Unlocking the secrets to healthy aging and longevity

GoldLab Symposium 2024

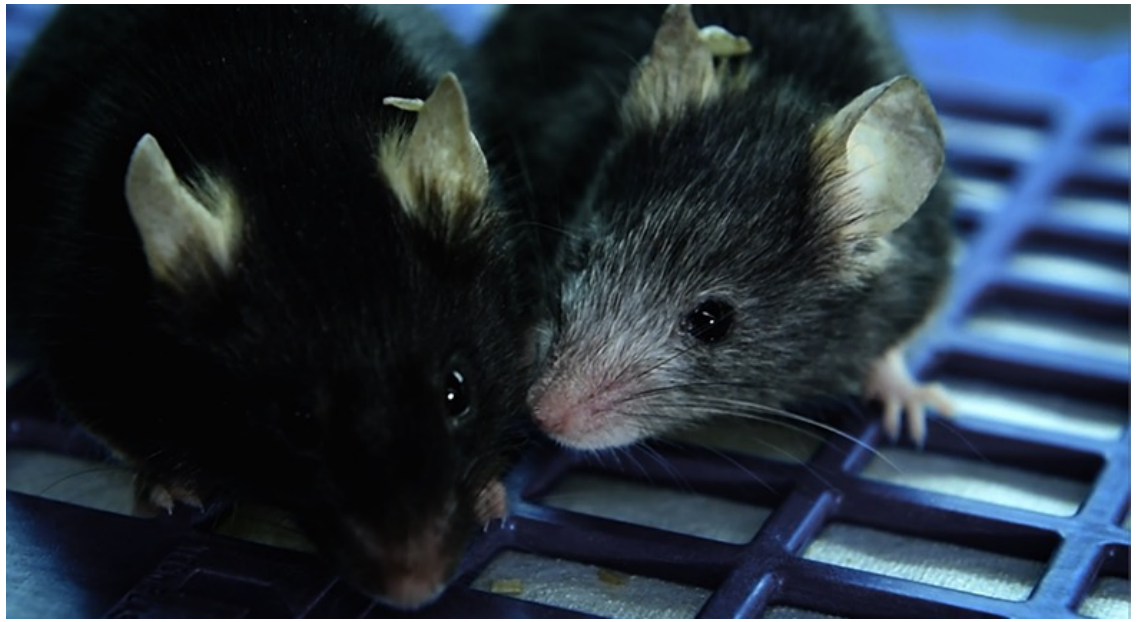
Hamilton Oh

PhD Student

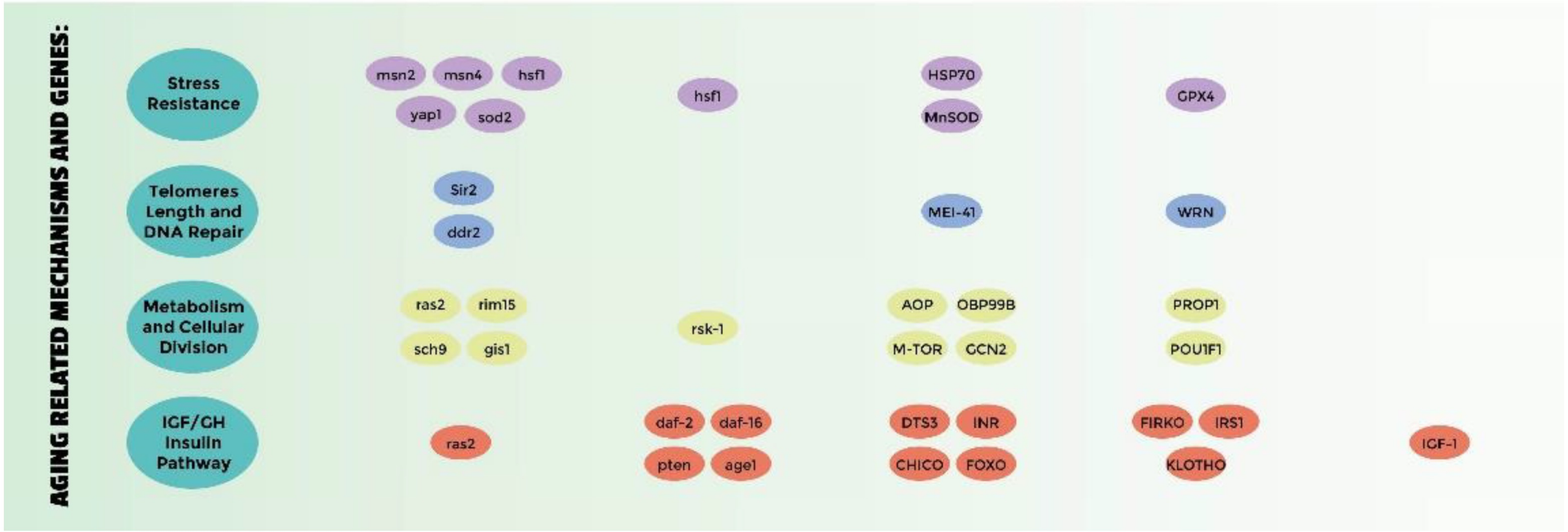
Tony Wyss-Coray lab

Stanford University

How do we age? Are there ways to slow aging and prevent disease?

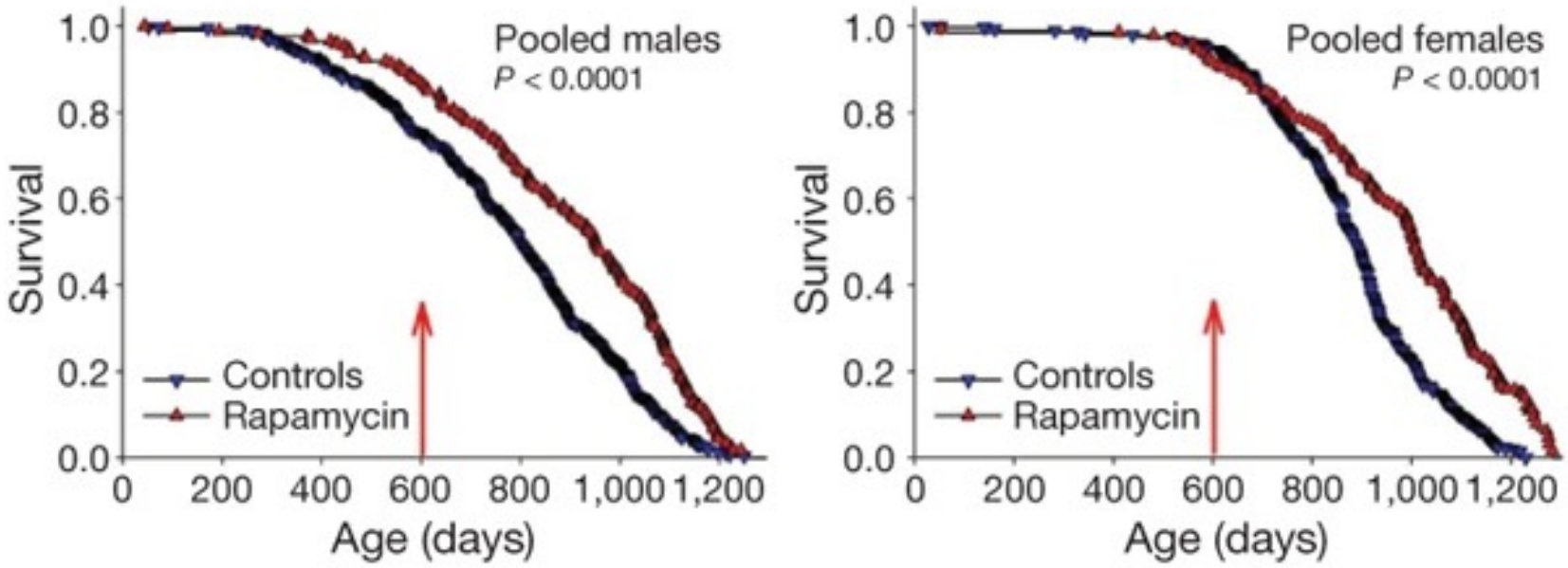


Animal studies have revealed evolutionarily conserved mechanisms of aging



Taormino, MDPI (2019)

Therapies that target aging mechanisms can extend health and lifespan in model organisms

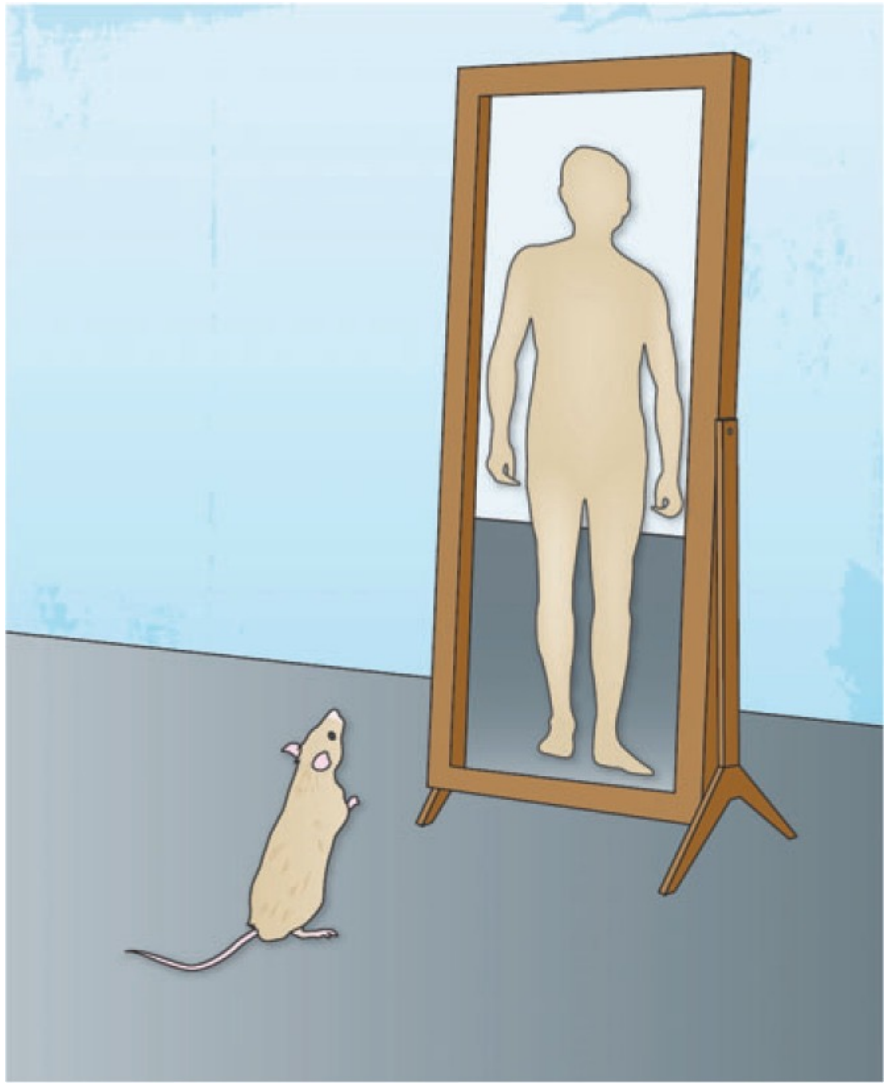


How do we translate these findings to humans?

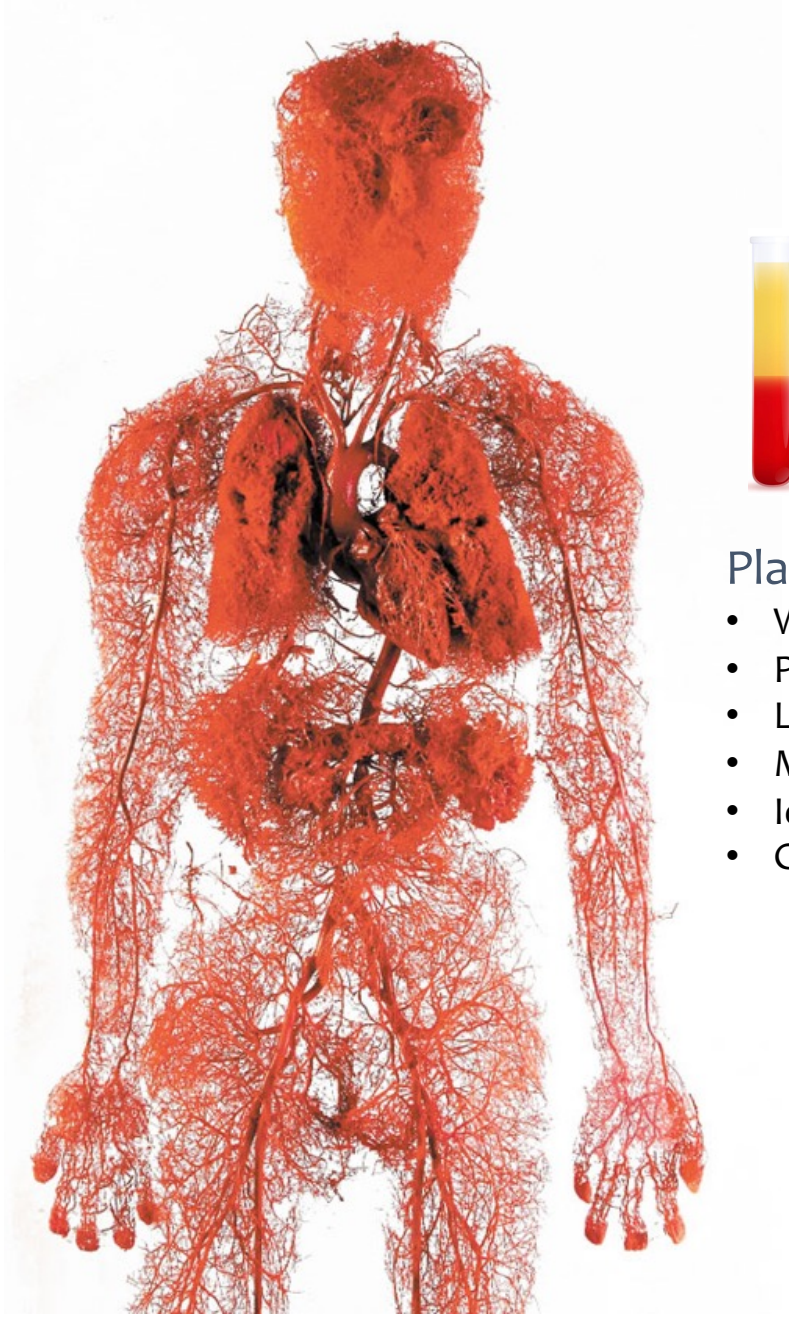
Harrison, Nature (2009)

