

A Call for a New National Institute for Longevity and Aging Research (NILAR)

Written by the Alliance for Longevity Initiatives (A4LI)

BLUF: In alignment with the Energy and Commerce Committee's call for reform at NIH, Congress should establish the National Institute for Longevity and Aging Research (NILAR), which will support the development of groundbreaking therapeutics that prevent multiple age-related conditions while emphasizing accountability and innovation within the institute.

Executive Summary

The U.S. is undergoing a substantial demographic transformation, with the proportion of individuals aged 65 and above anticipated to reach 23% by 2050. This trend is leading to a rise in the number of cases of age-related diseases, such as cardiovascular disease, dementia, and cancer. Our current healthcare model is siloed in its approach, focused on reactive treatment of individual diseases rather than addressing the root cause of these disorders– the biological processes of aging. As a result, many Americans spend nearly a quarter of their life in poor health, which has devastating implications for our economy.

With Congress prioritizing NIH reformation to better serve the needs of Americans, the Alliance for Longevity Initiatives (A4LI) proposes the establishment of the National Institute for Longevity and Aging Research (NILAR). NILAR's mission will focus on developing therapies that address multiple age-related diseases simultaneously, while enforcing accountability, encouraging innovation, and promoting collaboration among institutes. This approach aligns with Congress' goals of enhancing the transparency, efficiency, and responsiveness of the NIH.

NILAR's key strategic objectives include:

1. **Focus on Aging Biology:** Prioritize research and development in aging biology with the goal of developing interventions that prevent multiple chronic age-related diseases.
2. **Emphasis on Translation:** Create specialized divisions dedicated to translating research into applications for clinical practice and public health.
3. **Encourage Innovation:** Implement reforms that promote high-risk, high-reward research and bold initiatives, which should serve as an example for other institutes at the NIH.
4. **Increased Accountability:** Define clear, public objectives to ensure accountability and reallocate resources from underperforming programs to more promising projects.
5. **Collaboration with Related Agencies:** Collaborate with agencies, like FDA and related NIH institutes, to ensure a coordinated approach in advancing all biotechnology efforts.

NILAR is a response to Congress's proposal to merge the NIA into a siloed dementia-focused division. This proposal can serve as a blueprint for a new institute or as recommendations for enhancing the existing NIA, should it continue to exist. Our goal is to ensure geroscience research and development receives the focus and resources needed to revolutionize healthcare.

Background

Consequences of an Aging Demography

Since 1950, there has been a dramatic increase in the percentage of Americans aged 65 years and older. Older Americans made up 8% of the population in 1950, 18% in 2024 and will make up 23% of the population by 2050. Because more Americans have made it to older age, our medical system is treating an ever-increasing number of age-related diseases and conditions, placing immense pressure on healthcare systems and government budgets. In the U.S. today, roughly 28 million Americans have cardiovascular disease, 7 million people have dementia, and 1.5 million people have cancer – the three deadliest age-related diseases. By 2050, those numbers are projected to reach 45 million, 13.9 million, and 3 million, respectively.^{1,2,3}

A population that is aging in an unhealthy way will cause an increase in demand for healthcare services, pensions, and Social Security. The cost of Medicare and Social Security are growing at a faster rate than our Gross Domestic Product due to our aging population. The Centers for Medicare & Medicaid Services project that National Health Expenditures will grow to \$7.2 trillion by 2028.⁴ Couple that with our shrinking working-age population due to persistently low fertility rates over the last few decades and we're also poised to experience labor shortages and plummeting economic productivity. Japan reached this demographic situation in the early 1990s and currently has a smaller GDP than it did 30 years ago. The U.S. is approaching the edge of this cliff within the next decade. This aging demographic crisis is unprecedented in human history and thus, a completely novel approach is needed to combat the consequences.

The Development of “Longevity Biotechnology”

Modern medicine has made tremendous strides in treating acute illnesses, yet it remains largely unable to cure chronic, age-related diseases. This lack of progress can be largely attributed to two things. First, biomedical research (including drug development) and clinical practice are fundamentally reactive, waiting until people become sick before taking action. Second, these institutions have largely ignored the single greatest risk factor for - and mechanistic cause of - nine of the ten top killers in the United States: the biological aging process itself.

