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Sven Bulterijs

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Oxidative balance score as predictor of all-cause, cancer, and noncancer mortality in a biracial US cohort.

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Author information

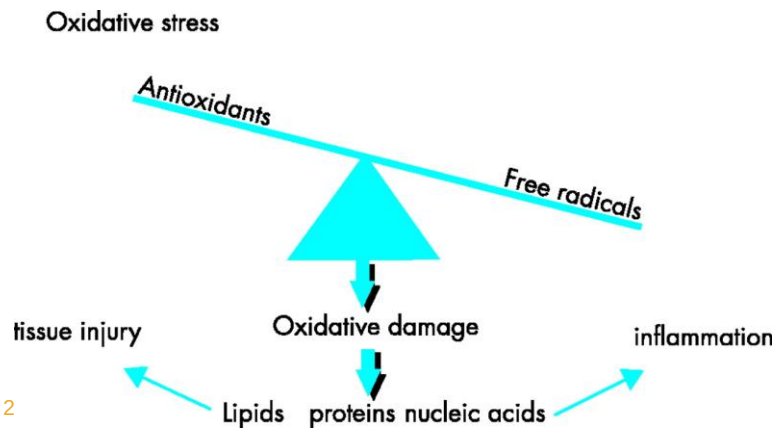
Abstract

PURPOSE: We previously proposed an oxidative balance score (OBS) that combines pro- and anti-oxidant exposures to represent the overall oxidative balance status of an individual. In this study, we investigated associations of the OBS with all-cause and cause-specific mortality, and explored alternative OBS weighting methods in the Reasons for Geographic and Racial Differences in Stroke Study cohort.

METHODS: The OBS was calculated by combining information from 14 a priori selected pro- and anti-oxidant factors and then divided into quartiles with the lowest quartile (predominance of pro-oxidants) as reference. Cox proportional hazard models were used to estimate adjusted hazard ratios and 95% confidence intervals for each OBS category compared with the reference.

RESULTS: Over a median 5.8 years of follow-up, 2079 of the 21,031 participants died. The multivariable-adjusted hazard ratios (95% confidence interval) for all-cause, cancer, and noncancer mortality for those in the highest versus the lowest equal-weighting OBS quartile were 0.70 (0.61-0.81), 0.50 (0.37-0.67), and 0.77 (0.66-0.89), respectively (P trend < .01 for all). Similar results were observed with all weighting methods.

CONCLUSIONS: These results suggest that individuals with a greater balance of antioxidant to pro-oxidant lifestyle exposures may have lower mortality.



OBS:

PUFA intake, total iron intake, total vit. C intake, total lycopene intake, total alpha-carotene intake, total beta-carotene intake, total lutein intake, total beta-cryptoxanthin intake, selenium intake, smoking history, regular aspirin use, regular NSAID use, and alcohol consumption

A Platform for Rapid Exploration of Aging and Diseases in a Naturally Short-Lived Vertebrate

