

**U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY
SUBCOMMITTEE ON INVESTIGATIONS AND OVERSIGHT**

HEARING CHARTER

The Fountain of Youth? The Quest for Aging Therapies

Thursday, September 15, 2022
10:00 a.m. EDT – 12:00 p.m. EDT
2318 Rayburn House Office Building and Online via Zoom

PURPOSE

The purpose of this hearing is to discuss the state of geroscience, the study of aging and age-related diseases, and leading research efforts to develop therapeutic interventions that target aging and age-related diseases. The hearing will examine the ethical and societal implications that may result as aging therapies grow closer to commercial readiness. It will also consider the role of the federal government and barriers that may be affecting the research effort.

WITNESSES

- **Dr. Jay Olshansky**, Professor of Epidemiology and Biostatistics, University of Illinois-Chicago; Research Associate, Center on Aging at the University of Chicago; Chief Scientist at Lapetus Solutions, Inc.
- **Dr. Laura Niedernhofer** (*KNEE-durn-ho-fer*), Director, Institute on the Biology of Aging and Metabolism; Medical Discovery Team on the Biology of Aging; Professor, Department of Biochemistry, Molecular Biology and Biophysics, University of Minnesota
- **Dr. Steve Horvath**, Principal Investigator, Altos Labs

OVERARCHING QUESTIONS

- What is the state of scientific knowledge on the basic biological processes behind aging?
- What is the state of research on drugs and therapies that can extend human life?
- What outcomes in a formal animal or a clinical trial would represent the achievement of “anti-aging?”
- What are the long term ethical and societal considerations associated with therapies that could significantly extend human lifespans and/or healthspans?
- What is the role of the federal government in both supporting and regulating research on strategies to increase lifespans and/or healthspans?

Background

“Fountains of youth” have been a mythical concept going back to Herodotus. Many an entrepreneur has profited off spurious claims that their miracle product can turn back the clock on human biology. But researchers are working today on therapies that may legitimately be able to mitigate or even reverse the natural aging processes. A 2015 conference of biology and genetics experts reached a consensus that “there is sufficient evidence that aging interventions will delay and prevent disease onset for many chronic conditions of adult and old age.”¹

The term “geroscience” was first coined when the National Institutes of Health awarded a long-term interdisciplinary research grant to the Buck Institute in 2007.² Geroscience seeks to advance the study of molecular and cellular biology of aging and translate those findings to age-related disease. A 2022 Symposium Report from the New York Academy of Sciences put it this way:

For many years, it was believed that the aging process was inevitable and that age-related diseases could not be prevented or reversed. The geroscience hypothesis, however, posits that aging is, in fact, malleable and, by targeting the hallmarks of biological aging, it is indeed possible to alleviate age-related diseases and dysfunction and extend longevity. This field of geroscience thus aims to prevent the development of multiple disorders with age, thereby extending healthspan, with the reduction of morbidity toward the end of life.³

Scientists are still working to defining the field

The concept of **healthspan** is not yet defined by objective validated metrics, but one common definition is “the period of life spent in good health, free from the chronic diseases and disabilities of aging.”⁴ The innovation frontier and associated funding for geroscience is primarily focused on the extension of healthspan, rather than extending the human lifespan beyond the record set by 122-year-old Jeanne Louise Calment in 1997.

As scientists are still working to resolve a more discrete and quantifiable definition of “healthspan,” success in geroscience today may be determined according to whether a therapy or drug can mitigate a wide range of diseases and ailments heavily associated with aging, even if those conditions are otherwise biologically unrelated. Statin drugs may already lower cholesterol and protect against heart attack or stroke, for example, but an aging therapy might mitigate the risk of heart attack, Alzheimer’s disease, osteoarthritis, and hearing loss all at once. Geroscientists include both fatal and non-fatal but still life-affecting maladies among the target conditions to be mitigated with potential therapies. In regulating both clinical trials on humans and the marketing of prescription drugs in interstate commerce, the U.S. Food and Drug Administration generally takes a “one drug, one indication” approach. A clinical trial or a drug approval application would articulate a single condition to be addressed by a given treatment,

¹<https://www.researchgate.net/publication/275354743> Interventions to Slow Aging in Humans Are We Ready

² [Buck Institute Awarded \\$25 Million to Establish New Scientific Discipline of Geroscience](#)

³ [Extending human healthspan and longevity: a symposium report - PubMed \(nih.gov\)](#)