¹ Cancer Statistics Center. Accessed on June 30, 2024. <https://cancerstatisticscenter.cancer.org/>

² 2024 Heart Disease and Stroke Statistics: A Report of US and Global Data From the American Heart Association. *Circulation*. Volume 149, Issue 8, 20 February 2024; Pages e347-e913 February 20, 2024. Accessed on June 30, 2024. <https://www.ahajournals.org/doi/epub/10.1161/CIR.0000000000001209>

³ Alzheimer's Facts and Figures. Accessed on June 30, 2024. <https://www.alz.org/alzheimers-dementia/facts-figures>

⁴ National Health Expenditure Fact Sheet (2022). Accessed on June 01, 2024.

<https://www.cms.gov/data-research/statistics-trends-and-reports/national-health-expenditure-data/nhe-fact-sheet>

This reactive approach has led to increases in lifespan without a corresponding increase in healthspan – the period of life spent in good health, free of chronic disease. As a result, many individuals spend their later years battling multiple chronic age-related diseases, diminishing their quality of life and placing a heavy burden on healthcare systems. Our current siloed approach to treating individual diseases also has significant limitations on extending life expectancy. Research from scientists at the University of Southern California has shown that even if all forms of cancer were cured, average life expectancy would only increase by roughly three years.⁵ This is because curing a single disease does not address the underlying aging processes that drive the development of all other age-related diseases– aging.

The longevity biotechnology industry has emerged from the realization that therapeutics targeting the biological mechanisms of aging could ameliorate multiple age-related diseases at once and extend healthy lifespans. There are hundreds of longevity biotechnology companies in the U.S. developing therapies that target aging with dozens entering Phase II and III trials within the next few years.⁶ Economists argue that the introduction of longevity medicine to society could drive massive gains in GDP from increases in citizen productivity and decreases in costly end-of-life medical care. Even in the most conservative estimates, the US stands to add trillions to its GDP from the addition of one year of average healthy life expectancy to its population.⁷

NIH's Lack of Focus on Longevity Research

The NIH has yet to shift its thinking from siloed, disease-specific efforts to research that advances the understanding and practical applications of the biology of aging. Today, less than 0.5% of NIH funding is allocated toward investigating and treating the biology of aging, despite the fact that biological aging is the primary risk factor for 9 out of 10 leading causes of death in the U.S. This is clearly a profound misallocation of federal resources.

In a recent report to Congress, the NIH detailed its ongoing geroscience (science of aging) research efforts, but the report revealed that there is little activity in this area and even less progress toward the development of new therapies targeting aging.⁸ As we prepare for the consequences of our aging population, the NIH must shift its focus and invest heavily in translational research on interventions that will effectively prevent or treat combat multiple age-related diseases at once and maintain good health for Americans as we age.

⁵ Wu, S. (October 2023). USC Today: Delayed aging is better investment than cancer, heart disease research. Accessed on March 27, 2024.

<https://today.usc.edu/delayed-aging-is-better-investment-than-cancer-heart-disease-research/>

⁶ The Rejuvenation Roadmap. Accessed on June 30, 2024.

<https://www.lifespan.io/road-maps/the-rejuvenation-roadmap/>

⁷ Scott, A.J et al, The economic value of targeting aging. *Nat Aging* 1, 616–623 (2021). Accessed on June 30, 2024. <https://doi.org/10.1038/s43587-021-00080-0>

⁸ Department of Health and Human Services. NIH Report on Geroscience. https://www.afar.org/imported/RTC-on-Geroscience_FINAL.signed.pdf

Proposing the National Institute for Longevity and Aging Research (NILAR)

The Alliance for Longevity Initiatives (A4LI) proposes the establishment of a new institute, the National Institute for Longevity and Aging Research (NILAR), within the NIH to better reflect the healthcare and societal needs of our country. NILAR will streamline NIH efforts by coordinating research on aging's biological processes, improving efficiency and accountability, and unifying age-related disease studies. The NILAR Director, who should have terms of no more than 10 years, will be tasked with setting time-bound goals and measuring progress against those timelines. This approach aligns with Congress's vision for a more focused and responsive NIH to the needs of Americans. NILAR's mission is to extend the healthy lifespan of Americans from roughly 66 years (where it currently stands) to 85 years by 2045.

