

BIOTECH & HEALTH EXTENSION

SPONSORED BY
100 PLUS CAPITAL

 **FORESIGHT**
INSTITUTE

Aaron King

Keynote Speakers



[Alex Zhavoronkov](#)
[Brian Kennedy](#)
[Christopher Leptak](#)
[Daniel Belsky](#)
[Daniel Ives](#)
[David Gobel](#)
[Dylan Livingston](#)

[Gordan Lauc](#)
[Greg Fahy](#)
[Irina Conboy](#)
[James L. Kirkland](#)
[James Peyer](#)
[Jamie Justice](#)
[Jean M. Hebert](#)

[Joris Deelen](#)
[Karl Pflieger](#)
[Keith Murphy](#)
[Lynne Cox](#)
[Michael Levin](#)
[Michael Snyder](#)
[Morgan Levine](#)

[Mike West](#)
[Nir Barzilai](#)
[Ronald Kohanski](#)
[Sonia Arrison](#)
[Steve Horvath](#)
[Terrie Moffitt](#)
[Vadim Gladyshev](#)

Table of Contents

Introduction	4
Biotech & health extension accelerator	5
<u>Industry blindspots: Non-incentivized work that could dramatically advance progress on aging</u>	6
<u>Tissue rejuvenation via plasma dilution</u>	7
<u>Academic perspective: Non-incentivized work that could dramatically advance progress on aging</u>	8
<u>Brain cell replacement as the cornerstone to beating aging</u>	9
<u>Clinical trials and senolytics Q & A</u>	10
<u>Institutional perspective: Promising aging work from an NIA perspective</u>	11
<u>How to fund and build geroprotectors</u>	12
<u>Biomarker development for FDA-recognized diseases</u>	13
<u>ALARMA (America's Longevity, Aging and Regenerative Medicine Association)</u>	14
<u>Thymus rejuvenation progress update</u>	15
<u>Longevity as a service: AI & aging clocks</u>	16
<u>Biomarker & aging clock development</u>	17
<u>Biomarker and aging clock development needed to spur progress on aging</u>	18
<u>Biomarker standardization</u>	19
<u>Patient trials in a dish</u>	20
<u>TAME Q&A: Lessons for progress on aging</u>	21
<u>Drug target discovery for cellular rejuvenation by the application of 'driver' clocks to cell reprogramming</u>	22
<u>Regenerative medicine focus</u>	23
<u>Monitoring personal health and ageotypes using big data</u>	24
<u>Quantification of the pace of biological aging: the DunedinPoAm DNA methylation algorithm</u>	25
Bountied biotech brainstorm	26

Introduction

[Biotech and Health Extension](#)

A group of scientists, entrepreneurs, funders, and institutional allies who cooperate to advance biotechnology to reverse aging, extend human healthspans, and improve cognition. Meetings are private and may be off the record. Those that are recorded can be found in our seminar summaries page and are overviewed in this report.



This group is sponsored by 100 Plus Capital. 100 Plus Capital invests in companies positively impacting human longevity. This can be directly targeted (for example, anti-aging companies) or broader reaching (clean food and water companies).

[Seminar Program](#)

[Seminar Summaries](#)

[Foresight Fellows](#)

[Apply to join](#)

[Support to join](#)

[About Foresight Institute](#)

[Foresight Institute](#) is a 30+ year-strong San Francisco-based institute to advance crucial science and technology for the long-term flourishing of life. We believe that, in addition to directly addressing existential risks, one relatively neglected area for impact is to directly support differential technology development in areas that make great futures more likely. We focus on working groups to advance:

- [Molecular Machines for atomically precise control of matter](#)
- [Biotech & Health Extension to reverse aging and improve cognition](#)
- [Computer Science to secure decentralized human AI cooperation](#)
- [Existential Hope to catalyze beautiful futures](#)

Thank you for your interest in our work. Please contact us with feedback, questions, and suggestions.



Allison Duettmann
[President, Foresight Institute](#)
a@foresight.org

Biotech & health extension accelerator

In addition to collaborations via our seminars, the 2021 Foresight Biotech & Health Extension Accelerator offered mentorship and support for particularly promising projects.

We are excited to congratulate our three winning projects:



Cellular Reprogramming



Biostasis



Brain Cell Replacement

Thank you to the mentors for supporting this accelerator.



[Sonia Arrison](#)
[Steve Horvath](#)
[Nils Regge](#)
[Andrew Scott](#)
[Jim O'Neill](#)
[Reason](#)

[Joe Betts-Lacroix](#)
[Tina Wood](#)
[Morgan Levine](#)
[Gordon Lauc](#)
[Daniel Bojar](#)

[Joris Deelen](#)
[Kristen Fortney](#)
[Felix Faber](#)
[Margaretta Colangelo](#)
[Petr Sramek](#)

[Arye Lipman](#)
[Adam Gries](#)
[Sourav Sinha](#)
[Alexandra Bause](#)
[Dina Radenkovic](#)

Industry blindspots: Non-incentivized work that could dramatically advance progress on aging

Sonia Arrison, 100+ Capital
Karl Pflieger, Agingbiotech
Mike West, AgeX

February 12, 2021



Summary

During this session, three speakers shared their opinion on what are the underappreciated opportunities in the field of aging and on the work that is currently not well incentivized but could dramatically advance the progress. Mike West (CEO at AgeX) discussed the need for treatments of chronic degenerative diseases associated with aging and the potential of partial reprogramming for induced tissue regeneration. Karl Pflieger (Investor at Agingbiotech.info) described the need for better “debuggers for biological blackboxes”, also the need for trialing combinations of therapies and aiming for robust mouse regeneration, as well as the overlooked opportunity of the professional sports market for longevity. Sonia Arrison (General Partner at 100 Plus Capital) mentioned immune system regeneration, regenerative medicine, and organ repair, as well as more focus on the brain enabled by a novel focus on brain research. Then the group together discussed a range of interesting ideas for instrumentation and tooling that could advance progress in the field, and also roadblocks and concerns that the community needs to be wary of, with a few concrete examples of what the field can do to prevent them.

Opportunities

What is a path for speeding up transcriptional reprogramming?

Chronic age-related degenerative disease is the largest challenge to humanity. Transcriptional reprogramming appears to offer simultaneously a means of reversing aging in human cells and also the ability to unlock intrinsic regenerative potential normally only present in the early stages of human development.

How can we (other fields?) develop assay/sensing technologies to validate and debug biological mechanisms and enhance our understanding of intended interventions?

We need better assays and sensing technology to validate and debug mechanisms, to look under the hood and not treat organisms as black boxes as much. We could use more combination therapies, like RMR, but how do we incentivize for more than just philanthropic money or government money? We should also rejuvenate from midlife/early old age, before chronic diseases get to clinical stage, to prime-of-life 20s & 30s health.

What is the most promising work in immunosenescence, regenerative medicine, and targeted brain therapies for aging?

Covid made the importance of the immune system and immunosenescence very clear. For regenerative medicine, this field was looking super promising 5-10 years ago and some companies came out of it, but it has stalled. Regarding the brain -- now that a significant amount of brain research work has been done and we have better technologies for studying it. It seems the time is right for more targeted brain therapies. Some for aging, some for mental health which impacts aging.

