

2023 Longevity Frontiers Workshop

R. K. Kalla

Chaired by

Allison Duettmann Foresight Institute

Sonia Arrison 100 Plus Capital

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About Foresight Institute

Foresight Institute is a research organization and non-profit that supports the beneficial development of high-impact technologies. Since our founding in 1987 on a vision of guiding powerful technologies, we have continued to evolve into a many-armed organization that focuses on several fields of science and technology that are too ambitious for legacy institutions to support. From molecular nanotechnology, to brain-computer interfaces, space exploration, cryptocommerce, and AI, Foresight gathers leading minds to advance research and accelerate progress toward flourishing futures.

Our focus areas include:

Molecular Machines to better control matter Biotechnology to reverse aging Computer Science to secure human AI cooperation Neurotechnology to support human flourishing Spacetechnology to further exploration



Workshop Sponsors



Executive Summary

As the longevity industry evolves, a multitude of intriguing avenues remain largely uncharted. These include aging biomarkers, the extracellular matrix, young plasma, epigenetic reprogramming, bioelectricity and aging, alongside machine-learning approaches for data processing. In our quest to delve deeper into these areas, we invited distinguished researchers, entrepreneurs, and funders to pinpoint areas of potential progress, resulting in the keynote presentations encapsulated in this report.

Upon evaluating these presentations, collaborative workgroups were established to probe into ways of fostering advancement in the identified sectors. This report contains recordings of the ensuing project presentations and concise outlines of their proposed projects. Some of the topics addressed include the use of biomarkers in clinical trials, brain aging, partial reprogramming rebound, master aging regulators, and a longevity-focused AI atlas, among others.

Workshop attendees were given an opportunity to vote for the project they deemed most promising. The winning project received a development grant to kickstart initiatives aimed at tackling their area of interest. The report also delves into societal impediments to longevity progress, which were extensively deliberated upon and are detailed in the notes at the end of the report.

This report introduces an interactive element: By clicking on the play icon in the images, you can view the corresponding presentations.

We were also honored to present the inaugural Longevity Hypothesis Prize to Carlos Galicia from the Buck Institute, whose proposal aims at leveraging embryogenesis' rejuvenation processes for longevity. Congratulations, Carlos!

We extend our heartfelt gratitude to all participants, to Sonia Arrison of 100 Plus for chairing the workshop, and we would especially like to acknowledge our generous sponsors: AgingBiotech.info, Methuselah Foundation, 100 Plus Capital, Quadrascope, Pebblebed, Retro, Tomorrowbio, The Longevity Prize, Juvenescence, and Aginginterventions.org. Without their support, this workshop would not have been possible.

We welcome those interested in bolstering ongoing progress to apply or reach out to us.

For an overview of the longevity field, including major needed technical capabilities, existing actors, and outstanding challenges, please see Foresight Institute's technology tree: https://foresight.org/ext/ForesightTechTree.

Best regards, Allison Duettmann Foresight Institute a@foresight.org







Participants

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Adrian Matysek FORESIGHT FELLOW

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Ben Alexander FORESIGHT FELLOW

Benjamin Anderson

Brad English HARVARD MEDICAL SCHOOL

Carlos Galicia BUCK INSTITUTE FOR RESEARCH ON AGING

Christin Glorioso NEUROAGE

Clinton Mielke GENENTECH

Workshop chairs

Collin Ewald UNIVERSITY OF ZURICH

Dane Gobel METHUSELAH FOUNDATION

David Furman BUCK INSTITUTE

Emil Kendziorra Tomorrow BIO

Fiona Miller QUADRASCOPE

Greg Fahy INTERVENE IMMUNE

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Jim O'Neill

JJ Ben-Joseph TENSORSPACE

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Lucy Fauth KARLSRUHE INSTITUTE OF TECHNOLOGY

Lynne Corner NEWCASTLE UNIVERSITY

Mahdi Moqri STANFORD UNIVERSITY

Mahmood Panjwani on deck

Manish Chamoli BUCK INSTITUTE

Mariëlle van Kooten STANFORD UNIVERSITY

Mark Hamalainen LONGEVITY BIOTECH FELLOWSHIP

Matthew Buckley RETRO BIOSCIENCES

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Workshop Chairs



Allison Duettmann PRESIDENT AND CEO, FORESIGHT INSTITUTE

Allison Duettmann is the president and CEO of Foresight Institute. She directs the Intelligent Cooperation, Molecular Machines, Biotech & Health Extension, Neurotech, and Space Programs, Fellowships, Prizes, and Tech Trees, and shares this work with the public. She founded Existentialhope.com, co-edited Superintelligence: Coordination & Strategy, co-authored Gaming the Future, and co-initiated The Longevity Prize. She advises companies and organizations, such as the Consortium for Space Health, and is on the Executive Committee of the Biomarker Consortium. She holds an MS in Philosophy & Public Policy from the London School of Economics, focusing on Al Safety.



