LIFE EXTENSION ADVOCACY FOUNDATION

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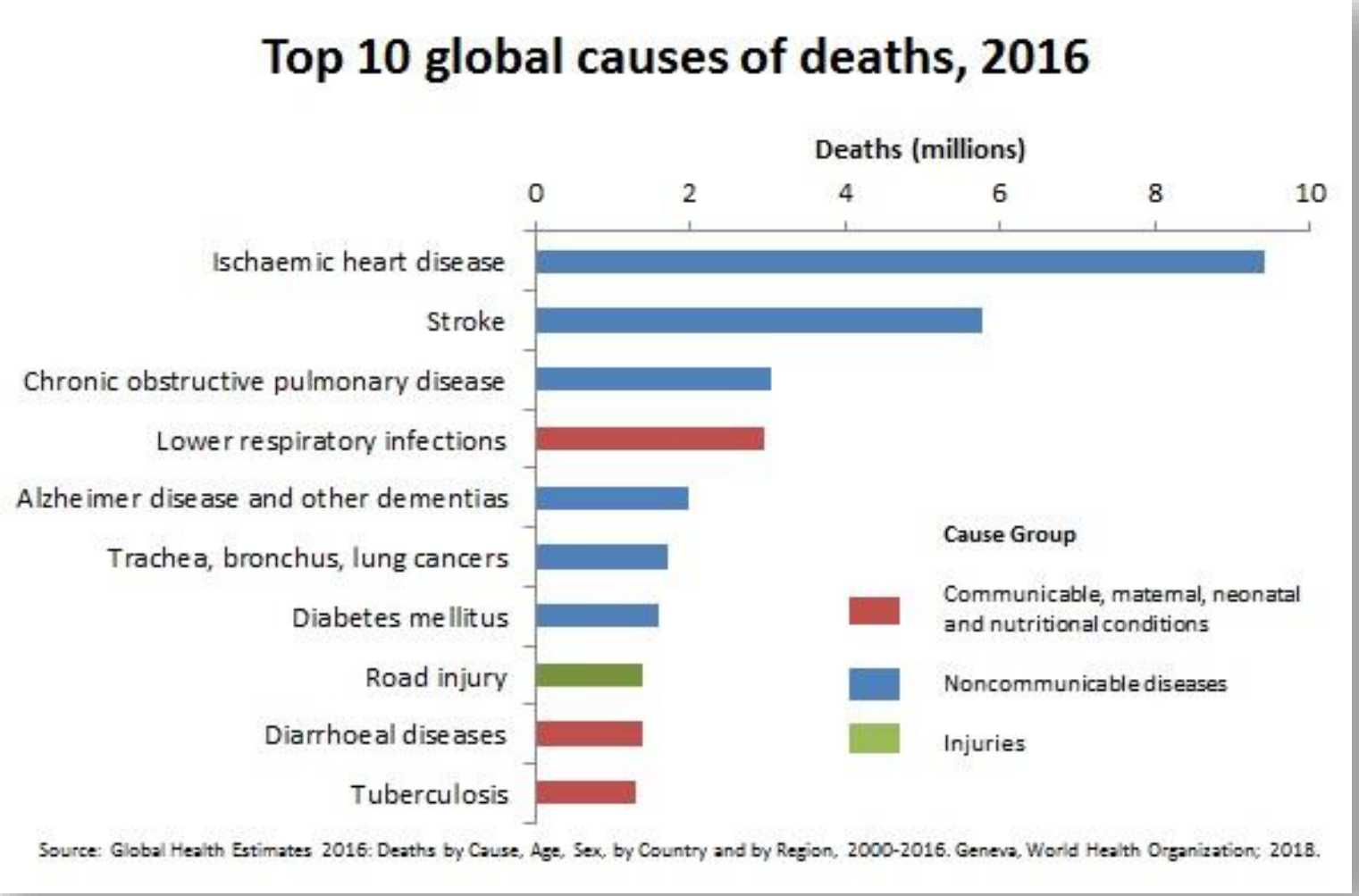
What is aging?
What are the root causes of aging?