[Access the full summary and recording](#)

Tissue rejuvenation via plasma dilution



Irina Conboy, UC Berkeley

February 24, 2021

Summary

During this presentation, Irina Conboy (Professor at UC Berkeley) presented the latest findings about tissue rejuvenation via plasma dilution, an already FDA approved procedure that seems to have major effects on aging related processes. Following that is an insightful discussion touching on theoretical and practical next steps and limitations. There is also information on the most likely path to market and the possibility of availability for the general public in the near future.

Opportunities

How can we safely calibrate the circulatory milieu to health-youth?

The way forward is through removal and dilution of age elevated proteins, and we need to have excellent screening systems and excellent computational and modeling capabilities to identify every single determinant age-elevated protein and to see how to calibrate them to precisely young levels. However, not just in general, but individually. Because people do not age identically, so even though there will probably be the same patterns in our aging, there will also be deviations in those patterns between people. So the safe calibration should be based on patient level, where for every person we will identify the key proteome, the levels, and composition of it, how it differs from the healthy and young proteome, and how we can reset it to that healthy and young proteome.

The effect – rejuvenation takes place without a putative cause – young blood; while “young” factors change with age, as well as many other things, this is not causal to either aging or to rejuvenation.

This does not mean that donating blood would make one young; it is a novel scientific “thread” for unraveling the cause of age-imposed health decline and a new meaningful medicine.

Rejuvenation of three germ layers tissues by exchanging old blood plasma with saline-albumin [Priority Research Paper Volume 12, Issue 10 pp 8790–8817](#)

Old plasma dilution is safer and more robust for rejuvenation than all other current approaches.

[Access the full summary and recording](#)

Academic perspective: Non-incentivized work that could dramatically advance progress on aging

Brian Kennedy, Buck Institute
Joris Deelen, Max Planck Institute
Lynne Cox, Oxford

March 12, 2021



Summary

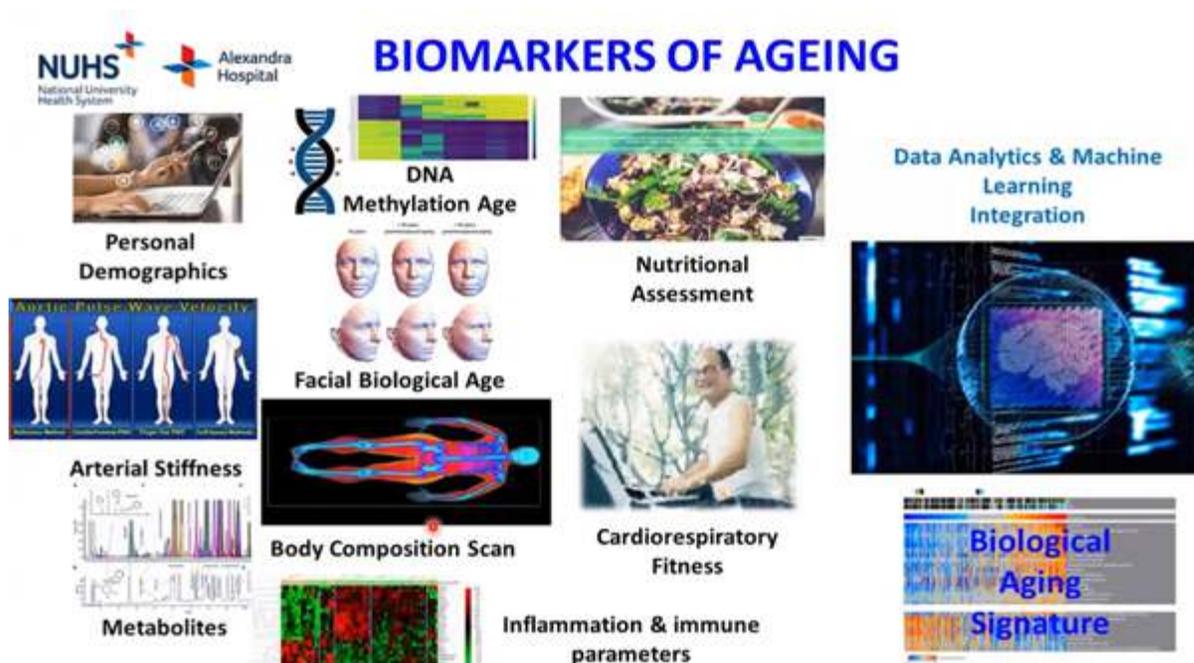
In this session, Brian Kennedy, (Director at NUHS Centre for Healthy Ageing) presented his assessment of the state of aging research in academia and the non incentivized academic research that could dramatically advance progress. After that, Lynne Cox (Professor at University of Oxford) introduced two progress opportunities she identified - new drug discovery approaches focusing on polypharmacology, and in silico systems modeling of aging. Following that was a last presentation from Joris Deelen (Research Group Leader at Max Planck Institute for Ageing), in which he presented ideas on how to get already discovered aging biomarkers into the clinic, as well as a novel approach to utilize genetics of long lived people to move the field forwards.

Opportunities

How would you develop an in silico human model for aging?

A major unmet need is determining ways to screen effectively for drugs that work on complex interconnected systems – phenotypic screens that fully reflect aging biology and look for reversal/rejuvenation in complex human systems.

How can we speed up translatability of model organisms to humans or human observational studies to clinical practice?



Access the full summary and recording

Brain cell replacement as the cornerstone to beating aging



Jean Hebert, Albert Einstein College

March 24, 2021

Summary

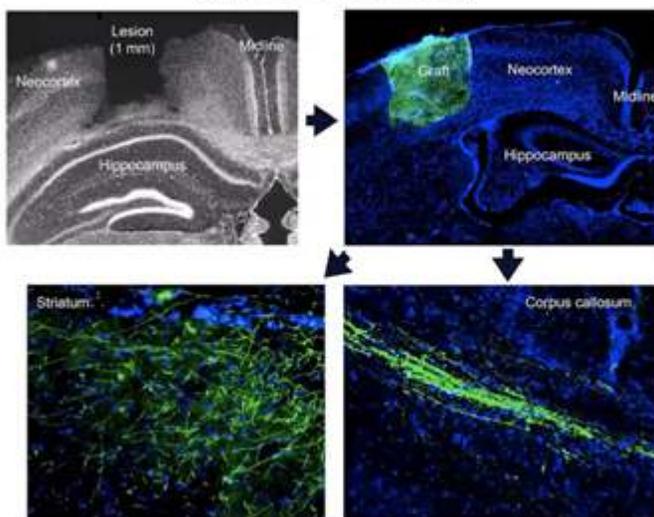
In this session, Jean Hebert (Professor at Albert Einstein School of Medicine) introduced the idea of brain tissue replacement as a necessary strategy for the long term defeat of aging. He went through the history of the field and research so far and presented a case for pursuing this approach further based on the available positive data. He also talked about the roadmap they have for this kind of research even with a pioneering experiment they are pushing for and for which they are now looking for funders.

