

Characterising antibody immunity and ageing in a short-lived teleost

William John Bradshaw

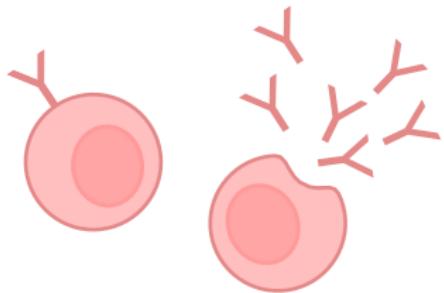
6th June 2019



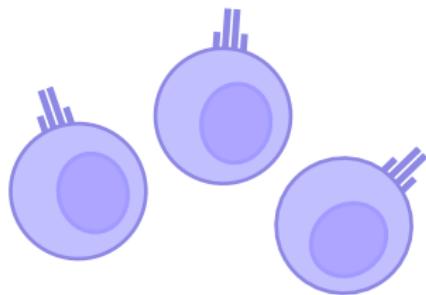
University of Cologne



Antibodies



T-cell receptors



B-cells

T-cells



Adaptive immune system

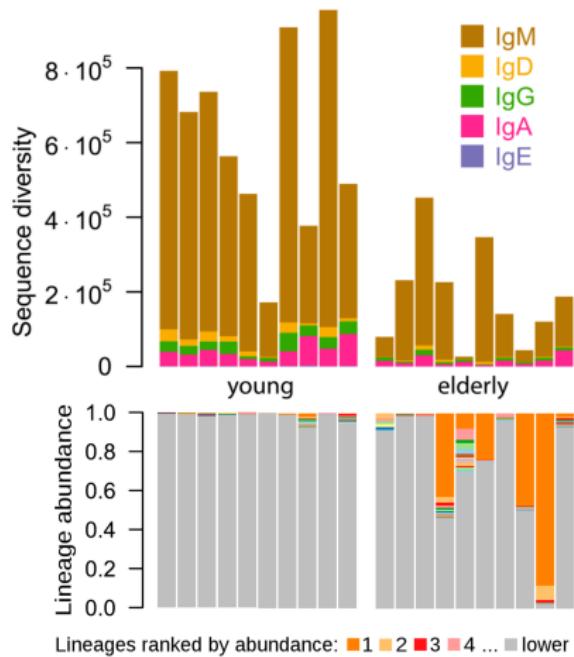
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- Impaired antibody quality
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Adapted from de Bourcey et al., PNAS 2017

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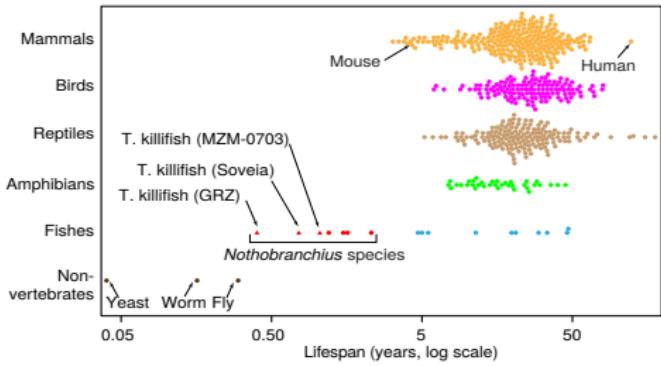
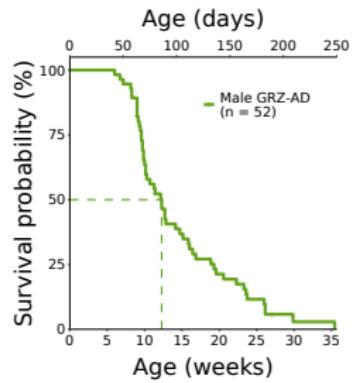
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The turquoise killifish as a model for antibody ageing

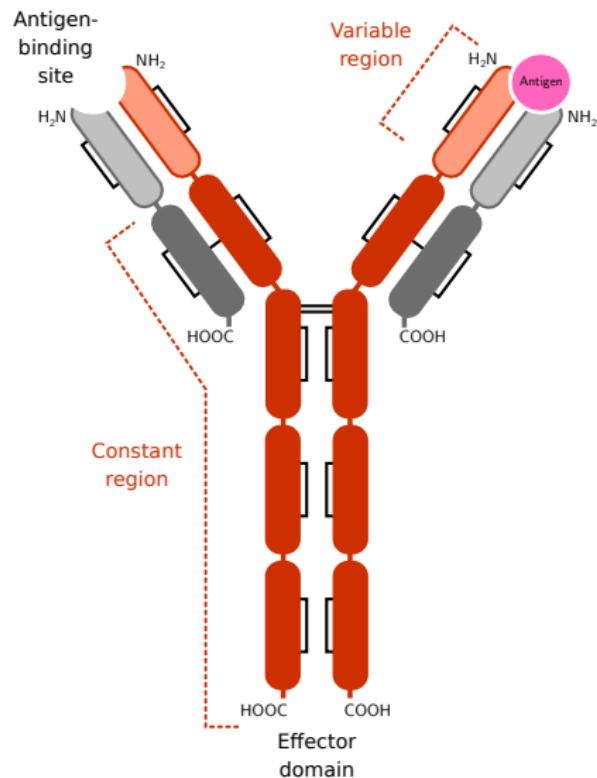


Valenzano et al., Cell 2015

- Shortest-lived vertebrate bred in captivity (median lifespan 12-16 wk)
- **Short-lived:** tractable for large, repeatable ageing experiments
- **Vertebrate:** possesses a mammal-like adaptive immune system

Understanding adaptive immune ageing in turquoise killifish

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VDJ recombination and primary antibody diversity

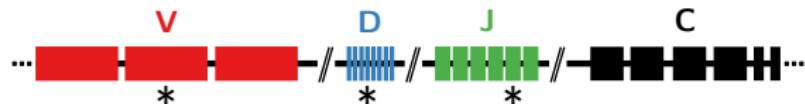
VDJ recombination and primary antibody diversity

(i) Native state



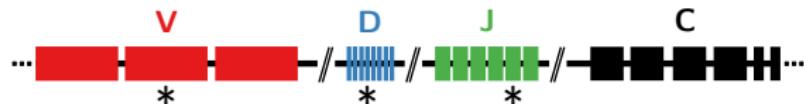
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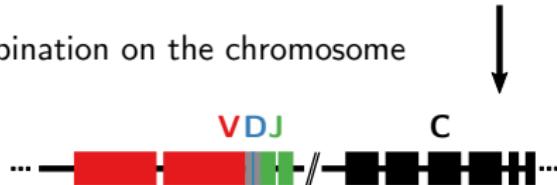


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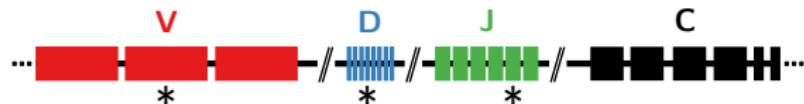


(ii) VDJ Recombination on the chromosome

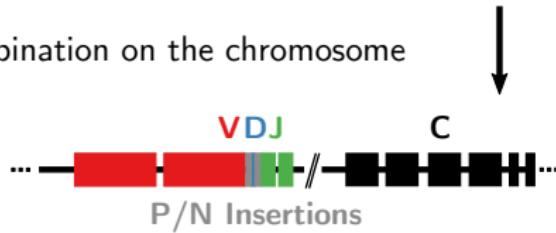


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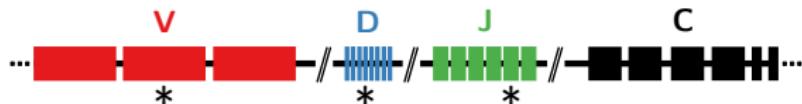


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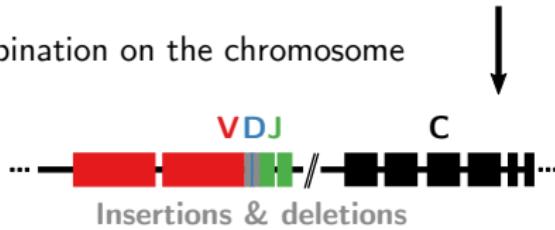


