

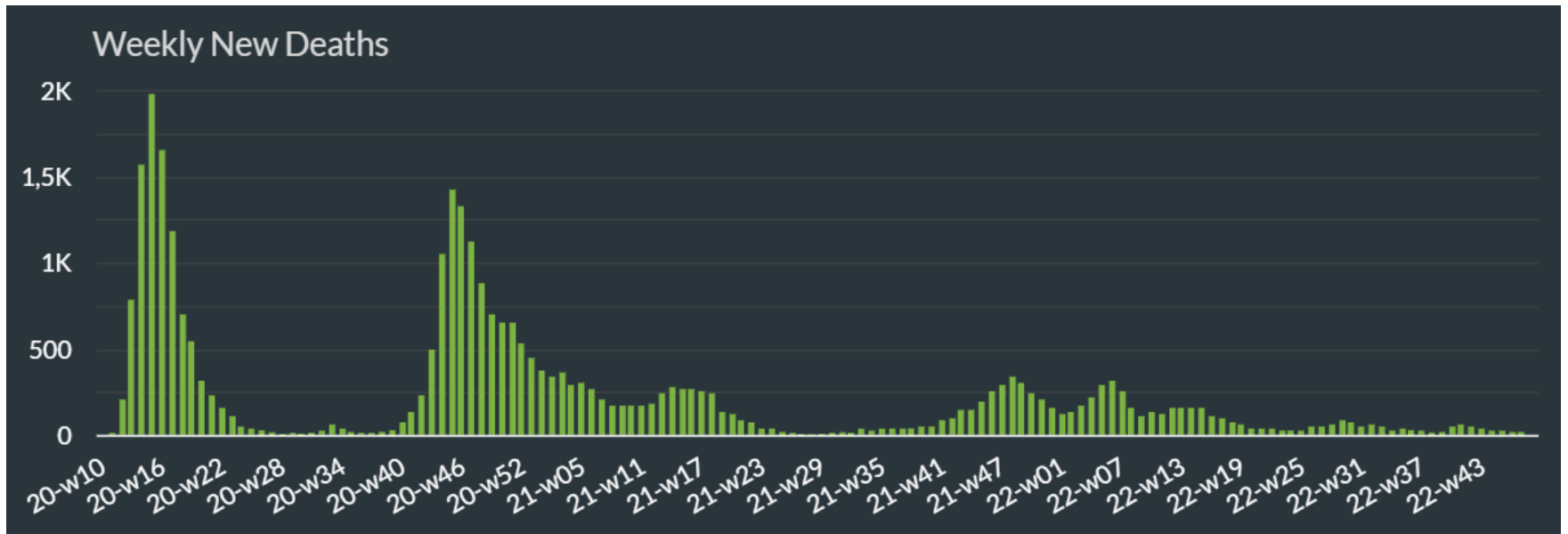
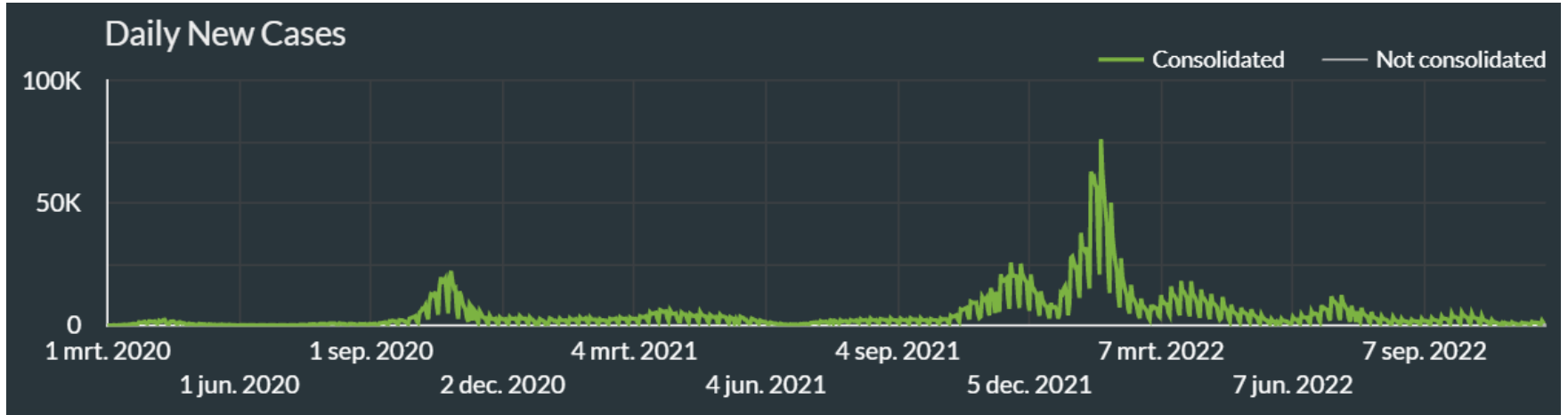


