Not everything gets bad when we get old.

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





The Interplay: Aging vs. Splicing



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Using RNASeq data to investigate the interplay







Dysregulation of the spliceosome **Differential splicing**

Not much differences between transcriptomes of different ages in <u>healthy</u> organisms.







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

× Age Gene

Threshold

× Age & Hk Gene

Old



</> Whippet, rMATs



Whippet, rMATs </>

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







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



ò

50 -

0 -

0 -

young mature

aged

old aged

50 -

How to find the interesting ones?



</> IsoformSwitchAnalyzeR

How to find the interesting ones?



</> 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.

> 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.















We: total RNAseq Other:

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

Longevity

	Young Aging	Late Aging	Longevity
MMU	blood - 20 25 32 39 93 48 50 34 34	blood - 15 46 27 46 84 48 56 26 38	blood - 0 33 16 26 100 44 44 12 4
	brain - 8 35 22 38 84 39 38 13 39	brain -10 40 19 41 80 42 39 19 31	brain - 9 34 20 39 80 40 31 14 3
	liver - 6 39 16 43 77 44 44 13 28	liver - 10 43 23 43 79 44 42 16 38	liver - 10 43 27 48 74 41 51 20 3
	skin - 10 37 30 42 88 39 47 21 38	skin - 9 37 27 45 80 41 42 19 38	skin - 8 37 18 39 78 46 38 12 3
DRE	brain -12 30 27 38 82 34 43 22 34	brain - 13 33 26 37 82 44 41 19 35	brain - 12 26 31 36 80 39 41 23 3
	liver - 15 30 23 38 67 30 30 18 39	liver - 11 30 27 34 80 42 37 21 30	liver - 7 34 20 34 87 42 35 16 3
	skin -13 28 31 35 86 40 47 27 37	skin - 12 34 30 43 82 40 45 22 37	skin - 12 35 25 42 78 36 36 19 3
NFU	brain -13 38 31 42 88 63 44 22 41	brain -10 44 29 48 81 56 33 17 29	brain - 15 35 30 47 81 55 45 28 2
	liver - 11 44 27 46 94 72 46 23 35	liver - 16 40 28 44 90 59 40 24 30	liver - 14 40 26 51 86 69 46 40 4
	skin - 0 50 19 56 88 62 38 25 12	skin - 12 43 29 51 90 61 49 21 35	skin - 10 44 27 49 90 56 47 19 3
	MOLESCOND & ECOLO		
	Leger Legere	0 20 40	60 80 100
	OF THE SOUTH	Consequenc per Gene [%]	
	to a		

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Intersection size

17