



11 Maggio 2022

Dall’Africa una formidabile macchina del tempo: Nothobranchius furzeri

Livia D’Angelo, DVM, Ph.D

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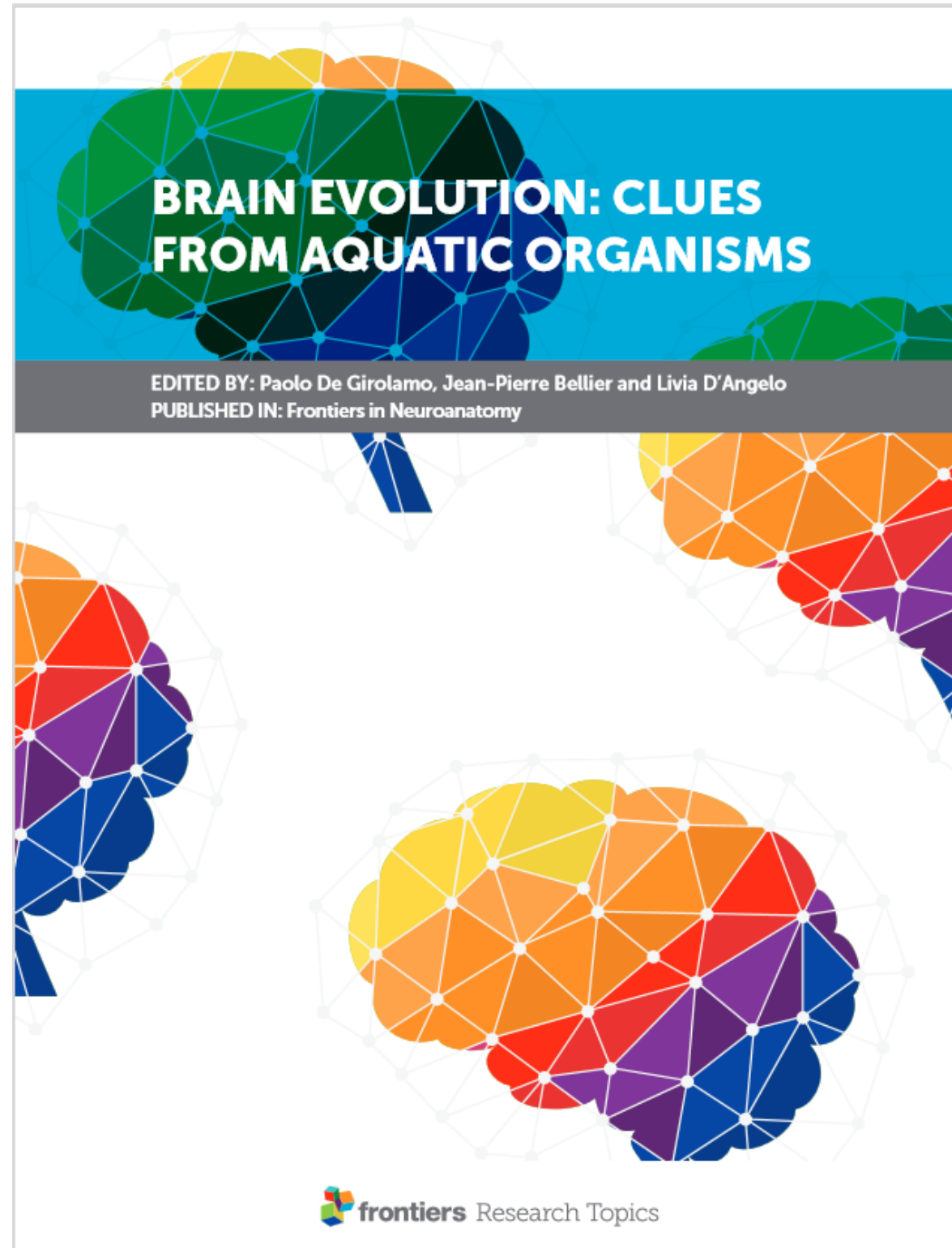
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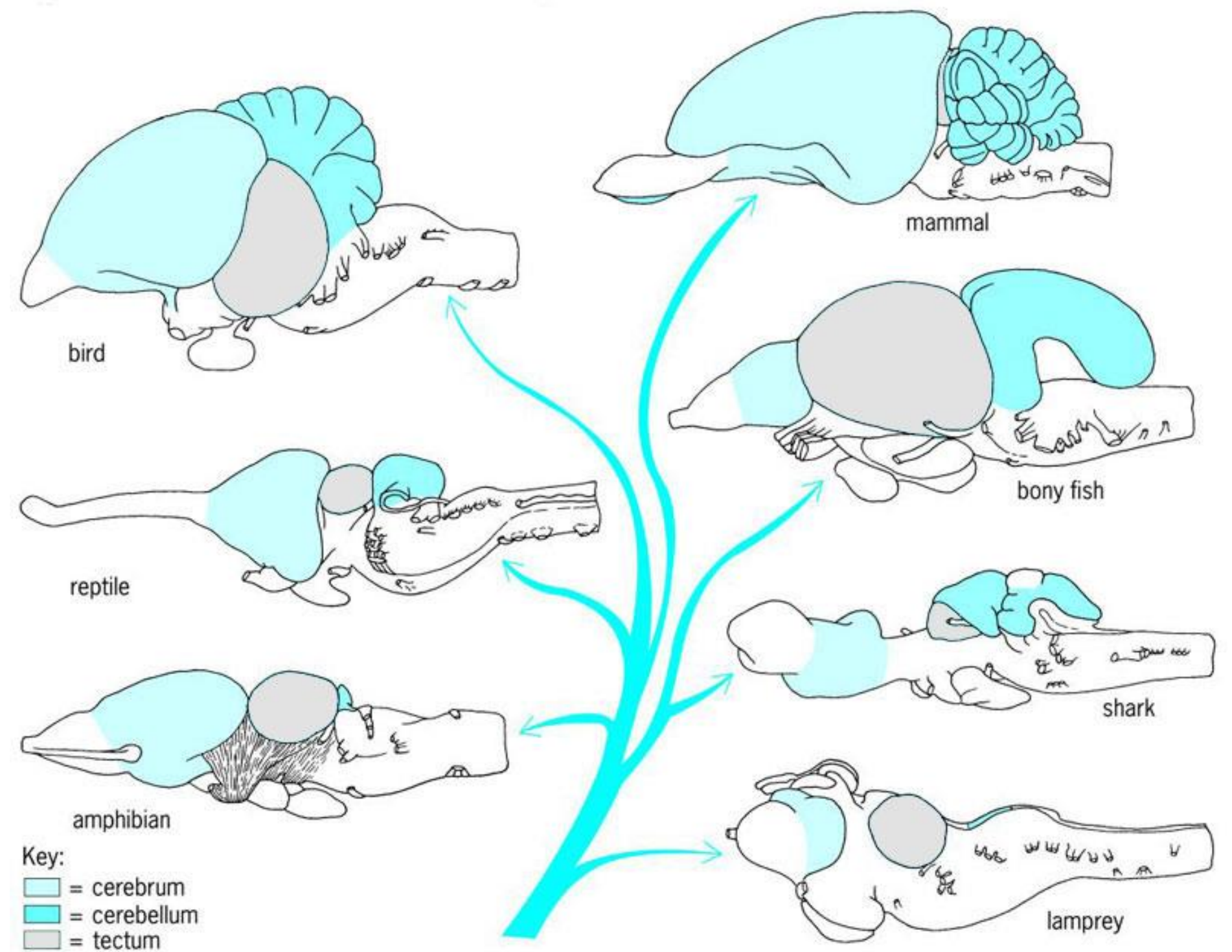
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**SCUOLA DI AGRARIA
E MEDICINA VETERINARIA**

Scientific Interest



Comparative Neuroanatomy

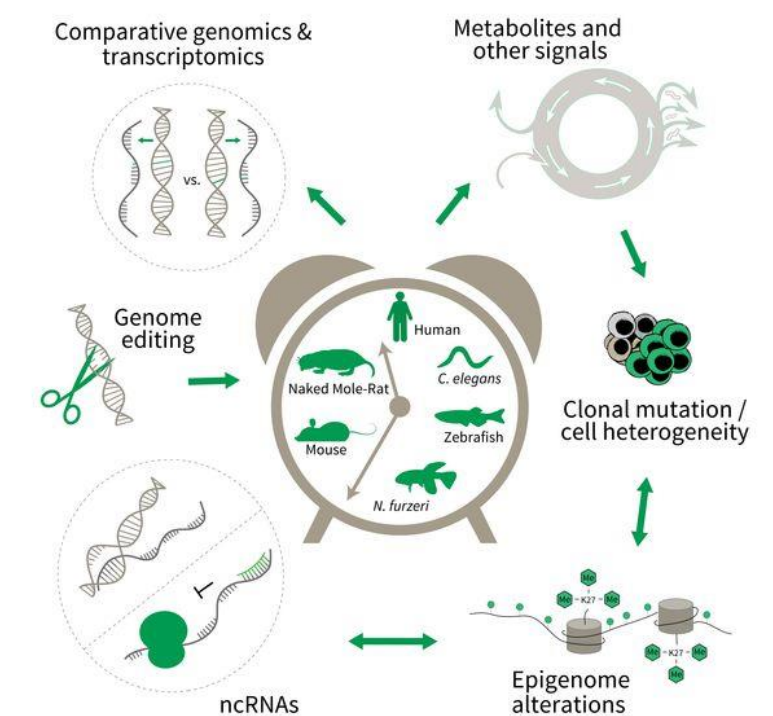


Ph.D «Model Organisms in Biomedical and Veterinary Research»

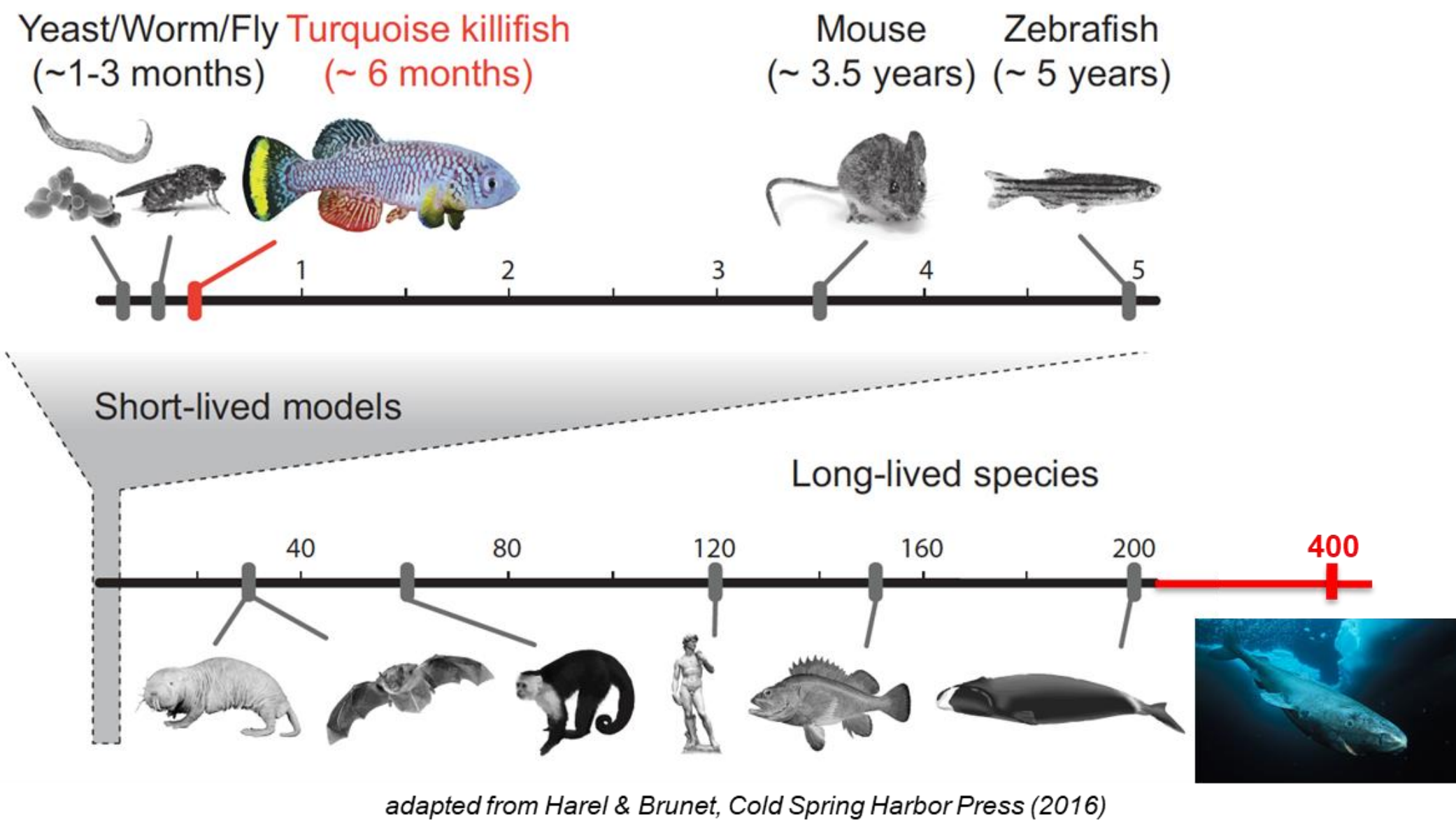


SCUOLA
NORMALE
SUPERIORE

Emerging teleost fish model in
ageing research,
focus on **neurobiology**



Short and long lived species



“

The reasons for some animals being long-lived and others short-lived, and, in a word, causes of the length and brevity of life call for investigation.

”

Aristotle,
On Longevity and Shortness of Life
(350 BC)

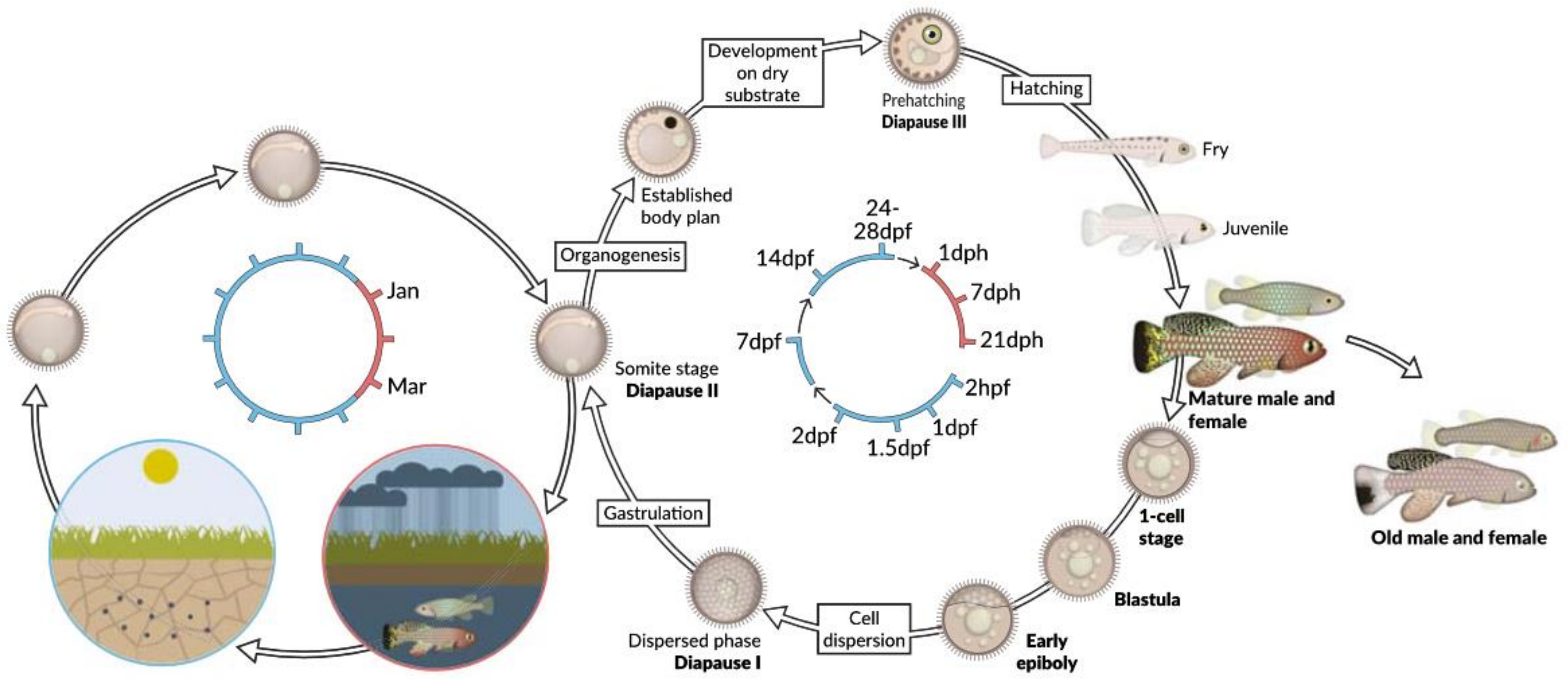


Features of turquoise killifish

Common life cycle in the wild
(Annual diapause trajectory: ~1 year)

Common life cycle in the lab
(Diapause skipping trajectory: ~6-8 weeks)

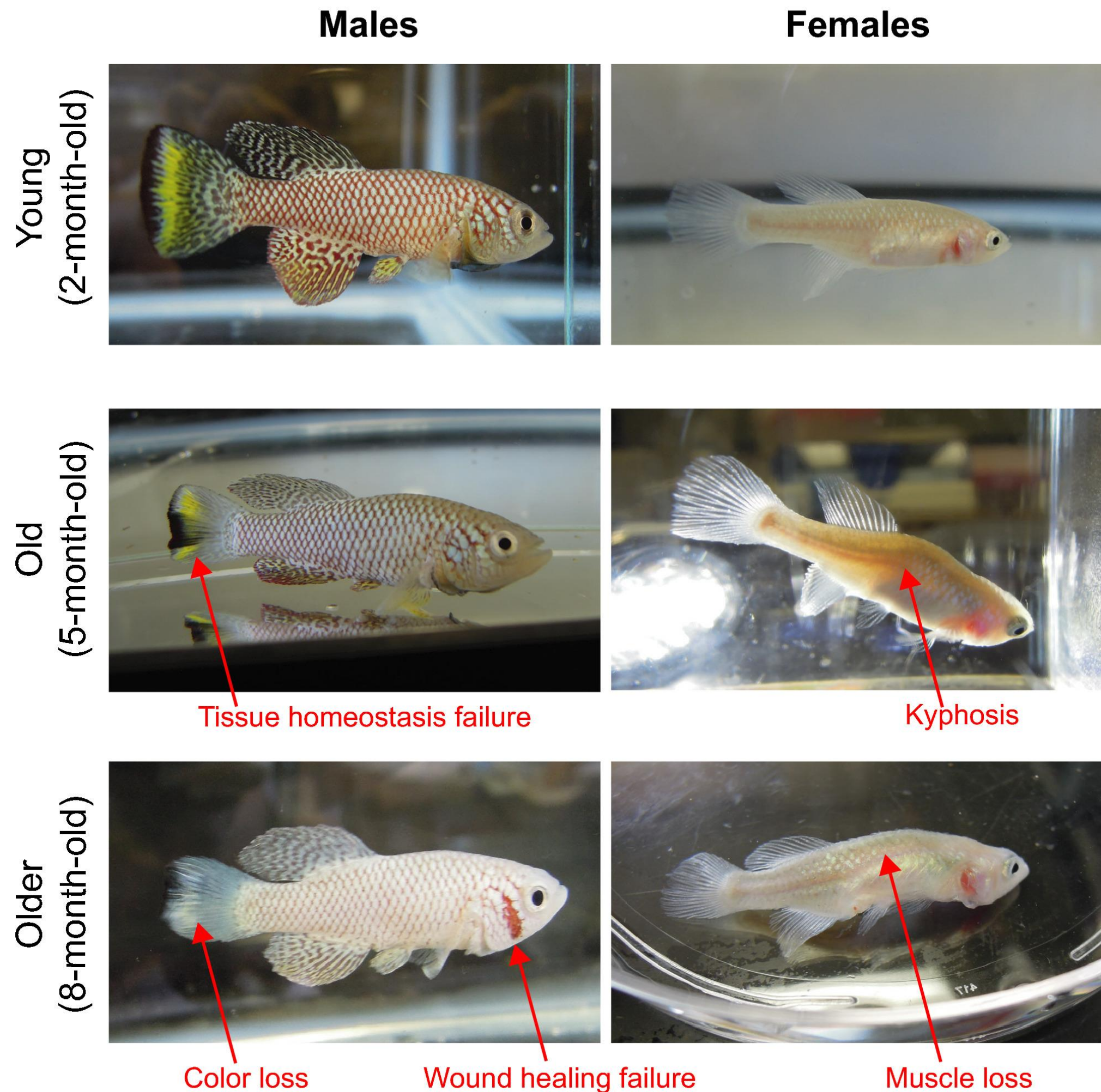
Common lifespan in the lab
(~4-6 months)



