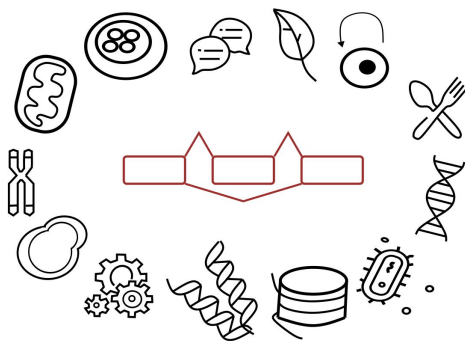


Not everything gets bad when we get old.

Maria Schreiber, 15th Feb. 2024
39th TBI Winterseminar in Bled

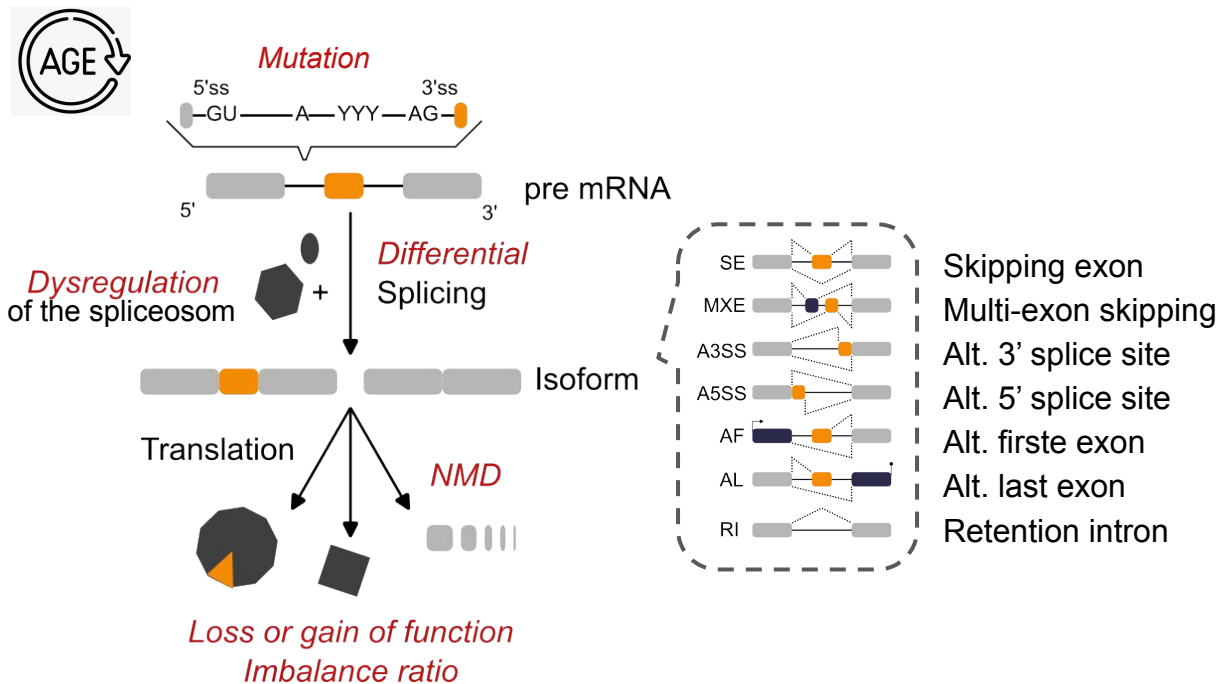


The Interplay: Aging vs. Splicing

