



Longevity Frontiers Workshop

Co-hosted by the Longevity Biotech Fellowship & Foresight Institute

MENLO PARK & STANFORD UNIVERSITY, CA, USA 28 & 29 July, 2024

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Foreword

The 2024 Longevity Frontiers Workshop, a collaborative effort between the Longevity Biotech Fellowship and Foresight Institute, brought together leading experts in science, engineering, entrepreneurship, and investment. Held over two days in San Francisco, the event aimed to advance a shared vision of a future free from disease and aging.

The workshop focused on five key areas critical to longevity research:

- Acceleration: Enhancing the pace of biotechnology progress
- Replacement: Exploring tissue replacement as an intervention for aging
- **Bioengineering:** Advancing measurement, modeling, and gene delivery techniques
- Biostasis: Developing reversible stasis for organs and humans
- **Healthcare 3.0:** Making health and lifespan extension accessible to all

On the first day, chaired by Mark Hamalainen, Longevity Biotech Fellowship, participants covered the first four areas. Michael Snyder, Stanford University led day two, focusing on Healthcare 3.0.

We are grateful to all participants for their valuable contributions and collaborative spirit. Special thanks to our sponsors—100 Capital, AgingBiotech.Info, Deep Origin, Open Cures, NfX Bio, Protocol <u>Labs</u> and <u>The Michael Antonov Foundation</u>—for their generous support, enabling junior researchers to attend.

Top-rated projects from the workshop were considered for funding by present funders, the LBF <u>Accelerator Fund</u> and the <u>Longevity Prize</u>. We look forward to next year's workshop to review progress and build on the initiatives launched this year.

If you are a researcher, practitioner, or funder interested in advancing this critical field, we encourage you to reach out and join our efforts.

Best regards,

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Bryan Johnson BLUEPRINT



Chelsea Voss **OPEN AI**



Christopher Bradley MATTER BIO



Daniel Ives SHIFT BIOSCIENCE



Danielle Ruiz **EVEREST HEALTH**



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Edward Lando PARETO HOLDINGS



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Emil Kendziorra TOMORROW BIO



Eric Bennett FRONTIER BIO



Heye Gross RETRO BIOSCIENCES



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Max Novendstern **MANA**



Niklas Anzinger **VITALIA**



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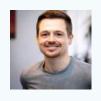
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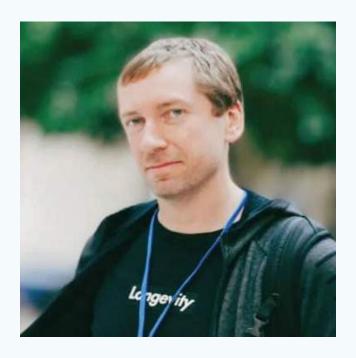


About Foresight Institute

Founded in 1986, we support the beneficial development of high-impact technology to make great futures more likely. We focus on science and technology that is too early-stage or interdisciplinary for legacy institutions to support, such as longevity biotechnology, molecular machines, brain-computer interfaces, multipolar AI, and space exploration. We award prizes, offer grants, support fellows, and host conferences and seminars to accelerate progress toward flourishing futures and mitigate associated risks.



Workshop Chairs





Mark Hamalainen
LONGEVITY BIOTECH FELLOWSHIP

Hamalainen's career has progressed from manual bench work in academia, to lab automation at Synthego, to longevity movement building - always seeking better methods and higher leverage ways to accelerate progress.

Michael Snyder

STANFORD UNIVERSITY

Snyder is a genomicist and the Stanford B. Ascherman Professor, and since 2009, chair of genetics and director of genomics and personalized medicine at Stanford University. He is the former director of the Yale Center for Genomics and Proteomics.

Introduction



* This video is clickable

Intro & Opening Remarks by Allison Duettmann @ LBF + Longevity Workshop 2024

Allison Duettmann, Foresight Institute

The 2024 Longevity Biotech Fellowship and Longevity Frontiers Workshop brought together participants to collaborate on advancing longevity science. Hosted by Foresight Institute and LBF, the event features speed talks, workshops, and networking opportunities focused on topics such as biostasis, bioengineering, and healthcare 3.0. Foresight's interactive tech tree was introduced, mapping longevity goals, challenges, and technologies to guide new talent and funders in the field. Sponsors were thanked for making the event accessible to a wider audience through subsidies. Participants were encouraged to actively engage and use the event to spark new ideas and connections, all aimed at accelerating progress toward healthier, longer lives.