Age-related diseases are the main causes of disability and death in the modern world*



***Infectious diseases are mostly defeated; chronic diseases prevail. [Source: WHO.]**

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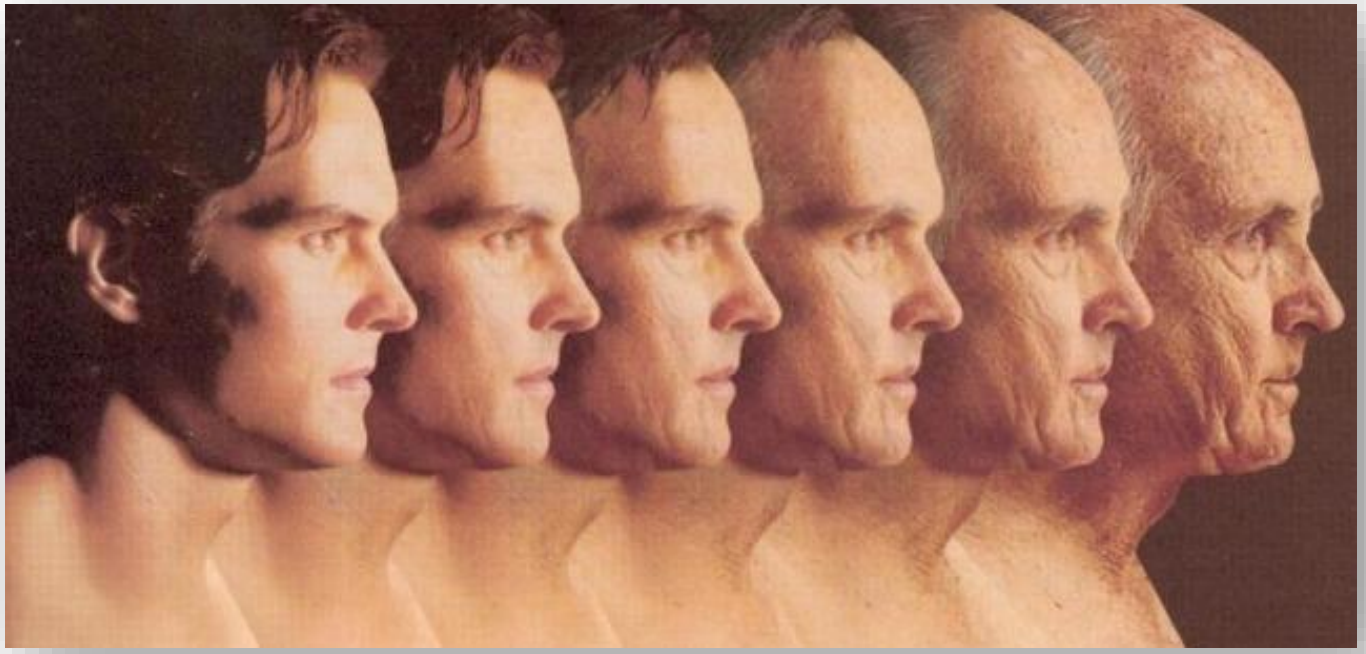
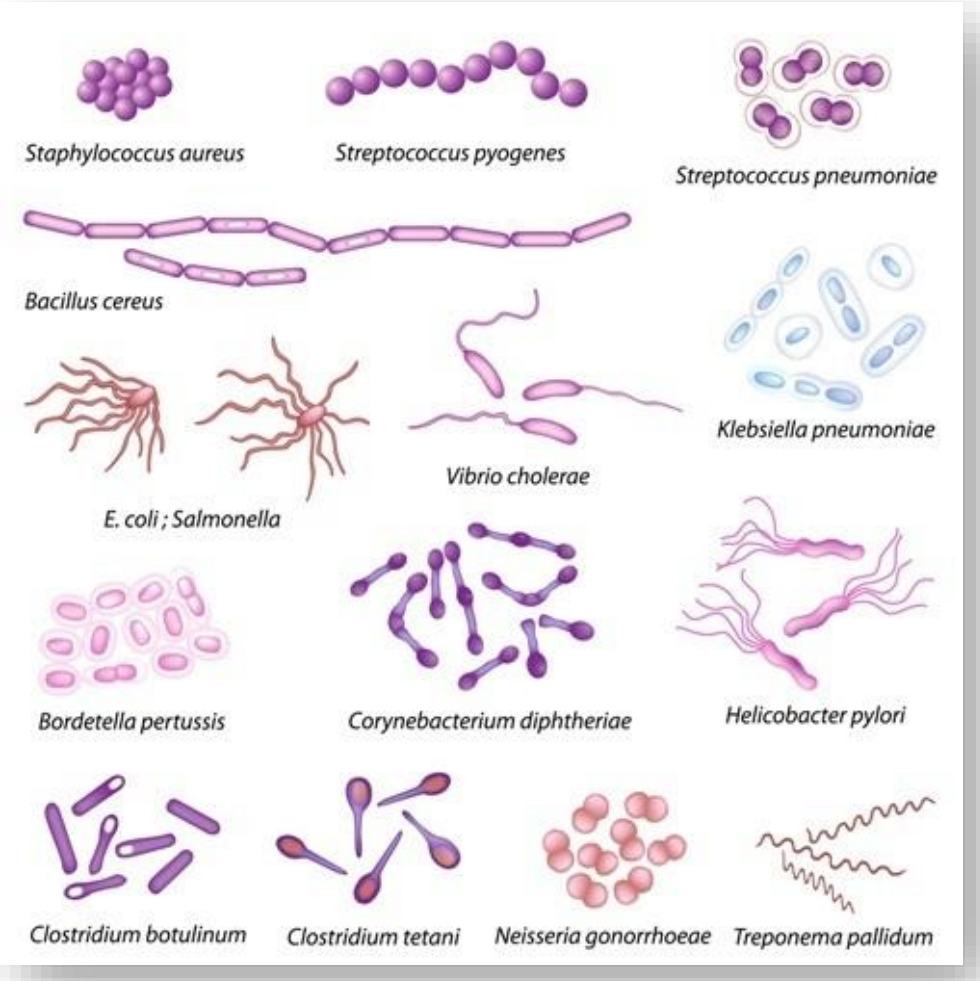