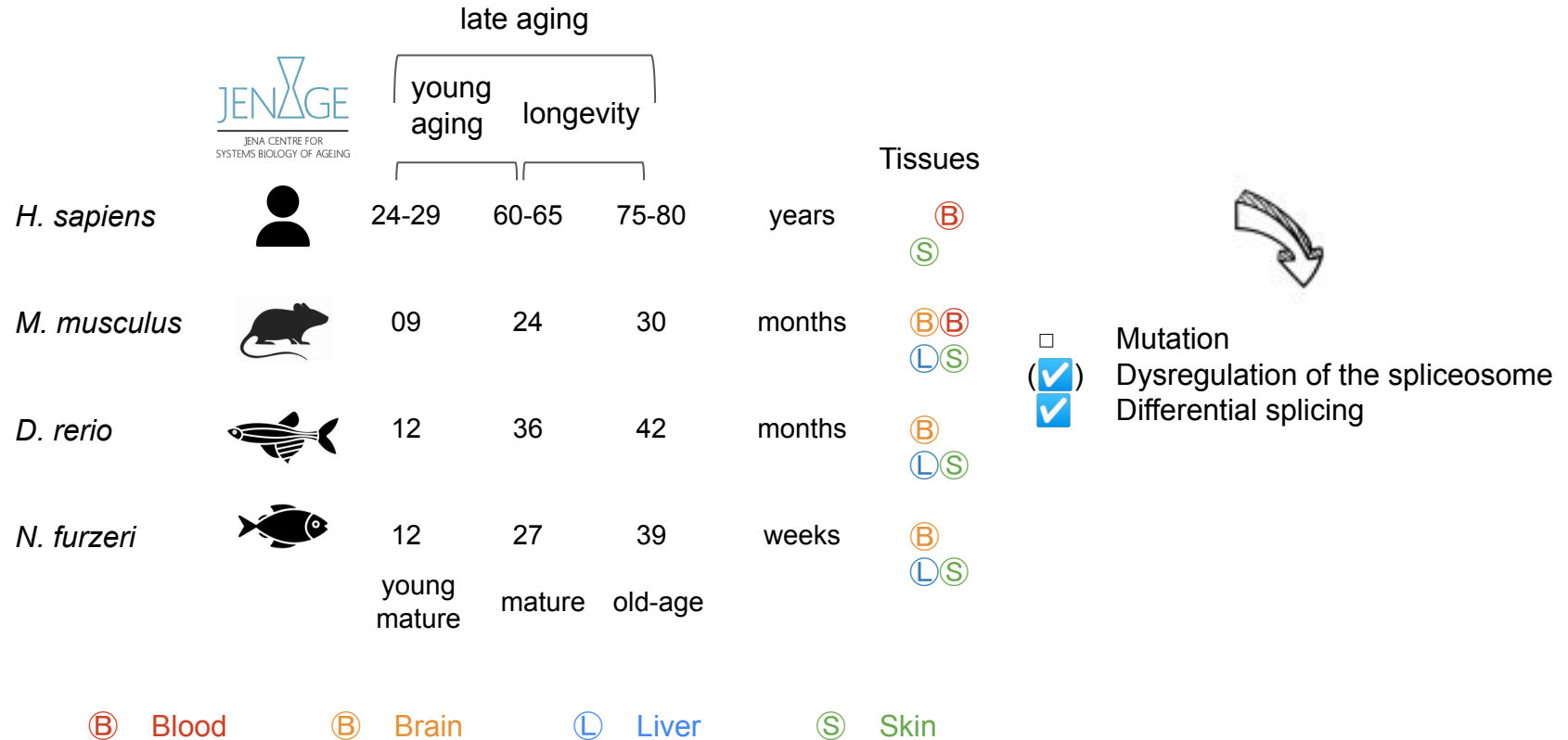


Hallmarks of aging

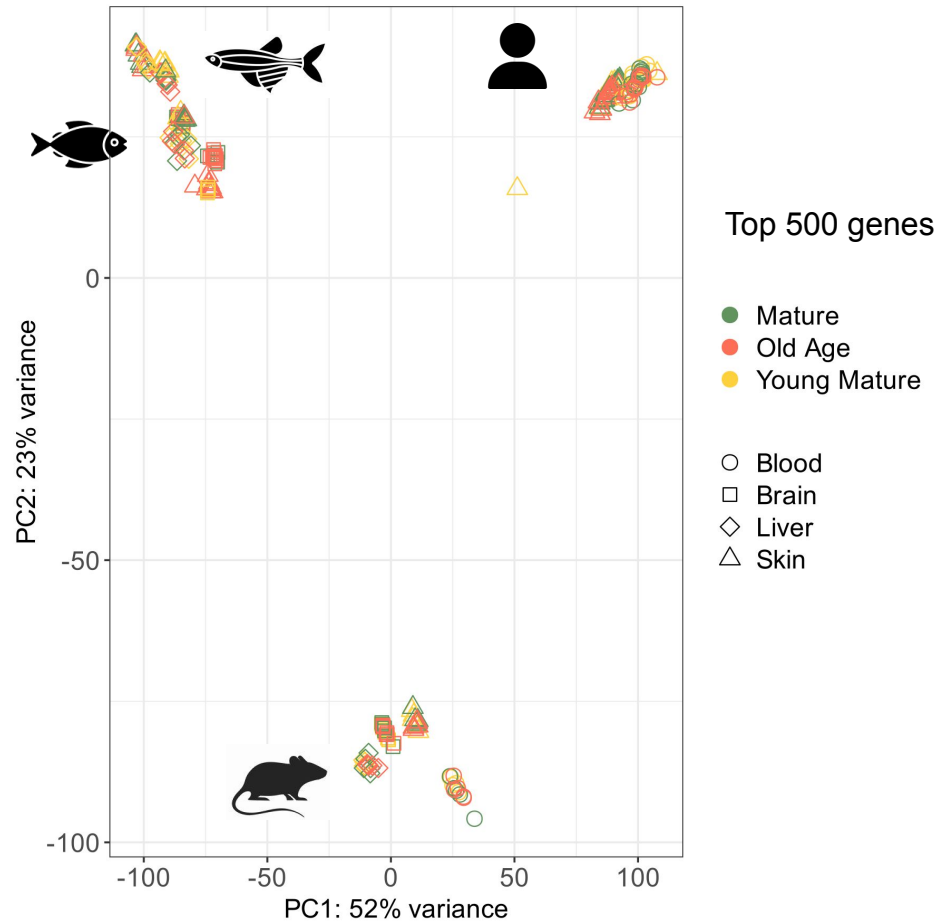
Schmauck-Medina, Tomas, *et al.* (2022)



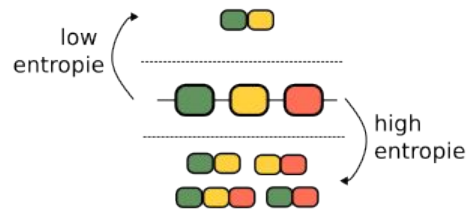
Using RNASeq data to investigate the interplay