ACCELERATION

Accelerating progress in biotechnology occurs at several levels. Funding innovations and regulatory reforms could help address legacy barriers that have prevented new approaches from taking root in practice. Automations in research and AI-driven tools and workflow optimization can help reduce costs, increase data utility, and enhance the pace of biotechnology advancements.



Acceleration: Tools to Increase the Rate of Progress in Biotech

Reason, Repair Biotechnologies

Reason addressed two major challenges in advancing therapies to clinical trials. First, he highlighted the difficulty in using existing off-label therapies due to lack of intellectual property and funding, advocating for organized philanthropy to support clinical trials for these therapies. Secondly, he discussed the barriers for IP-protected therapies, emphasizing the high costs and regulatory hurdles. He suggested exploring alternative regulatory environments outside the US, such as Honduras, the Bahamas, and Australia, to reduce costs and speed up trials. Reason called for innovative approaches to navigate these challenges and improve the efficiency of getting therapies to market.



Automating Longevity Research Michael Florea, Olden Labs

Florea discussed transforming animal research infrastructure to accelerate aging studies. Highlighting the limitations of current methods, which remain outdated and costly, he introduced his company's approach to automate and scale animal research using smart cages, robotics, and gene delivery. Smart cages provide comprehensive data through sensors and video, reducing the need for manual handling. Robotics automates animal care, aiming for significant cost reductions and scalability. Gene delivery technology accelerates the development of disease models. Florea emphasized that this integrated system offers up to 20x cost savings and 2,000x more data, which could dramatically increase the volume and quality of aging studies, ultimately aiming to standardize and enhance research efficiency.



Longevity Acceleration Roadmap

Mark Hamalaien, Longevity Biotech Fellowship

Hamalainen argued for the urgent need to address aging as a critical issue, emphasizing that society is not treating it with the necessary seriousness. He outlined the lack of approved interventions for aging, noting the field's stagnation despite progress in other areas. He distinguished between advanced bioengineering, which involves modifying biology to combat aging, and biostasis, which involves halting aging processes until a solution is found. Hamalainen stressed the importance of improving data generation and funding, and he advocated for open, critical discussions and innovative approaches to overcoming the challenges in longevity research.

REPLACEMENT

Advances in tissue engineering, genetic sequencing, and transplantation are creating new possibilities for replacing aging components in the human body. From synthetic stem cells to in vitro organogenesis, emerging approaches to personalized medicine will leverage our own genetic material to circumvent aging processes.



Organogenesis Max Novendstern, Mana

Novendstern argued that organogenesis is undervalued as a path to longevity and that in vitro development is the most viable technology for creating universal basic human organs. He explained that nature's robustness in tissue development supports this approach, and current technologies are now advanced enough to explore it. Novendstern contended that in vitro development offers the best prospects due to its biocompatibility, engineering freedom, and scalability. He outlined alternative approaches, including autologous scaffolding and xenotransplantation, but emphasized that in vitro development, focusing on creating representative tissue cross-sections and optimizing growth environments, presents a more promising path.



Renewing Human Health: Human Stem **Cell Derived Embryos**

Omri Amirav-Drory, NFX

Amirav-Drory presented groundbreaking work on synthetic embryos, a technology poised to revolutionize longevity research. He described how his firm invested in renewal's innovative approach, which involves creating human embryos from lab-grown stem cells, eliminating the need for sperm, eggs, or a uterus. This process, initially developed by Professor Yakov Kahana,

involves using stem cells to form embryos and studying their development. Amirav-Drory highlighted that synthetic embryos can replicate natural embryonic development with high accuracy, offering potential for personalized transplants and a deeper understanding of early human development. The technology aims to address aging and fertility issues by providing genetically identical tissue and organs. Current goals include advancing the technology to grow embryos up to day 35, addressing technical and ethical challenges, and expanding the capabilities for therapeutic applications.

