

Molekulare Manipulationen des Alterungsprozesses

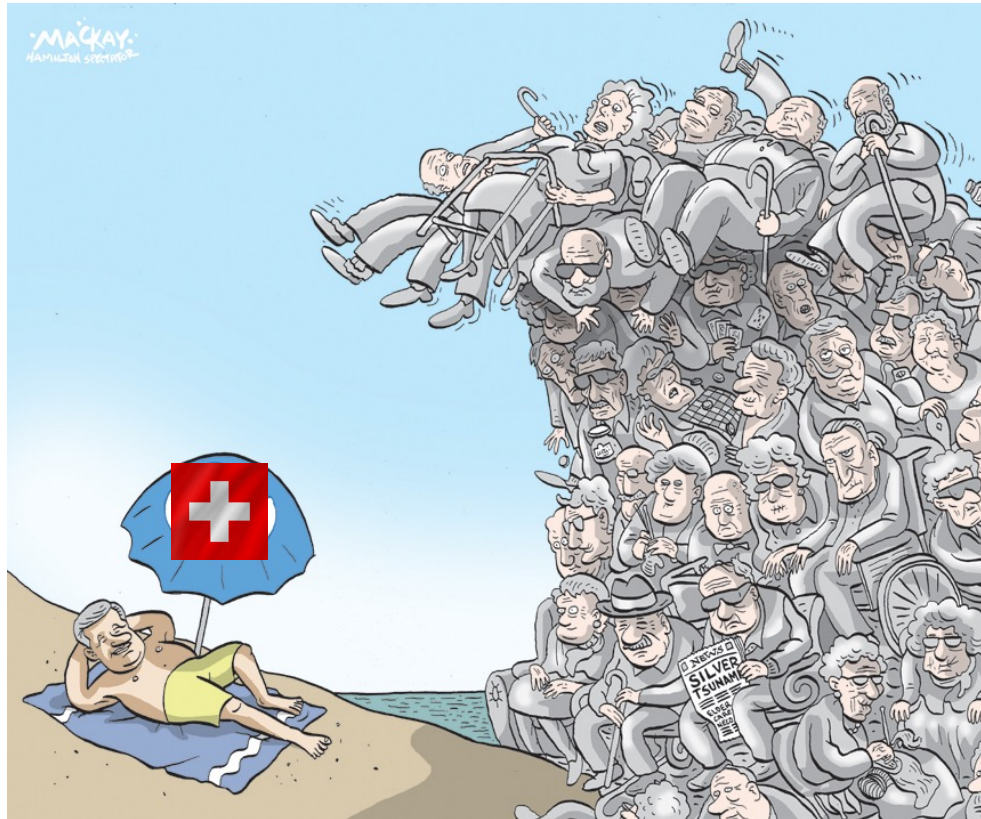
Collin Y. Ewald
 Institute of Translational Medicine
 Department of Health Sciences and Technology



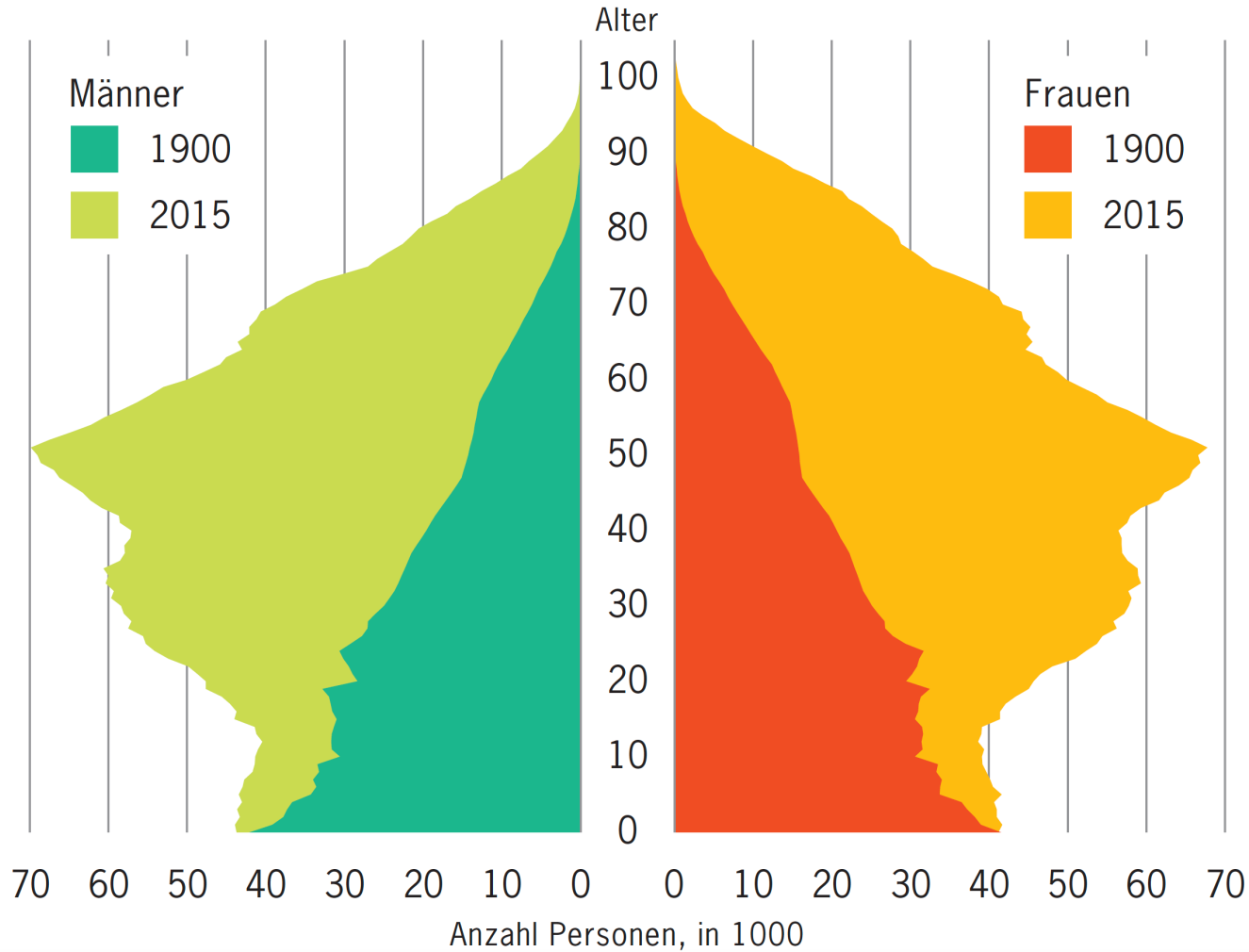
Major Challenge: Silver Tsunami

Prediction for 2030:

1 out 4 people will be older than 65 years
in Switzerland, Europe, or US

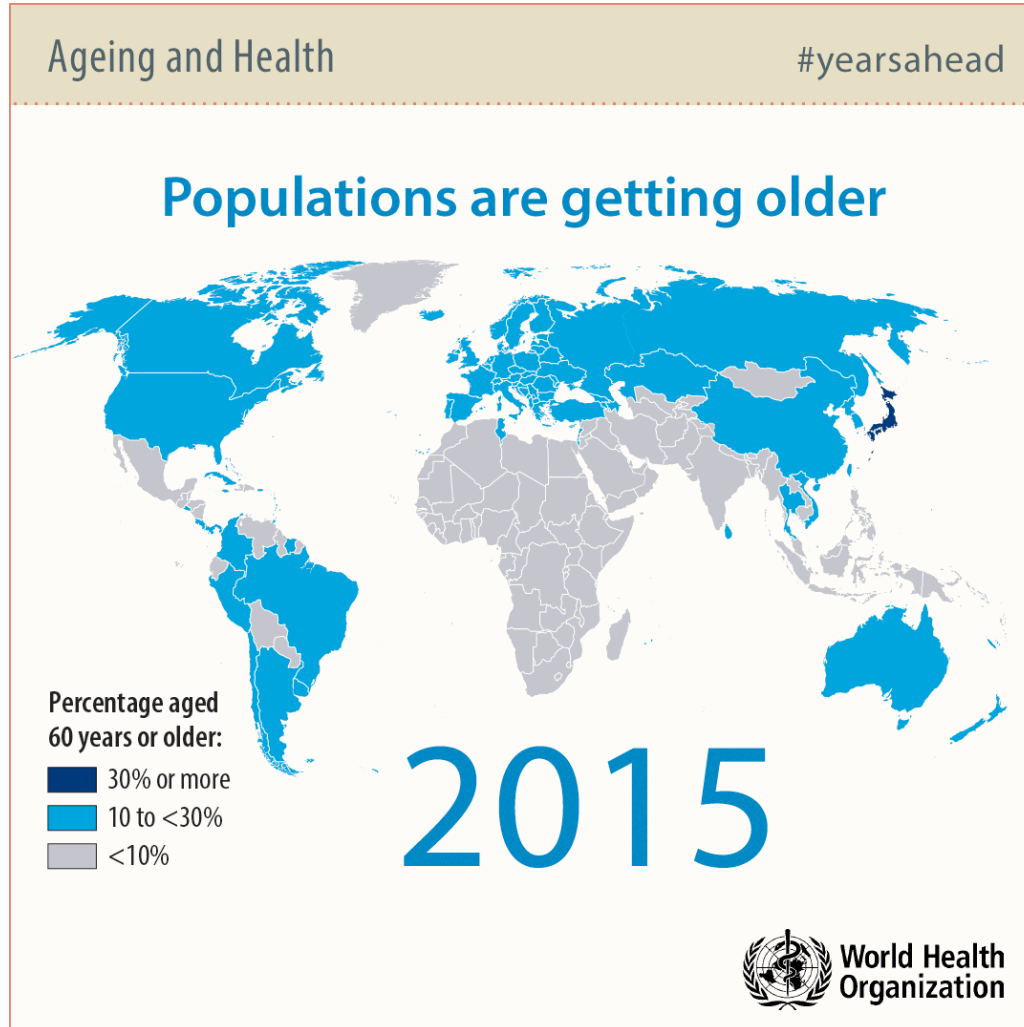


Aging Demographics of Switzerland













Bundesamt für Statistik BFS-Nummer do-d-00.01-pan-01
Veröffentlicht am 28.03.2017

We all become older and older...



