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Scientific News 11th of Oktober 2015
Sven Bulterijs

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Helft Vlamingen langdurig behandeld voor chronische ziekte

09/10/2015 om 05:00 door Maxie Eckert

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Foto: BELGA

‹ 1 van 3 ›

Te hoge bloeddruk, astma, depressie, diabetes. De helft van de Vlamingen moet langdurig worden behandeld voor een chronische aandoening, en dat aantal stijgt nog. Almaar meer patiënten nemen ook langdurig geneesmiddelencocktails. En daar houden de huidige richtlijnen voor behandelingen van ziekten nog te weinig rekening mee, klinkt het bij

MEEST RECENT · MEEST GELEZEN

1. Lonen stijgen, prijzen schadelijke producten ook
2. Parket opent onderzoek naar giften Burgerplatfo
3. Oppositie: 'Kosten onmiddellijk voelbaar, voorde
4. Jonge bestuurder overlijdt bij frontale aanrijding
5. Meer asielzoekers keren vrijwillig terug naar Irak

Volledig overzic

DE CORRESPONDENTEN Voor de tweede maal geeft d
redactie van De Standaard zeven van haar journalis
zes maanden lang tijd, ruimte en budgetten om te
onderzoeken wat onze wereld en uw leven overhoo

MitoSENS fundraiser: success!

http://www.lifespan.io/

MitoSENS fundraiser: success!

01 OCT 2015

Launching the Fight Aging! 2015 $125,000 Matching Fundraiser for SENS Rejuvenation Research

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Today I'm pleased to announce the launch of this year's Fight Aging! matching fundraiser in support of the work of the SENS Research Foundation, funding scientific programs to speed progress towards working rejuvenation therapies and an end to frailty and disease in aging. In 2013 we raised $60,000, in 2014 $150,000, and this year we're shooting at a cool quarter of a million dollars. You never know where the limits really are unless you forge ahead, and support for the treatment of aging as a medical condition is growing more rapidly today than at any time since the creation of Fight Aging!

- View the Fundraiser Page at Fight Aging!
- Donate at the SENS Research Foundation

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IgG Conformer's Binding to Amyloidogenic Aggregates

Monichan Phay, Alfred T. Welzel, Angela D. Williams, Helen P. McWilliams-Koeppen, Veronika Blinder, Tiernan T. O'Malley, Alan Solomon, Dominic M. Walsh, Brian O'Nuallain

Abstract

Amyloid-reactive IgGs isolated from pooled blood of normal individuals (pAbs) have demonstrated clinical utility for amyloid diseases by *in vivo* targeting and clearing amyloidogenic proteins and peptides. We now report the following three novel findings on pAb conformer's binding to amyloidogenic aggregates: 1) pAb aggregates have greater activity than monomers (HMW species > dimers > monomers), 2) pAbs interactions with amyloidogenic aggregates at least partially involves unconventional (non-CDR) interactions of F(ab) regions, and 3) pAb's activity can be easily modulated by trace aggregates generated during sample processing. Specifically, we show that HMW aggregates and dimeric pAbs present in commercial preparations of pAbs, intravenous immunoglobulin (IVIg), had up to ~200- and ~7-fold stronger binding to aggregates of Aβ and transthyretin (TTR) than the monomeric antibody. Notably, HMW aggregates were primarily responsible for the enhanced anti-amyloid activities of Aβ- and Cibacron blue-isolated IVIg IgGs. Human pAb conformer's binding to amyloidogenic aggregates was retained in normal human sera, and mimicked by murine pAbs isolated from normal pooled plasmas. An unconventional (non-CDR) component to pAb's activity was indicated from control human mAbs, generated against non-amyloid targets, binding to aggregated Aβ and TTR. Similar to pAbs, HMW and dimeric mAb conformers bound stronger than their monomeric forms to amyloidogenic aggregates. However, mAbs had lower maximum binding signals, indicating that pAbs were required to saturate a diverse collection of binding sites. Taken together, our findings strongly support further investigations on the physiological function and clinical utility of the inherent anti-amyloid activities of monomeric but not aggregated IgGs.