BIOENGINEERING

Age is just a number, but our growing ability to pinpoint biological health adds context to our lifespan that has never been possible before. Bioengineering is transforming aging research through advanced measurement, modeling, and gene delivery techniques. Personalized healthcare driven by novel biomarkers of aging will leverage organ- or tissue-level data and cutting edge data science and AI methods to make tailored treatments more accessible. Critically, as these technologies become more widespread, costs will come down, enabling broader availability for both a growing spectrum of aging related interventions, and a larger population of individuals.



Aging Biomarker Discoveries Aaron King, Aeon Biomarkers LLC

Aaron King from Aeon Biomarkers explored the concept of aging as a universal process characterized by changes with age. He analyzes biomarkers using scatter plots to identify agerelated patterns. King discussed the potential of personalized healthcare, highlighting the importance of understanding individual differences. He also presents a network diagram of biomarkers, differentiating those that change with age from those that remain constant. The talk touches on the idea of 'health span' and the use of plasma donation to potentially influence biomarker changes, suggesting a novel approach to managing aging.



Computational Tools for Drug Discovery and Longevity

Michael Antonov, Formic Ventures

Antonov discussed the application of computational tools in drug discovery and longevity, focusing on simulating cells. He emphasized the need for advanced software and modeling to understand complex biological systems, integrating AI, physics, and wet lab data. Antonov outlined the use of molecular dynamics, AI-enhanced docking, and protein folding models to simulate interactions at various levels, including cellular and molecular. He highlighted the challenges and advancements in simulating dynamic processes and pathways within cells. Antonov envisioned a future where comprehensive models will enable detailed understanding and manipulation of biological systems, with ongoing efforts to improve both computational methods and data integration.



Longitudinal Multi Omics Study of Biological Age

Andrea Cipriano, Stanford University

Cipriano presented a longitudinal study by the Biomarker Aging Consortium focused on building a multiomics dataset to advance aging research. He highlighted the challenge of defining aging, differentiating between chronological age (a measure of time) and biological age (reflecting cellular damage). The talk stressed the need for reliable biomarkers to evaluate aging and rejuvenation interventions, addressing current issues like inconsistent aging definitions, organspecific aging rates, and individual variability. Multiomics is suggested as the best approach for understanding aging comprehensively. The Consortium is working on guidelines and a new initiative by Harvard and Stanford will collect multiomic data from conference volunteers to create a longitudinal dataset over ten years. Cipriano concluded by addressing questions on extracellular damage and adaptive responses.



Preserving the Information of Life Chris Bradley, MatterBio

Bradley discussed the importance of maintaining genome integrity as a strategy for addressing aging. He explained that every cell in the body has a unique genome, resulting in a trillion different genomes per person, which are subject to damage and mutations over time. These mutations, including point mutations and structural variations, correlate with aging and lifespan across various organisms. Bradley's approach focuses on three strategies: (1) enhancing genome sequencing to detect mutations, (2) removing damaged or corrupted cells, and (3) renewing healthy tissue. He highlighted ongoing projects, including DNA fragment amplification and engineered bacteria for targeted therapies, with plans to enter clinical trials. Bradley emphasized the challenge of delivering treatments to specific cells and the potential to start with stem cell niches to address age-related diseases.



Systems Biology of Aging Sruthi Sivakumar, Retro Bioscience

Sivakumar traced the evolution of medical approaches from ancient qualitative treatments to modern reductionist methods that address diseases at a specific level. She argued that while these approaches have significantly extended human lifespan and managed infectious diseases, they fall short in tackling chronic diseases linked to aging. Sivakumar advocated for a systems biology approach, integrating various data types and mathematical models to address the complexity of aging. She highlighted the use of information theory to quantify and address disruptions in biological processes. At Retro Bio, Sivakumar explored innovative strategies for restoring and replacing tissues, aiming to use the growing body of biological data to develop novel solutions for aging-related challenges.

BIOSTASIS

Biostasis and cryopreservation are emerging technologies aimed at preserving human biology "in stasis," unlocking options for novel interventions and research opportunities. Advances in this frontier will enable organ preservation and regenerative medicine that could help cure diseases and reduce societal suffering while opening up new realms of research. The possibilities of whole-body preservation could also expand options for people and families, particularly in parallel with advances in monitoring and restoration methods following cryogenic sleep. Speakers covered foundational science, key technological trends and timelines, as well as nuances of ethical consideration, accessibility, and scalability, spanning disease treatment, fertility, brain rejuvenation, and other applications in biomedical research.