Heales
**HEALTHY LIFE EXTENSION
SOCIETY**

Scientific News
4th of December 2022
Sven Bulterijs

Business/Conferences/
General news

Belgium



COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU)

Last Updated at (M/D/YYYY)
4-12-2022 09:20

Total Cases
645,122,290

Total Deaths
6,640,618

Total Vaccine Doses Administered
13,054,668,703

Cases | Deaths by
Country/Region/Sovereignty

28-Day Cases
12,251,250

28-Day Deaths
38,916

28-Day Vaccine Doses Administered
168,524,355

Japan
28-Day: **2,517,053** | **3,114**
Totals: **25,242,594** | **50,352**

Korea, South
28-Day: **1,469,851** | **1,357**
Totals: **27,308,090** | **30,729**

US
28-Day: **1,225,320** | **8,582**
Totals: **98,967,906** | **1,081,431**

France
28-Day: **1,034,655** | **1,816**
Totals: **38,174,893** | **160,133**

China
28-Day: **854,442** | **342**
Totals: **3,852,218** | **16,031**

Italy
28-Day: **846,069** | **2,297**
Totals: **24,488,080** | **181,733**

Germany
28-Day: **734,090** | **3,663**
Totals: **36,557,861** | **158,198**

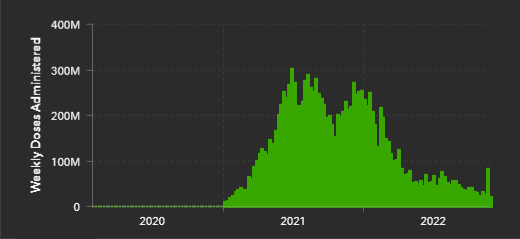
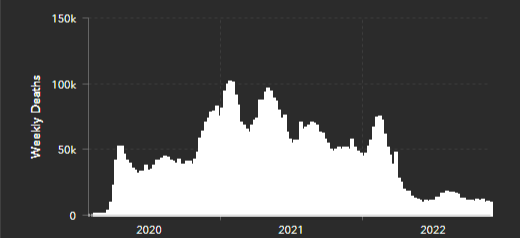
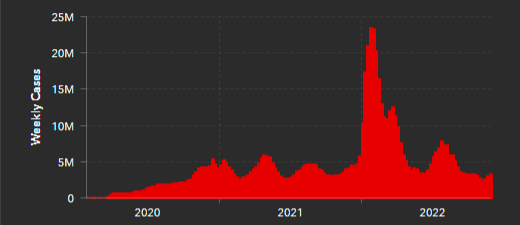
Taiwan*
28-Day: **493,024** | **1,298**
Totals: **8,356,217** | **14,449**

Brazil
28-Day: **488,493** | **1,742**



Esri, FAO, NOAA, USGS

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Admin0 Admin1 Admin2

28-Day Totals Incidence Case-Fatality Ratio Global Vaccinations US Vaccinations Terms of Use

Weekly 28-Day



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EHA 2022 - 2.10. Big data for longevity, how to better share (Didier Coeurnelle)

2 weergaven • 17 uur geleden



2.9. How Big Data of evidence based articles can reduce doctors mistakes & delay...

2 weergaven • 18 uur geleden



EHA 2022 - 2.7. EHDS - A Chance for the European Union to foster Citizen Longevity...

2 weergaven • 18 uur geleden



EHA 2022 - 2.6. A Democratic Use of our Digital Data (Stefan Sorgner)

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EHA 2022 - 2.8. Can a start-up develop big data and IA to adress Healthy Longevity? (...)

3 weergaven • 18 uur geleden



2.5. Tackling Aging: Limits of market economy only approaches and the case for...

3 weergaven • 18 uur geleden



EHA 2022 - 2.4. New Codes for Ageing and Ageing-Related Diseases in ICD11 of WHO...

12 weergaven • 1 dag geleden

Amid 'biotech winter,' Insilico turns up the heat with Sanofi deal worth \$1.2B in biobucks

By **Gabrielle Masson** • Nov 8, 2022 09:00am

The freshly inked multiyear research deal gives Sanofi access to Insilico's AI platform, dubbed Pharma.AI, to advance drug development candidates for up to six targets. The Big Pharma will pay out up to \$21.5 million to cover the upfront and target nomination fees, with further milestone payments stretching to over \$1.2 billion in addition to tiered royalties.