Age-related diseases affect our lives for 30-40 years

Most old people have several chronic diseases at the same time, which makes it difficult to treat them

Age-related diseases are humanity's greatest source of suffering, since, in most cases, they cannot be cured and only aggravate over time

Globally, 100,000 people die every day from age-related diseases



The key prerequisite for bringing infectious diseases under medical control was the identification of pathogens.

Understanding the root causes allowed us to develop effective measures to prevent and treat infectious diseases: hygiene, sanitation, water chlorination, vaccines, and antibiotics.

Can we identify the root causes of aging?

Dr. Aubrey de Grey

Dr. Aubrey de Grey was the first person to start and actively maintain the discussion about the plausibility of addressing the root causes of aging in order to eventually eradicate age-related diseases.

He identified 7 main categories of age-related damageand suggested ways of addressing each of them with a specific therapy. Aubrey founded SENS Research Foundation to support scientific studies on the main damages of aging and potential therapies.

www.sens.org

sens research foundation

reimagine aging

SENS Research Foundation: Reimagine Aging

The "seven deadly things" & their fixes

Damage type	The maintenance approach
Cell loss, cell atrophy	Replace, using stem cells
Division-obsessed cells	Reinforce, using telomere control
Death-resistant cells	Remove, using suicide genes etc
Mitochondrial mutations	Reinforce, using backup copies
Intracellular waste products	Remove, using foreign enzymes
Extracellular waste products	Remove, using immune system
Extracellular matrix stiffening	Repair, using crosslink-breakers