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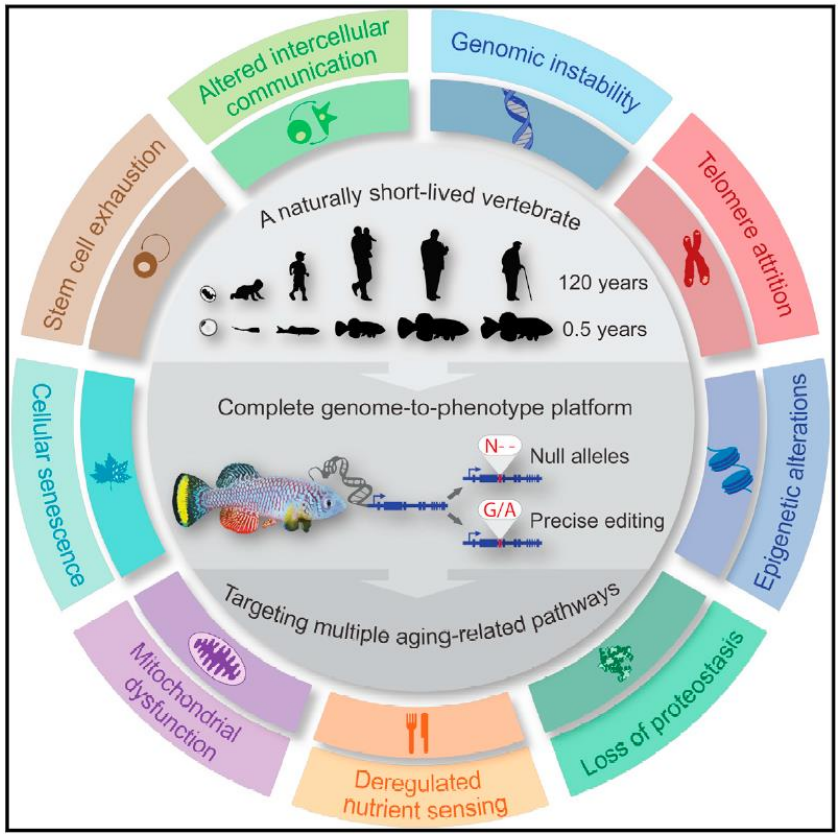
Aging is a complex process that affects multiple organs. Modeling aging and age-related diseases in the lab is challenging because classical vertebrate models have relatively long lifespans. Here, we develop the first platform for rapid exploration of age-dependent traits and diseases in vertebrates, using the naturally short-lived African turquoise killifish. We provide an integrative genomic and genome-editing toolkit in this organism using our de-novo-assembled genome and the CRISPR/Cas9 technology. We mutate many genes encompassing the hallmarks of aging, and for a subset, we produce stable lines within 2–3 months. As a proof of principle, we show that fish deficient for the protein subunit of telomerase exhibit the fastest onset of telomere-related pathologies among vertebrates. We further demonstrate the feasibility of creating specific genetic variants. This genome-to-phenotype platform represents a unique resource for studying vertebrate aging and disease in a high-throughput manner and for investigating candidates arising from human genome-wide studies.



"Mifepristone is often used in Drosophila aging research as the trigger for the conditional gene expression system called "Gene-Switch""

PDF version

The progesterone antagonist mifepristone/RU486 blocks the negative effect on life span caused by mating in female Drosophila

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Key words: *aging; sexual antagonistic pleiotropy; sexual conflict; life span trade-off*

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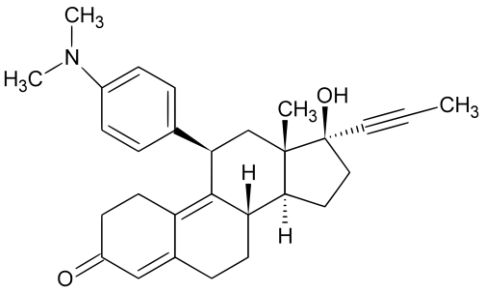
Abstract

Mating causes decreased life span in female Drosophila. Here we report that mifepristone blocked this effect, yielding life span increases up to +68%. Drug was fed to females after mating, in the absence of males, demonstrating function in females. Mifepristone did not increase life span of virgin females or males. Mifepristone reduced progeny production but did not reduce food intake. High-throughput RNA sequencing was used to identify genes up-regulated or down-regulated upon mating, and where the change was reduced by mifepristone. Five candidate positive regulators of life span were identified, including dosage compensation regulator Unr and three X-linked genes: multi sex combs (PcG gene), Dopamine 2-like receptor and CG14215. The 37 candidate negative genes included neuropeptide CNMamide and several involved in protein mobilization and immune response. The results inform the interpretation of experiments involving mifepristone, and implicate steroid hormone signaling in regulating the trade-off between reproduction and life span.