Cryopreservation WILL Be Needed!

Emil Kendziorra, Tomorrow Bio

Kendziorra discussed his commitment to cryopreservation as a solution for indefinite life extension. He expressed skepticism about the effectiveness of current longevity technologies, citing slow progress in cancer research despite significant investments. He also emphasized his belief that cryopreservation, whilst imperfect, is a preferable option compared to traditional burial or cremation when all other medical interventions fail. He described the operational aspects of his organization, including the use of mobile operating rooms and a cryopreservation storage facility in Switzerland. The organization plans to expand in the US, with a membership model and a one-time fee for cryopreservation services. Kendziorra also addressed scalability concerns, noting that increasing the number of cryopreserved individuals is manageable with current technology. He highlighted the competitive landscape, mentioning a few key players but asserting his organization's pioneering role in advancing the field.



Turning Old Brains into Young Brains Using Progressive Tissue Replacement

Jean Hebert, BE Therapeutics

Herbert explored the concept of Progressive Brain Tissue Replacement as a method to combat aging by rejuvenating the brain. He divided the process into two main components: removing old brain tissue without losing the information it contains, utilizing examples like benign tumors which, despite significant tissue removal, do not disrupt cognitive functions due to the brain's plasticity; and adding new, functional tissue progressively. He described efforts to develop young precursor tissue with necessary structural and cellular components to integrate effectively with existing brain structures. Herbert also discussed alternative methods such as growing fetal-like brain tissue from IPS cells, creating chimeras, and using human fetal tissue, though the latter is controversial. He emphasized the importance of incremental replacement to maintain function and self-identity, and notes that while some brain areas are highly plastic, others may require different strategies.



Ultrasound Awakening: Resurrecting Life From Cryogenic Sleep

Ramon Risco, Seville University

Risco discussed advancing cryopreservation using ultrasound to overcome challenges associated with ice formation during cooling. Traditional methods, like electromagnetic radiation, face limitations such as thermal runaway and inability to monitor via medical imaging. Ultrasound, with its precise control and real-time monitoring via MRI, presents a promising alternative. Risco's research demonstrates that ultrasound can effectively warm biological samples, like ovary tissue and adult C. elegans, rapidly and uniformly. Recent successes include preserving mouse hearts with near-perfect recovery. Ultrasound's potential extends to organ transplantation, fertility preservation, and biodiversity, suggesting a broad market impact.

HEALTHCARE 3.0

Research breakthroughs in human longevity will not meet their potential without enabling system-level access. The events' sessions concluded with a track led by Michael Snyder of Stanford University, who set the tone with a vision of affordable healthspan extension for all. As clinical practice adopts new methods like the exposome, genomics, wearables, health systems will enable Omics that are both personalized and longitudinally tracked. In the short term, this will enable earlier detection of cancers and other diseases, while shrinking the gap between research and practice over time.

Scaling beyond a single clinical model to a defined geography will also become possible. Longevity cities will require non-biomedical capital investments, impacting employment and public benefits in addition to healthcare spending. Investments in longevity as a field for practitioners will require unprecedented levels of collaboration, effective communication to translate research into practice.



Multi-Omics for Understanding Aging Michael Snyder, Stanford University

Snyder advocated for comprehensive health data collection to detect disease shifts and understand aging. He emphasizes integrating multiple data sources, including genomics, epigenomics, transcriptomics, and metabolomics. Recent advancements in machine learning have enabled identification of health-associated genes and risk prediction using combined genomic and EHR data. Snyder highlighted the potential of wearable technologies for early disease detection, sharing personal experiences demonstrating their effectiveness. He envisioned AI-driven personalized health recommendations but acknowledges challenges in data management and accessibility. Snyder called for convergence of health tracking services and financial incentives to broaden adoption. He noted the potential of microbiome and epigenetic data in understanding health variations and emphasizes the importance of collaborative ecosystems like Foresight in advancing aging research.



Building a New Biotech Jurisdiction Niklas Anzinger, Vitalia

Anzinger discussed practical challenges in building longevity-focused cities, such as those faced by his project, Vitalia. He highlighted issues like political instability, reputation building, unique capital needs due to land and real estate, and the difficulty in attracting and retaining talent. Anzinger noted the importance of secure capital investment and local employment to support such ventures. He drew parallels with historical examples of city-building and emphasized the need for a strong sense of mission and urgency to overcome these challenges.