Sonia Arrison is the founder of 100 Plus Capital, as well as an acclaimed author and investor. Her expansive career in tech research, underscored by her focus on the implications of rapidly evolving technologies, positions her as a sought-after thought leader in the realm of technological impacts on society. Her best-selling book, "100 Plus," delves into the transformative societal effects of extended human longevity. Beyond her writing, Sonia's influence extends to her roles as Chair of the Alliance for Longevity Initiatives and her prior association as a co-founder of Unsugarcoat Media and Singularity University. Arrison's work and vision have secured her spots on the boards of notable institutions like the Thiel Foundation, Foresight Institute, and Alliance for Longevity Initiatives. She holds additional recognition as a Senior Fellow at the Fraser Institute in Vancouver.



Many longevity areas are still underexplored. Some were surfaced by our 2022 workshop, some have been highlighted by the Longevity Prize, and some are entirely new. This two-day event invited leading researchers, entrepreneurs, and funders to drive progress. Together we explored new opportunities, formed lasting collaborations, and drove cooperation toward shared long-term goals.

Format

Rapid keynotes were followed by working groups to curate opportunities for talent and funders present at the workshop. Highlights also included mentorship hours, breakouts, and a speaker, sponsor & fellow gathering.



















































All workshop presentations are clickable via the play button



Longevity Frontiers Workshop 2023 **Recap**

SUMMARY

Allison Duettmann discusses the importance of collaboration. She expresses excitement about the growing interest in the field of longevity and the opportunities it presents for research, entrepreneurship, and funding. Duettmann highlights that aging is still an open question and estimates that a significant portion of individuals die as a result of aging after the age of 50. She further emphasizes the benefits of exercise as a free and accessible tool and suggests that it should be utilized as a motivating drug. The significance of regenerative abilities in combating aging is also discussed, with a focus on regenerative organisms that never develop cancer. Finally, she expresses gratitude for the effort put into the workshop and acknowledges the success of the conference.



Longevity Frontiers Workshop 2023 Introduction

SUMMARY

Allison Duettmann provides an overview of this workshop, and the work of Foresight Institute in general. She acknowledges that Foresight Institute supports individuals and projects that are often too early stage or ambitious for traditional institutions. Foresight Institute offers virtual seminars, fellowships, prizes, and events like the Longevity Frontiers Workshop. She dives into the work Foresight Institute does in the longevity field, through a project called Tech Trees – which aim to track progress and advancements within the ecosystem. The Tech Tree serves as a comprehensive resource, offering a condensed overview and Al assistance through a feature called Lateral, which allows users to perform natural language searches and obtain Al-generated answers specific to the sections.





Sonia Arrison & Duettmann
Longevity Investing 1-1

SUMMARY

Sonia Arrison and Allison Duettmann focus on longevity investing, specifically in the context of brain longevity research. Sonia Arrison highlights the evolution of the industry and the increasing interest in longevity over the years. She discusses the exciting developments happening in the field of brain longevity research, including organoid research, imaging work, and regenerative medicine. Arrison emphasizes the importance of evaluating the team and the stage of scientific development when considering investment opportunities. Challenges in brain-related research, such as overcoming the blood-brain barrier, are discussed. Collaborations and cooperation between scientists and business professionals are deemed crucial for successful commercialization. The lack of understanding regarding the underlying mechanisms of mental health conditions is highlighted, and the development of drugs for conditions like bipolar disorder and schizophrenia is compared to the early days of oncology. The preservation of memory, the concept of memory itself, Al advancements, and the importance of brain health and mental health are also discussed. Finally, organoid research is mentioned as a valuable tool for understanding the effects of drugs on brain tissue, particularly in the context of Alzheimer's disease.



Greg Fahy, Intervene Immune Thymus Regeneration: What's Next?

SUMMARY

Greg Fahy discusses the next steps in thymus regeneration, following a review of past progress and the current status of research. He highlights the importance of thymic functional mass, which declines significantly as we age, impacting our ability to defend against diseases and increasing mortality rates. Fahy mentions a previous clinical trial conducted from 2015 to 2017, which successfully regrew functional thymic mass in individuals up to the age of 65. Positive anti-aging effects were observed, such as reduced inflammation and changes in hair color. To replicate these results, a new trial called Trim X was initiated, with promising signs of replication already observed in the first phase (Trim XA). The results showed improvements in prostate cancer risk, decreased CRP levels, positive immunity, and epigenetic aging results. Additional findings included increases in lymphocyte count, improvement in lung function, muscle strength, and exercise tolerance. Fahy concludes by mentioning future research plans, such as conducting Trim X trials, validating an early cancer detection method through the ACE trial, exploring thymus regeneration without growth hormone, and investigating the epigenetic landscape for age reversal potential.



Joe Betts-Lacroix, Retro Biosciences Whose Lives Are We Extending?