Source: World Health Statistics 2016

Today's mean life expectancy

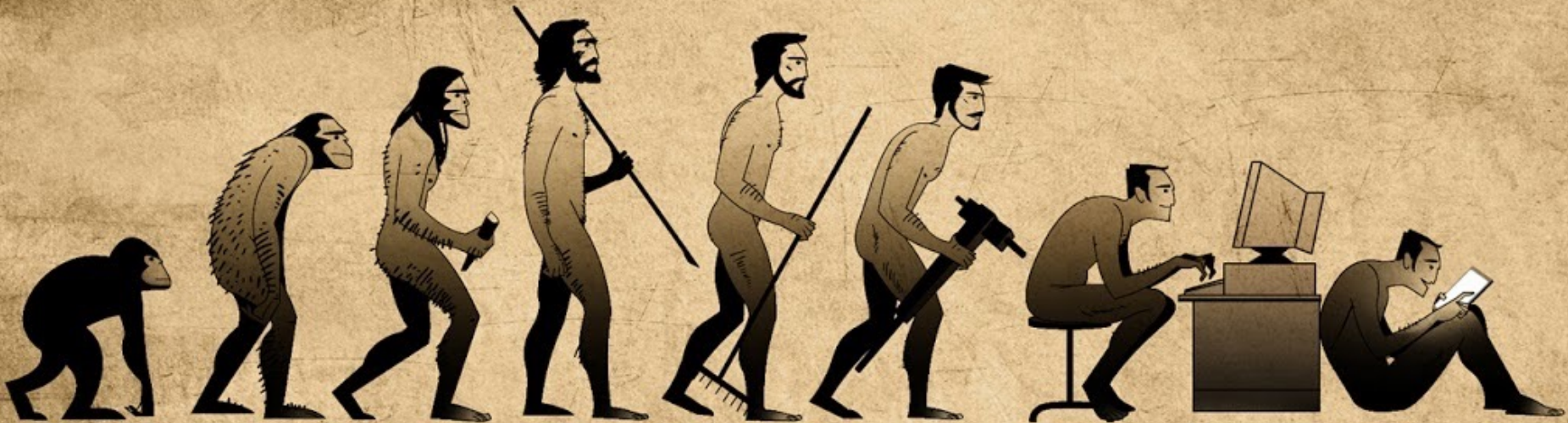
Land		Jahre
Japan		83.7
Schweiz		83.4
Singapur		83.1
Australien		82.8
Spanien		82.8
Island		82.7
Italien		82.7
Israel		82.5
Frankreich		82.4
Schweden		82.4

Source: World Health Statistics 2016

The history of human aging

4 million years:
20 → 31 years = 11 years

In the last 115 years:
31 → 71 years = 40 years



Picture source: jimintoblog; Data source: WHO

The question is: why do we live longer?

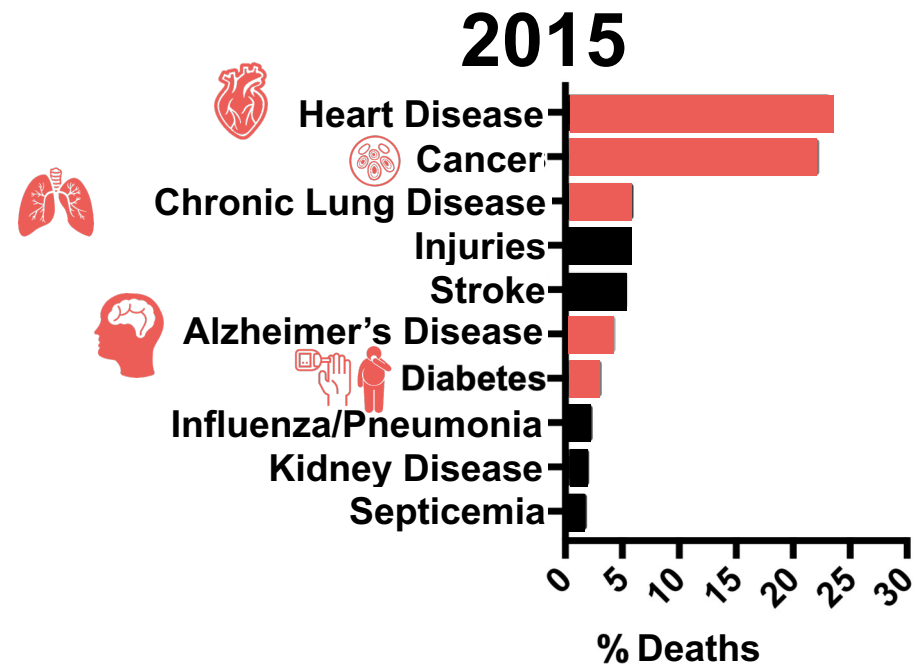
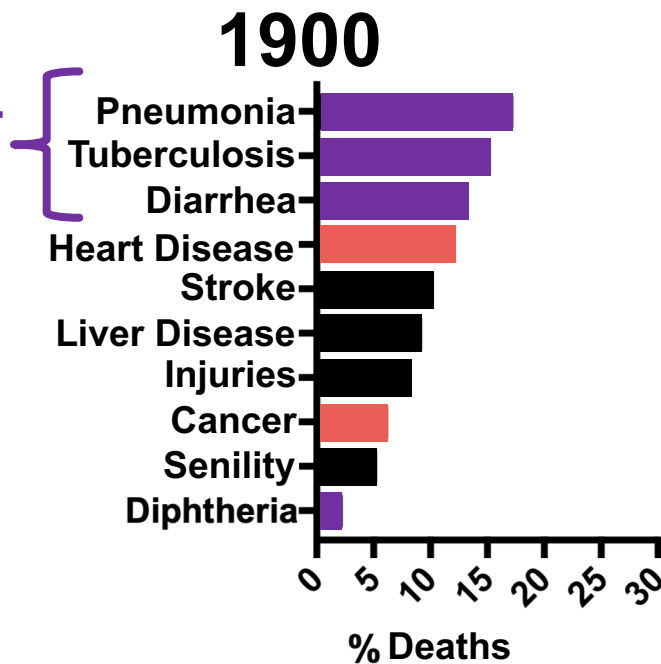


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Breakthroughs in medicine enabled a longer life