Existence of any 8th is looking increasingly unlikely

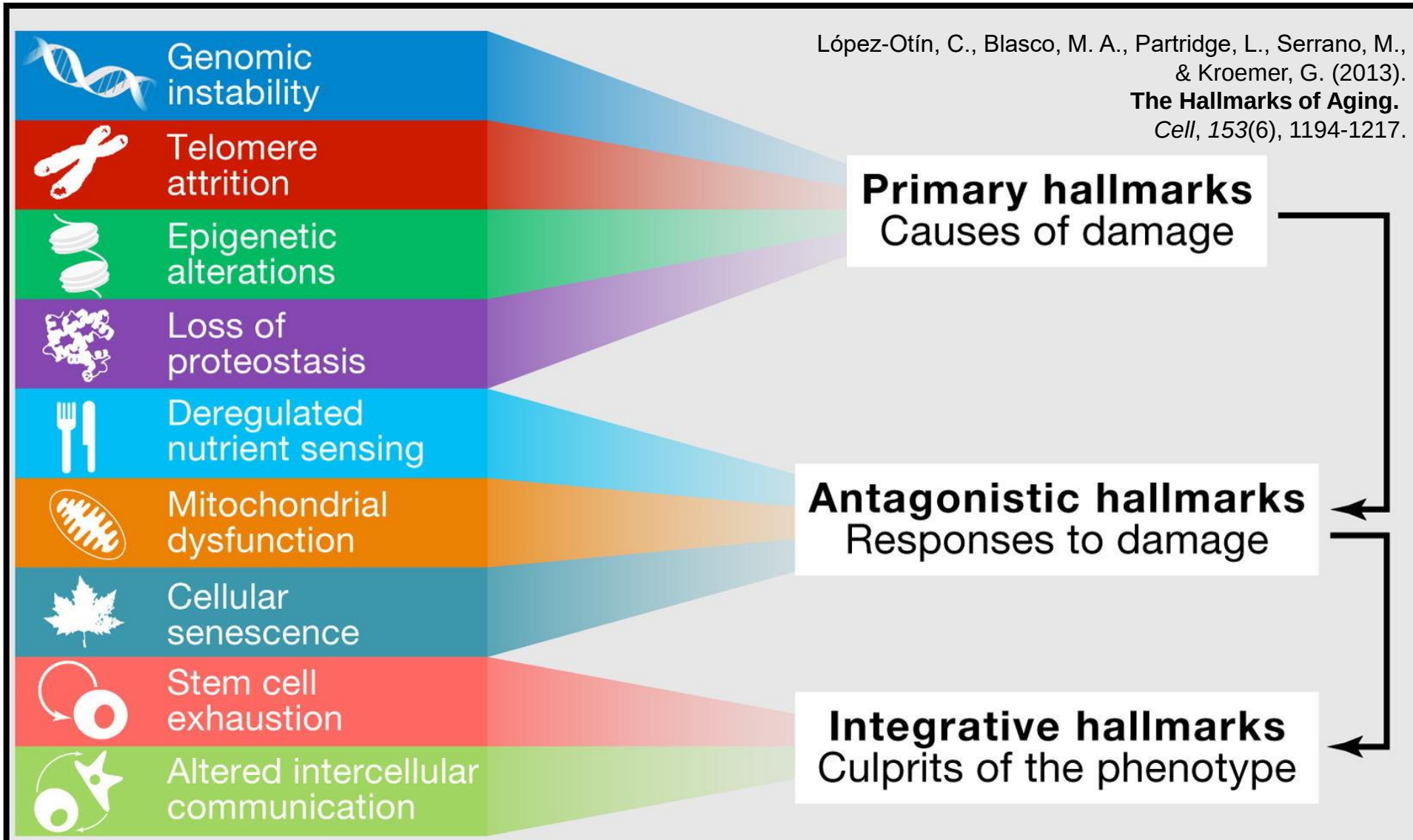
sens research foundation
reimagine aging

The publication introducing SENS provoked multiple discussions and, for many years, was subject to open and rough criticism.