Not much differences between transcriptomes of different ages in healthy organisms.



$$\psi = \frac{\text{Include Reads}}{\text{Exclude} + \text{Include Reads}}$$

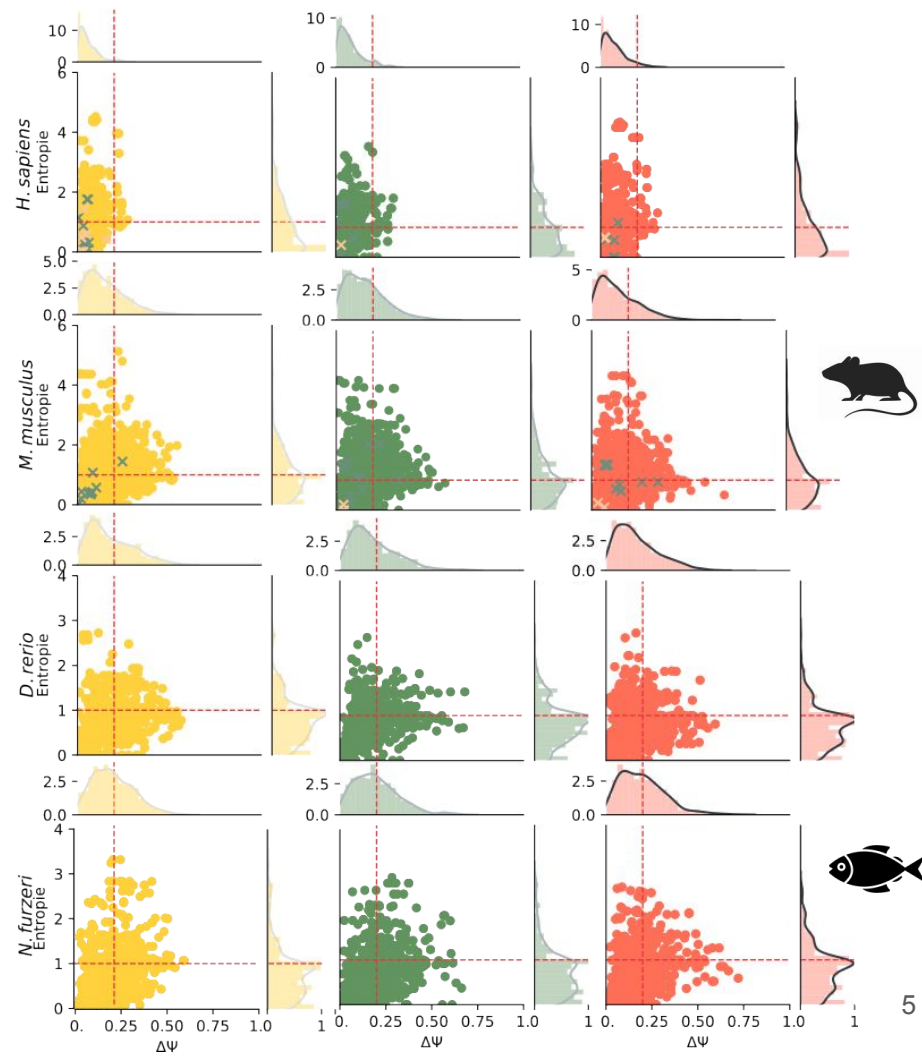


$$\text{Entropy} = -\sum_i \Psi_i \log_2 \Psi_i$$

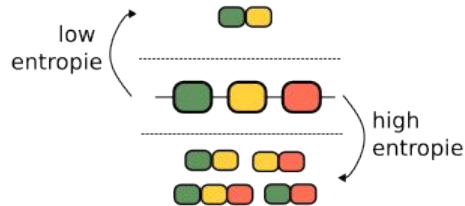


Whippet, rMATs

- × Age Gene
- × Age & Hk Gene
- Threshold
- Young
- Mature
- Old



$$\psi = \frac{\text{Include Reads}}{\text{Exclude} + \text{Include Reads}}$$

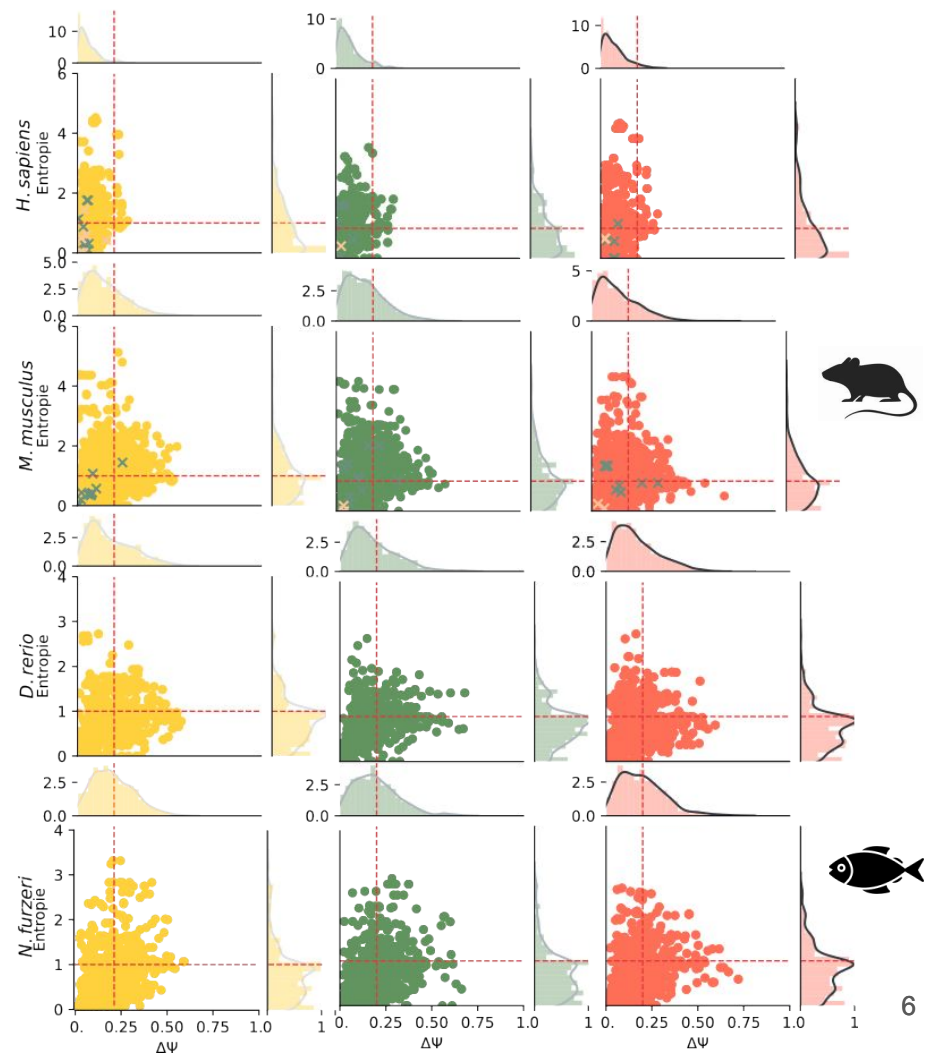


$$\text{Entropy} = -\sum_i \Psi_i \log_2 \Psi_i$$

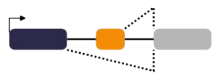