SUMMARY

Joe Betts-Lacroix discusses his work at Retro Biosciences, a biotech company focused on increasing healthy human lifespan. He addresses the challenge of choosing a target population and emphasizes the various factors that influence healthy longevity, including war, poverty, healthcare access, pollution, and lifestyle choices. Retro Biosciences aims to develop medicines to extend healthy lifespan rather than relying solely on apps or lifestyle interventions. Betts-Lacroix highlights the importance of exercise as a validated life-extending technology and encourages individuals to take advantage of its benefits. While Retro Biosciences considers developing an exercise pill, Joe emphasizes that exercise itself is already accessible and impactful for health. The company's target market is not those unwilling to make lifestyle changes, but rather a global population wishing to live longer and healthier lives. He argues that there comes a point where lifestyle modifications have limited effects, and technological interventions are necessary for a substantial increase in healthy lifespan. Betts-Lacroix emphasizes Retro Biosciences' commitment to developing high-impact technologies to extend healthy human lifespan worldwide. He disagrees with the idea of extending lifespan to those who are not already taking action, emphasizing the importance of creating products for those who are already making efforts. He raises questions about the potential benefits and asymmetry of developing a pill for already healthy and motivated individuals versus one for those still engaging in unhealthy behaviors. Finally, he suggests that solving the problem of extending lifespan for the already healthy and motivated individuals with access to healthcare would likely have a positive impact on the broader population.



Mahdi Moqri, Stanford University The Biomarkers of Aging Consortium

SUMMARY

Mahdi Moqri discusses the work of the Biomarkers of Aging Consortium in establishing reliable biomarkers for longevity interventions. The first manuscript generated by the Consortium focused on these aspects, although a complete consensus on definitions was not reached. The Consortium compiled a list of licensed and commercially used biomarkers of aging, including various omics, as well as identified epigenetic biomarkers used in clinical trials. Moqri argues that biomarker validation, including cross-species validation, is an important area of research, although he acknowledges that there are debates about its relevance due to biological complexity.





Michael Snyder, Stanford University **ML for Personalized Medicine**

SUMMARY

Michael Snyder discusses his team's use of big data and novel approaches for personalized medicine in order to extend health span. The current healthcare approach is based on population averages and lacks personalized tracking. Snyder's team collects deep data on individuals, including genomics, molecular measurements, clinical testing, questionnaires, and wearables, in order to track them individually and create personalized health programs. Through longitudinal sampling and deep data dives, the team has made significant health discoveries, detecting pre-symptomatic conditions such as lymphoma, pre-cancers, and heart issues. They also profile individuals' health trajectories to better understand aging. Snyder's team aims to bring healthcare measurements into the home, utilizing wearables and micro sampling. Wearables such as smartwatches and rings provide 24/7 monitoring and can detect infectious diseases pre-symptomatically. Micro sampling involves taking small blood samples for deep omics profiles and molecular measurements. By combining a lot of data, personalized food responses can now be measured. Personalized patterns can be identified using wearables and microsampling. Snyder also discusses the formation of Silicon Valley companies to scale and make these projects more affordable. He notes that preference is expressed for wearables. like smartwatches and continuous glucose monitors, due to their effectiveness and affordability, but implantable devices are also mentioned as a personal preference for continuous monitoring.



Benjamin Anderson, Independent **Bioelectricity & Aging**

SUMMARY

Benjamin Anderson discusses the importance of bioelectricity research in the field of biology, particularly in relation to aging interventions. He highlights the work of Dr. Michael Levin's lab, which studies planaria – a regenerative organism that does not develop cancer. By altering the bioelectric state of planaria, they were able to induce a two-headed phenotype that persisted through subsequent generations. Anderson notes that membrane voltage alterations in individual cells play a crucial role in bioelectricity research, with different cell types clustering towards polarized or depolarized states. He also emphasizes the role of epigenetic changes, which are influenced by tissue-wide voltage gradients that regulate cell-cell communication. He introduces the computational toolkit called Betsy, developed by Dr. Levin's lab, which allows researchers to map functional data and search for potential interventions. Anderson believes that bioelectricity is key to more efficient reprogramming strategies for aging interventions and could provide new avenues for exploration. Finally, he mentions the importance of understanding biological changes at the transcriptional level and references Clarence Cohn's research on reversible mitotic blocks.



