LE
MAGAZINE

The Prospect of Human Age Reversal

Age-reversal research is rapidly accelerating. Bill Faloon summarized many of these findings at a scientific conference, including delayed aging using young plasma, resetting youthful gene expression with transcription factors, elongating telomeres with hyperbaric oxygen, the first human trial using CRISPR gene therapy, and other exciting developments.

Scientifically reviewed by: **Dr. Gary Gonzalez**, MD, in May 2022. Written by: William Faloon.

Each year there are scientific conferences where presentations are made about slowing and reversing aging processes in lab models and people.

Groups that I fund send experts to many of these events to learn better ways of keeping people alive and healthy for as long as possible.

I announce these findings at a conference that **Life Extension** helps sponsor called **RAADfest**, which stands for **Revolution Against Aging and Death**.


William Faloon

Each year, about 1,000 people attend this event where speakers describe mechanistic ways for people to thwart degenerative processes.

This article summarizes highlights from my keynote presentation at **RAADfest 2021**.

My presentation opens by outlining the major topics I will discuss, as can be seen on the following slide.

TRANSCENDING TOWARD SUPER LONGEVITY

Today's Overview

- **Research findings since last year's RAADfest.**
- **What people can do now to live 5 more years.**
- **Repopulate bone marrow with autologous stem cells to reverse immune senescence.**
- **Transhumanist advances over last few months.**

I let the audience know that ***Life Extension®*** has been publishing groundbreaking research findings for the past **41 years** in our monthly publications:

Our contention that aging may be reversible today is controversial. I make it clear that we nonetheless proceed

forward no matter what obstacles stand in our way.

Most attendees at these conferences are aware of **research** dating back to the 1950s showing that when **young blood** is continually circulated into old animals, the old animals grow biologically ***younger***.

What's important about this research is that it proves a concept, i.e., it is possible to partially **regenerate** old animals.

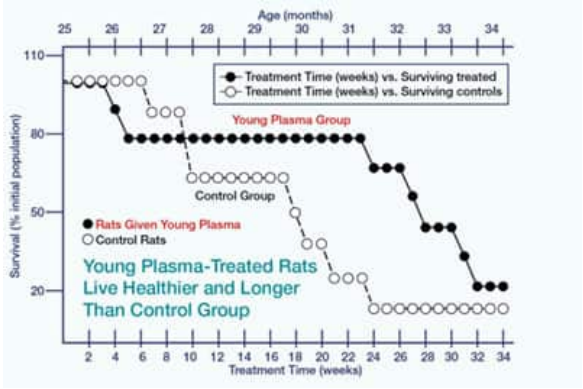
My first announcement was a study our groups funded showing that injecting **young plasma** into rats the **human** equivalent of **60 years** enabled quality-of-life enhancements and some longevity benefits.

The **young plasma**-treated rats looked and behaved *younger* than the same age control group.

The slide below shows that rats given **young plasma** (solid black dots) lived much longer before degenerative changes set in compared to the **control** group (blank circle dots).

The **young plasma**-treated rats may have lived seven additional human equivalent years compared to the control groups. I acknowledged that calculating **human equivalents** to rodent lab models is an imprecise science.

The box below summarizes highlights from this **young plasma** study that our groups helped to fund:



SURVIVAL + QUALITY-OF-LIFE IMPROVEMENTS IN RATS RECEIVING YOUNG PLASMA (I.P.) EVERY 2 WEEKS

- **Rats aged human equivalent of 60 years given Young Plasma via intraperitoneal injection.**
- **Transient improvement in quality of life.**
- **Average Lifespan of untreated group: 29.8 months (70 years in humans)**
- **Average Lifespan of treated group: 32 months (77 years in humans)**
- **On May 23, 2021, seven treated rats alive compared to one living control.**
- **On July 20, 2021, two treated rats alive compared to one living control.**

Email from Professor Rodolfo Goya to Bill Faloon August 16, 2021.

I reminded the audience of a separate study where a **young plasma fraction** cut a measure of aging in half in old rats. This was calculated by **epigenic age** using the "Horvath Clock." The Horvath Clock is the most reliable current measure of biological age, and this study is described on the following three slides:

My emphasis was on the **consistency of evidence** about **rejuvenating** factors in **young plasma**. I let the audience know our challenge in the box below:

YOUNG PLASMA FRACTION INDUCES AGE REVERSAL IN MAJOR TISSUES

bioRxiv April 21, 2020

Young plasma treatment more than **halved** the **epigenetic** ages of blood, heart, and liver tissues.