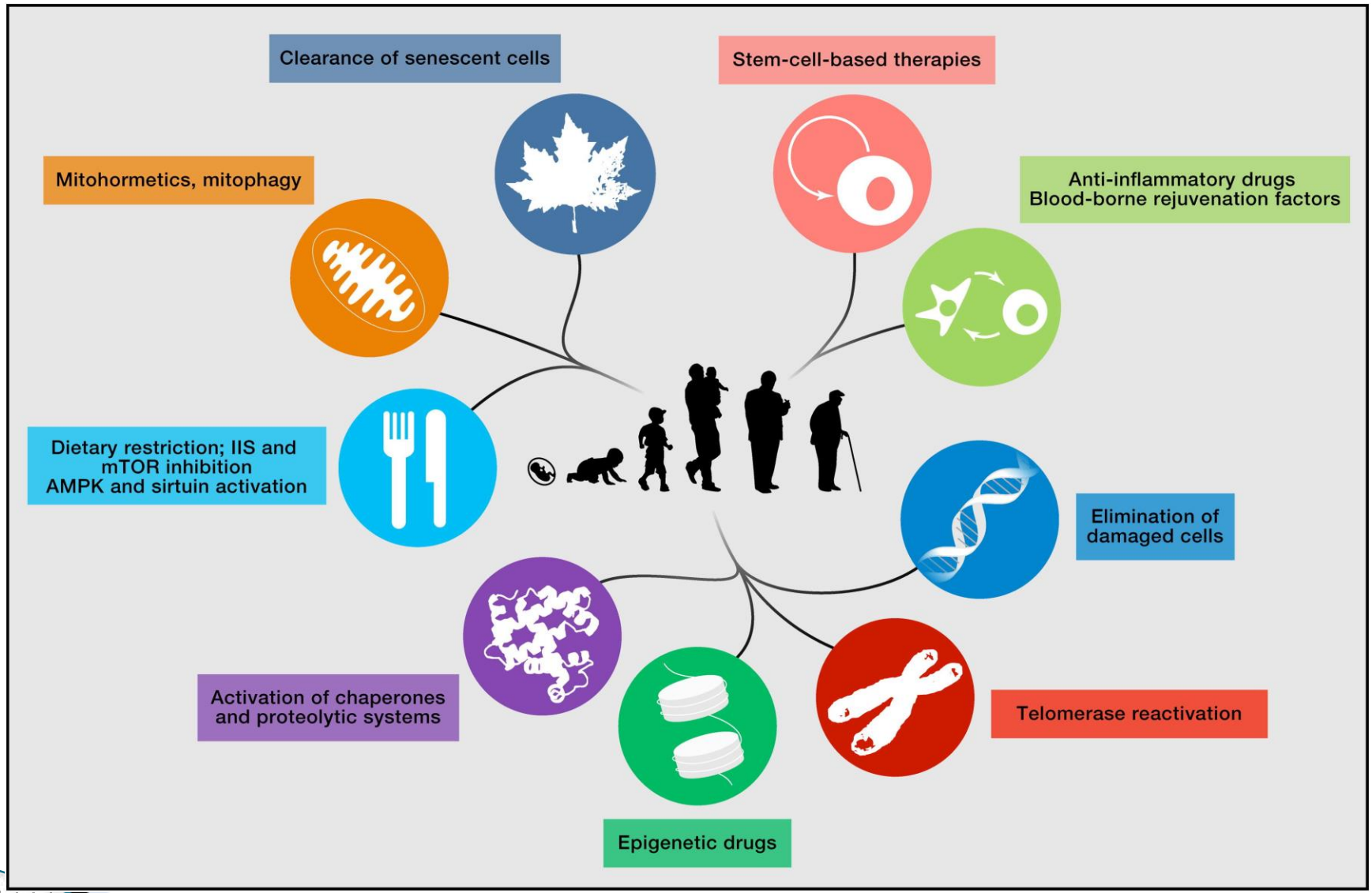
However, as scientific studies progressed, it became clear that the concept of dividing aging into specific processes and looking for potential ways to address them one by one was scientifically sound and viable.

In 2013, a group of renowned researchers published an article in Cell describing nine root causes of aging. As they were all experts in their respective fields of research, the article was taken very seriously, and it has been cited more than 3,000 times.