Carlos Galicia, Buck Institute for Research on Aging **Embryogenesis-Inspired Rejuvenation**

SUMMARY

Carlos Galicia presents his ideas, focusing on harnessing rejuvenation events that occur during embryogenesis for therapeutic approaches to combat age-related decline. He highlights the importance of understanding the biological processes that occur during embryogenesis, such as the generation of new tissue without replicative senescence or significant accumulation of molecular damage. He mentions a rejuvenation event during embryogenesis that resets the epigenetic age of cells to zero, discovered by the Gladyshev lab. Galicia proposes three phases for his proposal: identifying age-related changes in gametes, observing how the embryo rejuvenates, and applying rejuvenation mechanisms. He suggests using deep phenotyping and molecular characterization techniques to uncover molecular changes and transcriptional signatures associated with rejuvenation. He also discusses the benefits of deep phenotyping, such as performing complex screens and reconstructing mechanistic networks. The audience suggests exploring the role of the extracellular matrix and the influence of embryonic interactions in reprogramming tumor cells. Galicia welcomes collaboration and suggests forming a working group, leading to discussions of collaboration. Galicia also emphasizes the need for computational models to understand the effects of factors and design experiments, as well as the development of better computational tools to uncouple observed effects from computational ones. Overall, Galicia emphasizes the importance of understanding embryogenesis to harness rejuvenation mechanisms and provides his contact information for further inquiries or collaborations.



Johnny Adams, Aging Intervention Foundation Project Star Shot for Open Ended LIFE

SUMMARY

Johnny Adams discusses the reality of aging and the urgent need to find a solution, emphasizing the importance of aiming high and thinking big. Alongside solving aging, Adams encourages finding a purpose and making the world a better place. He highlights the need for collaboration, funding, and oversight in aging solutions development and shares his expertise and focus on aging intervention. Adams expresses interest in gene therapy, Al for biomarker analysis, and invites others to collaborate in these areas. He calls for innovators, donors, investors, visionaries, and scientists to connect and work together. Adams also emphasizes the need for long-term planning and sets a target date in 2049 for significant progress.



Steve Horvath, Altos Labs **Young Plasma**

SUMMARY

Steve Horvath discusses the importance of using graphics and visualizations to enhance understanding of epigenetic clocks. He presents Kaplan Meyer Curves representing different epidemiological cohort studies, demonstrating the ability of the Grim Age measure to stratify individuals. He introduces Grim H version 2, which expands on the previous version by adding estimators of certain biomarkers to the methylation estimators of plasma proteins. Horvath highlights associations between underlying biomarkers and mortality risk, particularly focusing on the association of gdf 15 with mortality. Regardless of data analysis or racial and ethnic groups, there is consistent separation between fast and slow agers according to Grim Age. He mentions studies where interventions reversed Grim Age and methylation-based component biomarkers. He also discusses the potential of young blood, plasma, and methionine restriction as interventions to reverse epigenetic age. The need to find interventions that can reverse epigenetic age and catalog them is expressed. Overall, Horvath emphasizes the potential for interventions to reverse epigenetic age in humans.



Tina Woods, Collider Health Quantum Healthy Longevity

SUMMARY

Tina Woods discusses the Quantum Healthy Longevity Innovation Mission, which has the goal of bringing scientific advancements out of the lab to benefit real people. The mission aims to promote healthy people, a healthy planet, and healthy economic growth. Woods highlights the importance of international collaboration and working with a range of partners. She addresses the problems of decreasing lifespan and widening health inequalities and expands upon how she aims to extend benefits of research to everyone. She also discusses the potential impact of research in healthy longevity on improving healthy life expectancy and the financial potential it holds. Woods advocates for a Quantum Leap Forward in thinking, shifting from a sick care model to a preventative health program. The mission focuses on the exposome, considering the wider determinants of health beyond the medical record, and plans to map exponential insights and develop an open platform accessible to all to spur ethical aging. The approach to Quantum Healthy Longevity is a Federated approach with citizens at the center, aiming to democratize knowledge and access to healthy longevity.



Mark Hamalainen, Longevity Biotech Fellowship Longevity Bottleneck's Results

SUMMARY

Mark Hamalainen discusses their organization (Less Death)'s focus on longevity biotech and the importance of getting more people involved in addressing the problem of aging. To gather input from the community, they conducted a survey to identify bottlenecks and potential solutions in longevity research. The survey was conducted during the Longevity Summer Camp, with participants coming up with a scheme for conducting the survey. The survey aimed to evaluate intervention strategies, identify bottlenecks, and gather diverse perspectives. The first survey was conducted qualitatively, allowing participants to freely express their ideas. The analysis of the survey responses involved extensive text reading and categorization. The survey reached out to a thousand people in the longevity community, receiving 800 initial responses and 400 completed surveys. Hamalainen emphasizes the importance of involving more people in addressing the significant challenges presented by aging.



J-J Ben Joseph, TensorSpace Early Stage Drug Discovery Using Natural Language Prompts

SUMMARY

JJ-Ben Joseph presents a venture called Tensor Space, which focuses on early-stage drug discovery using natural language prompts – it is AI horizontal product with various use cases, one of which is enabling natural language search on small molecule chemicals. He discusses how the search feature allows users to query drugs and non-drug substances using natural language prompts, returning results based on the input. Tensor Space also allows for prompt-based searches on non-drug substances, such as dangerous poison or deadly substances. The architecture of Tensor Space involves converting data modalities into embeddings, which are high-dimensional vectors representing the data. The system includes a vector database, a data database, and a UI layer shared across different data modalities. Currently, the relevance of search results is sorted based on the distance from the query, but improvements can be made to indicate relevance or confidence levels.