The stable splicing landscape does not shift in splicing event preferences or overall complexity with age.

Whippet, rMATs

- × Age Gene
- × Age & Hk Gene
- Threshold
- Young
- Mature
- Old



Changes in beginning and the end



Regulation of gene expression

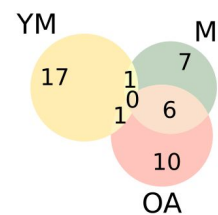
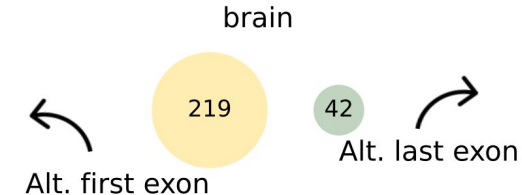
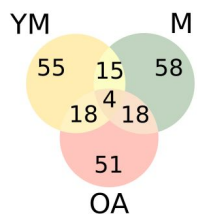
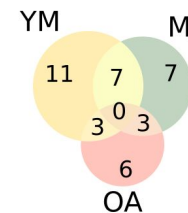
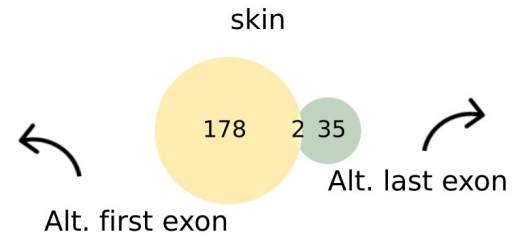
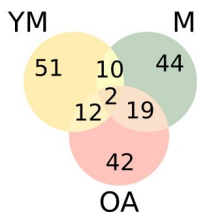
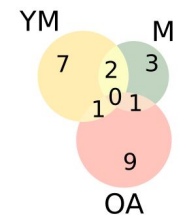
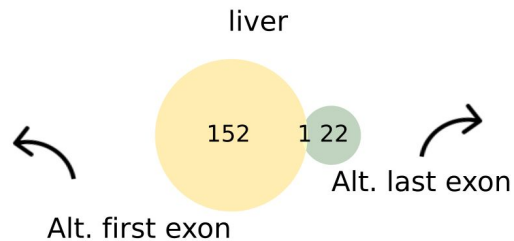
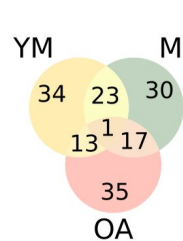
Tan, *et al.*(2006) & Robinson, *et al.*(2021)



