Anti-Aging: State of the Art

Felix Karg

22. Juli 2021

Seminar Bioinformatics



Why is aging a problem?

Is aging necessary?

What is aging?

How can we slow down aging?

What can I do?

How can bioinformatics help?

Why is aging a problem?

Is aging necessary?

What is aging?

How can we slow down aging?

What can I do?

How can bioinformatics help?

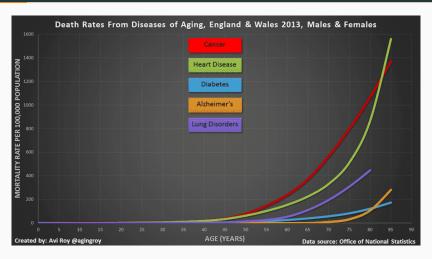
Corona Deaths correlate with Age



[Santesmasses et al., 2020]

Conclusion: They don't die due to Corona, they die due to old age!

All causes for Death correlate with Age



Same with all other primary causes!

Slowing aging has incredible potential



[Kaeberlein, 2019]
And yet it receives less than 1/100th of Funding!

Why is aging a problem?

Is aging necessary?

What is aging?

How can we slow down aging?

What can I do?

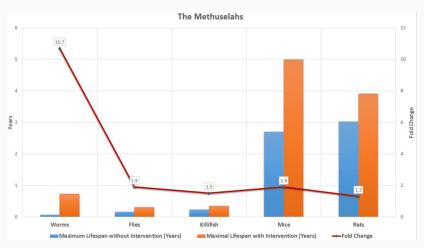
How can bioinformatics help?

Animals that don't senescence (age)

- hydra (biologically immortal) [Martiñez, 1998]
- naked mole rats [Ruby and Smith, 2018]
- tortoises [Miller, 2001]
- some sharks: 400y [Pennisi, 2016]
- some clams: 500y [Munro and Blier, 2012]

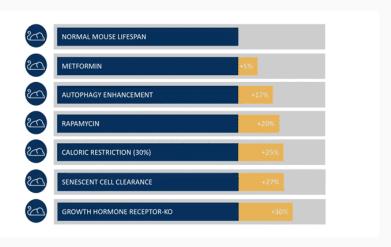
Conclusion: Biological creatures don't have to age

Extending Life in different animals



[Bulterijs et al., 2015]

Most effective Mice Treatments



[Brunemeier, 2020]

Why is aging a problem?

Is aging necessary?

What is aging?

How can we slow down aging?

What can I do?

How can bioinformatics help?

What is aging?

Definition and Hallmarks

Common Root Cause Existence
Assumed Root Causes

Aging

Definition

Ageing is characterized by a progressive decline in organismal fitness occurs with increasing age, ultimately ending in death.

But how can we measure it?

Hallmarks of Aging

According to [López-Otín et al., 2013]:

- Genomic instability
- Telomere attrition
- Epigenetic alterations
- Loss of proteostasis
- Deregulated nutrient-sensing
- Mitochondrial dysfunction
- Cellular senescence
- Stem cell exhaustion
- Altered intercellular communication

Hallmarks are mostly just side-effects we can measure!

What is aging?

Definition and Hallmarks

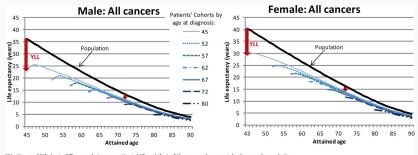
Common Root Cause Existence

Assumed Root Causes

Diabetes: Life Expectancy

Life Expectancy is at least 10 years lower with Diabetes Type 1 [Livingstone et al., 2015] and about 5 lower less with Type 2.

Cancer: Life Expectancy



YLL= Years of life lost, difference between patients' LE and that of the age and sex matched general population

[Botta et al., 2019]

Existence proof of common pathways

someone who has one severe illness early is likely to have others

Similarity of diseases of aging

[Wentworth, 2021] At the cellular level:

- decrease in cell count
- increase in damaged proteins/DNA/fats
- inflammation

Roughly this pattern for:

- alzheimers
- atherosclerosis
- muscle loss
- many others

What is aging?

Definition and Hallmarks

Common Root Cause Existence

Assumed Root Causes

Mitochondrial dysfunction

Turns out, mitochondrial dysfunction accounts for telomere-dependent senescence [Passos et al., 2007].

Assumed root causes: free radicals and transposon damage
Maybe not in too much detail? Could fill 30min itself [Wentworth, 2021]

p21 and reactive oxygen feedback for senescence [Passos et al., 2010]

Why is aging a problem?

Is aging necessary?

What is aging?

How can we slow down aging?

