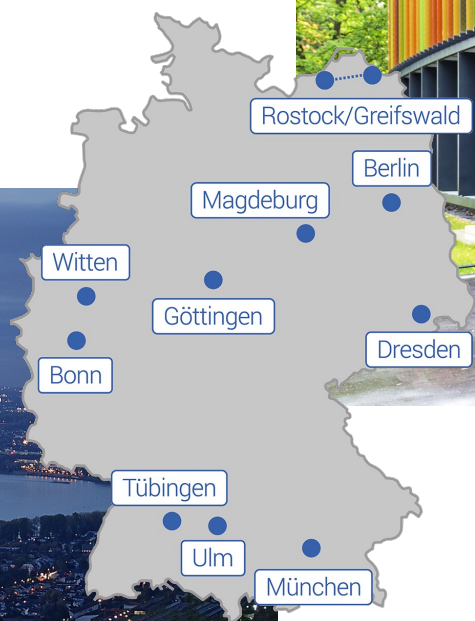
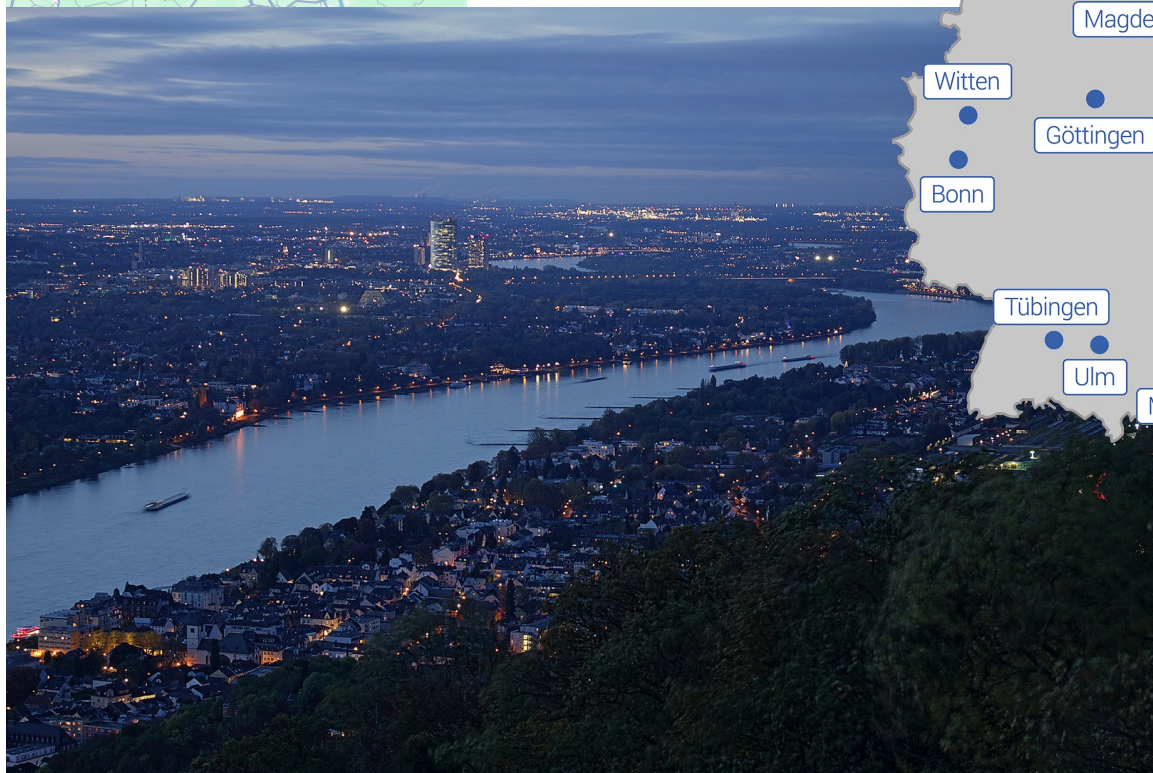
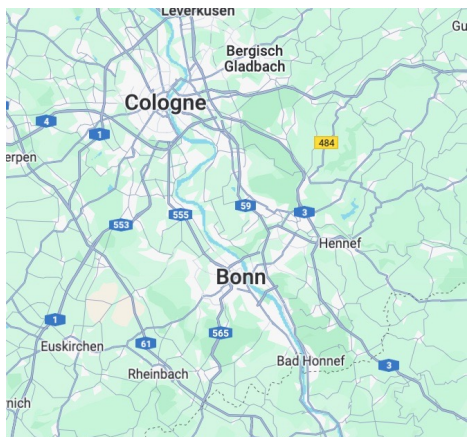




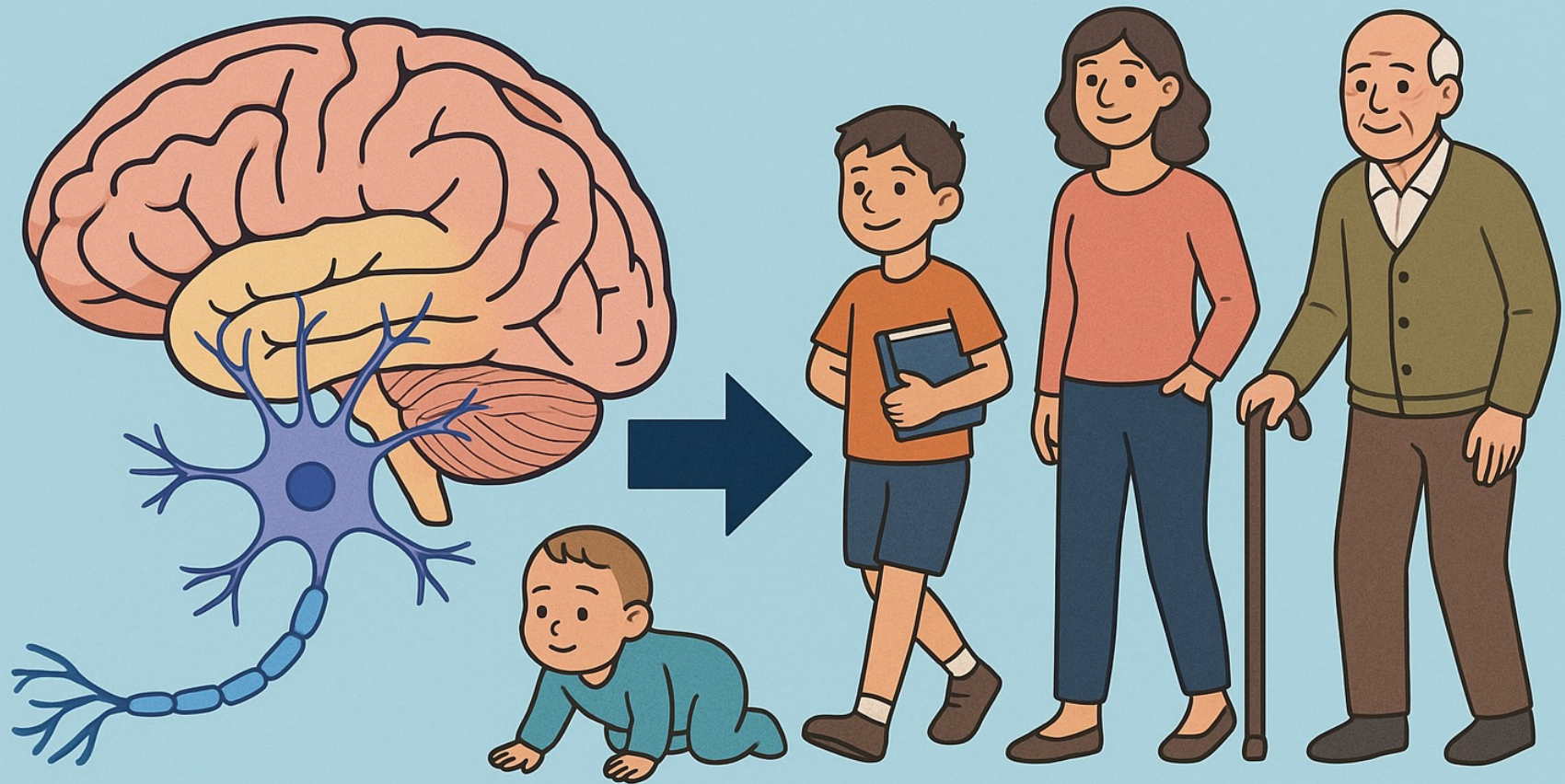
Korea–EU Horizon Europe Researcher Networking
Forum on Advanced Biotechnology
July 1-3, 2025

