REVIEW OF BIOLOGICAL RESEARCH IN AGING pdf

1: JOHNSON LAB PUBLICATIONS

The review reflects this ongoing ferment, providing a historical perspective as well as discussion of recent research and experimentation on the evolution of senescence, through late In addition to the general evolutionary theory, two proposed population genetic mechanisms for the evolution of senescence are presented: mutation.

How does life end? What is the true nature of death? Is it absoluteâ€”a fundamental state? Or is it relative and a matter of degree? Can it be defined as part of some basic reality, a detail of an unknown whole rather than merely an illusion? Although any living creature anytime can lose its life, no creature can lose its death. This is why death is safe and secure in all living things. Despite the fundamental nature and importance of both the process of dying and of death itself, the concepts have received almost no attention in the basic biological sciencesâ€”textbooks seldom contain any reference to death or dying. Studies on the biology of death are important because the literature that results from these studies would provide new insights into end-of-life events and processes and thus provide bioethicists, physicians and family members with a more secure biological foundation for considering ethical, legal and medical issues at the end-of-life. Understanding the biology of death will also shed light on questions concerned with time-to-death, and cause-of-death dependent patterns of death, and complex interactions among competing causes. Death as finitude One of the most creative thinkers in aging science was the late gerontologist George Sacher who, in a seminal but rarely cited paper Sacher , asserted that biological research on aging is the scientific response to three primitive questions. Why do we grow old? Why do we live as long as we do? Why do we die? However, the third question that situates death in the broader context of aging science has been completely ignored. He notes that questions about death are important because, among other reasons it is the problem of transition probabilities from the stochastic changes of state from health to disease or from living to death. He believed that the problem of death must be investigated in its own right since there was no necessary relationship between aging and dying. Many variations on this model can be considered. For example, the schema becomes a two-stage model for death that occurs instantaneously severe trauma â€”i. However, in both principle and in reality, they may live for decades suspended in this stage. One of the most difficult predictions is identifying when an individual has entered into the active dying process i. Although difficult, the ability to predict will never advance through physician-by-physician anecdotal observations. Systematic studies of death in model species should reveal whether it is possible a priori as distinct from retrospectively to identify markers indicating irreversible descent with specified levels of probability. The general model presented in Table 1 can be further refined to include additional phases or subphases such a pre-descent stage linking death with earlier events involving aging and disablement, and a post-expiration phase linking the death of the individual as a whole with postmortem biological processes. There are probably two main reasons why so little literature exists on the biology of death: Developing a literature based on the systematic study of the final stages of life the process of dying will begin to fill in an important gap in the study of lifeâ€”how life ends. The clinical definition of death is important because it defines the point at which to withdraw medical and care giving resources from decedent and, with prior consent, use the decedent as a source of organs that can be used in organ transplants. Likewise, developing a deeper understanding of dying through the use of experimental methods will be important because the knowledge will provide a more sound basis for identifying the point at which the end-phase has begun and for revealing the progressive stages in active dying that most and perhaps all living creatures experience that die naturally.

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2: Biology of Death | The Evolution and Medicine Review

Review of Biological Research in Aging, volume 1, admirably fills this gap, and it is hoped that further volumes in this planned series will materialize. This first volume has set a precedent for.