Top 10 Causes of Death



A longer life comes with a price: Old age is the highest risk factor for

Cardiovascular Diseases



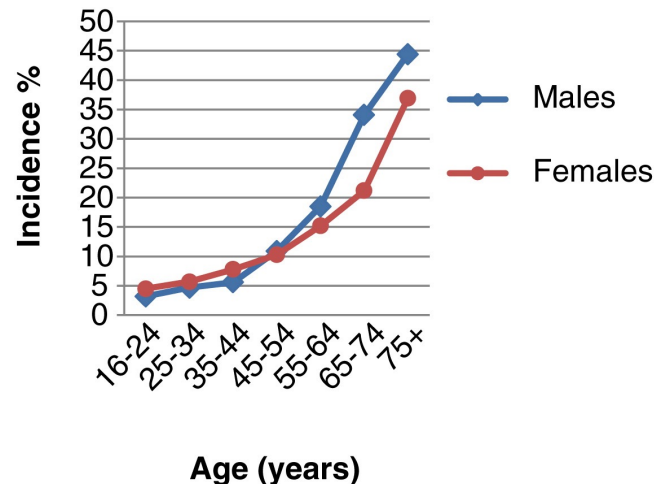
Dementia



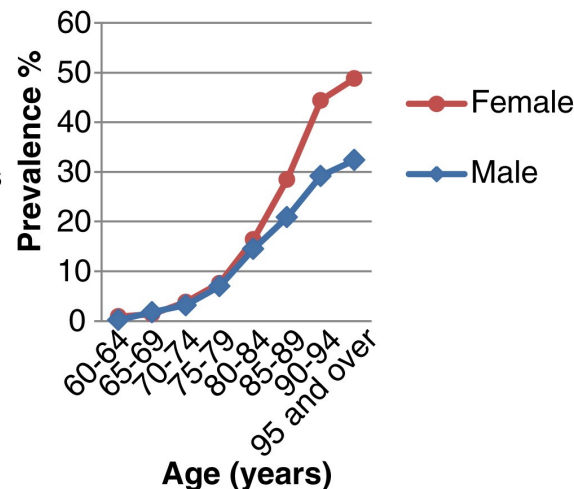
Cancer



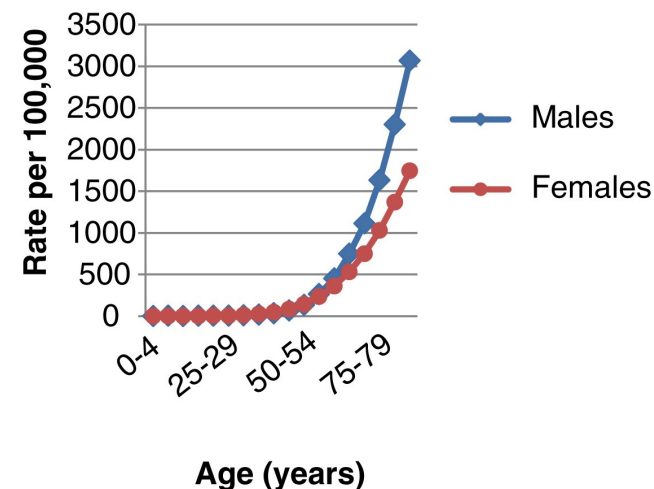
A England cardiovascular disease rates



B Europe dementia rates



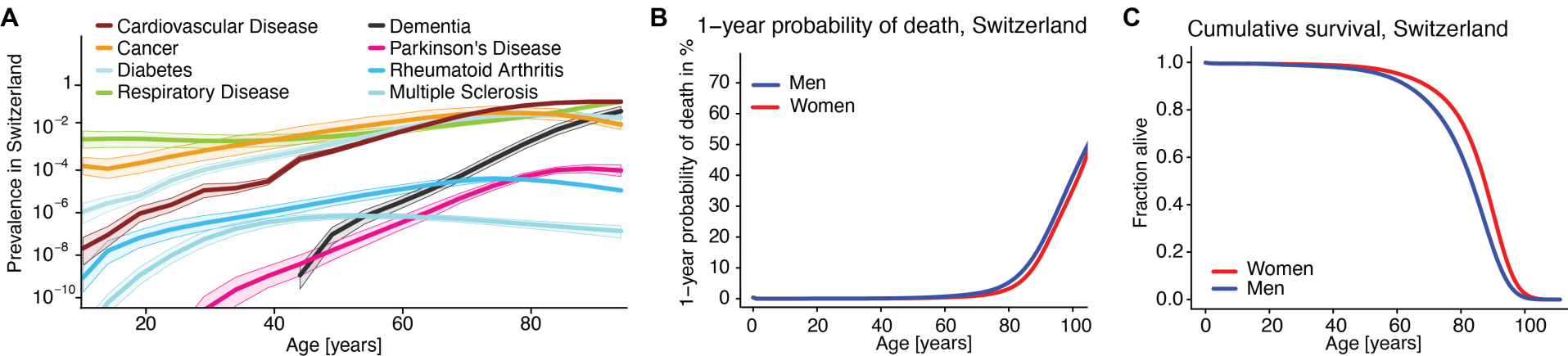
C UK cancer rates



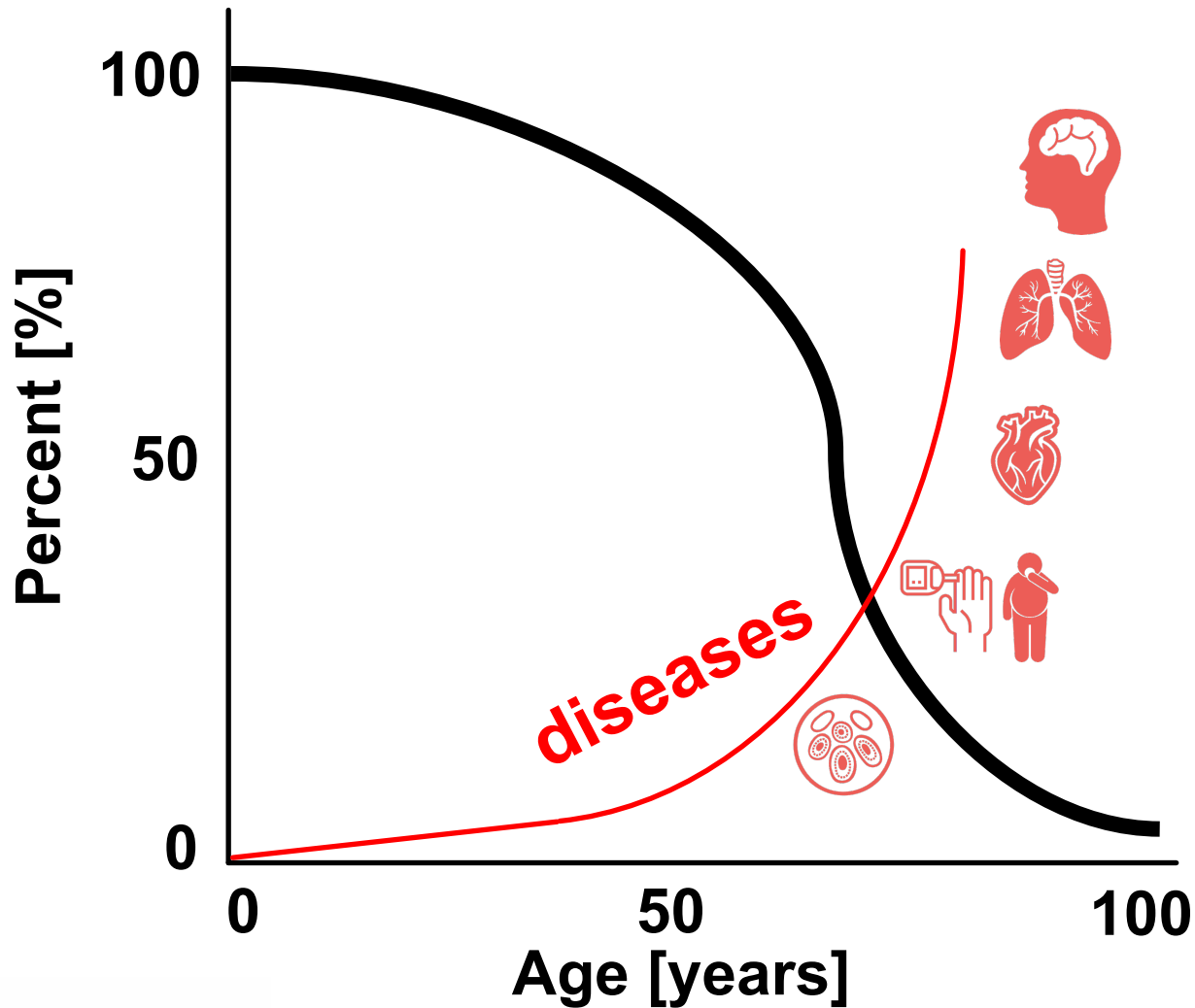
Current Biology

Niccoli & Partridge *Curr. Bio.* 2012

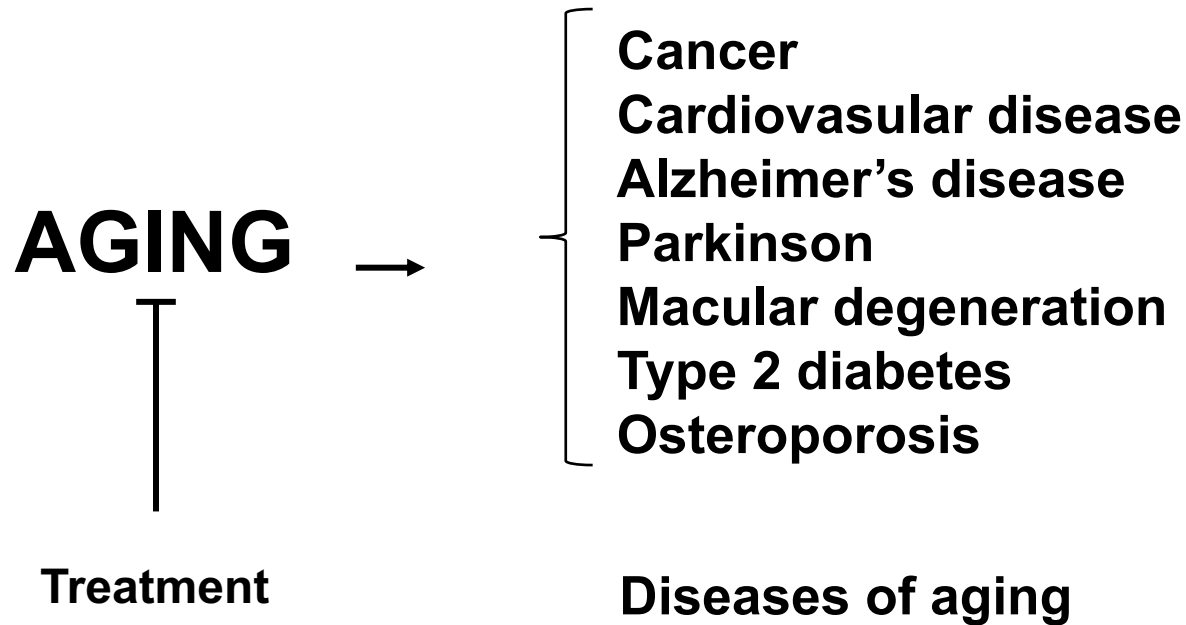
Old age highest risk factor for chronic diseases



Age-related Diseases and Lifespan



Goal of aging research (Geroscience) is to prolong healthspan



Systems Biology of Human Aging - Network Model 2019

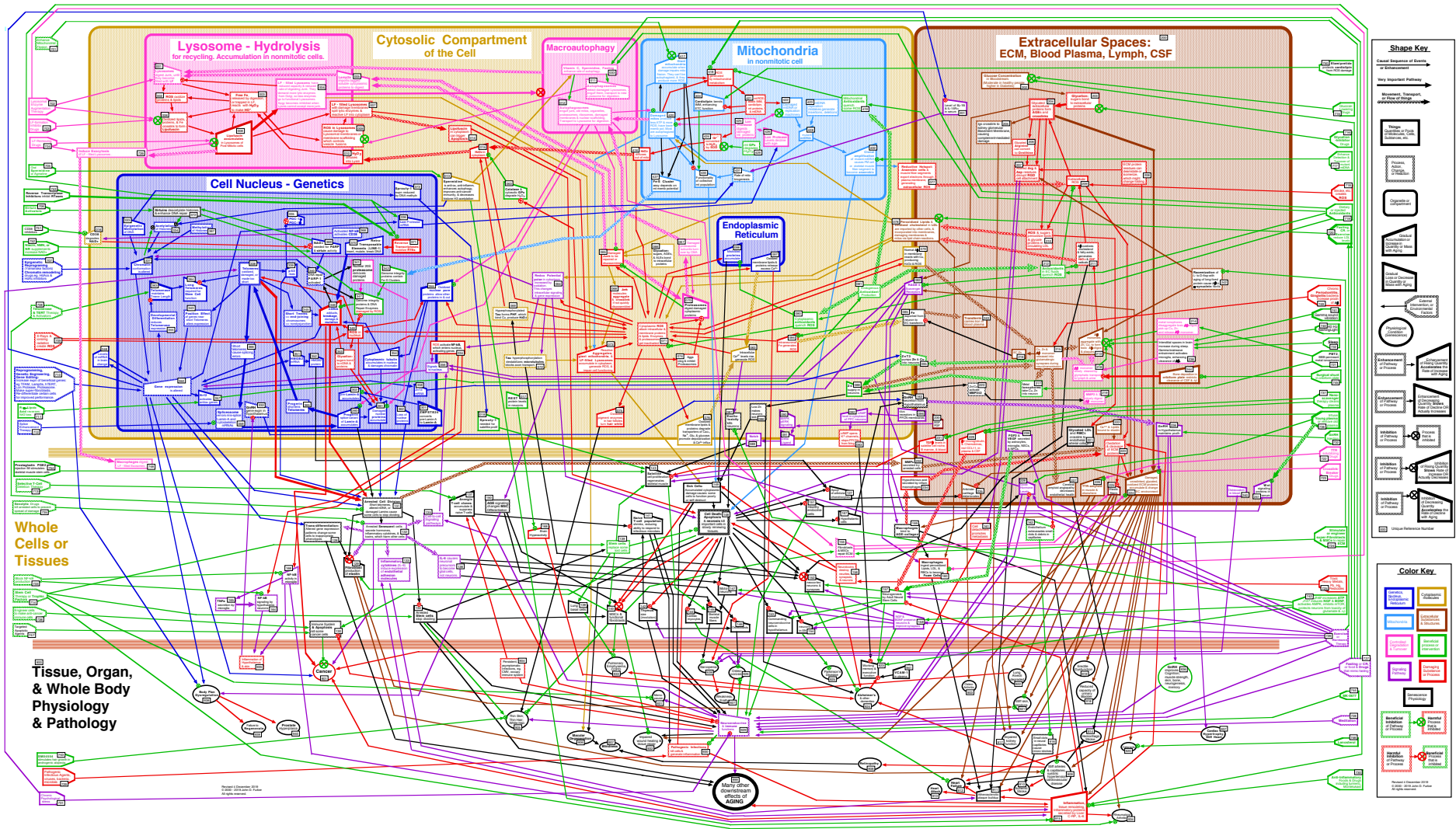
Revised 4 December 2019
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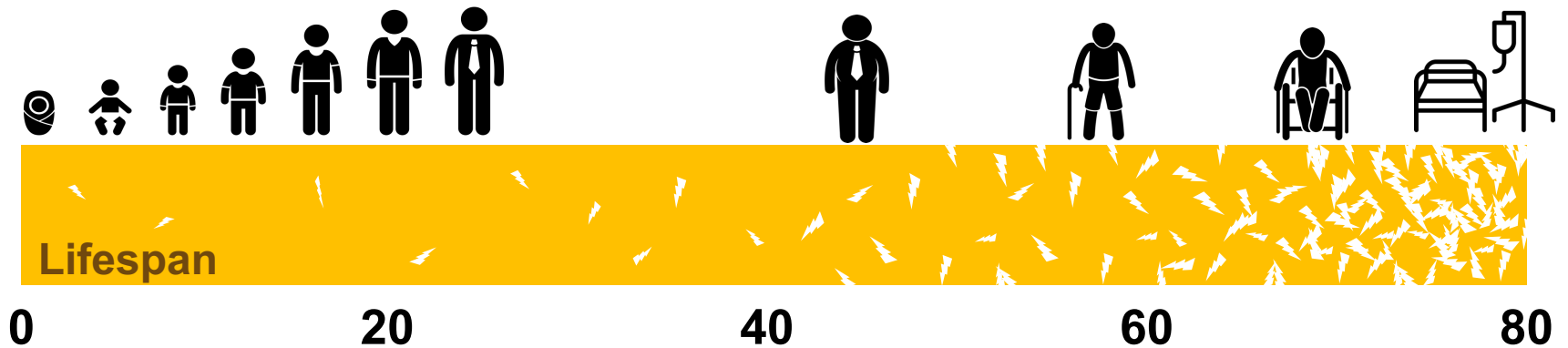
Legendary Pharmaceuticals
 PO Box 1425
 Gaithersburg, FL 32054-2000 USA
 JohnFurber@LegendaryPharma.com