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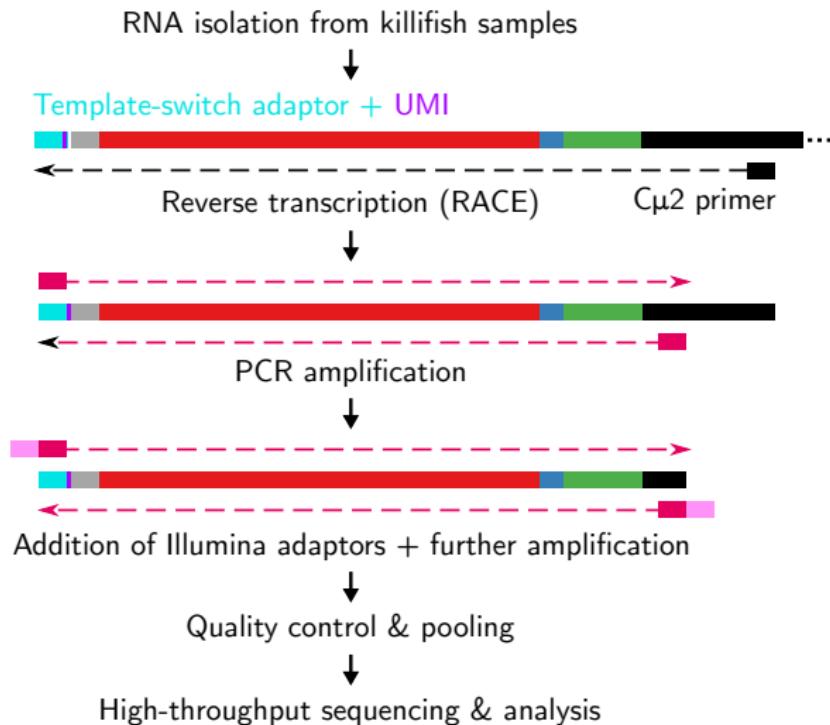
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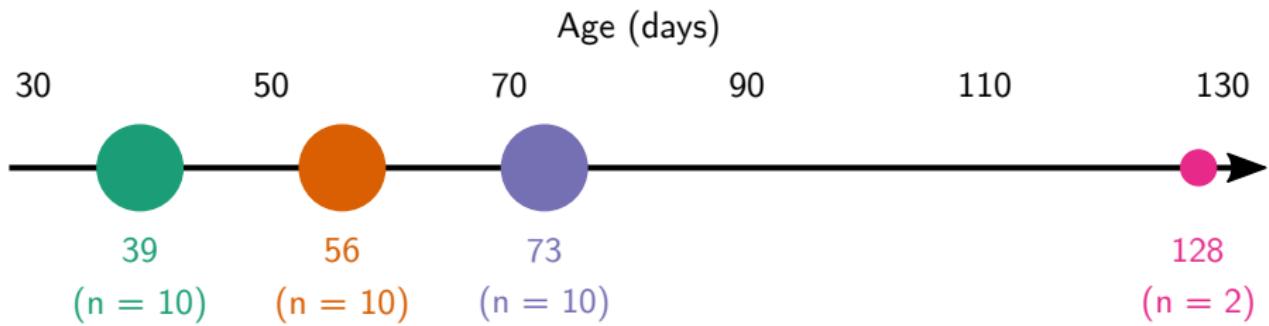
(iii) Transcription and splicing