Translational Neuroscience in Neurodevelopmental and Neurodegenerative Disorders

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TRANSLATIONAL NEUROSCIENCE ACROSS THE LIFESPAN



Translational neuroscience in neurodegenerative disorders

- Alzheimer's disease, dementias, brain and cognitive aging
- Disease mechanisms, risk factors, novel treatment approaches
- Methods: Animal models (mice and invertebrates), deep phenotyping, multi-omics, genetics, pharmacology, data science & AI

Scifo et al., EMBO J, in press
Xie et al., Cell Metabolism, 2025
Deng et al., Aging Cell, 2024
Deng et al., Cell Death Discov, 2024
Jackson et al., Cell Death Dis, 2024
Wischhof et al., Sci Rep, 2024
Papazoglou et al., PLoS One, 2024
Bano et al., Cell Death Discov, 2023
Papazoglou et al., Data Brief, 2023
Keshavarz et al., Mol Psychiatry 2023

Xie & Ehninger, Mech Ageing Dev, 2023
Keshavarz et al., Mech Ageing Dev, 2023
Xie et al., Nat Commun, 2022
Papazoglou et al., Int J Mol Sci, 2022
Piazzesi et al., EMBO Rep, 2022
Wischhof et al., J Biol Chem, 2022
Bano et al., Curr Opinion Pharmacol, 2021
Xie et al., Mech Ageing Dev, 2020
Lountzi et al., Mech Ageing Dev, 2020
Kumar et al., Mech Ageing Dev, 2020

Poll et al., Nat Neurosci, 2020
Bellantuono et al., Nat Protoc, 2020
Xie et al., PNAS, 2018
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Matthes et al., Cell Death Discov, 2018
Schweiger et al., Sci Rep, 2017
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Mitroi et al., Autophagy, 2017
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Papazoglou et al., Neural Plast, 2016
Lundt et al., Neural Plast, 2016
Wagner et al., Acta Neuropathol, 2015
Siwek et al., Neural Plast, 2015
Paesler et al., Neural Plast, 2015
Hettich et al., PLoS One, 2014
Ehninger et al., Cell Mol Life Sci, 2014
Neff et al., J Clin Invest, 2013
Kempermann et al., Front Neurosci, 2010
Kronenberg et al., Neurobiol Aging, 2006

AGING

major risk factor for neurodegenerative diseases...



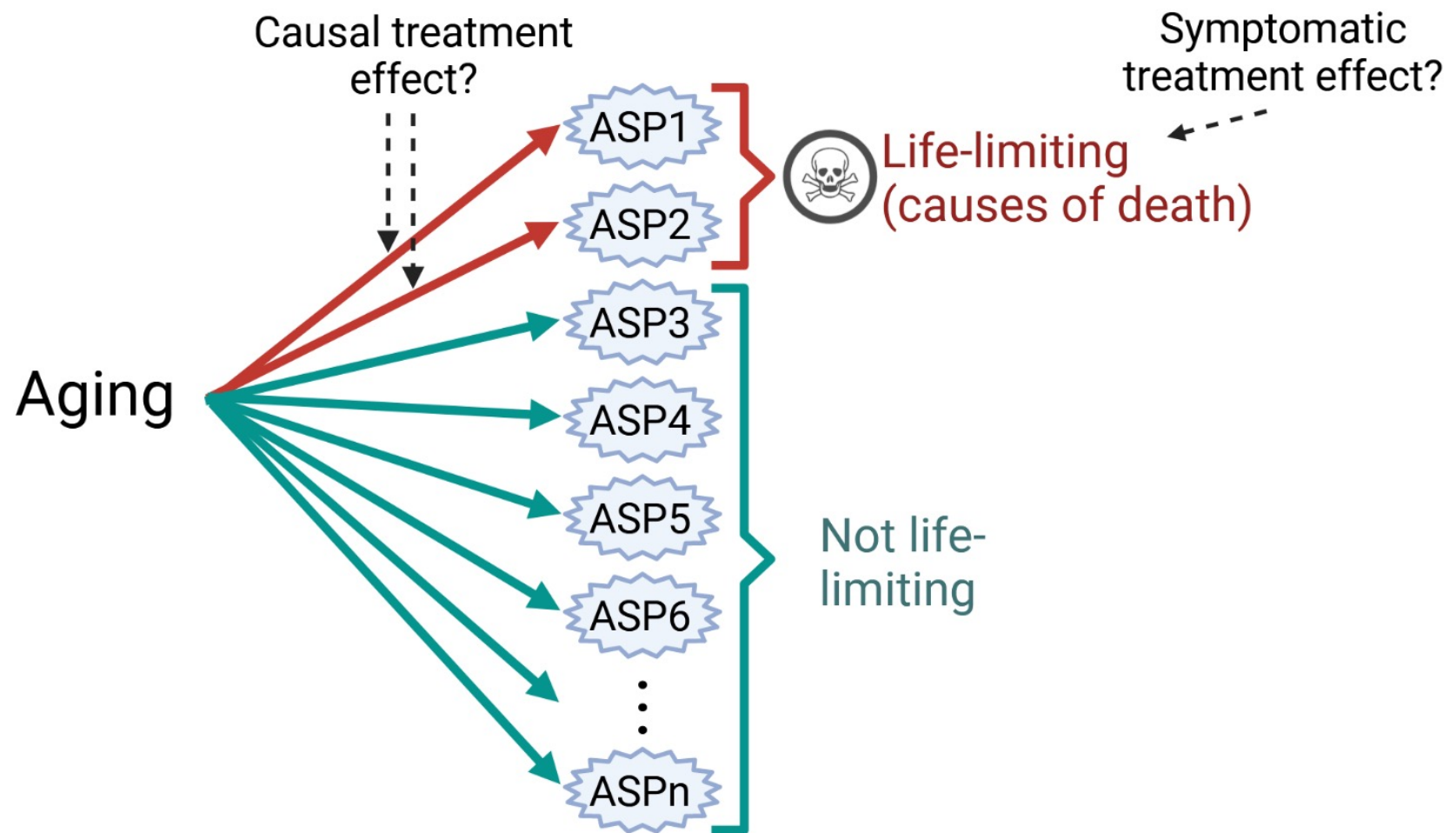
***What are genetic and environmental factors
that influence aging?***