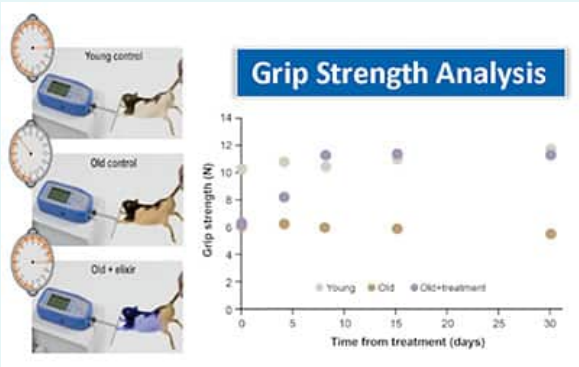
Epigenetic clock measures indicate systemic rejuvenation.

Horvath, S., Singh, K., Raj, K., Khairnar, S., Sanghavi, A., Shrivastava, A., … & Lehmann, M. (2020). Reversing Age: dual species measurement of epigenetic age with a single clock. bioRxiv.

REJUVENATING EFFECT ON GRIP STRENGTH IN OLD RATS

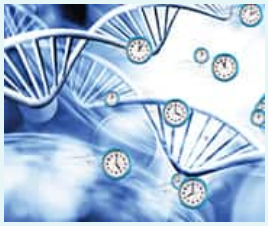
Within 10 days of **young plasma fraction** treatment the physical capabilities of **old rats** are indistinguishable from that of the **young rats**.

Horvath, S., Singh, K., Raj, K., Khairnar, S., Sanghavi, A., Shrivastava, A., … & Lehmann, M. (2020). Reversing Age: dual species measurement of epigenetic age with a single clock. bioRxiv.



bioRxiv April 21, 2020

DNA METHYLATION MEASURES EPIGENETIC AGE



DNA methylation controls the transcription (activation) of genes.

Without proper DNA methylation beneficial genes are deactivated while harmful genes can be overexpressed.

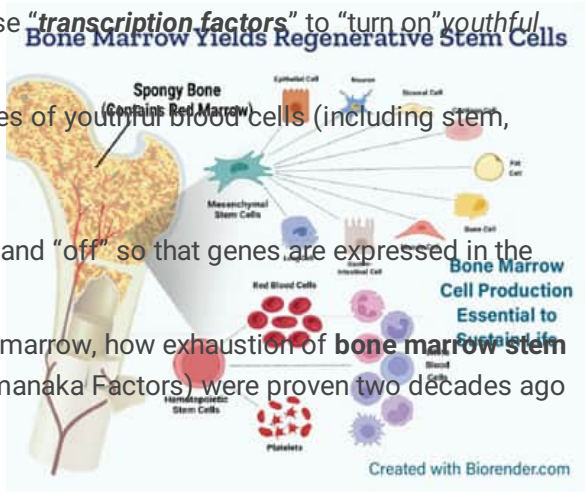
This is the principle of what is called “epigenetic aging.”

Young plasma treatment more than halved epigenetic ages.

Horvath, S., Singh, K., Raj, K., Khairnar, S., Sanghavi, A., Shrivastava, A., … & Lehmann, M. (2020). Reversing Age: dual species measurement of epigenetic age with a single clock. bioRxiv.

“How to Transition Young Plasma Benefits into Old Humans?”

The proposed solution as described in the following slides is to use “***transcription factors***” to “turn on” *youthful* **gene expression** in human **bone marrow**.



This may enable our own bone marrow to generate endless supplies of youthful blood cells (including stem, progenitor and immune cells) to induce **systemic age reversal** and keep us young.

Transcription factors are cellular proteins that turn our **genes** “on” and “off” so that genes are expressed in the right cell, at the right time, in the right amount.

The following five slides describe the importance of healthy bone marrow, how exhaustion of **bone marrow stem cells** limits lifespans, and how ***transcription factors*** (including Yamanaka Factors) were proven two decades ago to reverse aging in old cells.

I then announced a review article that we **funded** that was published in **February 2021** in a respected scientific journal. The purpose of this article was to summarize data that began accumulating in **2006** showing that it is possible to fully reverse **aging** in old cells using ***transcription factors*** to turn *youthful* **gene expression** back on.