Opportunities

How can we speed up engineering fully functional replacement brain cells and tissue?

A central challenge for current life extension approaches is slowing or reversing macromolecular damage (which at its core is aging). Regenerative medicine is on track to being able to replace all cells and tissues of the body in the foreseeable future, which could be used to reverse all forms of damage in one shot. Yet, the longevity field largely overlooks replacement as a strategy. The biggest challenge facing replacement therapy relates to the brain. Brain cell replacement for the purpose of age reversal is possible both in theory and in practice without a loss of function or self-identity if done progressively over the course of several years. The challenge, which remains technical (and therefore something we should be able to overcome), is engineering fully functional replacement brain cells and tissue.

Grafting method in mice as a platform for engineering human neocortical tissue.



Quezada et al., unpublished

[Access the full summary and recording](#)

Clinical trials and senolytics

Q & A



James Kirkland, Mayo Clinic

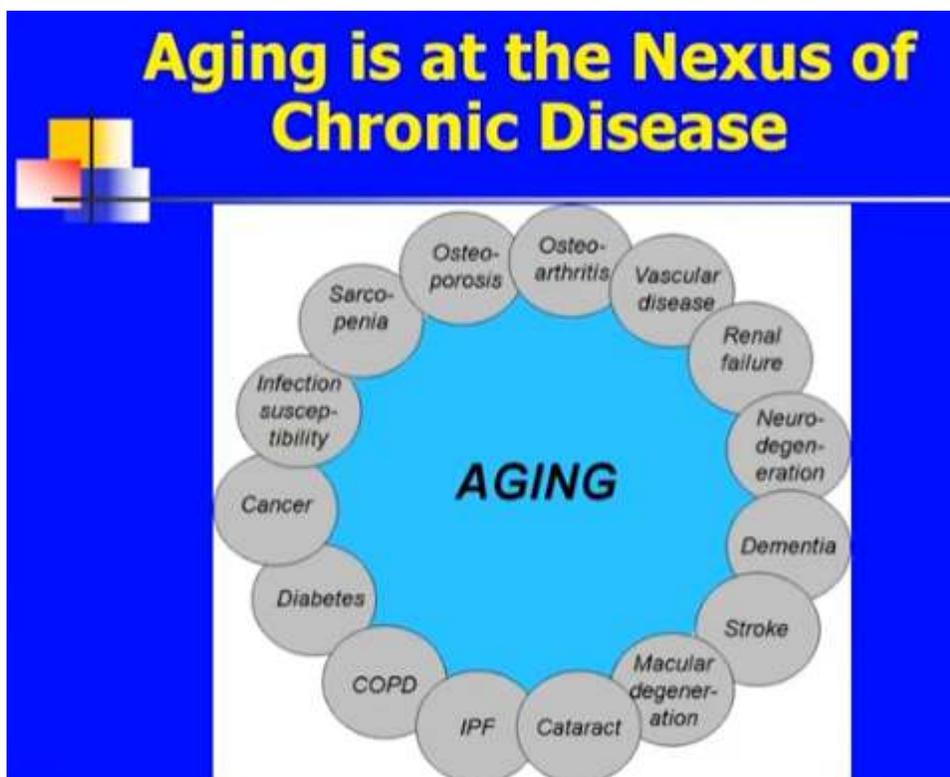
April 3, 2021

Summary

In this session, James Kirkland (Professor at Mayo Clinic) gave a comprehensive overview of the current state of research about senescent cells and senolytic clinical trials. He provided nuanced insights into how senescent cells become senescent, how they work, what kind of functions they can play, and much more. He also went through 15 clinical trials that are currently testing senolytics on different indications and provided explanations and motivations behind the trials and what are the studies already in the process of finding, or discovered recently.

Opportunities

We have a lot of help from the government and foundations. What is very important for people is to get the message out to not take the drugs in an uncontrolled way because we don't know whether these drugs are safe and effective. I give it maybe a 50:50 chance. We are doing the trials because we don't know if they are going to work. As a physician I am very concerned with the Hippocratic oath and the first principle – "first, do no harm". It's a very fundamental process we are playing with, so we'll have to see what happens and prefer a conservative approach at this point. But we are trying to move quickly because we feel it's important to know one way or the other, but I worry.



[Access the full summary and recording](#)

Institutional perspective: Promising aging work from an NIA perspective



Ronald Kohanski, NIA

April 9, 2021

Summary

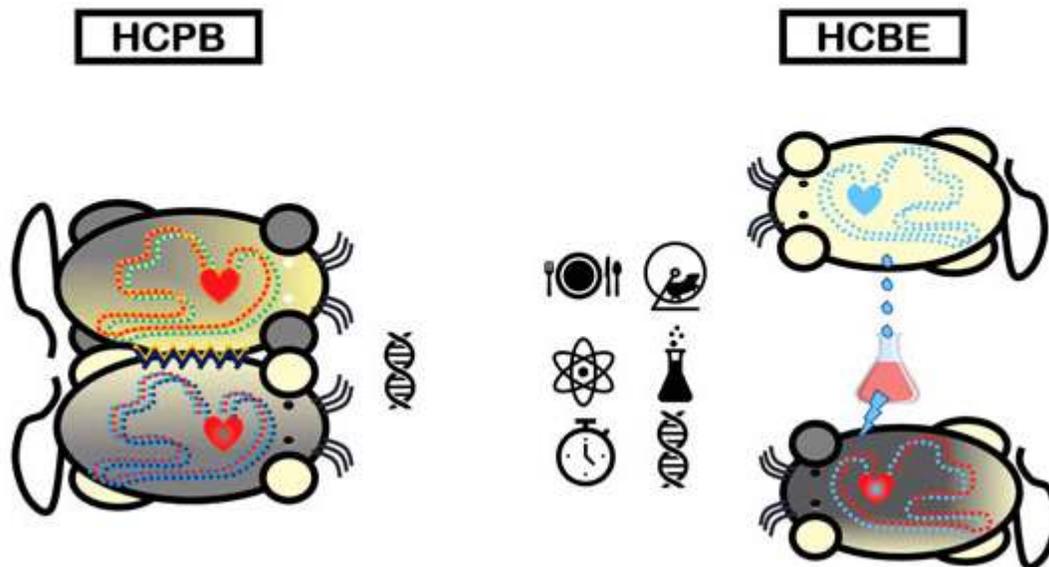
In this session, Ronald Kohanski (Director of Division of Aging Biology at the National Institute on Aging) presented his ideas and suggestions for a way forward from an NIA perspective. He covered many different areas in the field, starting with an overview of metrics and indices the field is using to track health, and the need for developing an aging scale focusing on health expectancy. Then he offered his opinion on interventions that seem promising, particularly on interesting research opportunities for heterochronic blood exchange.

Opportunities

We need to widen our understanding of the basic biology of aging in the human population. This includes widening and diversifying the human demographics we study and finding promising intermediary candidates between mice and humans to study aging.

The NIA could use more public private partnerships - partnering with industry on projects of common interests.