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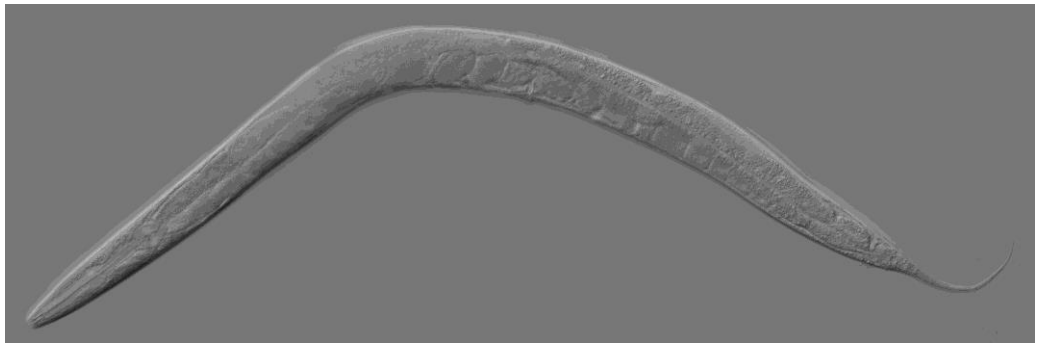
Uncoupling lifespan and healthspan in *Caenorhabditis elegans* longevity mutants

Ankita Bansal[a], Lihua J. Zhu[a,b,c], Kelvin Yen[a,1], and Heidi A. Tissenbaum[a,c,2]

Aging research has been very successful at identifying signaling pathways and evolutionarily conserved genes that extend lifespan with the assumption that an increase in lifespan will also increase healthspan. However, it is largely unknown whether we are extending the healthy time of life or simply prolonging a period of frailty with increased incidence of age-associated diseases. Here we use *Caenorhabditis elegans*, one of the premiere systems for lifespan studies, to determine whether lifespan and healthspan are intrinsically correlated. We conducted multiple cellular and organismal assays on wild type as well as four long-lived mutants (insulin/insulin-like growth factor-1, dietary restriction, protein translation, mitochondrial signaling) in a longitudinal manner to determine the health of the animals as they age. We find that some long-lived mutants performed better than wild type when measured chronologically (number of days). However, all long-lived mutants increased the proportion of time spent in a frail state. Together, these data suggest that lifespan can no longer be the sole parameter of interest and reveal the importance of evaluating multiple healthspan parameters for future studies on antiaging interventions.



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J Agric Food Chem. 2015 Feb 23. [Epub ahead of print]

Creatine Is a Scavenger for Methylglyoxal under Physiological Conditions via Formation of N-(4-Methyl-5-oxo-1-imidazolin-2-yl)sarcosine (MG-HCr).

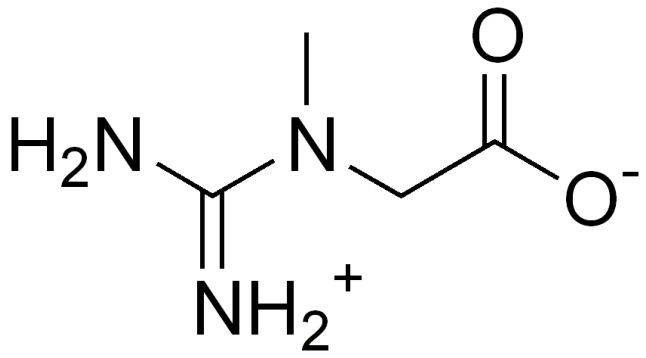
Löbner J[1], Degen J, Henle T.