⁴ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6136295/>

never a whole suite of conditions. As such, the small clinical trials being conducted now on some of the leading gerotherapy proposals generally identify a single target condition, but are informing the broader field of geroscience. For example, in 2019, in what may have been the first human trial for an aging therapeutic, scientists from Unity Biotechnology and Buck Institute used the target condition of osteoarthritis in the knee.⁵

Funding Support

At the federal level, many of the leading research efforts receive funding support from the National Institutes of Health. Since 1974, NIH's National Institute of Aging has supported intramural and extramural research on a broad range of topics associated with aging, including things like improving mental health in the elderly, treating Alzheimer's disease and strategies to prevent falls, but is increasingly supporting research on the basic biology of aging. NIA funds Nathan Shock Centers of Excellence in the Basic Biology of Aging at eight locations across the United States.⁶ In addition, in October 2021, NIH launched the Cellular Senescence Network (SenNet), a Common Fund Initiative.⁷ SenNet seeks to comprehensively identify and characterize senescent cells across the body over the next ten years.

In March 2017, the National Academy of Medicine initiated its Grand Challenge in Healthy Longevity. Its goal is to comprehensively address the challenges associated with global population aging and catalyze breakthroughs that will extend the human healthspan.⁸ The National Science Foundation, primarily through its Biological Sciences (BIO) and Social, Behavioral, and Economic Science (SBE) directorates, has also extended grants toward the study of cellular senescence and other biological factors that influence the pace of aging.^{9,10,11}

Over the last decade, a swell of private research funding has been committed to independent laboratories focused specifically on aging research, some of which issue their own extramural grants in turn. These include Altos Labs, the Buck Institute for Research on Aging, Calico Labs, Human Longevity Inc., the Salk Institute for Biological Studies, and the SENS Research Foundation. Some are non-profit, while others are for-profit. Some have received considerable attention in the media for the funding support they have received from American tech billionaires.¹² In addition, a number of independent biotech companies, some publicly traded, are also conducting research on specific therapeutic interventions to address aging. The larger, traditional pharmaceutical companies largely have not disclosed any active steps they might be taking toward the development or testing of new aging therapies.

Leading Research Frontiers

⁵ [A Safety and Tolerability Study of UBX0101 in Patients With Osteoarthritis of the Knee - Full Text View - ClinicalTrials.gov](#)

⁶ <https://nathanshockcenters.org/the-centers>

⁷ <https://www.preprints.org/manuscript/202207.0160/v1>

⁸ <https://nam.edu/initiatives/grand-challenge-healthy-longevity/>

⁹ [RoL: NSF-BSF: \(Dia\)pausing aging. The role of vitamin D synthesis and signaling in the control of development, aging, and pace of life](#)

¹⁰ [Brown Adipose Tissue, Biological Variation and Senescence in Humans](#)

¹¹ [Doctoral Dissertation Research: Cellular Senescence in Human Age-Related Mortality and Lifespan](#)

¹² <https://www.newyorker.com/magazine/2017/04/03/silicon-valleys-quest-to-live-forever>

Recent leading research topics on extending healthspan include, but are not limited to:

Cellular senescence: Geroscientists hypothesize that senescent, or “zombie” cells, accumulate in the body as it ages, eventually causing tissue degeneration and age-related diseases.

Researchers at the Mayo Clinic developed the first known senolytic drugs designed to clear out senescent cells. In a 2019 human clinical trial, these demonstrated that these drugs do boost proteins that help clear the bloodstream of senescent cells.¹³ When senolytic drugs were used to amplify the protein *a-klotho* in lab mice, their lifespan increased by 30%.^{14,15}

Metformin trials: Metformin is a drug approved by FDA to treat Type 2 diabetes. Recent research suggests it may also ward off a wide-range of age-related maladies. Animal studies have demonstrated metformin extended the life span of worms, flies, mice, and rats, and observational studies of adults already taking metformin have found that it “appears to show protection against cancer, inflammation, and age-related diseases.”^{16,17} A research team led by the Nathan Shock Center at Albert Einstein College of Medicine is currently launching an NIH-funded clinical trial called Targeting Aging with Metformin (TAME), which will for treat human subjects with metformin to evaluate its effects on a range of age-related morbidities among a cohort of 3,000.¹⁸