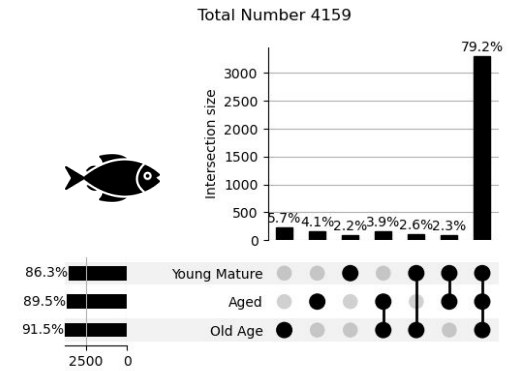
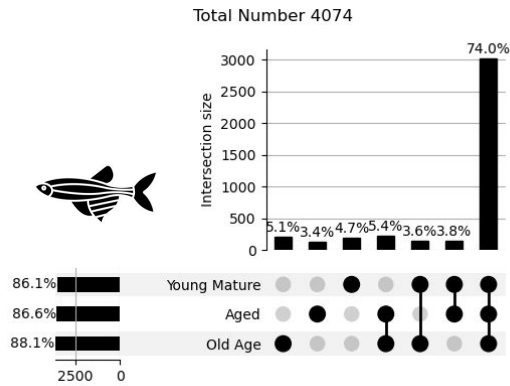
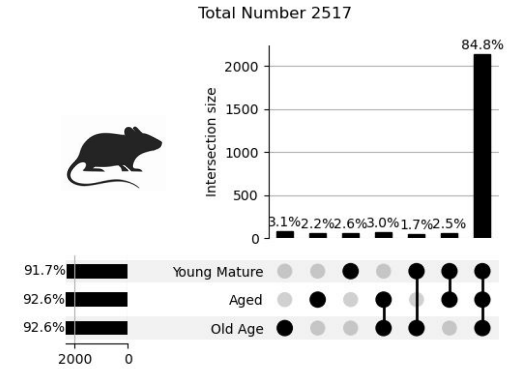
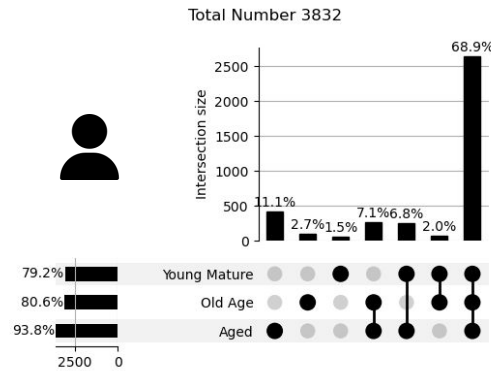
Localisation

Titus, *et al.*(2021)

● Young
● Mature
● Old

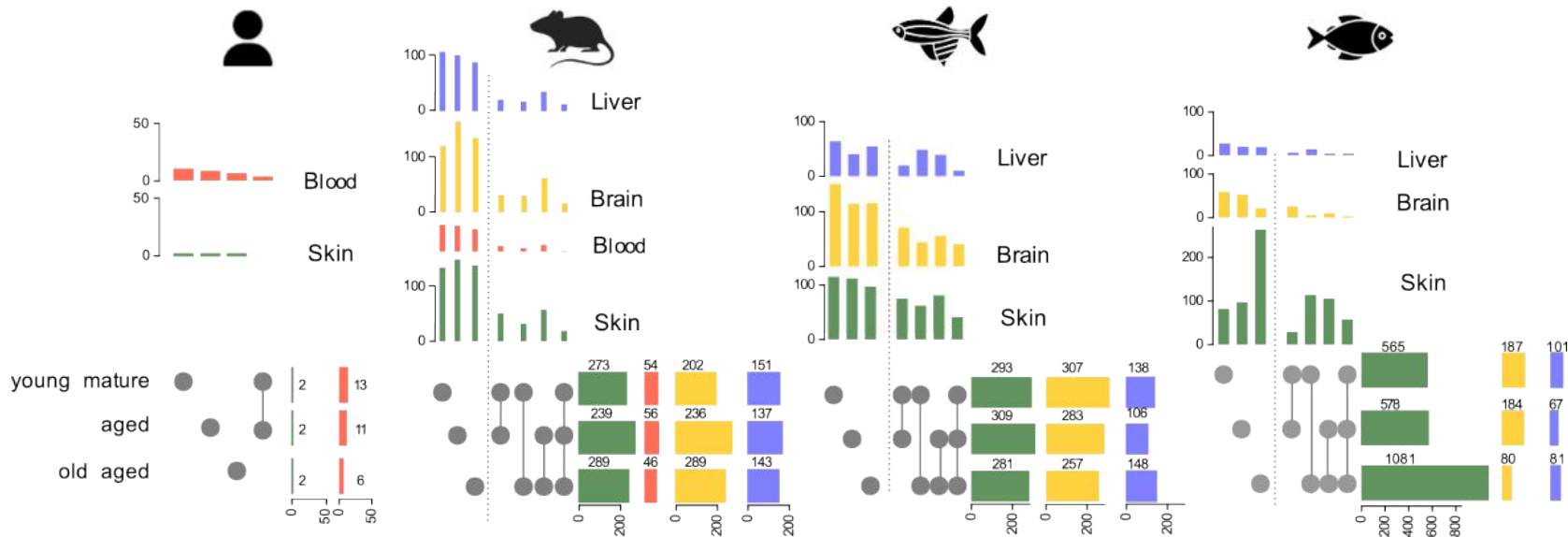
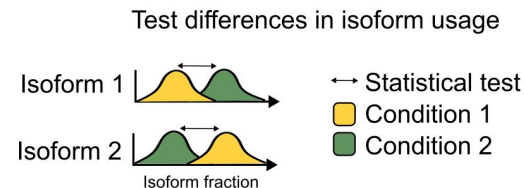
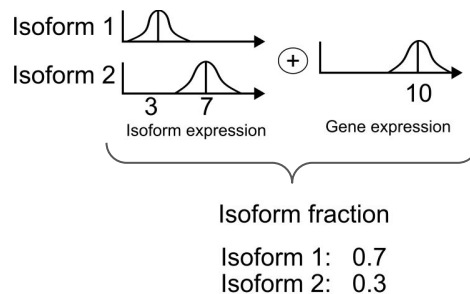