Maintained updated online.
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www.LegendaryPharma.com/chartbg.html



Accumulation of molecular damage

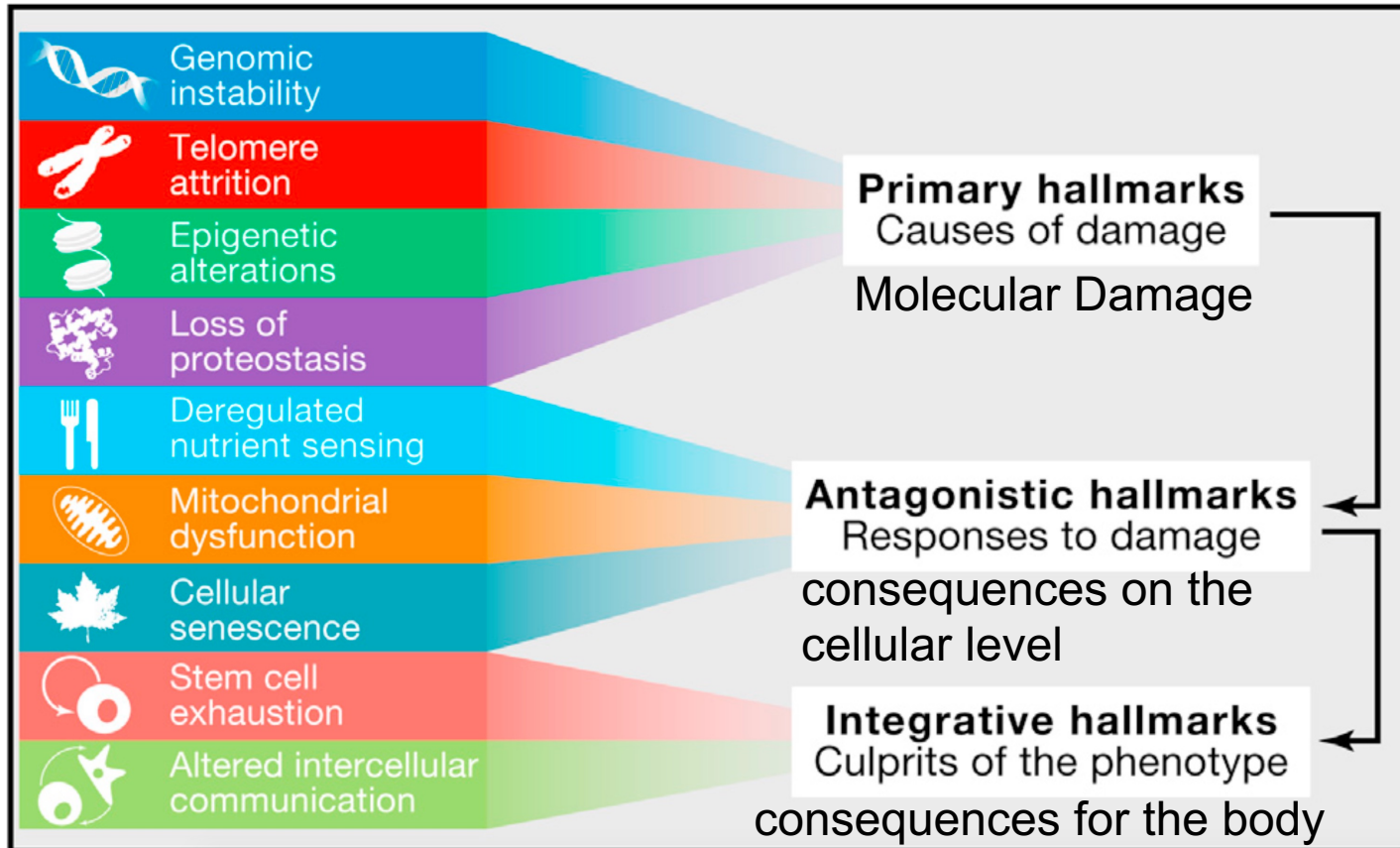


Molecular Repair Mechanisms

Progressive decline of repair- and maintaining- mechanisms during aging



Progressive loss of physiological integrity: Molecular Mechanisms



López-Otín et al., Cell 2013

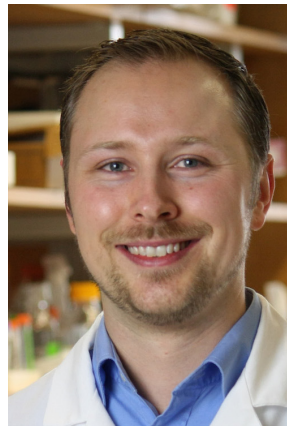
Current state of aging research

genes (TOR, Ins) & environmental factors (dietary restriction, exercise)