Astre et al. in *Laboratory Fish in Biomedical Research*, D'Angelo and de Girolamo Editors, Elsevier 2021

Physiological ageing

- **increased frailty** and decline in organ and physiological functions
- **loss of color**
- **reduced muscle mass** (sarcopenia)
- **bending of the spine** (kyphosis)



Physiological ageing

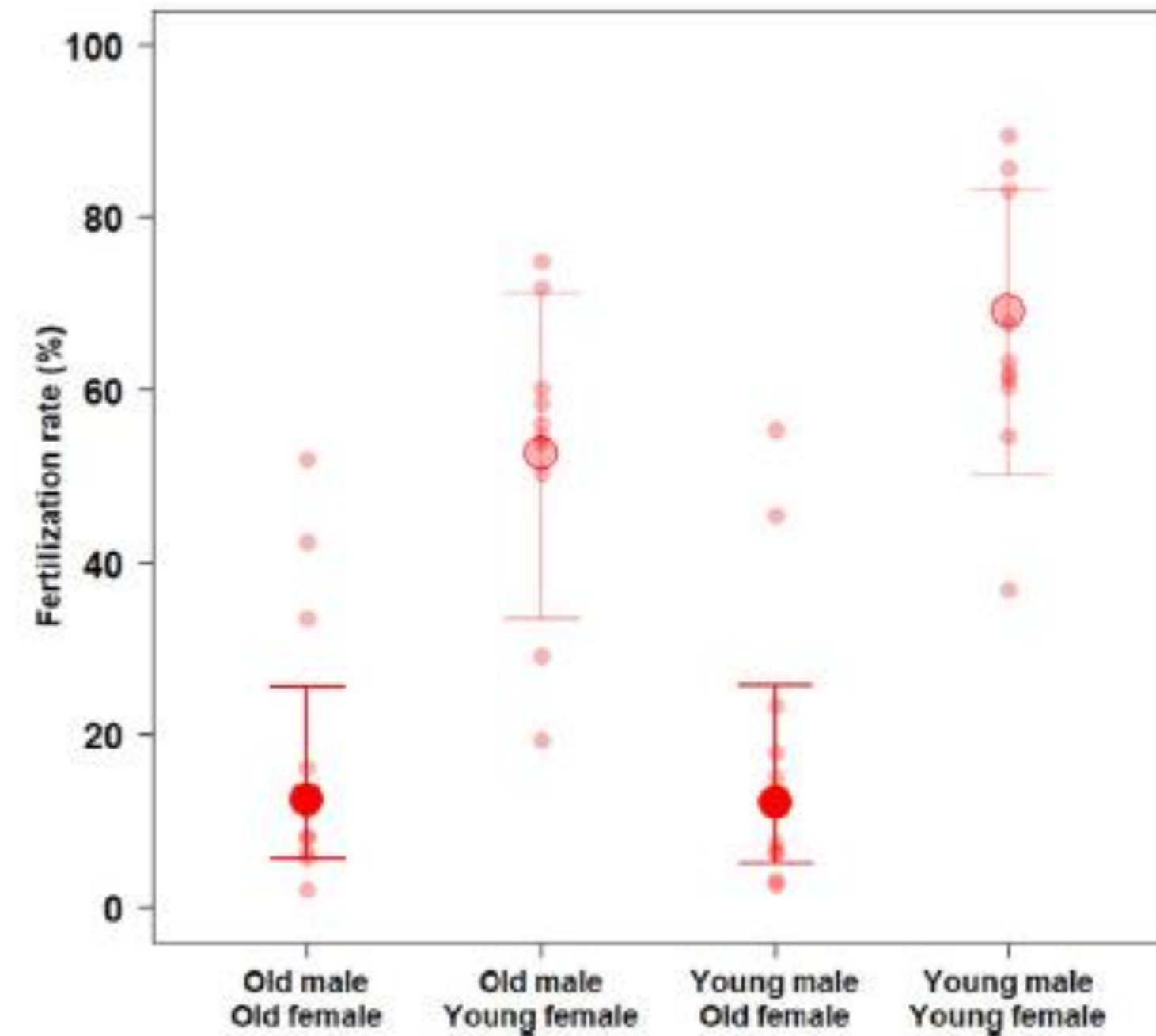
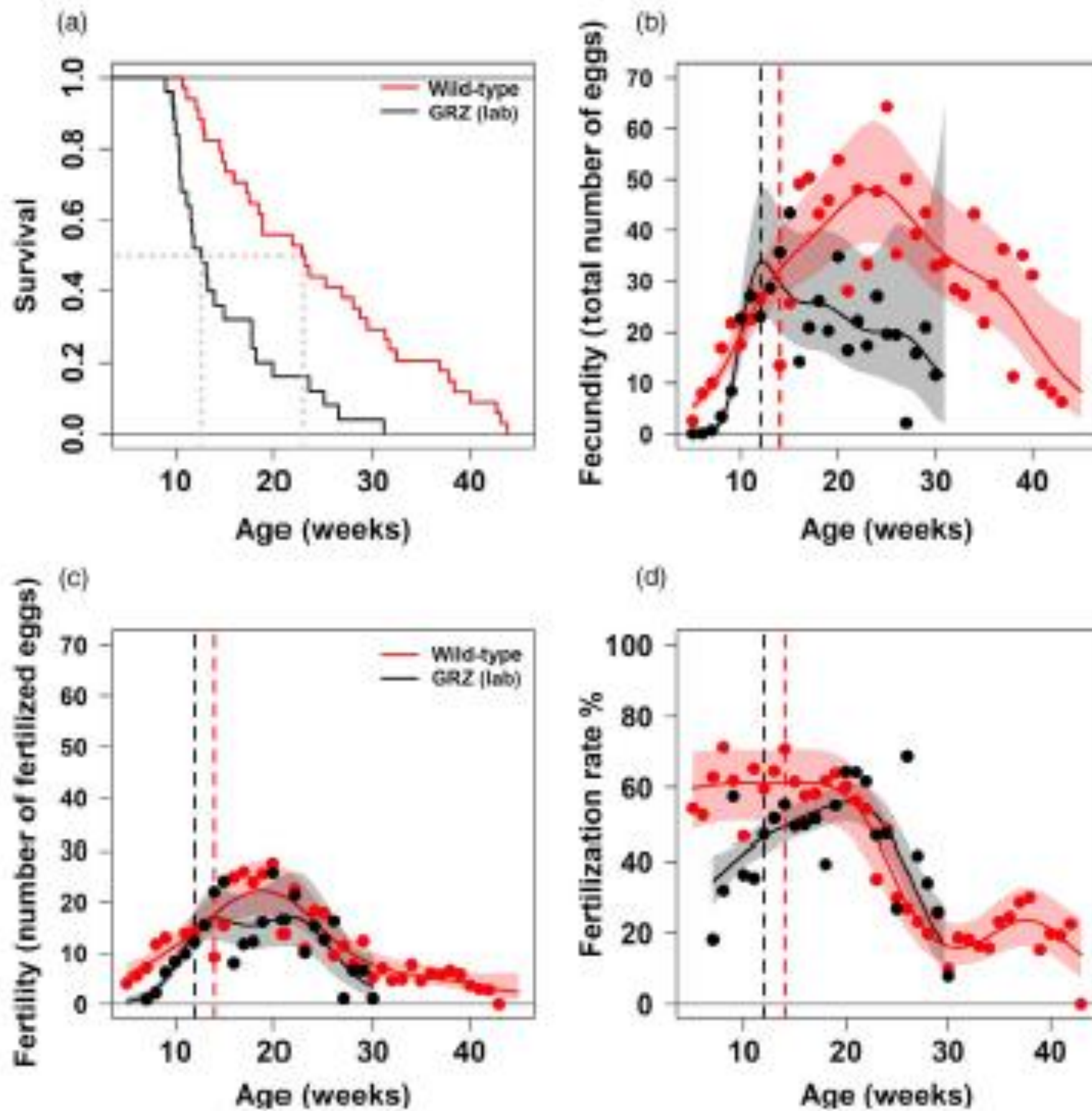
Received: 23 June 2020 | Accepted: 2 November 2020
DOI: 10.1111/1365-2656.13382

RESEARCH ARTICLE

Journal of Animal Ecology 

Reproductive senescence in a short-lived fish

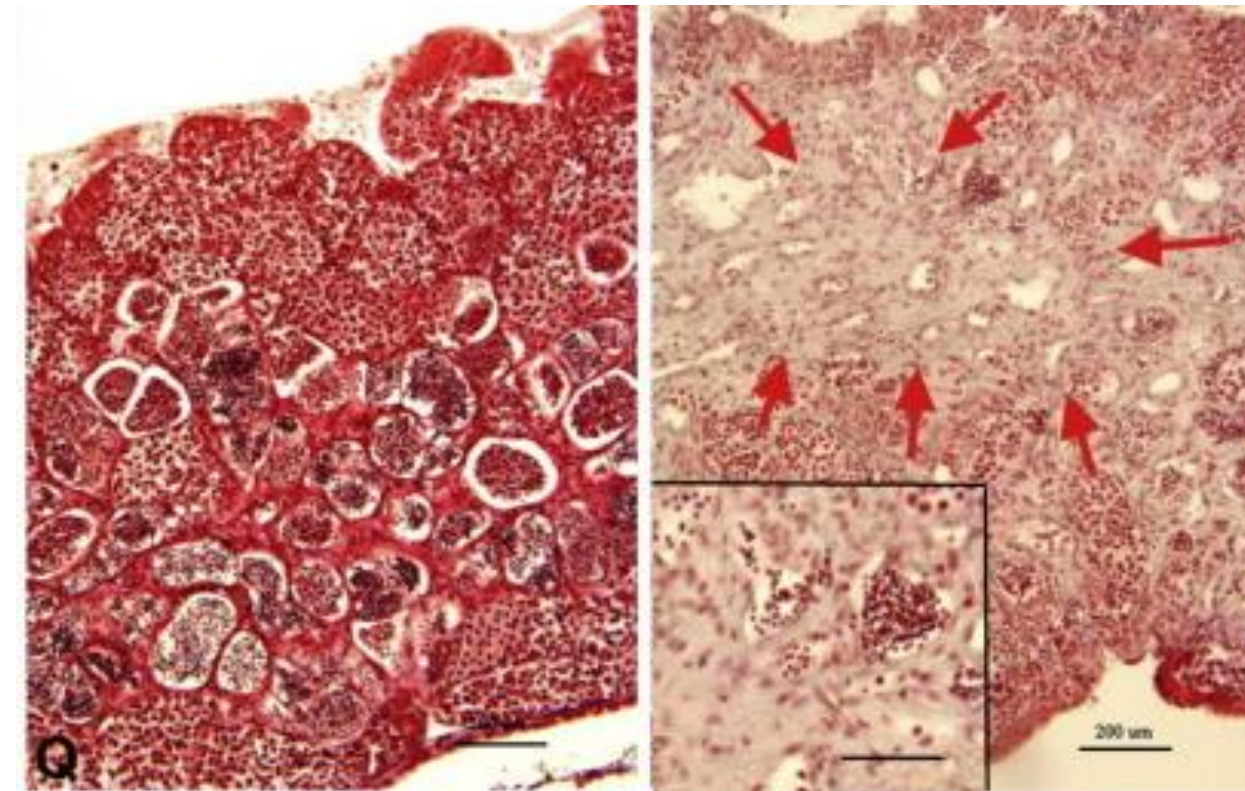
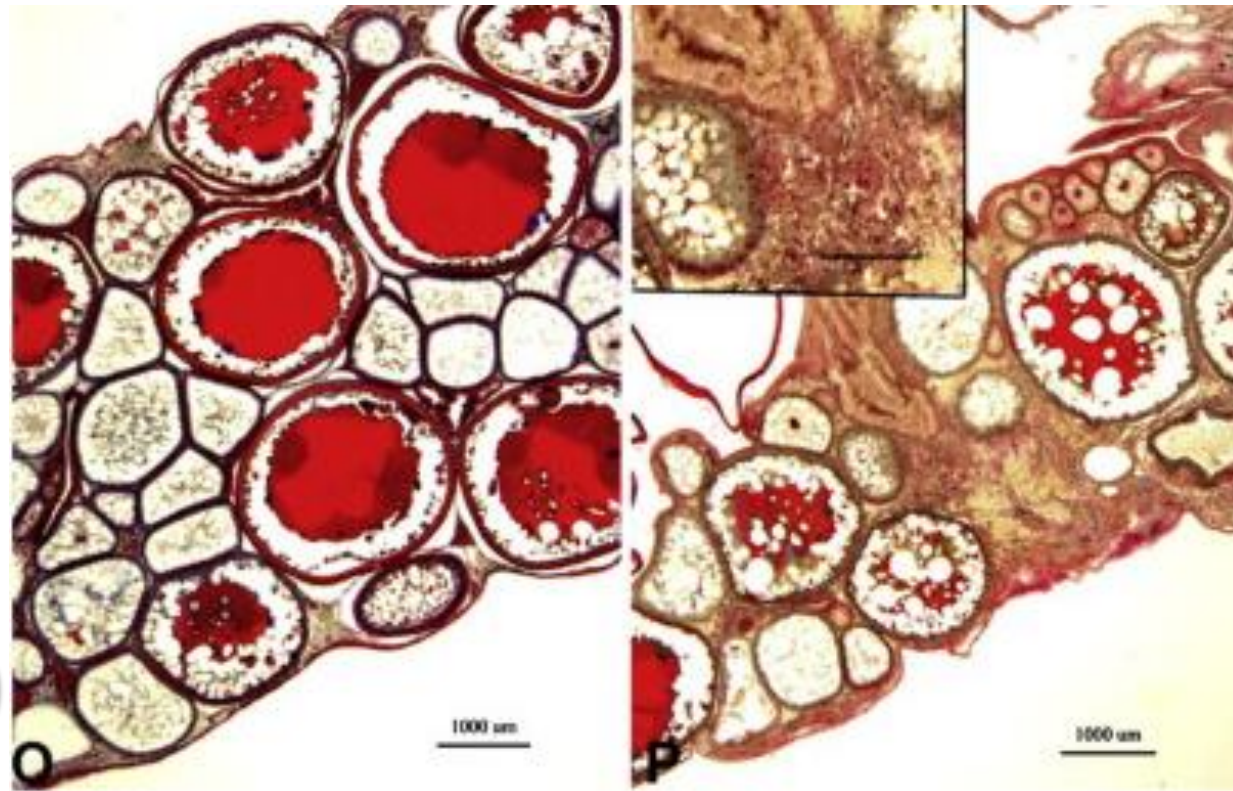
Jakub Žák^{1,2}  | Martin Reichard^{1,3} 