First, we need a deeper molecular understanding of human aging

(80% of lab mice die from cancer)



Probing the blood to understand and measure human aging



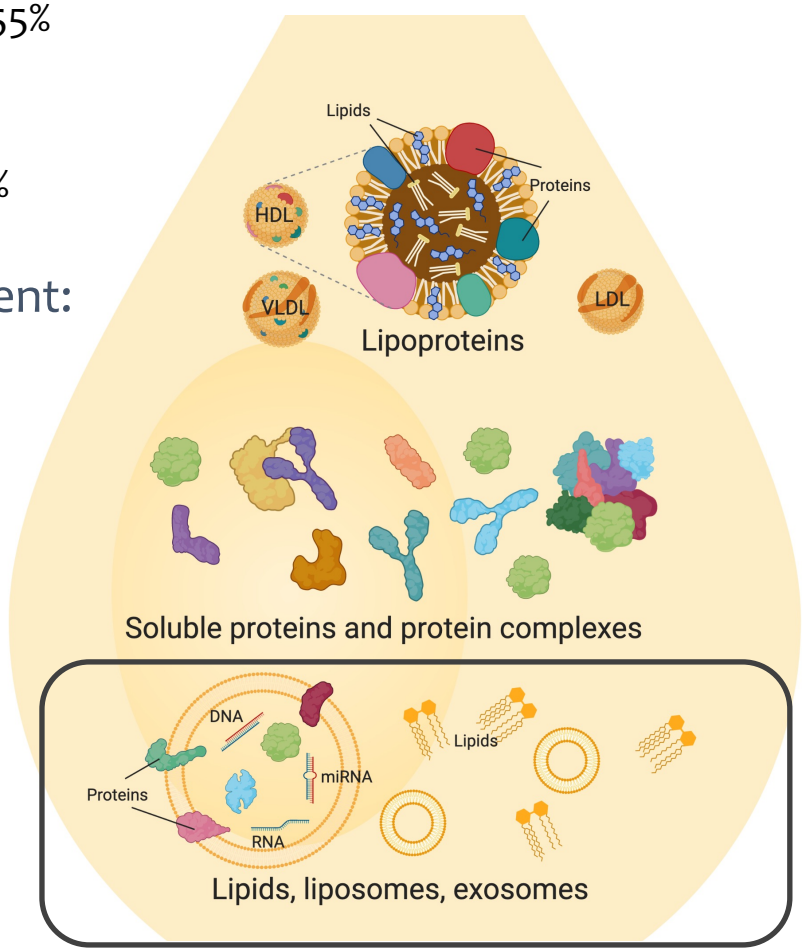
60,000 miles of blood vessels

Plasma - 55%

Blood Cells - 45%

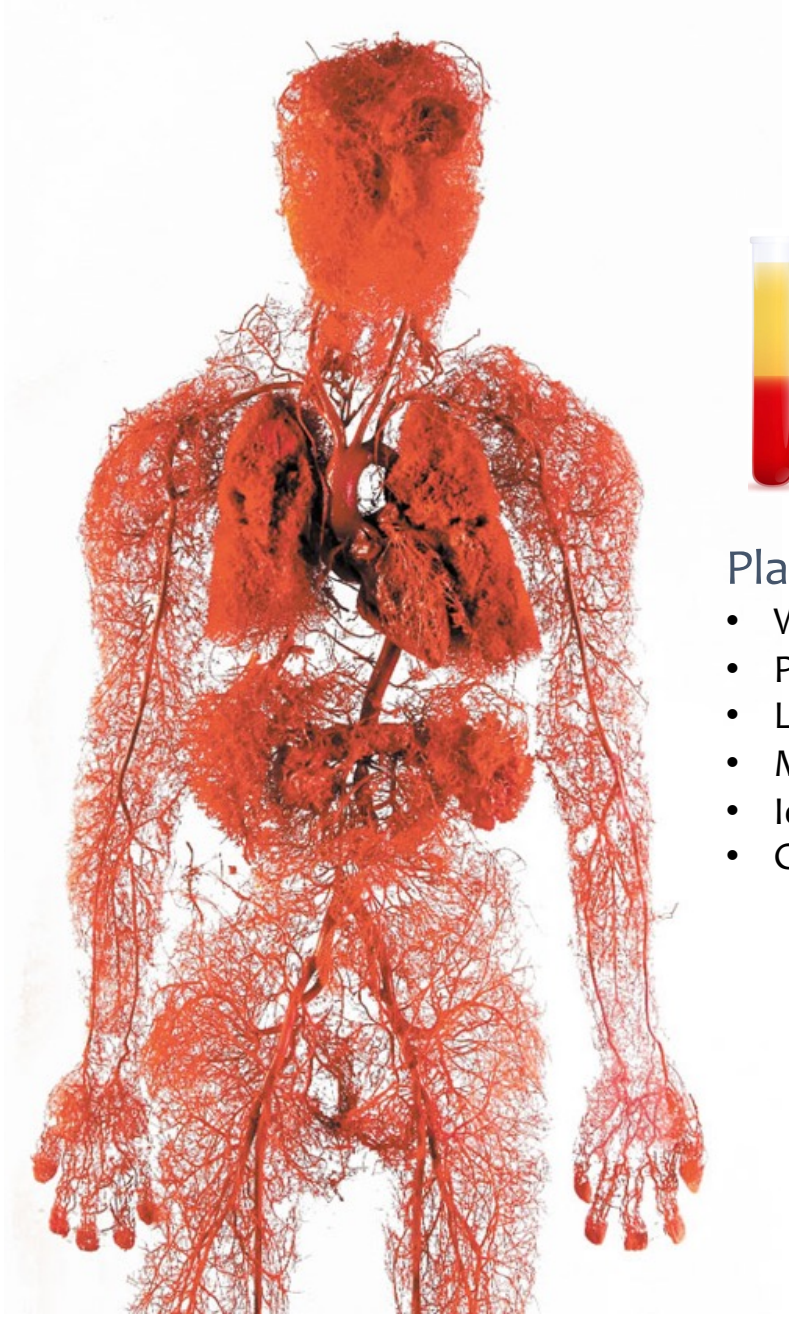
Plasma content:

- Water - 91%
- Proteins - 8%
- Lipids
- Metabolites
- Ions
- Gases



Blood cholesterol

Probing the blood to understand and measure human aging



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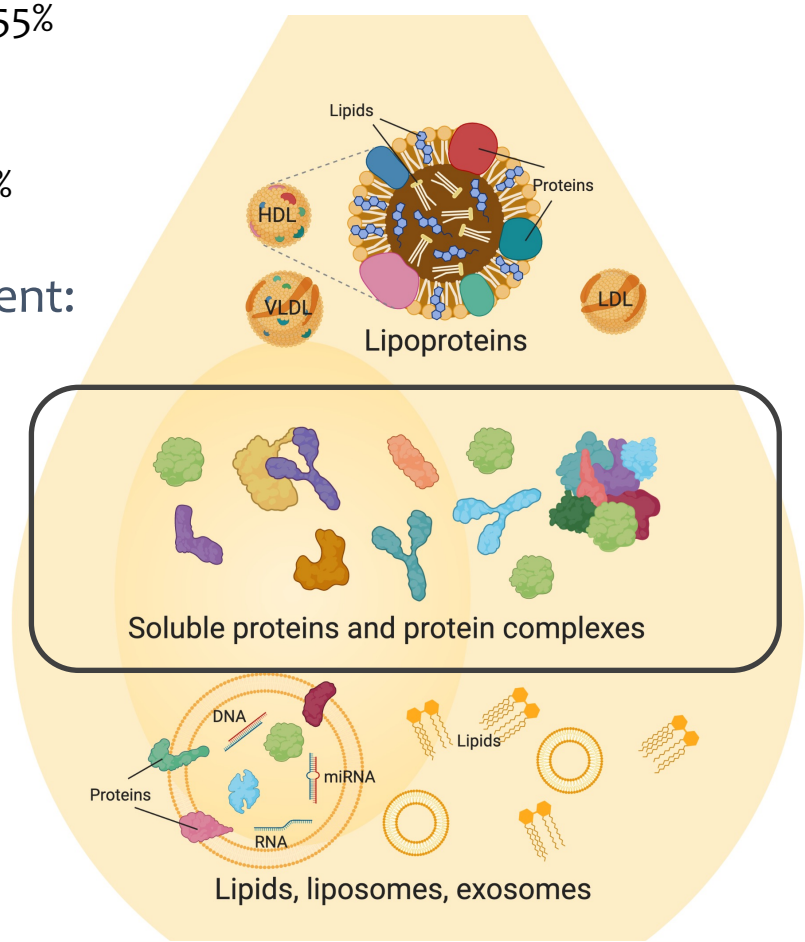
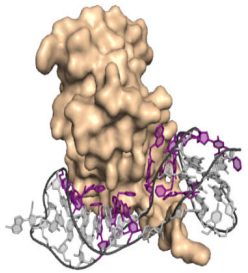
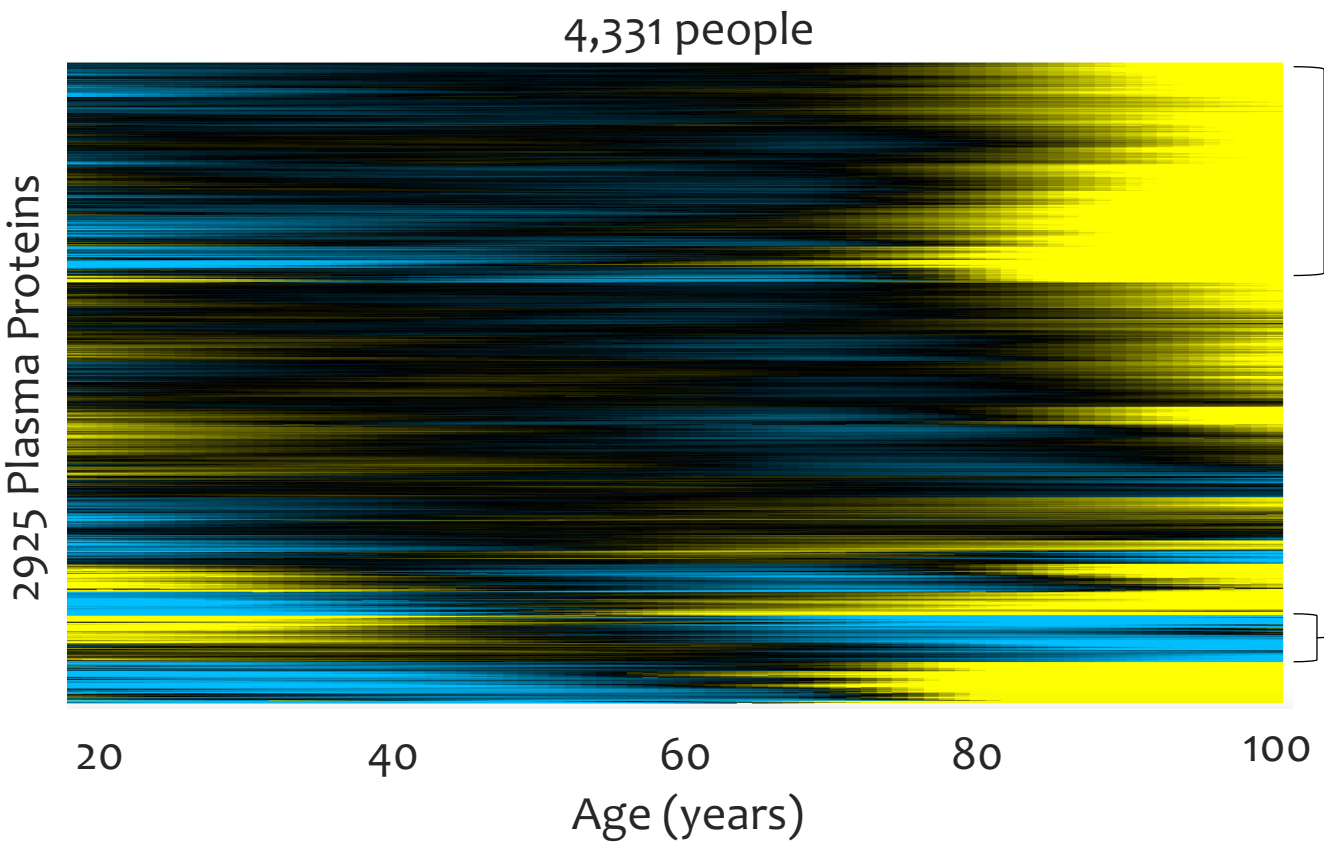
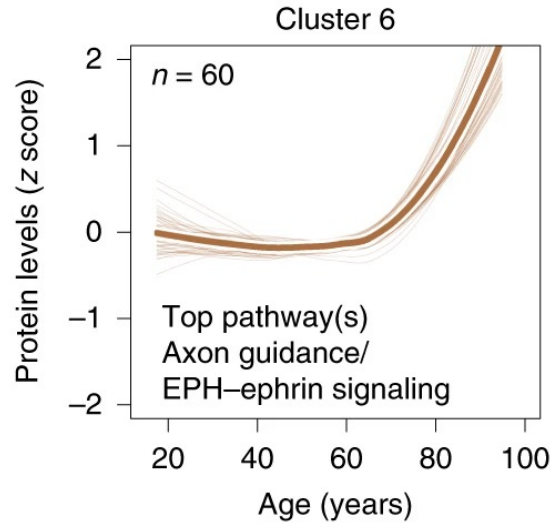