Fiona Miller, Quadrascope **Longevity Investing**

SUMMARY

Fiona Miller discusses the importance of accurate measurement in longevity science and the need for standardized measurement methods. She highlights the exponential nature of aging and its potential impact on knowledge and productivity, before diving into the financial and regulatory challenges in longevity research and development, and emphasizes the need to get politics right to overcome these barriers. She shares data on investment trends in longevity biotech and medicine, noting that a significant portion of VC money in 2021 went to longevity. Miller advocates for the consolidation and expansion of conferences and collaborations in the longevity investing. She also discusses the societal and behavioral factors that should be considered when discussing longevity investment. Lastly, Miller addresses the challenges in raising funds and attracting investors, seeking strategies to overcome barriers and improve funding opportunities.



Vittorio Sebastiano, Stanford University Epigenetic Reprogramming: The Path Ahead

SUMMARY

Vittorio Sebastiano discusses the concept of epigenetic reprogramming as a potential solution to the problem of aging. Aging is viewed as an epigenetic issue, where dysfunction in the epigenetic program of cells leads to age-related problems. Various factors like sun exposure, diet, stress, and lack of sleep can contribute to mistakes in the epigenetic program. He recognizes that the good news is that the epigenetic program is programmable and can be reset and reorganized. His lab has developed a technology called Epigenetic Reprogramming of Aging (ERA), which delivers a cocktail of factors into old and dysfunctional cells to reprogram the epigenetic landscape and impact multiple hallmarks of aging simultaneously. ERA has shown promising results in human cells and has potential applications in dermatology and immunology, showing increased expression of certain proteins and enhancing the functionality of immune cells. The short-term goal is to move towards clinical trials, and funding is being raised to support these programs. Epigenetic reprogramming has the potential to be applied across different tissues and cell types, and biomarkers are needed to measure the outcomes and effectiveness of rejuvenation interventions. He also emphasizes the importance of considering the duration of treatment during epigenetic reprogramming to ensure that cells maintain their identity, and mRNA plays a key role in achieving a transient and defined expression of factors. The duration may vary depending on the cell type and factors used.





Ashish Tripathy, Tzar Labs Quest for Pan-Cancer Early Diagnosis & Prognosis Ends with HrC Test

SUMMARY

Ashish Tripathy discusses the development of the HrC Test, a pan-cancer blood test that can detect cancer in its early stages. He claims three global firsts for their research, including the ability to predict that a person will not get cancer within the next year. Unlike other liquid biopsy companies, the HrC Test focuses on detecting cancer stem cells much earlier in the cancer formation process, allowing for effective intervention and treatment. The test achieves high accuracy through a comparison model coined by Benjamin Gimpel, and it has the potential to distinguish between metastatic and benign cancers. He highlights that the HrC Test has shown promising results in detecting cancer stem cells up to 18 months before a tumor even forms.



Collin Ewald, University of Zurich The Extracellular Matrix & Longevity

SUMMARY

Collin Ewald provides an overview of the Extracellular Matrix (ECM) and its relationship to aging and longevity. The ECM, composed of collagen and other proteins, plays a crucial role in maintaining cell health and predicting phenotypic characteristics. Collagen remodeling, which becomes fragmented and cross-linked with age, is identified as a key factor for longevity. The composition of the ECM can be used for drug discovery, with potential longevity drugs being identified by comparing ECM composition in young and aged tissues. Although dietary restriction and rapamycin interventions can slow down collagen cross-linking, current interventions are not effective in reversing it. The ECM is a dynamic system, with collagen remodeling occurring within days in certain tissues. The proximity of cells to the ECM influences its behavior, and certain collagen proteins are linked to circadian rhythm. Cross-linking becomes problematic when cells are distant from the ECM, leading to the loss of ECM protein homeostasis during aging. He notes that current interventions mainly focus on slowing down cross-linking, while the potential use of plasma and the relationship between gene expression and protein half-life in the ECM are areas of interest.





SUMMARY

Mariëlle van Kooten A Moonshot to Move the 13 Mitochondrial Genes to the Human Nucleus

Mariëlle van Kooten introduces the Moonshot project, which aims to relocate the 13 mitochondrial genes to the human nucleus in order to address aging-related issues. She highlights the importance of mitochondrial DNA in controlling cellular processes and the communication between the nuclear and mitochondrial genomes, with dysfunction in this communication leading to health problems. She mentions that most mitochondrial genes have already been transferred to the nucleus throughout human evolution, leaving only 13 genes in the mitochondria. The Moonshot project proposes a systematic approach involving interdisciplinary teams and recent technological advancements to achieve the relocation of these genes. Finally, Kooten presents the three milestones of the project, and encourages collaboration and questions. She also emphasizes the need for a panel of donors from different geographical regions to account for genetic diversity, before concluding with the challenge of convincing others about the potential benefits of gene therapy within the next 7-10 years.