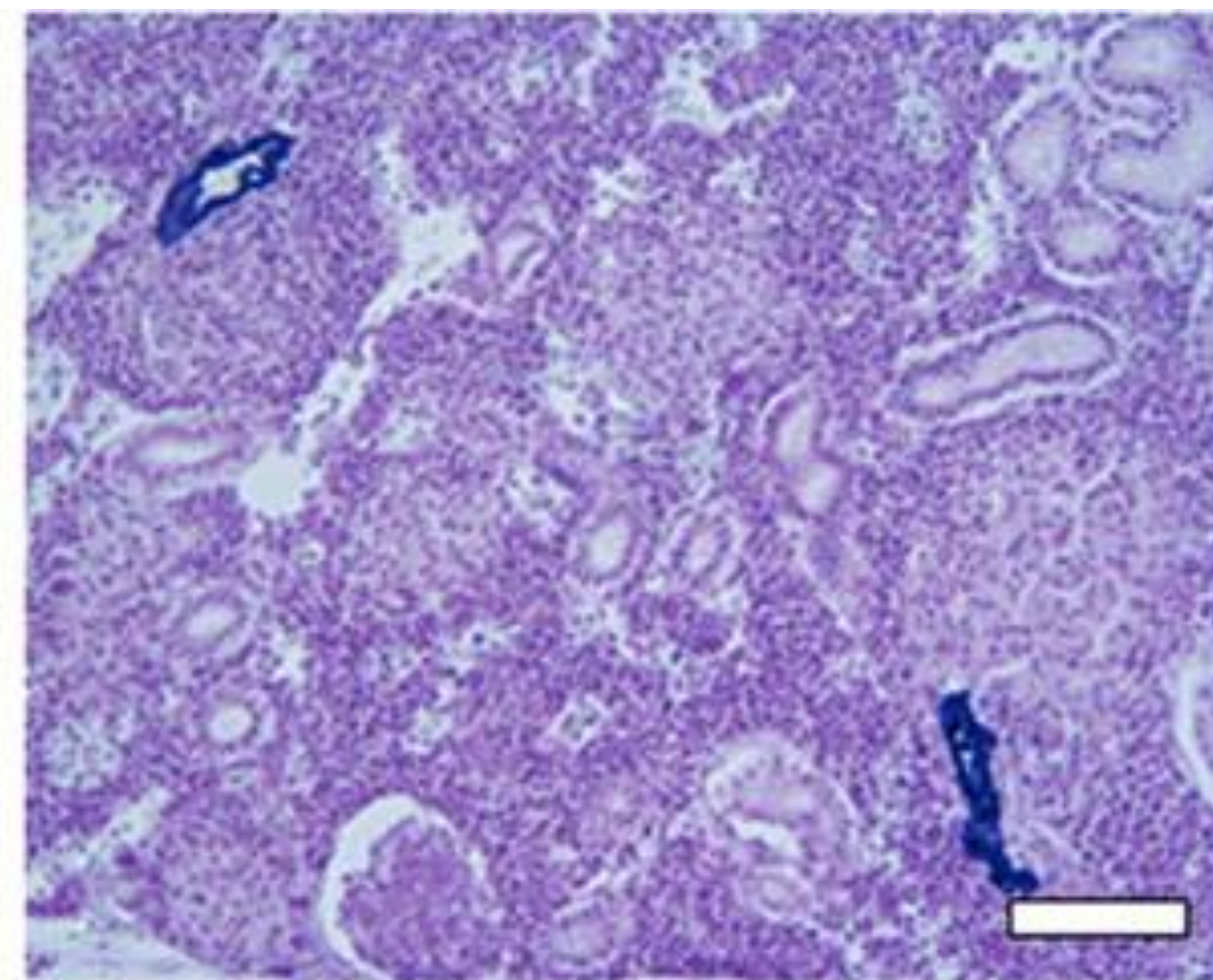
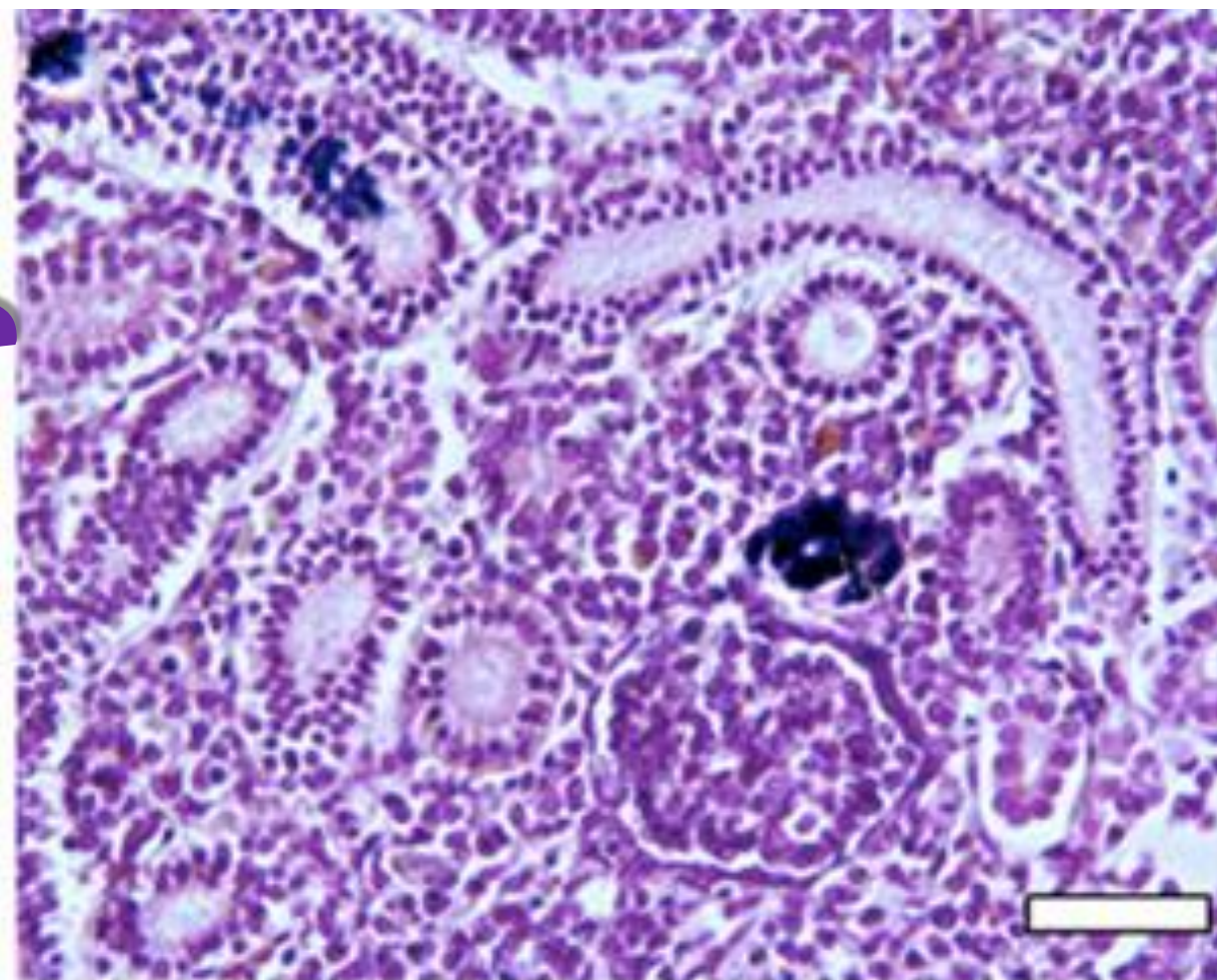
Ageing biomarkers

Degenerative lesions observed post mortem:

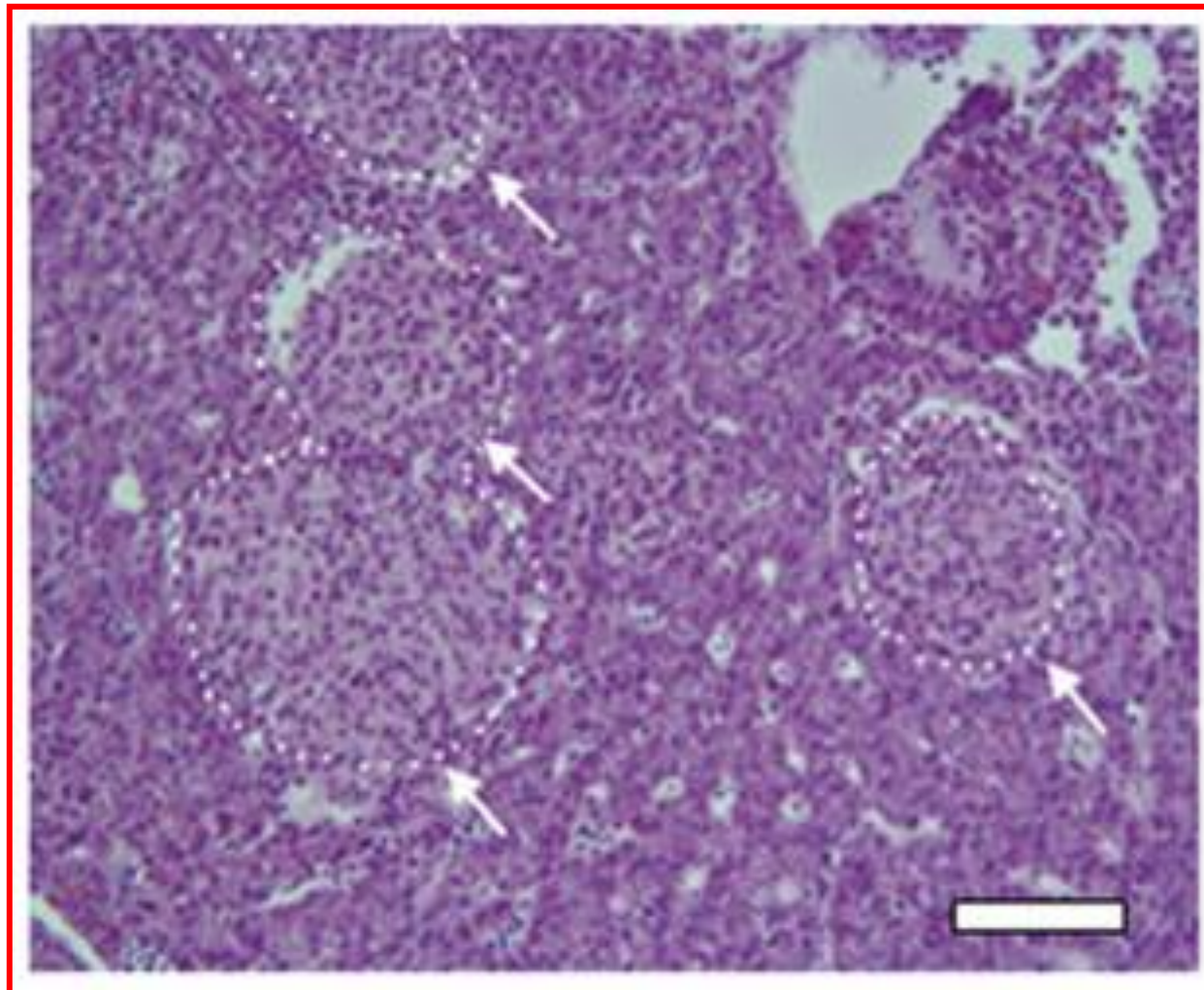
gonads



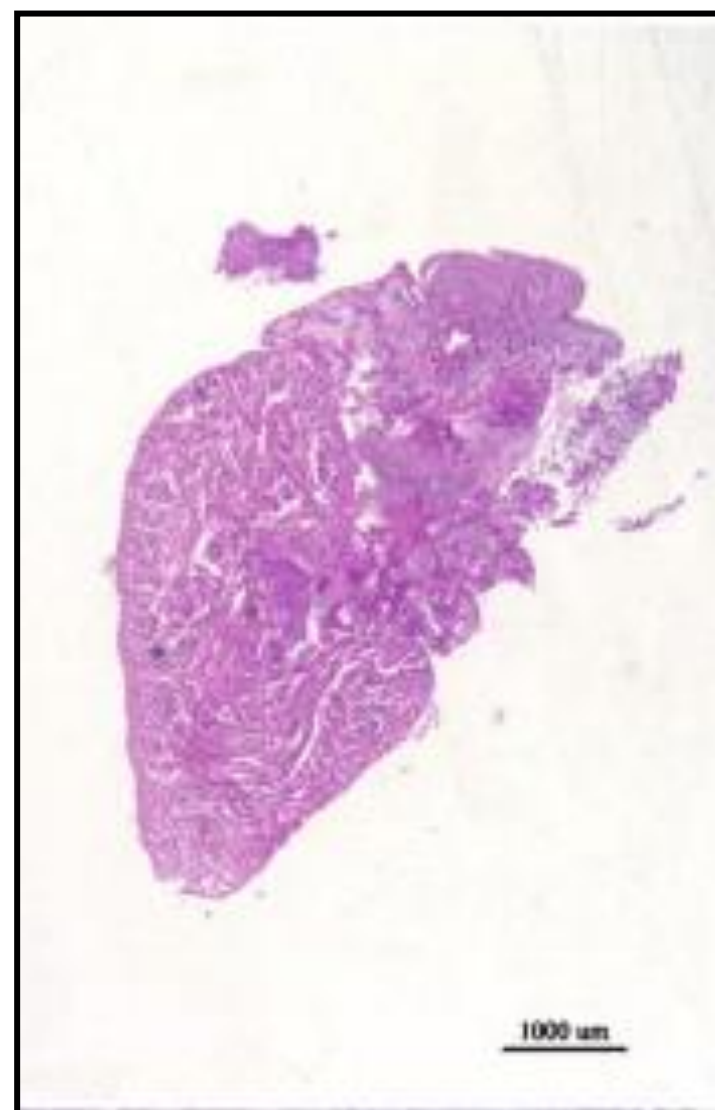
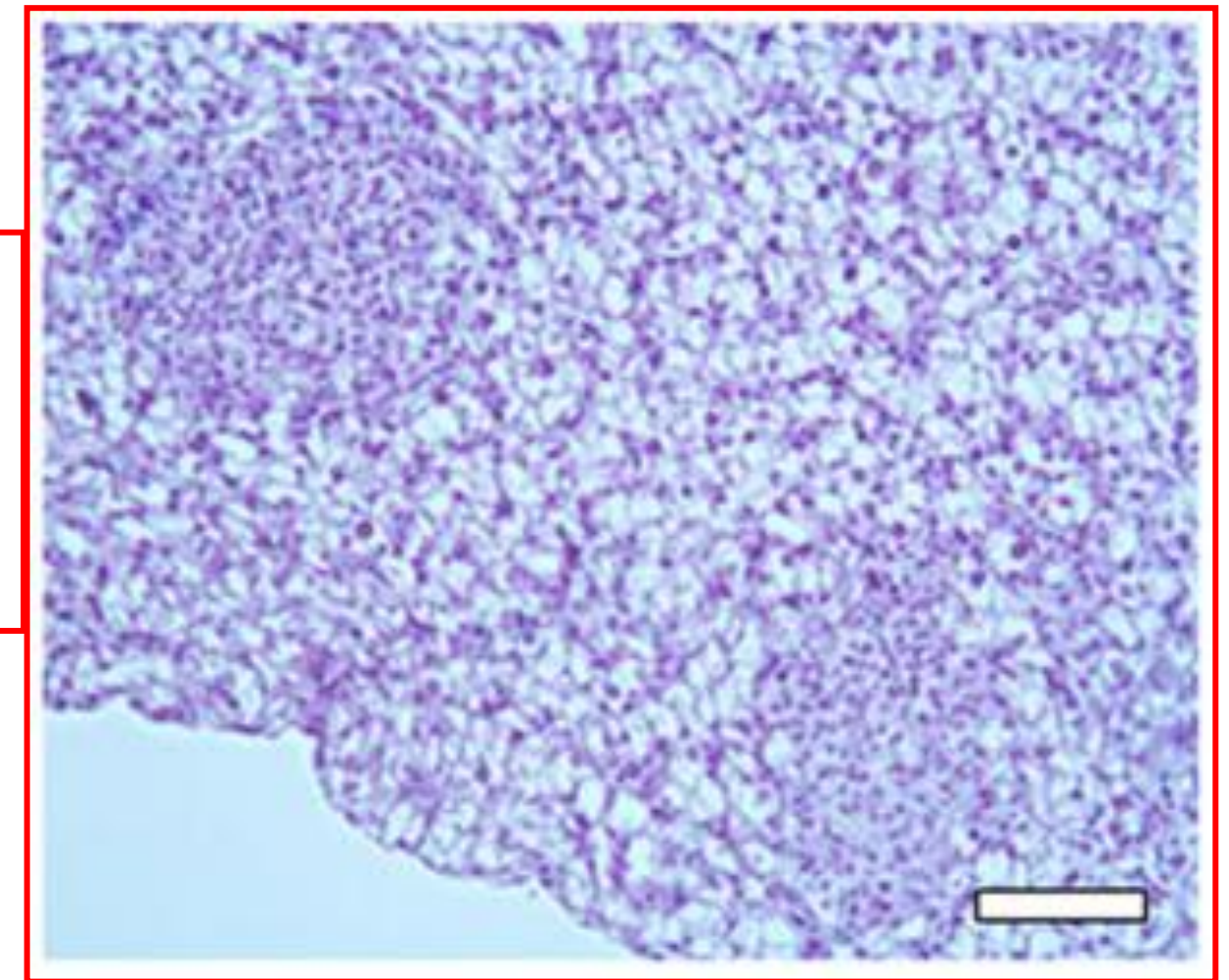
kidney



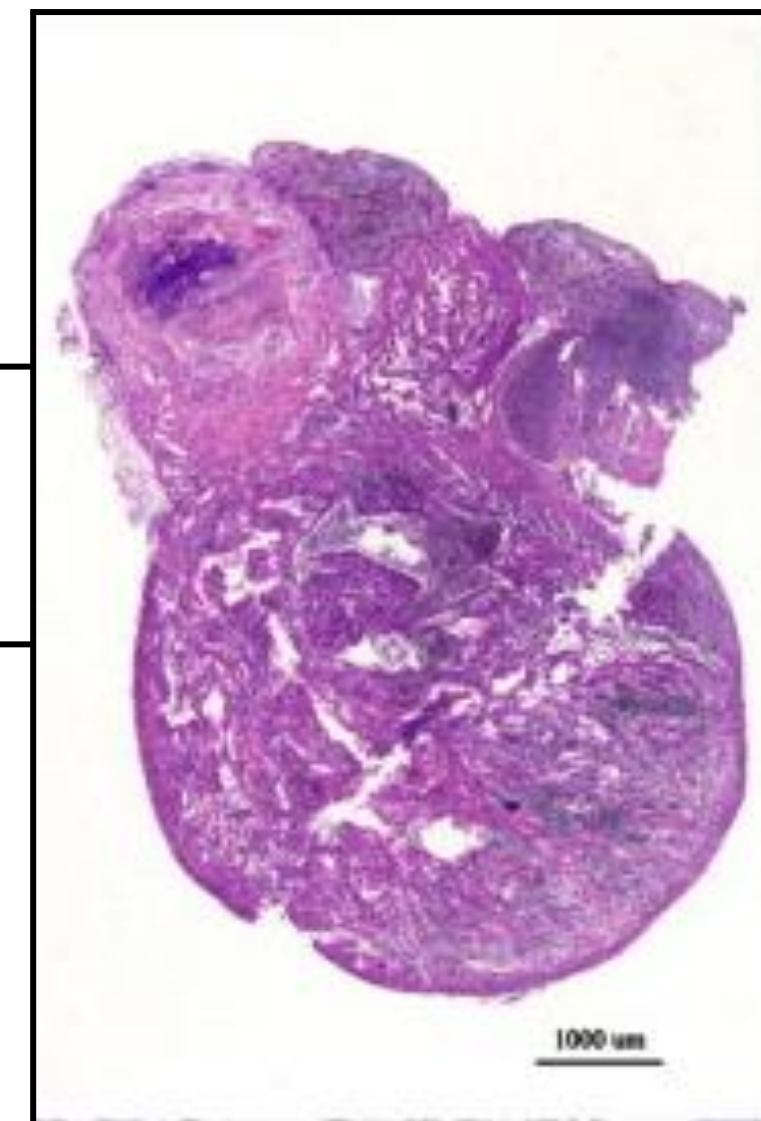
Ageing biomarkers



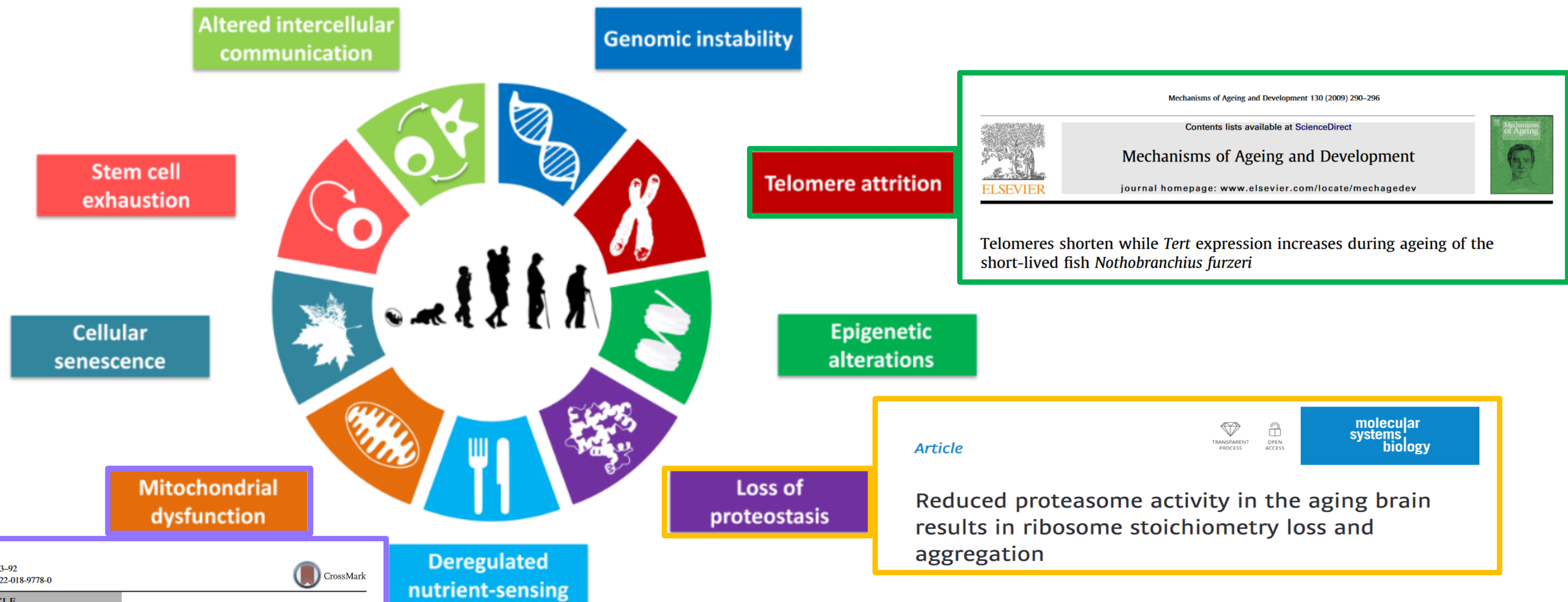
progressive
liver degeneration
up to steatosis