Aging

young



old

Aging



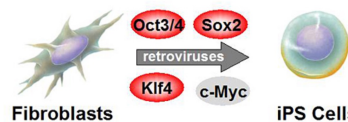
reverse



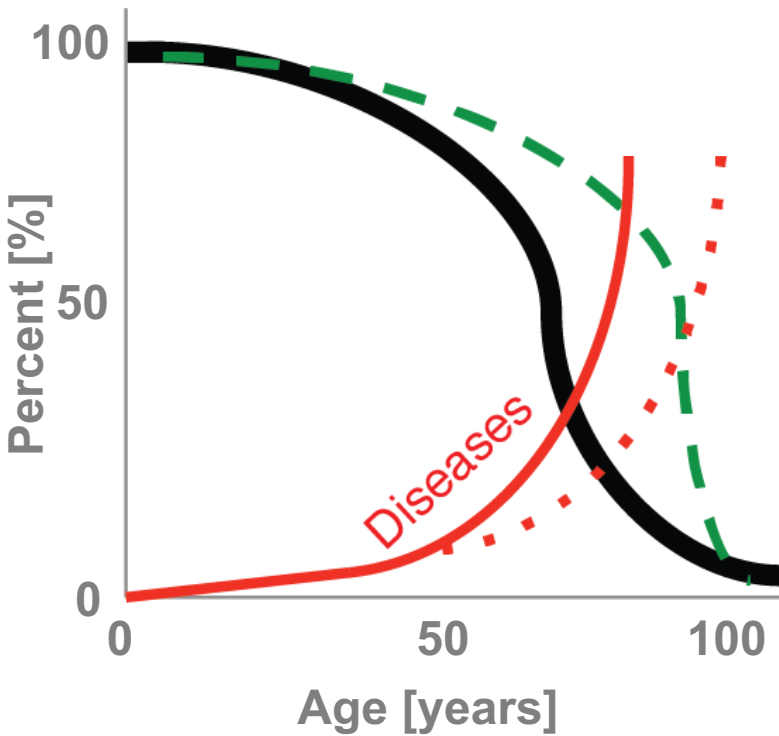
Conboy et al., Nature 2005

- parabiosis
- reprogramming (Yamanaka) factors iPS cells

Takahashi & Yamanaka Cell 2006

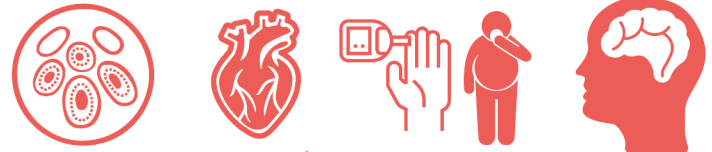


Summary: Goal of aging research is to extend healthspan



Age-related Diseases

Cancer Heart Disease Diabetes Alzheimer's Disease



Intervention Scenarios

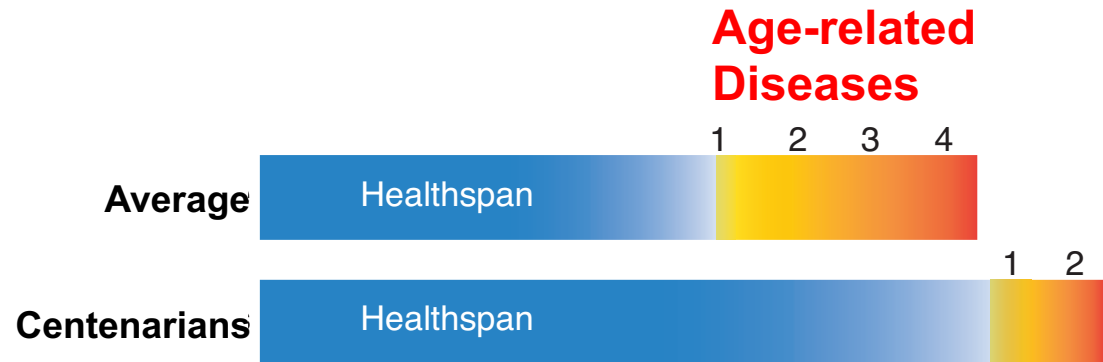
Cure 1 Disease



Extending Healthspan



Centenarians are protected from age-dependent diseases and environmental factors



85% very late disease onset
15% disease free

Evert et al., J. Gerontology 2003

Record: 122 years max. human lifespan



Jeanne Calment

Arles, France

Ultracentenarian, World's oldest person

Lived for 122 years, 164 days

Took up fencing at age 85

Rode a bicycle until age 100

Released a rap album on her 121st birthday

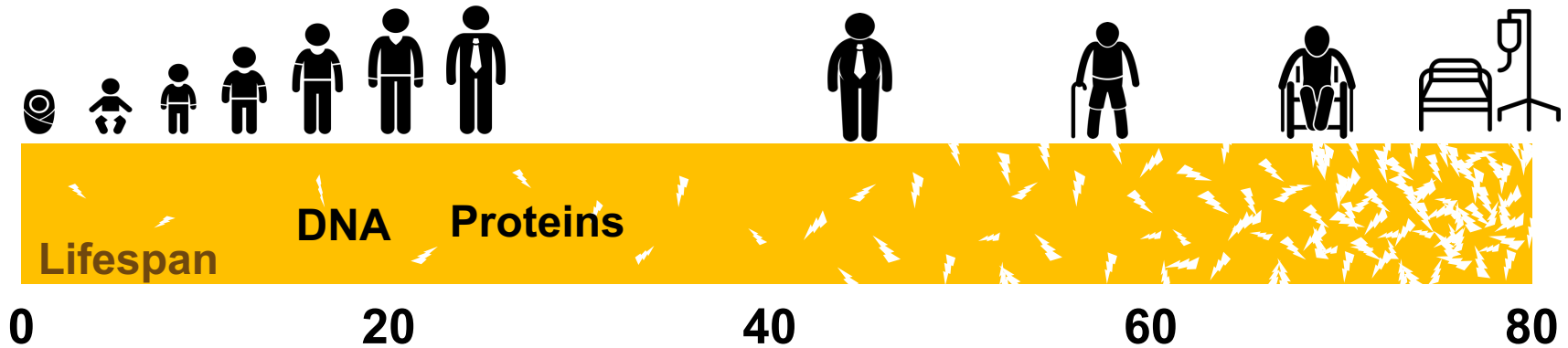
Drank alcohol until age 121

Smoked cigarettes for 100 years

Ate 2 lbs (1 kg) of chocolate every week

Calment met Vincent van Gogh when he came into her uncle's shop to buy canvas in 1888. She found him to be "Dirty, badly dressed and disagreeable".

Repair of molecular damage



Molecular Repair Mechanisms



Centenarian >100 years old



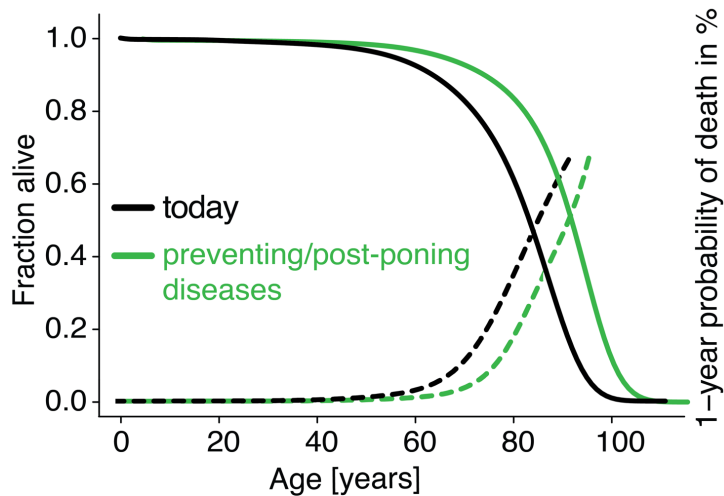
Molecular Repair Mechanisms



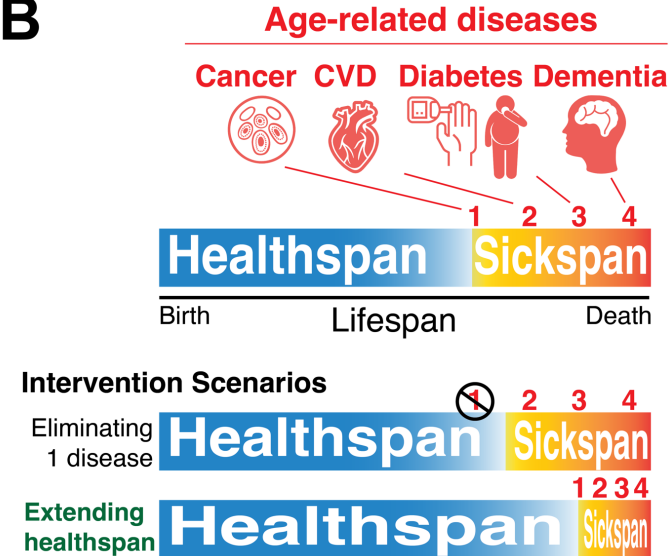
85% late disease onset
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Evert et al., J. Gerontology 2003

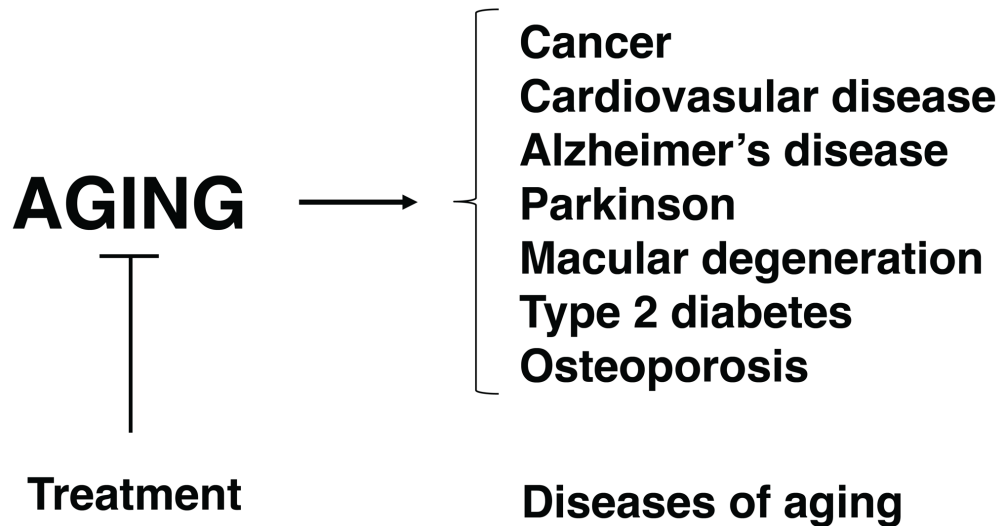
A



B

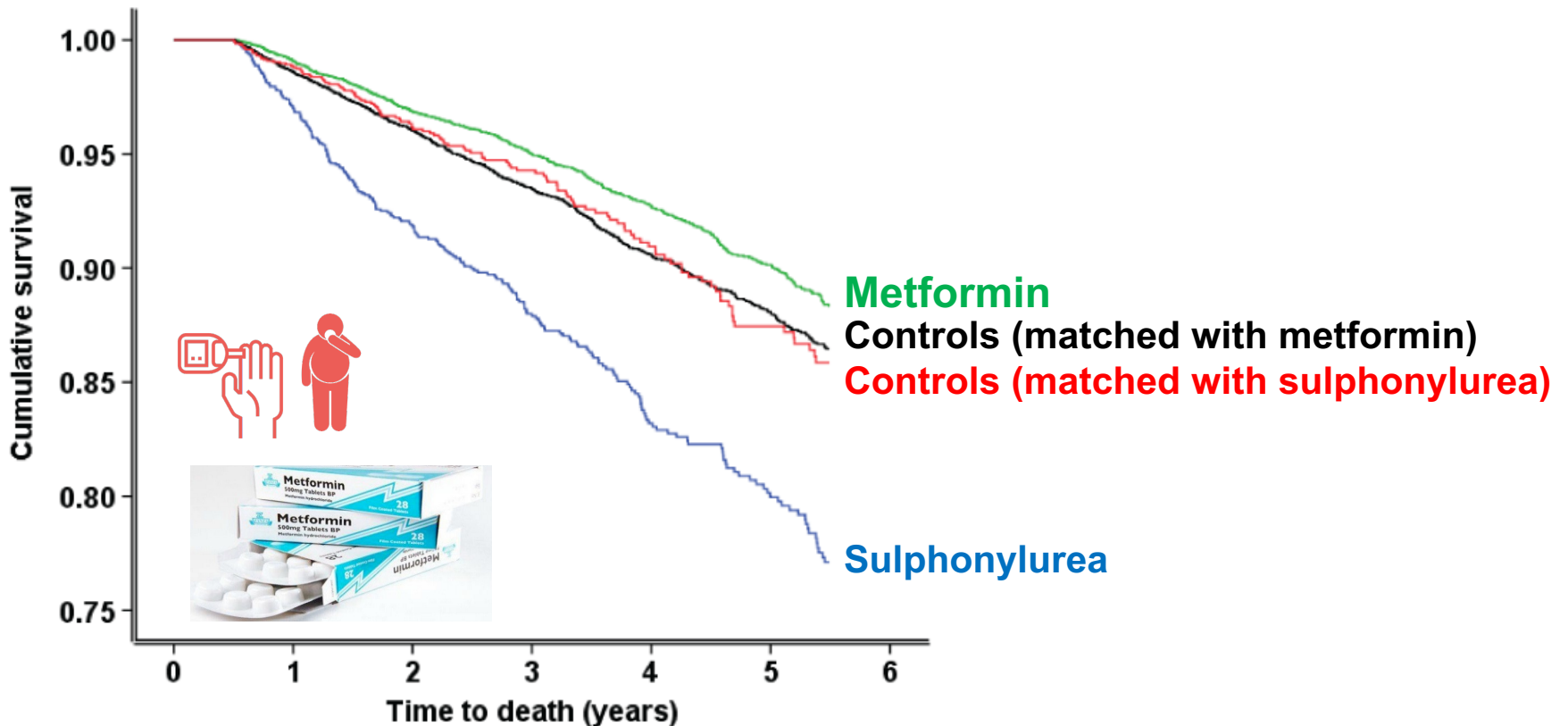


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Lack of next generation longevity drugs