Emil Kendziorra, Tomorrow Bio Cryonics 1-1

SUMMARY

Emil Kendziorra discusses cryonics as an alternative in the field of longevity. He highlights the concept of longevity escape velocity and the slow progress in extending lifespan. Kendziorra advocates for cryopreservation as a backup in case other treatments fail, explaining the process and emphasizing the need for backups. He acknowledges the challenges in cryopreservation, such as lack of funding and limited experiments. Animal cryopreservation is also addressed, with the current limitations due to funding constraints. The focus of cryopreservation is on preserving the connectome and potentially achieving consciousness preservation. Funding limitations in cryopreservation restrict research and development, but he has hope for increased funding in the future. Kendziorra expresses commitment to advancing cryopreservation and extending human lifespan, even with limited resources.



Reason, Repair Biotechnologies Repair Bio & Personal Longevity

SUMMARY

Reason discusses the problem of disrupted cholesterol transport and its implications for bio and personal longevity. He notes that when cholesterol transport is disrupted, excess cholesterol accumulates, which can be toxic to cells and disrupt tissue function. Aging and obesity are factors that contribute to cholesterol disruption. Current treatment approaches do not effectively address this issue; therefore, a different approach is needed. Cholesterol transport is vital as every cell in the body requires cholesterol, which is largely manufactured in the liver and transported throughout the body; however, excess cholesterol can overwhelm cells and lead to atherosclerosis. Specifically, free cholesterol, which forms when cholesterol overwhelms esterified cholesterol, is toxic to cell function. His proposed solution involves selectively clearing excess free cholesterol using a combination of human enzymes, which has shown promising results in animal models by reversing conditions such as Nash and atherosclerosis.



David Furman, Buck Institute Space Health: The Final Frontier

SUMMARY

David Furman discusses two main topics; firstly, the Thousand Immunomes Project, and secondly, the relationship between space health and accelerated aging. The Thousand Immunomes Project, which Furman and his team launched in 2007, aims to establish the normality of the immune system by measuring different omics in a large group of individuals. Through this project, they have derived a metric for immunological health that correlates with various health conditions and mortality. This metric is now being commercialized by a company that spun out of the project. Furman also shares his work on space health and accelerated aging. He explains that astronauts seem to age faster in space in several aspects, including cardiovascular health, cognition, muscle strength, and immune system reactivation. In response to this observation, Furman started the Consortium for Space Health and Human Longevity, a non-profit organization that funds research in the intersection of space biology and longevity research. The consortium aims to understand the biological constraints of space-aged accelerated aging and develop gero-protective compounds. They have also established a company called Cosmica Biosciences, which focuses on reversing accelerated aging in space. He concludes by thanking his team and acknowledging the work they do, as well as expressing gratitude to the institution's designer.



Development Grant Winners

1st Place \$3,000

Promote the Use of Biomarkers of Aging in Clinical Trials

2nd Place \$2,000

Partial Reprogramming Bounceback and Master Regulators of Aging

3rd Place \$1,000

Constructive Pessimism

Project Presentations (in order of votes)

3112

Promote the Use of Biomarkers of Aging in Clinical Trials



SUMMARY

This group proposes utilizing aging biomarkers in clinical trials to prevent failures due to biological age disparities and build a genomic database. The innovative approach includes using one blood tube from participants for proteomics and methylation, aiding in securing robust trial data and future research. Next steps encompass developing guidelines for biomarker use in trials and connecting with global stakeholders and organizations. With each methylation array costing under \$200 and a timeline of 6 months, immediate actions for a development grant (\$1k-\$3k) involve creating detailed guidelines and engaging with relevant consortiums and organizations in the biomarker and aging research sphere. Success hinges on preventing skewed trial outcomes and enhancing the future utility of the genomic database.



Partial Reprogramming Bounceback and Master Regulators of Aging



SUMMARY

This project group focuses on the relapse or reversal effect after stopping reprogramming related to aging. The crux lies in understanding whether the effects of partial reprogramming therapy, generally administered repeatedly until life's end to notably increase lifespan, revert after cessation. Some studies suggest short or single-bout reprogramming impacts, potentially indicating a reset to baseline epigenetic age post-therapy. Goals include discerning if a "bounceback" of epigenetic age happens post-reprogramming and any implications for aging comprehension and therapeutic target identification. Investigative approaches might involve studies with post-reprogramming time points and tissue biopsies to monitor epigenetic age and biomarkers. The costs are several hundred thousand to a million dollars, with about a year timeline for a preliminary inquiry. Immediate next steps could involve a \$2k grant to draft a detailed experimental protocol and establish lab settings. Success, risks, and comprehensive insights from these studies promise to direct future therapeutic strategies and aging research pathways efficiently.