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Structural basis of template-boundary definition in *Tetrahymena* telomerase

Linnea I Jansson, Ben M Akiyama, Alexandra Ooms, Cheng Lu, Seth M Rubin & Michael D Stone

Affiliations | **Contributions** | **Corresponding author**

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Received 19 June 2015 | Accepted 02 September 2015 | Published online 05 October 2015

Abstract

Abstract • Accession codes • References • Author information • Supplementary information

Telomerase is required to maintain repetitive G-rich telomeric DNA sequences at chromosome ends. To do so, the telomerase reverse transcriptase (TERT) subunit reiteratively uses a small region of the integral telomerase RNA (TER) as a template. An essential feature of telomerase catalysis is the strict definition of the template boundary to determine the precise TER nucleotides to be reverse transcribed by TERT. We report the 3-Å crystal structure of the *Tetrahymena* TERT RNA-binding domain (tTRBD) bound to the template boundary element (TBE) of TER. tTRBD is wedged into the base of the TBE RNA stem-loop, and each of the flanking RNA strands wraps around opposite sides of the protein domain. The structure illustrates how the tTRBD establishes the template boundary by positioning the TBE at the correct distance from the TERT active site to prohibit copying of nontemplate nucleotides.

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Potential Mechanisms for Cancer Resistance in Elephants and Comparative Cellular Response to DNA Damage in Humans

FREE ONLINE FIRST

Importance Evolutionary medicine may provide insights into human physiology and pathophysiology, including tumor biology.

Objective To identify mechanisms for cancer resistance in elephants and compare cellular response to DNA damage among elephants, healthy human controls, and cancer-prone patients with Li-Fraumeni syndrome (LFS).

Design, Setting, and Participants A comprehensive survey of necropsy data was performed across 36 mammalian species to validate cancer resistance in large and long-lived organisms, including elephants (n = 644). The African and Asian elephant genomes were analyzed for potential mechanisms of cancer resistance. Peripheral blood lymphocytes from elephants, healthy human controls, and patients with LFS were tested in vitro in the laboratory for DNA damage response. The study included African and Asian elephants (n = 8), patients with LFS (n = 10), and age-matched human controls (n = 11). Human samples were collected at the University of Utah between June 2014 and July 2015.

Exposures Ionizing radiation and doxorubicin.

Main Outcomes and Measures Cancer mortality across species was calculated and compared by body size and life span. The elephant genome was investigated for alterations in cancer-related genes. DNA repair and apoptosis were compared in elephant vs human peripheral blood lymphocytes.

Results Across mammals, cancer mortality did not increase with body size and/or maximum life span (eg, for rock hyrax, 1% [95% CI, 0%-5%]; African wild dog, 8% [95% CI, 0%-16%]; lion, 2% [95% CI, 0%-7%]). Despite their large body size and long life span, elephants remain cancer resistant, with an estimated cancer mortality of 4.81% (95% CI, 3.14%-6.49%), compared with humans, who have 11% to 25% cancer mortality. While humans have 1 copy (2 alleles) of *TP53*, African elephants have at least 20 copies (40 alleles), including 19 retrogenes (38 alleles) with evidence of transcriptional activity measured by reverse transcription polymerase chain reaction. In response to DNA damage, elephant lymphocytes underwent p53-mediated apoptosis at higher rates than human lymphocytes proportional to *TP53* status (ionizing radiation exposure: patients with LFS, 2.71% [95% CI, 1.93%-3.48%] vs human controls, 7.17% [95% CI, 5.91%-8.44%] vs elephants, 14.64% [95% CI, 10.91%-18.37%]; $P < .001$; doxorubicin exposure: human controls, 8.10% [95% CI, 6.55%-9.66%] vs elephants, 24.77% [95% CI, 23.0%-26.53%]; $P < .001$).

