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Sven Bulterijs

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Science. 2015 Apr 30. pii: aaa1356. [Epub ahead of print]

A Werner syndrome stem cell model unveils heterochromatin alterations as a driver of human aging.

Zhang W[1], Li J[2], Suzuki K[3], Qu J[4], Wang P[1], Zhou J[1], Liu X[2], Ren R[1], Xu X[1], Ocampo A[3], Yuan T[1], Yang J[1], Li Y[1], Shi L[5], Guan D[1], Pan H[1], Duan S[1], Ding Z[1], Li M[3], Yi F[6], Bai R[4], Wang Y[5], Chen C[1], Yang F[1], Li X[7], Wang Z[8], Aizawa E[3], Goebl A[9], Soligalla RD[3], Reddy P[3], Esteban CR[3], Tang F[10], Liu GH[11], Belmonte JC[12].

⊕ Author information

Abstract

Werner syndrome (WS) is a premature aging disorder caused by WRN protein deficiency. Here, we report on the generation of a human WS model in human embryonic stem cells (ESCs). Differentiation of WRN-null ESCs to mesenchymal stem cells (MSCs) recapitulates features of premature cellular aging, a global loss of H3K9me3, and changes in heterochromatin architecture. We show that WRN associates with heterochromatin proteins SUV39H1 and HP1α and nuclear lamina-heterochromatin anchoring protein LAP2β. Targeted knock-in of catalytically inactive SUV39H1 in wild-type MSCs recapitulates accelerated cellular senescence, resembling WRN-deficient MSCs. Moreover, decrease in WRN and heterochromatin marks are detected in MSCs from older individuals. Our observations uncover a role for WRN in maintaining heterochromatin stability and highlight heterochromatin disorganization as a potential determinant of human aging.

Biogerontology. 2015 Apr 10. [Epub ahead of print]

The influence of dietary fat source on liver and skeletal muscle mitochondrial modifications and lifespan changes in calorie-restricted mice.

Villalba JM[1], López-Domínguez JA, Chen Y, Khraiwesh H, González-Reyes JA, Del Río LF, Gutiérrez-Casado E, Del Río M, Calvo-Rubio M, Ariza J, de Cabo R, López-Lluch G, Navas P, Hagopian K, Burón MI, Ramsey JJ.

Author information

Abstract

The Membrane Theory of Aging proposes that lifespan is inversely related to the level of unsaturation in membrane phospholipids. Calorie restriction (CR) without malnutrition extends lifespan in many model organisms, which may be related to alterations in membrane phospholipids fatty acids. During the last few years our research focused on studying how altering the predominant fat source affects the outcome of CR in mice. We have established four dietary groups: one control group fed 95 % of a pre-determined ad libitum intake (in order to prevent obesity), and three CR groups fed 40 % less than ad libitum intake. Lipid source for the control and one of the CR groups was soybean oil (high in n-6 PUFA) whereas the two remaining CR groups were fed diets containing fish oil (high in n-3 PUFA), or lard (high in saturated and monounsaturated fatty acids). Dietary intervention periods ranged from 1 to 18 months. We performed a longitudinal lifespan study and a cross-sectional study set up to evaluate several mitochondrial parameters which included fatty acid composition, H^+ leak, activities of electron transport chain enzymes, ROS generation, lipid peroxidation, mitochondrial ultrastructure, and mitochondrial apoptotic signaling in liver and skeletal muscle. These approaches applied to different cohorts of mice have independently indicated that lard as a fat source often maximizes the effects of 40 % CR on mice. These effects could be due to significant increases of monounsaturated fatty acids levels, in accordance with the Membrane Theory of Aging.

Biogerontology. 2015 Apr 10. [Epub ahead of print]

Age-related change in γH2AX of Drosophila muscle: its significance as a marker for muscle damage and longevity.

Jeon HJ[1], Kim YS, Park JS, Pyo JH, Na HJ, Kim IJ, Kim CM, Chung HY, Kim ND, Arking R, Yoo MA.

Author information

Abstract

Muscle aging is closely related to unhealthy late-life and organismal aging. Recently, the state of differentiated cells was shown to be critical to tissue homeostasis. Thus, understanding how fully differentiated muscle cells age is required for ensuring healthy aging. Adult Drosophila muscle is a useful model for exploring the aging process of fully differentiated cells. In this study, we investigated age-related changes of γH2AX, an indicator of DNA strand breaks, in adult Drosophila muscle to document whether its changes are correlated with muscle degeneration and lifespan. The results demonstrate that γH2AX accumulation increases in adult Drosophila thoracic and leg muscles with age. Analyses of short-, normal-, and long-lived strains indicate that the age-related increase of γH2AX is closely associated with the extent of muscle degeneration, cleaved caspase-3 and poly-ubiquitin aggregates, and longevity. Further analysis of muscle-specific knockdown of heterochromatin protein 1a revealed that the excessive γH2AX accumulation in thoracic and leg muscles induces accelerated degeneration and decreases longevity. These data suggest a strong correlation between age-related muscle damage and lifespan in Drosophila. Our findings indicate that γH2AX may be a reliable biomarker for assessing muscle aging in Drosophila.