Lifespan vs. aging

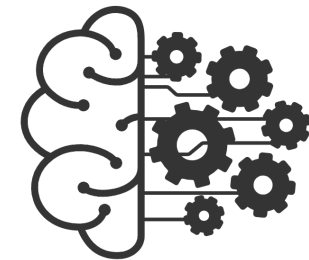
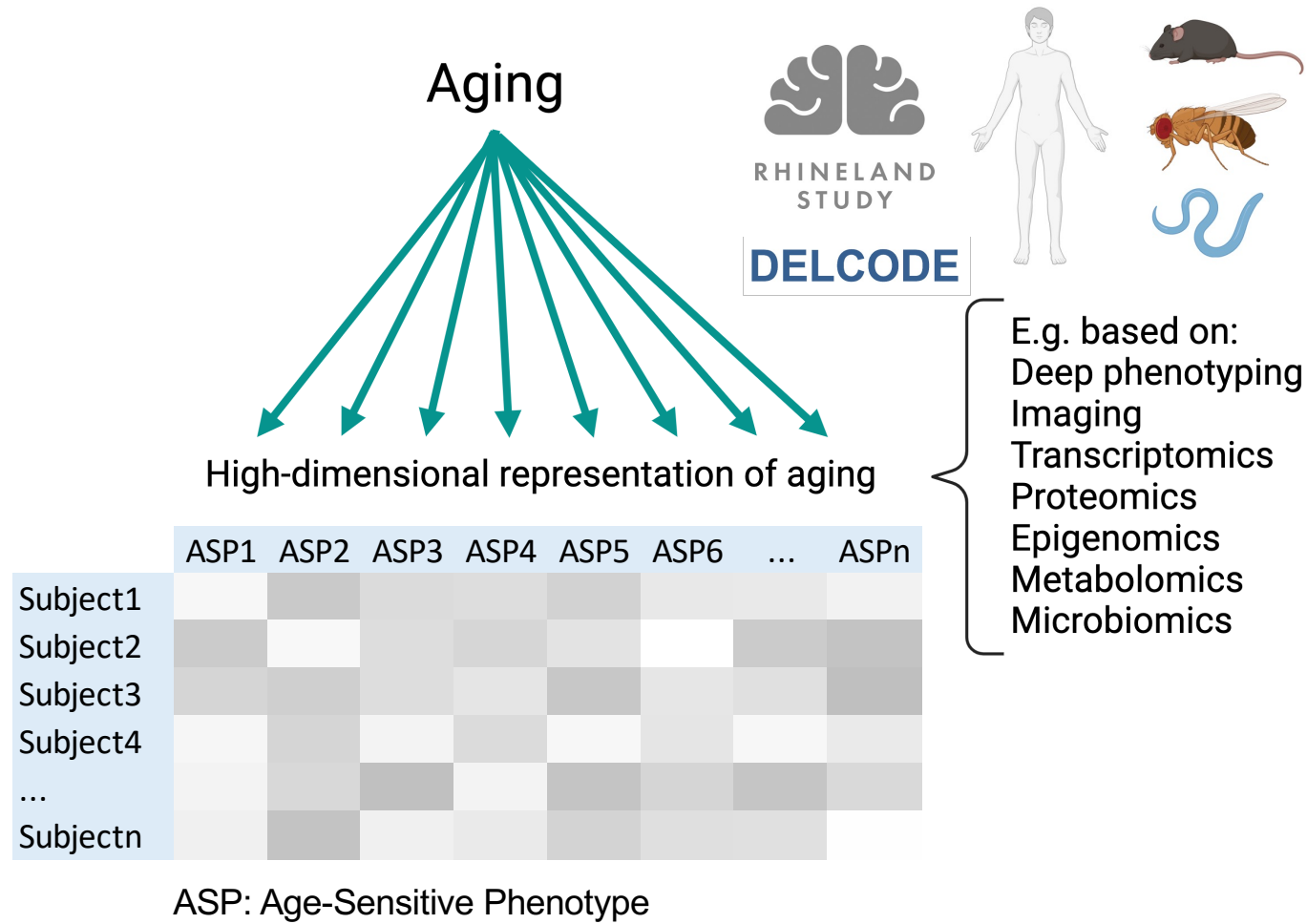
Lifespan vs. aging in mice



Main cause of death in old mice:
cancers (70-90%)



Tools & methods



e.g.,
 Scifo et al., *EMBO J*, in press
 Deng et al., *Aging Cell*, 2024
 Keshavarz et al., *Mol Psychiatry*, 2023
 Keshavarz et al., *Mech Ageing Dev*, 2023
 Xie et al., *Mech Ageing Dev*, 2023
 Xie et al., *Nat Commun*, 2022
 Bellantuono et al., *Nat Protoc*, 2020