cardiac
hypertrophy



Several hallmarks of ageing have been investigated in turquoise killifish

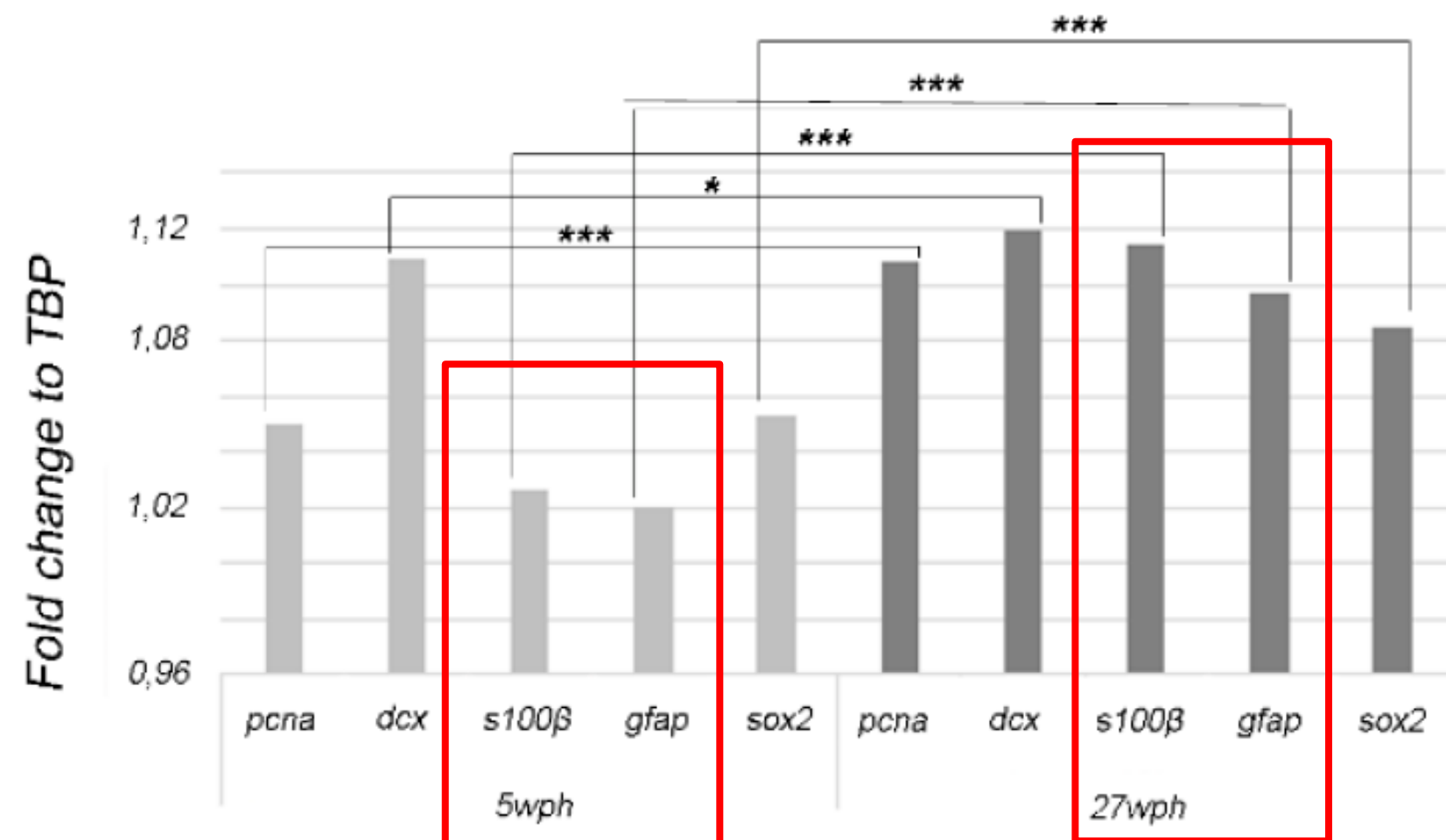
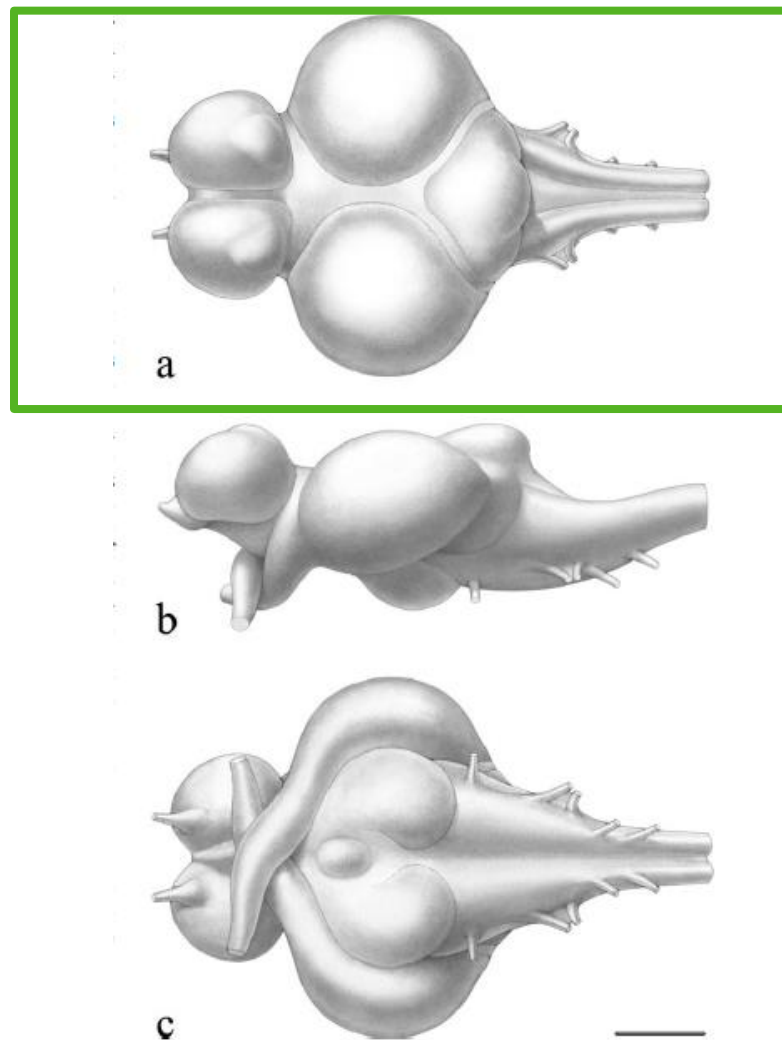


López-Otín et al., Cell. 2013

Brain Atlas of an Emerging Teleostean Model: *Nothobranchius furzeri*

LIVIA D'ANGELO*

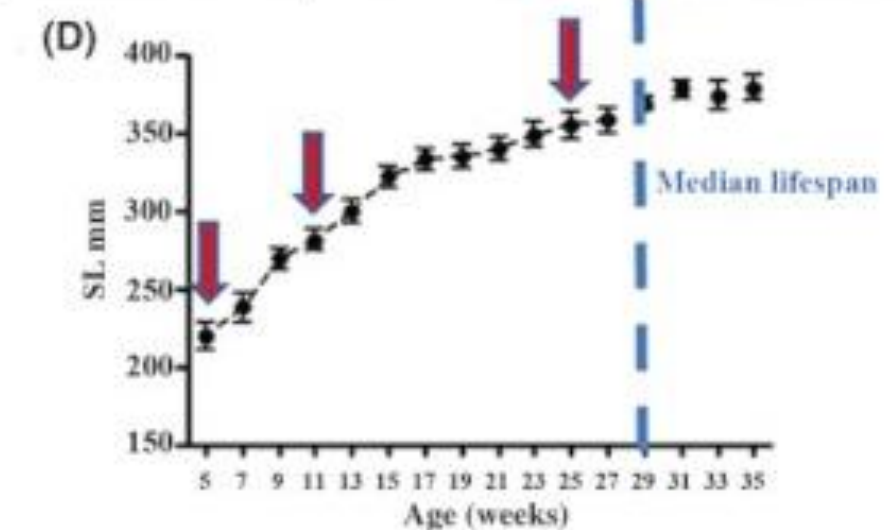
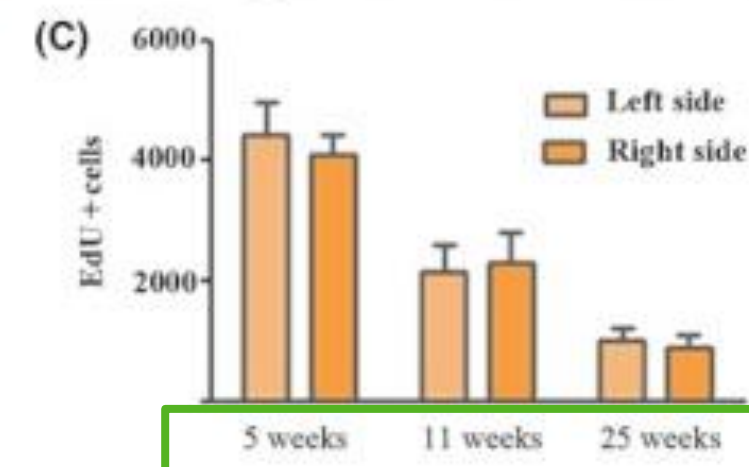
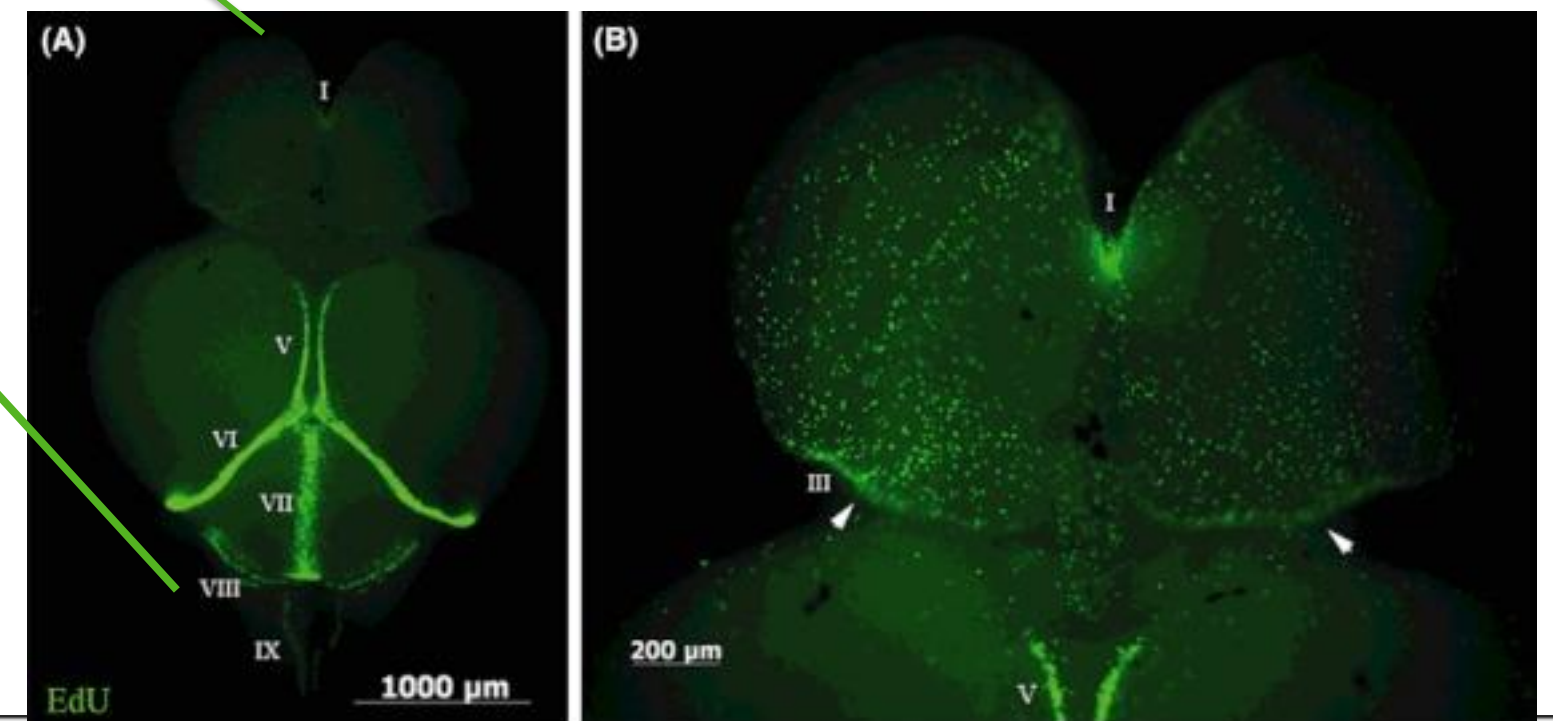
Department of Veterinary Medicine and Animal Productions, University of Naples Federico II, Italy



Leggieri et al, IJMS (2022)

Key morphological hallmarks of ageing

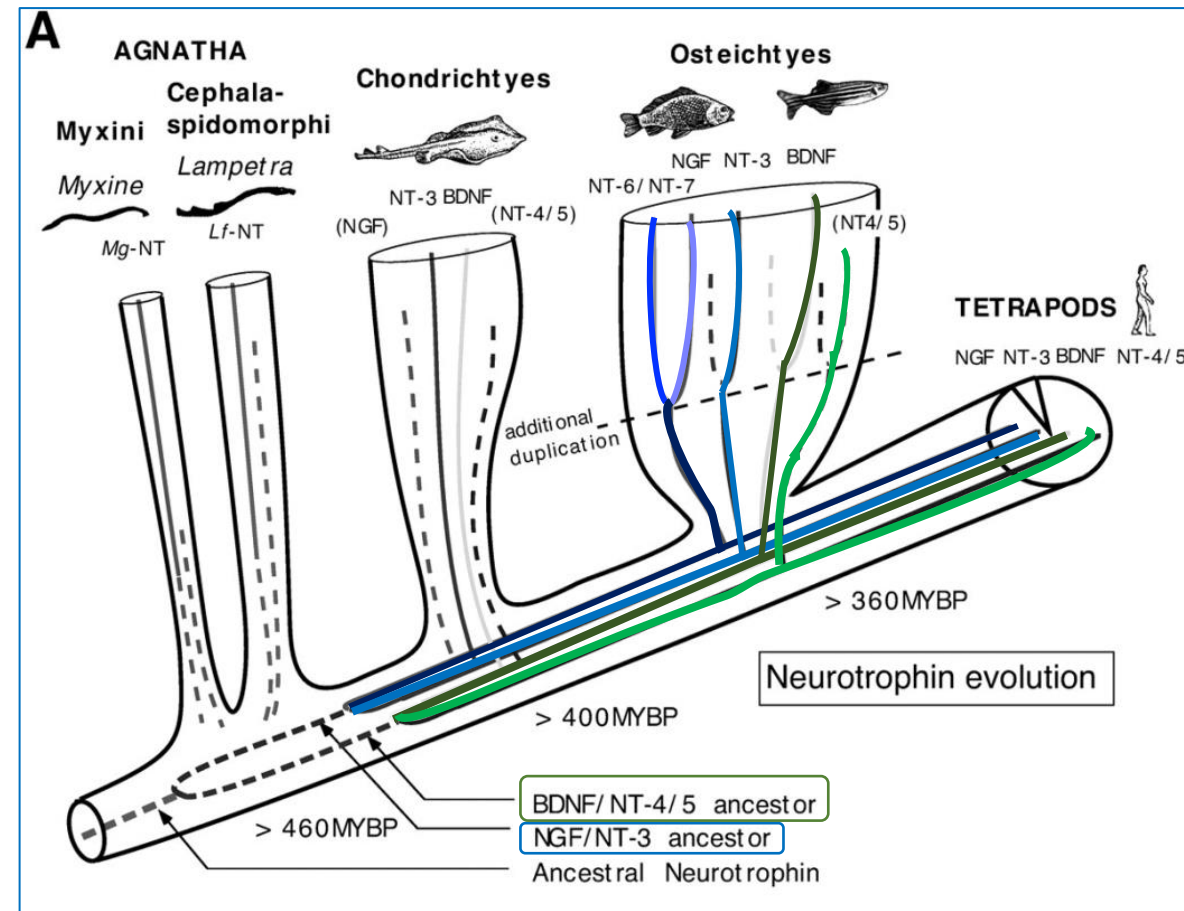
- age-related reduced mitotic activity of the neuronal progenitors
- up-regulation of GFAP, hallmark of gliosis
- neurodegeneration – measured by Fluoro-Jade B, which stains cell bodies, dendrites and axons of degenerating neurons
- accumulation of lipofuscin in the brain



Tozzini et al, Aging Cell (2012)