Conclusions and Relevance Compared with other mammalian species, elephants appeared to have a lower-than-expected rate of cancer, potentially related to multiple copies of *TP53*. Compared with human cells, elephant cells demonstrated increased apoptotic response following DNA damage. These findings, if replicated, could represent an evolutionary-based approach for understanding mechanisms related to cancer suppression.

Antisense therapy targeting apolipoprotein(a): a randomised, double-blind, placebo-controlled phase 1 study

Background

Lipoprotein(a) (Lp[a]) is a risk factor for cardiovascular disease and calcific aortic valve stenosis. No effective therapies to lower plasma Lp(a) concentrations exist. We have assessed the safety, pharmacokinetics, and pharmacodynamics of ISIS-APO(a)$_{Rx}$, a second-generation antisense drug designed to reduce the synthesis of apolipoprotein(a) (apo[a]) in the liver.

Findings

Between Feb 27, 2013, and July 15, 2013, 47 (23%) of 206 screened volunteers were randomly assigned to receive ISIS-APO(a)$_{Rx}$ as a single-dose or multi-dose of ascending concentrations or placebo. In the single-dose study, we assigned three participants to receive 50 mg ISIS-APO(a)$_{Rx}$, three participants to receive 100 mg ISIS-APO(a)$_{Rx}$, three participants to receive 200 mg ISIS-APO(a)$_{Rx}$, three participants to receive 400 mg ISIS-APO(a)$_{Rx}$, and four participants to receive placebo. All 16 participants completed treatment and follow-up and were included in the pharmacodynamics, pharmacokinetics, and safety analyses. For the multi-dose study, we assigned eight participants to receive six doses of 100 mg ISIS-APO(a)$_{Rx}$, nine participants to receive six doses of 200 mg ISIS-APO(a)$_{Rx}$, eight participants to receive six doses of 300 mg ISIS-APO(a)$_{Rx}$, and six participants to receive six doses of placebo. Whereas single doses of ISIS-APO(a)$_{Rx}$ (50–400 mg) did not decrease Lp(a) concentrations at day 30, six doses of ISIS-APO(a)$_{Rx}$ (100–300 mg) resulted in dose-dependent, mean percentage decreases in plasma Lp(a) concentration of 39·6% from baseline in the 100 mg group (p=0·005), 59·0% in the 200 mg group (p=0·001), and 77·8% in the 300 mg group (p=0·001). Similar reductions were observed in the amount of oxidized phospholipids associated with apolipoprotein B-100 and apolipoprotein(a). Mild injection site reactions were the most common adverse events.

Interpretation

ISIS-APO(a)$_{Rx}$ results in potent, dose-dependent, selective reductions of plasma Lp(a). The safety and tolerability support continued clinical development of ISIS-APO(a)$_{Rx}$ as a potential therapeutic drug to reduce the risk of cardiovascular disease and calcific aortic valve stenosis in patients with elevated Lp(a) concentration.

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Antidiabetic drugs restore abnormal transport of amyloid-β across the blood–brain barrier and memory impairment in *db/db* mice