Heterochronic Blood Exchange to Study Rejuvenation and Acceleration of Aging



[Access the full summary and recording](#)

How to fund and build geroprotectors



James Peyer, Cambrian Biopharma

April 18, 2021

Summary

In this session, James Peyer (CEO and founder of Cambrian Biopharma) shared his overview of the longevity biotech industry with insights into what it actually means to be a longevity biotech company, how Cambrian functions, what is a Distributed Drug Discovery Company model and why it will most likely replace single asset biotech companies model, and also the barriers that he sees are preventing us from starting clinical trials with the first geroprotectors. In the end, he also presented a preview of a paper calculating the potential societal value of geroprotectors.

Opportunities

How can we identify and validate a composite biomarker of multi-morbidity risk (MMR)? To get a properly validated biomarker takes three steps:

- Figure out what parameters we could measure, including -omics data, specific markers or assays, but also functional and phenotypic readouts.
- Put gathered data from healthy normals onto a risk curve and show how well the new MMR composite measures risk specificity and sensitivity.
- Validation of the biomarker can only be achieved by doing a placebo controlled interventional clinical trial wherein the MMR biomarker not only predicts whether a person will get a disease but also changes upon the use of an intervention and correctly predicts a decline in MMR over a long trial period.

▼ How to think about Longevity Biotech

- **New, usually patented, therapeutics that target the damage of aging**
- **Table stakes for the field – Choose the indication that gets to rapid evidence of human safety and efficacy**
- **Must have the possibility of either delaying or preventing diseases of aging to extend healthspan**
- **The hallmarks of aging are a useful guide, but not a gospel**
- **Longevity biotech companies must be structured to achieve value from both their first indication and their geroprotective potential, otherwise the “longevity” tag is just marketing**

[Access the full summary and recording](#)

Biomarker development for FDA-recognized diseases



Christopher Leptak, FDA

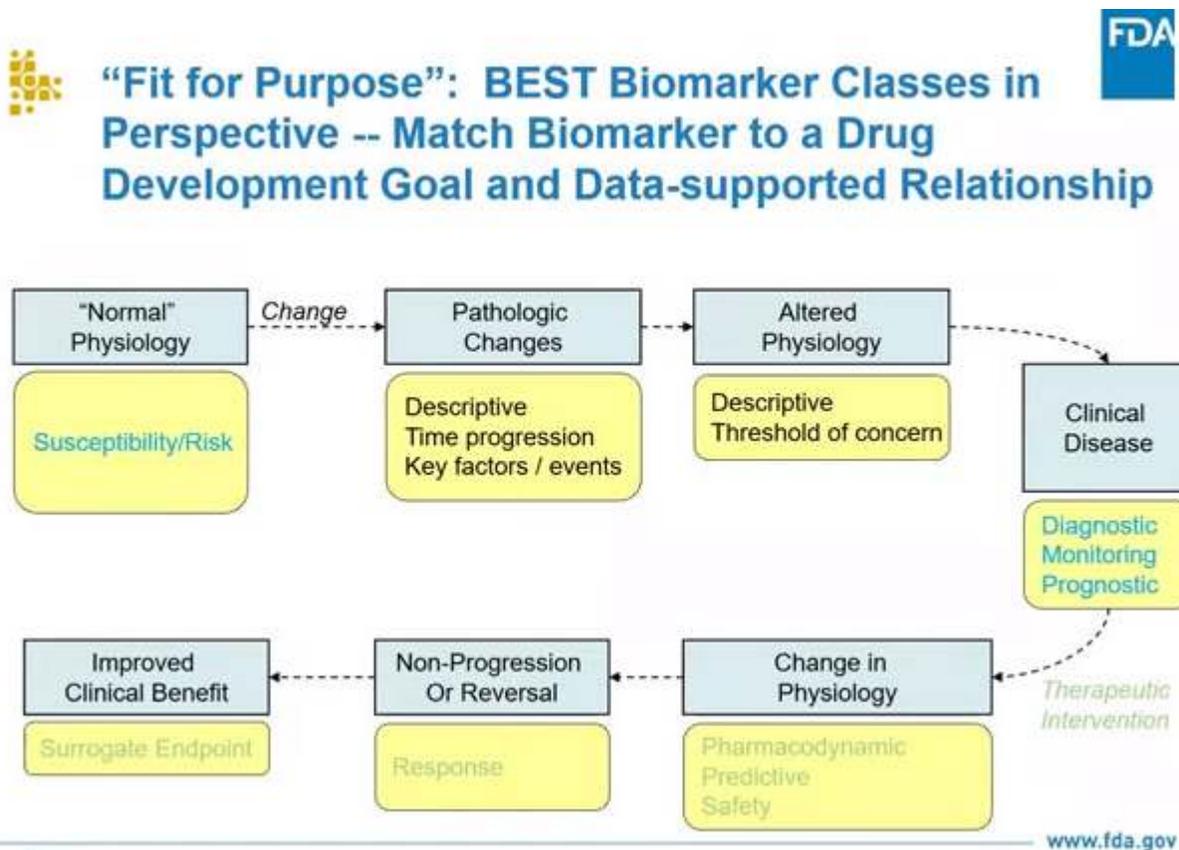
May 1, 2021

Summary

In this session, Christopher Leptak (Director at New Drug's Regulatory Science Program Office) in the FDA's Center for Drug Evaluation and Research, elucidated how the FDA is approaching biomarkers specifically for drug development, what is actually considered a biomarker and what needs to happen for a new biomarker to be used. Apart from valuable tips and insights about the process, and a range of resources on how to prepare for it, he also offered his opinion on the way the longevity field could approach biomarkers with relation to aging.

Opportunities

We are looking at certain things, for example for eye tracking for autism spectrum disorder, and that is also a biomarker that we are looking into in Alzheimer. The openness is there, but the hurdle is probably on the other end – which diseases are we going to target and how to convince the pharma partners. Focus on the people who have the power, and for whom these problems are in their paygrade. Commissioners, secretaries, folks in congress - talk to them.



[Access the full summary and recording](#)

ALARMA (America's Longevity, Aging and Regenerative Medicine Association)



Dylan Livingston, Alliance for Longevity Initiatives May 27, 2021

Summary

In this session, Dylan Livingston (Founder and Executive Director at The Alliance for Longevity Initiatives) introduced the first 501(c)(4) nonprofit organization focused on advocating for government-sponsored initiatives and policies to increase healthy human lifespan in the US. He went over the reasons why it was needed and teased the first draft of the action plan, based on which an insightful debate took place.

Why the time is right now...

- Geroscience therapeutics 1.0 will be released over the next decade, so let's establish this organization now so we can get out in front of the issues before it's too late.
- COVID has given everyone a wake up call about their day-to-day health and people are starting to understand that a preventative approach to healthcare is better.
- Eric Lander is the head of OSTP and while he isn't necessarily a longevity enthusiast, he has friends in our community
- Democrats may only be in power for another year and a half - not saying they are better or worse for the cause necessarily, but this is where my network is.
- Aubrey said so over a year ago!