Aging research articles

Disruption of Growth Hormone Receptor in Adipocytes Improves Insulin Sensitivity and Lifespan in Mice FREE

Growth hormone receptor knockout (GHRKO) mice have been used for 25 years to uncover some of the many actions of growth hormone (GH). Since they are extremely long-lived with enhanced insulin sensitivity and protected from multiple age-related diseases, they are often used to study healthy aging. To determine the effect that adipose tissue has on the GHRKO phenotype, our laboratory recently created and characterized adipocyte-specific GHRKO (AdGHRKO) mice, which have increased adiposity but appear healthy with enhanced insulin sensitivity. To test the hypothesis that removal of GH action in adipocytes might partially replicate the increased lifespan and healthspan observed in global GHRKO mice, we assessed adiposity, cytokines/adipokines, glucose homeostasis, frailty, and lifespan in aging AdGHRKO mice of both sexes. Our results show that disrupting the GH receptor gene in adipocytes improved insulin sensitivity at advanced age and increased lifespan in male AdGHRKO mice. AdGHRKO mice also exhibited increased fat mass, reduced circulating levels of insulin, c-peptide, adiponectin, resistin, and improved frailty scores with increased grip strength at advanced ages. Comparison of published mean lifespan data from GHRKO mice to that from AdGHRKO and muscle-specific GHRKO mice suggests that approximately 23% of lifespan extension in male GHRKO is due to GHR disruption in adipocytes vs approximately 19% in muscle. Females benefited less from GHR disruption in these 2 tissues with approximately 19% and approximately 0%, respectively. These data indicate that removal of GH's action, even in a single tissue, is sufficient for observable health benefits that promote long-term health, reduce frailty, and increase longevity.

Decreased lifespan in female "Munchkin" actors from the cast of the 1939 film version of The Wizard of Oz does not support the hypothesis linking hypopituitary dwarfism to longevity

Vince Fazekas-Pongor ^{# 1}, Anna Péterfi ^{# 1}, Dávid Major ¹, Zsófia Szarvas ¹, Monika Fekete ¹, Adam G Tabak ^{1 2 3}, Anna Csiszar ^{4 5 6 7}, William E Sonntag ⁴, Steven N Austad ⁸, Zoltan I Ungvari ^{9 10 11 12 13}





Affiliations + expand

PMID: 36334178 DOI: [10.1007/s11357-022-00680-7](https://doi.org/10.1007/s11357-022-00680-7)

Abstract

In laboratory mice, pituitary dwarfism caused by genetic reduction or elimination of the activity of growth hormone (GH) significantly extends lifespan. The effects of congenital pituitary dwarfism on human longevity are not well documented. To analyse the effects of untreated pituitary dwarfism on human lifespan, the longevity of a diverse group of widely known little people, the 124 adults who played "Munchkins" in the 1939 movie The Wizard of Oz was investigated. Survival of "Munchkin" actors with those of controls defined as cast members of The Wizard of Oz and those of other contemporary Academy Award winning Hollywood movies was compared. According to the Kaplan-Meier survival curves, survival of female and male "Munchkin" actors was shorter than cast controls and Hollywood controls of respective sexes. Cox regression analyses showed that female "Munchkin" actors had significantly higher risk ratios compared to both female cast controls (RR, 1.70; 95% CI, 1.05 to 2.77) and female Hollywood controls (RR, 1.52; 95% CI, 1.03 to 2.24). Similar trends were also discernible for men, albeit point estimates were not significant. The lack of lifespan extension in "Munchkin" actors does not support the hypothesis that hereditary GH deficiency regulates longevity in humans.

The memory B cell response to influenza vaccination is impaired in older persons

Alice R. Burton¹, Stephane M. Guillaume¹, William S. Foster¹, Adam K. Wheatley², Danika L. Hill^{1,3}, Edward J. Carr^{1,4,5,6,7}  , Michelle A. Linterman^{1,6}  

Influenza infection imparts an age-related increase in mortality and morbidity. The most effective countermeasure is vaccination; however, vaccines offer modest protection in older adults. To investigate how aging impacts the memory B cell response, we track hemagglutinin-specific B cells by indexed flow sorting and single-cell RNA sequencing (scRNA-seq) in 20 healthy adults that were administered the trivalent influenza vaccine. We demonstrate age-related skewing in the memory B cell compartment 6 weeks after vaccination, with younger adults developing hemagglutinin-specific memory B cells with an *FcRL5*⁺ “atypical” phenotype, showing evidence of somatic hypermutation and positive selection, which happened to a lesser extent in older persons. We use publicly available scRNA-seq from paired human lymph node and blood samples to corroborate that *FcRL5*⁺ atypical memory B cells can derive from germinal center (GC) precursors. Together, this study shows that the aged human GC reaction and memory B cell response following vaccination is defective.