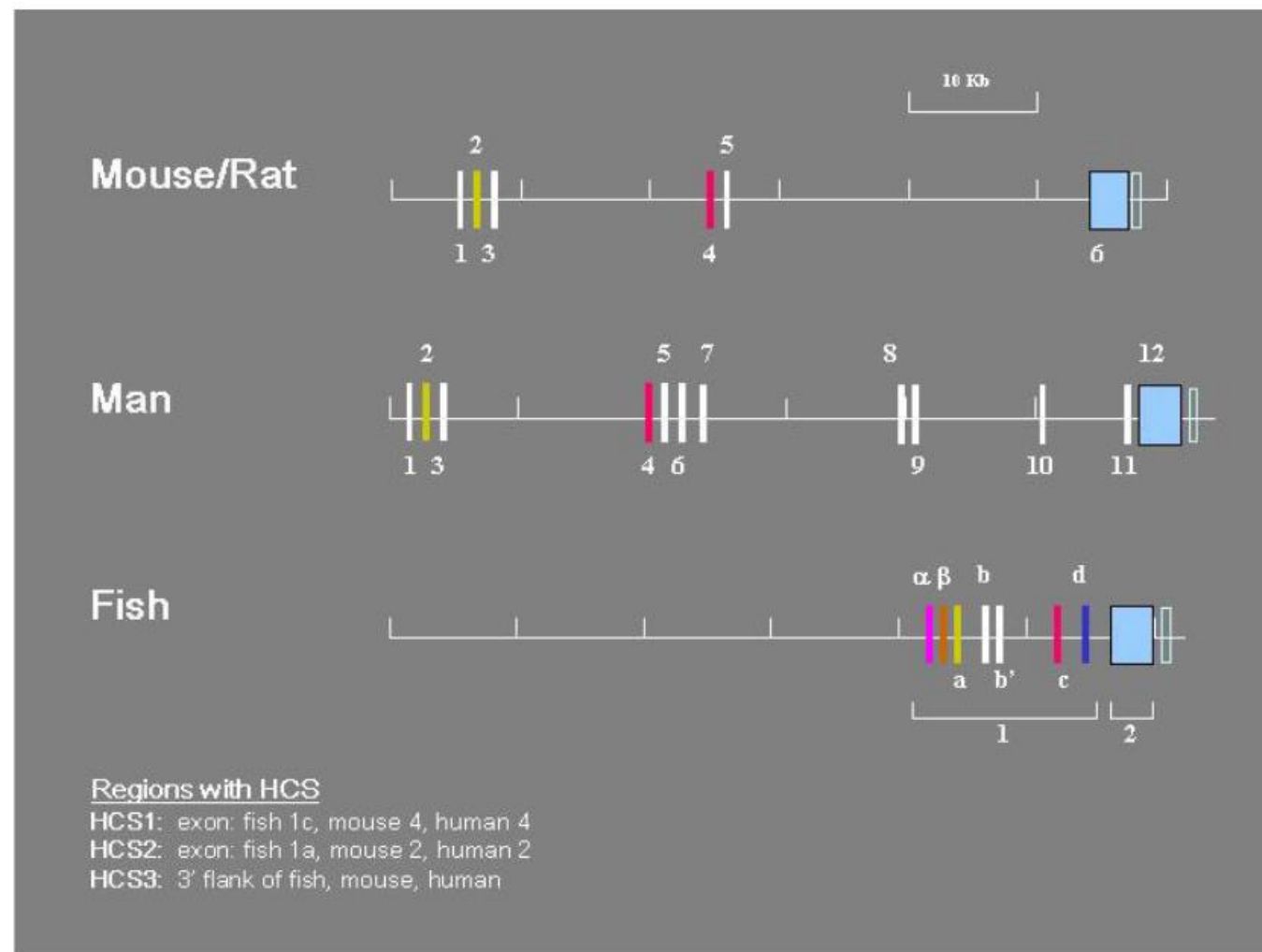
(A)

Evolution of Neurotrophins



Modified from Hallbook, *Curr Opin Neurobiol* 1999

Conserved *bdnf* exons structure

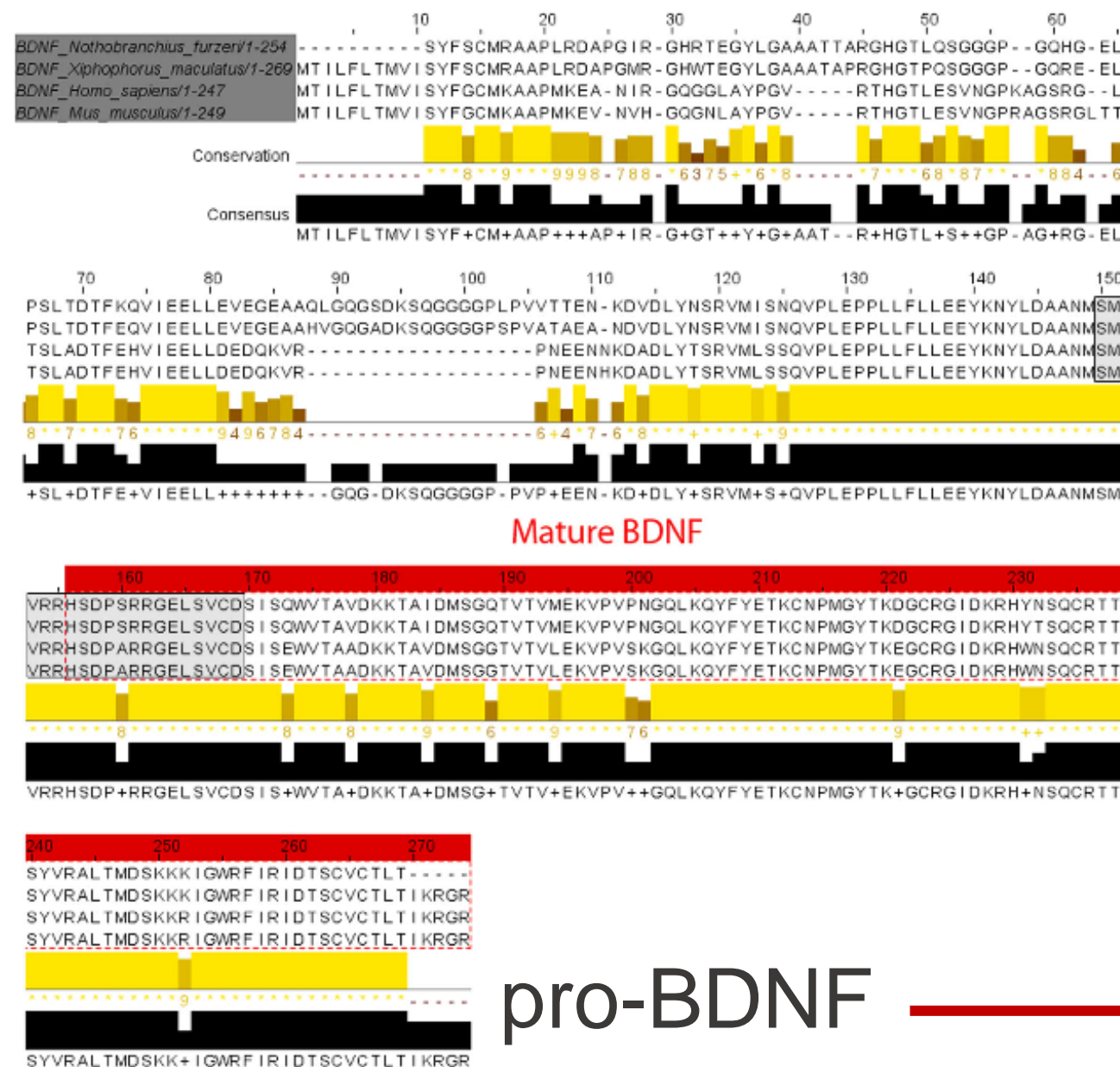


Heinrich and Pagtakhan, *BMC Neuroscience* (2004)

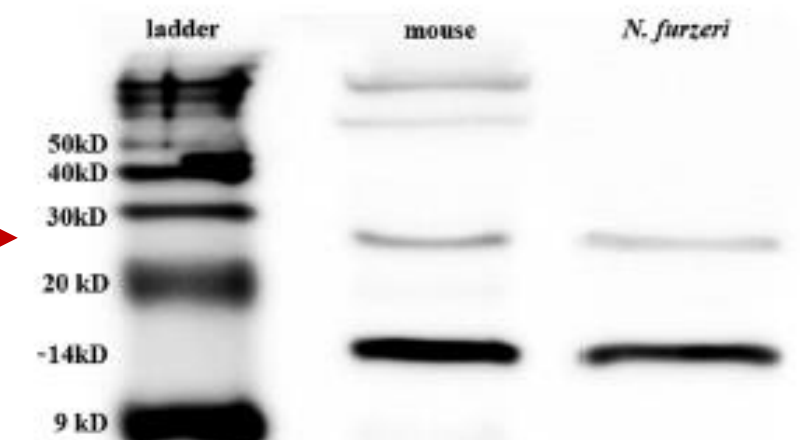
RESEARCH ARTICLE

Brain-Derived Neurotrophic Factor: mRNA Expression and Protein Distribution in the Brain of the Teleost *Nothobranchius furzeri*

Livia D'Angelo,^{1,2*} Paolo De Girolamo,¹ Carla Lucini,¹ Eva Tozzini Terzibasi,³ Mario Baumgart,² Luciana Castaldo,¹ and Alessandro Cellerino^{2,3}



pro-BDNF →
mature BDNF →

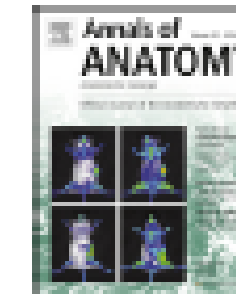




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Neurotrophin-4 in the brain of adult *Nothobranchius furzeri*

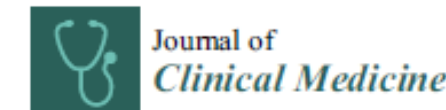
Annals of Anatomy 196 (2014) 183–191



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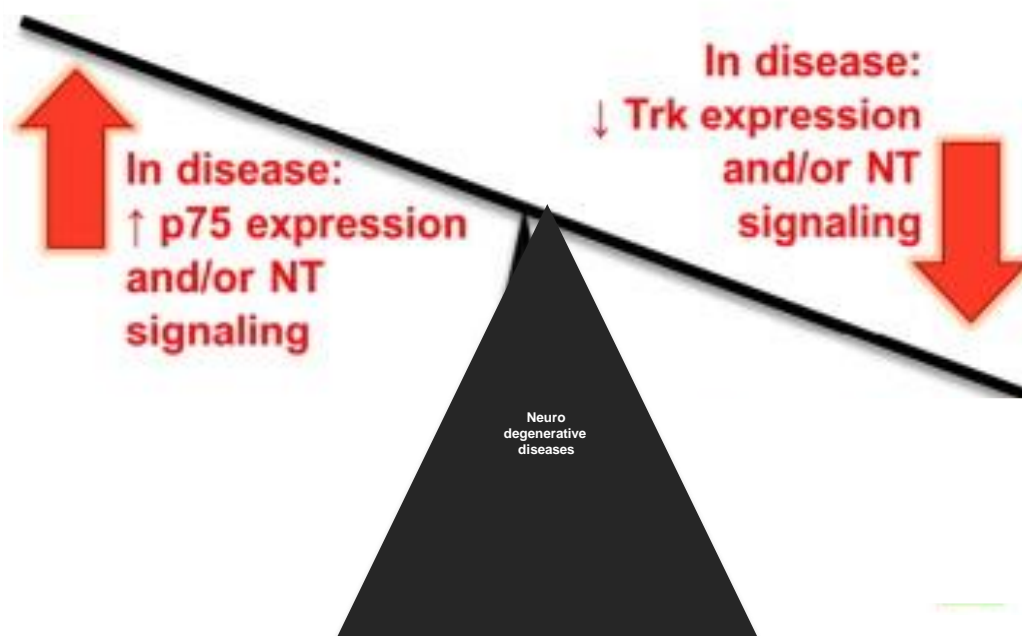
Nerve growth factor in the adult brain of a teleostean model for aging research: *Nothobranchius furzeri*



Article

Identification and Expression of Neurotrophin-6 in the Brain of *Nothobranchius furzeri*: One More Piece in Neurotrophin Research

Adele Leggieri ^{1,*}, Chiara Attanasio ^{1,2,3,4}, Antonio Palladino ², Alessandro Cellerino ^{4,5}, Carla Lucini ¹, Marina Paolucci ⁶, Eva Terzibaszi Tozzini ⁴, Paolo de Girolamo ¹ and Livia D'Angelo ^{1,7,*}



adapted by Josephy-Hernandez et al., *Neurobiology of disease* (2017)

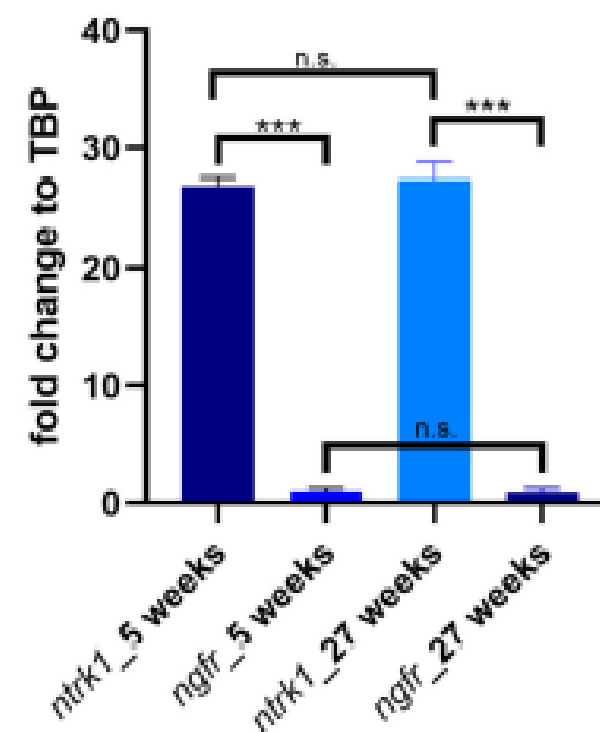


Article

Cholinergic System and NGF Receptors: Insights from the Brain of the Short-Lived Fish *Nothobranchius furzeri*

Paolo de Girolamo ^{1,*}, Adele Leggieri ¹, Antonio Palladino ², Carla Lucini ¹, Chiara Attanasio ¹ and Livia D'Angelo ¹

NGF receptors in the brain of *N. furzeri*



Neurotrophins in the Brain of Teleost Fish: The State of the Art

20

Paolo de Girolamo and Livia D'Angelo

Advances in experimental medicine and biology, Springer Nature (2021)

Experimental modulation of lifespan



RESEARCH ARTICLE



Regulation of life span by the gut microbiota in the short-lived African turquoise killifish

Patrick Smith^{1†}, David Willemsen^{1†}, Miriam Popkes^{1†}, Franziska Metge¹, Edson Gandiwa², Martin Reichard³, Dario Riccardo Valenzano^{1,4*}

Current Biology 16, 296–300, February 7, 2006 ©2006 Elsevier Ltd All rights reserved DOI 10.1016/j.cub.2005.12.038

Report

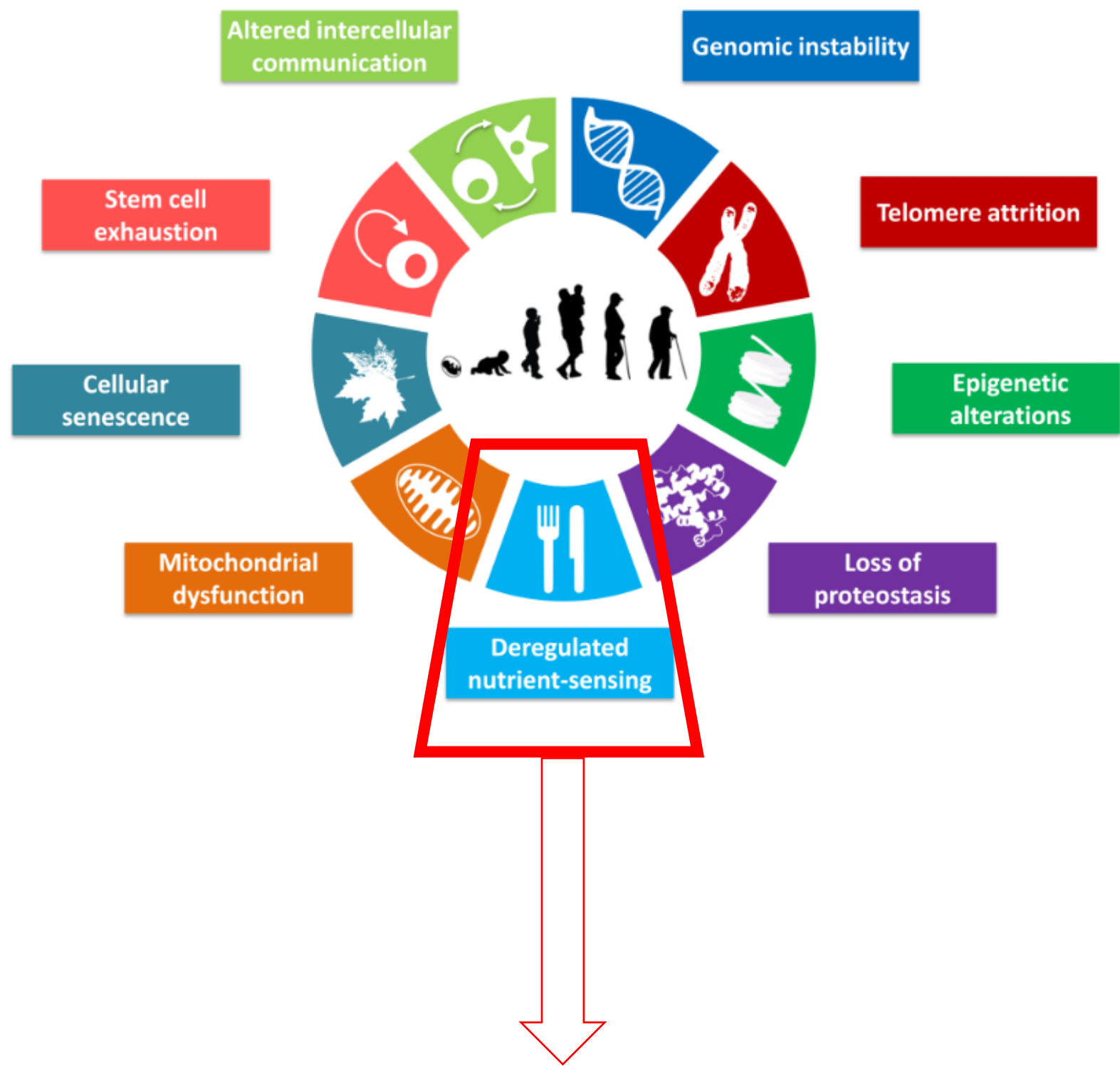
Resveratrol Prolongs Lifespan and Retards the Onset of Age-Related Markers in a Short-Lived Vertebrate