Received Mar 18; Accepted Jun 2. Non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly attributed, cited, and is not altered, transformed, or built upon in any way, is permitted. The moral rights of the named author s have been asserted. This article has been cited by other articles in PMC. Abstract Over a century ago, the zoologist Emile Maupas first identified the nematode, Rhabditis elegans, in the soil in Algiers. Subsequent work and phylogenic studies renamed the species Caenorhabditis elegans or more commonly referred to as C. However, it was not until , when Sydney Brenner, already successful from his work on DNA, RNA, and the genetic code, suggested the future of biological research lay in model organisms. Brenner believed that biological research required a model system that could grow in vast quantities in the lab, were cheap to maintain and had a simple body plan, and he chose the nematode C. Since that time, C. This paper reviews some initial identification of mutants with altered lifespan with a focus on genetics and then discusses advantages and disadvantages for using C. This review focuses on molecular genetics aspects of this model organism. In this influential paper Brenner , Brenner outlined methodology for isolation, complementation, and mapping of worm mutants. Importantly, the publication also included the successful isolation of several hundred mutants affecting behavior and morphology, a discussion of the number of defined genes, and an estimation of mutation frequency. Since that time, many discoveries including dissection of programmed cell death Coulson et al. In , Klass published that C. In these early studies, Klass found that altering either temperature or the amount of food resulted in a change in lifespan. In addition, only small effects on lifespan were observed based on parental age or parental lifespan. Klass performed a clonal genetic screen for mutants with altered lifespan and identified five mutants Klass This was the first breakthrough in aging research for studies based on C. From the initial characterization of mutants that altered lifespan, the words lifespan and aging have often been used interchangeably. However, lifespan is a single measureable parameter that defines the amount of time an organism is alive but does not give any indication for how an animal is actually aging. Lifespan as a measurement gives little detail about the health of the animal. For this reason, healthspan, defined as the time that an individual is active, productive and free from age-associated disease, is starting to become the focus of aging research reviewed in Tissenbaum Equally important for aging research is the use of the term regulation. A regulated process should indicate that this is a trait that would be selected for over time. However, fitness competitions between wild type and daf-2 mutants, show that after four generations, none of the daf-2 mutants remained primarily because of the early fertility defects in the daf-2 mutants Jenkins et al. Taken together, lifespan and aging should not be used interchangeably and the use of the word regulation should be monitored reviewed in Lithgow ; Tissenbaum Several years after the age-1 gene was identified, another gene was shown to modulate lifespan. Similar to mutation in age-1, daf-2 mutants showed adult lifespan extension Kenyon et al. Interestingly, previously, both daf-2 and age-1 had showed similarity based on a different phenotype. Under favorable growth conditions, C. In response to unfavorable growth conditions, in particular, high levels of a secreted pheromone i. Dauer German for enduring larvae alternate L3 maximize survival until conditions become more favorable, whereupon they will molt and form a reproductive adult. Genetic screens identified mutants affecting the ability to enter this dauer program. These mutants were named daf mutants indicating the dauer formation phenotype. Both daf-2 and age-1 were initially isolated in this type of screen because both daf-2 and age-1 originally identified as daf mutants show a dauer constitutive daf-c phenotype such that even under good growth conditions, mutants will enter the dauer stage Albert et al. These studies also revealed that both daf-2 and age-1 mutants could be suppressed by a mutation in the daf gene Albert et al. Subsequent molecular cloning beginning in , explained why these genes were separate and distinct from other pathways. Since then, studies have shown that the IIS pathway is evolutionarily conserved such that mutations in this pathway in flies and mice are also linked to lifespan extension Barbieri et al. Molecular and genetic studies in Drosophila