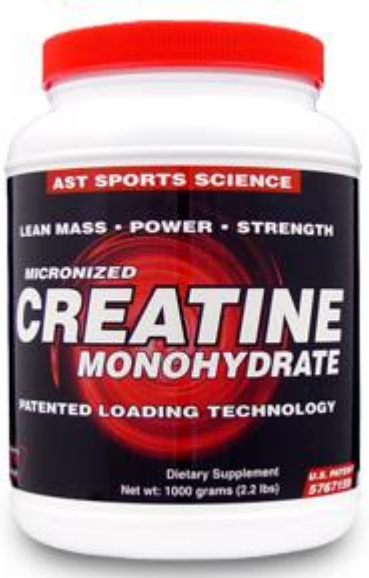
Author information

Abstract

Following incubation of methylglyoxal and creatine under physiological conditions, N-(4-methyl-5-oxo-1-imidazolin-2-yl)sarcosine (MG-HCr) was isolated and identified by NMR and mass spectrometry. Due to its rapid formation, MG-HCr represents a specific product following "scavenging" of methylglyoxal by creatine. Using hydrophilic interaction chromatography coupled to mass spectrometry, MG-HCr was analyzed in urine samples of healthy volunteers. Daily MG-HCr excretion of nonvegetarians ranged from 0.35 to 3.84 µmol/24 h urine (median: 0.90 µmol/24 h urine) and of vegetarians from 0.11 to 0.31 µmol/24 h urine (median: 0.19 µmol/24 h urine), indicating that formation of MG-HCr in vivo is influenced by the dietary intake of creatine. The trapping of methylglyoxal by creatine may delay the formation of advanced glycation compounds in vivo and, therefore, could be of special importance in situations in which the body has to deal with pathophysiologically increased amounts of dicarbonyl compounds ("carbonyl stress"), for instance in diabetic patients.

KEYWORDS: carbonyl stress; creatine; diabetes; dicarbonyl compounds; glycation; meat; methylglyoxal





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Aging Cell. 2015 Feb 14. doi: 10.1111/acel.12289. [Epub ahead of print]

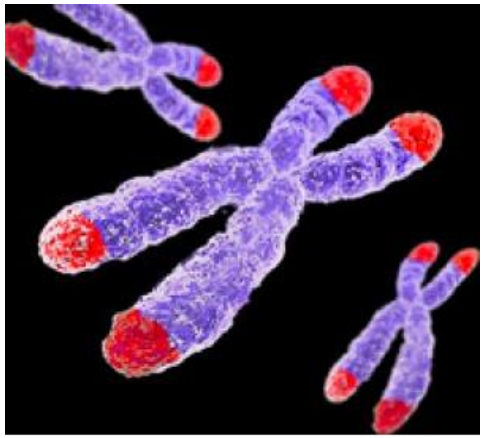
Stn1 is critical for telomere maintenance and long-term viability of somatic human cells.

Boccardi V[1], Razdan N, Kaplunov J, Mundra JJ, Kimura M, Aviv A, Herbig U.

⊕ Author information

Abstract

Disruption of telomere maintenance pathways leads to accelerated entry into cellular senescence, a stable proliferative arrest that promotes aging-associated disorders in some mammals. The budding yeast CST complex, comprising Cdc13, Stn1, and Ctc1, is critical for telomere replication, length regulation, and end protection. Although mammalian homologues of CST have been identified recently, their role and function for telomere maintenance in normal somatic human cells are still incompletely understood. Here, we characterize the function of human Stn1 in cultured human fibroblasts and demonstrate its critical role in telomere replication, length regulation, and function. In the absence of high telomerase activity, shRNA-mediated knockdown of hStn1 resulted in aberrant and fragile telomeric structures, stochastic telomere attrition, increased telomere erosion rates, telomere dysfunction, and consequently accelerated entry into cellular senescence. Oxidative stress augmented the defects caused by Stn1 knockdown leading to almost immediate cessation of cell proliferation. In contrast, overexpression of hTERT suppressed some of the defects caused by hStn1 knockdown suggesting that telomerase can partially compensate for hStn1 loss. Our findings reveal a critical role for human Stn1 in telomere length maintenance and function, supporting the model that efficient replication of telomeric repeats is critical for long-term viability of normal somatic mammalian cells.



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Nat Cell Biol. 2015 Mar;17(3):262-75. doi: 10.1038/ncb3101. Epub 2015 Feb 16.