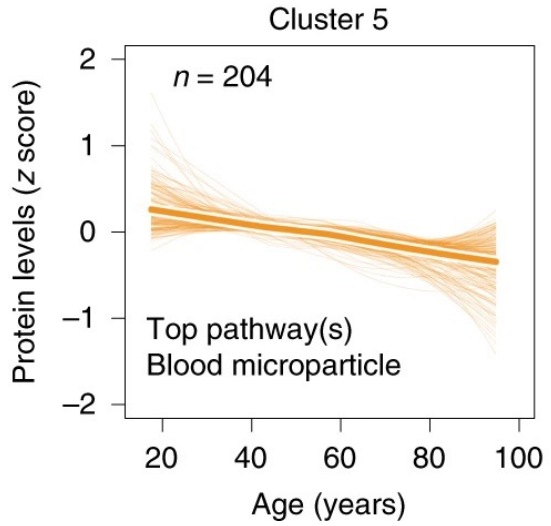
Somalogic Proteomics
Measure levels of 11,000 proteins using DNA aptamers



Thousands of proteins in our blood change in concentration with age



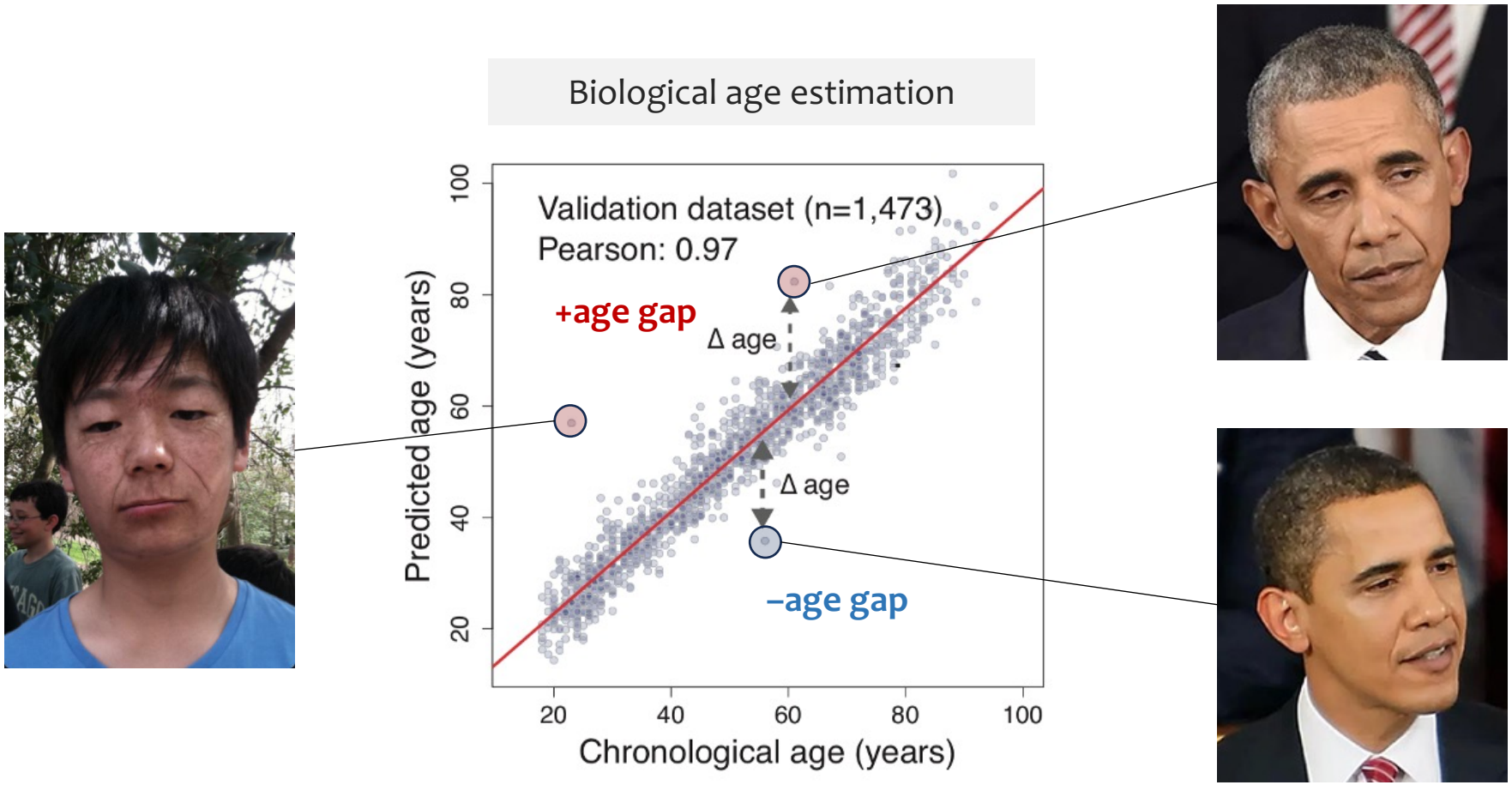




Benoit Lehallier

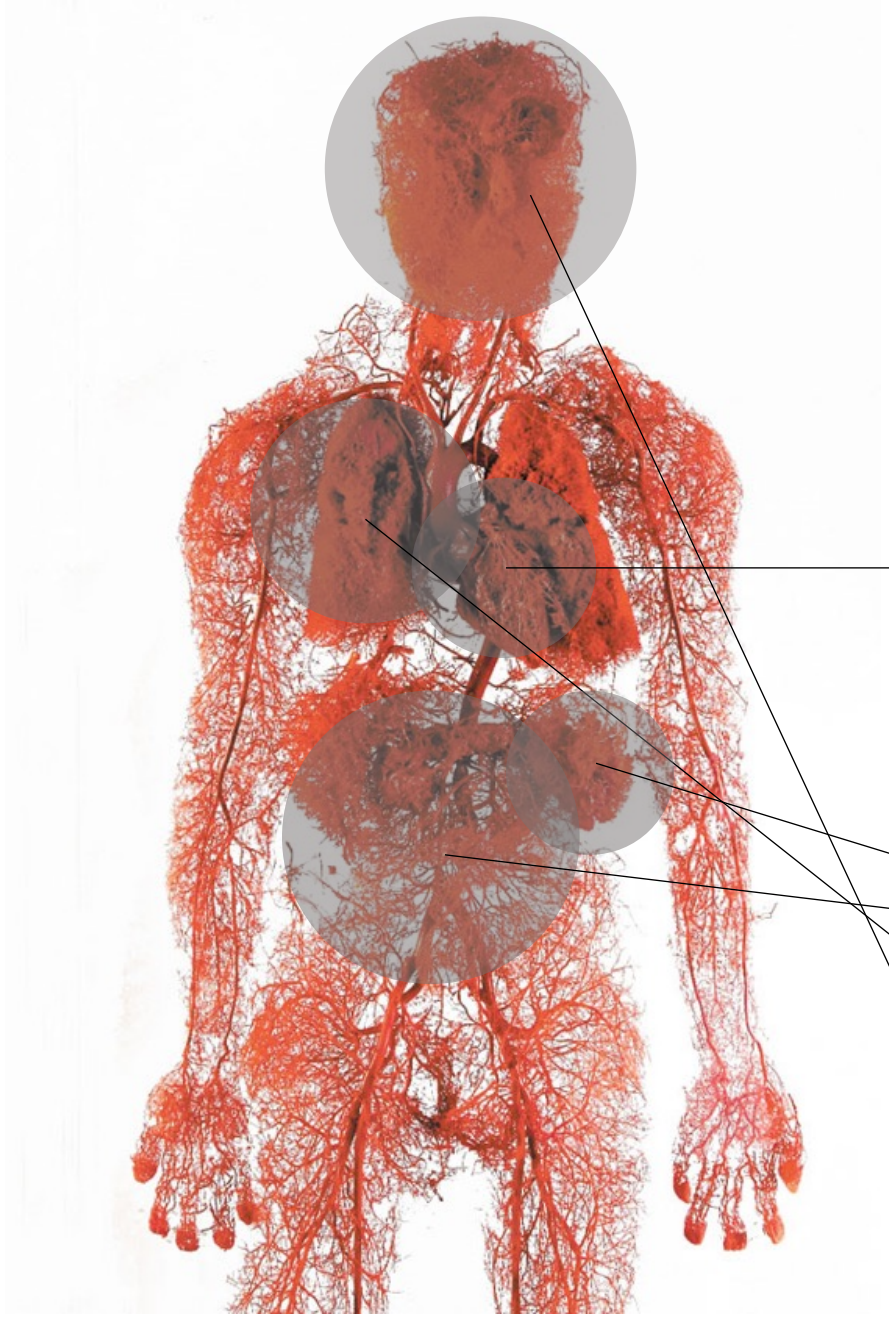
Lehallier, Nature Medicine (2019)

These proteins can provide information about how fast or slow we are aging



Lehallier, Nature Medicine (2019)

Human aging is multifaceted



What do people die from? Causes of death globally in 2019

Our World in Data

The size of the entire visualization represents the total number of deaths in 2019: 55 million.
Each rectangle within it is proportional to the share of deaths due to a particular cause.

74% died from noncommunicable diseases

14% died from infectious diseases

33% died from heart diseases
Heart attacks, strokes, and other cardiovascular diseases.
Per year: 18.5 million deaths
Per average day: 50,850 deaths

18% Cancers
Per year: 10 million deaths
Per average day: 27,600 deaths

7% Chronic respiratory diseases
COPD, Asthma, and others

4.5% Digestive diseases
Cirrhosis and others

2.7% Diabetes

3.9% Neurological diseases
Alzheimer's, Parkinson's, epilepsy, and others

5.7% Other noncommunicable diseases

4.4% Pneumonia
and other lower respiratory diseases
Per year: 2.5 million deaths
Per average day: 6800 deaths

2.7% Diarrheal diseases
Per year: 1.5 million deaths
Per average day: 4200 deaths

2% Tuberculosis

1.5% HIV/AIDS

1.1% Malaria

2.1% other infectious diseases

3.3% Neonatal deaths
babies who died within the first 28 days of life

0.4% Maternal deaths

0.4% Nutritional deficiencies

2.3% Transport accidents
Per year: 1.3 million deaths
Per average day: 3500 deaths

3.1% Other accidents
including falls, drownings, and fires.

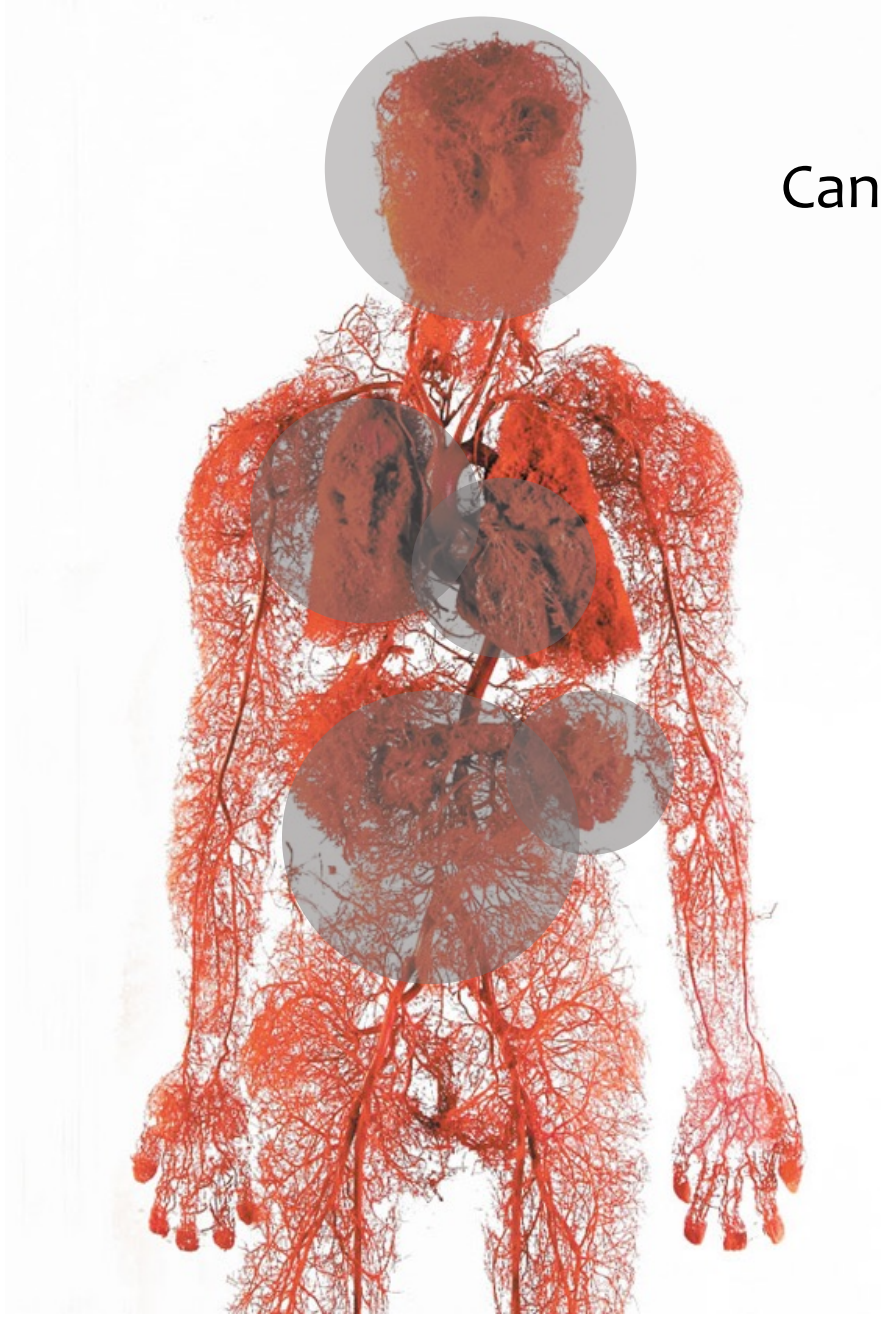
1.3% Suicides Per year: 760,000 deaths Per average day: 2080 deaths