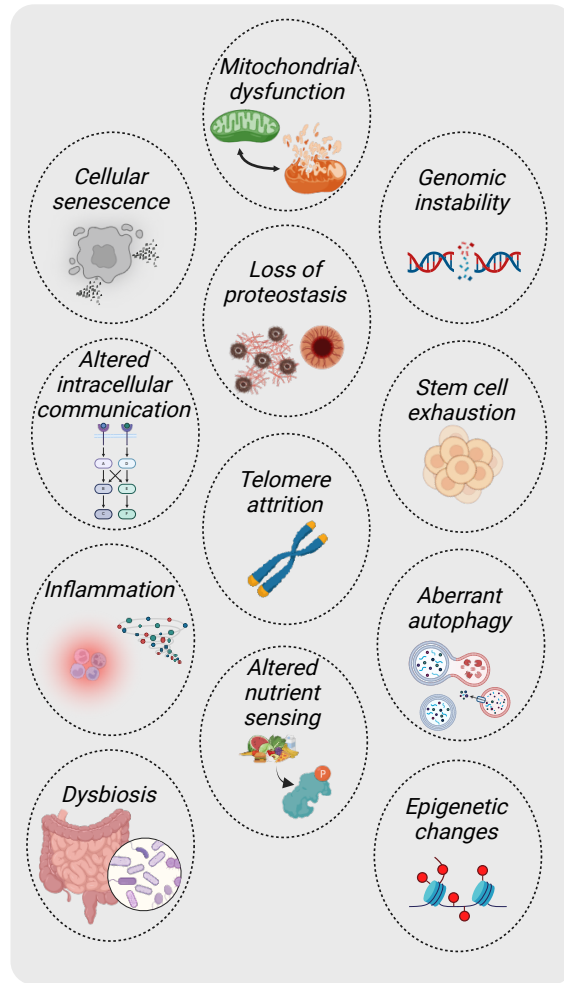
Models & cohorts



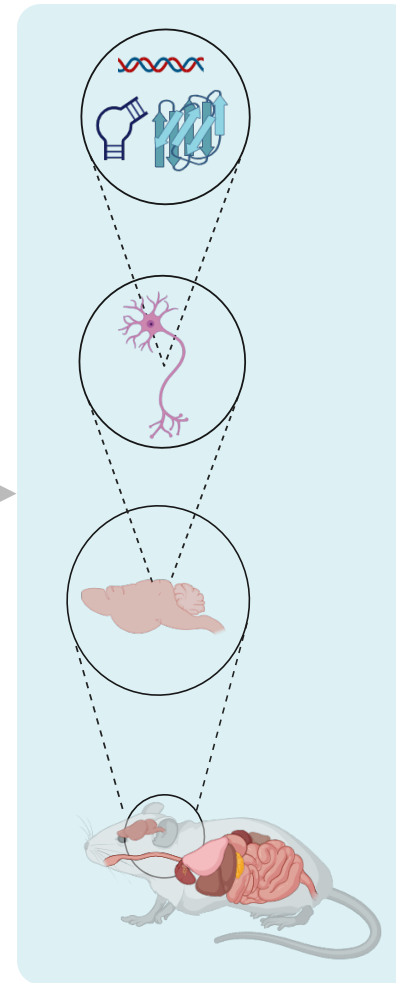
RHINELAND
STUDY

DELCODE

Hallmarks of aging



Age-dependent organismal change

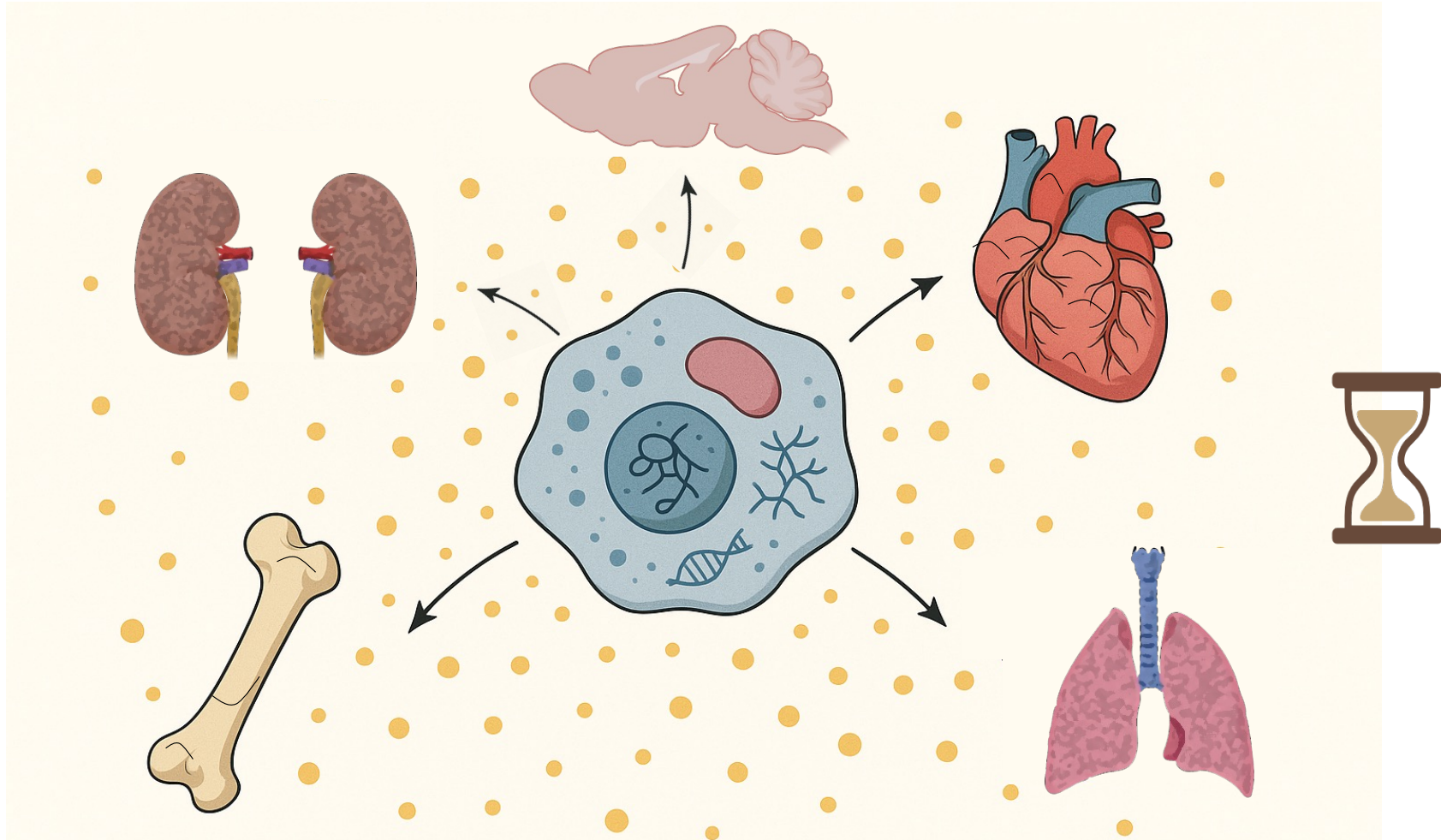


e.g.,
Scifo et al., *EMBO J*, in press
Keshavarz et al., *Mol Psychiatry*, 2023
Xie et al., *Nat Commun*, 2022

Potential collaborative research topic

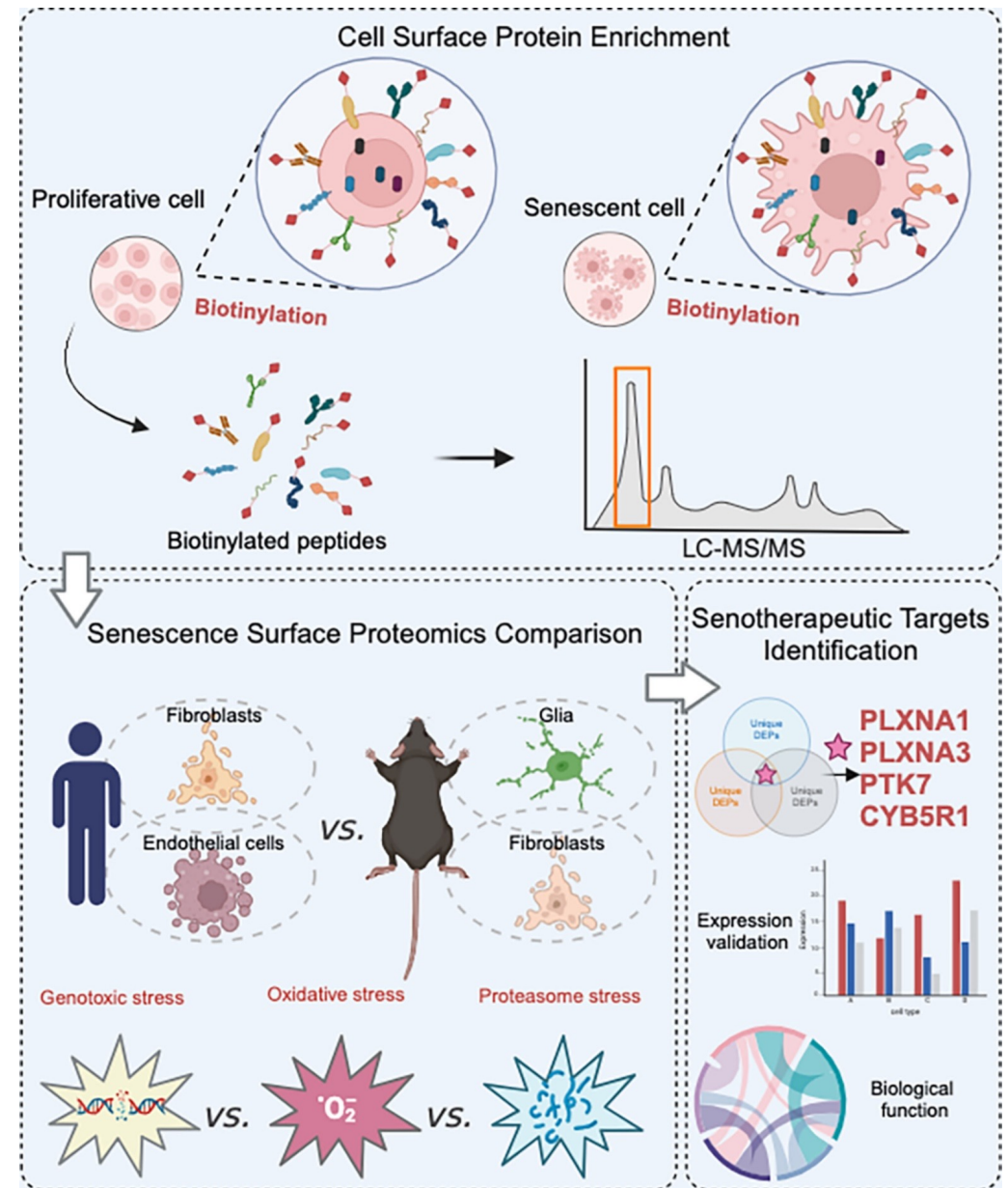
***Translating insights from aging biology to novel treatments for
age-related brain disorders***