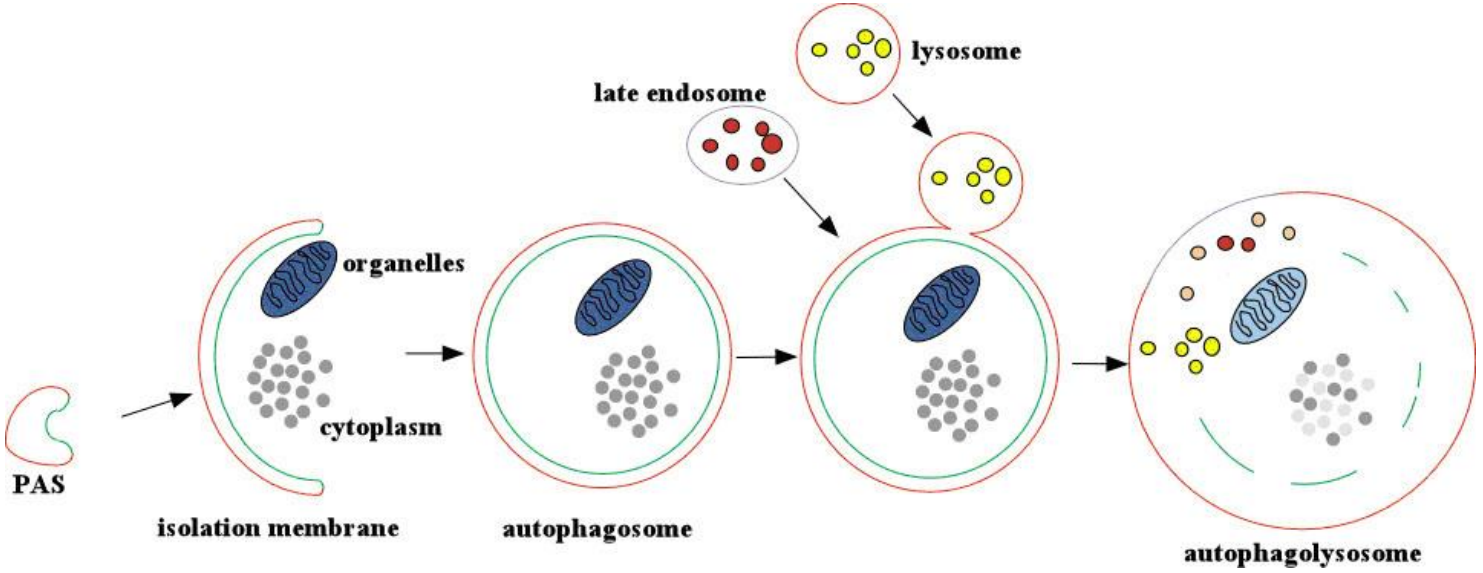
Huntingtin functions as a scaffold for selective macroautophagy.

Rui YN[1], Xu Z[1], Patel B[2], Chen Z[1], Chen D[1], Tito A[3], David G[4], Sun Y[1], Stimming EF[5], Bellen HJ[6], Cuervo AM[7], Zhang S[8].

Author information

Abstract

Selective macroautophagy is an important protective mechanism against diverse cellular stresses. In contrast to the well-characterized starvation-induced autophagy, the regulation of selective autophagy is largely unknown. Here, we demonstrate that Huntingtin, the Huntington disease gene product, functions as a scaffold protein for selective macroautophagy but it is dispensable for non-selective macroautophagy. In Drosophila, Huntingtin genetically interacts with autophagy pathway components. In mammalian cells, Huntingtin physically interacts with the autophagy cargo receptor p62 to facilitate its association with the integral autophagosome component LC3 and with Lys-63-linked ubiquitin-modified substrates. Maximal activation of selective autophagy during stress is attained by the ability of Huntingtin to bind ULK1, a kinase that initiates autophagy, which releases ULK1 from negative regulation by mTOR. Our data uncover an important physiological function of Huntingtin and provide a missing link in the activation of selective macroautophagy in metazoans.