Previous studies have shown significant changes in amyloid-β (Aβ) transport across the blood–brain barrier (BBB) under diabetic conditions with hypoinsulinemia, which is involved in diabetes-associated cognitive impairment. Present study employed *db/db* mice with hyperinsulinemia to investigate changes in Aβ transport across the BBB, hippocampal synaptic plasticity, and restorative effects of antidiabetic drugs. Our results showed that *db/db* mice exhibited similar changes in Aβ transport across the BBB to that of insulin-deficient mice. Chronic treatment of *db/db* mice with antidiabetic drugs such as metformin, glibenclamide and insulin glargine significantly decreased Aβ influx across the BBB determined by intra-arterial infusion of ^{125}I-A$\beta_{1\text{-}40}$, and expression of the receptor for advanced glycation end products (RAGE) participating in Aβ influx. Insulin glargine, but not, metformin or glibenclamide increased Aβ efflux across the BBB determined by stereotaxic intra-cerebral infusion of ^{125}I-A$\beta_{1\text{-}40}$, and expression of the low-density lipoprotein receptor related protein 1 (LRP1) participating in Aβ efflux. Moreover, treatment with these drugs significantly decreased hippocampal A$\beta_{1\text{-}40}$ or A$\beta_{1\text{-}42}$ and inhibited neuronal apoptosis. The drugs also ameliorated memory impairment confirmed by improved performance on behavioral tasks. However, insulin glargine or glibenclamide, but not metformin, restored hippocampal synaptic plasticity characterized by enhancing *in vivo* long-term potentiation (LTP). Further study found that these three drugs significantly restrained NF-κB, but only insulin glargine enhanced peroxisome proliferator-activated receptor γ (PPARγ) activity at the BBB in *db/db* mice. Our data indicate that the antidiabetic drugs can partially restore abnormal Aβ transport across the BBB and memory impairment under diabetic context.

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Nat Med. 2015 Oct;21(10):1154-62. doi: 10.1038/nm.3951. Epub 2015 Sep 21.

Critical role of acetylation in tau-mediated neurodegeneration and cognitive deficits.

Min SW[1,2], Chen X[1,2], Tracy TE[1,2], Li Y[1], Zhou Y[1], Wang C[1,2], Shirakawa K[3], Minami SS[1,2], Defensor E[4], Mok SA[5], Sohn PD[1,6], Schilling B[7], Cong X[7], Ellerby L[7], Gibson BW[7], Johnson J[8], Krogan N[8], Shamloo M[4], Gestwicki J[5], Masliah E[9], Verdin E[3], Gan L[1,2,6].

Author information

Abstract

Tauopathies, including frontotemporal dementia (FTD) and Alzheimer's disease (AD), are neurodegenerative diseases in which tau fibrils accumulate. Recent evidence supports soluble tau species as the major toxic species. How soluble tau accumulates and causes neurodegeneration remains unclear. Here we identify tau acetylation at Lys174 (K174) as an early change in AD brains and a critical determinant in tau homeostasis and toxicity in mice. The acetyl-mimicking mutant K174Q slows tau turnover and induces cognitive deficits in vivo. Acetyltransferase p300-induced tau acetylation is inhibited by salsalate and salicylate, which enhance tau turnover and reduce tau levels. In the PS19 transgenic mouse model of FTD, administration of salsalate after disease onset inhibited p300 activity, lowered levels of total tau and tau acetylated at K174, rescued tau-induced memory deficits and prevented hippocampal atrophy. The tau-lowering and protective effects of salsalate were diminished in neurons expressing K174Q tau. Targeting tau acetylation could be a new therapeutic strategy against human tauopathies.

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Burden of high fracture probability worldwide: secular increases 2010–2040

A. Odén, E. V. McCloskey, J. A. Kanis ✉, N. C. Harvey, H. Johansson

Abstract

Summary

The number of individuals aged 50 years or more at high risk of osteoporotic fracture worldwide in 2010 was estimated at 158 million and is set to double by 2040.

Introduction

The aim of this study was to quantify the number of individuals worldwide aged 50 years or more at high risk of osteoporotic fracture in 2010 and 2040.

Methods

A threshold of high fracture probability was set at the age-specific 10-year probability of a major fracture (clinical vertebral, forearm, humeral or hip fracture) which was equivalent to that of a woman with a BMI of 24 kg/m^2 and a prior fragility fracture but no other clinical risk factors. The prevalence of high risk was determined worldwide and by continent using all available country-specific FRAX models and applied the population demography for each country.