Senescent cells: drivers of multiple aging-associated pathologies

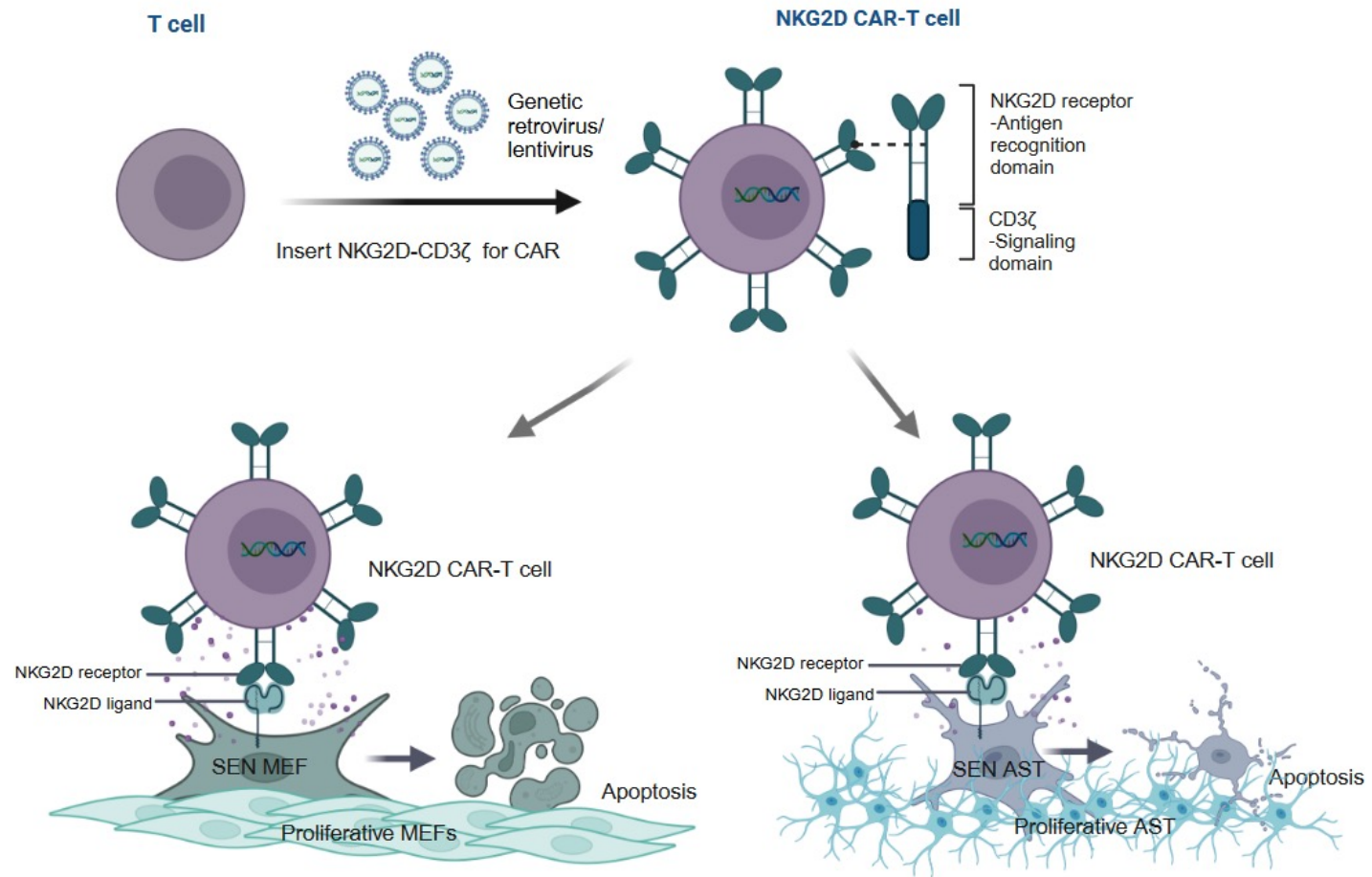


How to target senescent cells?

Immunotherapeutic targeting of senescent cells



Targeting senescent cells via CAR T cells



VENCELL

cellex.
Cell Professionals

Deng et al., *Cell Death Discov*, 2024

Potential collaborative research topic

***Develop targeted immunotherapies to eliminate senescent cells
to address neurodegenerative diseases***

AGING

An intergenerational risk factor for disease?



Advanced paternal age: Intergenerational risk factor for neurodevelopmental disorders

e.g.