and C. Importantly, advances in genomic research have led to new findings in the area of genome-wide association studies in humans. Multiple human population studies have found an association between single nucleotide polymorphisms SNPs in human FOXO3 and human lifespan extension Lunetta et al. Therefore, FOXO3 has emerged as a candidate longevity gene in humans. Taken together, just over a decade from the molecular identification of DAF in C. Therefore, it was thought that daf-2 and age-1 were long lived merely due to activation of part of the dauer program manifested in the adult. However, Kenyon et al. Moreover, recent studies Shaw et al. Taken together, multiple studies suggest that the longevity of daf-2 mutants is due to activation of the dauer program in the adult. Despite the fact that a dauer program, an alternative hibernation state to delay reproduction until growth conditions are favorable, seems worm specific, the signaling pathways that were identified to regulate dauer formation modulate longevity from worms to mice, and are associated with human longevity. Advantages of worms Why has C. What would make an organism suitable for aging research? As suggested by Sydney Brenner in , the ability to easily and cheaply grow large quantities of worms in the lab is very helpful for aging research, especially when identifying long-lived mutants. Additional benefits of using C. This has allowed for extensive forward and reverse genetic screens for genes that modulate lifespan. The RNAi library allows RNAi to be done by feeding worms bacteria that produce the desired dsRNA and then either the worm or their progeny are scored for a longevity phenotype Ahringer Using genome-wide RNAi feeding libraries, the importance of the mitochondria, signal transduction, the response to stress, protein translation, gene expression, and metabolism were found to modulate lifespan Dillin et al. Another advantage working with C. Therefore, statistical significance can be tested in addition to the analysis of mortality rates. Together, these techniques allow one to comprehensively survey the worm genome for genes that modulate lifespan. This has led to the identification of more than genes and regimens that modulate lifespan in C. Therefore, the combination of the short, invariant lifespan, ease of assays, ample genetic, molecular and genomic tools, and evolutionary conservation has allowed C. Disadvantages of worms Despite all the excellent advantages of working with C. Typically, all biochemistry, microarray, immunoprecipitation, and chromatin immunoprecipitation is performed on whole worm extracts of either mixed-stage animals or animals at a similar growth stage. This may lead to limited understanding of any tissue-specific signaling such as whether a gene is expressed in the hypodermis or the intestine. Thus far, research has focused on the use of lifespan as a measurement of the aging process. These studies have led to the identification of hundreds of genes and regimens that modulate lifespan. Although the initial studies identified genes that altered lifespan and affected dauer diapause, these signaling pathways have nonetheless identified longevity-associated pathways across phylogeny. However, to truly use C. Aging is much more than a lifespan measurement. Aging involves the coordination of multiple systems in an organism and how they change as a function of time. We should strive to use model systems to reveal this systemic coordination on a molecular and genetic level, and how this leads to healthy aging rather than simply lifespan extension. Due to lack of space, this article focused on molecular genetics and the aging process in C. For additional details of the C. For early studies, please refer to Nigon and Dougherty Sensory control of dauer larva formation in Caenorhabditis elegans. The Journal of Comparative Neurology. Experimental evolution reveals antagonistic pleiotropy in reproductive timing but not life span in Caenorhabditis elegans. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences. The natural history of Caenorhabditis elegans research. American Journal of Physiology - Endocrinology and Metabolism. The genetics of Caenorhabditis elegans. Green fluorescent protein as a marker for gene expression. Longevity determined by developmental arrest genes in Caenorhabditis elegans. A demographic analysis of the fitness cost of extended longevity in Caenorhabditis elegans. Toward a physical map of the genome of the nematode Caenorhabditis elegans. Proceedings of the National Academy of Sciences. Is life-span the best measure of aging? Science of Aging Knowledge Environment. Lifespan regulation by evolutionarily conserved genes essential for viability. Aging and the aggregating proteome. Journal of Proteome Research. Rates of behavior and aging specified by mitochondrial function during development. Genes required for the engulfment of cell corpses during programmed cell death in Caenorhabditis elegans. Genetic control of differential heat tolerance in two strains of the nematode Caenorhabditis elegans. Potent and specific genetic interference by double-stranded RNA in

Caenorhabditis elegans. A mutation in the age-1 gene in Caenorhabditis elegans lengthens life and reduces hermaphrodite fertility. Two pleiotropic classes of daf-2 mutation affect larval arrest, adult behavior, reproduction and longevity in Caenorhabditis elegans. A systematic RNAi screen for longevity genes in C.

REVIEW OF BIOLOGICAL RESEARCH IN AGING pdf

3: Journal of Aging Science- Open Access Journals

Review of Biological Research in Aging (Review of Biological Research in Aging) by Morton Rothstein, August , Alan R. Liss edition, Hardcover in English.