Divisions of NILAR

The divisions of NILAR will reflect its goals of advancing translational research and practical health improvements for our aging population. While prior areas of research within the NIA overlap with NILAR's focus areas, NILAR will direct this research towards concrete health improvements for our population. In service of this goal, NILAR will also create new translation-focused divisions to ensure a comprehensive approach to developing therapies targeting aging.

Division of Aging Biology: NILAR will house the existing Division of Aging Biology (DAB) and expand on the discovery of basic biological and genetic mechanisms underlying the processes of aging at the molecular, cellular, tissue, and organ levels.⁹ The DAB will also develop programs to support mammalian model development with species that better represent specific human disease conditions. The goal of this division is to develop and utilize high-throughput technology to better understand the fundamental processes that drive aging and age-related disease and identify new interventions to slow or reverse the aging process.

Division of Biomarkers of Health, Function and Aging: The Division of Biomarkers of Health, Function and Aging (DBHFA) will focus on identifying and validating biomarkers crucial for the early diagnosis, prevention, and monitoring of aging and age-related diseases. This division will engage in public-private partnerships in longitudinal data collection to establish baselines for normal aging and develop biomarkers of biological aging to measure age-dependent biological changes in individual patients. Discovery of these biomarkers will help measure responsiveness to therapies in older adults and develop technologies for early detection of age-related conditions. The DBHFA's goal is to ensure that the biomarkers developed are not

⁹ National Institute on Aging Division of Aging Biology. Accessed on 8/03/2024. <https://www.nia.nih.gov/research/dab>

only scientifically sound but also align with regulatory requirements, thereby facilitating the approval and clinical adoption of innovative treatments targeting aging.

Division of Translational Geroscience: The Division of Translational Geroscience (DTG) will focus on translating basic research findings into clinical applications and developing interventions that modify the biological mechanisms of aging that promote health and longevity. This division will fund proof-of-concept clinical trials for new interventions targeting aging mechanisms and support the technologies necessary for geroscience research and discovery. The goal of the DTG is to accelerate the development of interventions that modulate the aging processes and bring effective longevity interventions to clinical practice and patients as soon as possible.

Division of Economic and Societal Impact of Aging: The Division of Economic and Societal Impact of Aging (DESIA) will assess the economic and societal benefits of various approaches to treating or delaying chronic diseases and improving overall health and well-being. This division's tasks will also include developing economic analyses to understand the impact of quality-adjusted life years on healthcare costs and productivity, studying the societal benefits of improved health in aging populations, and measuring economic gains from increased healthspan. The goal of DESIA is to inform policy decisions on investments in longevity biotechnology.

It should be noted that there will be no division with a specific neuroscience research focus within the NILAR portfolio. Currently, there are eleven other institutes within the NIH that fund neuroscience research. We believe that neuroscience research should be consolidated into a single National Institute of Neuroscience to better enable effective coordination and goal-setting for understanding neurological and neurodegenerative diseases.

NILAR Budget

We propose a \$1.5B budget for NILAR, which is commensurate with the budget currently allocated to the NIA's Division of Aging Biology, Division of Geriatrics and Clinical Gerontology, and Division of Behavioral and Societal Research.¹⁰ With a \$1.5B budget, plus revamped leadership, a strategic vision, policy reform, the proposed restructuring, and a focus on understanding and addressing the biological mechanisms of aging, the longevity biotechnology industry is poised to advance rapidly. We propose that by 2030, Congress should grow the budget of NILAR to be at least comparable to those of other NIH institutes focused on individual age-related diseases (such as the NCI's \$7.22B budget)¹¹, given the central role of aging biology in chronic diseases, including cancer, dementia, and heart disease.

¹⁰ National Institute on Aging Fiscal Year 2025 Budget. Accessed on August 10, 2024. <https://www.nia.nih.gov/about/budget/fiscal-year-2025-budget#graphs>.

¹¹ National Cancer Institute. Accessed on August 10, 2024. <https://www.cancer.gov/about-nci/budget#what-is-ncis-current-fiscal-year-2024-fy24-budget>

Strategic Coordination at NILAR

Given aging's central role in driving diseases of aging, NILAR should serve as a hub for extensive collaboration with other agencies focused on age-related diseases. By fostering collaborations across various agencies and institutes, NILAR aims to streamline research activities, maximize resource efficiency, and accelerate the development of new therapies.