Deep phenotyping and lifetime trajectories reveal limited effects of longevity regulators on the aging process in C57BL/6J mice

Current concepts regarding the biology of aging are primarily based on studies aimed at identifying factors regulating lifespan. However, lifespan as a sole proxy measure for aging can be of limited value because it may be restricted by specific pathologies. Here, we employ large-scale phenotyping to analyze hundreds of markers in aging male C57BL/6J mice. For each phenotype, we establish lifetime profiles to determine when age-dependent change is first detectable relative to the young adult baseline. We examine key lifespan regulators (putative anti-aging interventions; PAAs) for a possible countering of aging. Importantly, unlike most previous studies, we include in our study design young treated groups of animals, subjected to PAAs prior to the onset of detectable age-dependent phenotypic change. Many PAA effects influence phenotypes long before the onset of detectable age-dependent change, but, importantly, do not alter the rate of phenotypic change. Hence, these PAAs have limited effects on aging.

Cell division drives DNA methylation loss in late-replicating domains in primary human cells

[Jamie L. Endicott](#), [Paula A. Nolte](#), [Hui Shen](#)  & [Peter W. Laird](#) 

Nature Communications **13**, Article number: 6659 (2022) | [Cite this article](#)

3897 Accesses | **68** Altmetric | [Metrics](#)



Abstract

DNA methylation undergoes dramatic age-related changes, first described more than four decades ago. Loss of DNA methylation within partially methylated domains (PMDs), late-replicating regions of the genome attached to the nuclear lamina, advances with age in normal tissues, and is further exacerbated in cancer. We present here experimental evidence that this DNA hypomethylation is directly driven by proliferation-associated DNA replication. Within PMDs, loss of DNA methylation at low-density CpGs in A:T-rich immediate context (PMD solo-WCGWs) tracks cumulative population doublings in primary cell culture. Cell cycle deceleration results in a proportional decrease in the rate of DNA hypomethylation. Blocking DNA replication via Mitomycin C treatment halts methylation loss. Loss of methylation continues unabated after *TERT* immortalization until finally reaching a severely hypomethylated equilibrium. Ambient oxygen culture conditions increases the rate of methylation loss compared to low-oxygen conditions, suggesting that some methylation loss may occur during unscheduled, oxidative damage repair-associated DNA synthesis. Finally, we present and validate a model to estimate the relative cumulative replicative histories of human cells, which we call “RepliTali” (Replication Times Accumulated in Lifetime).

Measurements of damage and repair of binary health attributes in aging mice and humans reveal that robustness and resilience decrease with age, operate over broad timescales, and are affected differently by interventions


As an organism ages, its health-state is determined by a balance between the processes of damage and repair. Measuring these processes requires longitudinal data. We extract damage and repair transition rates from repeated observations of binary health attributes in mice and humans to explore robustness and resilience, which respectively represent resisting or recovering from damage. We assess differences in robustness and resilience using changes in damage rates and repair rates of binary health attributes. We find a conserved decline with age in robustness and resilience in mice and humans, implying that both contribute to worsening aging health – as assessed by the frailty index (FI). A decline in robustness, however, has a greater effect than a decline in resilience on the accelerated increase of the FI with age, and a greater association with reduced survival. We also find that deficits are damaged and repaired over a wide range of timescales ranging from the shortest measurement scales towards organismal lifetime timescales. We explore the effect of systemic interventions that have been shown to improve health, including the angiotensin-converting enzyme inhibitor enalapril and voluntary exercise for mice. We have also explored the correlations with household wealth for humans. We find that these interventions and factors can affect both damage and repair rates, and hence robustness and resilience, in age and sex-dependent manners.

Predicting Lifespan-Extending Chemical Compounds with Machine Learning and Biologically Interpretable Features

Caio Ribeiro, Christopher K. Farmer,  João Pedro de Magalhães,  Alex A. Freitas

Recently, there has been a growing interest in the development of pharmacological interventions targeting ageing, as well as on the use of machine learning for analysing ageing-related data. In this work we use machine learning methods to analyse data from DrugAge, a database of chemical compounds (including drugs) modulating lifespan in model organisms. To this end, we created four datasets for predicting whether or not a compound extends the lifespan of *C. elegans* (the most frequent model organism in DrugAge), using four different types of predictive biological features, based on compound-protein interactions, interactions between compounds and proteins encoded by ageing-related genes, and two types of terms annotated for proteins targeted by the compounds, namely Gene Ontology (GO) terms and physiology terms from the WormBase Phenotype Ontology. To analyse these datasets we used a combination of feature selection methods in a data pre-processing phase and the well-established random forest algorithm for learning predictive models from the selected features. The two best models were learned using GO terms and protein interactors as features, with predictive accuracies of about 82% and 80%, respectively. In addition, we interpreted the most important features in those two best models in light of the biology of ageing, and we also predicted the most promising novel compounds for extending lifespan from a list of previously unlabelled compounds.