The global scientific community is been curious about this process and many interesting facts came up through extensive research. Multiple factors involved in aging is being analysed at laboratory scale individually and collectively. Aging science became a multidisciplinary branch of modern science. Journal of Aging Science offers an interesting platform for those who are interested in this area broadly where every aspect of aging is considered. This Aging Science Journal considers articles in the following areas: It also covers research on fast emerging areas of adults stem cells, brain imaging, calorie restriction, molecular diagnostics, pharmacology and clinical aspects of aging. Excellent quality contributions are welcome to address the recent important issues in the relevant subject and to achieve high impact factor. Editorial Manager System is being used to maintain high quality in peer review process. Online submission, review and tracking are possible through this system. Editorial board members of this journal or outside experts take part in review process where at least two independent reviewers approval followed by editor approval is required for acceptance of the submitted manuscript. Aging Science It is a branch of science which involves in biology of human aging. It deals with the treatment of age related diseases. Cognitive, psychological, social and biological aspects of aging are also included in aging science. Oxford Journals Aging Advancement in age of a human in which the mental and physical development gradually tends to decrease. Aging is known to be a major risk factor for several most diseases. It is also an important part in every human. Aging Skin Aging of the skin is a natural process in which wrinkles, age spots and dryness are common symptoms. Skin loses fat becomes slack and develops lesions. Senescence It is also known as biological aging. It refers to the gradual decrease in the ones daily functions. Various environmental factors are also responsible for senescence for example: Geriatrics It is the branch of medicine that deals with the health and care of older adults. It prevents and treats diseases in older population. It is important for older people in nursing them. It can also be called medical gerontology. Longevity It refers to duration of life or life expectancy. Exercise, diet and lifestyle are major factors that can affect longevity. Old Age Psychiatry Psychiatry is the most common problem in people aged over 65 and above associated with mental illness. Psychic disorder includes dementia, depression and schizophrenia. Biology of Aging Aging is said to be genetic. Longevity genes are responsible for aging in human and are complex to identify. These genes can be helpful in the future to support healthy aging. Cellular Senescense It refers to biological aging or biogerontology. Proliferation of cells occurs that leads to permanent cell cycle arrest. Senescense occurs due to the stress on the cells from exogenous and endogenous sources. Aging Population Aging Population is a phenomenon in which increase in the number of older adults in society. This increases when the population composed of children decreases. It is estimated that the population of older people is more in less developed countries. Antiaging Antiaging is to stop the normal process of cell death or senescence. Advanced technology to defeat aging has now been introduced such as cosmetic surgery which covers up all the signs of aging. Elder Care Elder care is showing special care to senior citizens regarding their daily needs. When their physical health begin to fail maintaining of the body becomes difficult. Seniors living in both home and senior living community, medical and non-medical home care should be provided. Advances in Age Test Aging of the skin can be noticed by wrinkles on the skin due to lack of production of collagen. Skin in older adults produces less oil making the skin dry and saggy. Antiaging Diet Diet plays a major role in aging. The intake of colorful fruits and vegetables containing antioxidant s help stop damaging of healthy cells in your body. Antiaging Creams Antiaging creams are usually used to protect the skin from natural signs of aging such as wrinkles, age spots, pigmentation. These creams rejuvenate the skin to look younger. Aging Research Aging biology research involves two or similar species that have different life expectancy. Diseases related aging and process of aging can be identified by genetic, biological, clinical, behavioral, social, and economic research on animals.

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4: The New Age of Aging Research â€“ Harvard Science Review