Bertram et al., Neurogenetics 1998

Zhang et al., Am J Epidemiol 1999

Malaspina et al., Arch Gen Psychiatry 2001

Reichenberg et al., Arch Gen Psychiatry 2006

Buizer-Voskamp et al., Schizophr Res 2011

Hultman et al., Mol Psychiatry 2011

Hamlyn et al., Neurobiol Dis 2013

Wu et al., Psychiatry Res 2012

Lampi et al., J Autism Dev Disord 2013

Grath et al., JAMA Psychiatry 2014

Carslake et al., Sci Rep 2019

Monaghan et al., Trends Ecol Evol 2020

Aging affects traits across generations

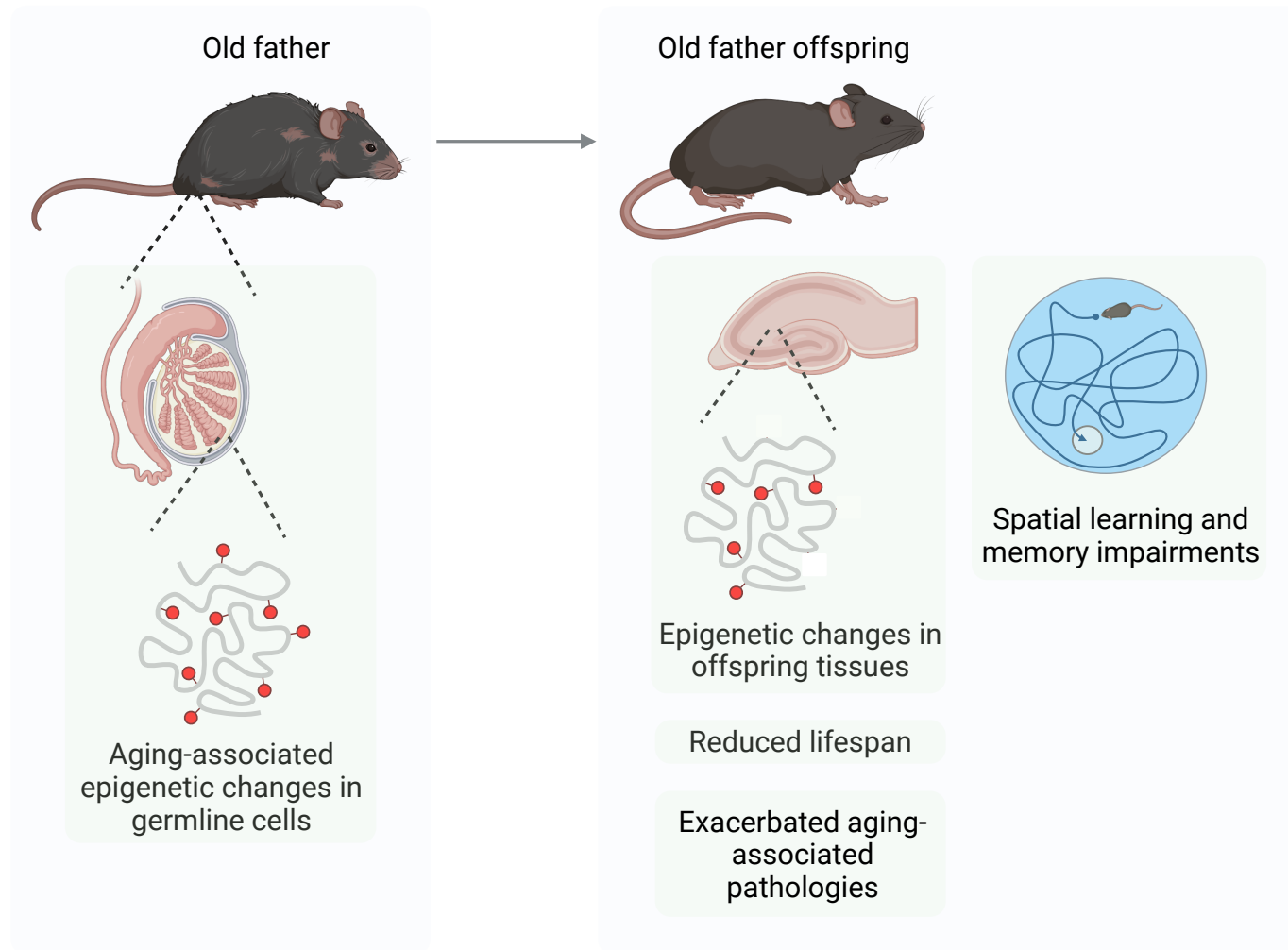



Young father offspring




Old father offspring

Aging affects traits across generations



Xie, Ryan, Pearson et al., PNAS, 2018

***Does paternal dietary restriction prevent
intergenerational effects of advanced paternal age?***

Two major forms of dietary restriction

Chronic caloric restriction (CR)



ad libitum



60%

Intermittent fasting (IF)



ad libitum



day1



ad libitum

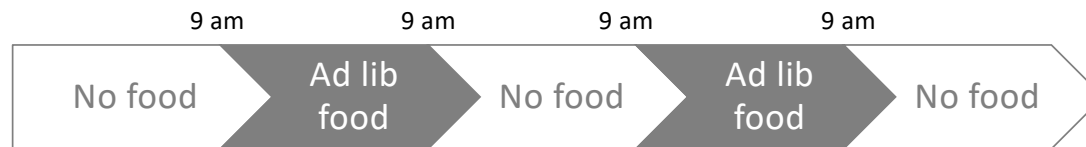
day2

no food

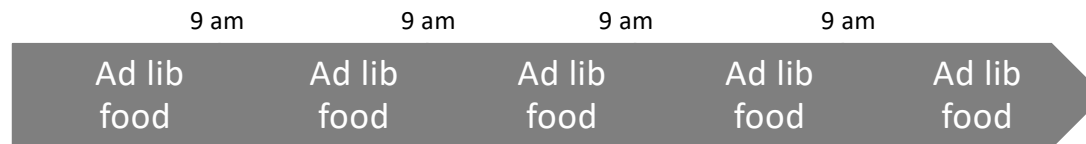
VS.

Intermittent fasting (IF)

Restricted groups (intermittent fasting, every-other-day feeding)



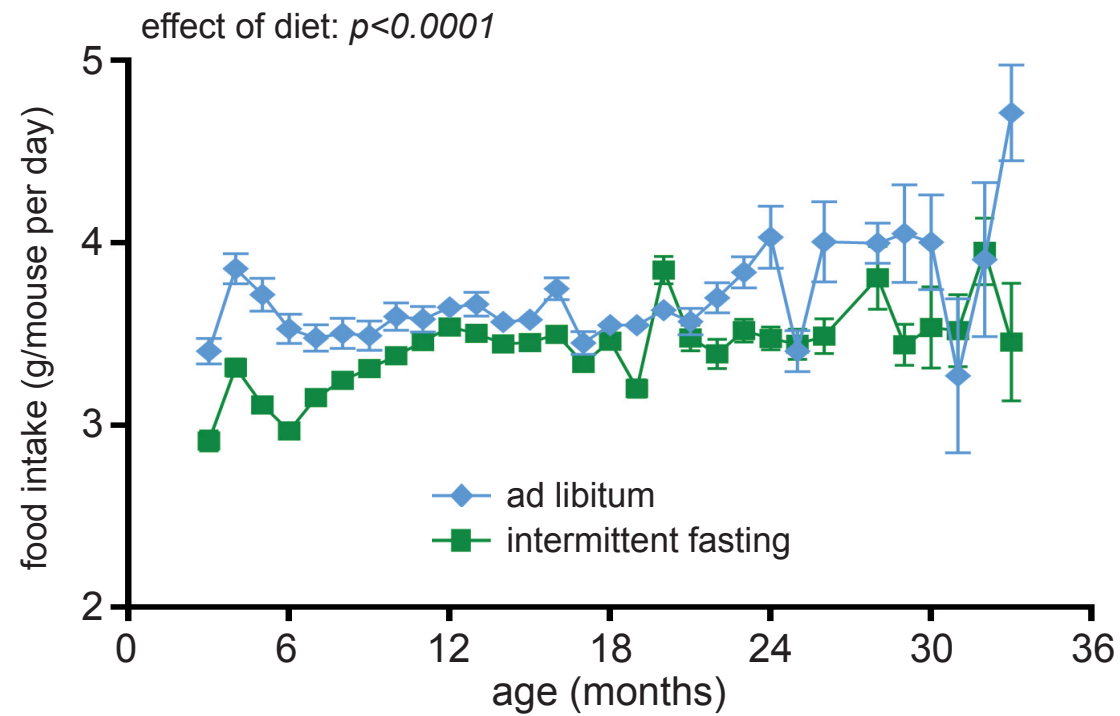
Control groups (ad libitum access to food)