Longevity of a solitary mole-rat species and its implications for the assumed link between sociality and longevity in African mole-rats (Bathyergidae)

P. Dammann, G. Šaffa and R. Šumbera 

Published: 23 November 2022 | <https://doi.org/10.1098/rsbl.2022.0243>

Abstract

Sociality and cooperative breeding are associated with enhanced longevity in insects and birds, but whether this is also true for mammals is still subject to debate. African mole-rats (Bathyergidae) have recently been claimed to be the only mammalian family in which such an association may exist because cooperatively breeding bathyergids seem to be substantially longer lived than solitary bathyergids. However, although ample longevity data are available for several social bathyergids, almost nothing is known about mortality distribution and lifespan in solitary bathyergids. Here we present robust long-term data on the longevity of a solitary African mole-rat, the silvery mole-rat *Heliophobius argenteocinereus*. Our findings show that this species is much longer-lived than previously believed. Nonetheless, our comparative analysis suggests that sociality has indeed a positive effect on longevity in this family. We argue that the extreme longevity seen particularly in social bathyergids is probably caused by a combination of subterranean lifestyle and cooperative breeding.

Unified epigenomic, transcriptomic, proteomic, and metabolomic taxonomy of Alzheimer's disease progression and heterogeneity

Yasser Iturria-Medina ^{1 2 3}, Quadri Adewale ^{1 2 3}, Ahmed F Khan ^{1 2 3}, Simon Ducharme ^{2 4}, Pedro Rosa-Neto ⁵, Kieran O'Donnell ^{3 6}, Vladislav A Petyuk ⁷, Serge Gauthier ⁵, Philip L De Jager ⁸, John Breitner ^{9 10}, David A Bennett ^{11 12}

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PMID: 36399579 PMCID: [PMC9674284](#) DOI: [10.1126/sciadv.abo6764](#)

[Free PMC article](#)

Abstract

Alzheimer's disease (AD) is a heterogeneous disorder with abnormalities in multiple biological domains. In an advanced machine learning analysis of postmortem brain and in vivo blood multi-omics molecular data ($N = 1863$), we integrated epigenomic, transcriptomic, proteomic, and metabolomic profiles into a multilevel biological AD taxonomy. We obtained a personalized multilevel molecular index of AD dementia progression that predicts severity of neuropathologies, and identified three robust molecular-based subtypes that explain much of the pathologic and clinical heterogeneity of AD. These subtypes present distinct patterns of alteration in DNA methylation, RNA, proteins, and metabolites, identifiable in the brain and subsequently in blood. In addition, the genetic variations that predispose to the various AD subtypes in brain predict distinct spatial patterns of alteration in cell types, suggesting a unique influence of each putative AD variant on neuropathological mechanisms. These observations support that an individually tailored multi-omics molecular taxonomy of AD may represent distinct targets for preventive or treatment interventions.

Lifelong temporal dynamics of the gut microbiome associated with longevity in mice

The effect of lifelong dynamics on host longevity of the gut microbiome is largely unknown. Herein, we analyzed the longitudinal fecal samples of seven sibling mice across their lifespan from birth to natural death, spanning over 1,000 days of age, and maintained them under controlled environmental and dietary conditions. Our 16S-rRNA sequencing analysis revealed 38 common “life-core” bacterial species/OTUs (operational taxonomic units) detected in $\geq 80\%$ of all samples collected across the lifespan of individual mice. Despite the shared genetic background and dietary habits, the gut microbiome structure significantly diversified with age and among individuals. We found a strong positive correlation between longevity and the alpha diversity in middle age (500-700 days) and negative correlation in old age (> 800 days). Furthermore, host longevity was significantly associated with the abundance of 17 bacterial species/OTUs, most of which were “life-core” species. Our data suggest that temporal dynamics of the gut microbiome are strongly linked to host longevity.

Dietary restriction fails to extend life in stressful environments

 Felix Zajitschek,  Susanne R.K. Zajitschek,  Ana C.O.Vasconcelos,  Russell Bonduriansky

doi: <https://doi.org/10.1101/2022.10.17.512576>

This article is a preprint and has not been certified by peer review [what does this mean?].



Abstract

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ABSTRACT

Moderate dietary restriction often prolongs life in laboratory animals, and this response has been interpreted as an adaptive strategy that promotes survival during famine. However, dietary restriction can also increase frailty, and it therefore remains unclear whether restricted diets prolong life under stressful conditions like those experienced by wild animals. We manipulated adult dietary protein of *Drosophila melanogaster* across a gradient of ambient temperature. We found that protein restriction increased longevity of both sexes at benign ambient temperatures (25-27°C), but failed to extend or even reduced longevity of flies maintained in cold (21-23°C) or hot (29°C) conditions. Protein restriction also generally reduced reproductive performance, and did not consistently enhance performance of F1, F2 or F3 descendants. Our results challenge the long-held idea that extended longevity of diet-restricted laboratory animals represents an adaptive survival strategy in natural populations, and suggest instead that this response is an artefact of benign laboratory conditions.