0.7% Homicides Per year: 415,000 deaths Per average day: 1140 deaths

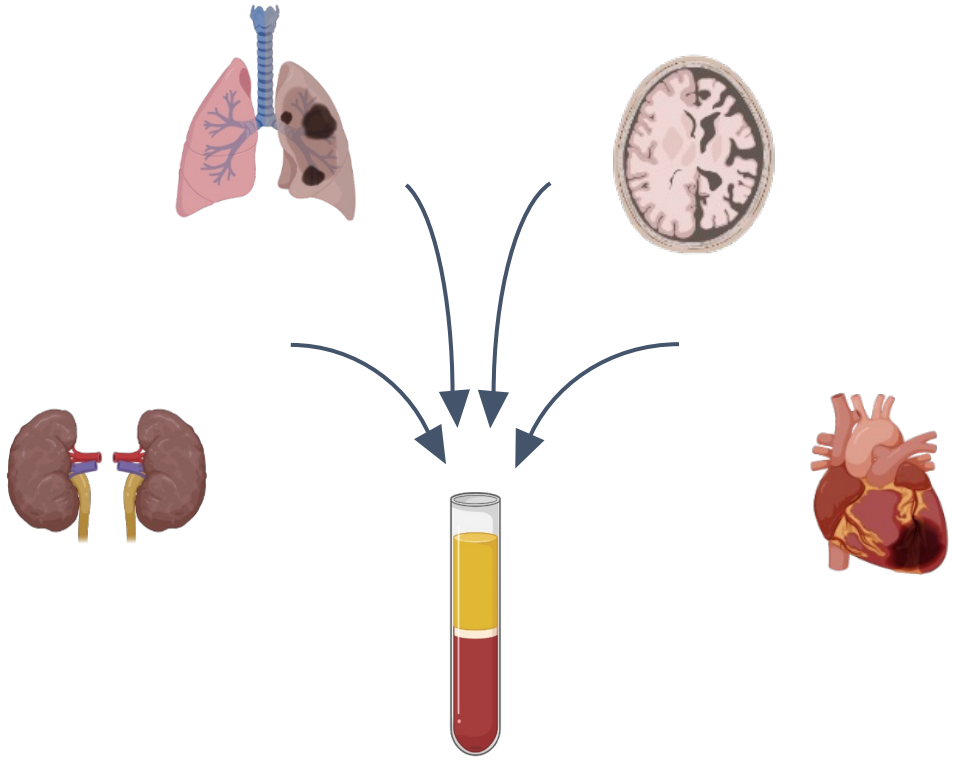
0.2% War battle deaths | 0.05% Terrorism

Less than 1% died due to interpersonal violence

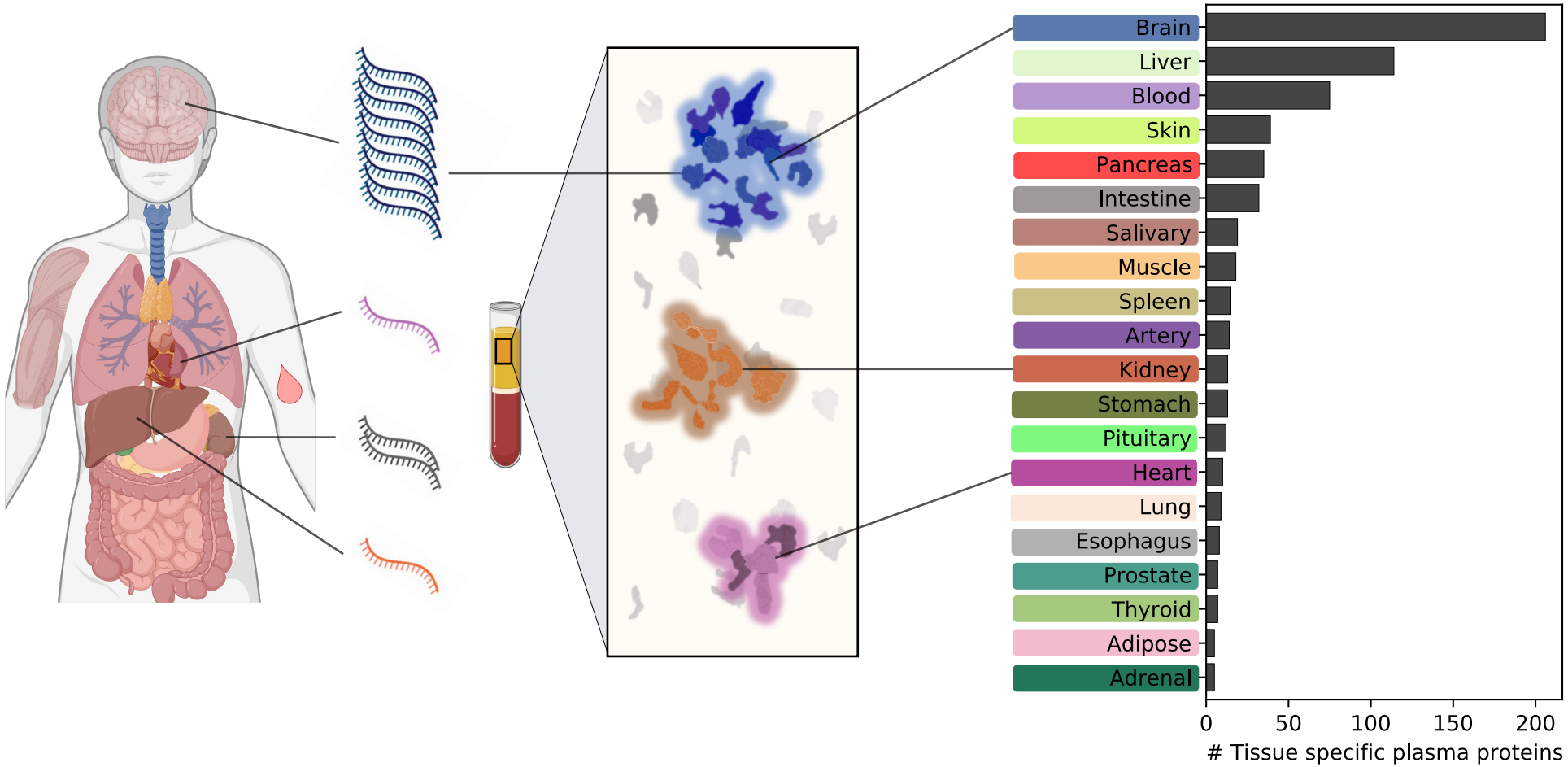
Data source: IHME Global Burden of Disease and Global Terrorism Database
OurWorldinData.org – Research and data to make progress against the world's largest problems.



Can we estimate biological age at organ-resolution?



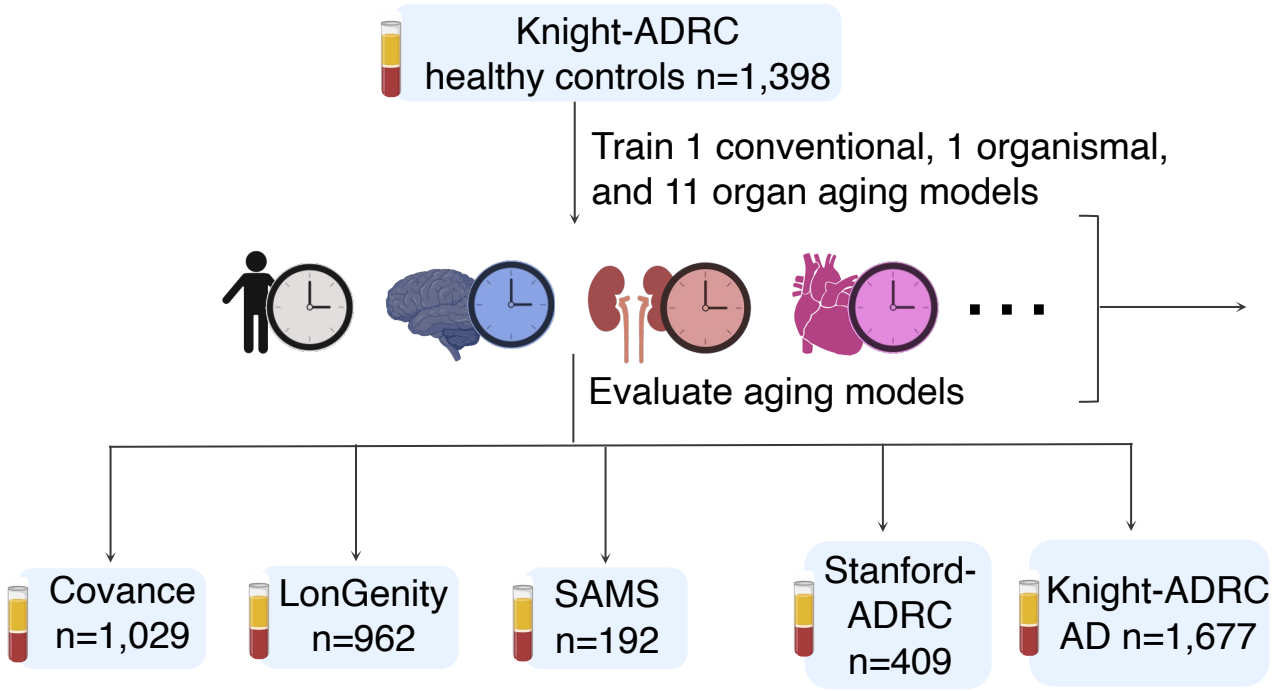
Mapping the origins of the plasma proteome