Immunoglobulin sequencing in the turquoise killifish

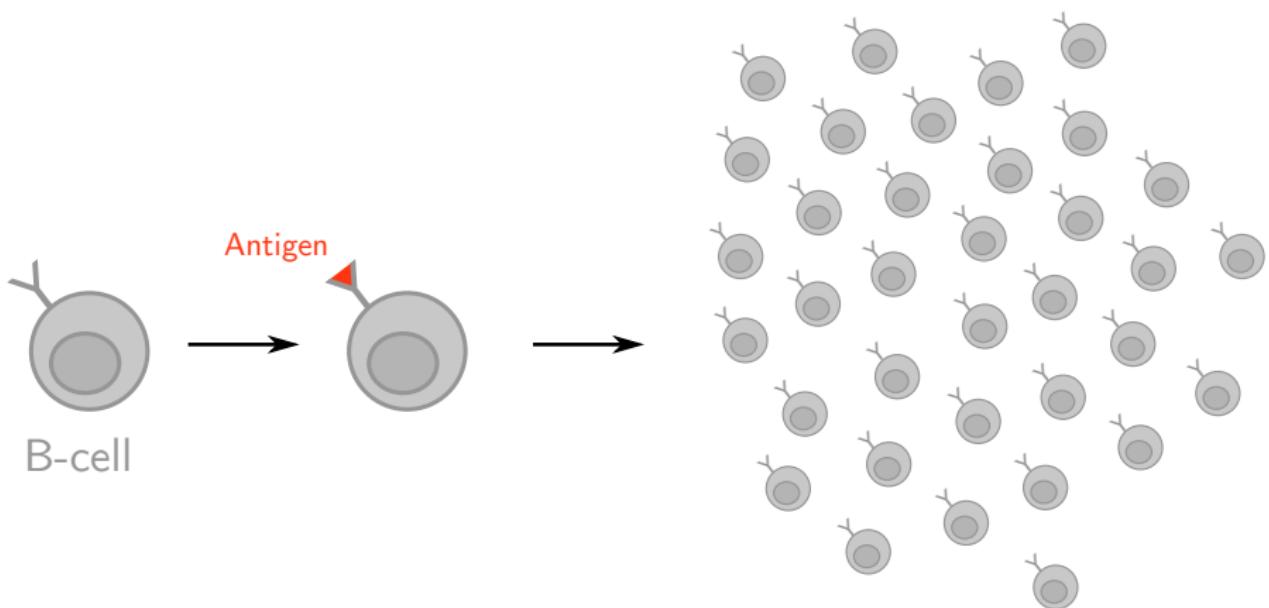


Sample design – killifish ageing study

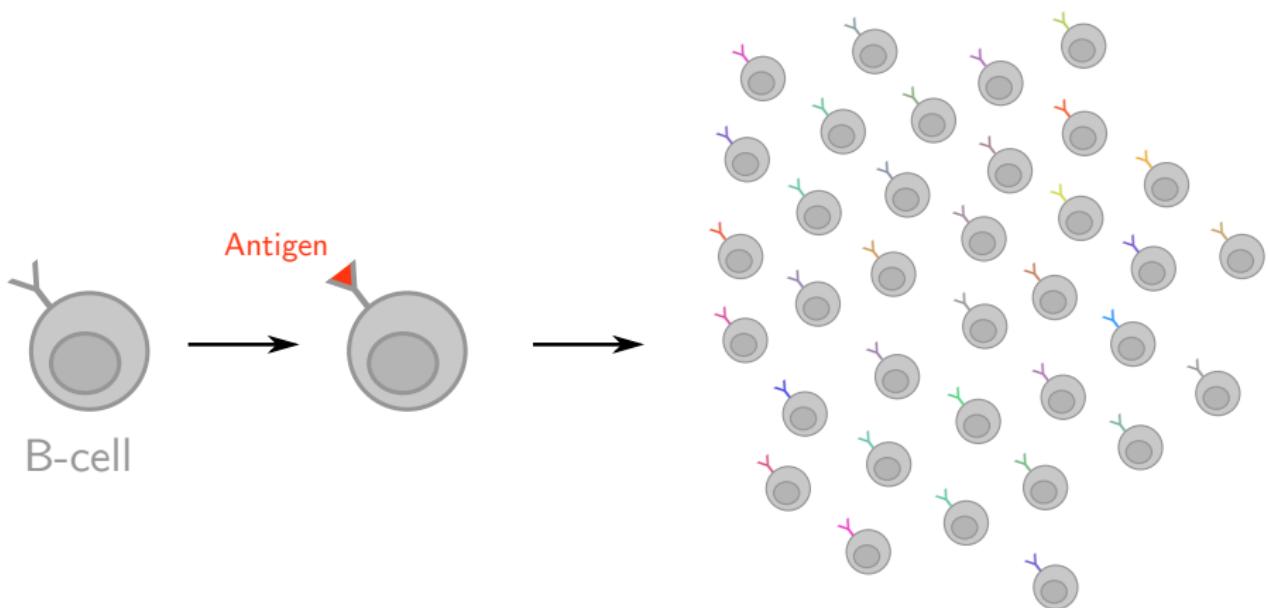


Clonal antibody diversity

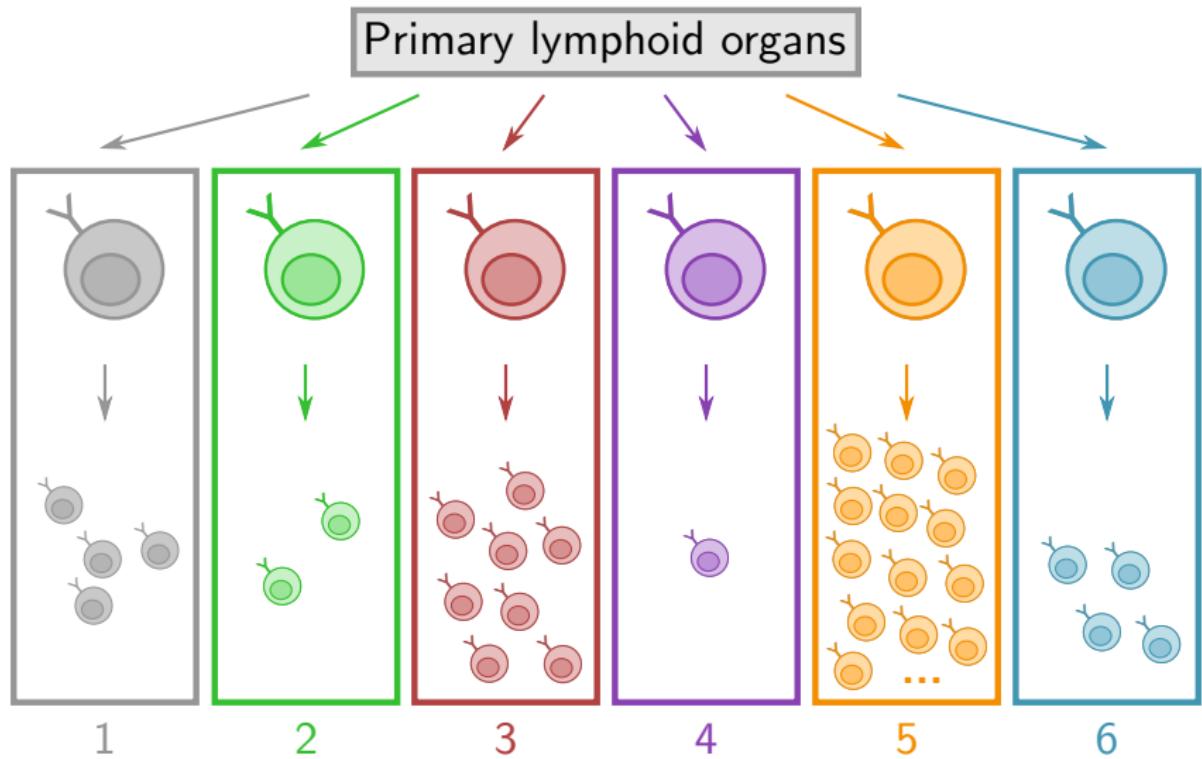
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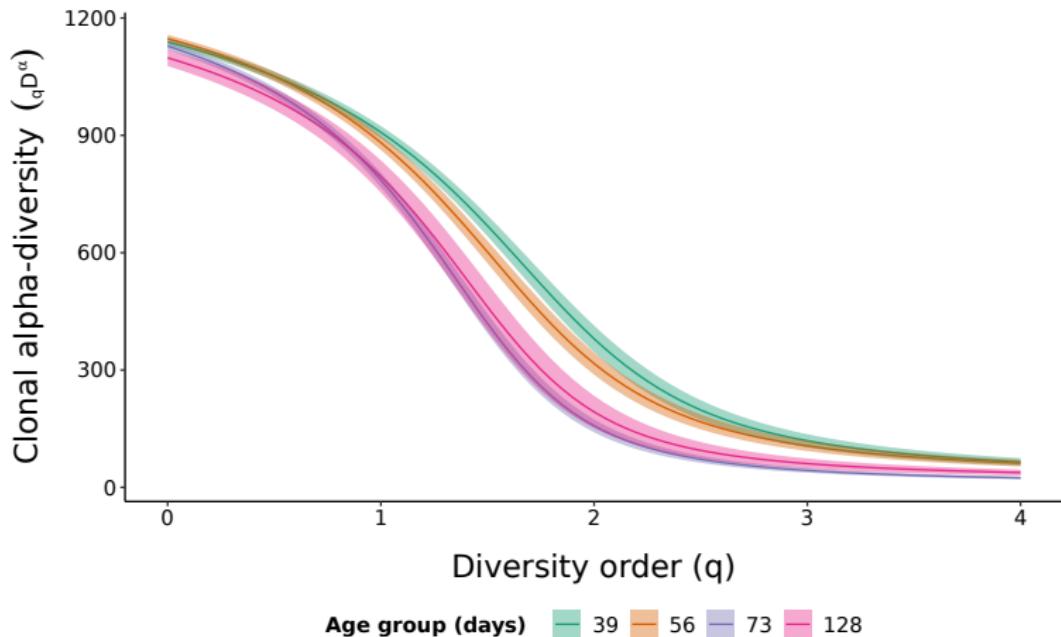


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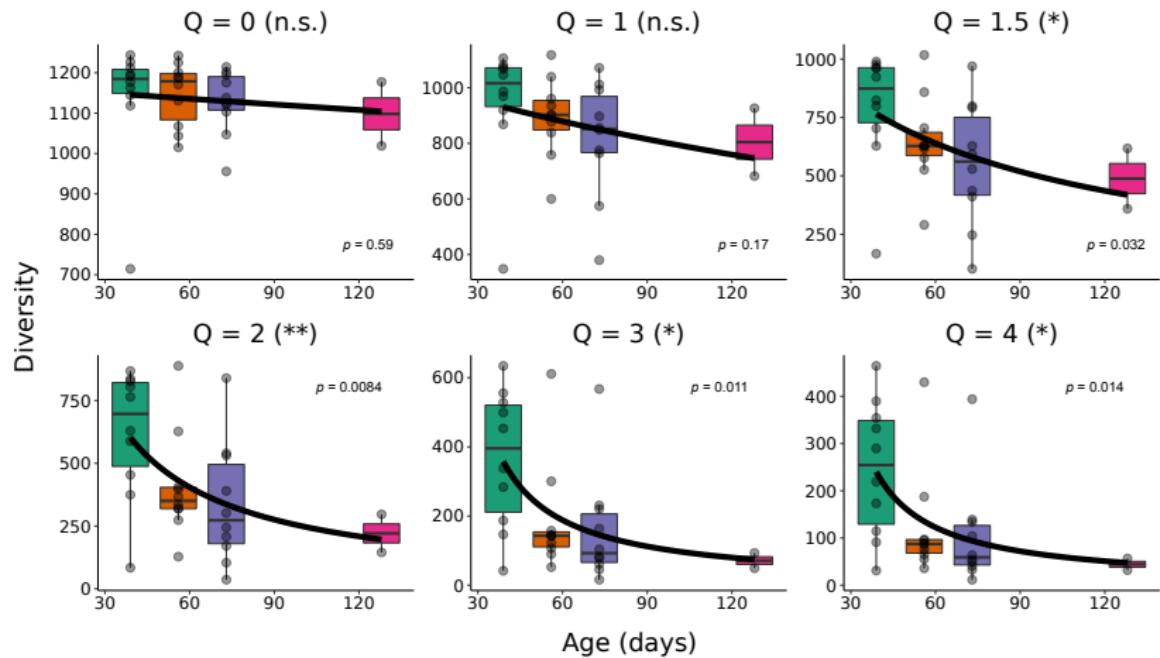


Clonal alpha-diversity in the killifish antibody repertoire

Clonal alpha-diversity in the killifish antibody repertoire declines with age



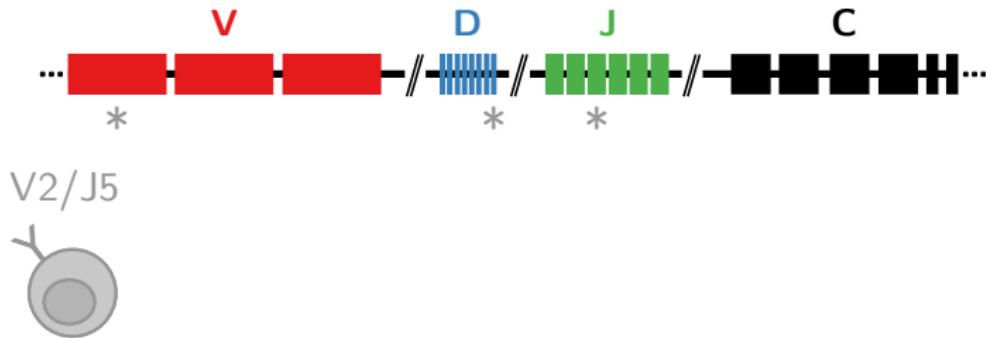
Clonal alpha-diversity in the killifish antibody repertoire declines with age at high diversity orders