THE NOBEL PRIZE IN PHYSIOLOGY OR MEDICINE

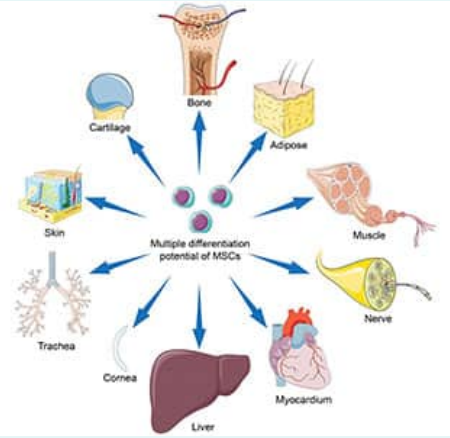
“For the discovery that mature cells can be reprogrammed to become pluripotent.”

Four specific genes encode *transcription factors* that can convert somatic cells into pluripotent stem cells that can propagate indefinitely. **“Yamanaka Factors”**

The Nobel Prize was awarded to John B. Gordon and Shinya Yamanaka—two scientists who discovered that mature, specialized cells can be reprogrammed to become embryonic cells capable of developing into all tissues of the body.

https://www.nobelprize.org/prizes/medicine/2012/yamanaka/facts/

STEM CELLS NATURALLY ENABLE SYSTEMIC REJUVENATION



But our supply of hematopoietic and mesenchymal stem cells is limited.

Transcription factors can reprogram old cells into induced pluripotent **stem cells** that can theoretically regenerate our tissues forever.

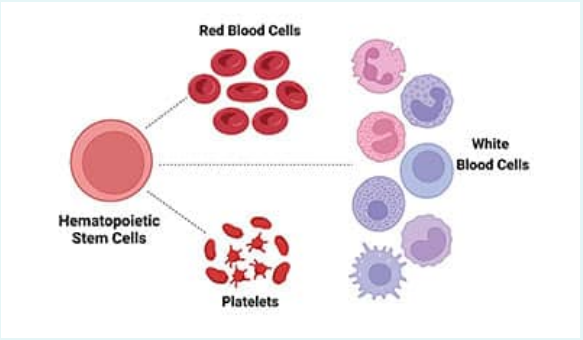
HEMATOPOIETIC STEM CELLS

can develop into all types of blood cells and are found in peripheral blood and bone marrow.

With age, hematopoietic stem cells become depleted and contribute to **immune senescence** and anemia.

Healthy hematopoietic stem cells are needed to sustain life.

https://www.cancer.gov/publications/dictionaries/cancer-terms/def/hematopoietic-stem-cell



HOW BLOOD CAN BE REJUVENATED

Lund University February 2017

- Blood stem cells generate around a thousand billion new blood cells every day.
- The capacity of hematopoietic stem cells to produce new blood cells diminishes with age.
- Older people are more susceptible to anemia, lowered immunity, and blood cancers.
- Researchers at Lund University (Sweden) rejuvenate blood stem cells in aged mice.

"We found that there was no difference in blood-generating capacity when we compared the reprogrammed blood stem cells with healthy blood stem cells from a young mouse. This is, as far as we know, the first time someone has directly succeeded in proving that it is possible to recreate the function of young stem cells from a functionally old cell."

Wahlestedt, M. et al. Clonal reversal of ageing-associated stem cell lineage bias via a pluripotent intermediate. Nat. Commun. 8, 14533 doi: 10.1038/ncomms14533 (2017).

Authors of this review discuss several studies, including one demonstrating that cells from **100-year-old** people can be "**reprogrammed**" into induced pluripotent **stem cells**.

The next step in transitioning this science to **whole-body regeneration** is to **multiply** the reprogrammed **stem cells** (genetically identical to the donor host) and then transplant the **reprogrammed** stem cells back into the same donor. The objective is **systemic rejuvenation**.

By highlighting key findings from eight independent studies, this review article (published **February 28, 2021**) urged that this technology be transitioned into whole-animal studies and then **people** if the animals safely grow

biologically *younger*.

The **regenerative** potential of these **cellular reprogramming** discoveries is so profound that on **September 4, 2021**, MIT announced that **Jeff Bezos** and another billionaire are committing hundreds of millions of dollars to enable this technology to allow older people to grow biologically **younger**.