[Access the full summary and recording](#)

Thymus rejuvenation progress update



Greg Fahy

May 27, 2021

Summary

In this session, Greg Fahy (Co-Founder of Intervene Immune and Principal Investigator of the TRIIM and TRIIM-X clinical trials) offered a sneak peek at some preliminary data from the TRIIM-X clinical trial along with updates about its development, progress, and conditions of the enrollment, as well as optimistically looking first preliminary results. Following discussion touched on possible next steps for their company, like developing a much cheaper growth hormone alternative, the possibility of prolonging the lifespan of kidney transplants, or reprogramming thymus with grafts to completely solve transplant rejections and autoimmune diseases.

Opportunities

- Tell your friends that TRIIM-X is open for enrollment, we keep things going by enrolling more people. It is our only source of income and knowledge. So anyone who is interested in the trial and is able to invest \$18k into it – which is pretty steep I know, we are working on it – will be appreciated.
- Tell your investment friends about TRIIM-X as well, just in case they might be interested in some of the things we have talked about, be it the GH alternative or the bioengineering and thymus reprogramming aspect.
- www.interveneimmune.com

BACKGROUND: THE GENERAL IDEA

The **Thymus** is the site at which **T cells** are generated.
T cells are major effectors of the adaptive immune system.
Loss of competent T cells is a major component of **immune system aging**.
T cell loss is apparently driven by **reduced thymic function** with age.
Reduced thymic function is due to programmed **thymic involution**.

THYMUS ORGAN MORPHOLOGY

HISTOLOGICAL PATTERN OF A THYMIC LOBULE

NEWBORN 10 YEARS OLD 25 YEARS OLD 50 YEARS OLD 70 YEARS OLD

Vessels Perivascular space Adipose tissue in perivascular space

Thymus

T cell incompetence is a **major cause of age-related morbidity and mortality**.
Therefore:
It is imperative to **reverse thymic involution**.

[Access the full summary and recording](#)

Longevity as a service: AI & aging clocks



Alex Zhavoronkov, Insilico Medicine

June 4, 2021

Summary

In this session, Alex Zhavoronkov (CEO and Founder of Insilico Medicine and Deep Longevity) offered his roadmap for what he calls Longevity as a Service. He explained the approach Deep Longevity and Young.ai are taking, the various clocks and machine learning methods they are using, the necessity for physician education, and coordinated building of a longevity ecosystem spanning physicians, clinics, insurers, academia, pharma, and more. And he also went into detail about a promising new interesting field of longevity psychology and connected subjective and psychological clocks.

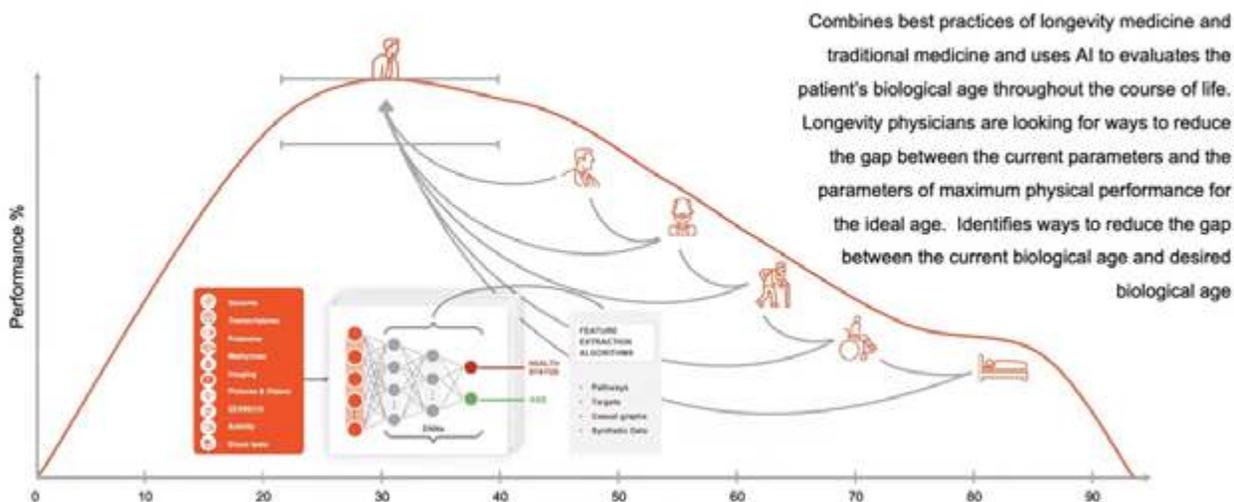
Opportunities

In the short term we are looking at the Deep Longevity app for which we are hiring.

Insurers will not change without medicine, medicine will not change without insurers, pharma companies will not change without medicine and insurers, academia is not going to accelerate without a huge consumer business. In order for us to drive Longevity as a Service vision, we need to ensure that all those areas are progressing very quickly and at the right pace, and we cannot progress faster than physicians and medicine, so that's why we need to ensure that medical doctors are engaged, involved, and educated.

I would also suggest growing a wider array of aged monkeys. Most experimental monkeys are around 3 years old, and longitudinal data is lacking.

Longevity Medicine



[Access the full summary and recording](#)

Biomarker & aging clock development



**Gordon Lauc, GlycanAge
Vadim Gladyshev, Harvard**

June 14, 2021

Summary

In this session, Gordon Lauc and Vadim Gladyshev gave their point of view on biomarkers & aging clocks development. Gordon Lauc went through the interesting glycomic data they recently and insights it generated about aging and menopause, exceptional predictive capability of glycans for hypertension, and much more. Vadim Gladyshev then went through the approach to molecular signatures and biomarkers that they are employing to find and test interventions to extend lifespan. Part of it is also a new epigenetic clock called scAge functioning on a single cell basis. This clock enabled them to find when aging actually begins during embryonic development.

Opportunities

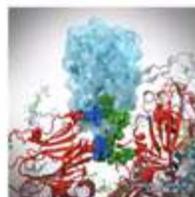
How can we make our immunoglobulins young again?

While we are young, glycans on immunoglobulins effectively suppress inflammation, but as we get older, glycans change and immunoglobulins lose the capability to suppress inflammation. We have mapped a network of over 40 genes that work together to regulate IgG glycosylation and through future research specific activators or inhibitors can be developed that could rejuvenate our immunoglobulins and suppress inflammation.

How can we accelerate the process of validating near-term interventions for lifespan extension to convince more money and talent that radical progress is possible?

It might be rejuvenation technologies that partially reprogram subsets of cells in an organism, bioengineering approaches that support cell replacement, genome editing strategies informed by cross-species analyses, or complex metabolic interventions that alter the organism itself. These advances will prove that it is possible to extend human lifespan, bringing more money and talent required for radical progress.