Do We Need a Longevity Standard of Care?

Mark Hamalaien, Longevity Biotech Fellowship

Hamalainen explored the vision of "Healthcare 3.0," – a seamless, data-integrated system where all personal health data is automatically collected, analyzed, and managed without user intervention. He advocated for AI-driven recommendations, easy access to preventive and experimental treatments, and the ability to participate in community-based health experiments. While acknowledging potential concerns about AI and centralized data, he envisioned a future where health management is highly automated and integrated, with minimal human oversight and greater personalization. He also raised concerns about privacy, data-sharing, and the need for a balance between AI and human expertise in healthcare.



Healthcare 3.0 – The Future of Longevity Medicine

Jacob Peters, Superpower.com

Peters shared his personal journey from nearly dying due to healthcare inefficiencies to founding his company. He highlighted systemic problems in healthcare, such as its reactive nature, fragmented data, and outdated protocols. Despite initial misdiagnoses and ineffective treatments, he discovered the benefits of advanced preventive and personalized medicine. Peters advocates for a shift to "Healthcare 3.0," which emphasizes preventive care, data-driven insights, and personalized treatment. He envisioned a future where high-end, individualized medical care becomes accessible to the broader public through technology. Superpower aims to revolutionize healthcare by integrating cutting-edge tools and innovations to offer comprehensive, personalized care. This approach seeks to address the root causes of health issues rather than merely treating symptoms.



Lifespan.io

Stephanie Dainow, Lifespan.io

Dainow discussed the recent merger between Lifespan and the SENS Research Foundation. The merger highlights the growing collaboration and momentum within the industry. Lifespan, a decade old, and SENS, sixteen years old, now share resources, including a state-of-the-art research facility. Dainow emphasized the importance of collaboration, effective communication, and marketing in advancing longevity research. She outlined Lifespan's role in providing visibility, funding, and support for startups. Key points included the need for better public understanding of longevity, framing it as a crucial race similar to the space race, and improving communication through storytelling and empathy to engage diverse audiences effectively.



Vitalism

Nathan Cheng, Longevity Biotech Fellowship

Cheng introduced Vitalism, a movement he co-founded to address challenges in longevity, alongside roles at Longevity Biotech Fellowship and Health Spun Capital. Vitalism's core belief is that life is good and death is bad, advocating for extended health and postponement of aging. Cheng highlighted the current lack of approved interventions for aging and the minimal funding in the field compared to its importance. He proposed a "moonshot" approach requiring significant resource allocation, akin to the Apollo program's scale. Vitalism aims to unify supporters, counteract death apologetics, and create a global push for substantial investment in longevity. The Vitalism Foundation plans to establish a "Longevity State" and coordinate efforts through initiatives like pop-up cities and the Vitalist Republic.

OTHER TALKS



Longevity Investing Q&A

Karl Pfleger, AgingBiotech.info

Pfleger's presentation offered a discussion into the intricacies of the aging and biotechnology sector, focusing on the interplay between comprehensive resources and strategic investments. AgingBiotech.com, with its detailed listings and public transparency, serves as a foundational tool for anyone looking to explore this burgeoning field. As investment strategies and scientific discoveries continue to evolve, the future of longevity research holds immense promise, potentially unlocking new frontiers in health and well-being.

Day 1 Lightning Presentations and Winner



End of Day Project Lighting Presentations

The session featured presentations from several groups on advancing various focus areas:

- Life Cell Age Clock: The team proposed genetically encoded age indicators that would work in vivo. They suggested using single-cell resolution fluorescent and multiplexed biomarkers based on CpG methylation sites to monitor and potentially control aging processes online. Challenges include achieving in vivo implementation and managing multiple signals for accurate readings.
- High Throughput Cryoprotectant Screening: This group aimed to develop an automated workflow to discover better cryoprotectants for biostasis. The goal is to screen 100,000 compounds per day to find solutions with minimal critical cooling/warming rates and toxicity. The plan includes using automation tools from organometallic catalysis and various assays to assess cryopreservation efficiency.
- Embryonic Rejuvenation: This idea involves generating younger organs by combining two advancements: creating embryos from naive IPS cells and studying natural rejuvenation processes occurring during mid-embryogenesis. The focus is on understanding and applying embryonic rejuvenation to obtain organs with the lowest biological age for replacement.
- AI-Driven Surgical Robots: The team proposed developing AI-assisted surgical robots for organ replacement. They suggested starting with VR simulations to train and test AI in surgery, addressing scalability, precision, and cost. They highlighted the need for supervised solutions and ethical considerations in deploying AI for surgeries.