Few novel exons, few novel introns, few novel transcripts.



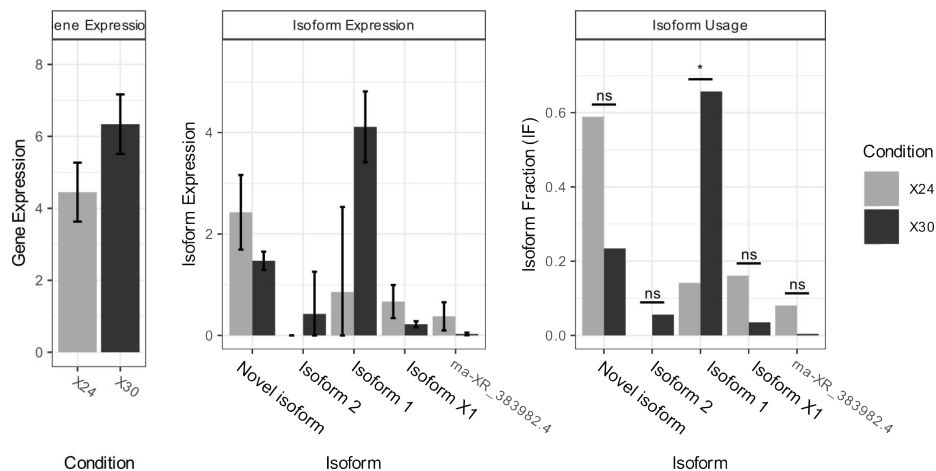
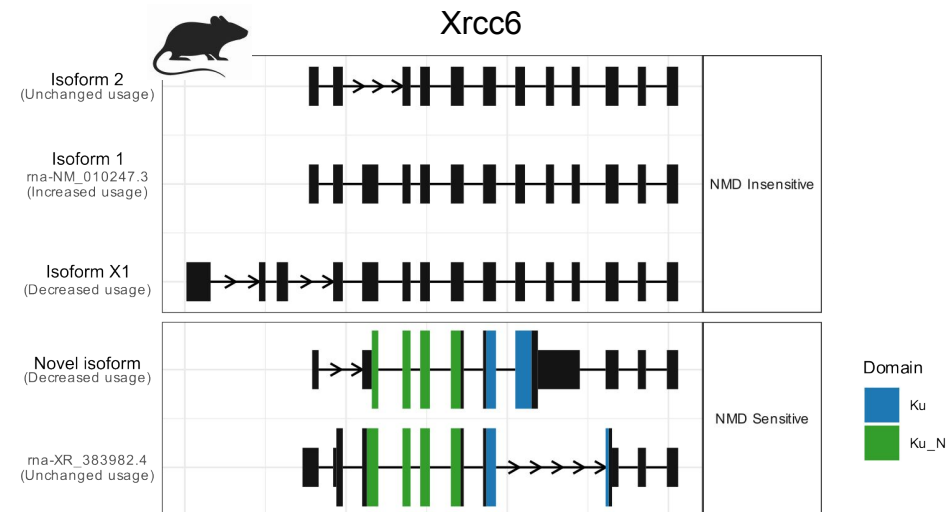
</> Stringtie, gffcompare

In response to healthy ageing, several hundred genes show dominant isoforms, usually in one age group.



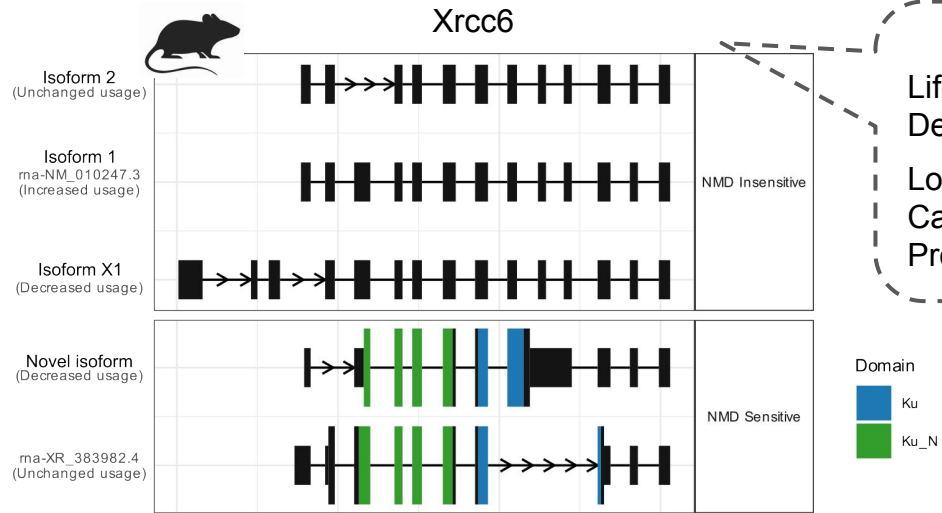
</> IsoformSwitchAnalyzER

How to find the interesting ones?