Another resveratrol failure...

Rejuvenation Res. 2015 Apr 7. [Epub ahead of print]

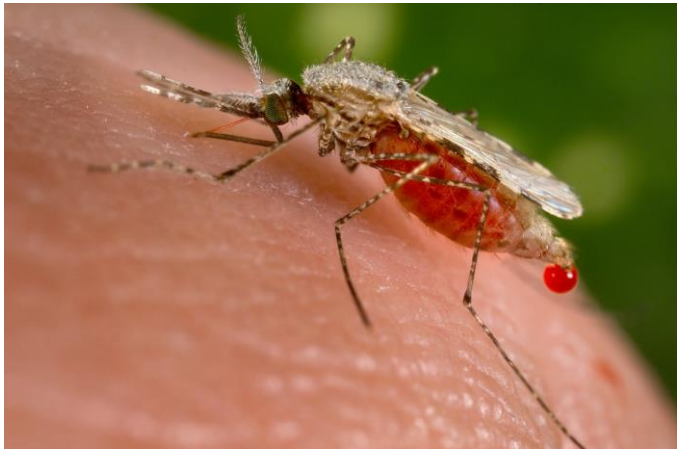
Resveratrol fails to extend lifespan in the mosquito Anopheles stephensi.

Johnson AA[1], Riehle MA.

Author information

Abstract

Resveratrol, a plant polyphenol present in grape skins, has been theorized to account for the "French Paradox" by explaining how red wine may decrease the health risks associated with unhealthy diets. Resveratrol has been reported to extend lifespan in several different species. Other studies, however, have failed to find a resveratrol-induced lifespan effect. A recent meta-study analyzing previously published survival data concluded that, while resveratrol reliably and reproducibly extends lifespan in some species, its lifespan effects show diminished reliability in other organisms. The data are mixed and it remains unclear how evolutionarily conserved resveratrol's effects on lifespan are. To gain further insight into this controversy, we studied the effects of various concentrations (200 μM, 100 μM, 50 μM, or 0 μM) of orally fed resveratrol on the lifespan of the mosquito Anopheles stephensi, an important vector of human malaria, under two different feeding treatments - sugar-fed only or sugar-fed with intermittent bloodmeals. Each treatment was repeated three times and both survivorship and mortality rates were analyzed for each replicate. For the majority of experiments, resveratrol failed to mediate a statistically significant effect on lifespan. While there was one instance where resveratrol significantly increased lifespan, there were five other instances where resveratrol significantly decreased lifespan. We conclude from these data that, under normal conditions, resveratrol does not extend lifespan in the A. stephensi mosquito.



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Circulation. 2015 Apr 10. pii: CIRCULATIONAHA.115.015489. [Epub ahead of print]

Polygenic Overlap Between C-Reactive Protein, Plasma Lipids and Alzheimer's Disease.

Desikan RS[1], Schork AJ[2], Wang Y[3], Thompson WK[2], Dehghan A[4], Ridker PM[5], Chasman DI[5], McEvoy LK[2], Holland D[2], Chen CH[3], Karow DS[2], Brewer JB[2], Hess CP[6], Williams J[7], Sims R[7], O'Donovan MC[7], Choi SH[8], Bis JC[9], Ikram MA[10], Gudnason V[11], DeStefano AL[12], van der Lee SJ[10], Psaty BM[13], van Duijn CM[10], Launer L[14], Seshadri S[15], Pericak-Vance MA[16], Mayeux R[17], Haines JL[18], Farrer LA[19], Hardy J[20], Ulstein ID[21], Aarsland D[22], Fladby T[23], White LR[24], Sando SB[24], Rongve A[25], Witoelar A[26], Djurovic S[27], Hyman BT[28], Snaedal J[29], Steinberg S[30], Stefansson H[30], Stefansson K[31], Schellenberg GD[32], Andreassen OA[3], Dale AM[3].

Author information

Abstract

BACKGROUND: -Epidemiological findings suggest a relationship between Alzheimer's disease (AD), inflammation and dyslipidemia, although the nature of this relationship is not well understood. We investigated whether this phenotypic association arises from a shared genetic basis.