The winning proposal was Embryonic Rejuvenation to Generate Younger Organs, which received the prize for its innovative approach to organ replacement.

Day 2 Group Presentations and Winner

During the workshop, participants self-assembled into groups to explore key areas where advances and innovative approaches could accelerate progress in the field. Following discussions, groups delivered presentations which were evaluated on their merit, feasibility, and impact, with a prize awarded to the most compelling idea, as voted on by the participants.



Biomarkers

Group 1 focused on the development of "Plasma AI," a project aimed at profiling blood plasma to determine the age of different organs. By analyzing plasma components from various organs, the goal is to identify weak links in an individual's health and design targeted interventions. This approach would move beyond universal treatments, offering personalized solutions based on specific organ needs. The group discussed the challenges of establishing quality control and managing the costs of multi-omic profiling, which can be expensive. They considered using targeted methods to reduce costs and suggested incorporating polygenic risk scores to enhance the robustness of the model. Despite the feasibility of the project, concerns about balancing interventions to avoid negative impacts on other organs were raised. The team concluded that personalized, organ-specific interventions could be a significant advancement in longevity research.

Day 2 Group Presentations and Winner



Funding

Group 2 addressed the funding challenges for longevity biotech companies, particularly during the preclinical stage when raising significant amounts of money can be difficult. They highlighted that many investment firms are unaware of the potential in longevity biotech. Notably, Puerto Rico, with its tax incentives and presence of family offices and big Pharma companies, presents a promising funding opportunity. The group proposed sending a representative, Carl, to Puerto Rico to engage with these firms and promote investment in longevity research. They also noted that such efforts could lead to additional funding through required annual donations by these organizations.



Replacement

Group 3 presented a proof-of-concept plan for full-body replacement in humans, focusing on a small-scale experiment involving fewer than ten individuals. Their approach involves two main components: creating a replacement body and performing nerve connection surgery to integrate a human head onto the new body. They emphasized that brain replacement and large-scale public convincing are not necessary for their proof of concept. The plan involves cloning a non-sentient human and growing it to maturity, with initial experiments in monkeys to refine the procedure. They estimated costs at \$60 million for monkey experiments and an additional \$100 million for human trials, suggesting that this could make significant progress toward full-body replacement. They acknowledged challenges including the high cost, ethical concerns, and public pushback but noted that the relatively low cost makes it an appealing area for research.

Day 2 Group Presentations and Winner



Open Source Repository

Group 4 proposed creating an open-source repository to help individuals evaluate the efficacy of health interventions they use or purchase. They suggested developing detailed protocols for testing various interventions, such as probiotics or supplements, which could include baseline measurements and follow-up tests to assess effectiveness. The platform could also incorporate crowdsourced input to refine and improve evaluation methods over time. Key considerations include ensuring accurate baseline data, managing placebo controls, and implementing blinding procedures. The goal is to empower individuals with better tools to determine the value of interventions, which could lead to more informed purchasing decisions and potentially reduce market demand for ineffective products.



Closing Remarks

The workshop concluded with the announcement of the winner: Group 3 focusing on Replacement technologies as a highly promising direction within longevity biotechnology.

What's Next?

Accelerating longevity progress requires the long-term, collective effort of a dedicated talent and funding pool.

The longevity field is finally growing. But the high-impact areas explored at this workshop, from replacement to healthcare 3.0, are still in their infancy. It's possible to generate entirely novel approaches for progress in each of these subfields during a two-day workshop. Yet, realizing them beyond the workshop requires both funding and domain-expertise.

If you are a researcher, practitioner, or funder seeking collaboration in the frontier of aging and longevity, we encourage you to avail yourself of the resources on the Longevity Biotech Fellowship and Foresight websites.

Longevity Biotech Fellowship: https://www.longbiofellowship.org

Foresight Institute: https://foresight.org

Please reach out to discuss how you can get involved in our collective mission to advance the progress and well-being of humanity.











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