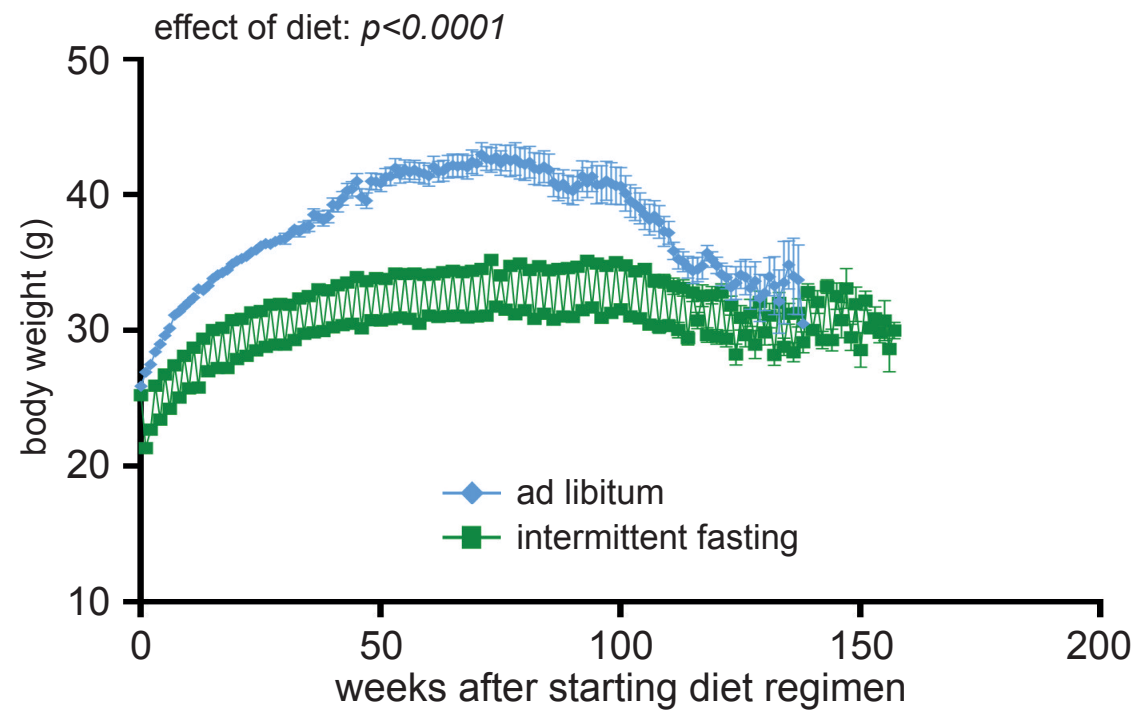
Feeding regime initiated at 8 weeks of age; chow: Altromin 1314 diet

Xie et al., Cell Metabolism, 2025
Xie et al., Nat Commun, 2022
Xie et al., Nat Commun, 2017