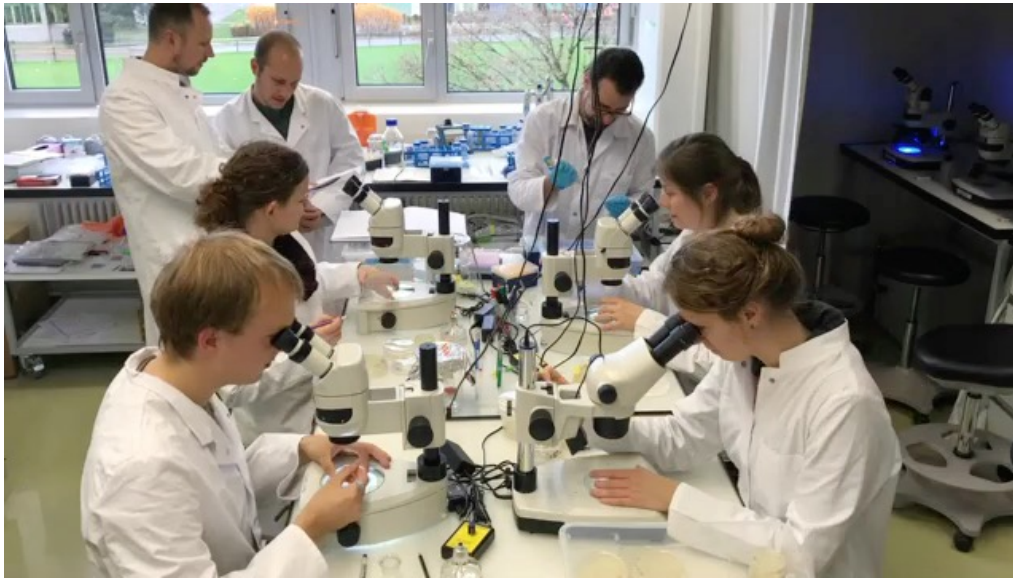
Bannister et al., Diabetes Obes. Metab. 2014



Question: How to we find new medications for healthy aging?

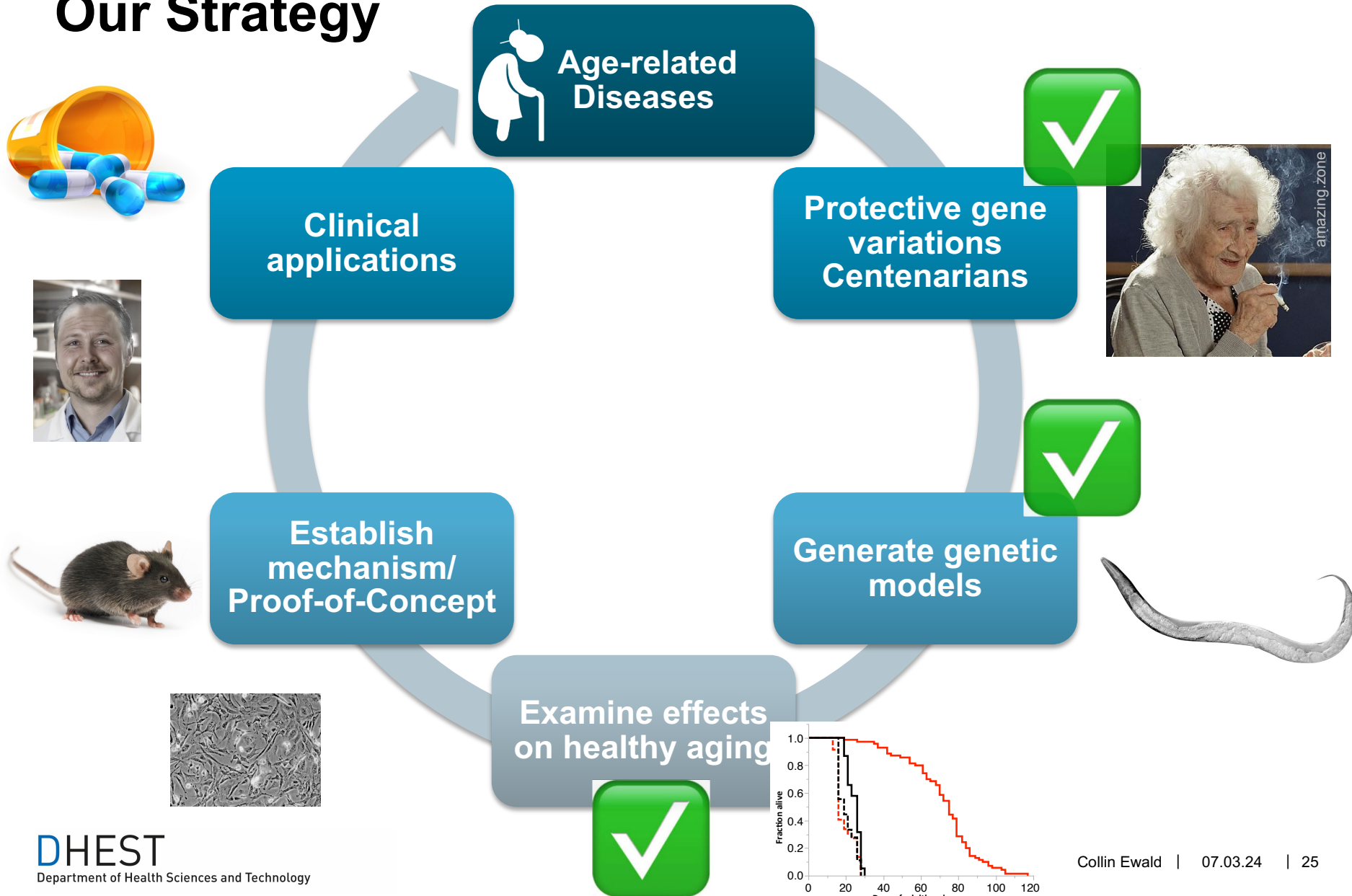
- current medications have side-effects
- not the best drugs; found by serendipity

Our Research

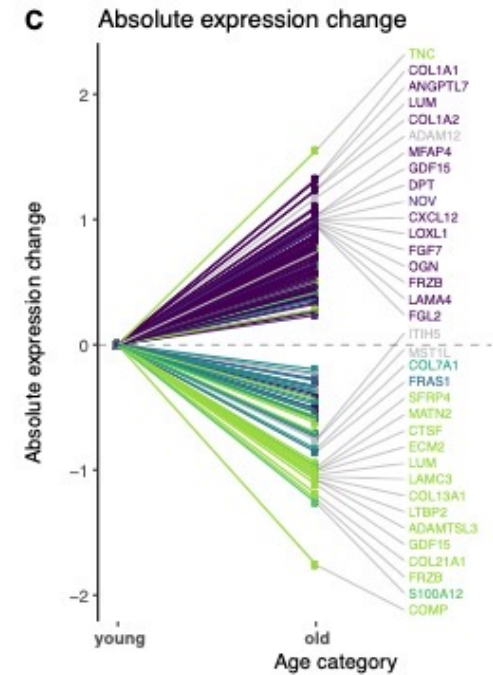
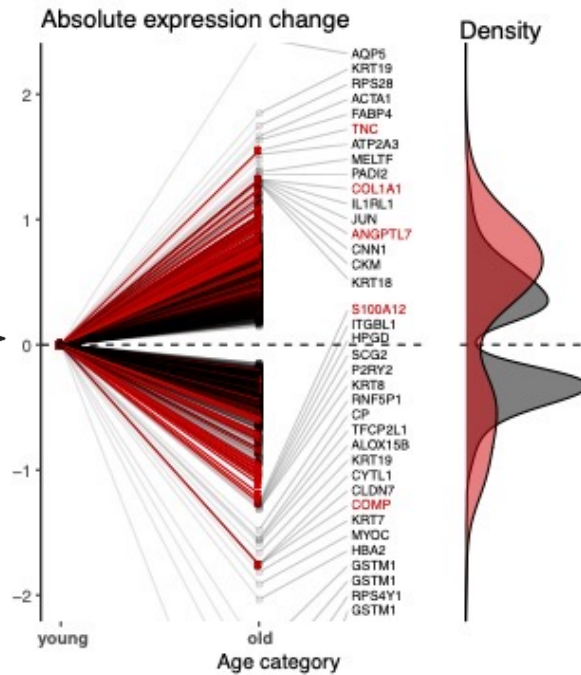
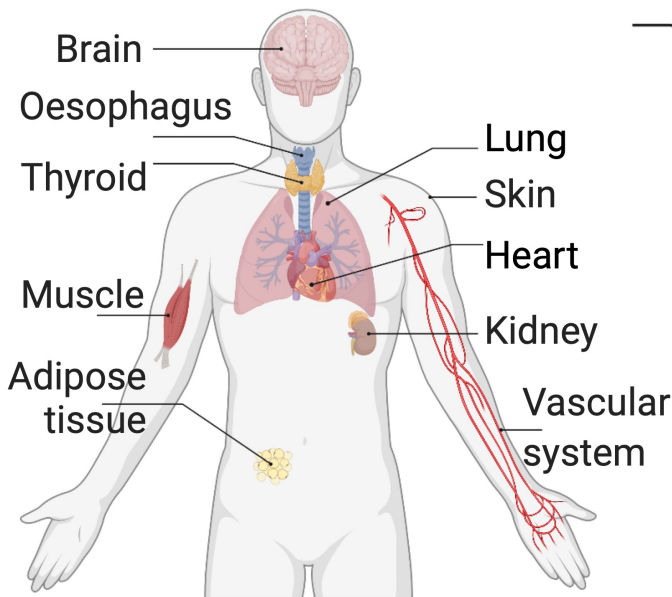


EWALD LAB.