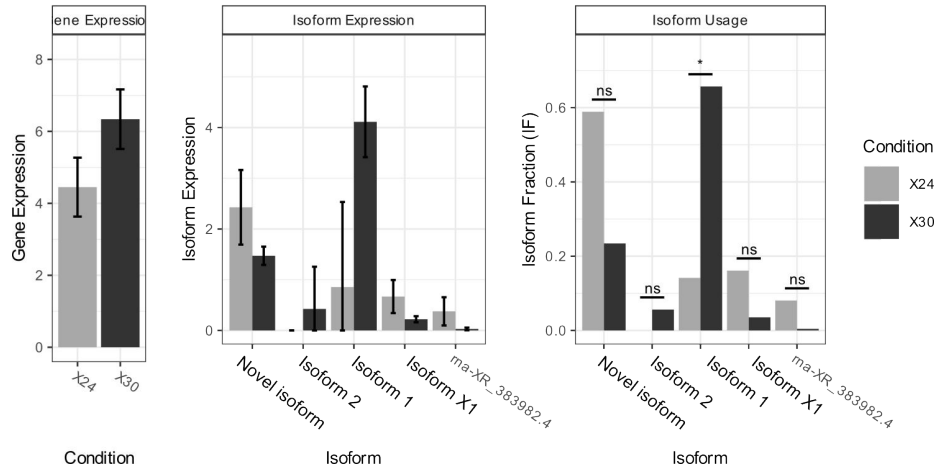


</> IsoformSwitchAnalyzer

How to find the interesting ones?



GenAge:
 Lifespan Effect:
 Decrease
 Longevity
 Category:
 Pro-Longevity



</> IsoformSwitchAnalyzer

Take Home Message: Stay healthy, be stable.

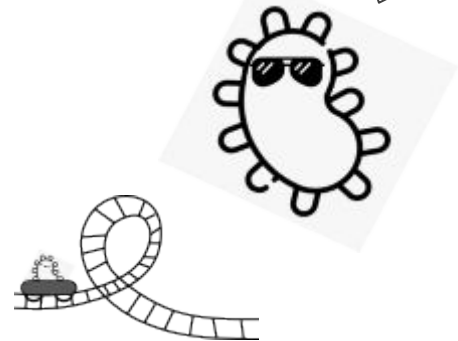
Acknowledgement



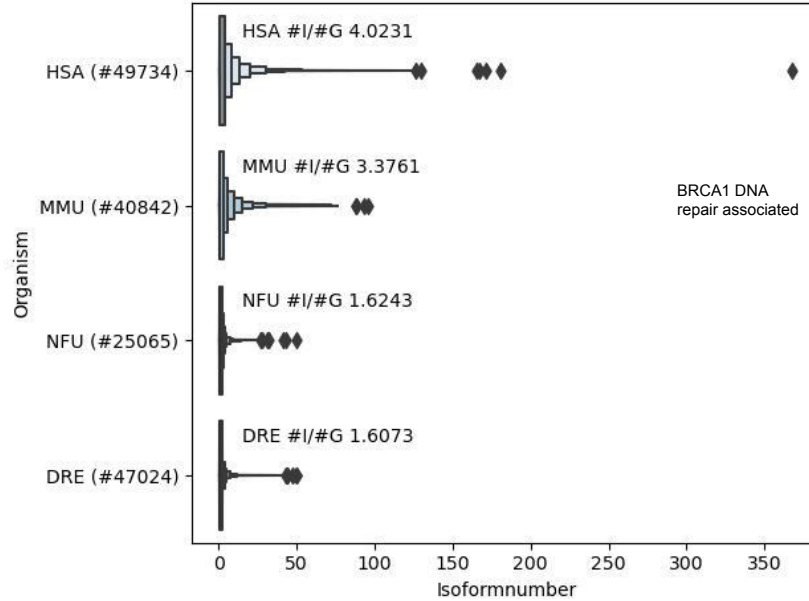
Many thanks to the whole group, especially Manja and Emanuel.

And thank you for your attention.

I'll be bac.