METHODS AND RESULTS: -Using summary statistics (p-values and odds ratios) from genome-wide association studies of over 200,000 individuals, we investigated overlap in single nucleotide polymorphisms (SNPs) associated with clinically diagnosed AD and C-reactive protein (CRP), triglycerides (TG), high- (HDL) and low-density lipoprotein (LDL) levels. We found up to 50-fold enrichment of AD SNPs for different levels of association with CRP, LDL, HDL and TG SNPs using an FDR threshold < 0.05. By conditioning on polymorphisms associated with the four phenotypes, we identified 55 loci associated with increased AD risk. We then conducted a meta-analysis of these 55 variants across four independent AD cohorts (total n = 29,054 AD cases and 114,824 healthy controls) and discovered two genome-wide significant variants on chromosome 4 (rs13113697, closest gene HS3ST1, odds ratio (OR) = 1.07, 95% confidence interval (CI) = 1.05-1.11, $p = 2.86 \times 10^{-8}$) and chromosome 10 (rs7920721, closest gene ECHDC3, OR = 1.07, 95% CI = 1.04-1.11, $p = 3.38 \times 10^{-8}$). We also found that gene expression of HS3ST1 and ECHDC3 was altered in AD brains compared with control brains.

CONCLUSIONS: -We demonstrate genetic overlap between AD, CRP, and plasma lipids. By conditioning on the genetic association with the cardiovascular phenotypes, we identify novel AD susceptibility loci including two genome-wide significant variants conferring increased risk for Alzheimer's disease.

Mol Neurodegener. 2015 Apr 10;10(1):19. [Epub ahead of print]

TREM2 is associated with increased risk for Alzheimer's disease in African Americans.

Jin SC[1], Carrasquillo MM[2], Benitez BA[3], Skorupa T[4], Carrell D[5], Patel D[6], Lincoln S[7], Krishnan S[8], Kachadoorian M[9], Reitz C[10,11], Mayeux R[12,13], Wingo TS[14,15], Lah JJ[16], Levey AI[17], Murrell J[18], Hendrie H[19,20], Foroud T[21], Graff-Radford NR[22], Goate AM[23,24,25,26,27], Cruchaga C[28,29], Ertekin-Taner N[30,31].

Author information

Abstract

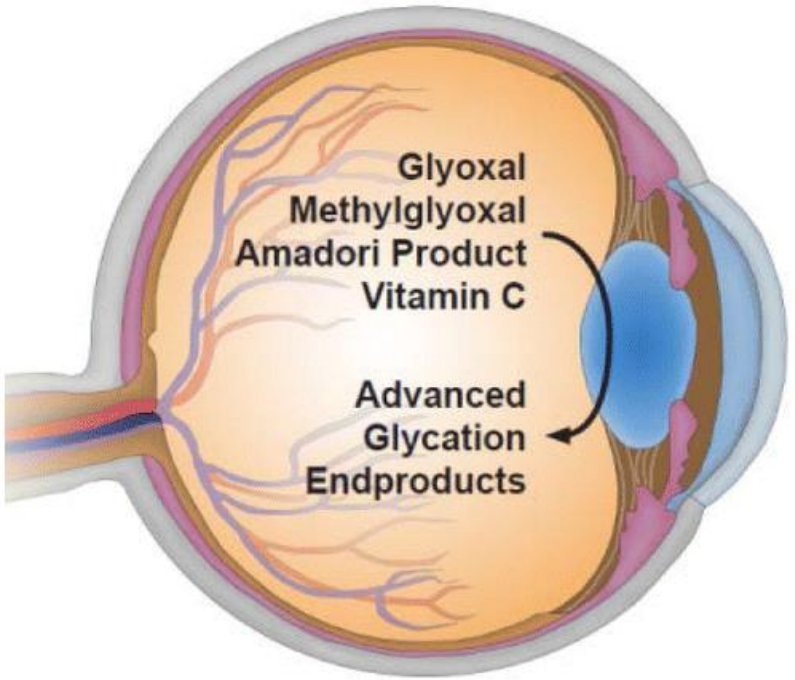
BACKGROUND: TREM2 encodes for triggering receptor expressed on myeloid cells 2 and has rare, coding variants that associate with risk for late-onset Alzheimer's disease (LOAD) in Caucasians of European and North-American origin. This study evaluated the role of TREM2 in LOAD risk in African-American (AA) subjects. We performed exonic sequencing and validation in two independent cohorts of >800 subjects. We selected six coding variants (p.R47H, p.R62H, p.D87N, p.E151K, p.W191X, and p.L211P) for case-control analyses in a total of 906 LOAD cases vs. 2,487 controls.

RESULTS: We identified significant LOAD risk association with p.L211P (p = 0.01, OR = 1.27, 95%CI = 1.05-1.54) and suggestive association with p.W191X (p = 0.08, OR = 1.35, 95%CI = 0.97-1.87). Conditional analysis suggests that p.L211P, which is in linkage disequilibrium with p.W191X, may be the stronger variant of the two, but does not rule out independent contribution of the latter. TREM2 p.L211P resides within the cytoplasmic domain and p.W191X is a stop-gain mutation within the shorter TREM-2V transcript. The coding variants within the extracellular domain of TREM2 previously shown to confer LOAD risk in Caucasians were extremely rare in our AA cohort and did not associate with LOAD risk.