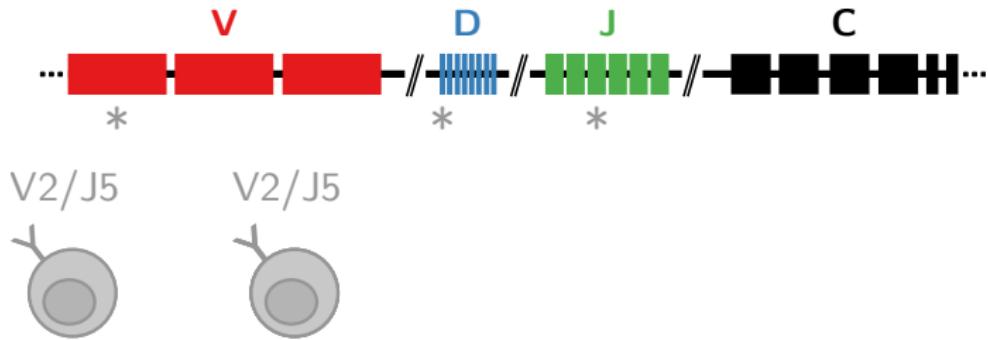
VJ alpha-diversity in the killifish antibody repertoire



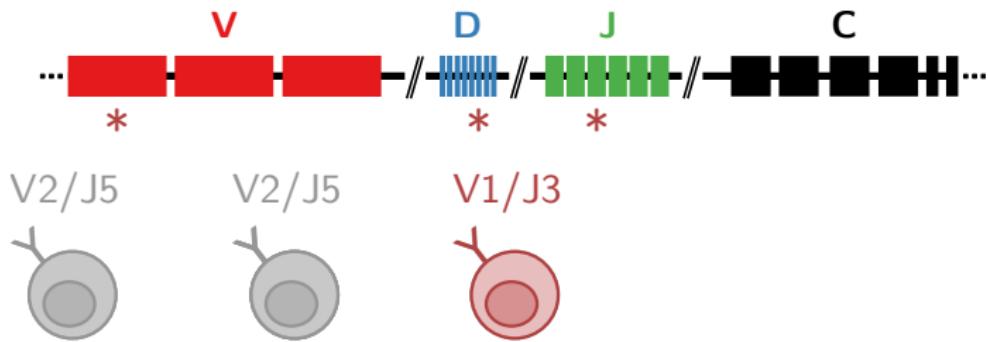
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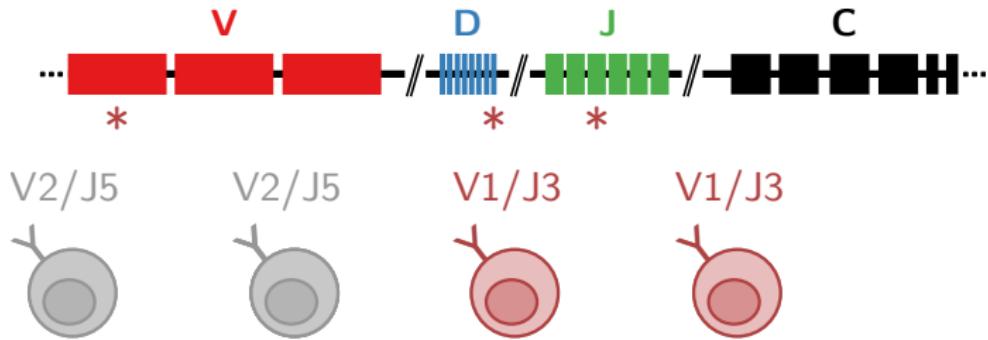
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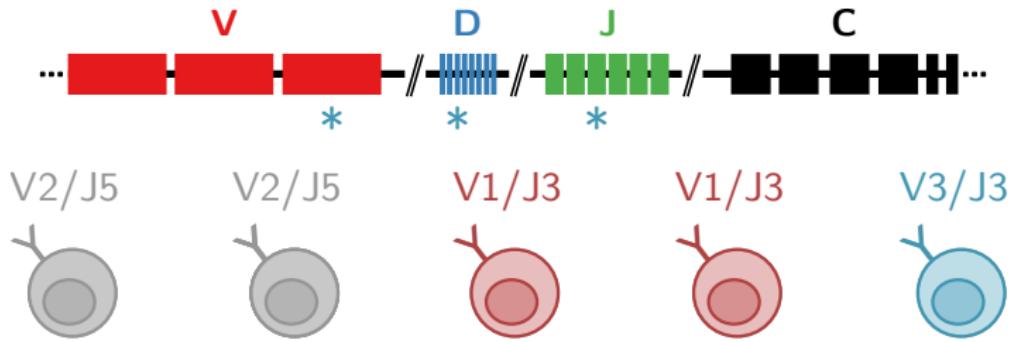
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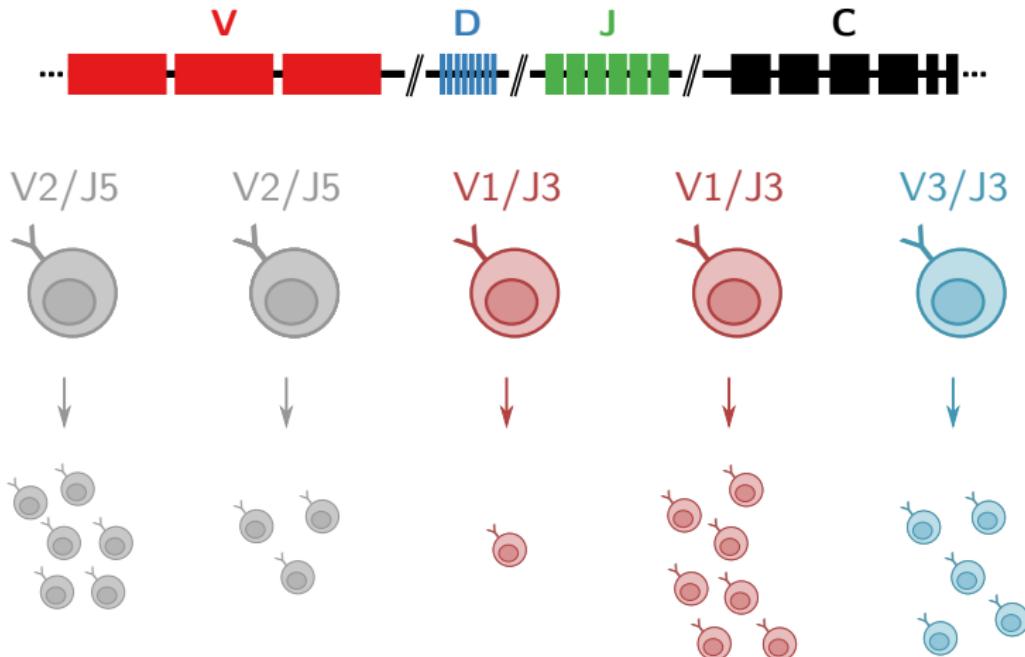
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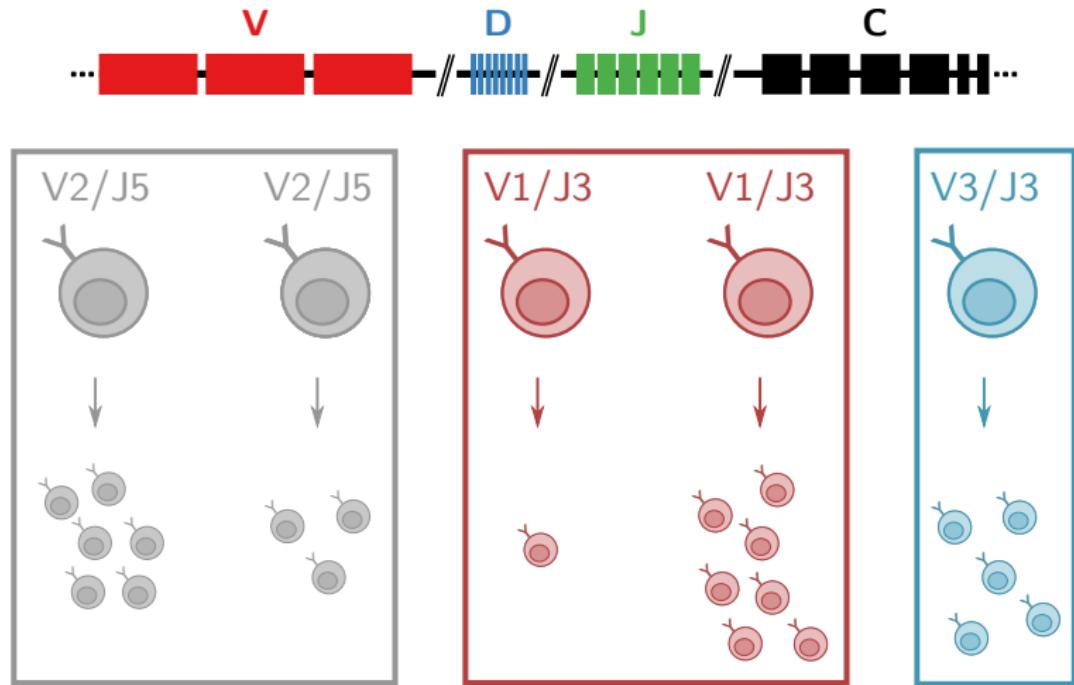
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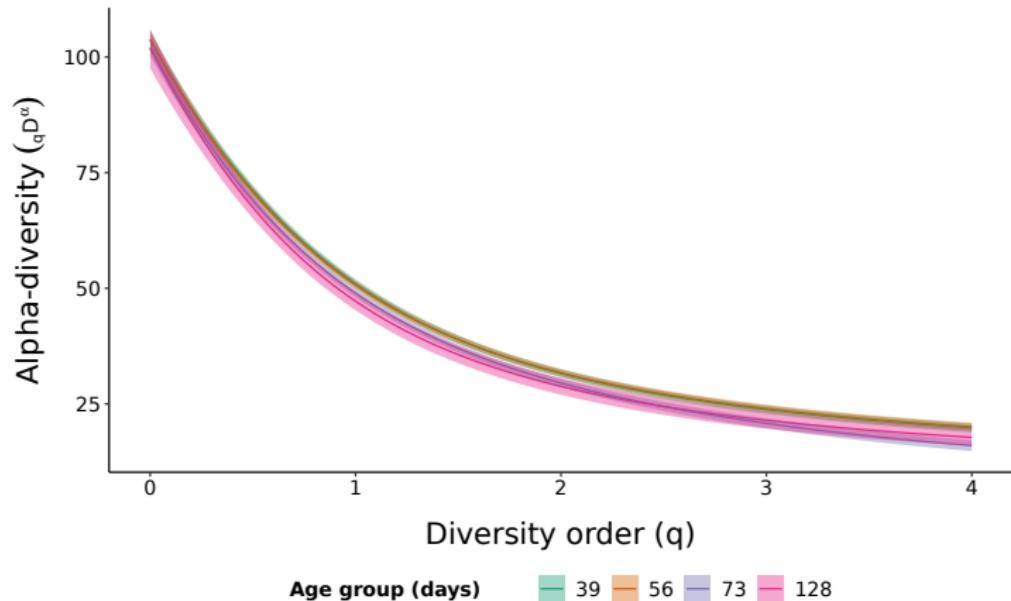