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To some, this word symbolizes equality, wisdom, and progress; to others, this word represents weakness, disease, and death. To me, aging has taken on a mixed meaning. When I was a small child, I remember lying awake in bed and counting my heartbeats as if the thumping in my chest was also the ticking of my biological clock. I imagined that each person was given a certain number of heartbeats in a lifetime. Aging, to my young mind, was simply the slow and eventual countdown of these limited heartbeats. Although not many people will admit it, the fear of aging and death is extremely common 1. Throughout history, our fascination with mortality has contributed to the rise and spread of religions and legends. Despite numerous efforts, there are no records of any successful attempts at synthesizing the object. After the discovery of the Americas, there was growing interest in the possibility of uncovering the fountain of youth in this uncharted territory. Birren developed the field of gerontology, which is the study of aging, and expanded it firstly socially and secondly scientifically. At this time, aging research was widely considered a pseudoscienceâ€"a label that was not helped by the unscientific blood and serum transfusions championed by charlatans as anti-aging treatments. Ironically, a recent study reported that old mice that received plasma transfusions from younger mice were physiologically healthier, although this has yet to be validated in humans and although it was quite clear that these results were unknown in the early s 2. Notable Advances In the following years, aging research underwent a series of profound, exciting breakthroughs. Perhaps the most famous discovery was that of the telomere. Telomeres are the repeating DNA sequences at the end of each of the chromosomes. Through the DNA replication mechanism, the telomeres deteriorate after each cycle of replication and the chromosomes become shorter. Although telomeres themselves do not appear to have any significant function outside of protecting other DNA sequences from degradation, when a cell exhausts its telomeres, each successive division results in deterioration of essential genes and deleterious effects that often result in cellular death 3. Hayflick, considered by many to be the father of modern aging research, carried out a groundbreaking experiment that indicated that somatic cells could only divide a finite number of times 1. At the time, it was widely accepted that cell lineages were immortal and that each body cell was capable of an indefinite number of divisions. This limit to cellular division was typically divisions for human somatic cells 1. In the s, Jack Szostak discovered the existence of telomeres at the end of chromosomes, which explained the Hayflick limit phenomenon 3. If cell replication was restricted by the length of the telomere, and the telomere was of a finite length, then surely cell lineages are finite. Szostak garnered a Nobel Prize for his work. Soon after the discovery of telomeres, the enzyme that extends telomeres on chromosomes, telomerase, was discovered. In recent years, overexpression of telomerase has been linked to the vicious proliferation and immortality of cancer cells 3. Telomeres serve as the switch for immortalityâ€"at least on a cellular level. An often overlooked, but perhaps even greater breakthrough was the development of several notable theories of aging. Imagine an organism as a car. Cars, no matter how well kept or maintained, begin to lose function with time. At first, there may be a few scratches to the windshield, buildup in the exhaust pipe, and worn-out tires. These are minor issues that can be amended relatively easily. Then, the engine starts to malfunction, the wires begin to rust, and the car becomes unsalvageable. Like a car, the organism has many parts that are being used daily. Similarly, an organism can break down through continuous wear and tear. This seemingly obvious idea has been revolutionary in the field of aging research. Contrary to other theories that proposed that humans were genetically programmed to age, the cumulative damage theory presented aging as a random process 1. As such, it may be reasonable to conclude that aging is the byproduct of environmental effects. Surely, this would mean that after centuries of medical advancement, which included vaccines, antibiotics, and surgery among its ranks, humans have been able to increase their life spans considerably. Yet, despite significant increases in life expectancy, meaning more humans are realizing the full extent of their maximum lifespans, the actual human lifespan has stayed relatively the same 3. A more recent theory proposed that the maximum lifespan is

determined genetically and that environmental factors can only contribute to expedited biological aging. Given the saturation of human population survival curves, this theory is especially convincing 3. As a corollary to the cumulative damage theory of aging, aging is regarded as a holistic processâ€"a process that is affected by a multitude of genes and environmental factors. One suspected contributor to the aging process is free radical damage. Free radicals are byproducts of cellular respiration and can damage DNA. In particular, mtDNA mitochondrial DNA is at risk of oxidative damage due to both its proximity to free radical formation, as cellular respiration occurs in mitochondria, and significantly lower levels of DNA repair. The free radical theory of aging has become especially popular in the health industry where antioxidants, compounds that neutralize free radicals, have become synonymous with anti-aging treatments. Other notable candidates for contributing to aging include protein aggregation, cross linkage, and induced apoptosis 1. In order to discern other contributing factors, several longitudinal studies on aging have been implemented. The Baltimore Longitudinal Study of Aging BLSA is the most prominent of these studies and was started in by Nathan Shock, a pioneer in the field of aging research, along with over 1, participants 4. Since then, several other studies have taken root including The SardiNIA Project executed by the National Institute on Aging that includes 6, participants from the island of Sardinia off the coast of Italy 3. Armed with the powerful tools of bioinformatics, these studies have become potential windows from which to understand the intricacies of human aging. Aging Research Today Aging research has gained steady momentum in recent years. In fact, one of the most famous aging experiments was conducted in by Cynthia Kenyon, a professor at UCSF and now vice president at Calico. Kenyon discovered that mutations in the daf-2 and daf- 16 genes doubled the lifespan of C. Her future work saw increasingly lengthened lifespans from modulating these two gene 5. The search for homologous counterparts in humans is ongoing. A recent subset of aging research has focused on life extension treatments in more complex model organisms such as D. Recently, other molecular mechanisms have been implicated with aging. These include reservatrol, sirtuins, and rapamycin. Reservatrol, a compound commonly found in red wines, activates sirtuin deacetylases, which extend the lifespan of lower organisms and may also be involved in human aging 6. Reservatrol has also been related to cardioprotective benefits. Treatments involving rapamycin, an immunosuppressant, have increased the longevity of mice 7. The search for contributing molecular factors of aging is an active and promising facet of aging research. In the past decade, the advent of computational tools for large-scale data analysis has revealed fascinating insights into aging. Computational biology and bioinformatics have expedited the search for biomarkers of aging. Traditionally, pulse wave velocity and telomere length served as the gold standards of biological age measurement, but only explained a fraction of individual variance in aging 3. Recent research has implicated a litany of cardiovascular traits, physical and mental characteristics, and genetic mutations as potential biomarkers. In , Steve Horvath, a professor at UCLA, developed a method for deriving an estimate of biological age DNAm from DNA methylation patterns, which was highly correlated with chronological age and seemed to explain several tendencies in both aging and disease 8. There is ongoing research in detection of a central aging signal that explains most physiological causes of aging. Aging research has garnered considerable public spotlight in the past several years. Aubrey de Grey, a computer scientist turned biologist and founder of the SENS foundation, gave an extremely well-received TED talk on a strategy that he has proposed to tackle the obstacle of aging. The strategy involves partitioning the aging process into several major factors: By targeting medical advancements in each field separately, the problem becomes more manageable and the human lifespan could potentially be elongated in small increments over a long period of breakthroughs 9. Other social movements such as transhumanism have highlighted the potential of anti-aging treatments in the near future. Transhumanism embraces emerging technologies and their potential in bettering the human body or quality of lifeâ€"including extension of the healthy lifespan 9. Controversies Since the age of alchemy, aging research has been a field brewing with controversy. Today, there are two major concerns with developments in aging research and rejuvenation technology. First, critics of anti-aging research are concerned with the very real possibility of overpopulation. The current age distribution of ages in the United States is a micro-example of what an ageless population might entail. There are already concerns that the aging Baby Boomers generation may overburden the healthcare and Social Security systems. Imagine this