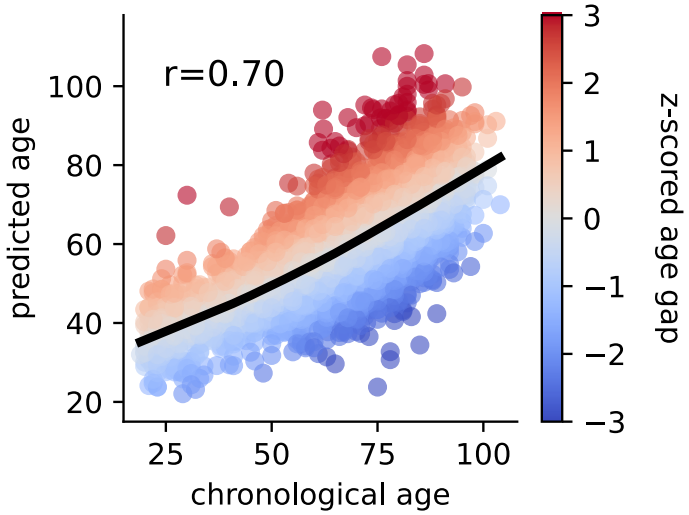


Jarod Rutledge

Oh and Rutledge, Nature 2023

Deriving estimates of organ-specific biological age

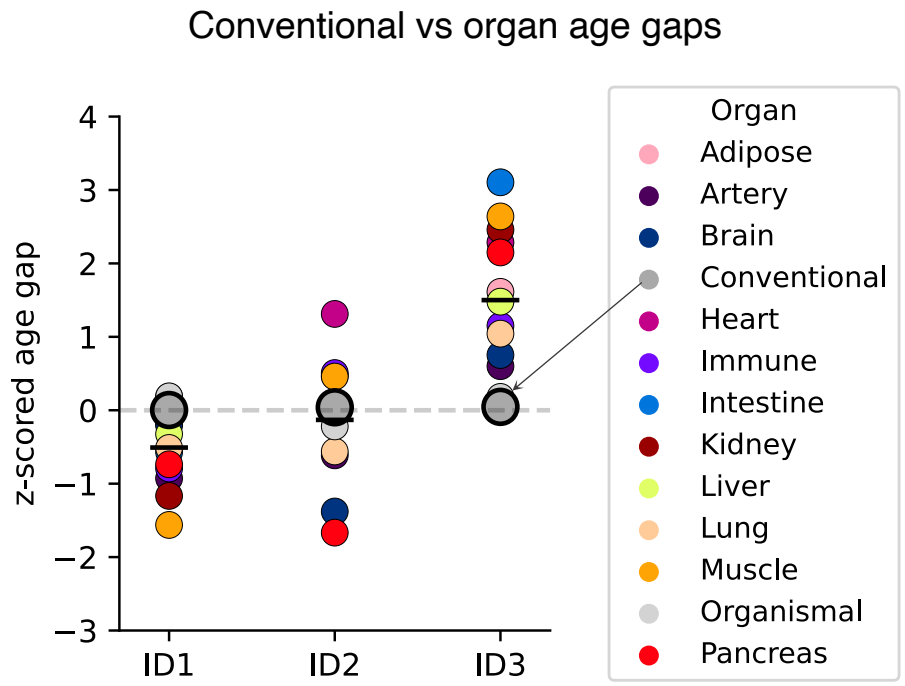


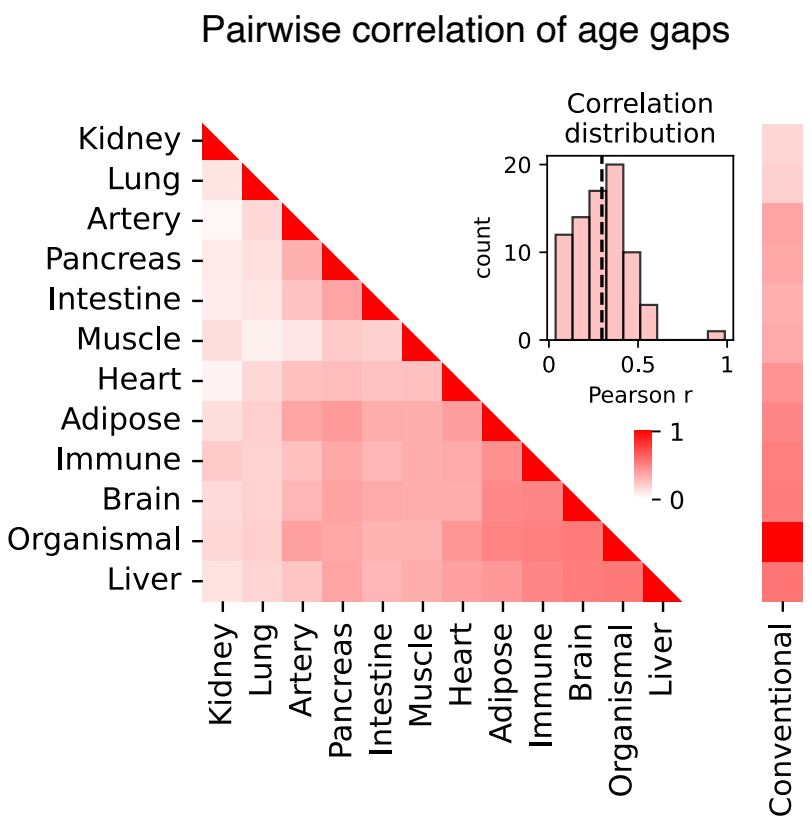


Carlos Cruchaga, Nir Barzilai, Sofiya Milman, Anthony Wagner, Beth Mormino, Somalogic

Oh and Rutledge, Nature 2023

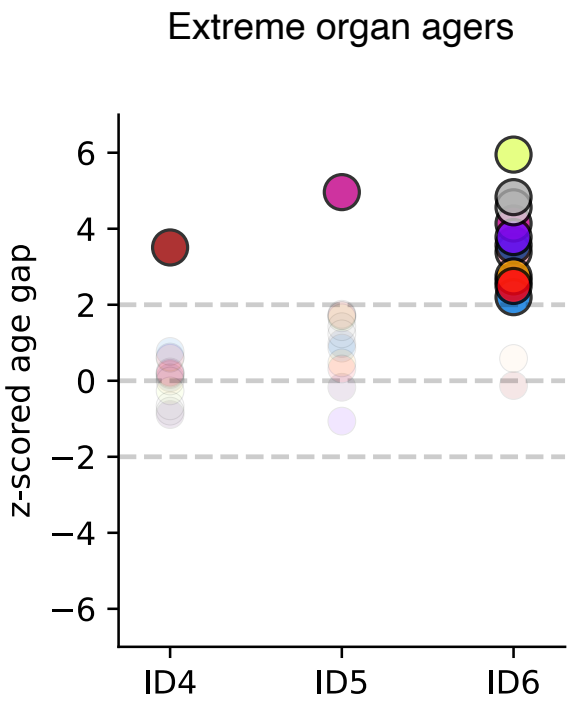
Organ age gaps are only mildly correlated

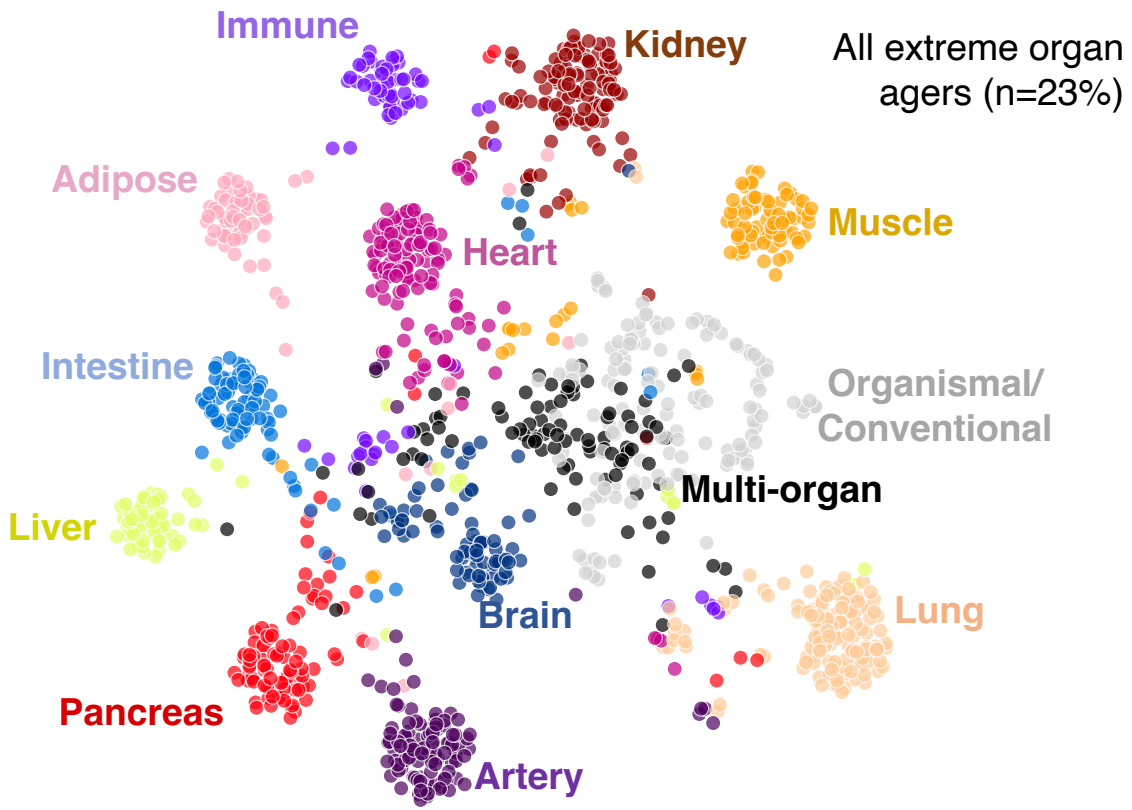




Oh and Rutledge, Nature 2023

Different types of agers in the population





Oh and Rutledge, Nature 2023

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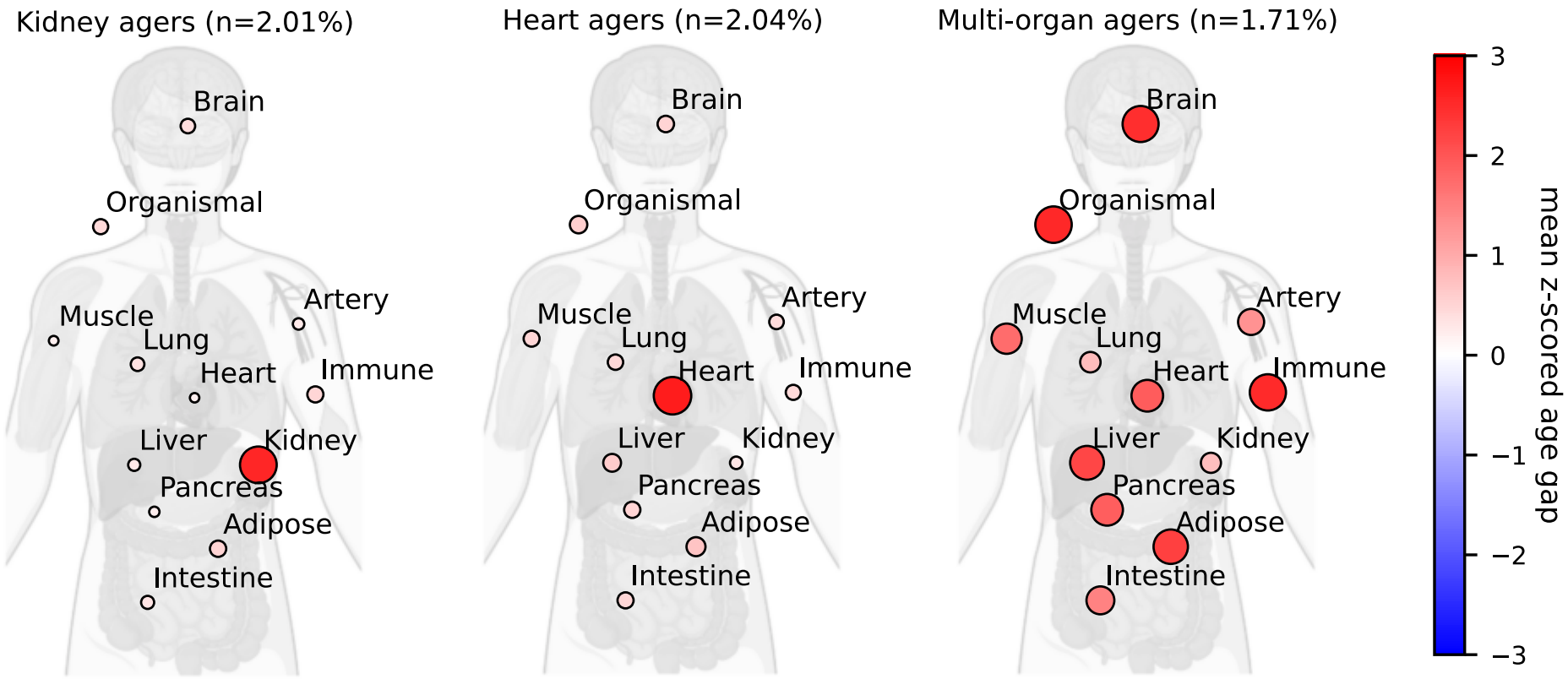
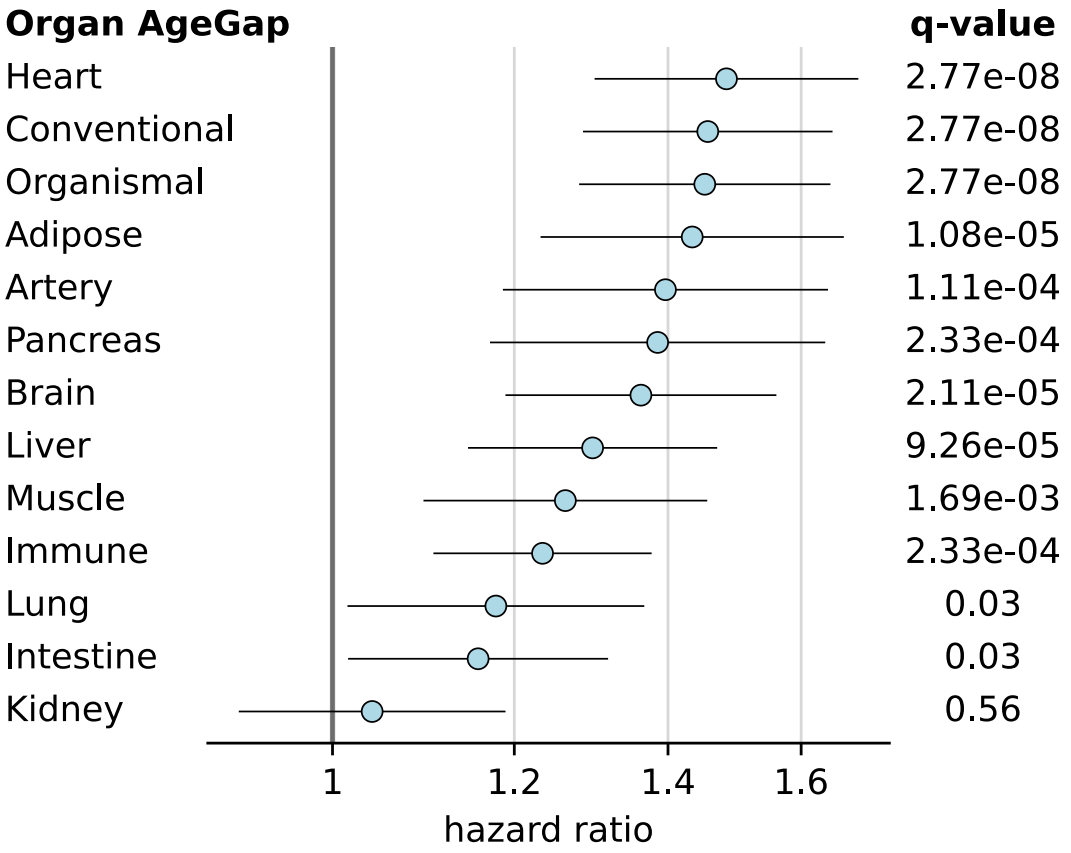