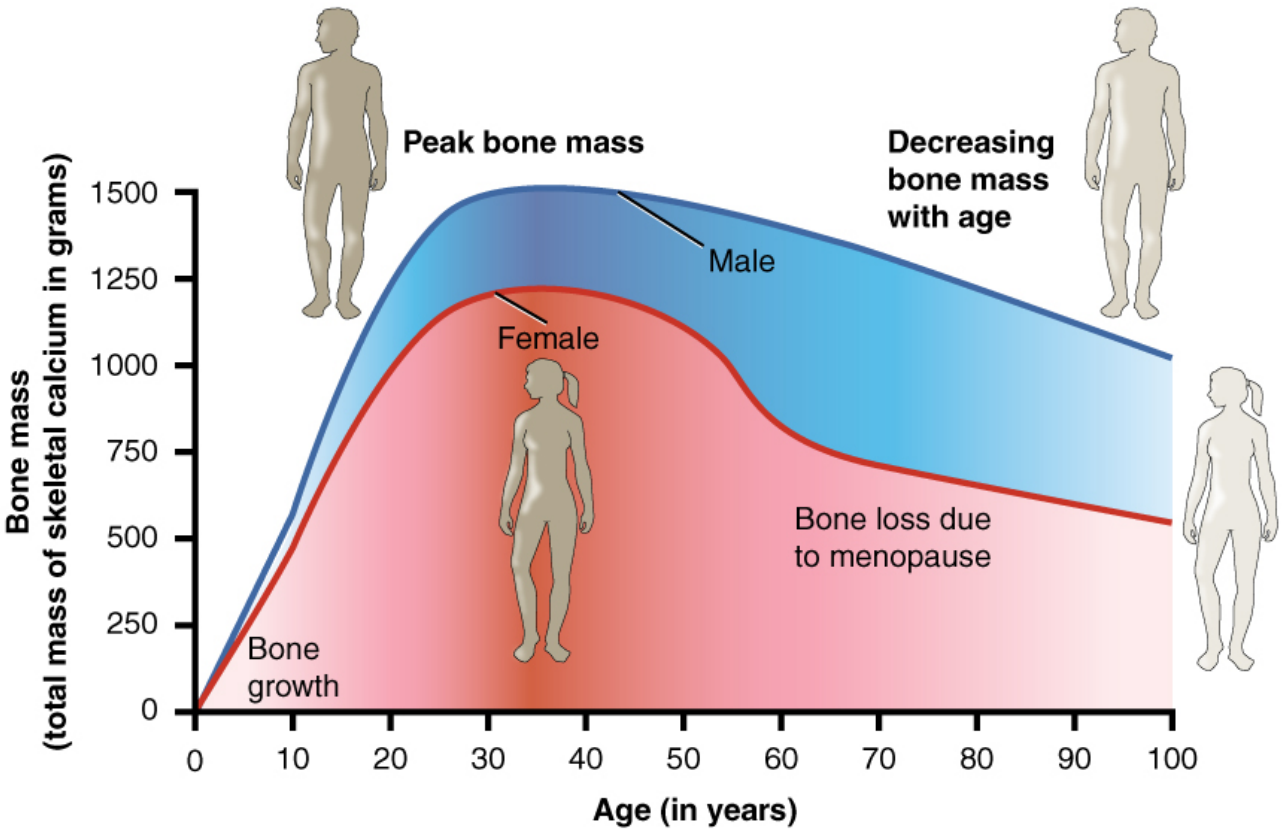
Results

Twenty-one million men and 137 million women had a fracture probability at or above the threshold in the world for the year 2010. The greatest number of men and women at high risk were from Asia (55 %). Worldwide, the number of high-risk individuals is expected to double over the next 40 years.

Conclusion

We conclude that individuals with high probability of osteoporotic fractures comprise a very significant disease burden to society, particularly in Asia, and that this burden is set to increase markedly in the future. These analyses provide a platform for the evaluation of risk assessment and intervention strategies.