The Hallmarks of Aging:
9 mechanisms, 4 of them primary

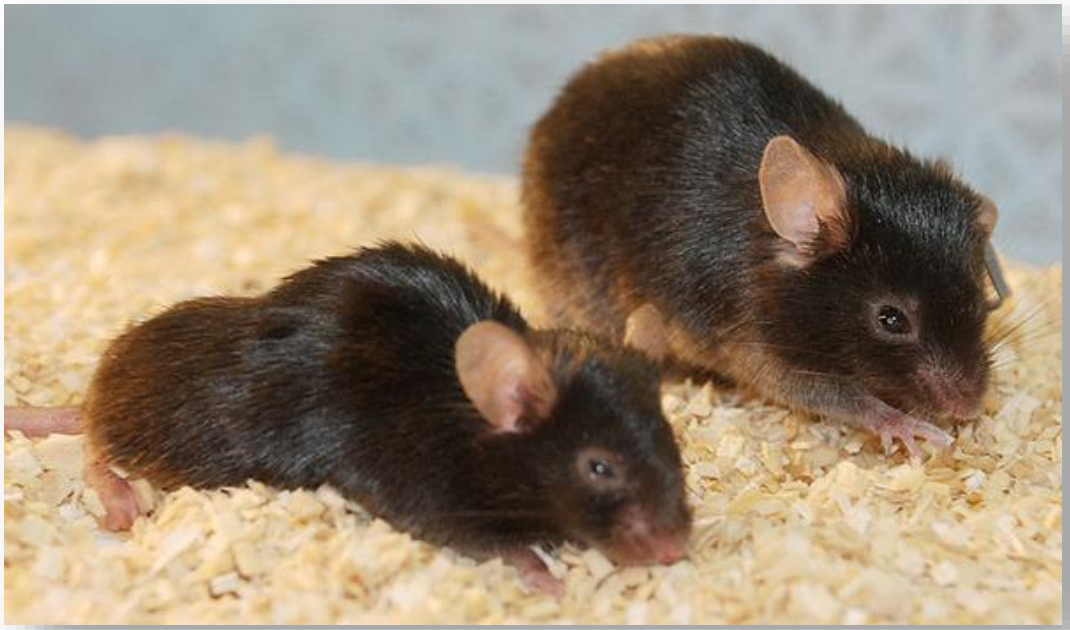


Solutions?



López-Otín, C., Blasco, M. A., Partridge, L., Serrano, M., & Kroemer, G. (2013). **The Hallmarks of Aging.** *Cell*, *153*(6), 1194-1217.

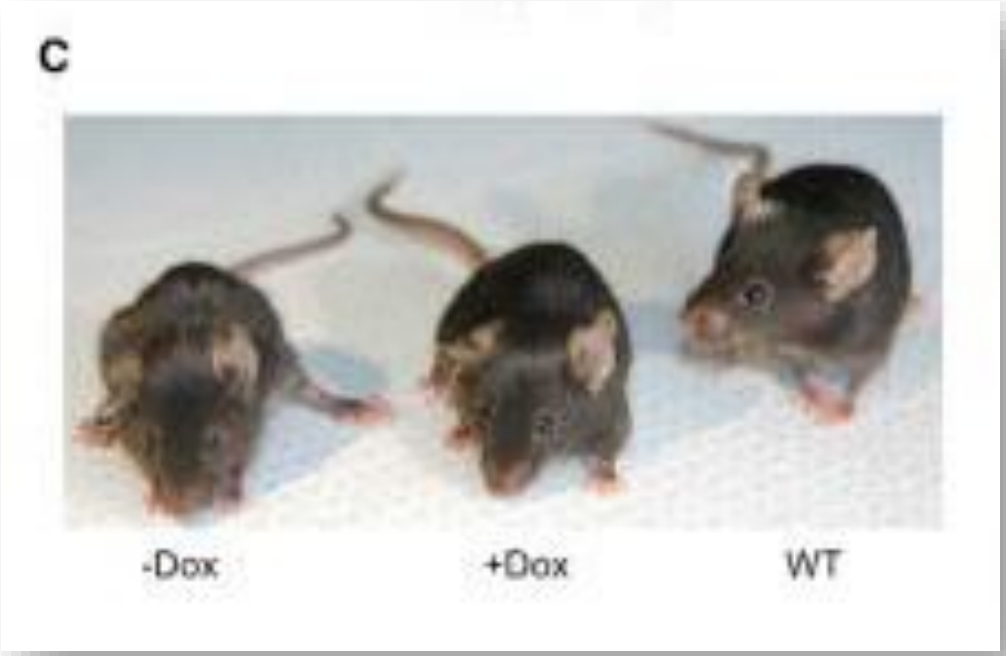
What happens when we target cellular senescence (one of the root causes of aging)

