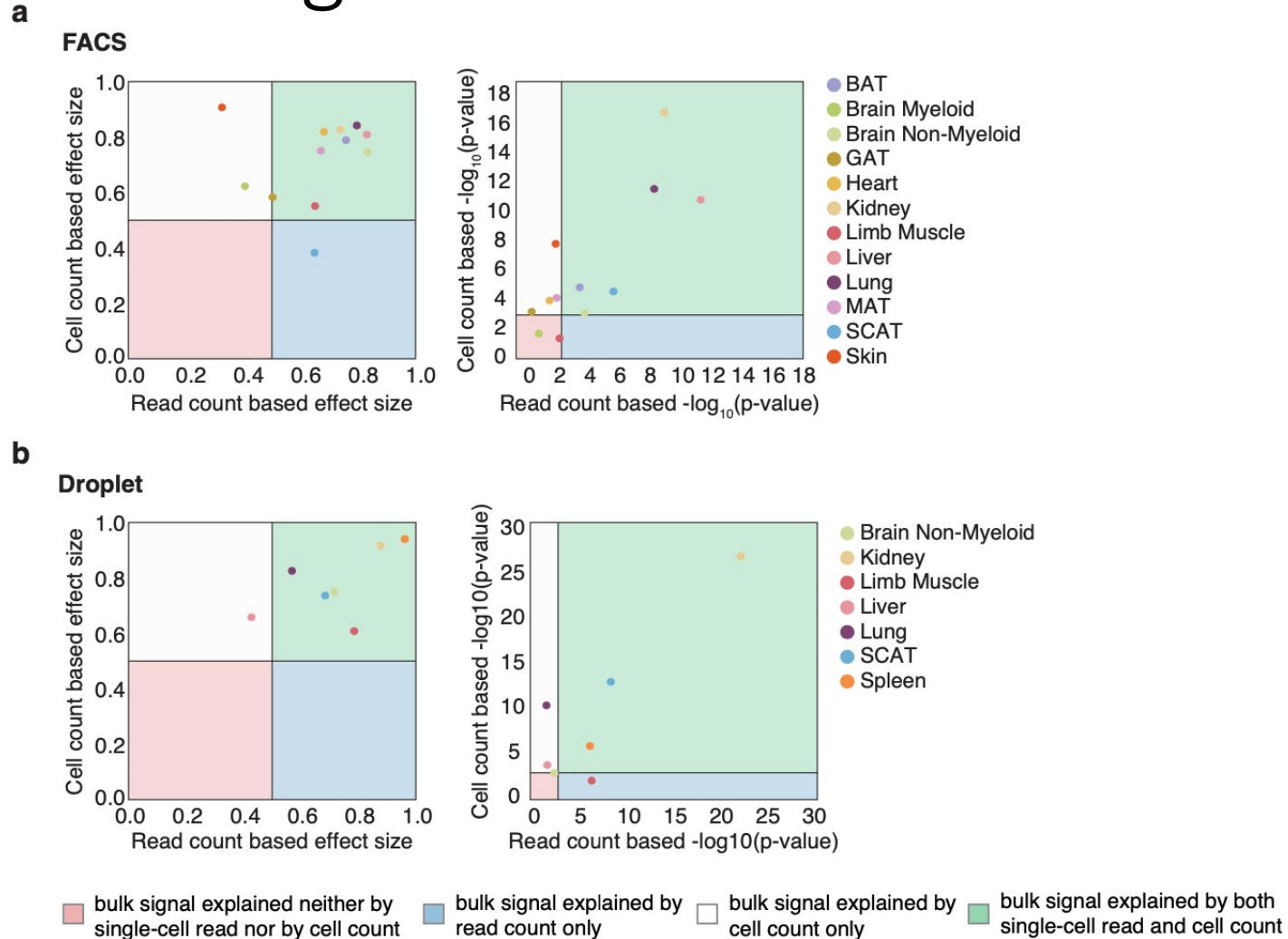


Fig. S8: Pseudo-Bulk Raw Gene Counts