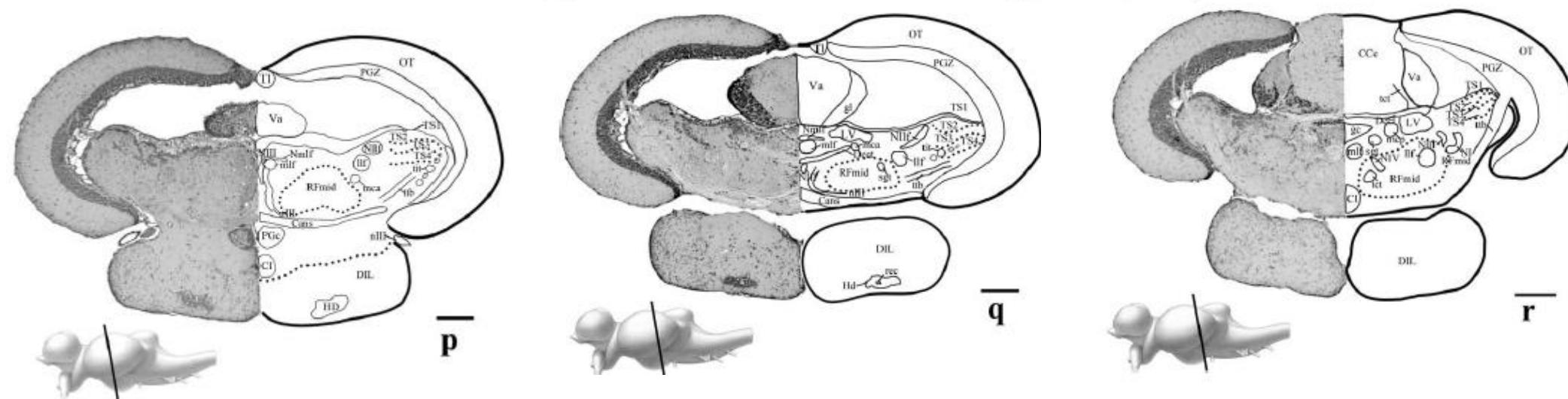
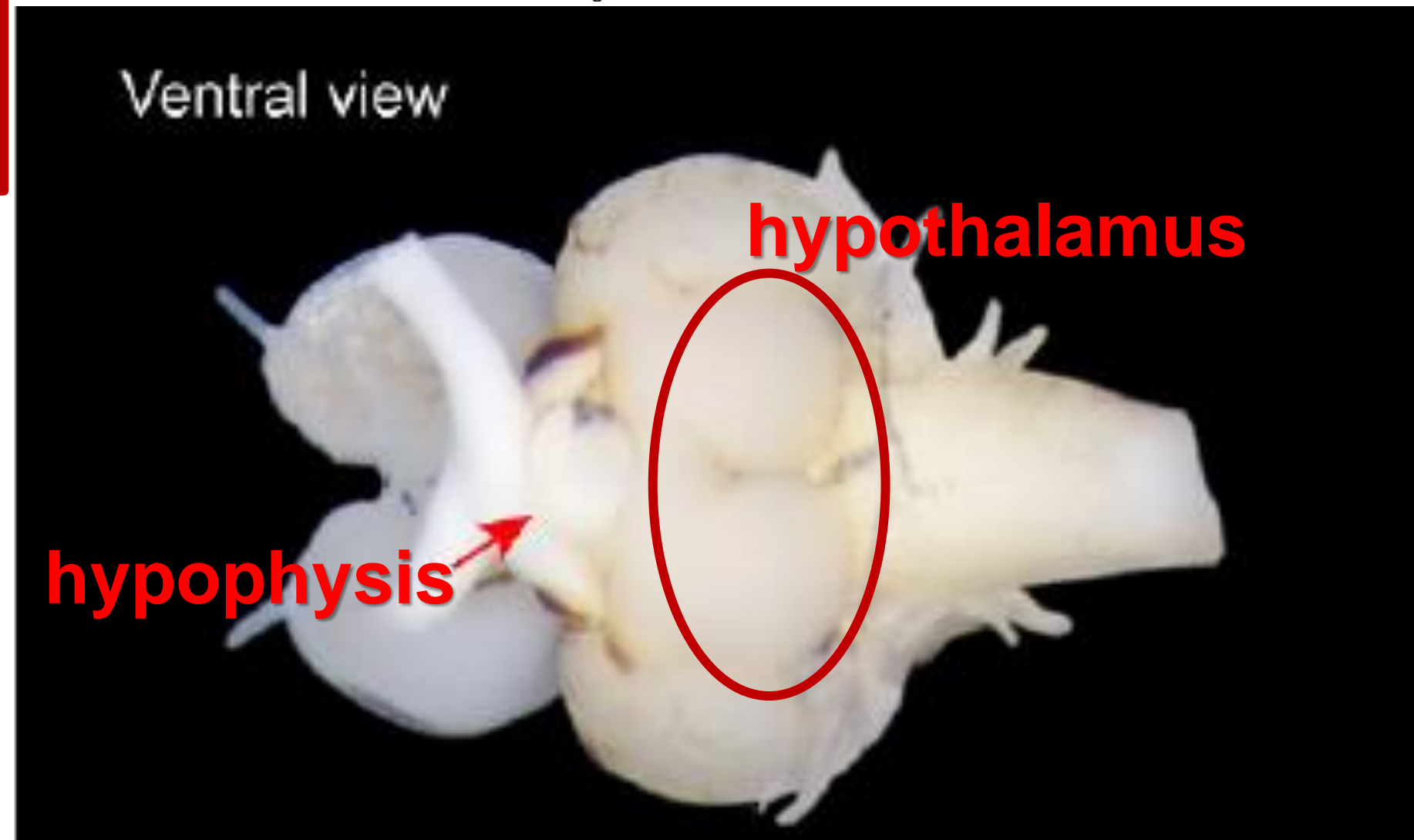
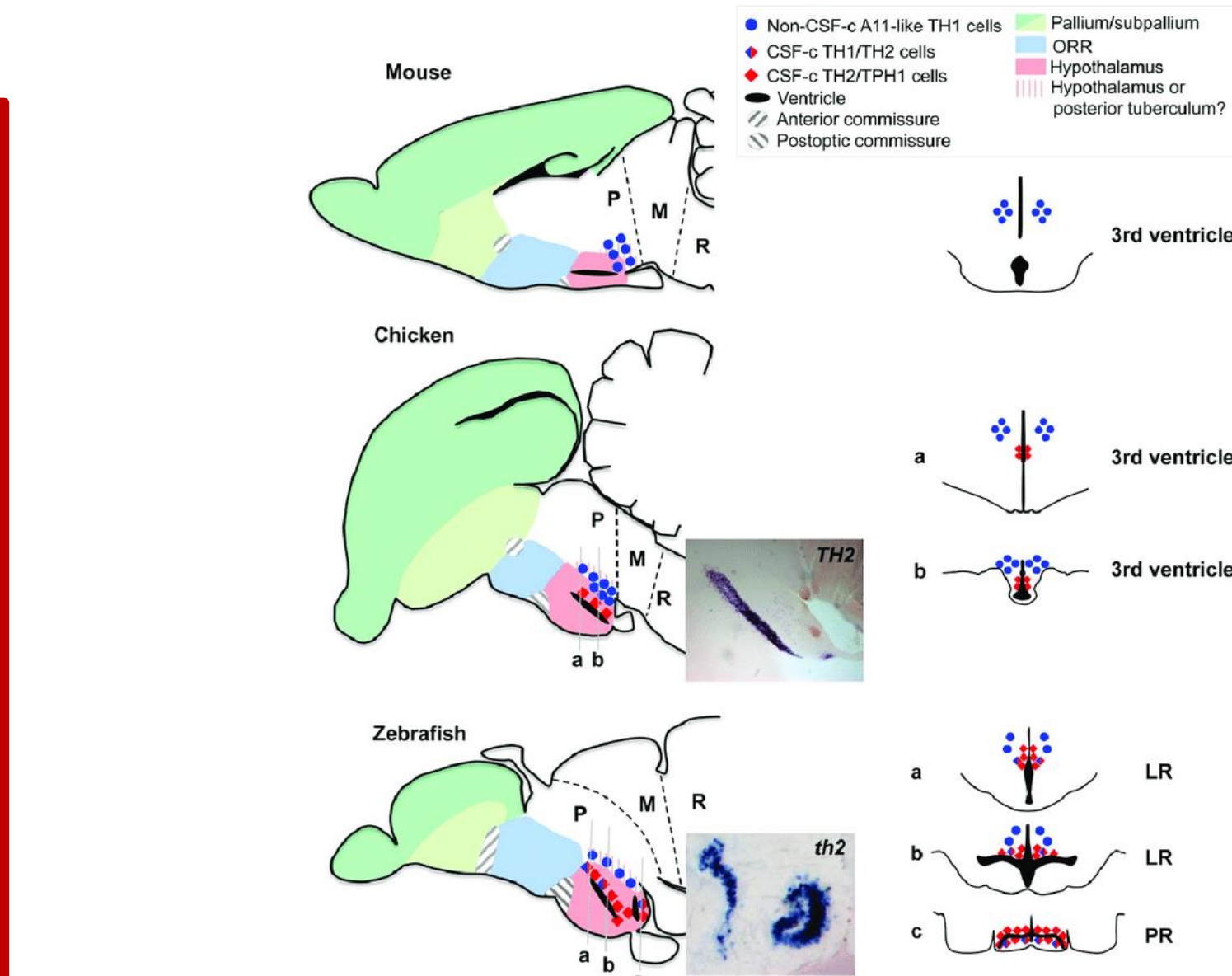
Aging Cell (2009) 8, pp88–99

Doi: 10.1111/j.1474-9726.2009.00455.x

Effects of dietary restriction on mortality and age-related phenotypes in the short-lived fish *Nothobranchius furzeri*



hypothalamus:
 evolutionary conservation of
 anatomy and molecular pathways



ARTICLE

doi:10.1038/nature12143

Hypothalamic programming of systemic ageing involving IKK- β , NF- κ B and GnRH

Guo Zhang^{1,2,3*}, Juxue Li^{1,2,3*}, Sudarshana Purkayastha^{1,2,3*}, Yizhe Tang^{1,2,3*}, Hai Zhang^{1,2,3*}, Ye Yin^{1,2,3}, Bo Li^{1,2,3}, Gang Liu^{1,2,3} & Dongsheng Cai^{1,2,3}

ageing can be globally influenced by hormones produced in the brain is of great interest to scientists



Food intake related neuropeptides as markers of age-related nutrient sensing

Chapter 19 The Suitability of Fishes as Models for Studying Appetitive Behavior in Vertebrates

Pietro Amodeo, Enrico D'Aniello, Fanny Defranoux, Angela Marino, Livia D'Angelo, Michael T. Ghiselin, and Ernesto Mollo

Results and Problems in Cell Differentiation, Springer Nature (2019)



Molecular and Cellular Endocrinology 497 (2019) 110437

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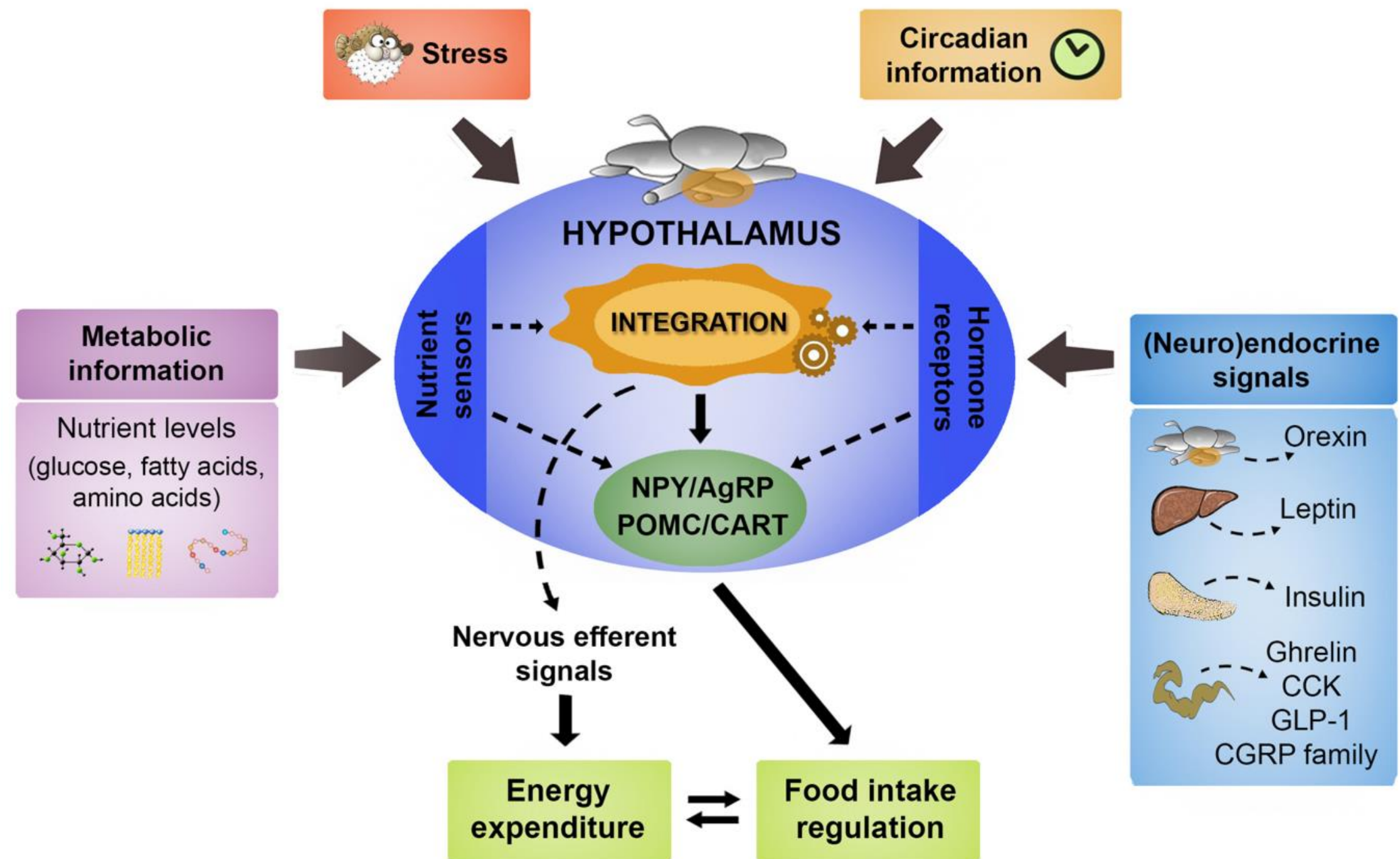
Fish as models for understanding the vertebrate endocrine regulation of feeding and weight

Helene Volkoff



Hypothalamic Integration of Metabolic, Endocrine, and Circadian Signals in Fish: Involvement in the Control of Food Intake