CONCLUSIONS: Our findings suggest that TREM2 coding variants also confer LOAD risk in AA, but implicate variants within different regions of the gene than those identified for Caucasian subjects. These results underscore the importance of investigating different ethnic populations for disease risk variant discovery, which may uncover allelic heterogeneity with potentially diverse mechanisms of action.

Comprehensive Analysis of Maillard Protein Modifications in Human Lenses: Effect of Age and Cataract

Mareen Smuda †, Christian Henning †, Cibin T. Raghavan ‡, Kaid Johar §, Abhay R. Vasavada §, Ram H. Nagaraj ‡, and Marcus A. Glomb *†



In human lens proteins, advanced glycation endproducts (AGEs) originate from the reaction of glycating agents, e.g., vitamin C and glucose. AGEs have been considered to play a significant role in lens aging and cataract formation. Although several AGEs have been detected in the human lens, the contribution of individual glycating agents to their formation remains unclear. A highly sensitive liquid chromatography–tandem mass spectrometry multimethod was developed that allowed us to quantitate 21 protein modifications in normal and cataractous lenses, respectively. N^{ε}-Carboxymethyl lysine, N^{ε}-carboxyethyl lysine, N^{δ}-carboxyethyl arginine, methylglyoxal hydroimidazolone 1, and N^{ε}-lactoyl lysine were found to be the major Maillard protein modifications among these AGEs. The novel vitamin C specific amide AGEs, N^{ε}-xylonyl and N^{ε}-lyxonyl lysine, but also AGEs from glyoxal were detected, albeit in minor quantities. Among the 21 modifications, AGEs from the Amadori product (derived from the reaction of glucose and lysine) and methylglyoxal were dominant.

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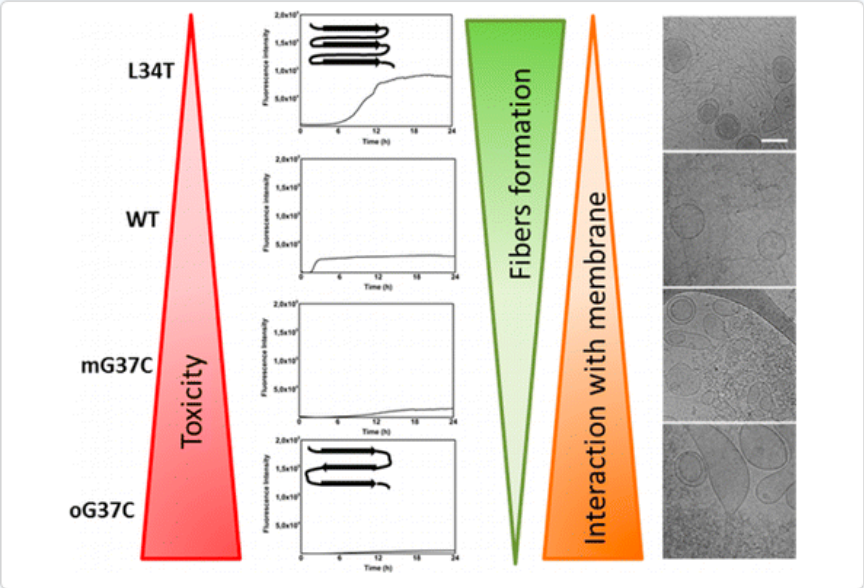
Interaction of $A\beta_{1-42}$ Amyloids with Lipids Promotes "Off-Pathway" Oligomerization and Membrane Damage

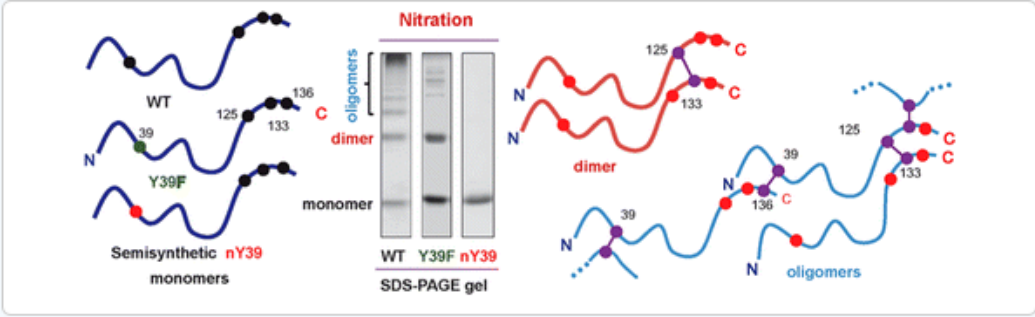
Sarah Henry †, Hélène Vignaud ‡, Claude Bobo ‡, Marion Decossas †, Oliver Lambert †, Etienne Harte †, Isabel D. Alves †, Christophe Cullin ‡, and Sophie Lecomte *†