Metabolic and physical function are improved with lifelong 15% calorie restriction in aging male mice

Emily C Peters ¹, Luke Safayan ¹, Tyler J Marx ², Emily Ngu ², Anastasiia Vasileva ², India Zappia ², William H Powell ¹, Frank A Duca ^{3 4}, Jennifer H Stern ^{5 6 7}

Affiliations + expand

PMID: 36315375 DOI: 10.1007/s10522-022-09996-5

Abstract

Chronic calorie restriction (CR) results in lengthened lifespan and reduced disease risk. Many previous studies have implemented 30-40% calorie restriction to investigate these benefits. The goal of our study was to investigate the effects of calorie restriction, beginning at 4 months of age, on metabolic and physical changes induced by aging. Male C57BL/6NCrI calorie restricted and ad libitum fed control mice were obtained from the National Institute on Aging (NIA) and studied at 10, 18, 26, and 28 months of age to better understand the metabolic changes that occur in response to CR in middle age and advanced age. Food intake was measured in ad libitum fed controls to assess the true degree of CR (15%) in these mice. We found that 15% CR decreased body mass and liver triglyceride content, improved oral glucose clearance, and increased all limb grip strength in 10- and 18-month-old mice. Glucose clearance in ad libitum fed 26- and 28-month-old mice is enhanced relative to younger mice but was not further improved by CR. CR decreased basal insulin concentrations in all age groups and improved insulin sensitivity and rotarod time to fall in 28-month-old mice. The results of our study demonstrate that even a modest reduction (15%) in caloric intake may improve metabolic and physical health. Thus, moderate calorie restriction may be a dietary intervention to promote healthy aging with improved likelihood for adherence in human populations.

C. elegans aging research

Identifying *C. elegans* lifespan mutants by screening for early-onset protein aggregation

Daniel F Midkiff ¹, Javier Huayta ¹, James D Lichty ¹, Joseph P Crapster ¹, Adriana San-Miguel ¹

Affiliations + expand

PMID: 36388964 PMCID: PMC9664360 DOI: 10.1016/j.isci.2022.105460

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Abstract

Genetic screens are widely used to identify genes that control specific biological functions. In *Caenorhabditis elegans*, forward genetic screens rely on the isolation of reproductively active mutants that can self-propagate clonal populations. Screens that target post-reproductive phenotypes, such as lifespan, are thus challenging. We combine microfluidic technologies and image processing to perform high-throughput automated screening for short-lived mutants using protein aggregation as a marker for aging. We take advantage of microfluidics for maintaining a reproductively active adult mutagenized population and for performing serial high-throughput analysis and sorting of animals with increased protein aggregation, using fluorescently-labeled PAB-1 as a readout. We demonstrate that lifespan mutants can be identified by screening for accelerated protein aggregation through quantitative analysis of fluorescently labeled aggregates while avoiding conditional sterilization or manual separation of parental and progeny populations. We also show that aged wildtypes and premature aggregation mutants differ in aggregate morphology, suggesting aggregate growth is time-dependent.

Further Extension of Lifespan by *Unc-43/CaMKII* and *Egl-8/PLC β* Mutations in Germline-Deficient *Caenorhabditis elegans*

Hildegard I D Mack¹, Laura G Buck¹, Sonja Skalet¹, Jennifer Kremer², Hao Li³,
Elisabeth K M Mack²

Affiliations + expand

PMID: 36428956 DOI: [10.3390/cells11223527](https://doi.org/10.3390/cells11223527)

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Abstract

Reduction of insulin/insulin-like growth factor 1 (IGF1) signaling (IIS) promotes longevity across species. In the nematode *Caenorhabditis elegans*, ablation of germline stem cells (GSCs) and activity changes of the conserved signaling mediators *unc-43/CaMKII* (calcium/calmodulin-dependent kinase type II) and *egl-8/PLC β* (phospholipase C β) also increase lifespan. Like IIS, these pathways depend on the conserved transcription factor *daf-16/FOXO* for lifespan extension, but how they functionally interact is unknown. Here, we show that altered *unc-43/egl-8* activity further increases the lifespan of long-lived GSC-deficient worms, but not of worms that are long-lived due to a strong reduction-of-function mutation in the insulin/IGF1-like receptor *daf-2*. Additionally, we provide evidence for *unc-43* and, to a lesser extent, *egl-8* modulating the expression of certain collagen genes, which were reported to be dispensable for longevity of these particular *daf-2* mutant worms, but not for other forms of longevity. Together, these results provide new insights into the conditions and potential mechanisms by which CaMKII- and PLC β -signals modulate *C. elegans* lifespan.

Keywords: RNA-seq; aging; collagen; germline stem cells; insulin signaling; stress resistance.