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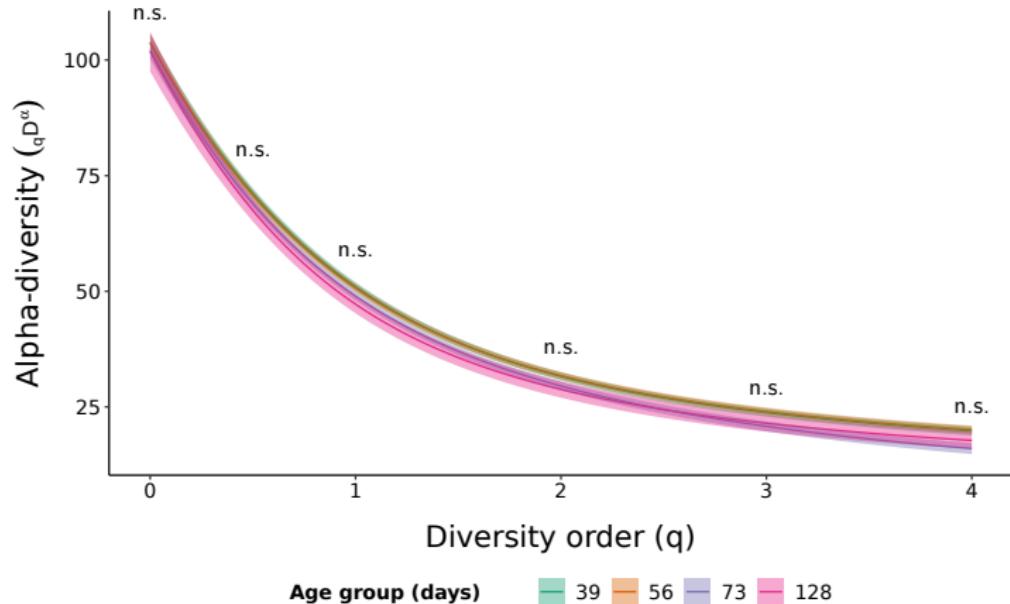


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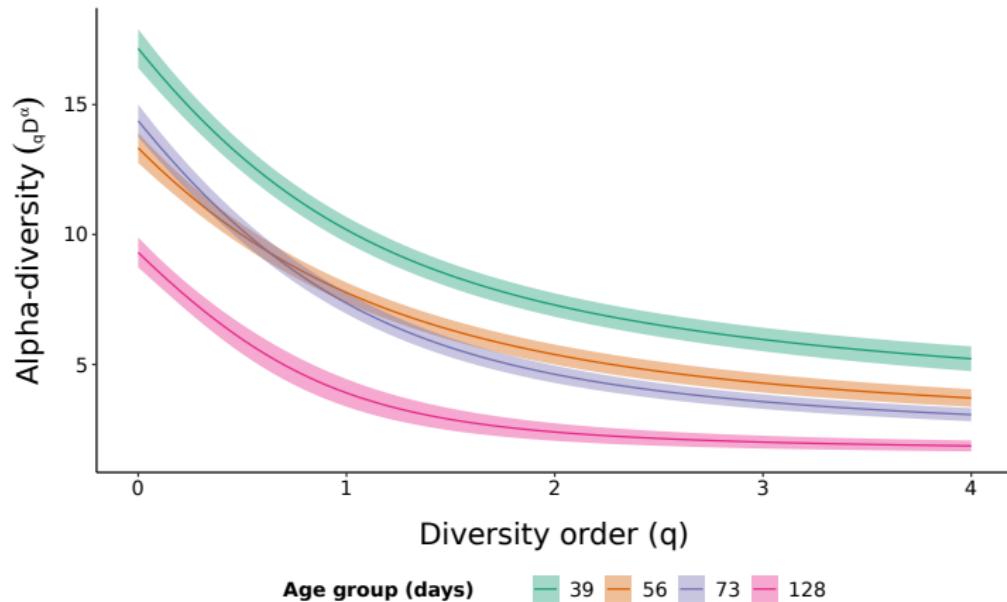
VJ alpha-diversity in the killifish antibody repertoire **does not decline** with age