Our Aging World: The Striking Statistics About Bone Fractures



158 million people worldwide over the age of 50 are already at high risk for bone fractures. This number could double by 2040.

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PDF version

Metabolic profiling distinguishes three subtypes of Alzheimer's disease

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Key words: *inflammation, neurodegeneration, cognition, insulin resistance, biomarkers, dementia, dyscalculia*

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Abstract

The cause of Alzheimer's disease is incompletely defined, and no truly effective therapy exists. However, multiple studies have implicated metabolic abnormalities such as insulin resistance, hormonal deficiencies, and hyperhomocysteinemia. Optimizing metabolic parameters in a comprehensive way has yielded cognitive improvement, both in symptomatic and asymptomatic individuals. Therefore, expanding the standard laboratory evaluation in patients with dementia may be revealing. Here I report that metabolic profiling reveals three Alzheimer's disease subtypes. The first is inflammatory, in which markers such as hs-CRP and globulin:albumin ratio are increased. The second type is non-inflammatory, in which these markers are not increased, but other metabolic abnormalities are present. The third type is a very distinctive clinical entity that affects relatively young individuals, extends beyond the typical Alzheimer's disease initial distribution to affect the cortex widely, is characterized by early non-amnestic features such as dyscalculia and aphasia, is often misdiagnosed or labeled atypical Alzheimer's disease, typically affects ApoE4-negative individuals, and is associated with striking zinc deficiency. Given the involvement of zinc in multiple Alzheimer's-related metabolic processes, such as insulin resistance, chronic inflammation, ADAM10 proteolytic activity, and hormonal signaling, this syndrome of Alzheimer's-plus with low zinc (APLZ) warrants further metabolic, genetic, and epigenetic characterization.

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J Gerontol A Biol Sci Med Sci. 2015 Sep;70(9):1097-104. doi: 10.1093/gerona/glv057. Epub 2015 Jul 17.

A 2-Year Randomized Controlled Trial of Human Caloric Restriction: Feasibility and Effects on Predictors of Health Span and Longevity.

Ravussin E[1], Redman LM[2], Rochon J[3], Das SK[4], Fontana L, Kraus WE[5], Romashkan S[6], Williamson DA[2], Meydani SN[4], Villareal DT[7], Smith SR[8], Stein RI[7], Scott TM[4], Stewart TM[2], Saltzman E[4], Klein S[7], Bhapkar M[5], Martin CK[2], Gilhooly CH[4], Holloszy JO[7], Hadley EC[6], Roberts SB[4]; CALERIE Study Group.

Author information

Abstract

BACKGROUND: Caloric restriction (CR), energy intake reduced below ad libitum (AL) intake, increases life span in many species. The implications for humans can be clarified by randomized controlled trials of CR.

METHODS: To determine CR's feasibility, safety, and effects on predictors of longevity, disease risk factors, and quality of life in nonobese humans aged 21-51 years, 218 persons were randomized to a 2-year intervention designed to achieve 25% CR or to AL diet. Outcomes were change from baseline resting metabolic rate adjusted for weight change ("RMR residual") and core temperature (primary); plasma triiodothyronine (T3) and tumor necrosis factor-α (secondary); and exploratory physiological and psychological measures.

RESULTS: Body mass index averaged 25.1 (range: 21.9-28.0kg/m(2)). Eighty-two percent of CR and 95% of AL participants completed the protocol. The CR group achieved 11.7±0.7 %CR (mean ± standard error) and maintained 10.4±0.4% weight loss. Weight change in AL was negligible. RMR residual decreased significantly more in CR than AL at 12 months ($p = .04$) but not 24 months (M24). Core temperature change differed little between groups. T3 decreased more in CR at M12 and M24 ($p < .001$), while tumor necrosis factor-α decreased significantly more only at M24 ($p = .02$). CR had larger decreases in cardiometabolic risk factors and in daily energy expenditure adjusted for weight change, without adverse effects on quality of life.