Only ~10% reduction in calorie intake under IF

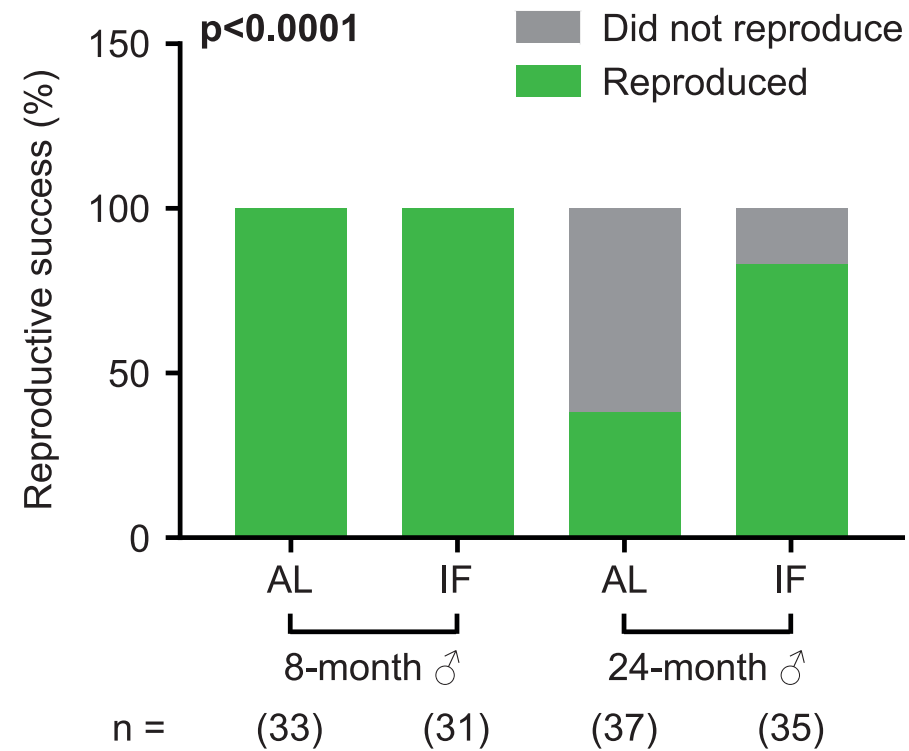


Substantial body weight reduction under IF

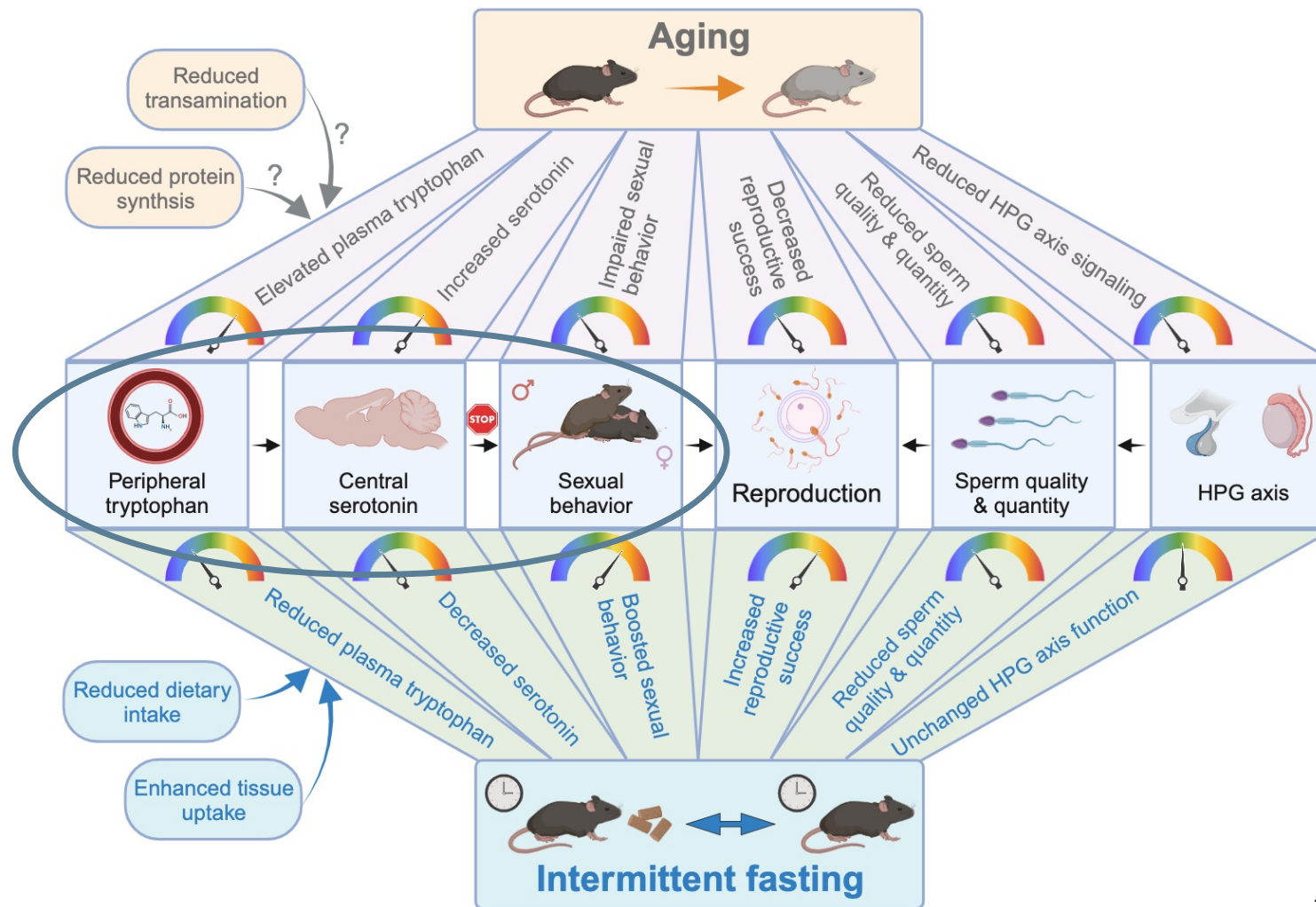


***Does paternal intermittent fasting prevent
intergenerational effects of advanced paternal age?***

IF promoted mating behavior in aged male mice



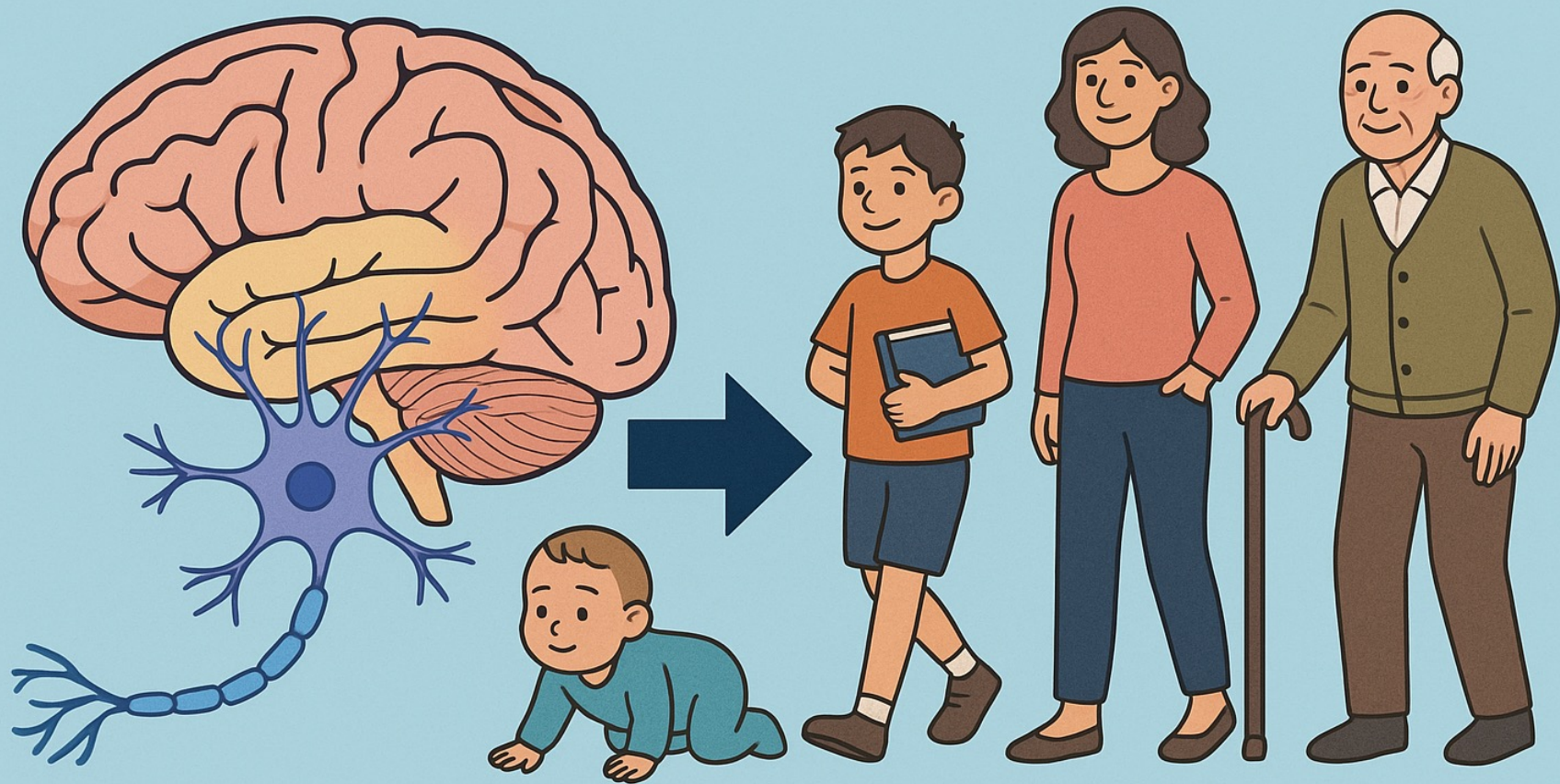
IF boosts sexual behavior by limiting the central availability of tryptophan and serotonin



Potential collaborative research topic

***Develop metabolic interventions to target clinical conditions
associated with libido impairments***

TRANSLATIONAL NEUROSCIENCE ACROSS THE LIFESPAN



Translational Neuroscience in Neurodevelopmental Disorders

- Autism, schizophrenia, intellectual disabilities, learning disabilities, ADHD, epilepsy
- Disease mechanisms, risk factors, novel treatment approaches
- Methods: Mouse models, genetics, behavioral biology, omics, pharmacology, neurophysiology, data science & AI



Sanz-Moreno et al., Sci Adv, 2025
Wormuth, Neural Plast, 2024
Papazoglou, BMC Res Notes, 2024
Wischhof et al., EMBO J, 2022
Jackson et al., Mol Metab, 2022
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Ryan et al., Mol Psychiatry, 2018
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Pearson & Ehninger, Epigenomics, 2018
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Wischhof et al., Sci Rep, 2017
Lee et al., Nat Neurosci, 2014
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Zhou et al., Neuron, 2013
Ehninger, Neuropharmacology, 2013
Heinen et al., Neural Plast, 2012
Ehninger et al., Mol Psychiatry, 2012
Ehninger et al., Trends Mol Med, 2011

Ehninger & Silva, Behav Genet, 2011
Shilyansky et al., PNAS, 2010
Zhao et al., Mol Psychiatry, 2010
Ehninger et al., Nat Med, 2009
Silva & Ehninger, J Neurodev Disord, 2009
Ehninger et al., J Intellect Disabil Res, 2009
Ehninger et al., Neuron, 2008
Ehninger et al., Nat Med, 2008
Li et al., PNAS, 2007

Potential collaborative research topics

Where and when do genetic and environmental risk factors act to cause neuropsychiatric disease?

- Where in the brain? Which cell types?
- Which ontological stage?



Neuron
Review

Reversing Neurodevelopmental Disorders in Adults

Dan Ehninger,¹ Weidong Li,¹ Kevin Fox,² Michael P. Stryker,³ and Alcino J. Silva^{1,*}

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²Cardiff School of Biosciences, Cardiff University, Museum Avenue, Cardiff CF10 3US, UK

³Department of Physiology, W.M. Keck Foundation Center for Integrative Neuroscience, University of California, San Francisco, San Francisco, CA 94143-0444, USA

*Correspondence: silvaa@ucla.edu

DOI 10.1016/j.neuron.2008.12.007

Lee et al., Nat Neurosci, 2014

Ehninger, Neuropharmacology, 2013

Ehninger et al., Trends Mol Med, 2011

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Silva & Ehninger, J Neurodev Disord, 2009

Ehninger et al., J Intellect Disabil Res, 2009

Ehninger et al., Neuron, 2008

Ehninger et al., Nat Med, 2008

Potential collaborative research topics

Where and when do genetic and environmental risk factors act to cause neuropsychiatric disease?

What are late-life manifestations of neurodevelopmental disorders?
How do neurodevelopmental factors predispose for the development of neurodegenerative diseases?

Acknowledgements



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