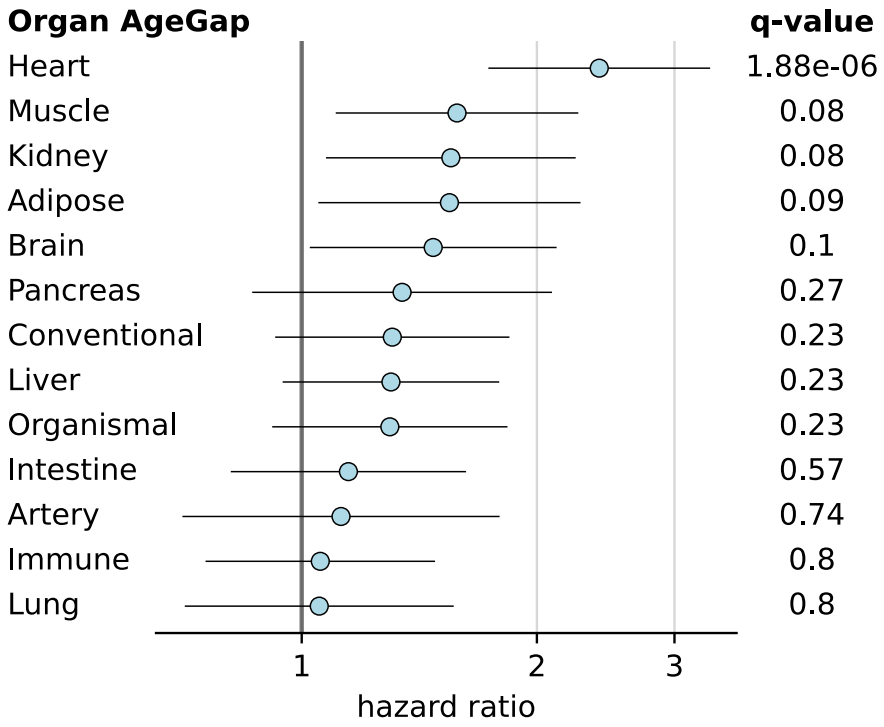
Oh and Rutledge, Nature 2023

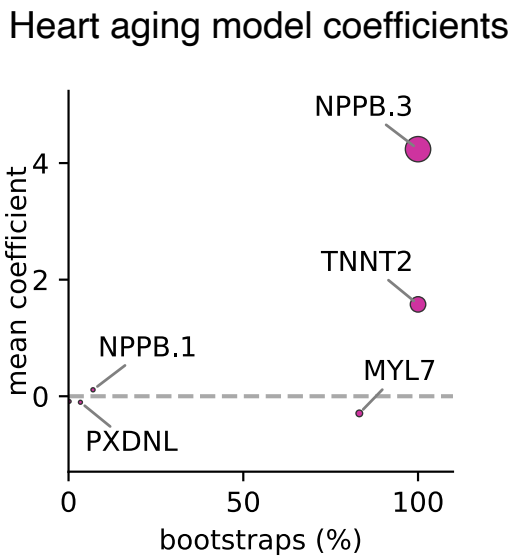
Organ aging is associated with future mortality risk

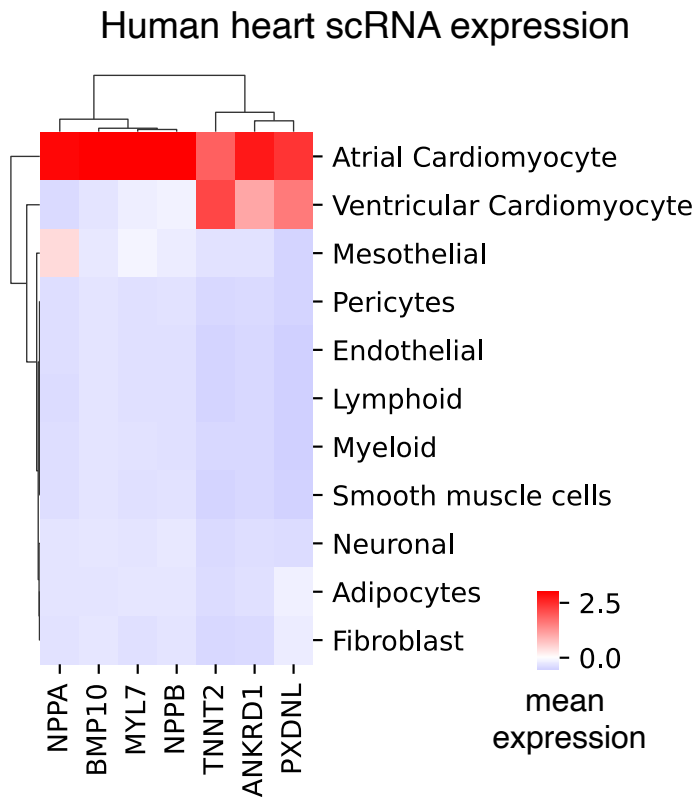


Oh and Rutledge, Nature 2023

Heart aging is associated with future heart failure





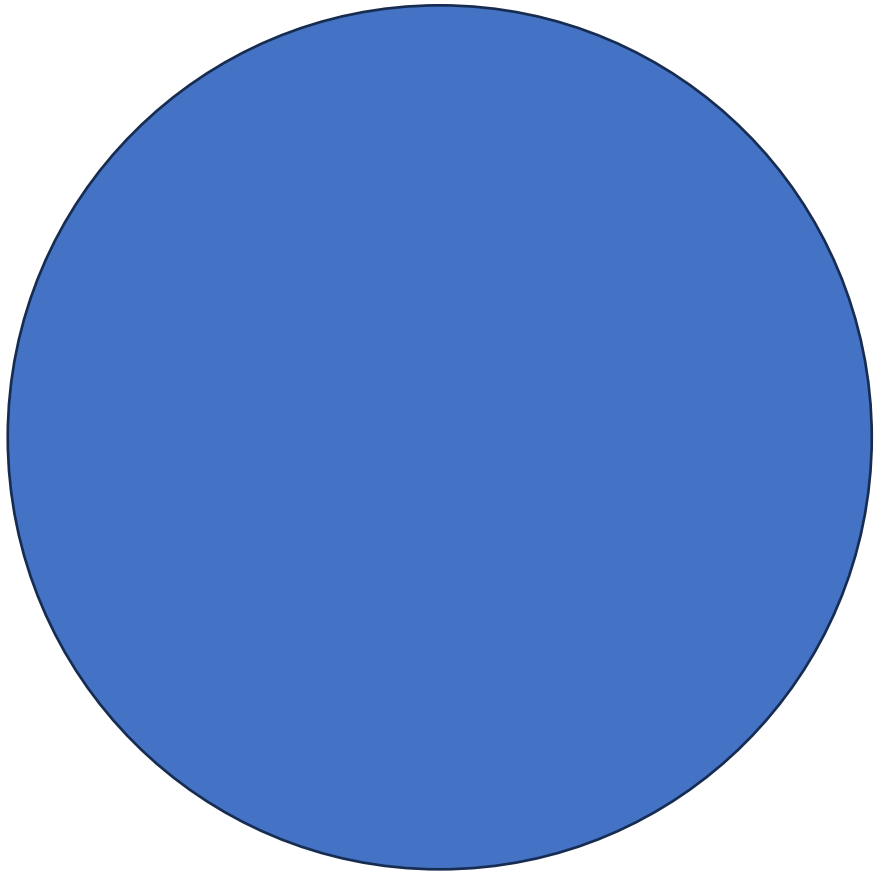


Oh and Rutledge, Nature 2023

Organ aging in the UK Biobank

UK Biobank
(n=50,000)

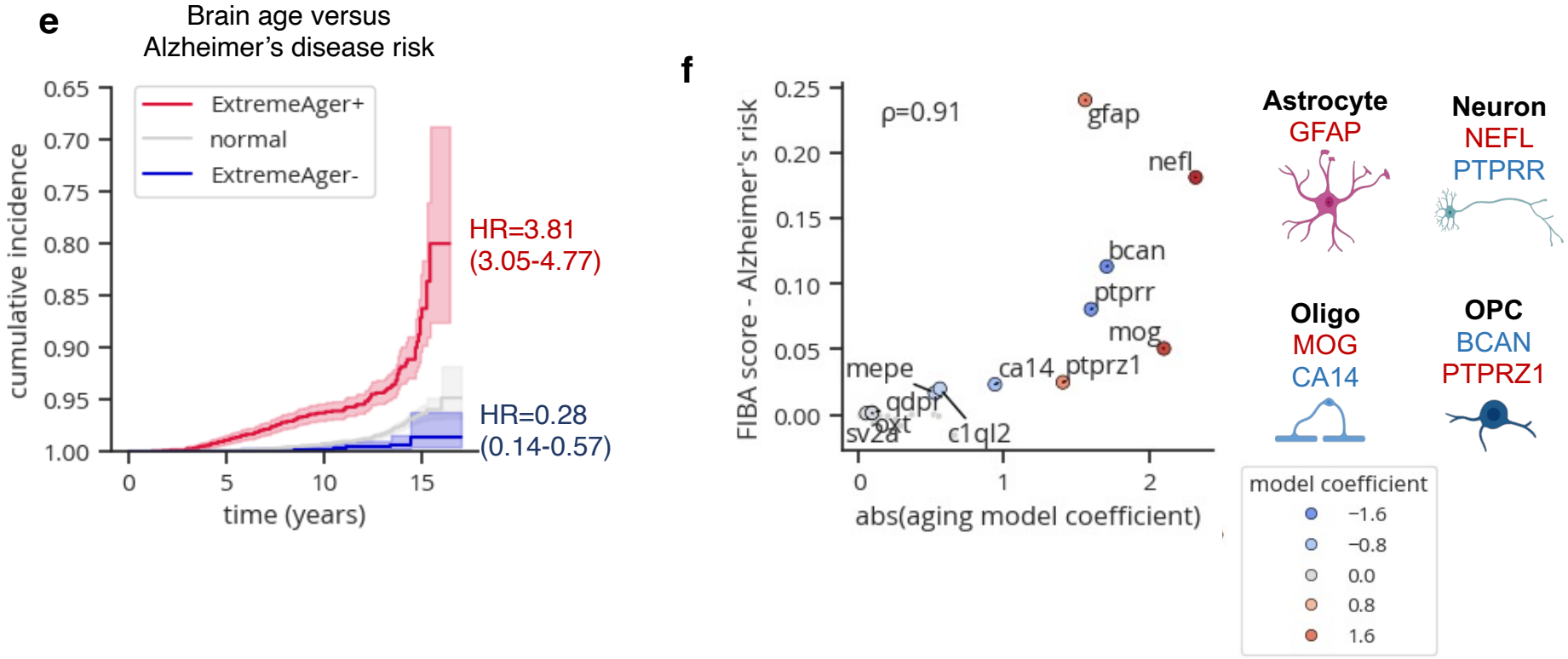
Our Nature study
(n=5,700)