The toxicity of amyloids, as $A\beta_{1-42}$ involved in Alzheimer disease, is a subject under intense scrutiny. Many studies link their toxicity to the existence of various intermediate structures prior to fiber formation and/or their specific interaction with membranes. In this study we focused on the interaction between membrane models and $A\beta_{1-42}$ peptides and variants (L34T, mG37C) produced in *E. coli* and purified in monomeric form. We evaluated the interaction of a toxic stable oligomeric form (oG37C) with membranes as comparison. Using various biophysical techniques as fluorescence and plasmon waveguide resonance, we clearly established that the oG37C interacts strongly with membranes leading to its disruption. All the studied peptides destabilized liposomes and accumulated slowly on the membrane (rate constant 0.02 min^{-1}). Only the oG37C exhibited a particular pattern of interaction, comprising two steps: the initial binding followed by membrane reorganization. Cryo-TEM was used to visualize the peptide effect on liposome morphologies. Both oG37C and mG37C lead to PG membrane fragmentation. The PG membrane promotes peptide oligomerization, implicated in membrane disruption. WT ($A\beta_{1-42}$) also perturbs liposome organization with membrane deformation rather than disruption. For all the peptides studied, their interaction with the membranes changes their fibrillization process, with less fibers and more small aggregates being formed. These studies allowed to establish, a correlation between toxicity, fiber formation, and membrane disruption.

Elucidating the Role of Site-Specific Nitration of α-Synuclein in the Pathogenesis of Parkinson's Disease via Protein Semisynthesis and Mutagenesis

Ritwik Burai , Nadine Ait-Bouziad , Anass Chiki , and Hilal A. Lashuel *



Parkinson's disease (PD) is characterized by the loss of dopaminergic neurons in the *substantia nigra* and the presence of intraneuronal inclusions consisting of aggregated and post-translationally modified α-synuclein (α-syn). Despite advances in the chemical synthesis of α-syn and other proteins, the generation of site-specifically nitrated synthetic proteins has not been reported. Consequently, it has not been possible to determine the roles of nitration at specific residues in regulating the physiological and pathogenic properties of α-syn. Here we report, for the first time, the site-specific incorporation of 3-nitrotyrosine at different regions of α-syn using native chemical ligation combined with a novel desulfurization strategy. This strategy enabled us to investigate the role of nitration at single or multiple tyrosine residues in regulating α-syn structure, membrane binding, oligomerization, and fibrils formation. We demonstrate that different site-specifically nitrated α-syn species exhibit distinct structural and aggregation properties and exhibit reduced affinity to negatively charged vesicle membranes. We provide evidence that intermolecular interactions between the N- and C-terminal regions of α-syn play critical roles in mediating nitration-induced α-syn oligomerization. For example, when Y39 is not available for nitration (Y39F and Y39/125F), the extent of cross-linking is limited mostly to dimer formation, whereas mutants in which Y39 along with one or multiple C-terminal tyrosines (Y125F, Y133F, Y136F and Y133/136F) can still undergo nitration readily to form higher-order oligomers. Our semisynthetic strategy for generating site-specifically nitrated proteins opens up new possibilities for investigating the role of nitration in regulating protein structure and function in health and disease.

Acta Neuropathol Commun. 2014 Aug 17;2(1):83. doi: 10.1186/s40478-014-0083-0.

Soluble amyloid beta levels are elevated in the white matter of Alzheimer's patients, independent of cortical plaque severity.

Collins-Praino LE[1,2], Francis YI[3], Griffith EY[4], Wiegman AF[5], Urbach J[6], Lawton A[7], Honig LS[8,9], Cortes E[10], Vonsattel JP[11], Canoll PD[12], Goldman JE[13,14], Brickman AM[15,16].

Author information

Abstract

Alzheimer's disease (AD) is the most common neurodegenerative disease and the leading cause of dementia. In addition to grey matter pathology, white matter changes are now recognized as an important pathological feature in the emergence of the disease. Despite growing recognition of the importance of white matter abnormalities in the pathogenesis of AD, the causes of white matter degeneration are still unknown. While multiple studies propose Wallerian-like degeneration as the source of white matter change, others suggest that primary white matter pathology may be due, at least in part, to other mechanisms, including local effects of toxic Aβ peptides. In the current study, we investigated levels of soluble amyloid-beta (Aβ) in white matter of AD patients (n=12) compared with controls (n=10). Fresh frozen white matter samples were obtained from anterior (Brodmann area 9) and posterior (Brodmann area 1, 2 and 3) areas of post-mortem AD and control brains. ELISA was used to examine levels of soluble Aβ -42 and Aβ -40. Total cortical neuritic plaque severity rating was derived from individual ratings in the following areas of cortex: mid-frontal, superior temporal, pre-central, inferior parietal, hippocampus (CA1), subiculum, entorhinal cortex, transentorhinal cortex, inferior temporal, amygdala and basal forebrain. Compared with controls, AD samples had higher white matter levels of both soluble Aβ -42 and Aβ -40. While no regional white matter differences were found in Aβ -40, Aβ -42 levels were higher in anterior regions than in posterior regions across both groups. After statistically controlling for total cortical neuritic plaque severity, differences in both soluble Aβ -42 and Aβ -40 between the groups remained, suggesting that white matter Aβ peptides accumulate independent of overall grey matter fibrillar amyloid pathology and are not simply a reflection of overall amyloid burden. These results shed light on one potential mechanism through which white matter degeneration may occur in AD. Given that white matter degeneration may be an early marker of disease, preceding grey matter atrophy, understanding the mechanisms and risk factors that may lead to white matter loss could help to identify those at high risk and to intervene earlier in the pathogenic process.