same effect but with continuous, cumulative addition to the old end of the age spectrum. Critics espousing this belief, however, do not take into consideration what current aging research implies about future anti-aging therapies. Nearly all current testing in model organisms has indicated that anti-aging treatments tend to promote extended, healthy aging. That is, the relative age of individuals would simply be stretched across a longer temporal span. Individuals under treatment who are chronologically 70 years old may instead be 50 years old biologically. As such, fears of skewing towards an elderly population are largely unfounded in a relative world. Additionally, longer healthy life spans would entail greater productivity from an individual over their lifetime 9. Other opponents of aging research cite religious and ethical concerns After all, if we are extending our lifespans beyond their natural limit, are we not playing God? There is no simple solution to address these concerns. There will always be advocates and critics of aging research and scientists should be attentive to these ethical concerns as they continue to pursue this line of research. In the end, if an anti-aging treatment is procured, it is only an additional opportunity that has been extended and would be by no means obligatory. The Path Ahead Aging research is an exciting and growing field. Aging is still a relatively underpopulated field of research and looks to benefit from the recent explosion of biotechnology and big data-aided research In the coming decades, one can expect to see greater innovation and progress in aging research. Nature , , Why We Age, 1st ed. Aging Cell , 4, Genome Biology , 14, R

REVIEW OF BIOLOGICAL RESEARCH IN AGING pdf

5: Ageing Research Reviews - Journal - Elsevier

Note: Citations are based on reference standards. However, formatting rules can vary widely between applications and fields of interest or study. The specific requirements or preferences of your reviewing publisher, classroom teacher, institution or organization should be applied.