February 28, 2021

NATIONAL LIBRARY OF MEDICINE

"Aging and Rejuvenation – A Modular Epigenome Model"

"When cells were reprogrammed with a 6-factor cocktail the (degenerative) alterations were fully reversed and cells fully rejuvenated."

This 2021 published review and additional investigations summarize age-reversal impact of cell reprogramming.

- Human trials being investigated.
- Funded by Bill Faloon and other charitable donors.

Chiavellini P, Canatelli-Mallat M, Lehmann M, et al. Aging and rejuvenation—a modular epigenome model. Aging (Albany NY). 2021;13(4):4734-4746. doi:10.18632/aging.202712

My next announcement was how we plan to implement this **bone marrow restoration** research as can be seen in the slide below:

REBUILD BONE MARROW TO RESTORE YOUTH

Human Research Initiative:

Step 1: Selectively remove senescent bone marrow cells.

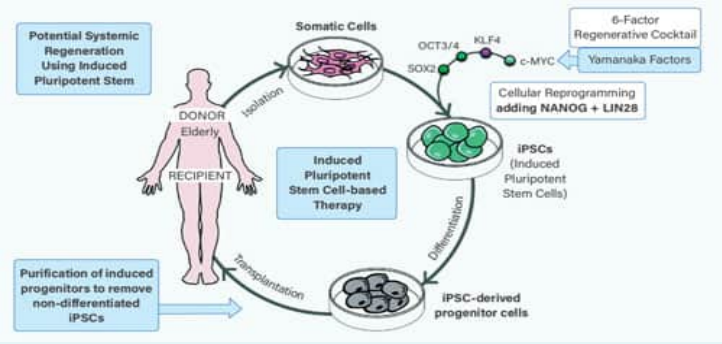
Step 2: Replace with induced autologous pluripotent hematopoietic stem cells to rebuild immunity.

Step 3: Also use transcription factors to make autologous mesenchymal stem cells for systemic regeneration.

Large-animal pilot studies will first evaluate safety and regenerative efficacy.

I created the following diagram to outline the step-by-step process that we will help fund over the next two to three years to use donor cells that will be **reprogrammed** back to **pluripotent stem cells** using ***transcription factors*** and then **transplanted** into the original **donor host**:

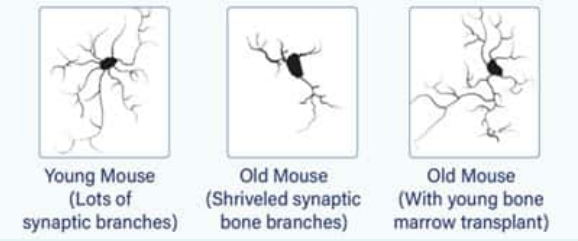
Old **fibroblasts** reprogrammed into **autologous** induced pluripotent **stem/progenitor cells**. **(This kind of rejuvenation research is now being funded by Jeff Bezos and others.)**



The next two slides demonstrate *in vivo* **brain regeneration** and systemic energizing effects that occur when **young** bone marrow is transplanted into **old** rats.

Medical Xpress February 28, 2021

YOUNG BONE MARROW REJUVENATES AGING MOUSE BRAINS

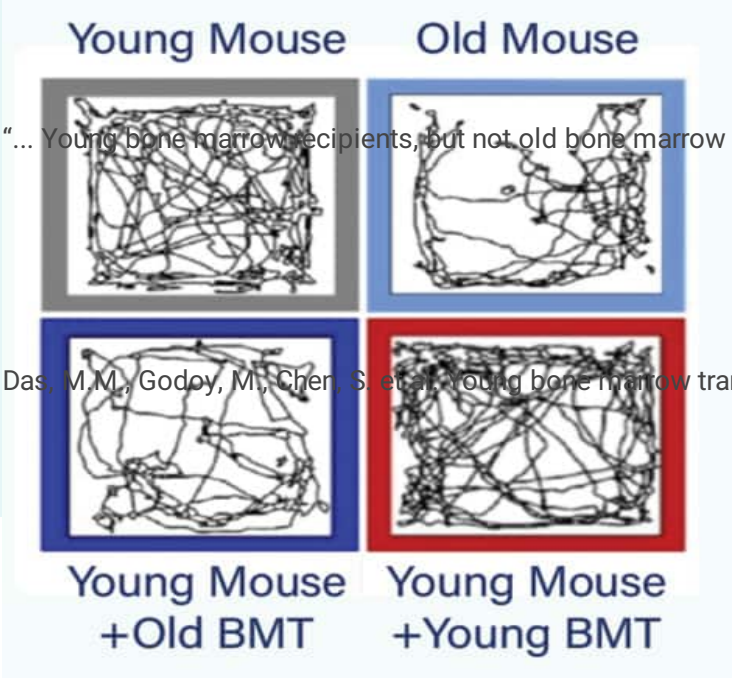


Microglia in brains of old mice have fewer/shorter branches than young mice.