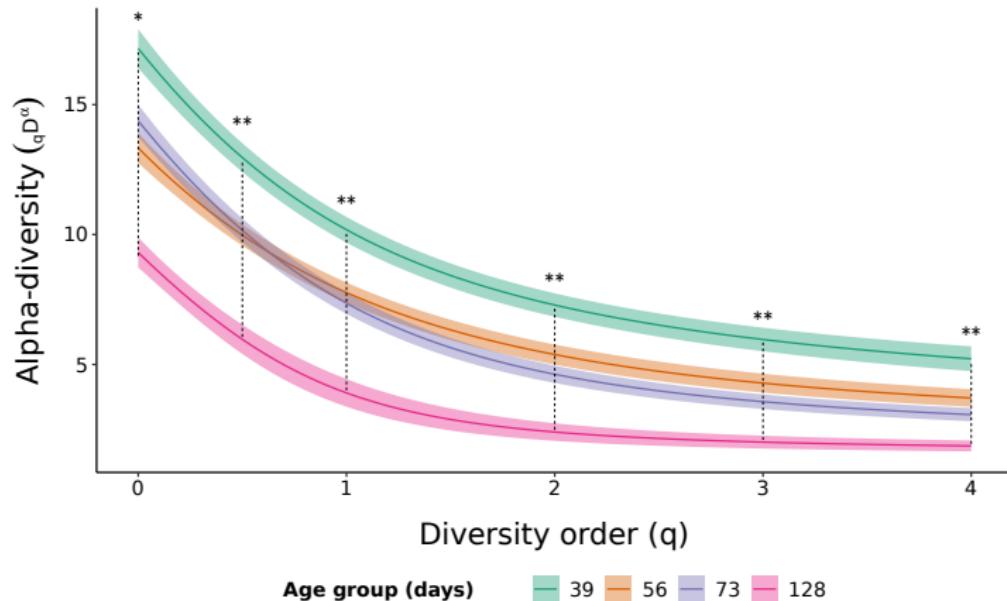
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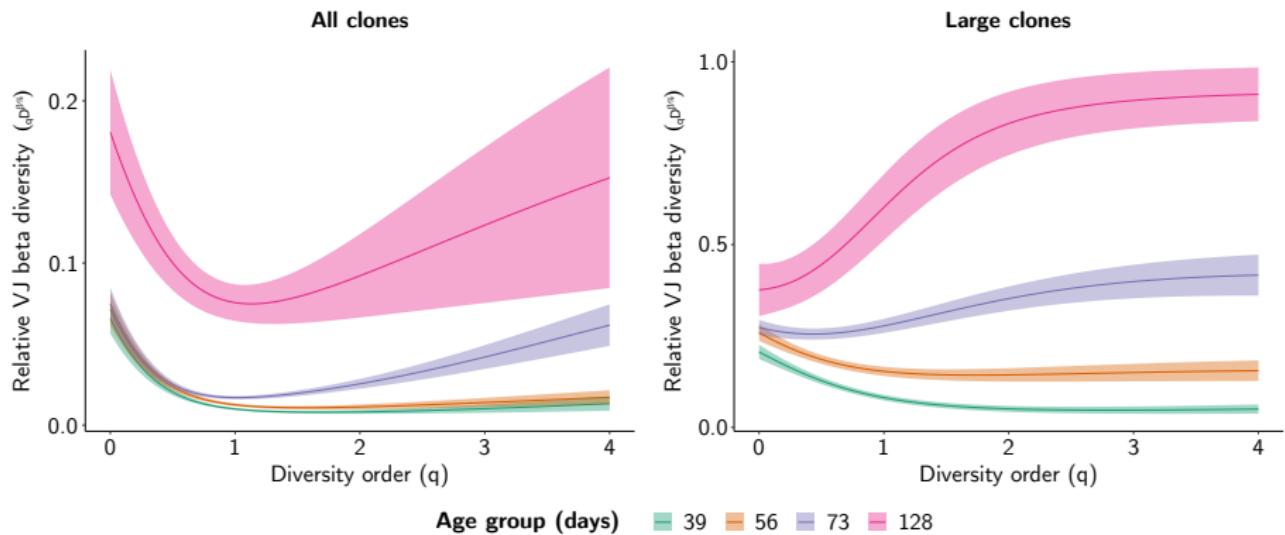
VJ alpha-diversity of large clones does decline with age



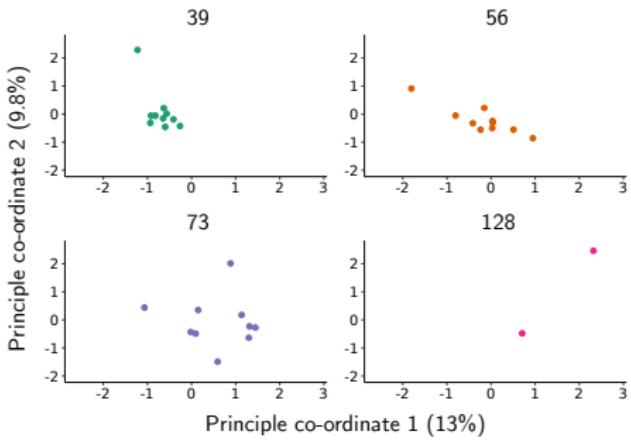
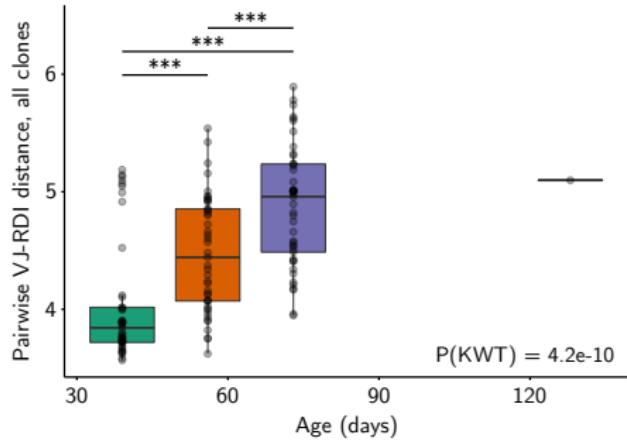
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Killifish VJ repertoires become **more dissimilar** with age



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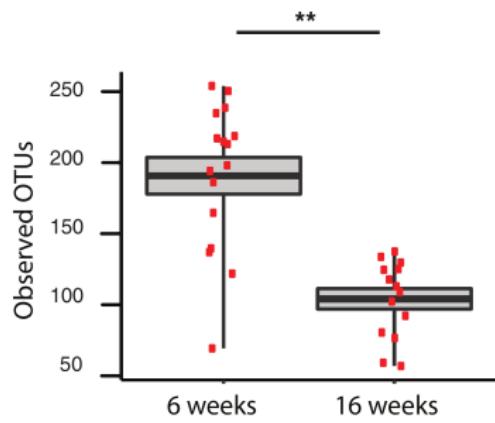
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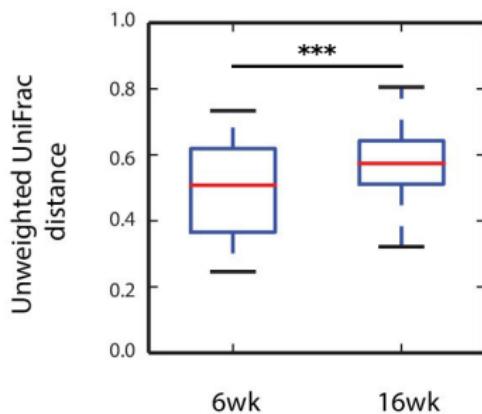
Killifish gut microbiota also show decreasing alpha- and increasing beta-diversity with age



Alpha diversity

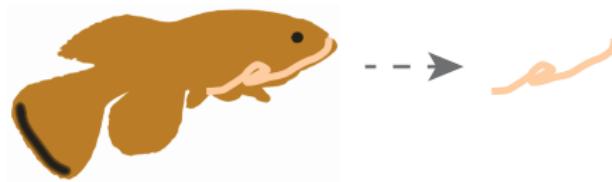
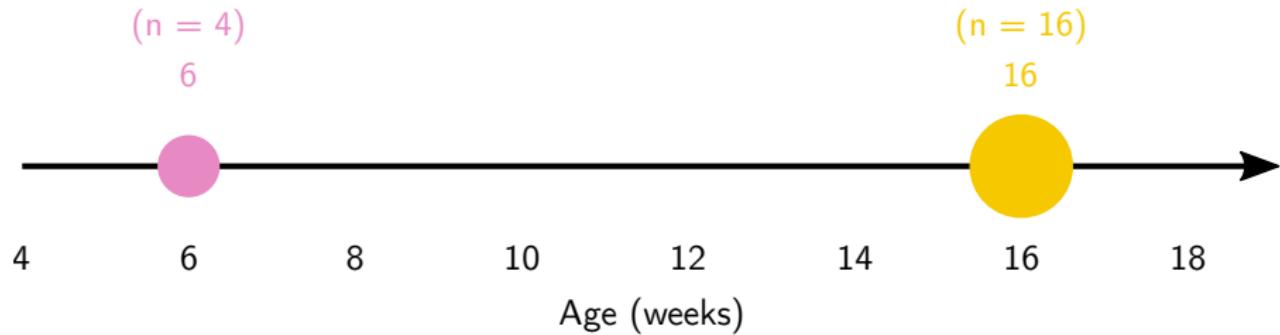