Constructive Pessimism



SUMMARY

This project addresses the necessity for self-criticism and scrutiny in the longevity field, advocating for a transparent, critical assessment of its methods and results. The goal is to bring visibility to negative results and skepticism within the science of longevity, thereby promoting critical thinking and saving resources. The proposed approach involves funding scientific writers to conduct interviews about research reservations, creating a repository of these critical insights for researchers and other stakeholders. Success entails integrating critical evaluations into public discourse, normalizing the seeking of work criticism, and educating the community about existing reservations in the field. Mitigating the risk of causing offense involves employing professional journalists and writers adhering to strict journalistic integrity standards. With an estimated cost of \$15,000 - \$25,000 per article and a timeline of 2-3 months per article, the first milestones involve publishing a preprint of the initial article for peer review, feedback incorporation, and eventual publication. The initial next step for development, priced at \$1k, includes launching a wiki-style site and commissioning the first critique article, while ensuring critiques are anonymous yet affiliated for credibility vetting.



Morpheia- Continuous Biotracking Implantables



SUMMARY

This working group aims to craft affordable, user-friendly biomarkers for home use, emphasizing global availability and predicting health and longevity in relation to nutrition. The objective involves creating easily adoptable biomarkers, considering factors like user-friendly implantable devices, without frequent charging, and simple upgrades to promote adherence. Data privacy and cybersecurity are pivotal, addressing continuous tracking and ensuring customer trust. The open-source API allows user choice and development in trusted applications, while future exploration will delve into sensor technologies and drug delivery mechanisms integrated with devices. The goal is a comprehensive implantable biosensor and data platform, granting easy access to detailed health data, facilitating large-scale health and longevity studies. Key challenges include implant reliability and data privacy, to be mitigated by involving medical experts and ensuring user control and standardized access. Initial costs are estimated at \$1-3K for talent and prototypes, with a subscription model considered for future financing. Success will be gauged through enhanced quality of life metrics, earlier disease detection, and novel health insights, with reliability and user adoption serving as mid-term assessments. Next developmental steps involve seed funding for prototype development and demonstration studies.



Consortium for Stage 0 Cancer Intervention



SUMMARY

This project group highlights the vital importance and challenges of developing interventions for stage 0 cancer - a stage of cancer undetectable due to lack of a tumor. The project aspires to foster the creation and enhancement of interventions for this early cancer stage by addressing detection and treatment challenges. The goal is to facilitate the early detection of Stage 0 cancers and create new treatment modalities, using a consortium to harmonize efforts. While current diagnostics can only detect cancer from Stage 1 onwards and pose ethical questions regarding early detection without available treatments, the novel approach emphasizes improving surveillance, diagnostics for Stage 0 cancers, and developing new treatment modalities through consortium-driven efforts. The risks involve the precision of diagnostics, ethical concerns about early information/treatment, and lengthy timelines, which will be mitigated through validation studies, consortium-derived benefits, and focusing on achievable short-term goals. The costs and timeline range from <\$3K for initial steps and 1-3 years for preliminary coordination, with robust validation extending beyond a decade. Success will manifest as improved early detection and the development of new preventive or interception modalities for cancers. The next steps under a development grant encompass forming a consortium, scheduling symposia, validating Stage 0 diagnostics, and exploring new modalities for targeted Stage 0 treatments.



AgeNet: The Longevity Al Atlas



SUMMARY

This working group explores utilizing AI to comprehend and manipulate human biology by establishing a diffusion model, linking cell attributes to descriptions and enabling the transition of biological systems between states. Aiming to construct the Single Cell Longevity Atlas Dataset and a reference diffusion model for public access via a cloud service, they stress the need for a unified data set and model. While the current approach is segmented and lacks holistic datasets, the proposed strategy applies advanced AI to form a comprehensive dataset and model, offering researchers expansive, diversified data. Success, defined by the creation, utilization, and citation of the dataset/model, seems achievable with anticipated low risks given the health-oriented nature of the project. With a budget of \$100,000 and a timeline of 3 months (2 for dataset creation, 1 for model training), mid- and final-term exams will evaluate model performance and usability. Development grant steps include hiring a technical writer to refine the proposal and documentation, and pursuing additional funding.



LongevityAction.org



SUMMARY

This project group underscores the necessity of crafting a comprehensive action list for those intrigued by longevity, addressing the lack of straightforward guidance and structure in the longevity community. By aiming to consolidate resources and initiatives on a centralized website, the project endeavors to make engagement in the longevity field tangible and actionable for individuals, providing various options beyond merely jobs and investments. Though the present landscape lacks a unified guide for longevity engagement, this novel approach seeks to bridge people with organizations, opportunities, and companies in the field. Success hinges on notable user engagement and action-taking, with a modest budget of \$3,000 and a 2-month timeline. Mid-term objectives include compiling a list and testing QR code postcards at an event (SynBioBeta), while final examinations will scrutinize website launch success and user engagement analytics from event attendees. Subsequent steps for utilizing development grants involve finalizing action lists, website launching, and QR code postcard distribution at diverse venues.