Advanced Search Abstract Telomeres, the DNAâ€"protein structures located at the ends of chromosomes, have been proposed to act as a biomarker of aging. In this review, the human evidence that telomere length is a biomarker of aging is evaluated. Although telomere length is implicated in cellular aging, the evidence suggesting telomere length is a biomarker of aging in humans is equivocal. These studies would benefit from longitudinal measures of both telomere length and aging-related parameters. Telomere length , Biomarker of Aging INCREASED inter-individual and intra-individual variability is observed within sensory, motor, and cognitive and health domains with increasing chronological age 1â€"6. Biomarkers of aging are quantifiable parameters that reflect biological aging, which potentially can identify those at risk of aging-related conditions, disease, and mortality. Biomarkers could also be used to monitor and evaluate interventions designed to delay the onset or retard the progression of aging-related conditions and disease. Even though there has been little agreement on the validation criteria for candidate biomarkers 7â€"10 , the promise of the utility of biomarkers of aging continues to be a driving force for research 11 , Telomere length has been proposed as a candidate biomarker of aging 7 , 10 , 13â€" Telomeres are nucleoprotein structures located at the ends of eukaryotic chromosomes. The observation that telomeres shorten with increasing age and are implicated in cellular aging has led to the proposal that telomere length is a biomarker of aging. Support for this hypothesis is provided by human studies that have found a significant inverse relationship between telomere length and several age-sensitive measures, aging-related conditions, disease, and mortality. However, the evidence is equivocal. In a review of the in vitro and in vivo evidence, von Zglinicki and Martin-Ruiz 16 found that telomere length satisfied several criteria for a biomarker of aging, as it changes with age, has high inter-individual variability, is linked to basic biology, and correlates with aging and aging-related disease. The authors acknowledged that the majority of the evidence was cross-sectional and that many studies were underpowered. Since this review, a wide range of human studies have been published examining the relationship of telomere length with aging-related measures and mortality, prompting the need to reexamine the evidence using a set of well-defined biomarker of aging criteria developed by the American Federation of Aging Research 10 , It must predict the rate of aging. In other words, it would tell exactly where a person is in their total life span. It must be a better predictor of lifespan than chronological age. It must monitor a basic process that underlies the aging process, not the effects of disease. It must be able to be tested repeatedly without harming the person. For example, a blood test or an imaging test. It must be something that works in humans and in laboratory animals, such as mice. This is so that it can be tested in lab animals before being validated in humans. PubMed, Web of Science, and Scopus. Various combinations of the following keywords were used as search criteria: Studies were included if they used a representative population sample and had a sample size of or more. Conference proceedings were excluded. Other published articles were identified by cross-checking cited references. All relevant studies were examined and compiled into tables detailing the age of sample, size of sample, sex ratio, adjustments, type of telomere length assay, the result, and, in addition for longitudinal studies, the length of follow-up Tables 1 and 2. Over 3, studies were examined with only 19 meeting the criteria for this review Tables 1 and 2.

6: Mechanisms of Aging | Open Philanthropy Project

Of all published articles, the following were the most read within the past 12 months.

Back to Top Our process Our scientific advisors, Chris Somerville and Heather Youngs , are biochemists and scientific generalists with no prior expertise in aging research. We asked them to survey the field of aging, divide it into subfields, identify promising projects that were not being pursued, and help us understand the potential impact on healthy lifespan if various potential long-term research projects were successful. The latter question was not discussed in the literature, and we had to approach it very speculatively. We excluded investigation of science mainly relevant only to one specific age-related disease e. Our advisors conducted literature reviews, spoke with several people in the field, and wrote rough internal memos for other staff to review. This was their main priority for roughly one and a half months. Back to Top What is the problem? Back to Top What currently available interventions can address this problem? There are a large number of symptoms associated with aging. Some are widely recognized as diseases and are subject to a variety of treatments e. There are approaches that have been hypothesized to fit in this category, such as caloric restriction. While some of these have been tested in model systems, they have not been tested in humans for the purpose of extending healthy lifespan, and we would guess that they would not have radical effects on healthy lifespan if they were tested but plausibly could be substantially positive. Back to Top How could the problem be substantially alleviated? This section focuses on imagining, very speculatively, how scientific advances could eventually make it possible to prevent or substantially alleviate some problems associated with aging. Claims not cited are generally based on the internal memos produced by, and subsequent conversations with, our advisors along the lines of the process described above. This list highlights some imaginable scientific advances that attracted the interest of our scientific advisors because of their potential to extend healthy lifespan. The list is not exhaustive. With those caveats and clarifications in mind, we would guess that healthy lifespan might be extended if scientists eventually were able to: Prevent the accumulation of epigenetic errors associated with aging, or restore more youthful epigenetic states in cells. Various alterations of epigenetic state 4 are correlated with both chronological age and symptoms of aging, and there are theoretical reasons to expect that these alterations would cause symptoms of aging. As animals age, senescent cells i. Research suggests that senescent cells contribute to damaging inflammation and may also suppress tissue regeneration by stem cells. We mean to raise the above generic strategies only as plausible possibilities and do not have confidence in the feasibility or timeline for success of particular approaches. Reverse stem cell exhaustion. Somatic stem cells are induced by factors such as growth, normal senescence, and tissue damage to divide and replenish other cells. We see a few speculative possibilities for addressing stem cell exhaustion, and we discuss three of them in a footnote. Some of us see several years of healthy life extension as the plausible potential upside and others see larger possible gains, but all of us involved in creating this report expect that any increase in healthy lifespan would keep average lifespan within the range of natural lifespans observed in humans today barring a historically exceptional increase in the rate of scientific progress. We would guess that much more radical life extension would likely require a larger number of successes like these and likely multiple successes that are not listed here, and we accordingly assign it much lower probability in the next few decades with some caveats. We held this view about the difficulty of radical life extension prior to this investigation. Our findings fit with this prior view, and the investigation did not strongly affect our views on the matter. The themes covered in less detail here include: We may investigate inflammation and decline of the immune system more thoroughly in the future because these topics caught the interest of our scientific advisors. We compare our list of highlighted topics with a plan proposed by researchers at the SENS Foundation in a footnote. Common obstacles to achieving the goals stated above include lack of ability to selectively deliver agents to desired cell types, measure and control the epigenetic state of cells, and understand and control differentiation and functioning of stem cells plausibly closely related to the previous item. Therefore, progress on these more general themes may assist with extending healthy lifespan. Our reasoning for thinking this work will be more important in the long run can be made clearer by