Reviews/Editorials/Commentaries

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The Critical Need to Promote Research of Aging and Aging-related Diseases to Improve Health and Longevity of the Elderly Population

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Abstract

Due to the aging of the global population and the derivative increase in aging-related non-communicable diseases and their economic burden, there is an urgent need to promote research on aging and aging-related diseases as a way to improve healthy and productive longevity for the elderly population. To accomplish this goal, we advocate the following policies: 1) Increasing funding for research and development specifically directed to ameliorate degenerative aging processes and to extend healthy and productive lifespan for the population; 2) Providing a set of incentives for commercial, academic, public and governmental organizations to foster engagement in such research and development; and 3) Establishing and expanding coordination and consultation structures, programs and institutions involved in aging-related research, development and education in academia, industry, public policy agencies and at governmental and supra-governmental levels.

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Annu Rev Anim Biosci. 2015 Feb 16;3:283-303. doi: 10.1146/annurev-animal-022114-110829.

Animal models of aging research: implications for human aging and age-related diseases.

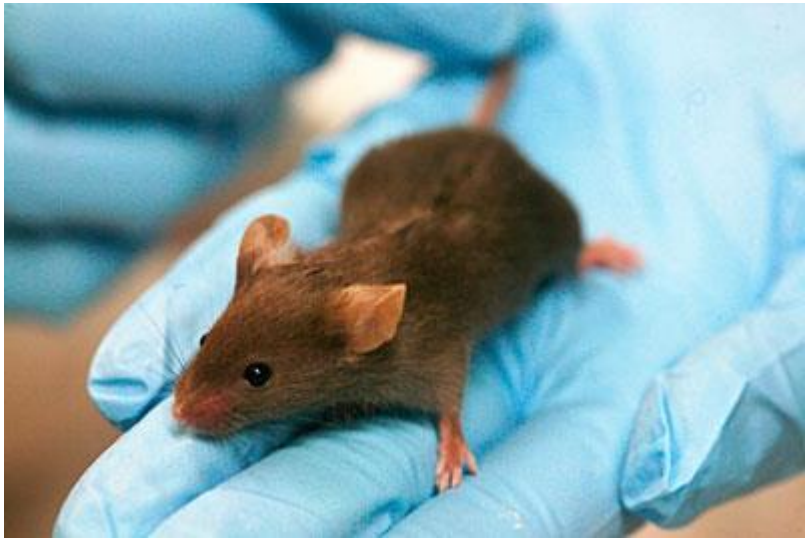
Mitchell SJ[1], Scheibye-Knudsen M, Longo DL, de Cabo R.

Author information

Abstract

Aging is characterized by an increasing morbidity and functional decline that eventually results in the death of an organism. Aging is the largest risk factor for numerous human diseases, and understanding the aging process may thereby facilitate the development of new treatments for age-associated diseases. The use of humans in aging research is complicated by many factors, including ethical issues; environmental and social factors; and perhaps most importantly, their long natural life span. Although cellular models of human disease provide valuable mechanistic information, they are limited in that they may not replicate the in vivo biology. Almost all organisms age, and thus animal models can be useful for studying aging. Herein, we review some of the major models currently used in aging research and discuss their benefits and pitfalls, including interventions known to extend life span and health span. Finally, we conclude by discussing the future of animal models in aging research.

KEYWORDS: aging; animal models; nonhuman primates; rodents



Metab Syndr Relat Disord. 2015 Feb 24. [Epub ahead of print]

A Perspective on Sirtuins in the Metabolic Syndrome.

Albiero M[1], Avogaro A, Fadini GP.

Author information

Abstract

The metabolic syndrome is a cluster of risk factor for diabetes and cardiovascular diseases. The metabolic syndrome pandemic reflects poor cardiometabolic health due to sedentary lifestyles and excess caloric intake over the background of an aging population. Sirtuins are protein deacetylases that represent master regulators of senescence, metabolism, and substrate utilization. In this perspective, we underline the pervasive role of sirtuins in the development of the typical features of metabolic syndrome and describe how sirtuins are becoming an attractive target of therapy.

PMID: 25710702 [PubMed - as supplied by publisher]