Synaptic branches of microglia of old mice who received **bone marrow** transplants from **young** mice resembled those of young mice.

Credit: Cedars-Sinai / Communications Biology Available at:
https://medicalxpress.com/news/2019-02-young-bone-marrow-rejuvenates-aging.html

Nature February 20, 2019



YOUNG BONE MARROW TRANSPLANTS RESTORE EXPLORATORY ACTIVITY IN OLD MICE

"... Young bone marrow recipients, but not old bone marrow recipients, were more active than old control mice."

(BMT means bone marrow transplant)

https://www.nature.com/articles/s42003-019-0298-5/figures/1

Das, M.M., Godoy, M., Chen, S. et al. Young bone marrow transplantation preserves learning and memory in old mice. Commun Biol 2, 73 (2019). **https://doi.org/10.1038/s42003-019-0298-5**

I explained that **young bone marrow transplants** are not yet feasible for **humans** because of graft versus host disease. (This does not occur in mice because they are so genetically similar.)

What these data highlight are the importance of using one's own cells (autologous) to be turned back into young cells using ***transcription factors*** and then transplanted back into the host donor (described in the humanoid graphic on the immediate left-hand column).

The next portion of my RAADfest presentation summarized research findings and news articles that had published over the past 12 months.

A consistent theme is the number of **ultra-wealthy** people donating to or investing in biomedical research that aims to reverse or eradicate pathological **aging** in humans.

My next set of slides described a study announced in **November 2020** that made **headline news** around the world. This **hyperbaric oxygen** study showed that **telomeres** lengthened by **20%** in these **human** study subjects.[25]

As Seen on CNBC September 30, 2020

BILLIONAIRE JIM MELLON'S LIFE EXTENSION START-UP TO GO PUBLIC IN 6 TO 12 MONTHS

Mellon's company, Juvenescence, has privately raised about $170 million.

Mellon said he wants to live longer than a century, and another billionaire, Michael Bloomberg, reportedly wants to live to be 125.

https://www.cnbc.com/2020/09/29/billionaire-jim-mellon-plans-to-take-life-extension-start-up-public.html

I showed slides of the media proclaiming that **aging** had been reversed for the first time in humans.

To achieve these **telomere elongation** benefits, study subjects underwent **hyperbaric oxygen therapy** plus breathed in **pure oxygen** five days a week for three consecutive months.

Telomeres are tips at the end our chromosomes that shorten with each cell division. When there is no more telomere structure, cells die.

I announced that a study will soon publish showing **hyperbaric therapy** combined with healthy behavior patterns **elongated telomeres** an average of **40%** in older people!

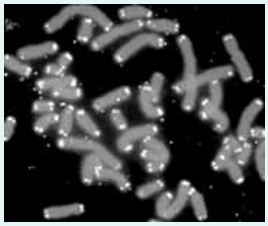
The audience was told that we are monitoring this research and interacting with the scientists to validate whether this **telomere elongation** is associated with indicators of systemic **age reversal**.

My next slides described what people can do today to reduce their rate of **telomere shortening** by:[25]

- **Engaging in healthy lifestyles**
- **Doing high intensity interval training**
- **Ensuring adequate antioxidant intake**
- **High consumption of omega-3s**
- **Including walnuts in your diet**
- **Restricting your calorie intake**

Tel Aviv University November 20, 2020

"STUDY FINDS HYPERBARIC OXYGEN TREATMENTS REVERSE AGING PROCESS"



A new study from Tel Aviv University and the Shamir Medical Center in Israel indicates that hyperbaric oxygen treatments in healthy aging adults can stop the aging of blood cells and reverse the aging process.

In the biological sense, the adults' blood cells actually grow younger as the treatments progress.

CREDIT: PD-NASA; PD-USGOV-NASA **https://medicalxpress.com/news/2020-07-hyperbaric-oxygen-therapy-protocol-cognitive.html**

NOVEL HYPERBARIC OXYGEN PROTOCOL EXTENDS TELOMERE LENGTH AND IMPROVES IMMUNE MARKERS

Some immune cell telomeres elongated by 20%.