Nonstop Neurons - Addressing Brain Aging



SUMMARY

This workshop group aimed to tackle neurodegeneration and brain health amid aging by proposing a consolidation of existing brain aging data into a usable, accessible resource. The goal is to expedite the development of therapies to reverse brain aging through integrated data analysis from an aging-biology perspective. Currently, exercise and diet are the main but limited approaches to brain aging, so the novel approach seeks to understand aging-biology-based risk factors and unique brain aging aspects, testing strategies like reducing inflammation. Success equates to finding a neurodegeneration cure, ensuring lifelong cognitive function. Risks include possible neglect of this research area, which may be mitigated by lobbying for support and collaborations. With costs of a 30-patient clinical trial at \$1 million and research status reformation in the billions, expected timelines are 2-3 years for small clinical trials and over 20 years for community research reformation. Immediate next steps involve surveying top neurodegeneration researchers and exploring potential collaborations, leveraging a possible \$3k development grant.



Addressing Meta Challenges in the Longevity Ecosystem

In addition to addressing crucial technical bottlenecks, such as the ones highlighted in this report, the longevity field still faces a few meta challenges that slow its progress and potential:

- 1. Funding constraints arise from factors such as the current economic downturn, as well as the historically risky perception of biotech and its historically relatively poor return on investment. This is further exacerbated by a concentration of funds in a few approaches, such as senescent cells and reprogramming, potentially sidelining other innovative approaches. Previous failures in the field have led to skepticism, and there is some tension between the infectious optimism of the field and genuine science and pragmatism. The absence of a concrete business model for preventive measures, inefficiencies in connecting funders with scientists and entrepreneurs, challenges in locating and onboarding donors, and companies' forced acceptance of lower valuations due to the constrained funding landscape are among other meta pain points slowing down the industry. Increased focus on lobbying, such as via organizations like A4LI, could help garner more political support to fill these systemic funding gaps. In addition, onboarding potential majors funders, such as investment banking firms specializing in longevity would help alleviate the funding shortage. Finally, starting novel longevity-focused incubators, or increasing the focus on longevity-focused companies within existing incubators could help kickstart early-stage companies.
- 2. Regulatory progress is impeded by the lengthy and risky nature of clinical trials, which often prioritize interventions only after damage has occurred, revealing a flawed strategic approach. The Kefauver–Harris Amendments to the FDA that skew towards efficacy over safety, and the absence of organizations that can navigate outside the U.S. regulatory framework, further compound the problem. The FDA's lack of a clear pathway for geroprotectors, and the fact that individual aging hallmarks are not acknowledged, requires the use of analogue targets. This, coupled with the issue of liability and an aggressive plaintiffs' bar, hinders advancements. Rectifying incentive misalignments between governmental bodies and researchers is a pressing problem. A shift towards human volunteer studies, a refocusing of the FDA on safety over efficacy, and bolstering the pipeline of companies for the FDA are areas of potential reform.
- **3. Talent acquisition** is potentially held back by the field's branding as 'longevity,' making it less appealing for mainstream researchers, even though there has been an encouraging recent increase in interest from junior researchers wanting to work on longevity itself. Aligning individual skills and interests with potential job opportunities, providing work environment flexibility, and counteracting the bystander effect, where potential actors assume someone else will address the challenges, are vital for placing top talent in effective roles.



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- **4. Collaboration** is hampered by the general problems holding back scientific progress across the board, such as the publish or perish norms in academia, incentivizing incremental progress, and poor peer review. The absence of key technologists in aging, and the often narrow-focus of existing funding sources further straight-jackets interdisciplinary work. Intellectual property rights issues, resistance to data-sharing, the lack of incentives to disclose failed data, replication bias, and a lack of mutual support within the community are additional barriers to cohesive action. A shift from prose-driven to data-driven science would be helpful in advancing the field.
- **5. Public education** about longevity faces significant challenges. The user experience in communicating complex longevity concepts is less than optimal, and a vast majority remains unaware of the importance of longevity. There is a shortfall in recognizing successes publicly, and some jargony terminologies need revamping for broader understanding. Societal culture plays a role; too many talented individuals opt for mundane jobs rather than ambitious, groundbreaking projects. Establishing credibility for results in the longevity field, rethinking public involvement strategies, and shifting from outdated dissemination methods to engaging the public as proactive agents of change in exciting creative ways are pivotal for widespread awareness and support.

Technical progress in longevity is advancing and the longevity ecosystem is rapidly growing. Addressing some of the meta challenges highlighted here could further accelerate the encouraging progress observable across the field.





Workshop Sponsors