Yann Le Guen

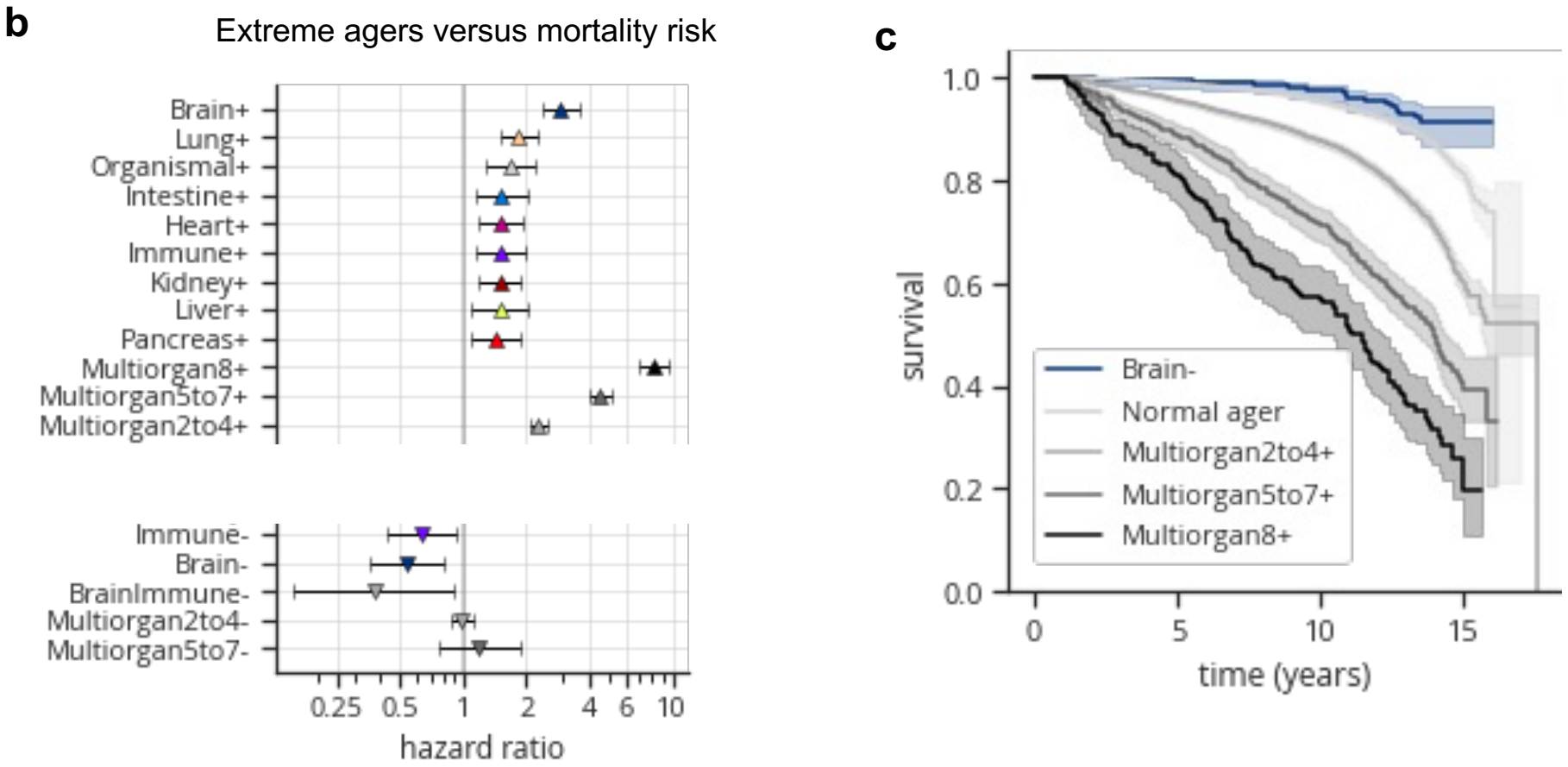
Unpublished

Brain age predicts future Alzheimer's disease



Unpublished

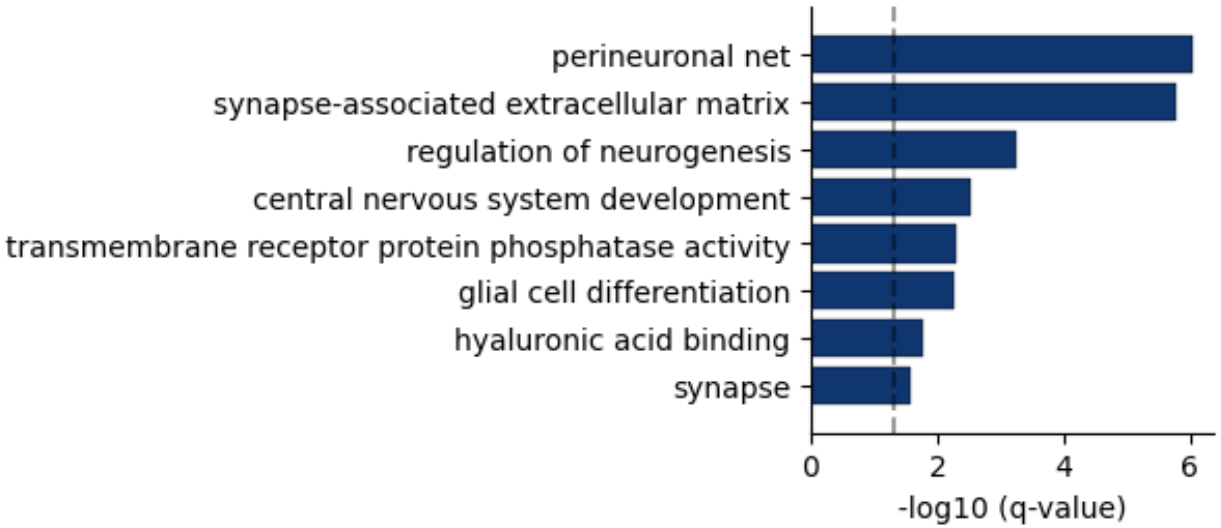
Accumulation of aging organs compounds risk of death and young immune system and brain reduces risk of death



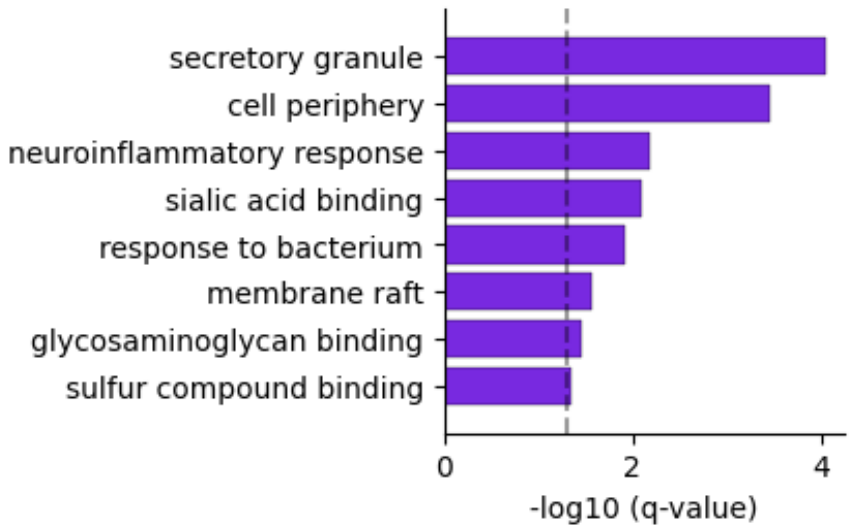
Unpublished

The biology of brain and immune system aging

Top10 brain-longevity protein pathways

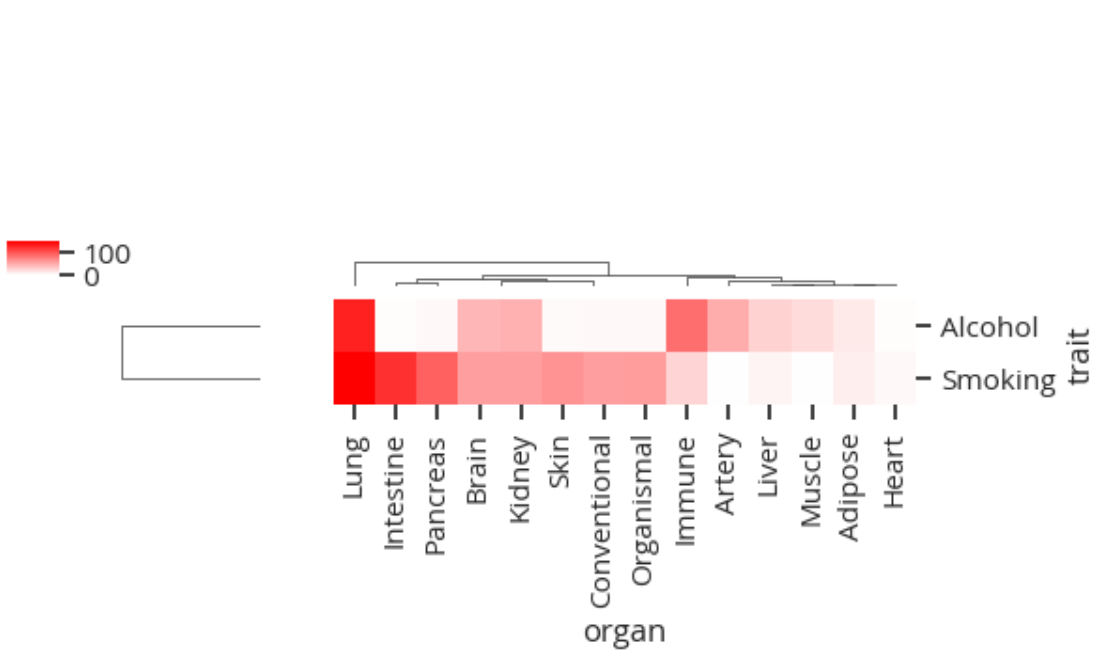


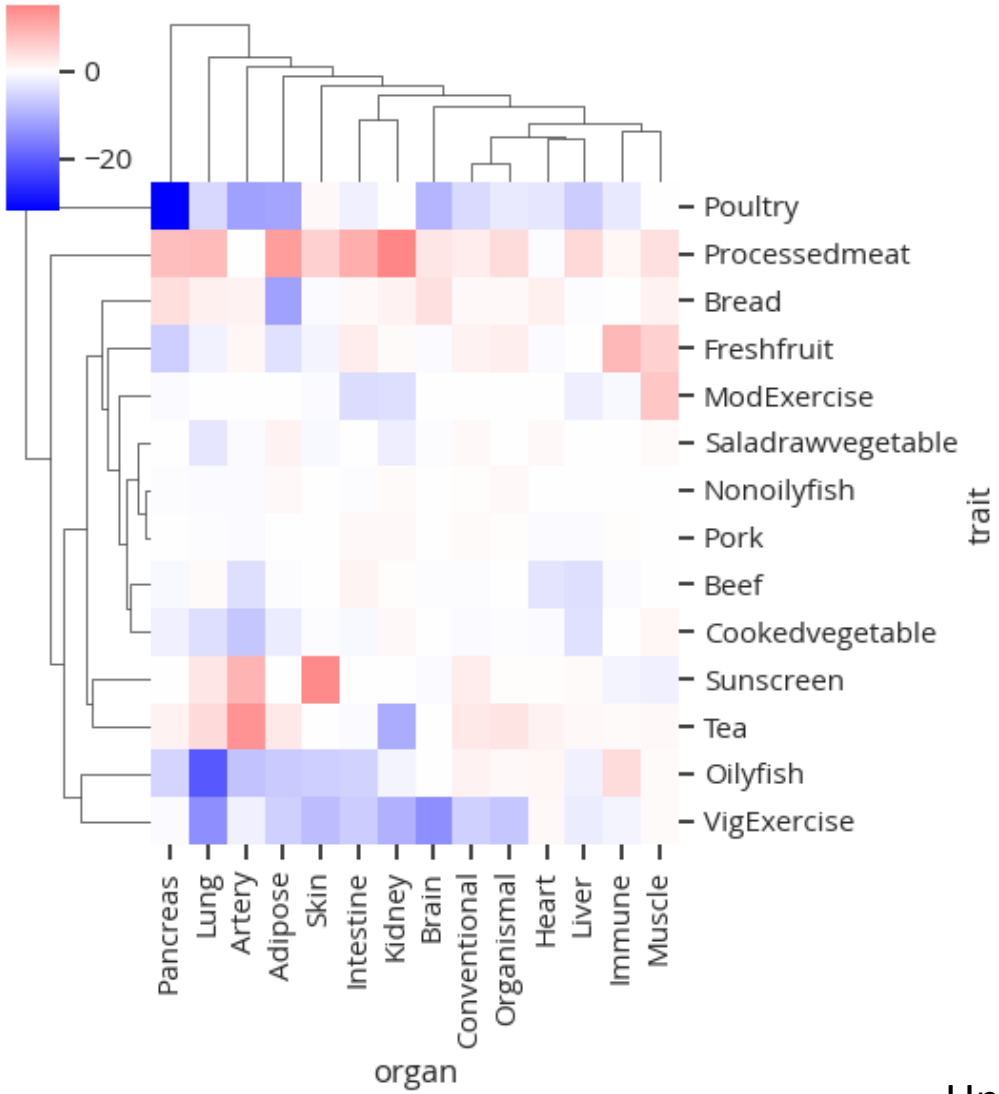
Top10 immune system-longevity protein pathways