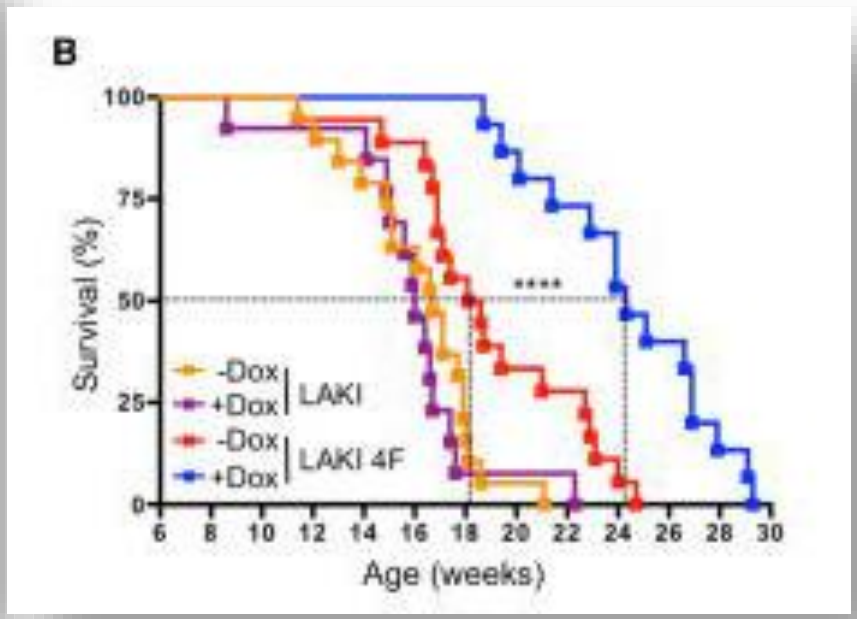


Baker, D. J., Childs, B. G., Durik, M., Wijers, M. E., Sieben, C. J., Zhong, J., ... & Khazaie, K. (2016). Naturally occurring p16Ink4a-positive cells shorten healthy lifespan. *Nature*, *530*(7589), 184. (+35% median lifespan extension)

- Animals remain healthy for longer
- Age-related diseases are postponed
- Some damages of aging are reversed
- Healthspan and lifespan extension of 30-40% in mammals, 10-fold in worms and yeast
- Lifespan is sometimes extended beyond the known maximum

What happens when we target epigenetic alterations (one of the root causes of aging)

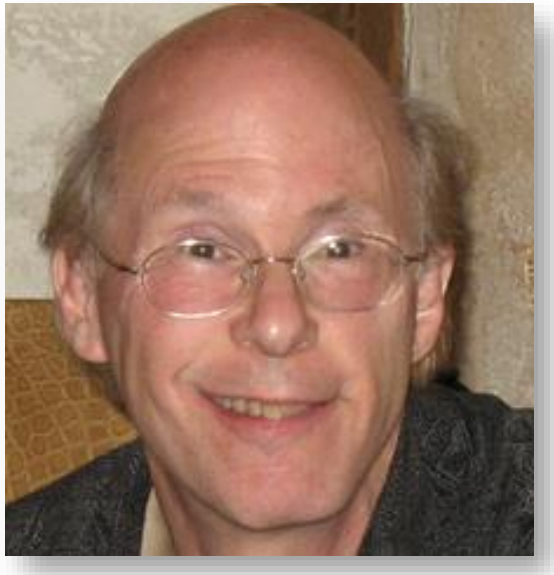




Ocampo, A., Reddy, P., Martinez-Redondo, P., Platero-Luengo, A., Hatanaka, F., Hishida, T., ... & Araoka, T. (2016). In vivo amelioration of age-associated hallmarks by partial reprogramming. *Cell*, *167*(7), 1719-1733.