CONCLUSIONS: Sustained CR is feasible in nonobese humans. The effects of the achieved CR on correlates of human survival and disease risk factors suggest potential benefits for aging-related outcomes that could be elucidated by further human studies.

Proc Natl Acad Sci U S A. 2015 Sep 22;112(38):11977-82. doi: 10.1073/pnas.1506054112. Epub 2015 Sep 8.

Systematic analysis of asymmetric partitioning of yeast proteome between mother and daughter cells reveals "aging factors" and mechanism of lifespan asymmetry.

Yang J[1], McCormick MA[2], Zheng J[3], Xie Z[4], Tsuchiya M[2], Tsuchiyama S[2], El-Samad H[3], Ouyang Q[5], Kaeberlein M[6], Kennedy BK[7], Li H[8].

Author information

Abstract

Budding yeast divides asymmetrically, giving rise to a mother cell that progressively ages and a daughter cell with full lifespan. It is generally assumed that mother cells retain damaged, lifespan limiting materials ("aging factors") through asymmetric division. However, the identity of these aging factors and the mechanisms through which they limit lifespan remain poorly understood. Using a flow cytometry-based, high-throughput approach, we quantified the asymmetric partitioning of the yeast proteome between mother and daughter cells during cell division, discovering 74 mother-enriched and 60 daughter-enriched proteins. While daughter-enriched proteins are biased toward those needed for bud construction and genome maintenance, mother-enriched proteins are biased towards those localized in the plasma membrane and vacuole. Deletion of 23 of the 74 mother-enriched proteins leads to lifespan extension, a fraction that is about six times that of the genes picked randomly from the genome. Among these lifespan-extending genes, three are involved in endosomal sorting/endosome to vacuole transport, and three are nitrogen source transporters. Tracking the dynamic expression of specific mother-enriched proteins revealed that their concentration steadily increases in the mother cells as they age, but is kept relatively low in the daughter cells via asymmetric distribution. Our results suggest that some mother-enriched proteins may increase to a concentration that becomes deleterious and lifespan-limiting in aged cells, possibly by upsetting homeostasis or leading to aberrant signaling. Our study provides a comprehensive resource for analyzing asymmetric cell division and aging in yeast, which should also be valuable for understanding similar phenomena in other organisms.

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Autologous iPSC-derived dopamine neuron transplantation in a nonhuman primate Parkinson's disease model

Shuyan Wang, **Chunlin Zou**, **Linlin Fu**, **Bin Wang**, **Jing An**, **Gongru Song**, **Jianyu Wu**, **Xihe Tang**, **Mo Li**, **Jian Zhang**, **Feng Yue**, **Chengyun Zheng**, **Piu Chan**, **Y Alex Zhang** & **Zhiguo Chen**

Affiliations | **Contributions** | **Corresponding author**

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Received 29 March 2015 | Accepted 17 April 2015 | Published online 26 May 2015

Abstract

Abstract • **Introduction** • **Results** • **Discussion** • **Materials and Methods** • **References** • **Acknowledgements** • **Author information** • **Supplementary information**

Autologous dopamine (DA) neurons are a new cell source for replacement therapy of Parkinson's disease (PD). In this study, we tested the safety and efficacy of autologous induced pluripotent stem cell (iPSC)-derived DA cells for treatment of a cynomolgus monkey PD model. Monkey bone marrow mesenchymal cells were isolated and induced to iPSCs, followed by differentiation into DA cells using a method with high efficiency. Autologous DA cells were introduced into the brain of a cynomolgus monkey PD model without immunosuppression; three PD monkeys that had received no grafts served as controls. The PD monkey that had received autologous grafts experienced behavioral improvement compared with that of controls. Histological analysis revealed no overgrowth of grafts and a significant number of surviving A9 region-specific graft-derived DA neurons. The study provided a proof-of-principle to employ iPSC-derived autologous DA cells for PD treatment using a nonhuman primate PD model.