Unpublished

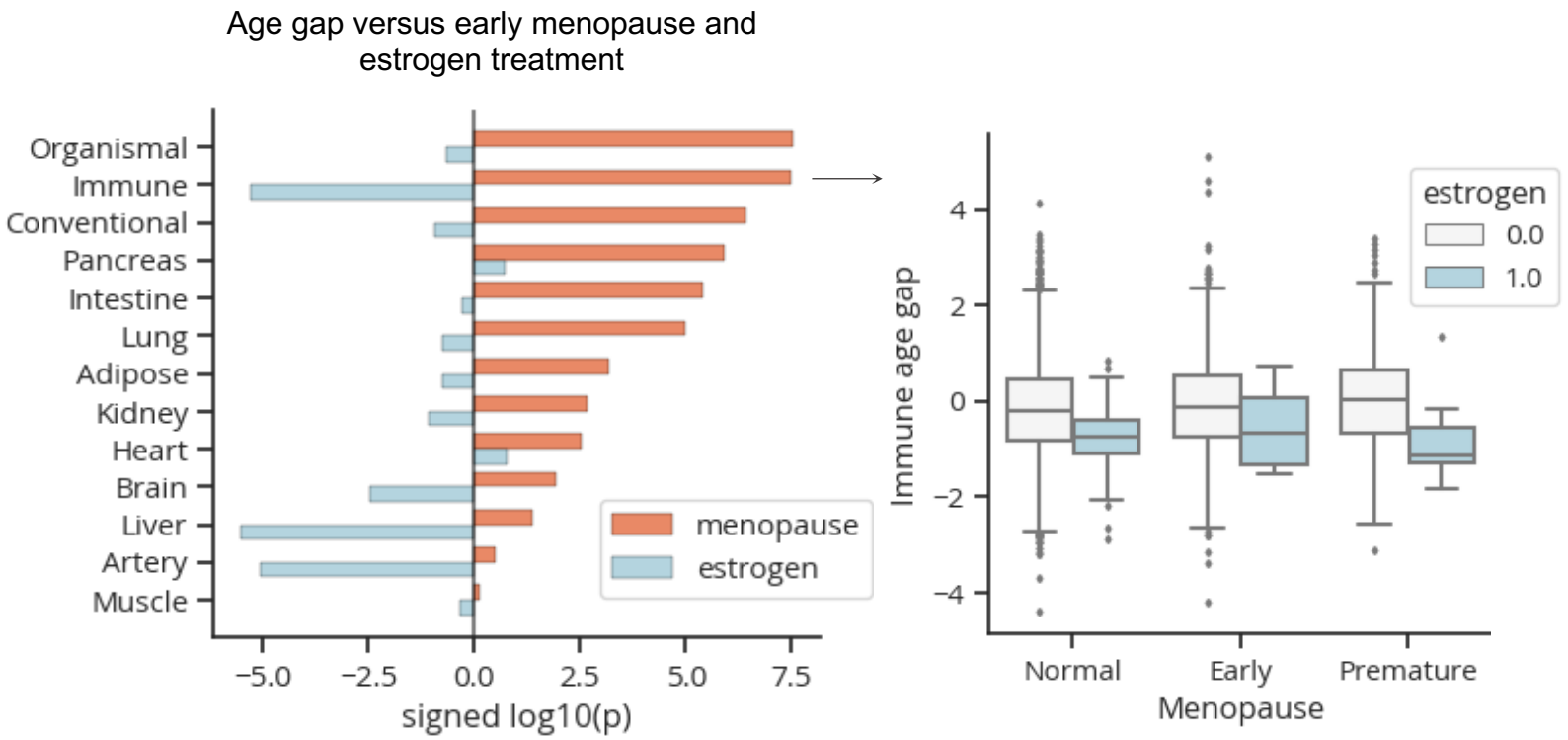
Organ aging is associated with lifestyle choices





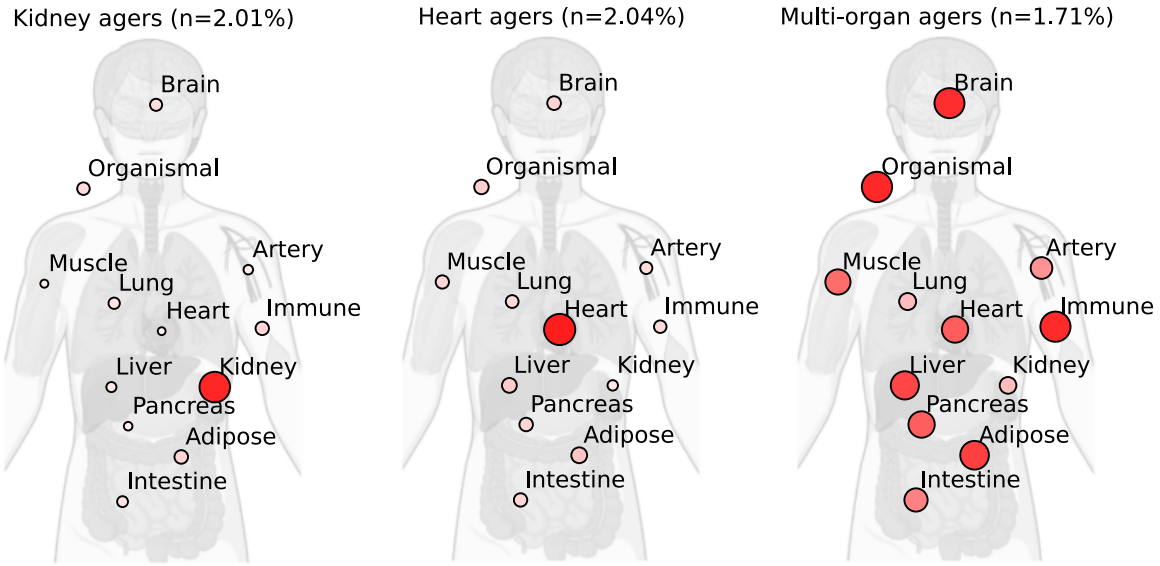
Unpublished

Estrogen treatment for post-menopausal symptoms is associated with immune system youth



Unpublished

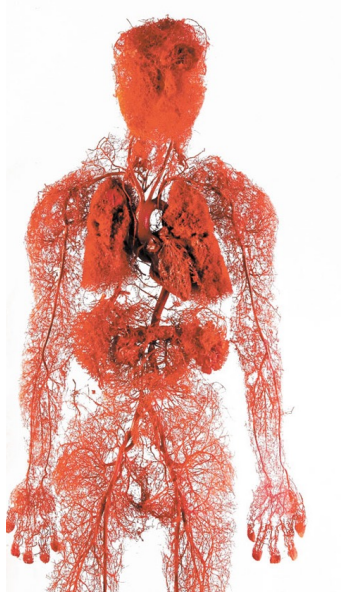
Monitoring organ aging in living people

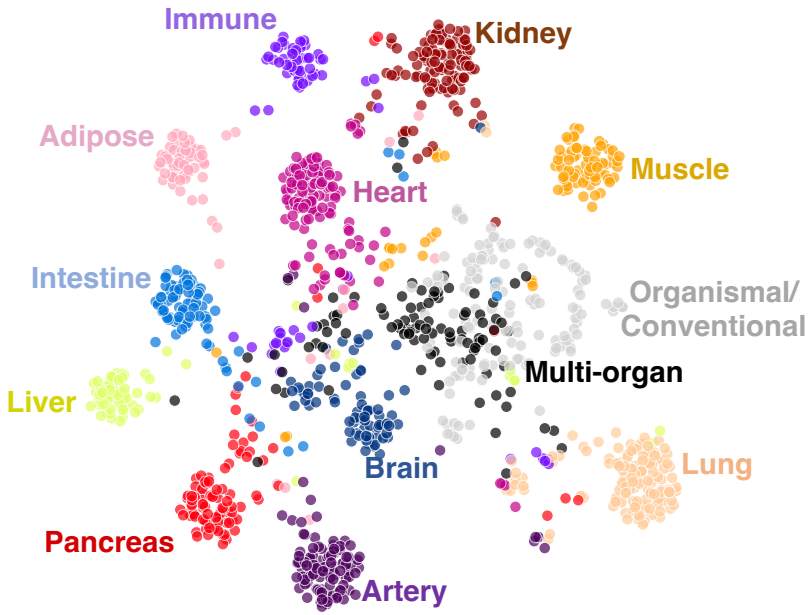


1. How do certain lifestyle interventions or drugs affect organ aging at an individual level?

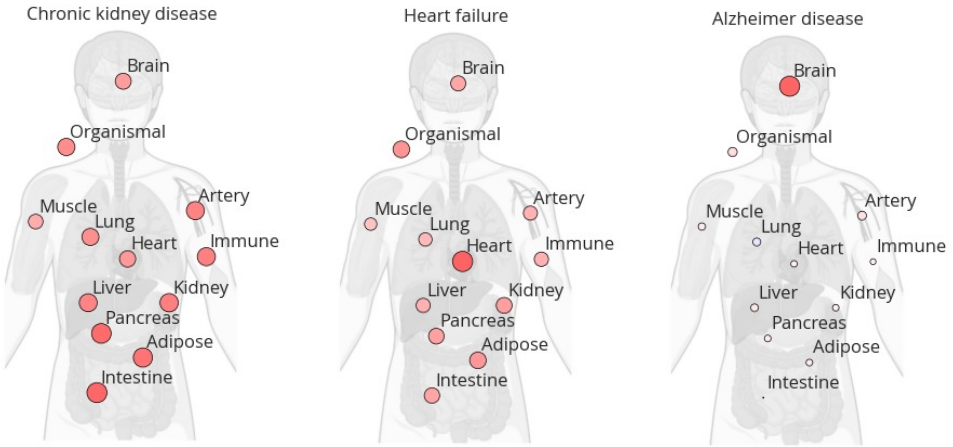
2. Do interventions rejuvenate the whole body or specific organs? Are there accelerated aging side effects in all/a subset of people?

3. Can the proteins we measure to monitor aging also be drug targets (ie. cholesterol)?

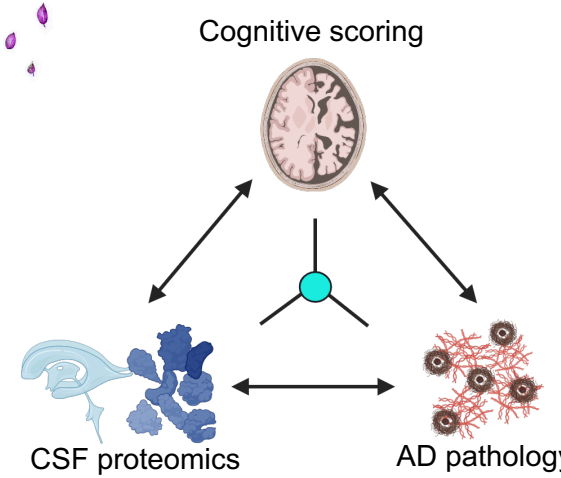


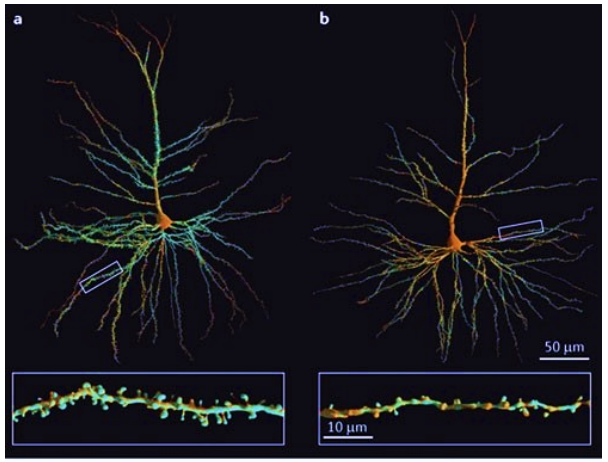


Organ aging in health and disease



Synaptic aging in Alzheimer's disease





Acknowledgments

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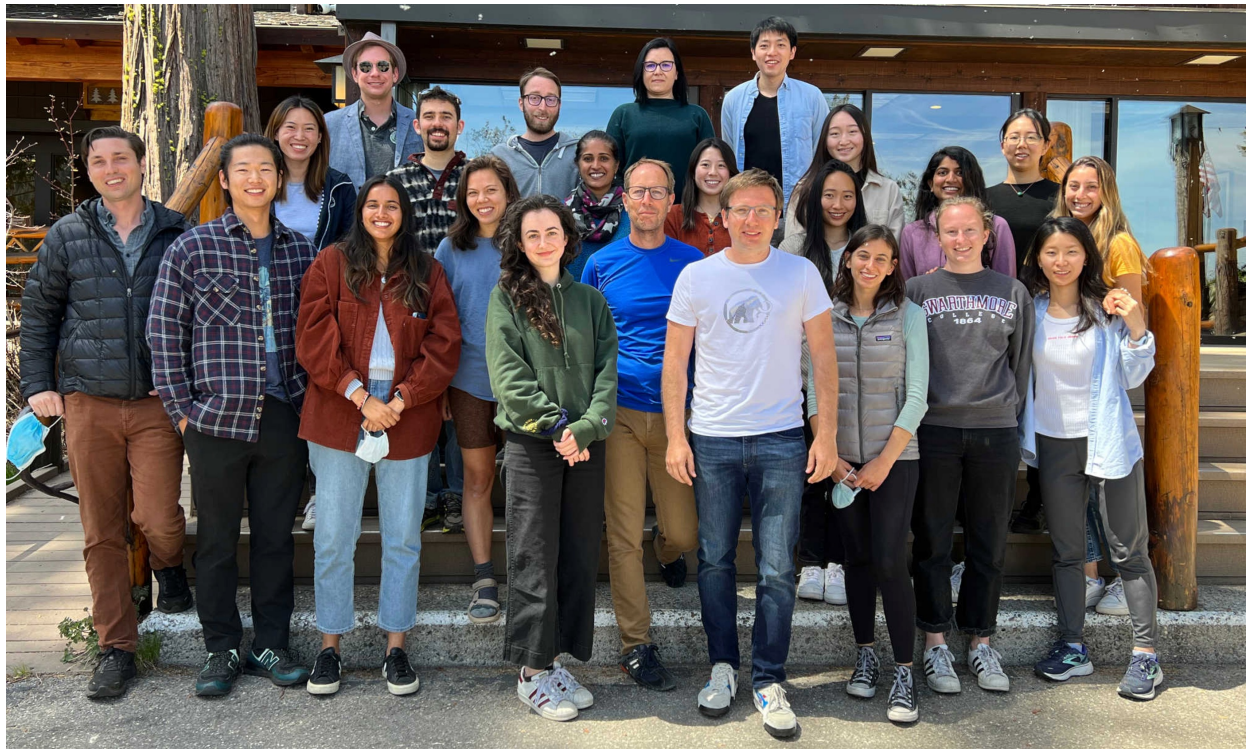
Amelia Farinas
Divya Channappa
David Gate

Collaborators

Anthony Wagner
Beth Mormino
Ola Abiose
Carlos Cruchaga lab
Nir Barzilai
Sofiya Milman



somalogic™

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NIH National Institutes of Health

NIH National Institute on Aging

NAN FUNG LIFE SCIENCES 南豐生命科技

ZENITH SOCIETY alzheimer's association

NSF GRFP