Mitochondria-originated redox signalling regulates KLF-1 to promote longevity in *Caenorhabditis elegans*

Alternations of redox metabolism have been associated with the extension of lifespan in roundworm *Caenorhabditis elegans*, caused by moderate mitochondrial dysfunction, although the underlying signalling cascades are largely unknown. Previously, we identified transcriptional factor Krüppel-like factor-1 (KLF-1) as the main regulator of cytoprotective longevity-assurance pathways in the *C. elegans* long-lived mitochondrial mutants. Here, we show that KLF-1 translocation to the nucleus and the activation of the signalling cascade is dependent on the mitochondria-derived hydrogen peroxide (H_2O_2) produced during late developmental phases where aerobic respiration and somatic mitochondrial biogenesis peak. We further show that mitochondrial-inducible superoxide dismutase-3 (SOD-3), together with voltage-dependent anion channel-1 (VDAC-1), is required for the life-promoting H_2O_2 signalling that is further regulated by peroxiredoxin-3 (PRDX-3). Increased H_2O_2 release in the cytoplasm activates the p38 MAPK signalling cascade that induces KLF-1 translocation to the nucleus and the activation of transcription of *C. elegans* longevity-promoting genes, including cytoprotective cytochrome P450 oxidases. Taken together, our results underline the importance of redox-regulated signalling as the key regulator of longevity-inducing pathways in *C. elegans*, and position precisely timed mitochondria-derived H_2O_2 in the middle of it.

REVIEWS/COMMENTS/
METHODS/EDITORIALS

Epigenetic regulation of aging: implications for interventions of aging and diseases

[Kang Wang](#), [Huicong Liu](#), [Qinchao Hu](#), [Lingna Wang](#), [Jiaqing Liu](#), [Zikai Zheng](#), [Weiqi Zhang](#), [Jie Ren](#) ,
[Fangfang Zhu](#)  & [Guang-Hui Liu](#) 

Signal Transduction and Targeted Therapy **7**, Article number: 374 (2022) | [Cite this article](#)

5699 Accesses | 92 Altmetric | [Metrics](#)

Abstract

Aging is accompanied by the decline of organismal functions and a series of prominent hallmarks, including genetic and epigenetic alterations. These aging-associated epigenetic changes include DNA methylation, histone modification, chromatin remodeling, non-coding RNA (ncRNA) regulation, and RNA modification, all of which participate in the regulation of the aging process, and hence contribute to aging-related diseases. Therefore, understanding the epigenetic mechanisms in aging will provide new avenues to develop strategies to delay aging. Indeed, aging interventions based on manipulating epigenetic mechanisms have led to the alleviation of aging or the extension of the lifespan in animal models. Small molecule-based therapies and reprogramming strategies that enable epigenetic rejuvenation have been developed for ameliorating or reversing aging-related conditions. In addition, adopting health-promoting activities, such as caloric restriction, exercise, and calibrating circadian rhythm, has been demonstrated to delay aging. Furthermore, various clinical trials for aging intervention are ongoing, providing more evidence of the safety and efficacy of these therapies. Here, we review recent work on the epigenetic regulation of aging and outline the advances in intervention strategies for aging and age-associated diseases. A better understanding of the critical roles of epigenetics in the aging process will lead to more clinical advances in the prevention of human aging and therapy of aging-related diseases.

Epigenetic regulation of aging: implications for interventions of aging and diseases

Kang Wang ^{# 1 2 3}, Huicong Liu ^{# 4}, Qinchao Hu ^{# 1 5 6 7}, Lingna Wang ^{# 4}, Jiaqing Liu ^{# 4},
Zikai Zheng ^{3 5}, Weiqi Zhang ^{3 5 8}, Jie Ren ^{9 10 11}, Fangfang Zhu ¹²,
Guang-Hui Liu ^{13 14 15 16 17}

Affiliations [+](#) expand

PMID: 36336680 PMCID: [PMC9637765](#) DOI: [10.1038/s41392-022-01211-8](#)

[Free PMC article](#)

Abstract

Aging is accompanied by the decline of organismal functions and a series of prominent hallmarks, including genetic and epigenetic alterations. These aging-associated epigenetic changes include DNA methylation, histone modification, chromatin remodeling, non-coding RNA (ncRNA) regulation, and RNA modification, all of which participate in the regulation of the aging process, and hence contribute to aging-related diseases. Therefore, understanding the epigenetic mechanisms in aging will provide new avenues to develop strategies to delay aging. Indeed, aging interventions based on manipulating epigenetic mechanisms have led to the alleviation of aging or the extension of the lifespan in animal models. Small molecule-based therapies and reprogramming strategies that enable epigenetic rejuvenation have been developed for ameliorating or reversing aging-related conditions. In addition, adopting health-promoting activities, such as caloric restriction, exercise, and calibrating circadian rhythm, has been demonstrated to delay aging. Furthermore, various clinical trials for aging intervention are ongoing, providing more evidence of the safety and efficacy of these therapies. Here, we review recent work on the epigenetic regulation of aging and outline the advances in intervention strategies for aging and age-associated diseases. A better understanding of the critical roles of epigenetics in the aging process will lead to more clinical advances in the prevention of human aging and therapy of aging-related diseases.