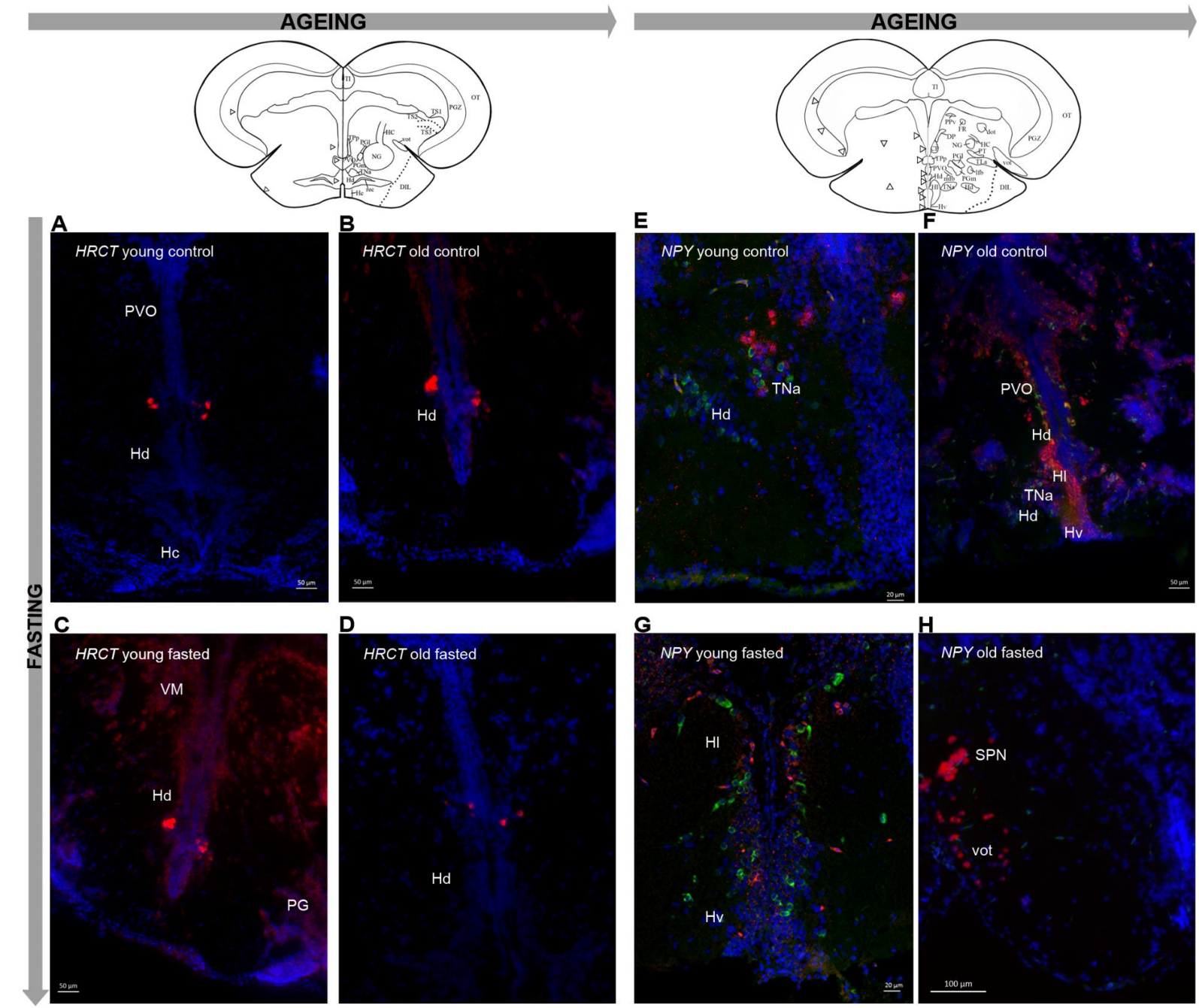
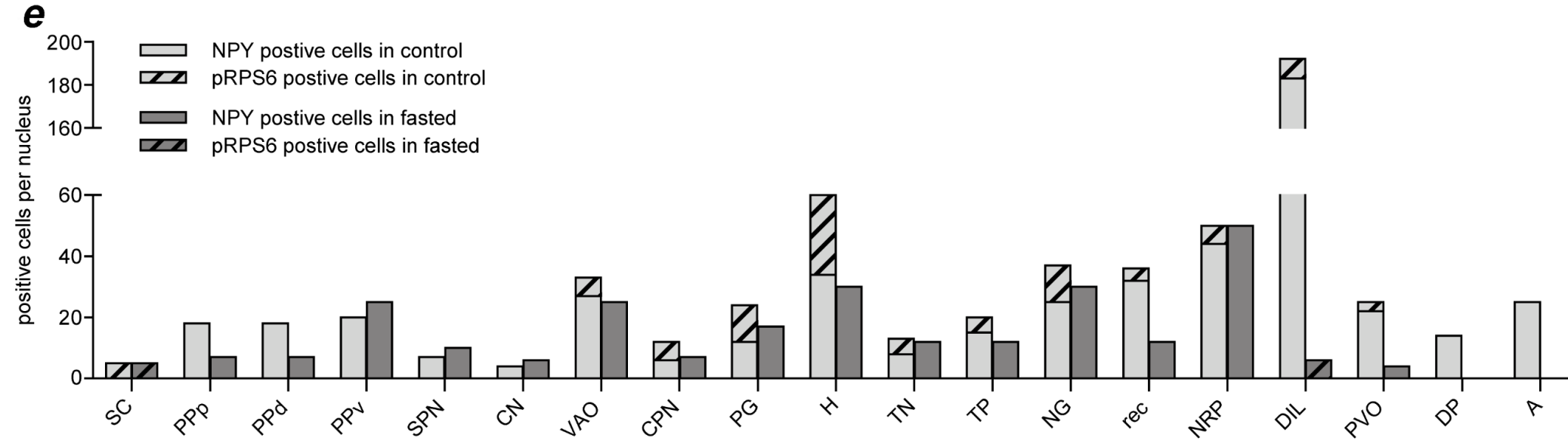
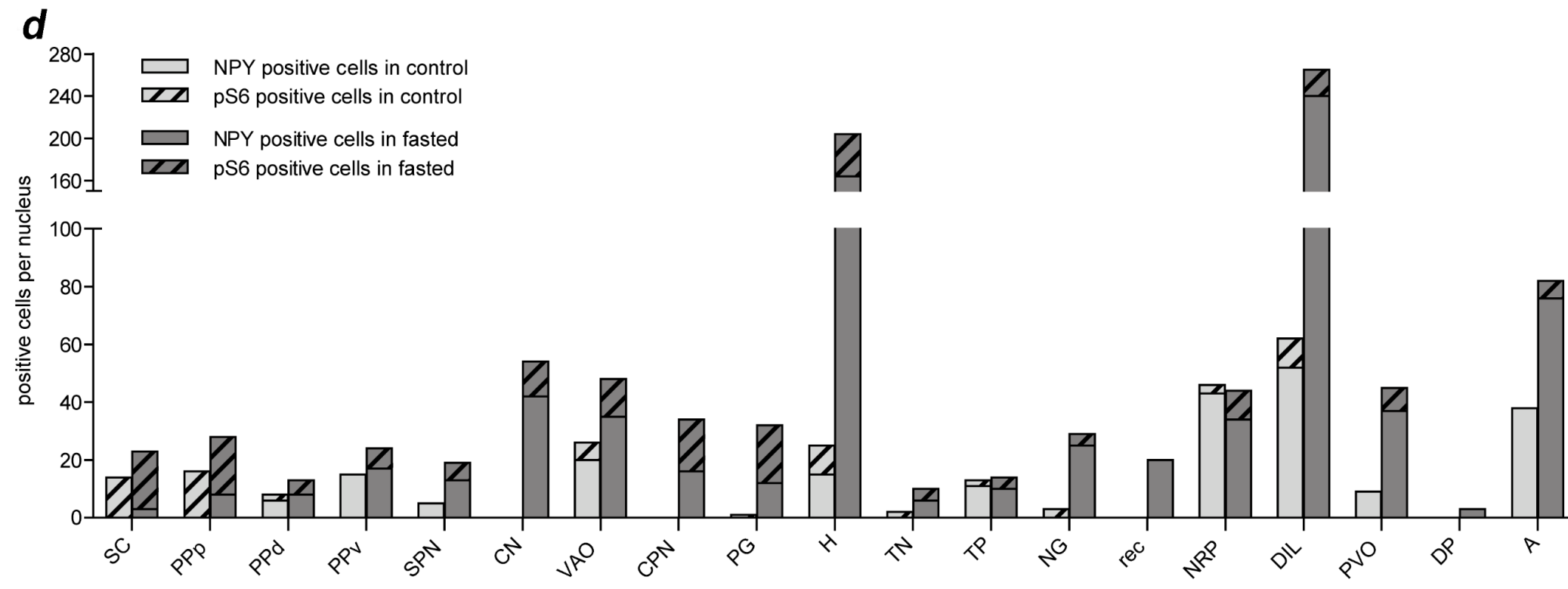
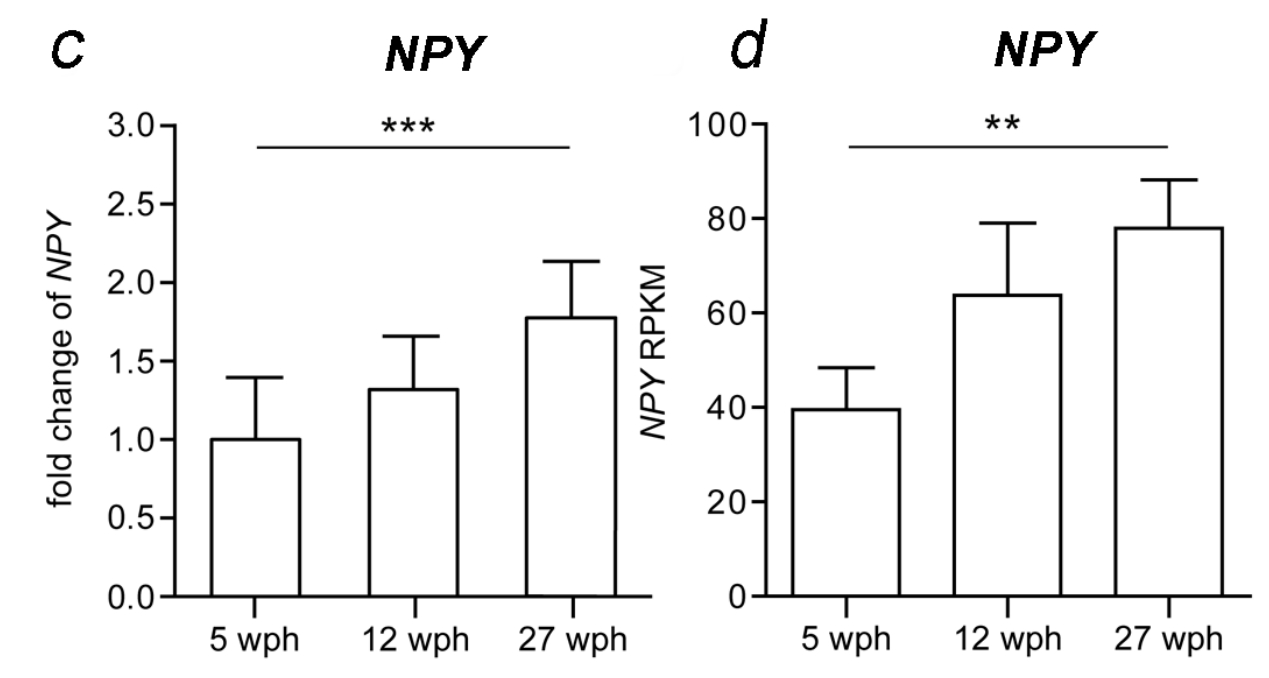
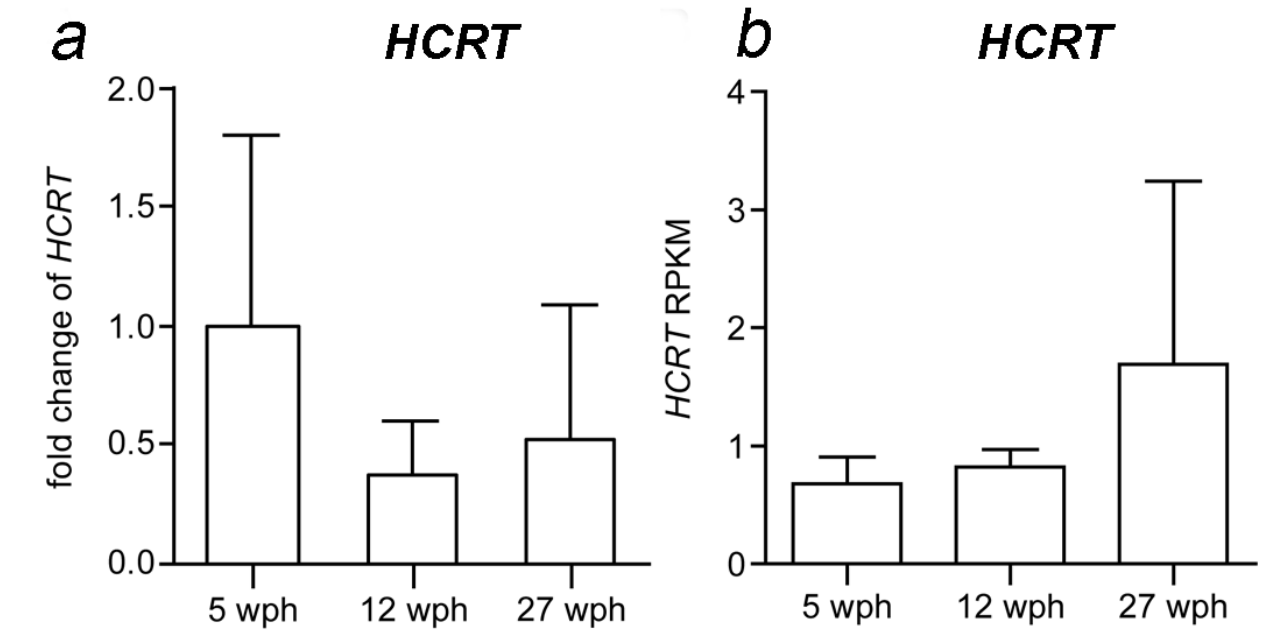
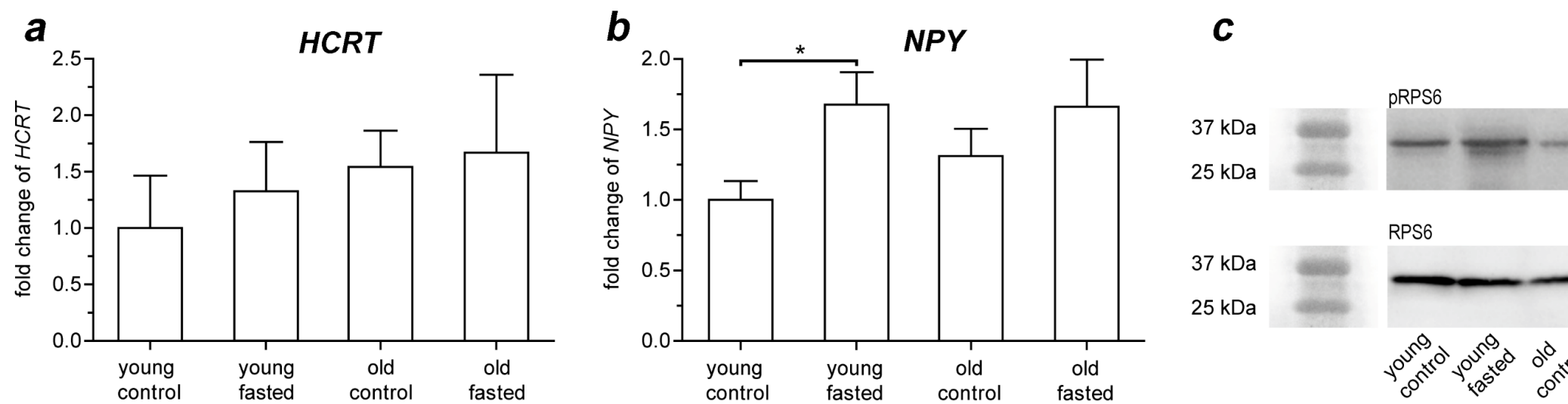
Maria J. Delgado¹, José M. Cerdá-Reverter² and José L. Soengas^{3*}



RESEARCH ARTICLE

Age-related central regulation of orexin and NPY in the short-lived African killifish *Nothobranchius furzeri*

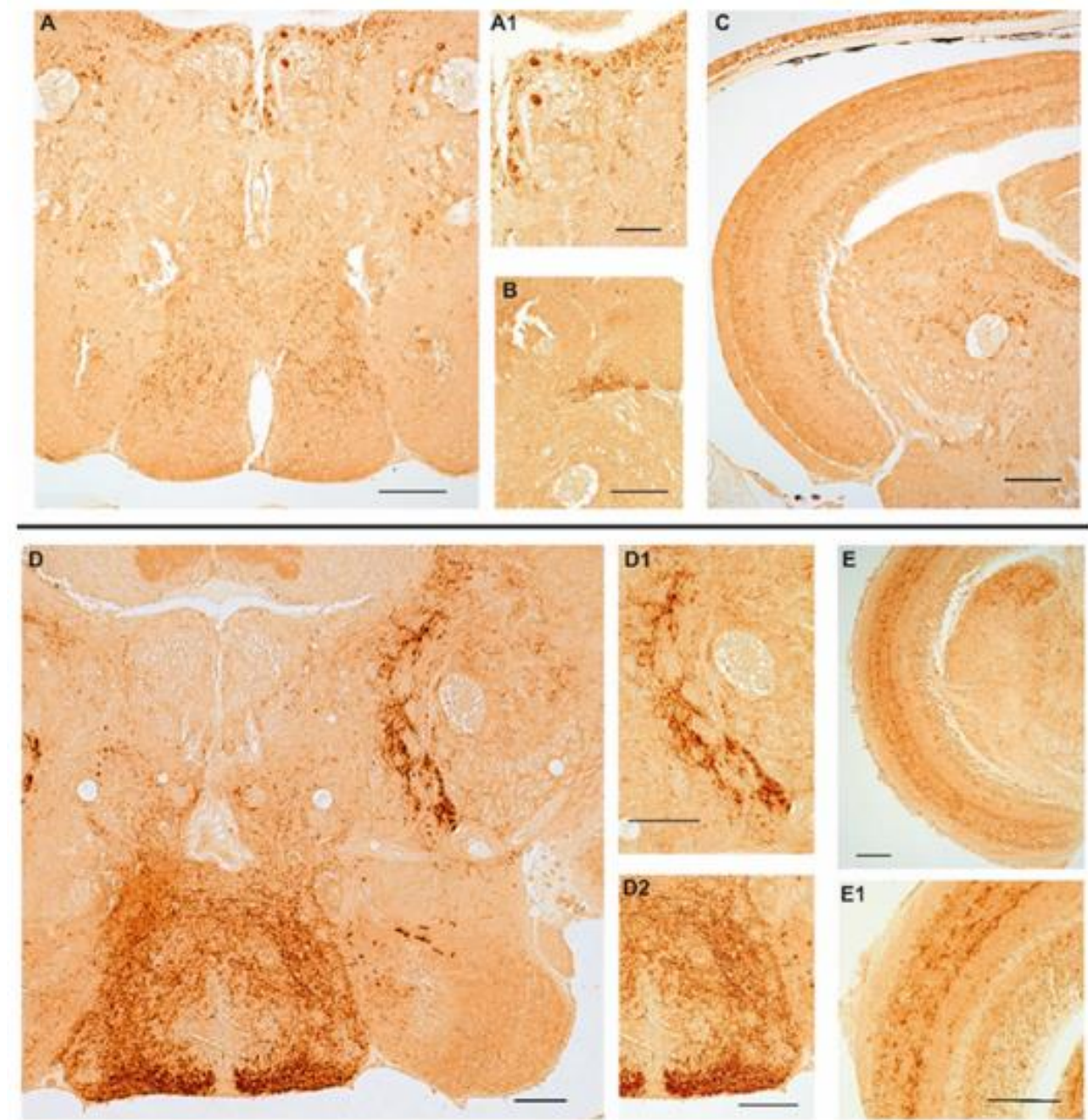
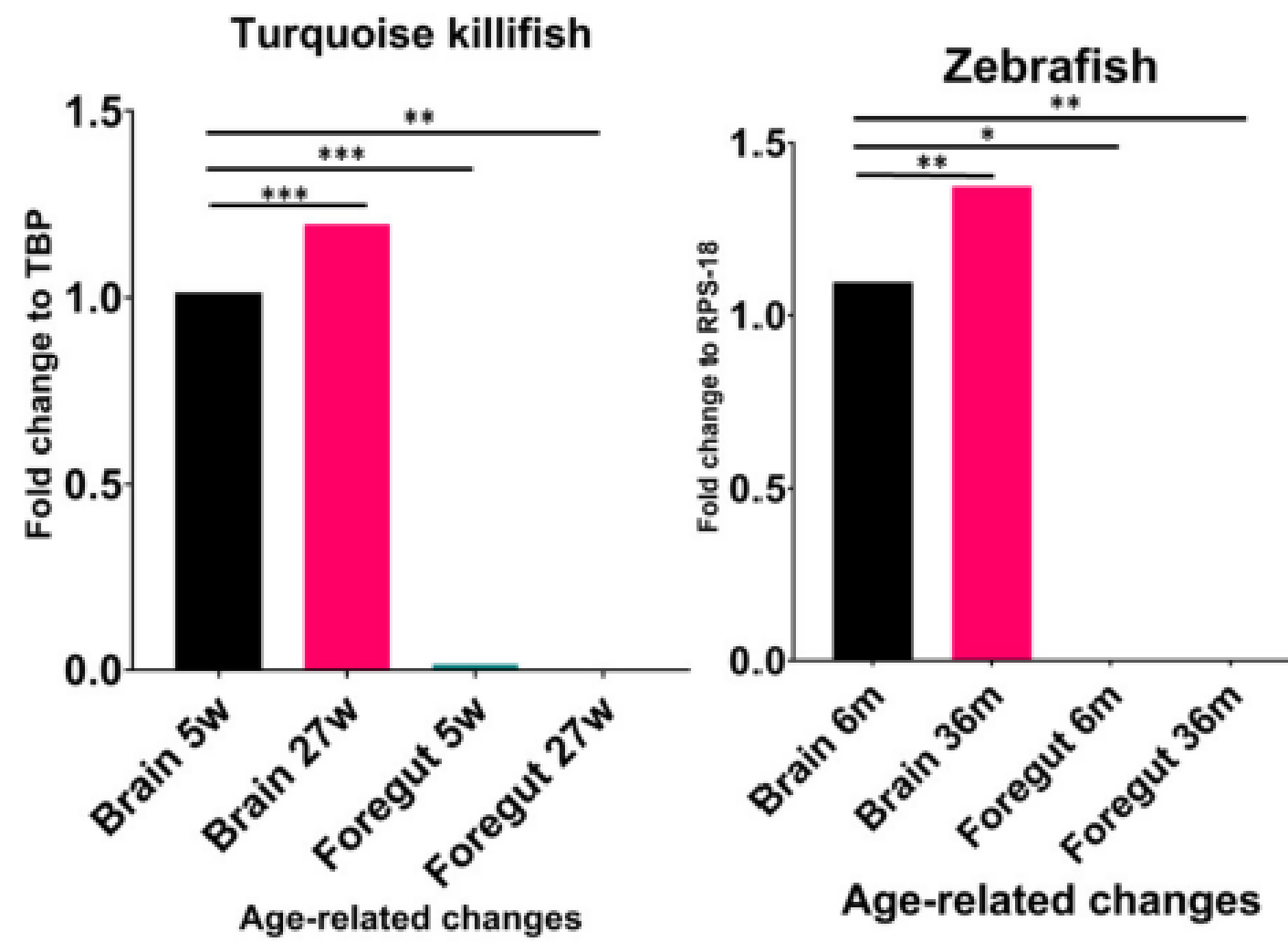
Alessia Montesano^{1,2} | Mario Baumgart² | Luigi Avallone¹ | Luciana Castaldo¹ |
 Carla Lucini¹ | Eva Terzibas Tozzini³ | Alessandro Cellerino^{2,3} | Livia D'Angelo^{1,4} |
 Paolo de Girolamo¹