Beta diversity



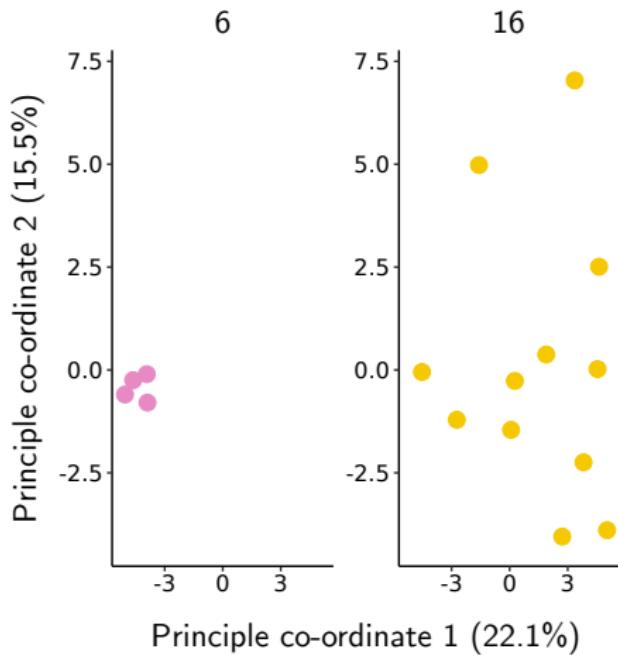
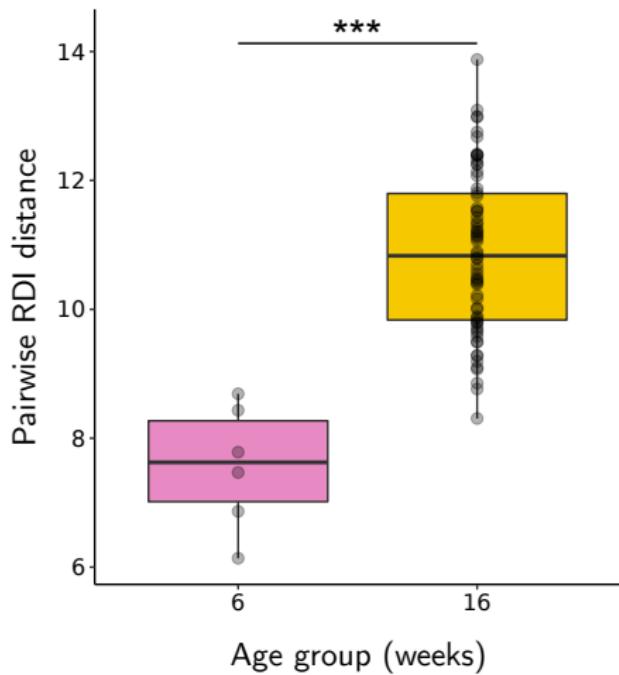
Smith et al., eLife 2017

Sample design – gut repertoire study

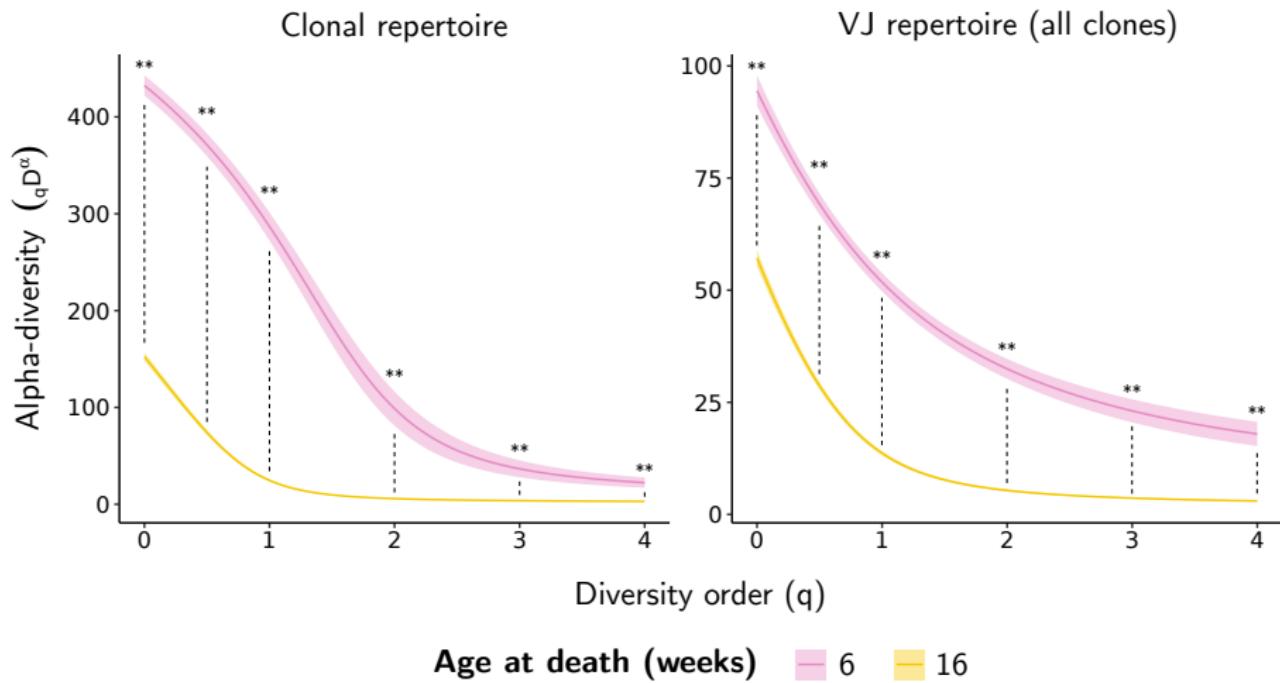


Samples collected for Smith et al., eLife 2017

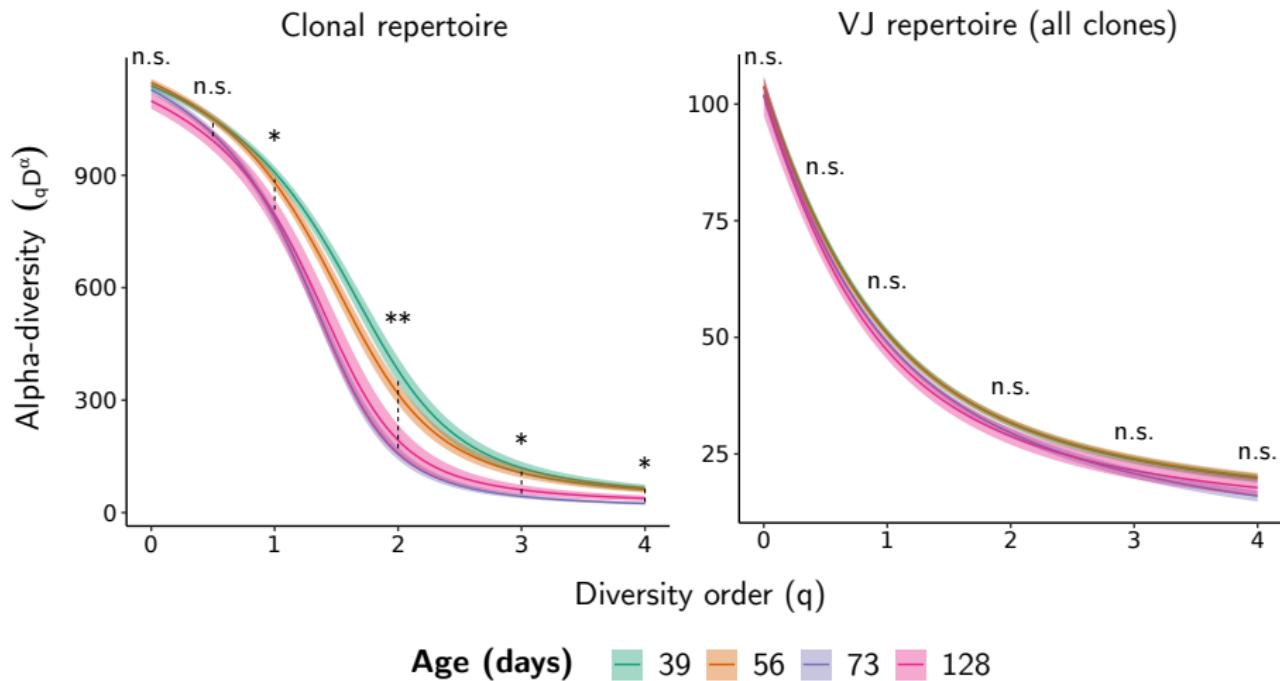
Killifish gut repertoires become much more dissimilar with age