Coordination with Age-Related Disease Institutes

The biology of aging plays a crucial role in age-related diseases such as cancer, heart disease, dementia, kidney disease, diabetes, and others. For example, research funded by the NIA on mitochondrial dysfunction has led to the development of drugs that enhance mitochondrial function. These drugs are being explored for their potential to treat neurodegenerative diseases and metabolic disorders by improving cellular energy production. By investigating the underlying mechanisms of aging, researchers can develop targeted therapies to prevent, mitigate, or cure multiple major age-related diseases. Therefore, we recommend mandating that both NILAR and age-related disease institutes (including but not limited to NCI, NHLBI, NIDCR, and NIAID) make all relevant data available to each other, including longitudinal study data, genomic and phenomic data, biomarkers, imaging data, clinical trial results. NILAR's coordination with centers like the Clin-STAR will strengthen the field's transdisciplinary collaboration and develop a more comprehensive research approach to aging that will increase visibility and attract more interest and talent to the field.

Coordination with FDA

A significant challenge for longevity biotechnology companies is the lack of clarity on appropriate indications areas, approval pathways and endpoints, and intermediate metrics of success. Conversely, efforts by the FDA to establish such pathways ahead of time, or alternatively to reserve personnel time to facilitate their creation in collaboration with applicants, would be highly beneficial to achieving societal benefits derived from NILAR's mission via the approval of aging-biology-targeted therapeutics. We believe that part of NILAR's mission should involve coordinating with the FDA to develop appropriate biomarkers and metrics for companies entering clinical trials for therapies targeting aging, as well as approval pathways that acknowledge the potential multi-indication benefits of aging therapeutics. This coordination would significantly reduce uncertainty which currently hinders the private longevity biotechnology industry. Congress should direct the FDA to collaborate with NILAR, specifically the DBHFA and DTG, to develop a plan to resolve these issues.

Accountability at NILAR

Accountability will be a cornerstone of NILAR's mission, ensuring that the institute operates with transparency, efficiency, and a clear focus on delivering measurable outcomes. NILAR will establish rigorous oversight mechanisms and set specific, public objectives to evaluate the effectiveness of its initiatives and the efficient allocation of resources.

Centers of Excellence on Aging Research

The NIA, like most other NIH institutes, sponsors several Centers of Excellence. While these centers have made valuable contributions, there has been room for improvement in terms of creating synergy and meeting specific objectives. Under NILAR-DAB, these Centers of Excellence will be tasked with setting clear, measurable goals to enhance their impact and ensure alignment with the institute's mission of advancing aging research. Centers that fail to meet their objectives and fail to clearly justify their continued support via substantial contributions will have their funding reallocated to other institutions. This includes the Nathan Shock Centers of Excellence, which were established to provide national leadership and research resources in the basic biology of aging, and the Claude D. Pepper Older Americans Independence Centers, which play a vital role in providing research and training opportunities for clinician-scientists, equipping them with the best practices for caring for individuals of advanced age. Centers will also now be required to incorporate training in aging-biology-focused therapeutics and biomarkers, to help leverage and disseminate the translational advances coming out of NILAR. Collaborations with industry or industry-focused training programs will be created to encourage the development of new therapies based on research coming out of NILAR.

Centers for Data and Biobanks

NILAR-DBHFA will continue to support several data centers and biobanks. To ensure that their utility is maximized by the research community, each biobank will set clear, actionable goals regarding the volume and diversity of data collection. Any data centers or biobanks that cannot reach their own self-imposed goals will be assessed for reallocation, and assessments will be made public. The data centers and biobanks to be housed under NILAR-DBHFA include the Intervention Testing Program, the Caenorhabditis Intervention Testing Program, the Aged Rodent Colonies, the Aged Rodent Tissue Bank, the Aging Cell Repository, the Non-Human Primate Tissue Bank, the Primate Aging Database, the AgingResearchBioBank, the NIA Aging Cell Repository, the Baltimore Longitudinal Study of Aging (BLSA) Biorepository, the Health, Aging, and Body Composition (Health ABC) Study Biobank, and the Long Life Family Study (LLFS) Biobank.