Reprogramming: In 2006, Dr. Shinya Yamanaka identified a small number of genes within the genome of mice that can allow mature cells to return to an immature state, as stem cells. In effect, he found that cells are “rewritable,” and was awarded the Nobel Prize for this discovery. In 2016, researchers at the Salk Institute for Biological Studies reported that it was possible for Yamanaka factors to be used to counter aging and increase life span in mice with premature aging.¹⁹ In 2021, the Salk team, supported by a NIH / National Cancer Institute Cancer Center Support Grant, found that cellular reprogramming can be used to boost muscle regeneration and rebuild tissue in older mice.^{20,21} This hypothesis has not been piloted on humans.²²

Thymus regeneration: In 2019, researchers from Stanford and Intervene Immune published the results of a 9-person pilot study called TRIIM. They found that the natural decline of the thymus, a central immune organ, leads to the decline in overall immune competence with age.²³ They are now finalizing the results of a pilot clinical trial called TRIIM-X that evaluates proposed therapies for thymus regeneration. The study directors hypothesize that a combination of the

¹³ <https://newsnetwork.mayoclinic.org/discussion/mayo-researchers-demonstrate-senescent-cell-burden-is-reduced-in-humans-by-senolytic-drugs/>

¹⁴ <https://mcpres.mayoclinic.org/research-innovation/senolytic-drugs-boost-key-protective-protein/>

¹⁵ <https://www.technologyreview.com/technology/anti-aging-drugs/>

¹⁶ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4772077/>

¹⁷ <https://www.medicalnewstoday.com/articles/280725#Cheap-and-widely-prescribed-diabetic-drug-may-have-beneficial-effects-for-all>

¹⁸ <https://pubmed.ncbi.nlm.nih.gov/27304507/>

¹⁹ <https://www.salk.edu/news-release/turning-back-time-salk-scientists-reverse-signs-aging/>

²⁰ <https://www.salk.edu/news-release/new-study-shows-how-to-boost-muscle-regeneration-and-rebuild-tissue/>

²¹ <https://www.nature.com/articles/s41467-021-23353-z>

²² <https://www.salk.edu/news-release/new-study-shows-how-to-boost-muscle-regeneration-and-rebuild-tissue/>

²³ <https://www.nature.com/articles/d41586-019-02638-w>

prescription drugs metformin, DHEA, and somatropin will lead to thymus regeneration, which could in turn “potentially prevent or reverse key parts of the aging process more generally.”²⁴

NAD+ restoration: Researchers are learning more about the role of nicotinamide adenine dinucleotide (“NAD+”), an enzyme in cells used for energy metabolism, and loss of SIRT3, a mitochondrial protein, in age-related metabolic decline.²⁵ The Buck Institute for Research on Aging recently published a paper suggesting that many age-associated diseases can be slowed down and even reversed by restoring NAD+ levels.²⁶

Biomarkers and identifiers of aging: The naturally short life span of model organisms evaluated in animal studies – worms, flies, and mice – make it possible to observe the effect of proposed aging interventions in a reasonable period of time. But as clinicians seek to translate these findings, it is not practical to wait for their human subjects to age over several decades to see how their aging interventions may have performed. Some geroscientists are focused on defining biomarkers of aging in human, such as DNA methylation, so that the effects of an intervention could be evaluated within months or just a few years. Well-established biomarkers will be key to efficiency and cost-effectiveness to carrying out larger clinical trials on humans.

Societal Implications and Long-Term Questions for Policymakers

Some researchers project that within the next decade or two, therapies that can add add ten years or more to the human healthspan will be demonstrated successfully in a clinical setting. Several of the proposed interventions being evaluated, such as metformin, are already largely low-cost and widely available. As such, commercial application of a clinically proven anti-aging therapy could ultimately be quite widespread. The implications for society would be substantial on:

- Demographic projections
- Healthcare costs
- The workforce
- Social security and other financial implications for retirement
- Health insurance

The advent of low-cost gerotherapies would also introduce philosophical, ethical, and policy questions, such as:

- What is the obligation of insurance companies to make gerotherapies widely accessible?
- What is the obligation of government to ensure the equitable availability of gerotherapies?
- Would a longer healthspan enabled by prescription drugs justify a later retirement age?
- When would it be appropriate for a physician to stop a patient’s access to prescription gerotherapies?

²⁴ <https://clinicaltrials.gov/ct2/show/NCT04375657>

²⁵ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5088772/>

²⁶ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7963035/>