Our Strategy

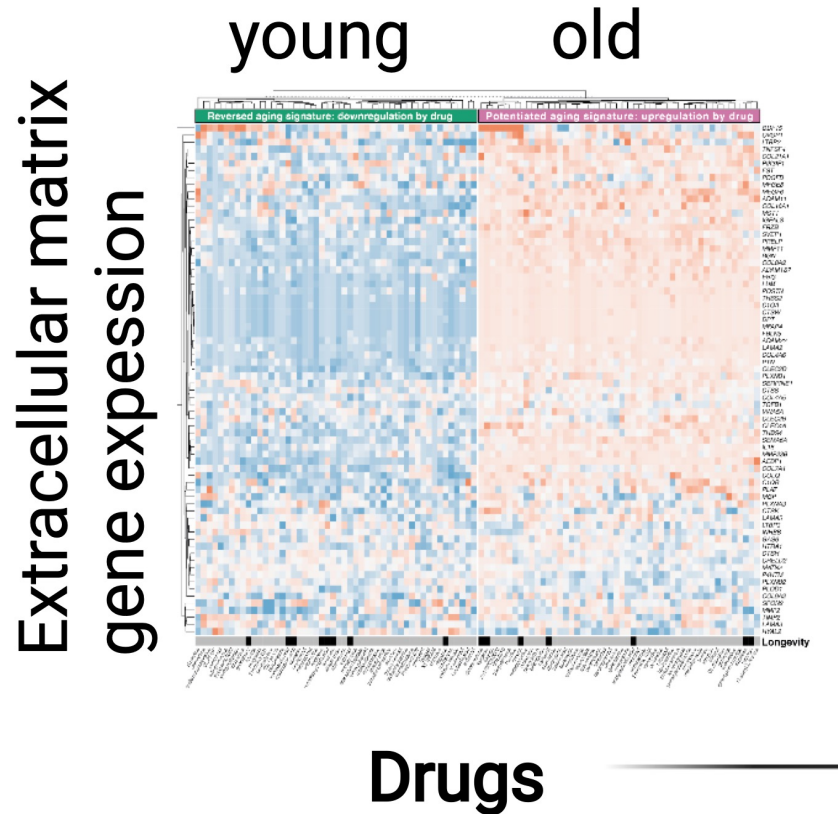


Define the youthful matreotype



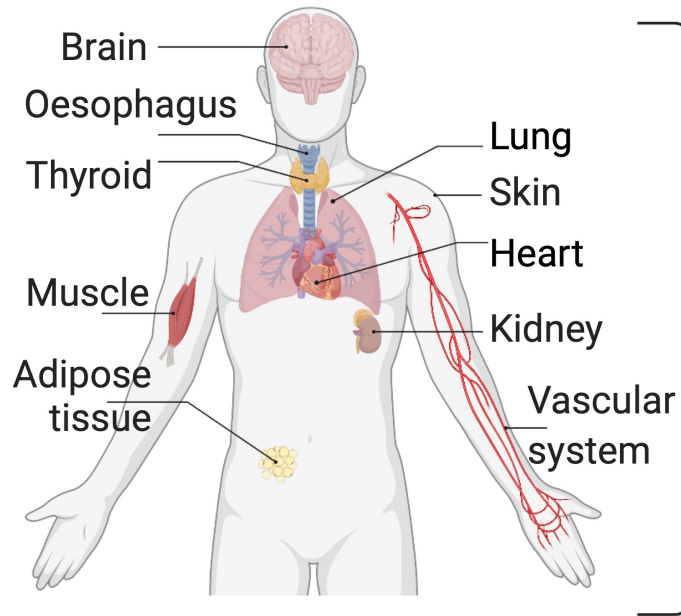
Statzer... Ewald (2021) *Aging Cell*
 DOI: [10.1111/ace.13441](https://doi.org/10.1111/ace.13441)

Identified 180 potential geroprotective compounds using the youthful matreotype



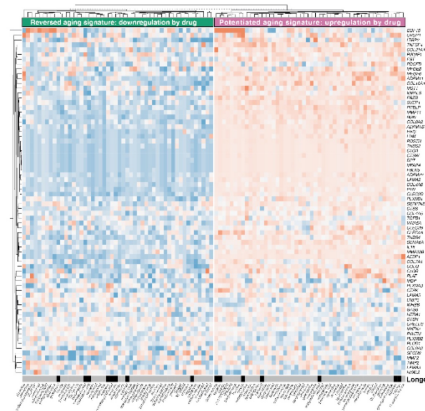
Statzer... Ewald (2021) Aging Cell
 DOI: [10.1111/ace.13441](https://doi.org/10.1111/ace.13441)

Matreotype for drug screening

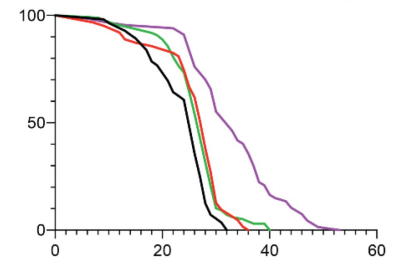


Matreotype

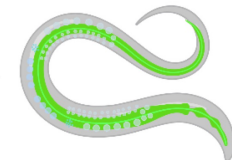
Extracellular matrix gene expression



Geroprotective drugs

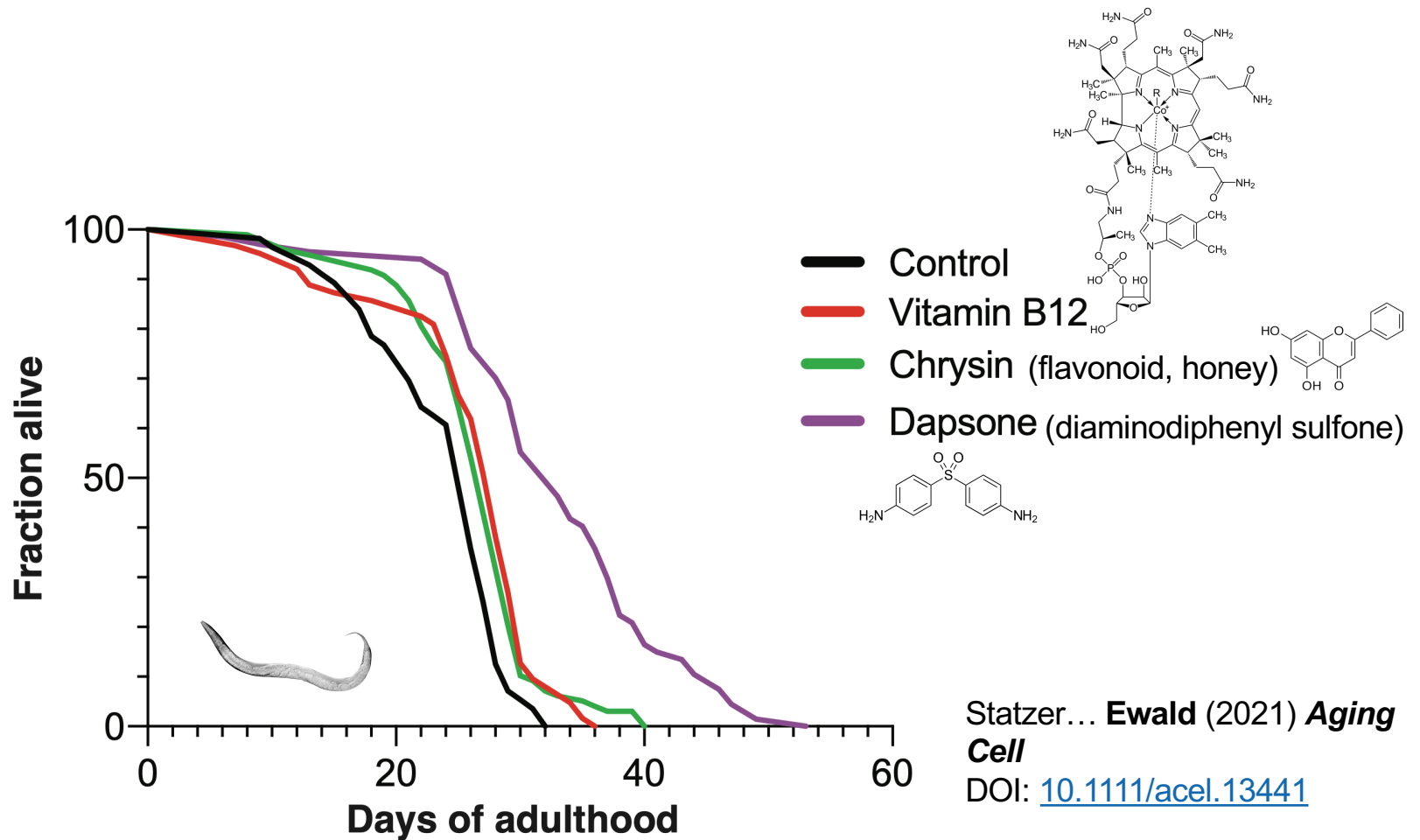


Collagen::GFP surrogate marker for Longevity

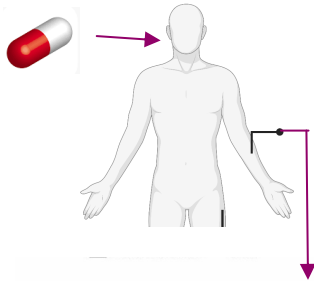


Statzer... Ewald (2021) *Aging Cell*
DOI: [10.1111/ace.13441](https://doi.org/10.1111/ace.13441)