NILAR and NIH-Wide Suggested Reforms

To create a more efficient and responsive agency, we have identified four key areas for reform that will be integral to the success of NILAR. These reforms are designed to foster innovative research and promote transparency, reducing redundancy in both public and private longevity sectors. While these reforms will be a core part of NILAR, we recommend implementing them NIH-wide to facilitate the development across all realms of biotechnology.

SBIR Reform

By statute, 3.5% of the NIH research budget must be used to support small businesses through the SBIR and STTR programs. However, the majority of program managers do not have a private sector background, which should be required when reviewing grants for small businesses. Furthermore, these programs are not structured in a way that reflects the reality of starting and running a small biotechnology company. The application process remains burdensome and slow, causing many eligible companies to refrain from applying for these grants and openly considering the SBIR and STTR programs as a hindrance to their fundraising abilities.

We recommend that the NIH centralize its SBIR and STTR programs into a single office at the NIH and that funds be allocated proportionally based on the relative budgets of the institutes. If such consolidation cannot be achieved across the NIH, NILAR's DTG should manage the SBIR and STTR programs. Improving the SBIR and STTR programs hinges on hiring dedicated program managers with private-sector experience to make award decisions. Additionally, these programs would benefit significantly from substantially reducing the application burden on private sector applicants, who currently invest more effort for less funding from the NIH compared to private capital sources. If NIH Institutes aim to attract better applicants for these programs, then the application process and time to award must be substantially reduced to better reflect the needs and norms of private sector funding. Furthermore, SBIR and STTR applicants are often academic researchers looking to commercialize their discoveries but lack entrepreneurial experience, leading to an unacceptably high failure rate for SBIR and STTR-funded companies. To address this, NILAR should fund, with remaining SBIR dollars, entrepreneurship training and accelerator programs for their funded researchers and provide expedited review consideration for scientists who have completed these programs.

Raising Standards for Grant Review Committees

NIH review committees have evolved into panels that tend to reward incremental advances over risk-taking. This has been a perennial challenge that limits innovation in favor of surety. We believe that Congress should direct NIH and NILAR in particular to develop clear standards and instructions for review committees that reward risk-taking and cutting-edge technology development over incremental advancements. This step alone is perhaps one of the most

important things that Congress could do to invigorate academic biological research in the United States and would unleash the creativity and vigor of our nation's scientists.

Intramural Research Reform

The NIH Intramural Program receives 10% of NIH funding and was established as a means to allow scientists to take risks and break completely new ground in the fields of study. However, the NIH Intramural Program has functionally evolved into the equivalent of a university campus, where risk aversion prevails and scientists stay for decades. A4LI urges the Committee to consider a wholesale reinvigoration of the NIH Intramural Program to ensure NIH campuses become the place where scientists go to establish themselves professionally by pursuing groundbreaking research. Appointments should be limited in duration, and investigators should be incentivized to take risks that substantially advance their fields of study. The NILAR Intramural Research Program should be tied to the NIH Clinical Center and promote research that breaks new ground in longevity and aging research. NILAR should use its program to take risks that accelerate the translation of research discoveries into practical applications.

Scientific Reproducibility and Publicizing Negative Results

NILAR-DAB will develop a clear strategy for reproducing research findings to verify the validity of these findings and reduce time and resource waste. The reproducibility strategy should be made public, and annual findings should be publicly available for all reproducibility grants. NILAR-DAB will also develop a public archive for negative research results and require all NILAR-funded scientists to publish their negative results. By making negative results readily available, the program will reduce wasted resources and accelerate the development of effective treatments through a more comprehensive understanding of what does not work.

Concluding Call to Action

As the urgency of our aging population crisis grows day by day, the time has come for Congress to establish an agency focused directly on researching and developing therapeutics that target the biology of aging to ameliorate multiple age-related diseases at once—the National Institute for Longevity and Aging Research (NILAR). The breakthroughs made possible through the projects that NILAR would fund could profoundly transform public health by extending healthy lifespans, enhancing quality of life, and easing the economic strain of an aging population. This initiative aligns with Congress's vision for a more efficient and responsive NIH that meets the needs and realities of Americans today. We urge policymakers, stakeholders, and the public to support NILAR and take decisive action to secure a healthier, more prosperous future for all Americans before the demographic challenge becomes insurmountable.