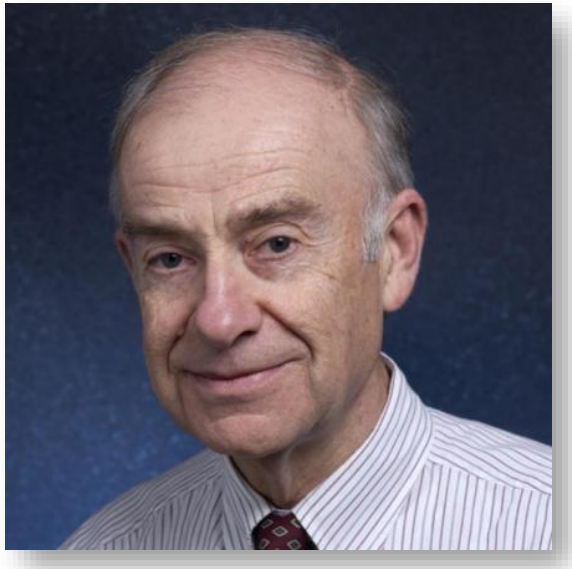
- Animals remain healthy for longer
- Age-related diseases are postponed
- Some age-related changes and damages are reversed
- Healthy period of life and lifespan in mice is extended by ~ 30%
- Note: this experiment was done in mice with accelerated aging

Records in manipulating aging



Robert Shmookler Reis
C. elegans (round worms) Lifespan extended 10-fold

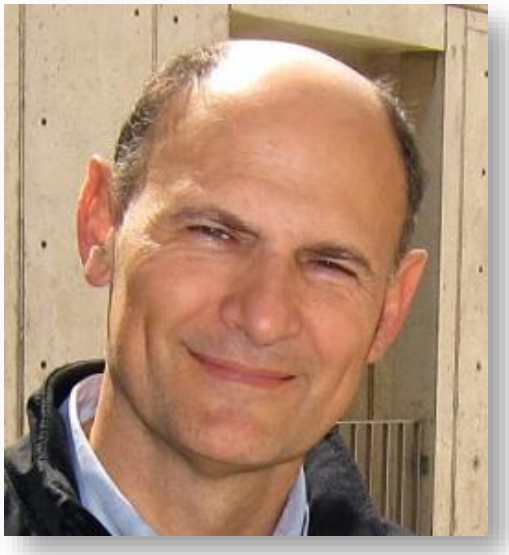
Valter Longo
Calorie restriction Lifespan in yeast extended 10-fold



Andrzej Bartke
Dwarf mice on caloric restriction +60% lifespan compared to normal mice

Records in manipulating aging

Jan van Deursen
Eliminating senescent cells with senolytics in mice
+35% lifespan



Juan Carlos Izpisua Belmonte
Rejuvenation of living mice with Yamanaka factors
+30% lifespan

Maria Blasco
Gene therapy to extend telomeres in mice
+24% lifespan

Conclusion

Dr. de Grey was first to begin the discussion on whether it is possible to define the root causes of aging and prevent age-related diseases by addressing these processes.

Over time, the concept was proven in scientific studies, and after several years of criticism and discussion, it was accepted by academia.

The studies show that by addressing even one of the root processes of aging, it is possible to keep animals healthy for longer, reverse some damages of aging, and postpone age-related decline. They also show that, as a consequence of health improvement, lifespan can be extended beyond the known maximum.

The good news is that some of these interventions against the processes of aging are already in clinical trials in humans.

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Thank you!

If you have an interesting research project in mind to investigate one of the main mechanisms of aging and longevity or you would like to support such a project, you are welcome to contact us at info@lifespan.io.

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