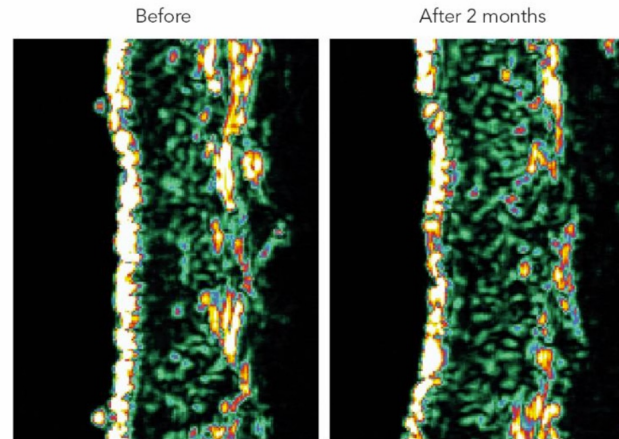
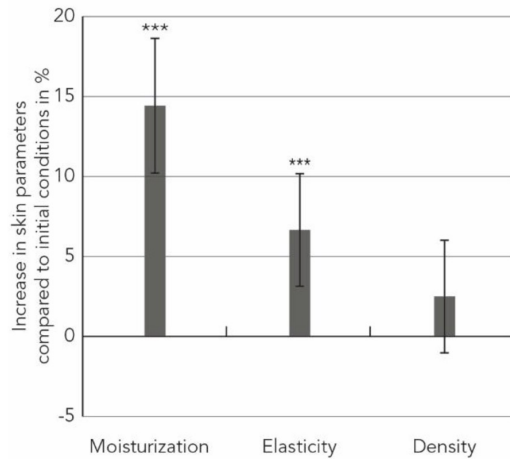
Vitamine B12 extending lifespan



Follow up: Pilot clinical trial with Dracobelle™ Nu

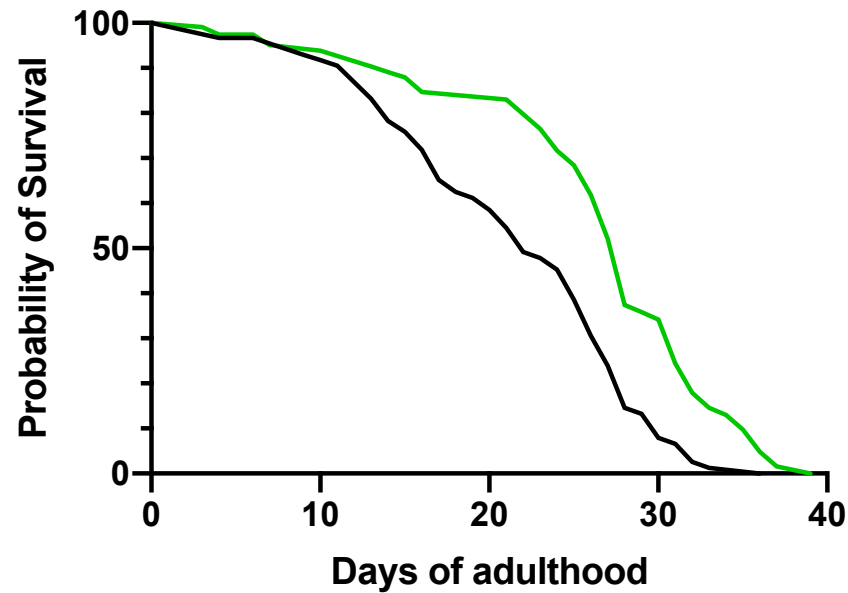


32 subjects with sun-damaged skin
Oral 200 mg daily for 2 months



Collaboration with Mibelle Biochemistry AG

AVEA001 as longevity supplement



— cont
— AVEA001

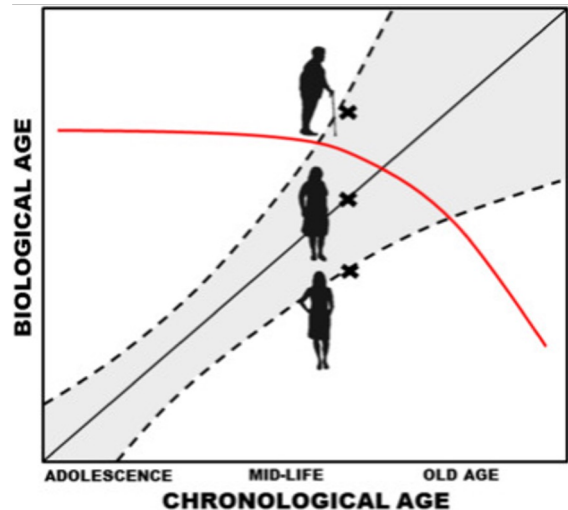
Patent application

AVEA



maximon

How we test Supplement works in humans?



42



Jylhävä et al., 2017 *eBioMedicine*

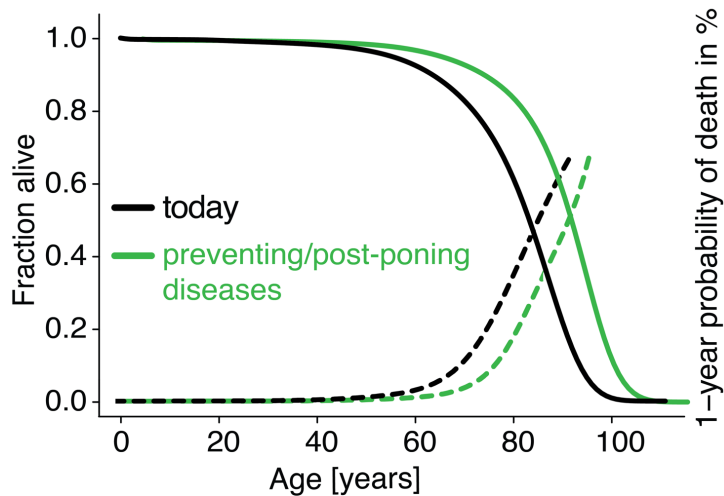
Clinical trial:

Epigenetic test → Supplement 6 months → Epigenetic test

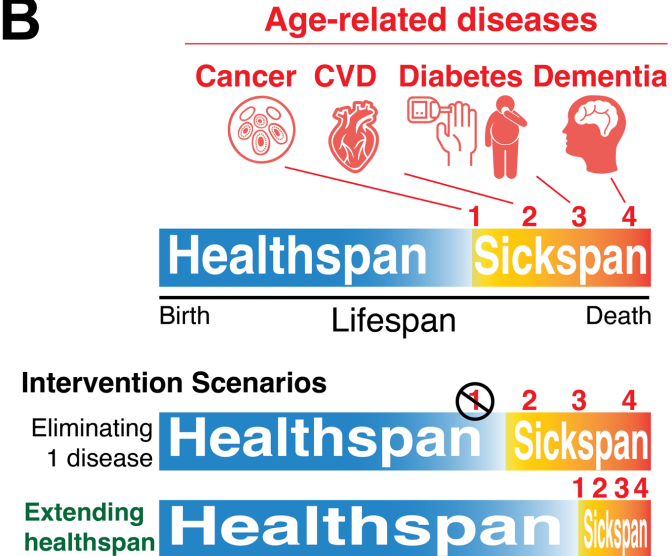
Mode of operation

- 1) Innovation at university
- 2) then spin out into start-ups
- 3) Clinical trials
- 4) then market

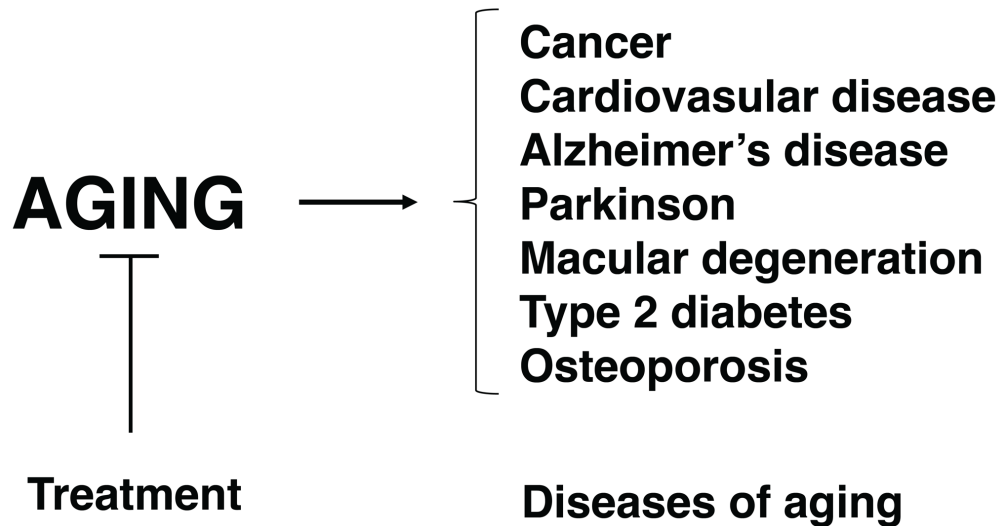
A



B

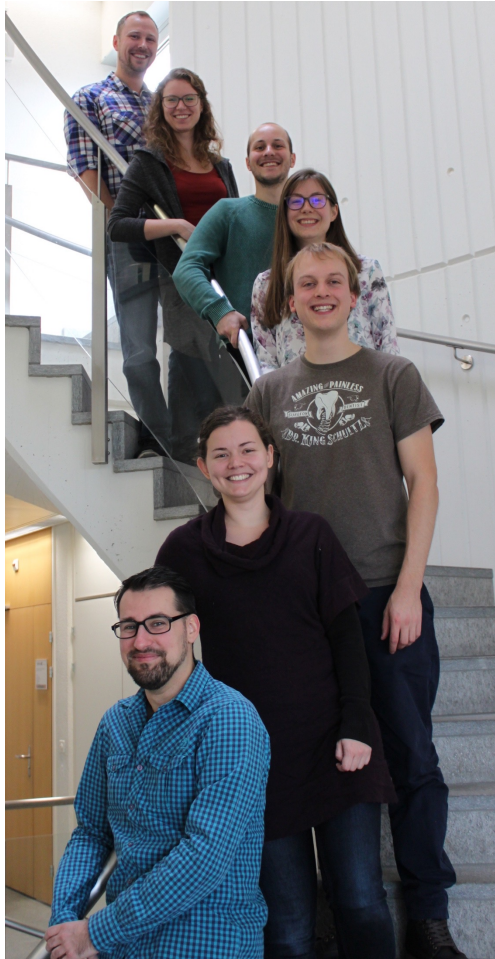


C



Ruckstuhl ... Ewald, in press

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Società svizzera di ricerca sull'invecchiamento

www.ssfar.ch

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<http://ewaldlab.com>