What can I do?

How can bioinformatics help?

Goal

Goal of anti-aging research: stop aging / neglegible senescence intermediate goals: slow down aging, increase QUALYs (QUality-Adjusted-Life-Years)

Potential strategies

Picture with blood exchange, senolytics, cellular reprogramming and others full slide for each of them

Why is aging a problem?

Is aging necessary?

What is aging?

How can we slow down aging?

What can I do?

How can bioinformatics help?

Pharmacological

Some medicaments: Not medical advice!

Lifestyle

Exercise, low-calorie-diet, others

Research!

A lot to be done, just see what you can do

Donate!

A lot of money is needed

Why is aging a problem?

Is aging necessary?

What is aging?

How can we slow down aging?

What can I do?

How can bioinformatics help?

How can bioinformatics help?

Analysis

Simulation

Analysis

Large datasets, ever-more data

Analysis

Will need new tools and software

How can bioinformatics help?

Analysis

Simulation

Simulation

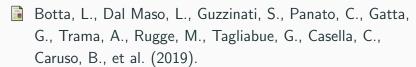
current Pharmaceutical battle: better simulator

Simulation II

AlphaFold2 and others

Questions?

Sources i



Changes in life expectancy for cancer patients over time since diagnosis.

Journal of advanced research, 20:153-159.

Brunemeier, S. (2020).

Geroscience and Biotech Venture Capital - YouTube.

https:

//www.youtube.com/watch?v=AM97A_5jFgk&t=645s.

Sources ii

(Accessed on 2021-05-26).

Bulterijs, S., Hull, R. S., Björk, V. C., and Roy, A. G. (2015).

It is time to classify biological aging as a disease. *Frontiers in genetics*, 6:205.

Kaeberlein, M. (2019).

It is Time to Embrace 21st-Century Medicine.

Public Policy & Aging Report, 29(4):111-115.

Sources iii

Livingstone, S. J., Levin, D., Looker, H. C., Lindsay, R. S., Wild, S. H., Joss, N., Leese, G., Leslie, P., McCrimmon, R. J., Metcalfe, W., et al. (2015).

Estimated life expectancy in a Scottish cohort with type 1 diabetes, 2008-2010.

Jama, 313(1):37-44.

López-Otín, C., Blasco, M. A., Partridge, L., Serrano, M., and Kroemer, G. (2013).

The hallmarks of aging.

Cell, 153(6):1194-1217.

Sources iv



Martiñez, D. E. (1998).

Mortality patterns suggest lack of senescence in hydra.

Experimental gerontology, 33(3):217-225.



Miller, J. (2001).

Escaping senescence: demographic data from the three-toed box turtle (Terrapene carolina triunguis).

Experimental Gerontology, 36(4-6):829-832.

Sources v



Munro, D. and Blier, P. U. (2012).

The extreme longevity of Arctica islandica is associated with increased peroxidation resistance in mitochondrial membranes.

Aging cell, 11(5):845-855.



Passos, J. F., Nelson, G., Wang, C., Richter, T., Simillion, C., Proctor, C. J., Miwa, S., Olijslagers, S., Hallinan, J., Wipat, A., et al. (2010).

Feedback between p21 and reactive oxygen production is necessary for cell senescence.

Molecular systems biology, 6(1):347.

Sources vi



Passos, J. F., Saretzki, G., Ahmed, S., Nelson, G., Richter, T., Peters, H., Wappler, I., Birket, M. J., Harold, G., Schaeuble, K., et al. (2007).

Mitochondrial dysfunction accounts for the stochastic heterogeneity in telomere-dependent senescence.

PLoS Biol, 5(5):e110.

Sources vii



Pennisi, E. (2016).

Greenland shark may live 400 years, smashing longevity record — Science — AAAS.

https://www.sciencemag.org/news/2016/08/ greenland-shark-may-live-400-years-smashing-longevi

(Accessed on 2021-05-24).



Ruby, J. G. and Smith, M. (2018).

Naked mole-rat mortality rates defy Gompertzian laws by not increasing with age.

elife, 7:e31157.

Sources viii

Santesmasses, D., Castro, J. P., Zenin, A. A., Shindyapina, A. V., Gerashchenko, M. V., Zhang, B., Kerepesi, C., Yim, S. H., Fedichev, P. O., and Gladyshev, V. N. (2020). COVID-19 is an emergent disease of aging. *Aging Cell*, 19(10):e13230.

Wentworth, J. S. (2021).

Core Pathways of Aging - LessWrong.

https://www.lesswrong.com/posts/ui6mDLdqXkaXiDMJ5/core-pathways-of-aging. (Accessed on 2021-05-26).