There is no single universal biomarker yet to estimate overall health status and longevity prospects. Moreover, a consensual approach to the very concept of aging and the means of its assessment are yet to be developed. Markers of aging could facilitate effective health control, more accurate life expectancy estimates, and improved health and quality of life. Clinicians routinely use several indicators that could be biomarkers of aging. Duly validated in a large cohort, models based on a combination of these markers could provide a highly accurate assessment of biological age and the pace of aging. Biological aging is a complex characteristic of chronological age (usually), health-to-age concordance, and medically estimated life expectancy. This study is a review of the most promising techniques that could soon be used in routine clinical practice. Two main selection criteria were applied: a sufficient sample size and reliability based on validation. The selected biological age calculators were grouped according to the type of biomarker used: (1) standard clinical and laboratory markers; (2) molecular markers; and (3) epigenetic markers. The most accurate were the calculators, which factored in a variety of biomarkers. Despite their demonstrated effectiveness, most of them require further improvement and cannot yet be considered for use in standard clinical practice. To illustrate their clinical application, we reviewed their use during the COVID-19 pandemic.

Keywords: biological age; molecular clock; age-related diseases; life expectancy; COVID-19

Telomeres expand sphere of influence: emerging molecular impact of telomeres in non-telomeric functions

Soujanya Vinayagamurthy ¹, Sulochana Bagri ¹, Jean-Louis Mergny ², Shantanu Chowdhury ³

Affiliations + expand

PMID: 36404192 DOI: 10.1016/j.tig.2022.10.002

Free article

Abstract

Although the impact of telomeres on physiology stands well established, a question remains: how do telomeres impact cellular functions at a molecular level? This is because current understanding limits the influence of telomeres to adjacent subtelomeric regions despite the wide-ranging impact of telomeres. Emerging work in two distinct aspects offers opportunities to bridge this gap. First, telomere-binding factors were found with non-telomeric functions. Second, locally induced DNA secondary structures called G-quadruplexes are notably abundant in telomeres, and gene regulatory regions genome wide. Many telomeric factors bind to G-quadruplexes for non-telomeric functions. Here we discuss a more general model of how telomeres impact the non-telomeric genome - through factors that associate at telomeres and genome wide - and influence cell-intrinsic functions, particularly aging, cancer, and pluripotency.

Age reprogramming: cell rejuvenation by partial reprogramming

Prim B Singh ¹, Assem Zhakupova ¹

Affiliations + expand

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Abstract

'Age reprogramming' refers to the process by which the molecular and cellular pathways of a cell that are subject to age-related decline are rejuvenated without passage through an embryonic stage. This process differs from the rejuvenation observed in differentiated derivatives of induced pluripotent stem cells, which involves passage through an embryonic stage and loss of cellular identity.

Accordingly, the study of age reprogramming can provide an understanding of how ageing can be reversed while retaining cellular identity and the specialised function(s) of a cell, which will be of benefit to regenerative medicine. Here, we highlight recent work that has provided a more nuanced understanding of age reprogramming and point to some open questions in the field that might be explored in the future.

Keywords: Age reprogramming; Cellular identity; Epigenetic rejuvenation; H3K9me3; OSKM; Partial reprogramming.

OTHER RESEARCH & REVIEWS

GeneFriends: gene co-expression databases and tools for humans and model organisms

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Abstract

Gene co-expression analysis has emerged as a powerful method to provide insights into gene function and regulation. The rapid growth of publicly available RNA-sequencing (RNA-seq) data has created opportunities for researchers to employ this abundant data to help decipher the complexity and biology of genomes. Co-expression networks have proven effective for inferring the relationship between the genes, for gene prioritization and for assigning function to poorly annotated genes based on their co-expressed partners. To facilitate such analyses we created previously an online co-expression tool for humans and mice entitled GeneFriends. To continue providing a valuable tool to the scientific community, we have now updated the GeneFriends database and website. Here, we present the new version of GeneFriends, which includes gene and transcript co-expression networks based on RNA-seq data from 46 475 human and 34 322 mouse samples. The new database also encompasses tissue-specific gene co-expression networks for 20 human and 21 mouse tissues, dataset-specific gene co-expression maps based on TCGA and GTEx projects and gene co-expression networks for additional seven model organisms (fruit fly, zebrafish, worm, rat, yeast, cow and chicken). GeneFriends is freely available at <http://www.genefriends.org/>.