Reviews/Editorials/Commentaries

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Epigenetic regulation of ageing: linking environmental inputs to genomic stability

Abstract

Abstract • References • Author information • Supplementary information

Ageing is affected by both genetic and non-genetic factors. Here, we review the chromatin-based epigenetic changes that occur during ageing, the role of chromatin modifiers in modulating lifespan and the importance of epigenetic signatures as biomarkers of ageing. We also discuss how epigenome remodelling by environmental stimuli affects several aspects of transcription and genomic stability, with important consequences for longevity, and outline epigenetic differences between the 'mortal soma' and the 'immortal germ line'. Finally, we discuss the inheritance of characteristics of ageing and potential chromatin-based strategies to delay or reverse hallmarks of ageing or age-related diseases.

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Late-onset dementia: a mosaic of prototypical pathologies modifiable by diet and lifestyle

Idiopathic late-onset dementia (ILOD) describes impairments of memory, reasoning and/or social abilities in the elderly that compromise their daily functioning. Dementia occurs in several major prototypical neurodegenerative disorders that are currently defined by neuropathological criteria, most notably Alzheimer's disease (AD), Lewy body dementia (LBD), frontotemporal dementia (FTD) and hippocampal sclerosis of aging (HSA). However, people who die with ILOD commonly exhibit mixed pathologies that vary within and between brain regions. Indeed, many patients diagnosed with probable AD exhibit only modest amounts of disease-defining amyloid β-peptide plaques and p-Tau tangles, and may have features of FTD (TDP-43 inclusions), Parkinson's disease (α-synuclein accumulation), HSA and vascular lesions. Here I argue that this 'mosaic neuropathological landscape' is the result of commonalities in aging-related processes that render neurons vulnerable to the entire spectrum of ILODs. In this view, all ILODs involve deficits in neuronal energy metabolism, neurotrophic signaling and adaptive cellular stress responses, and associated dysregulation of neuronal calcium handling and autophagy. Although this mosaic of neuropathologies and underlying mechanisms poses major hurdles for development of disease-specific therapeutic interventions, it also suggests that certain interventions would be beneficial for all ILODs. Indeed, emerging evidence suggests that the brain can be protected against ILOD by lifelong intermittent physiological challenges including exercise, energy restriction and intellectual endeavors; these interventions enhance cellular stress resistance and facilitate neuroplasticity. There is also therapeutic potential for interventions that bolster neuronal bioenergetics and/or activate one or more adaptive cellular stress response pathways in brain cells. A wider appreciation that all ILODs share age-related cellular and molecular alterations upstream of aggregated protein lesions, and that these upstream events can be mitigated, may lead to implementation of novel intervention strategies aimed at reversing the rising tide of ILODs.

Mitochondrion. 2015 Oct 2. pii: S1567-7249(15)30024-6. doi: 10.1016/j.mito.2015.09.003. [Epub ahead of print]

Mitoepigenetics: The different shades of grey.

Ghosh S[1], Singh KK[2], Sengupta S[1], Scaria V[3].

Author information

Abstract

Epigenetic modifications of the nuclear genome have been well studied and it is established that these modifications play a key role in nuclear gene expression. However, the status of mitochondrial epigenetic modifications has not been delved in detail. The recent technological advancements in the genome analyzing tools and techniques, have helped in investigating mitochondrial epigenetic modifications with greater resolution and studies have indicated a regulatory role of the mitochondrial epigenome. Association of mitochondrial DNA methylation with various disease conditions, drug treatment, aging, exposure to environmental pollutants etc. has lent credence to this belief. Herein, we have reviewed studies on mitochondrial epigenetic modifications with a focus to comprehend its regulatory role in gene expression and disease association.

KEYWORDS: Epigenetics; Methylation; Mitochondria; Mitochondrial DNA methylation; Mitoepigenetics