reference to a thought experiment: We suspect something similar is still true today. One observation we can offer in support of this is that many of the important questions relevant to extending lifespan could not even have been asked 30 years ago e. Some of the themes listed above do not seem to have as many basic obstacles as others. For example, it seems plausible to us that some of the above objectives related to senescent cell removal and heterochronic parabiosis could be achieved in the next couple of decades. Back to Top Indefinite vs. Some thoughts on this: However, we would have some concerns about indefinite life extension, mainly related to entrenchment of power and culture. By January 1, , there will be no collection of medical interventions for adults that are healthy apart from normal aging, which, according to conventional wisdom in the medical community, have been shown to increase the average lifespan of such adults by at least 25 years compared with not taking the interventions. The prediction excludes diet, exercise, and lifestyle, as well as existing medical interventions for healthy people such as currently available vaccines. Back to Top Who else is working on it? A brief Google search revealed the following non-profit organizations working in the space, with all funding totals reflecting amounts dedicated to aging-related research: We have a limited sense of the absolute and relative neglectedness of the various categories of research discussed in this report. However, our scientific advisors identified specific unfunded projects related to the following themes: Understanding the mechanism s driving regeneration associated with heterochronic parabiosis: Experiments have indicated that the blood of older animals can have deleterious effects on younger ones, and that the blood and organ functioning of younger animals can improve the functioning of old ones, though to date the hypothetical increase in healthy lifespan has not been tested. Back to Top Questions for further investigation How neglected are the various themes discussed in this document e. What are the most promising unfunded projects related to these themes? What is the comparative potential upside of accomplishing the core objectives related to these various themes for extending healthspan? With what probability and on what timescale could such successes be achieved? What other general-application tools and basic research areas might be important for accomplishing these core objectives? What research programs could help scientists discover all aspects of the epigenetic state of cells and make it possible to measure and intervene on those aspects of cells? To what extent are the most important research programs of this nature being pursued already? How likely is it that advances in drug delivery including delivery of other agents to cells would be required for effective senescent cell removal or interventions to correct or prevent the accumulation of epigenetic errors? If such advances are needed, what are these advances? What research programs could lead to these advances? What are the most important mechanisms of aging that were not investigated in this write-up? To what extent are the hallmarks of aging traceable to a few basic mechanisms, vs.

7: Editions of Review of Biological Research in Aging by Morton Rothstein

Review of Biological Research in Aging > Editions expand details. by Morton Rothstein First published Sort by.

8: Using C. elegans for aging research

Review of Biological Research in Aging: Volume 1 Edited by Morton Rothstein Alan R. LISS; New York, pages. E This is the first of a series to provide a.

9: Journal of Aging Researchâ€" An Open Access Journal

Aging is still a relatively underpopulated field of research and looks to benefit from the recent explosion of biotechnology and big data-aided research (11). In the coming decades, one can expect to see greater innovation and progress in aging research.

REVIEW OF BIOLOGICAL RESEARCH IN AGING pdf

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