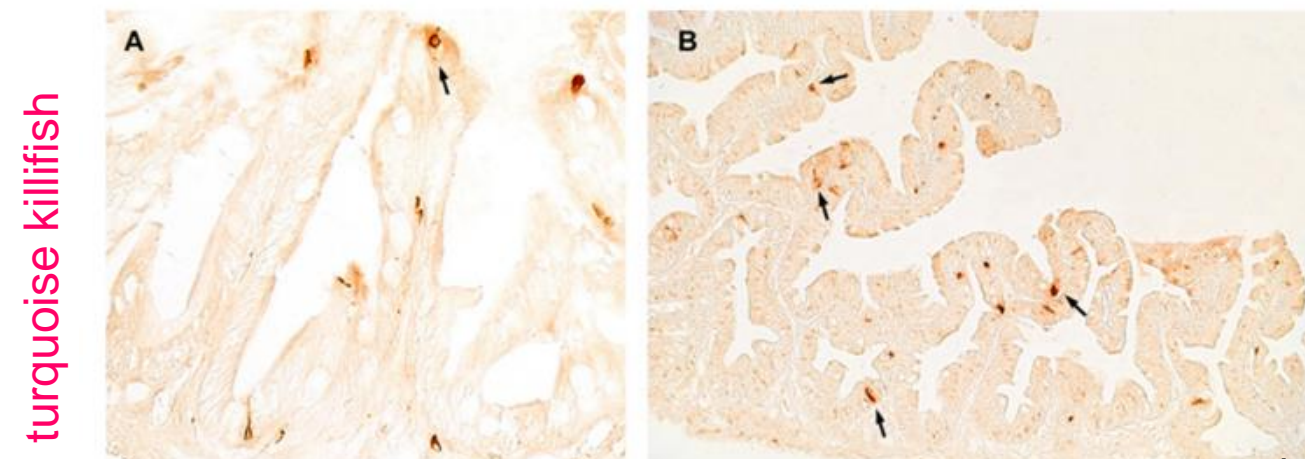
Article

Central and Peripheral NPY Age-Related Regulation: A Comparative Analysis in Fish Translational Models

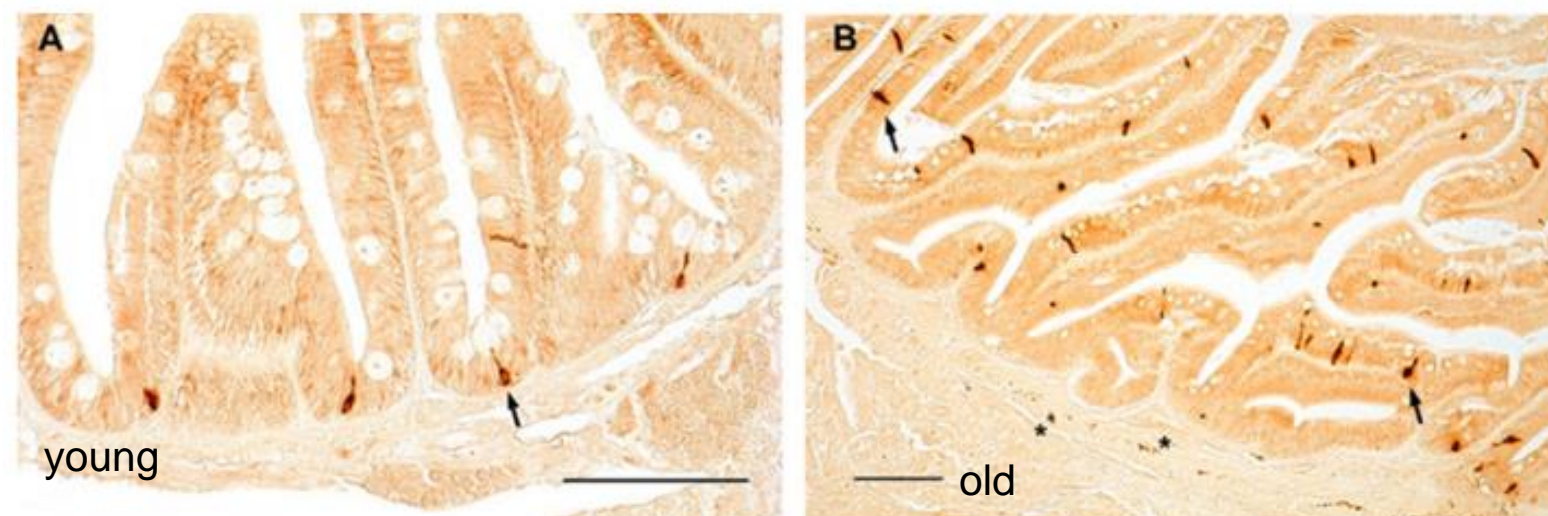
Daniela Giaquinto ^{1,†}, Elena De Felice ^{2,†}, Chiara Attanasio ¹, Antonio Palladino ³, Valentina Schiano ¹, Ernesto Mollo ⁴, Carla Lucini ¹, Paolo de Girolamo ¹ and Livia D'Angelo ^{1,*,†}



hypothalamic region of zebrafish



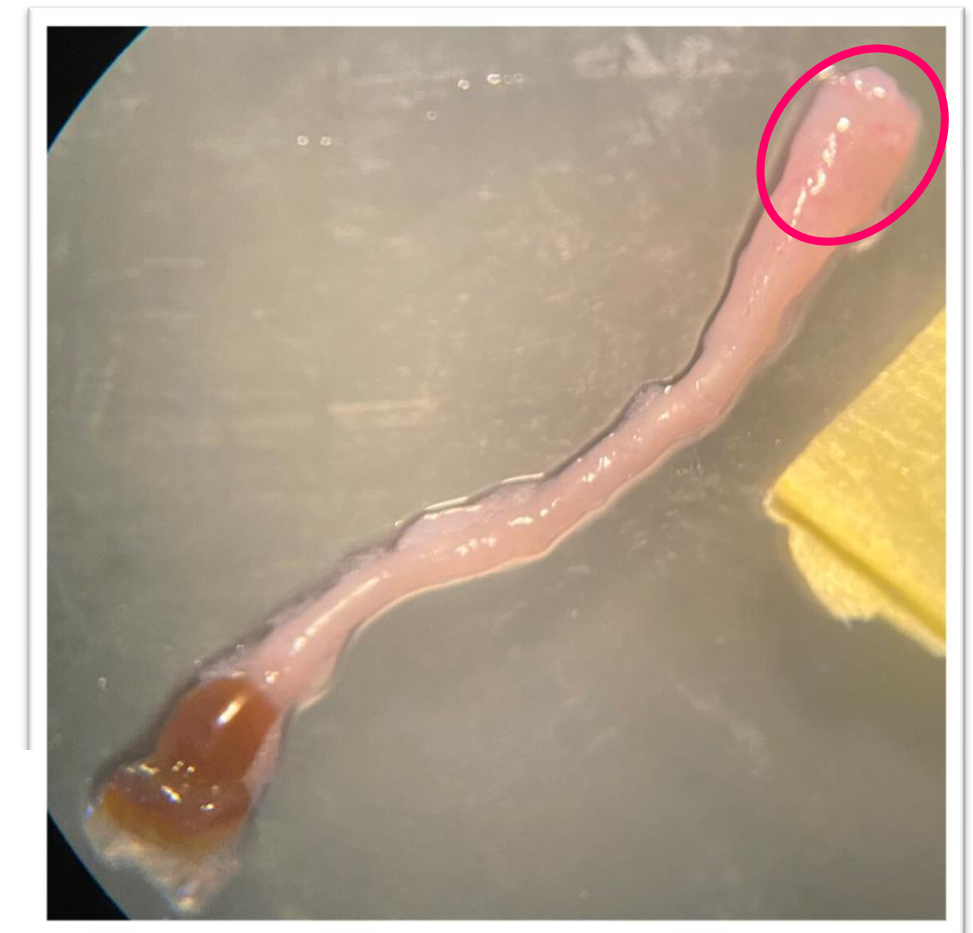
turquoise killifish



zebrafish

young

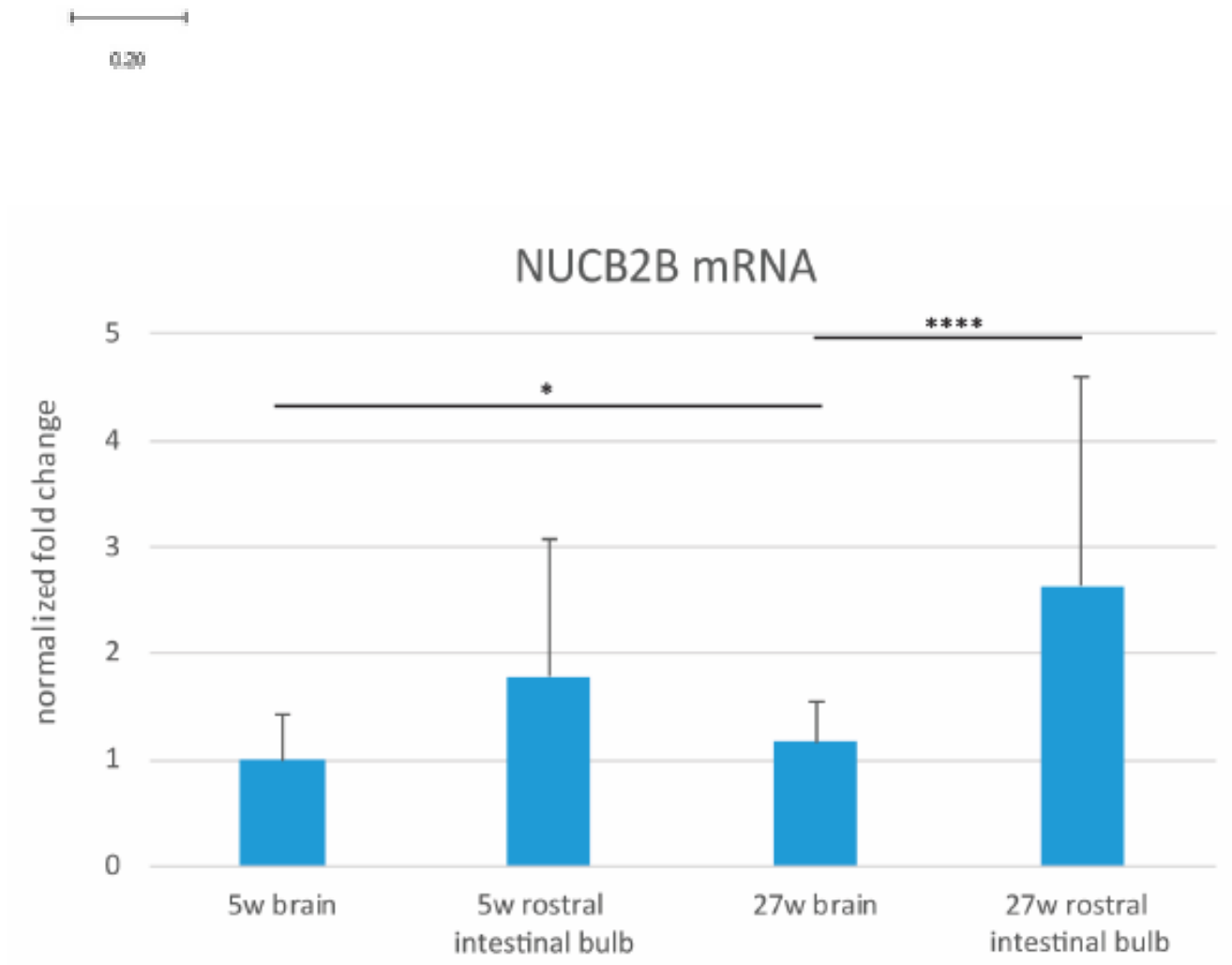
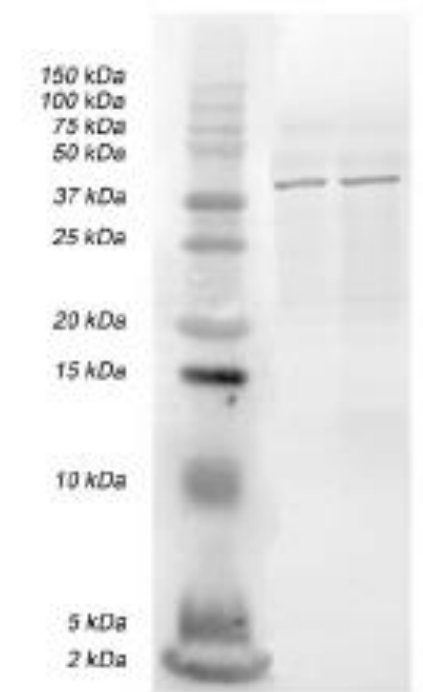
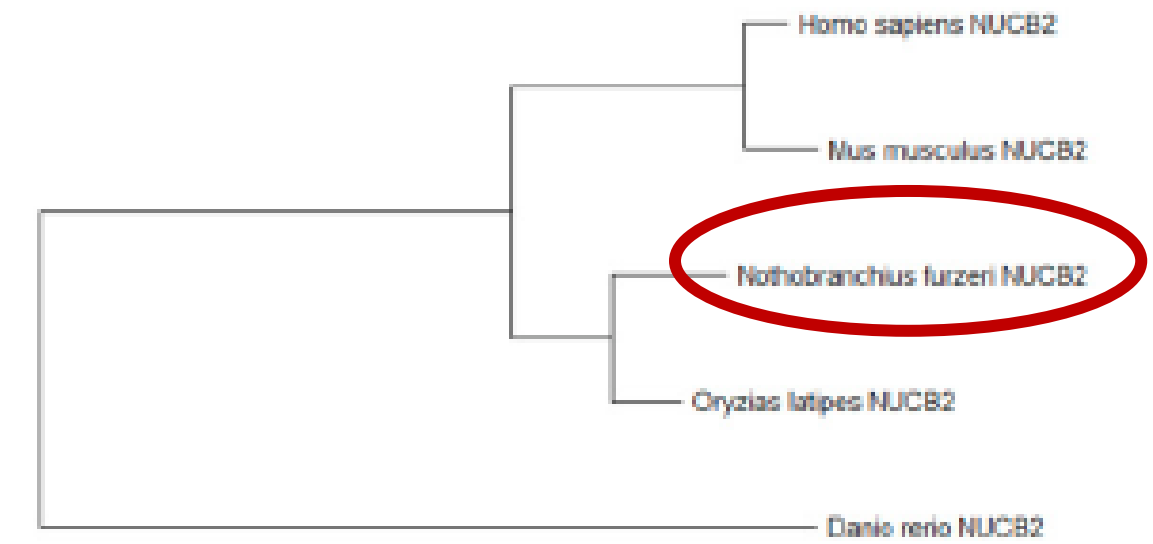
old



Article

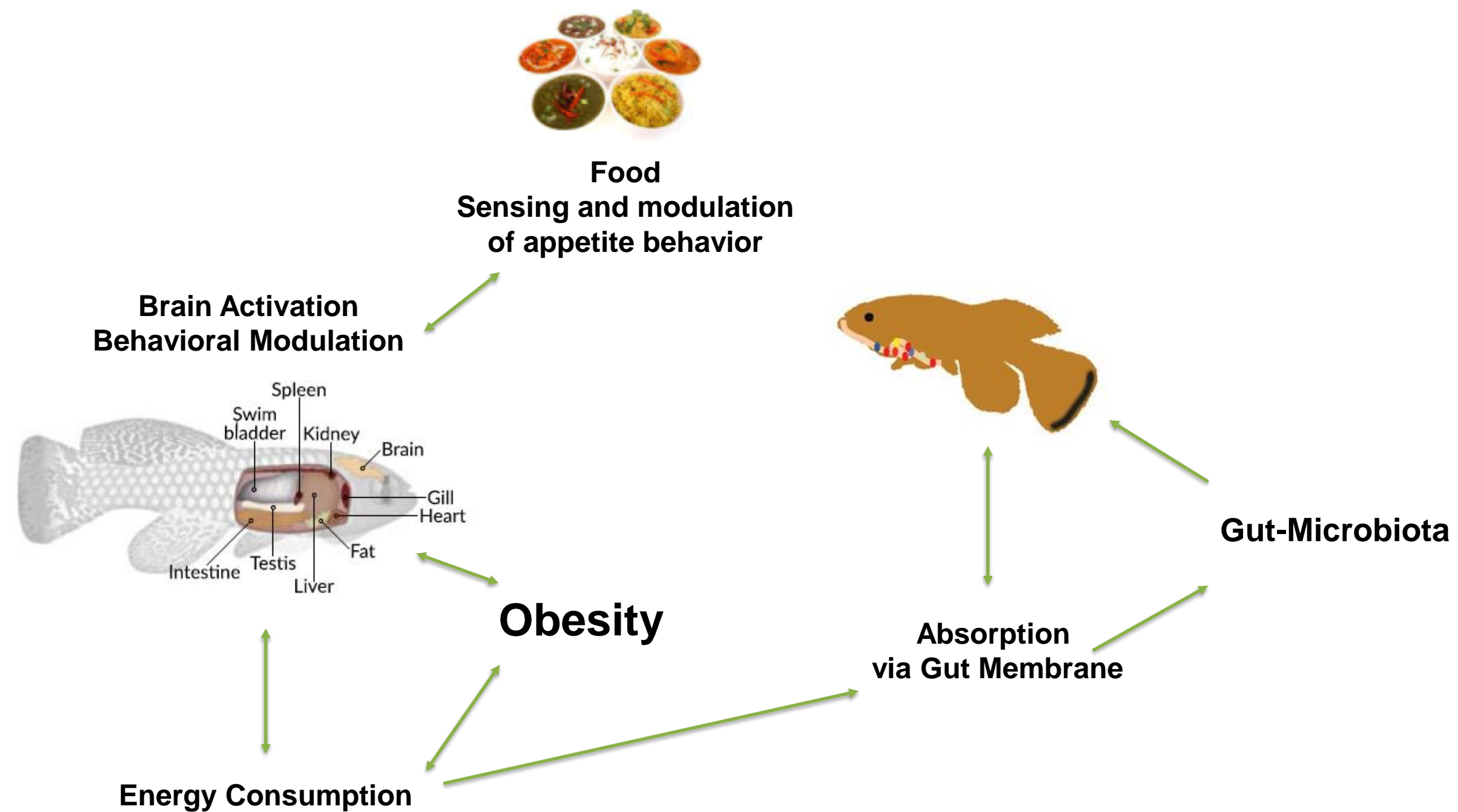
Ontogenetic Pattern Changes of Nucleobindin-2/Nesfatin-1 in the Brain and Intestinal Bulb of the Short Lived African Turquoise Killifish

Alessia Montesano ^{1,2,3,†}, Elena De Felice ^{4,†}, Adele Leggieri ¹, Antonio Palladino ⁵, Carla Lucini ¹, Paola Scocco ⁴, Paolo de Girolamo ¹, Mario Baumgart ^{2,‡} and Livia D'Angelo ^{1,6,*‡}



Ongoing research activities

Metabolic control via nutrient-sensing mechanisms:
role of taste receptors and the gut-brain neuroendocrine axis



Acknowledgment



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Prof. Valerio Cirillo

**Verso la funzionalizzazione
delle sostanze biostimolanti**

8 Giugno 2022

Main references

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Singh PP, Demmitt BA, Nath RD, Brunet A. The Genetics of Aging: A Vertebrate Perspective. *Cell*. 2019 177(1):200-220. doi: 10.1016/j.cell.2019.02.038.

Reichard M, Polačik M. *Nothobranchius furzeri*, an 'instant' fish from an ephemeral habitat. *Elife*. 2019 8:e41548. doi: 10.7554/eLife.41548.

Cellerino A, Valenzano DR, Reichard M. From the bush to the bench: the annual *Nothobranchius* fishes as a new model system in biology. *Biol Rev Camb Philos Soc*. 2016 91(2):511-33. doi: 10.1111/brv.12183.

D'Angelo L, Lossi L, Merighi A, de Girolamo P. Anatomical features for the adequate choice of experimental animal models in biomedicine: I. Fishes. *Ann Anat*. 2016 205:75-84. doi: 10.1016/j.aanat.2016.02.001.



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