PLoS One. 2015 Apr 29;10(4):e0124837. doi: 10.1371/journal.pone.0124837. eCollection 2015.

Resveratrol Induced Premature Senescence Is Associated with DNA Damage Mediated SIRT1 and SIRT2 Down-Regulation.

Kilic Eren M[1], Kilincli A[2], Eren Ö[2].

Author information

Abstract

The natural polyphenolic compound resveratrol (3,4,5-trihydroxy-trans-stilbene) has broad spectrum health beneficial activities including antioxidant, anti-inflammatory, anti-aging, anti-cancer, cardioprotective, and neuroprotective effects. Remarkably, resveratrol also induces apoptosis and cellular senescence in primary and cancer cells. Resveratrol's anti-aging effects both in vitro and in vivo attributed to activation of a (NAD)-dependent histone deacetylase family member sirtuin-1 (SIRT1) protein. In mammals seven members (SIRT1-7) of sirtuin family have been identified. Among those, SIRT1 is the most extensively studied with perceptive effects on mammalian physiology and suppression of the diseases of aging. Yet no data has specified the role of sirtuins, under conditions where resveratrol treatment induces senescence. Current study was undertaken to investigate the effects of resveratrol in human primary dermal fibroblasts (BJ) and to clarify the role of sirtuin family members in particular SIRT1 and SIRT2 that are known to be involved in cellular stress responses and cell cycle, respectively. Here, we show that resveratrol decreases proliferation of BJ cells in a time and dose dependent manner. In addition the increase in senescence associated β-galactosidase (SA-β-gal) activity and methylated H3K9-me indicate the induction of premature senescence. A significant increase in phosphorylation of γ-H2AX, a surrogate of DNA double strand breaks, as well as in levels of p53, p21CIP1 and p16INK4A is also detected. Interestingly, at concentrations where resveratrol induced premature senescence we show a significant decrease in SIRT1 and SIRT2 levels by Western Blot and quantitative RT-PCR analysis. Conversely inhibition of SIRT1 and SIRT2 via siRNA or sirtinol treatment also induced senescence in BJ fibroblasts associated with increased SA-β-gal activity, γ-H2AX phosphorylation and p53, p21CIP1 and p16INK4A levels. Interestingly DNA damaging agent doxorubicin also induced senescence in BJ fibroblasts associated with decreased SIRT1/2 levels. In conclusion our data reveal that resveratrol induced premature senescence is associated with SIRT1 and SIRT2 down regulation in human dermal fibroblasts. Here we suggest that the concomitant decline in SIRT1/2 expression in response to resveratrol treatment may be a cause for induction of senescence, which is most likely mediated by a regulatory mechanism activated by DNA damage response.

Reviews/Editorials/Commentaries

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Ageing Res Rev. 2015 Apr 8. pii: S1568-1637(15)00036-7. doi: 10.1016/j.arr.2015.04.002. [Epub ahead of print]

Programmed cell death in aging.

Tower J[1].

Author information

Abstract

Programmed cell death (PCD) pathways, including apoptosis and regulated necrosis, are required for normal cell turnover and tissue homeostasis. Mis-regulation of PCD is increasingly implicated in aging and aging-related disease. During aging the cell turnover rate declines for several highly-mitotic tissues. Aging-associated disruptions in systemic and inter-cell signaling combined with cell-autonomous damage and mitochondrial malfunction result in increased PCD in some cell types, and decreased PCD in other cell types. Increased PCD during aging is implicated in immune system decline, skeletal muscle wasting (sarcopenia), loss of cells in the heart, and neurodegenerative disease. In contrast, cancer cells and senescent cells are resistant to PCD, enabling them to increase in abundance during aging. PCD pathways limit life span in fungi, but whether PCD pathways normally limit adult metazoan life span is not yet clear. PCD is regulated by a balance of negative and positive factors, including the mitochondria, which are particularly subject to aging-associated malfunction.

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Curr Biol. 2015 Apr 20;25(8):R339-41. doi: 10.1016/j.cub.2015.02.047.

Cell competition: dying for communal interest.

Courgeon M[1], Konstantinides N[1], Desplan C[2].