Glycans are the ultimate layer of molecular complexity
most neglected molecules of cellular communication



Casalino L et al
ACS Cent. Sci., 2020

The majority of proteins are glycosylated

SEE THE COMPLETE PICTURE
INCLUDE GLYCANS
IN YOUR STUDY

Access the full summary and recording

Biomarker and aging clock development needed to spur progress on aging

Steve Horvath, UCLA

June 28, 2021



Summary

In this session, Steve Horvath (Professor at the University of California Los Angeles), provided an overview of the current state of the epigenetic clock field and the new developments in it. He then went on to talk about what is missing in regards to methylation clocks and the longevity field itself, as well as what might be the next steps - the holy grails we should strive toward. He also went on to address some of the common misconceptions tied to epigenetic clocks at the end.

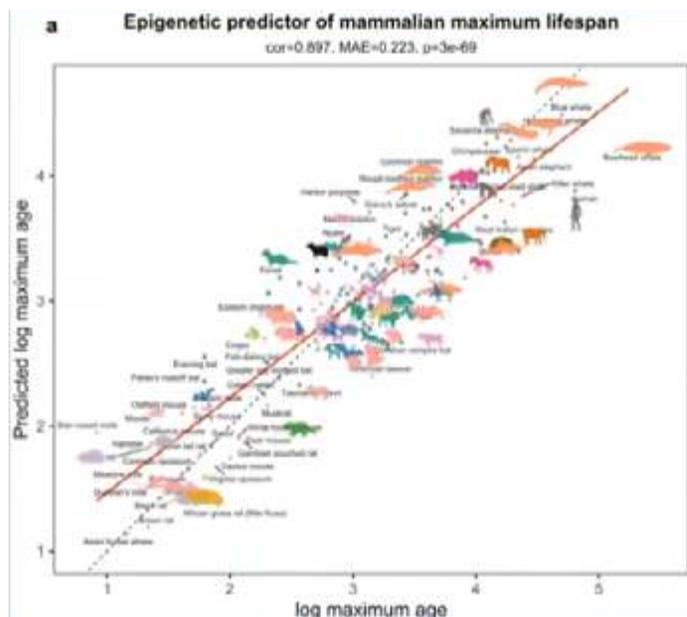
Opportunities

How can we develop causal aging clocks that apply to humans?

The answer is difficult due to two fundamental problems - we don't have validated anti-aging interventions in humans and we don't have consensus on the true causes of aging. This leads to a catch 22 situation. Without biomarkers, we cannot validate anti aging interventions in humans. Without anti-aging interventions, we cannot validate biomarkers.

Potential workarounds:

- Build a clock based on genes/proteins/pathways that are causally involved in aging. Problem: which ones?
- Use non-validated interventions. Simply ASSUME that certain interventions reverse human aging. Ex. Exercise, caloric restriction, rapamycin, metformin, etc
- Multi-species clocks that track validated anti-aging interventions in animal models.



[Access the full summary and recording](#)

Biomarker standardization

Jamie Justice, Wake Forest
Morgan Levine, Yale

July 9, 2021



Summary

In this session, Morgan Levine (Assistant Professor at Yale), gave a sneak peek into the new epigenetic clock they are developing that is able to probe into multiple organ systems, as well as on a new approach how to calculate clocks that is much more reliable, enabling to generate insights from methylation clocks with much smaller samples required. The second talk was given by Jamie Justice (Assistant Professor at Wake Forest) that covered the current ways and strides the longevity field is making towards validating biomarkers of aging through clinical trials, shown on examples of a few senolytic trials they made. In the end she also explained how exactly the TAME trial, which she is a coordinator of, should serve as a vehicle for the field to move further and have a flagship trial to validate new aging biomarkers against in the future.

Opportunities

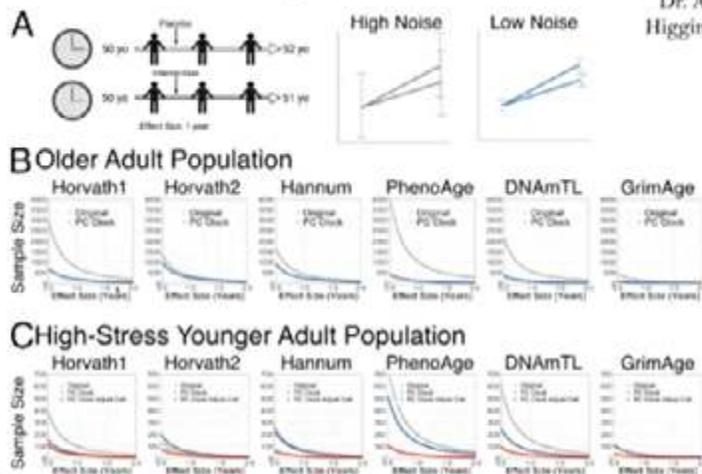
- We have no fundamental understanding of what drives DNA methylation changes with aging or how they directly connect to manifestations of aging at the tissue or organismal level. We need to focus on understanding the causal nature of methylation clocks.
- We need to define feasible trial designs and outcomes that require multidisciplinary communication from investigators and key stakeholders.
- Right now we are not only testing promising therapeutics that may target aging, but also our approaches to demonstrate that they are effective. Defining and testing the populations, designs, outcomes, and biomarkers in a harmonized and transparent way is as essential as testing the investigational agent.
- Biomarkers for clinical trials in geroscience are desperately needed.

Reliability

Power Analysis for interventions



Dr. Albert Higgins-Chen



[Access the full summary and recording](#)

Patient trials in a dish



Keith Murphy, Organovo

July 13, 2021

Summary

In this session, Keith Murphy (founder of Organovo and CEO and founder of Viscient Biosciences), covered the recent developments in the field of 3D tissue bioprinting and human organ models on a chip or sometimes also called patient trials in a dish. He went into the different technologies that are being used and trialed, applications and markets that are going to be the first affected by these innovations, and also tissue examples that are currently possible to develop. He also provided a good overview of the regulatory hurdles that the field will have to go through with some examples of companies and organizations paving the way.

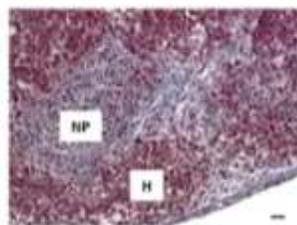
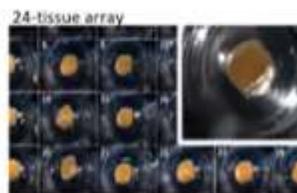
Opportunities

How do we create a permissive clinical paradigm for longevity products that allows informed and consenting volunteers to readily participate in research on potentially transformational interventions, to speed their development?

Cautious clinical advancement is important in the context of for-profit medicine and when drawing from a pool of the entire population, but by drawing from a more educated and informed pool, the pace of testing could be improved. Longevity research in particular has a dedicated and well-informed following, and a volunteer clinical trial scheme could allow them to push rigorous knowledge forward. Current regulations around enrolling people in clinical trials protect individuals from participation that would be inappropriate, but a scheme could be developed that allows certain willing, informed, and consenting participants with a particularly sound understanding of the risks and benefits to participate.