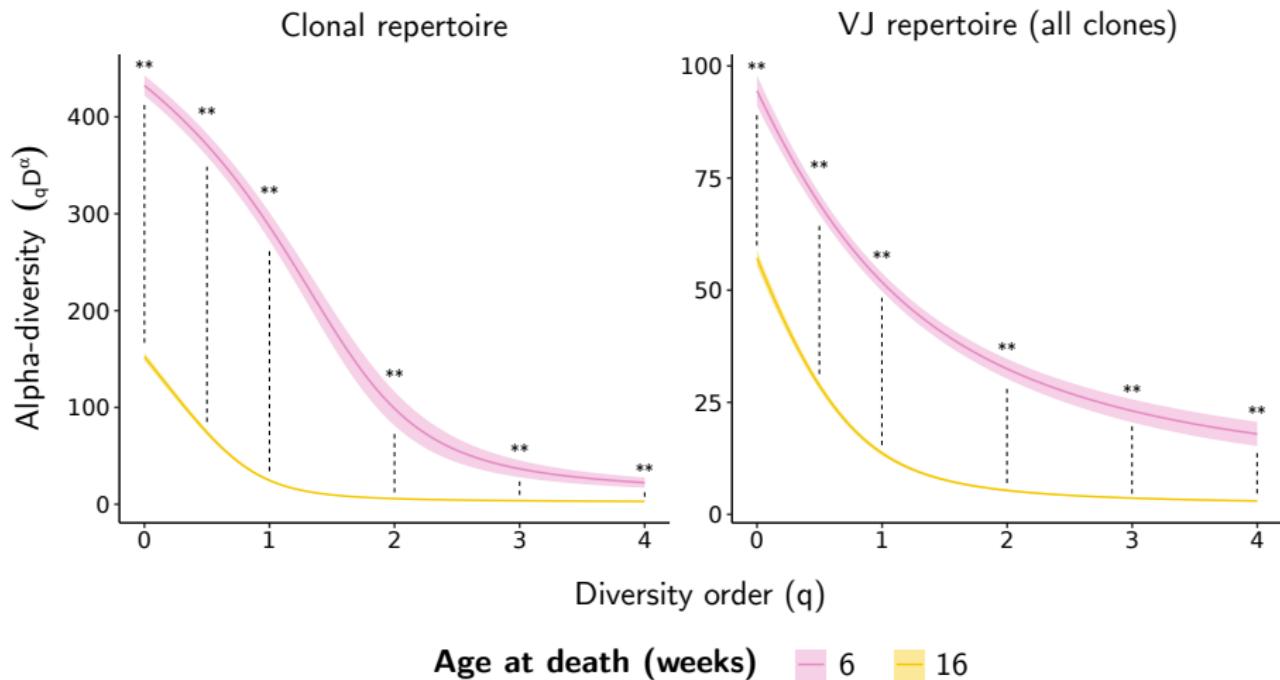
Gut repertoire alpha diversity declines dramatically with age in turquoise killifish



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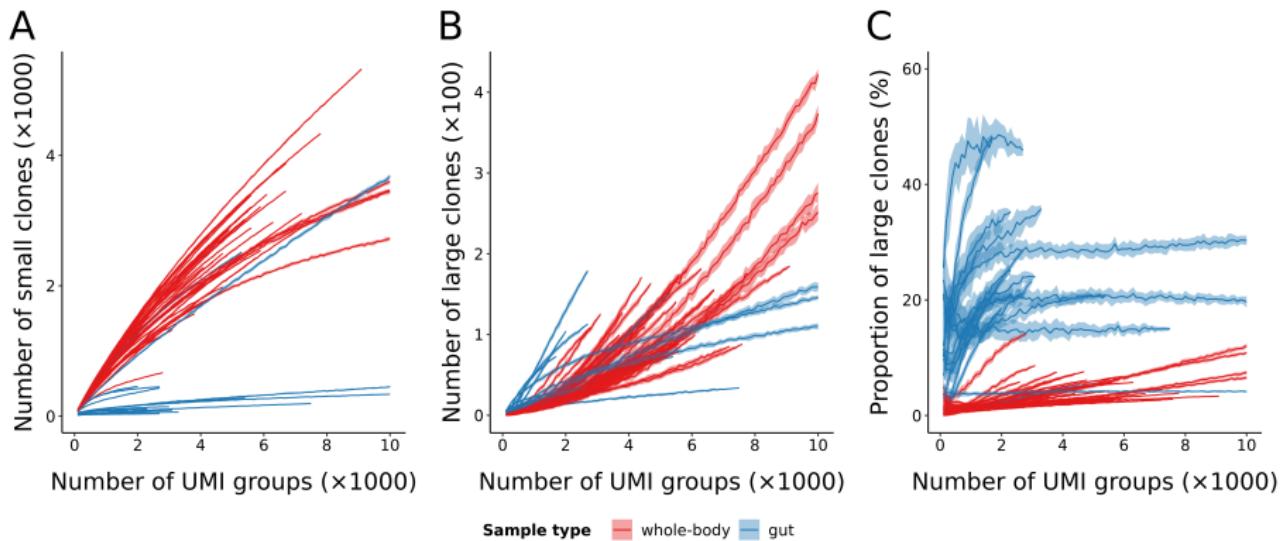
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2. Difference in **clonal composition**?

- Whole body includes primary lymphoid organs, intestine does not
- → More small naïve clones in whole-body samples than gut samples
- Larger clones more age-sensitive → stronger age effect in gut samples

Killifish gut repertoires contain fewer **small** clones than whole-body repertoires



Summary II

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- Killifish intestinal samples show a much more dramatic decline in alpha-diversity with age than in the whole body
- Both gut and whole-body repertoires show an increase in beta-diversity with age

Acknowledgements

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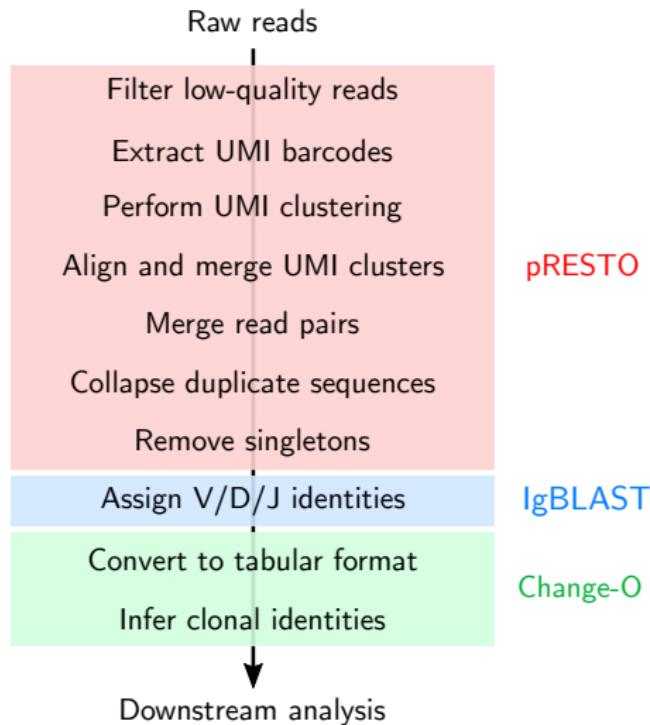


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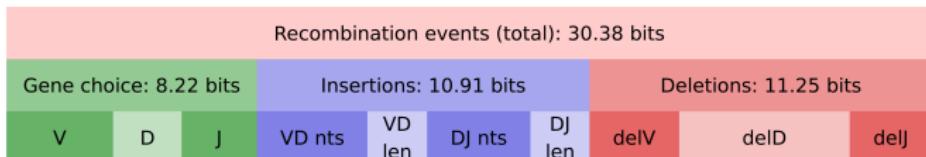
Thank you!

Bioinformatics pipeline

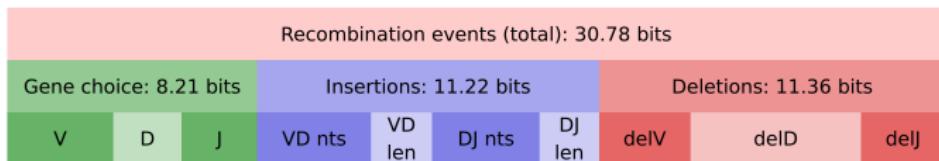


The generative entropy of the naïve antibody repertoire does not change with age

Age (days) = 39



Age (days) = 56



Age (days) = 73