Author information

Abstract

Viable but slower growing cells are eliminated during embryonic development through the process of cell competition. Two new studies highlight a role for cell competition during adulthood as a surveillance mechanism that ensures tissue integrity during homeostasis, regeneration, and aging.

Biochem Biophys Res Commun. 2015 Mar 6;458(2):221-6. doi: 10.1016/j.bbrc.2015.01.140. Epub 2015 Feb 7.

Dicarbonyl stress in cell and tissue dysfunction contributing to ageing and disease.

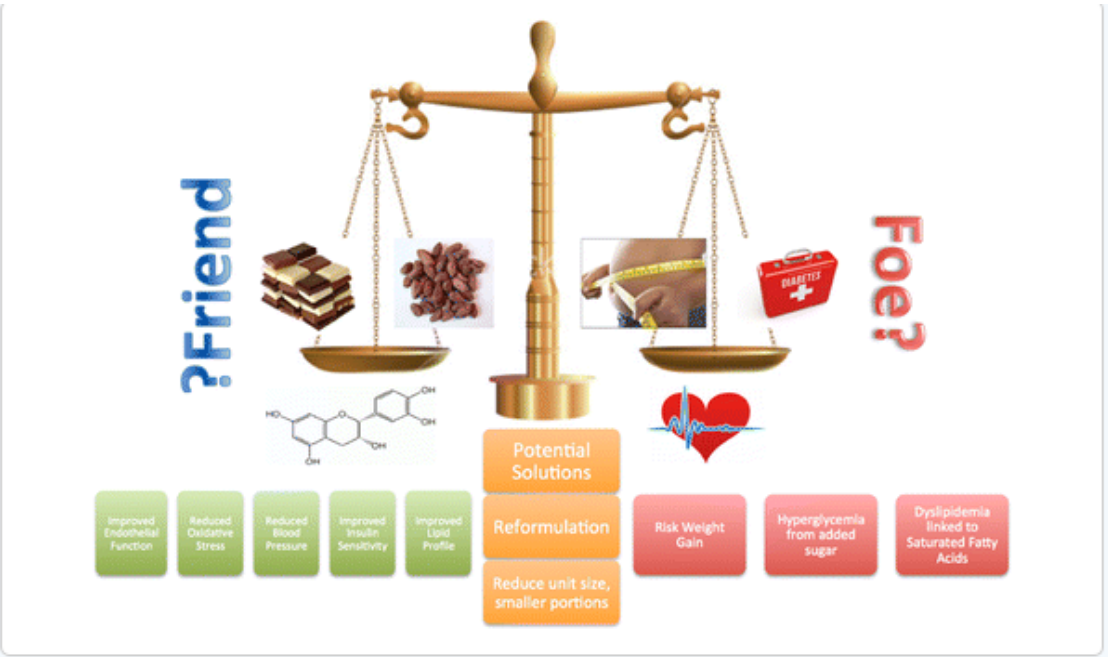
Rabbani N[1], Thornalley PJ[2].

Author information

Abstract

Dicarbonyl stress is the abnormal accumulation of dicarbonyl metabolites leading to increased protein and DNA modification contributing to cell and tissue dysfunction in ageing and disease. Enzymes metabolising dicarbonyls, glyoxalase 1 and aldoketo reductases, provide an efficient and stress-response enzyme defence against dicarbonyl stress. Dicarbonyl stress is produced by increased formation and/or decreased metabolism of dicarbonyl metabolites, and by exposure to exogenous dicarbonyls. It contributes to ageing, disease and activity of cytototoxic chemotherapeutic agents.

Diabetes and Chocolate: Friend of Foe?



Polyphenols and other compounds found in cocoa and chocolate have therapeutic potential in the management of diabetes in humans. Polyphenol benefits have been proposed supported by in vitro studies, animal work, and clinical trials, which have been conducted mostly in healthy volunteers. The energy-dense formulations of many cocoa and chocolate products, which can be up to 50% sugar by weight, have given the perception that chocolate may be harmful through its contribution to obesity. A review of both clinical trial databases and published literature yielded 15 registered trials and 7 published studies. The published data interventions reported are diverse and vary widely in quality, including poor selection of control products or inadequate blinding procedures. There are also inconsistencies in reporting of data with limited information on the effect of cocoa and chocolate supplementation on weight and glycemic control despite the potential benefits reported with respect to the cardiovascular risk factors of endothelial function and lipids. More studies are required powered for primary clinical outcomes together with the development of standardized product formulations that optimize the dose of polyphenols within a palatable and energy-restricted product.