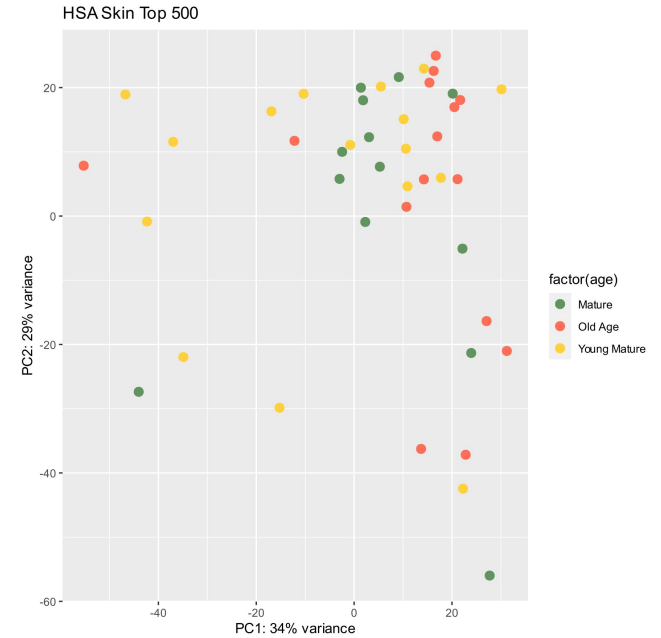
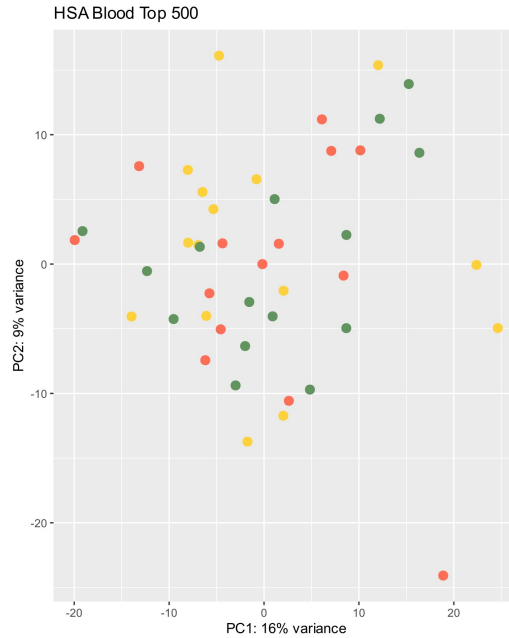
> How many isoforms per gene are possible?



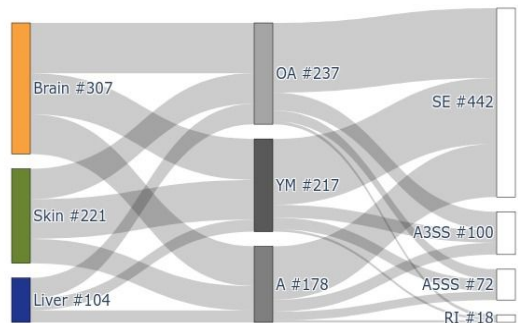
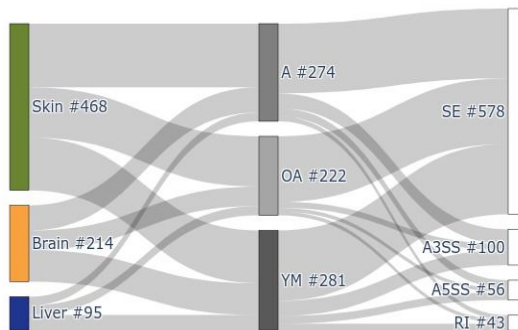
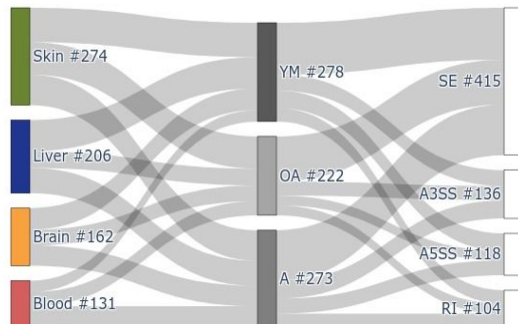
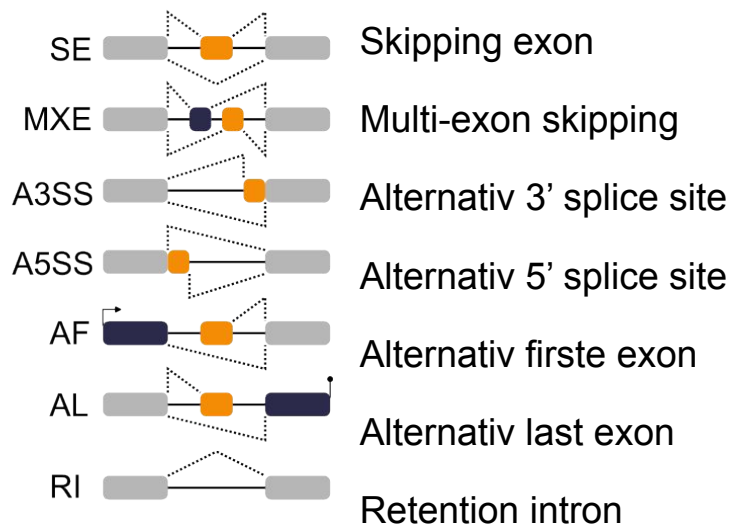
Just because a gene has many isoforms does not mean it is more likely to be differentially spliced.



Human data is not a bug but a a troublesome feature.



Alternative splicing types



We: total RNAseq

Other:

- disease
- tissue
- organism (e.g. worm)
- RNA extraction