Organovo's 3D bioprinting platform enables unique liver tissue model, ExVive Liver Tissue

- Fully human multicellular structure, three cell types, all primary human cells
 - Hepatocytes
 - Stellates
 - Endothelial Cells
- Patterned architecture in 3D, specific cell types in specific positions
- Architecture supports sustained function and viability (e.g., >6 weeks), enabling low-dose, chronic toxicity modeling



Distinct zones of hepatocytes (H) and non-parenchymal cells (NP)

[Access the full summary and recording](#)

TAME Q&A: Lessons for progress on aging



Nir Barzilai, NIA

July 27, 2021

Summary

In this session, Nir Barzilai (Professor at Albert Einstein School of Medicine and director of Institute for Aging Research), presented the current state of the groundbreaking TAME trial serving as a framework and data springboard for the whole longevity field, as well as the future plans for TAME-like trials with other drugs with high potential for repurposing for aging. At the end he and Jamie Justice answered questions about the trial design as well as broader inquiries about Metformin - like its effect on muscle building with exercise and the ideal dosing.

Opportunities

Phase 1 (now): We need to have clinical examples of aging that we can target so we can move on with newer and better science. We need several TAME like trials with other drugs that can be repurposed soon.

Phase 2 (science) is using our capacity as a species to live ~115 years at a time where the best life span is ~80. Many centenarians are an example of slow aging and their longevity genes have been identified. We need to capture all the genetic data to identify pathways, not just individual genes. We need to recruit and sequence the genomes of >10,000 centenarians/supercentenarians to develop drugs based on human data.

Phase 3 (in parallel) to help in healthspan by focusing on stem cells and organ replacement for older adults, or by erasing aging monthly in young people.

Metformin Attenuates Biological Hallmarks of Aging

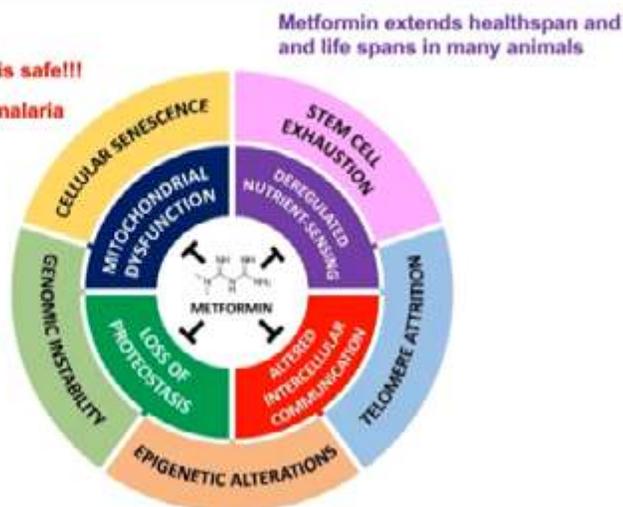
Its been used for 70 years and is safe!!!

It was used to prevent flu and malaria

Its generic and cheap

TAME will show it targets aging

Kulkarni et al Cell Met 2020



[Access the full summary and recording](#)

Drug target discovery for cellular rejuvenation by the application of 'driver' clocks to cell reprogramming



Daniel Ives, Shift Bioscience

July 29, 2021

Summary

In this session, Daniel Ives (founder of Shift Bioscience) introduced their transcriptomic driver clock which enabled them to identify putative drug targets for safer cellular rejuvenation, which might avoid the challenges coupled to therapeutic use of Yamanaka factors. Daniel goes into detail on what the clock enables, how they are planning to validate these putative targets, his wishlist for tools that could help speed up and de-risk longevity and aging focused drug development, and their upcoming capital raise.

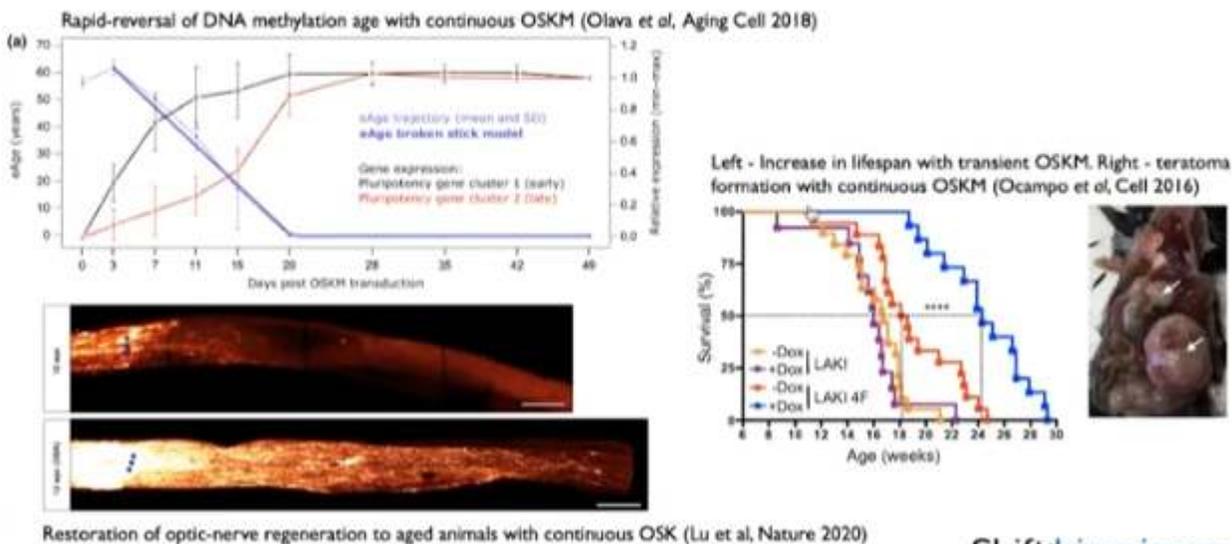
Opportunities

How can we gauge changes in biological age (not just chronological age) in human cells in vitro and mice to speed the development of rejuvenation interventions?

How can we expand the capability of multi-omic techniques, so that 'causal' or 'driver' aging biomarkers can be trained across a multitude of molecular layers?

How can we redirect the 'causal' or 'driver' biomarker approach to extract causal/driver biology specific to a given age-linked disease?

A powerful rejuvenation paradigm, with risks



Shiftbioscience

[Access the full summary and recording](#)

Regenerative medicine focus



Michael Levin, Tufts University

August 19, 2021

Summary

In this session, Michael Levin (director of the Tufts Center for Regenerative and Developmental Biology) introduced the field of bioelectricity, and the impressive regenerative potential it harbors. Michael showcased techniques that enable regrowth of limbs and formation of different organs using bioelectricity and cocktails of repurposed ion channel drugs. And he also gave an answer to the fundamental question of where does shape come from and how we could possibly program it in any way we want.

Opportunities

- Develop technology to non-invasively read and write the bioelectric states of body tissues (not just neurons),
- Crack the bioelectric code by which cellular networks process anatomical information
- Produce simulator platforms that enable us to choose ion channel stimulation protocols to control the activity of cell collectives.