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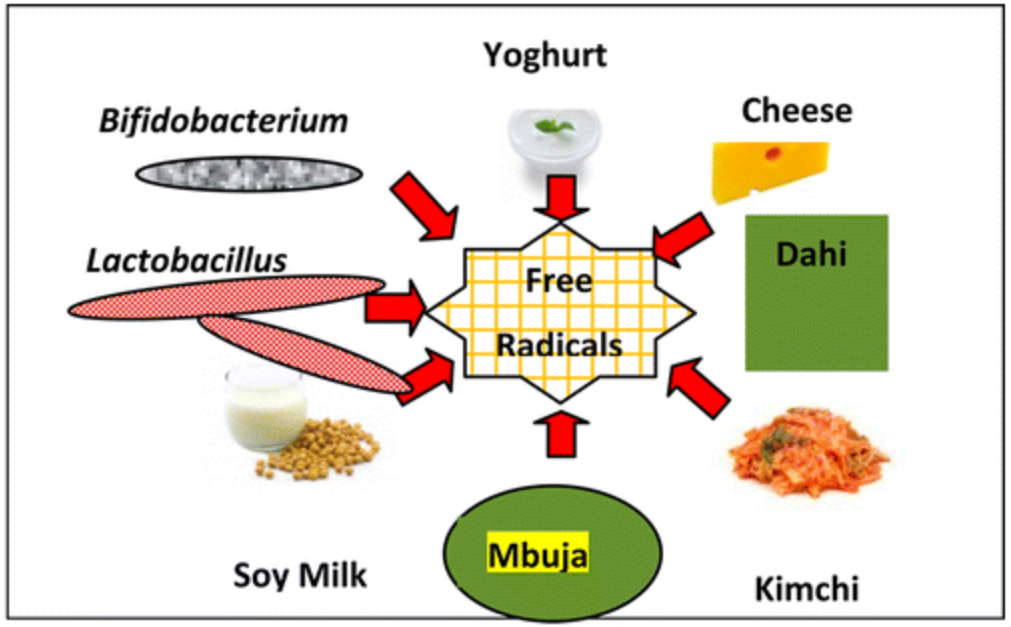
Probiotics as Potential Antioxidants: A Systematic Review

Vijendra Mishra [*†], Chandni Shah [§], Narendra Mokashe [†], Rupesh Chavan [†], Hariom Yadav [#], and Jashbhai Prajapati [§]



Probiotics are known for their health beneficial effects and are established as dietary adjuncts. Probiotics have been known for many beneficial health effects. In this view, there is interest to find the potential probiotic strains that can exhibit antioxidant properties along with health benefits. In vitro and in vivo studies indicate that probiotics exhibit antioxidant potential. In this view, consumption of probiotics alone or foods supplemented with probiotics may reduce oxidative damage, free radical scavenging rate, and modification in activity of crucial antioxidative enzymes in human cells. Incorporation of probiotics in foods can provide a good strategy to supply dietary antioxidants, but more studies are needed to standardize methods and evaluate antioxidant properties of probiotics before they can be recommended for antioxidant potential. In this paper, the literature related to known antioxidant potential of probiotics and proposing future perspectives to conduct such studies has been reviewed.

PLoS Biol. 2015 Apr 29;13(4):e1002131. doi: 10.1371/journal.pbio.1002131. eCollection 2015.

Why Is Aging Conserved and What Can We Do about It?

Pitt JN[1], Kaeberlein M[1].

Author information

Abstract

The field of aging research has progressed rapidly over the past few decades. Genetic modulators of aging rate that are conserved over a broad evolutionary distance have now been identified. Several physiological and environmental interventions have also been shown to influence the rate of aging in organisms ranging from yeast to mammals. Here we briefly review these conserved pathways and interventions and highlight some key unsolved challenges that remain. Although the molecular mechanisms by which these modifiers of aging act are only partially understood, interventions to slow aging are nearing clinical application, and it is likely that we will begin to reap the benefits of aging research prior to solving all of the mysteries that the biology of aging has to offer.

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Metabolites. 2015 Apr 27;5(2):232-51. doi: 10.3390/metabo5020232.

Mathematical modelling of metabolic regulation in aging.

Auley MT[1], Mooney KM[2], Angell PJ[3], Wilkinson SJ[4].

⊕ Author information

Abstract

The underlying cellular mechanisms that characterize aging are complex and multifaceted. However, it is emerging that aging could be regulated by two distinct metabolic hubs. These hubs are the pathway defined by the mammalian target of rapamycin (mTOR) and that defined by the NAD+-dependent deacetylase enzyme, SIRT1. Recent experimental evidence suggests that there is crosstalk between these two important pathways; however, the mechanisms underpinning their interaction(s) remains poorly understood. In this review, we propose using computational modelling in tandem with experimentation to delineate the mechanism(s). We briefly discuss the main modelling frameworks that could be used to disentangle this relationship and present a reduced reaction pathway that could be modelled. We conclude by outlining the limitations of computational modelling and by discussing opportunities for future progress in this area.

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http://www.ncbi.nlm.nih.gov/pubmed/25885886
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http://www.ncbi.nlm.nih.gov/pubmed/25839782
http://www.ncbi.nlm.nih.gov/pubmed/24628815
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