By developing voltage imaging technology that can reach beyond the outer surface of the skin (the current state of the art) and reveal the bioelectric states of the body tissues, we would be able to design electroceutical approaches for regeneration of complex organs, repairing of birth defects, and reprogramming tumor cells into healthy tissues. More broadly, we would be able to exploit endogenous bioelectric networks as the computational medium that enables cells to cooperate toward the construction and repair of anatomical structure. Better access to this instructive software of life would enable us to communicate structure and function goals to the cellular collective intelligence, instead of trying to micromanage pathways bottom up as modern molecular medicine seeks to do. This would get around the complexity problems that limit the impact of genomic editing and stem cell approaches, enabling transformative applications in regenerative medicine.

Remodeling until a "correct frog face" is made

Normal

Picasso-like

Genetics does not specify hardwired rearrangements: it specifies a system that executes a highly flexible program that can recognize unexpected states and take corrective action.

Cannot just follow a rote set of steps. How does it know when it's "right"?

Change bioelectric prepatterning

Craniofacial mispatterning

Metamorphosis

Morphometric analysis and modeling reveals: faces fix themselves!!

dorsal profile

unaffected

unaffected eyes

[Access the full summary and recording](#)

Monitoring personal health and ageotypes using big data



Michael Snyder, Stanford University

August 26, 2021

Summary

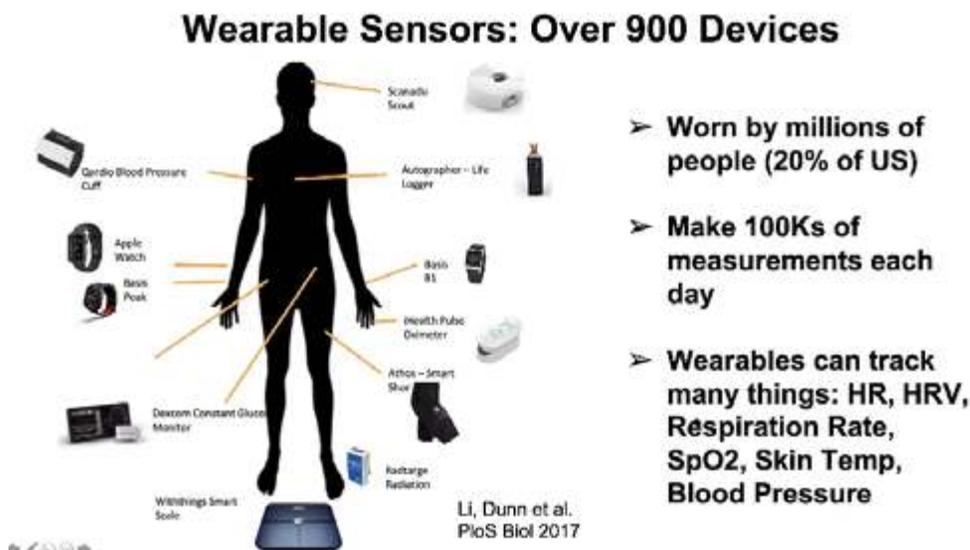
In this session, Michael Snyder (Professor in Genetics at Stanford University) reported the latest findings from their longitudinal trials of healthy people being profiled using various omics and wearables. The first part was focused on the necessity of collecting a healthy personal baseline, because the differences between people are much larger than significant variations from personal baseline. Trying to apply a standard value for something like weight or heart rate across the board is impossible. It is much more effective to measure an individual's baseline and then track changes in relation to that.

He brought up "ageotypes", patterns of aging that were found in clinical markers collected over time, which cluster aging data in a more actionable way. The last part of the talk was about COVID in the context of wearable data and how they can predict the onset of infectious diseases.

Opportunities

Join the Stanford diet and cognition study: <https://snyderlabs.stanford.edu/fiberandcognition/>

The immediate future of health diagnostics appears to be focused on wearable devices. Development of these wearables to collect massive amounts of data is going to radically alter how we approach healthcare over the next decade.



[Access the full summary and recording](#)

Quantification of the pace of biological aging: the DunedinPoAm DNA methylation algorithm

Terrie Moffitt, Duke University
Daniel Belsky, Columbia

September 13, 2021



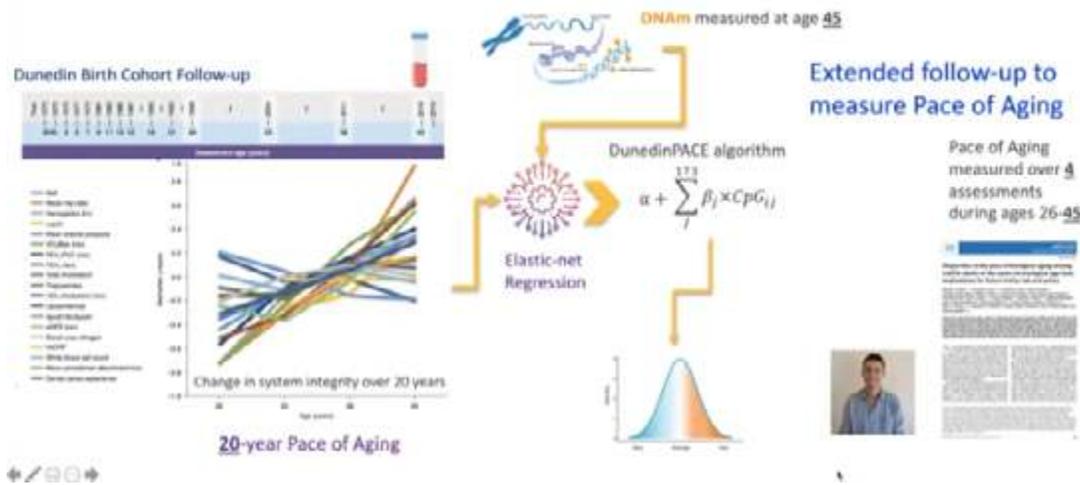
Summary

In this session, Terrie Moffitt (Professor at Duke University) and Daniel Belsky (Assistant Professor at Columbia University), dove into the details of a new approach to measuring aging using DNA methylation. Their Pace of Aging approach, based on which a second generation DunedinPACE algorithm was developed, looks at multiple timepoints and assesses how fast or slow a person ages (like a spinometer), compared to previous methylation based diagnostics (working more like a clock). They discuss the advantages of this new method and announce the availability to researchers and the public as well. The Dunedin longitudinal study plays an important part, which is why that is a significant part of the discussion.

Opportunities

There are numerous DNA methylation-based clocks for measuring age in clinical trial participants. And DunedinPACE is a DNA methylation-based tool for measuring the current pace of aging in trial participants. But whole-genome methylation is still expensive. What's the solution for translating methylation measures to something cheaper that is feasible for repeat administration throughout a gero-protective clinical trial? Aging measures need to be validated as sensitive to therapeutic change by giving them to participants in already proven-effective drug or behavioral treatments to slow aging. How can we get this work going? What are the barriers?

A 2nd Generation DNAm Pace of Aging: DunedinPACE



[Access the full summary and recording](#)

Biotech bountied brainstorm

The Bountied Brainstorm allows participants to ask open-ended questions, answer questions posed by others, and vote on the best answers. Foresight pays monetary bounties for each contribution and the best answers. Some questions are private, others are public. For instance, check out the answer to:

[What will our lives look like once we hit escape velocity in longevity?](#)