Some senescent immune cells reduced by 37%.

Improved immune markers.

https://www.aging-us.com/article/202188/text

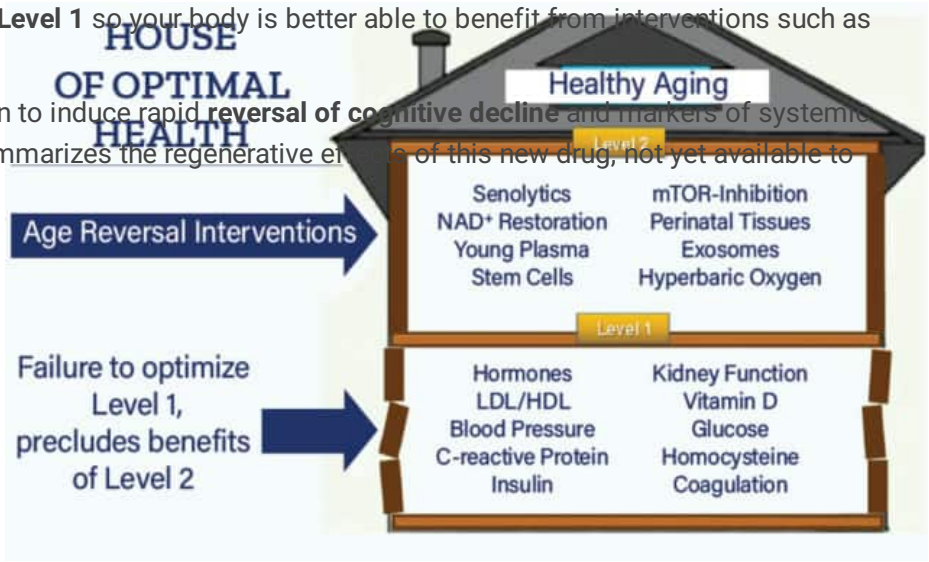
Our representative (on top right) inside multi-patient hyperbaric room at The Villages in Central Florida. This is much more comfortable than conventional hyperbaric chambers.

At this point in my presentation, it was important to remind the group that these regenerative therapies are unlikely to work if we don't pay attention to health basics learned decades ago.

Level 1 as depicted on the next slide is what *everyone* should be doing now to extend their healthy lifespan. My

emphasis has always been to correct **Level 1** so your body is better able to benefit from interventions such as **NAD⁺ restoration** and **young plasma**.

I next described a drug that was shown to induce rapid **reversal of cognitive decline** and markers of systemic aging in old mice. The slide below summarizes the regenerative effects of this new drug, not yet available to people:



Medical Xpress December 1, 2020

"DRUG REVERSES AGE-RELATED COGNITIVE DECLINE WITHIN DAYS"

UC San Francisco scientists show a few doses of new small-molecule integrated stress inhibitor:

- Rapid restoration of cognitive function in aged mice
- Reverse cognitive impairments in Down syndrome
- Restore memory function after traumatic brain injury
- Immune cell rejuvenation
- Enhanced cognition in healthy mice

"Just a few doses of an experimental drug can reverse age-related declines in memory and mental flexibility in mice."

https://medicalxpress.com/news/2020-12-drug-reverses-age-related-cognitive-decline.html
DOI:10.7554/eLife.62048

The value of ***transcription factors*** in restoring **eyesight** was published on **December 3, 2020** and showed **cell programming** therapy to be effective in a whole body model (beyond the petri dish).

This **Harvard** study was published in the journal ***Nature*** and received widespread media coverage because it showed reversal of vision loss as can be seen in my next two slides appearing at the top of the next column:

Nature December 3, 2020

"REPROGRAMMING RETINAL CELLS CAN REVERSE AGE-RELATED VISION LOSS"

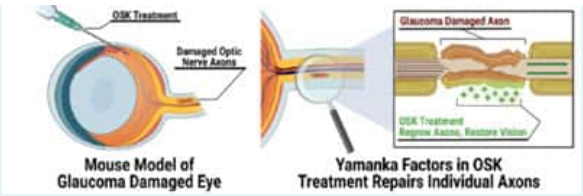
Harvard researchers used three Yamanaka transcription factors to restore youthful DNA methylation pattern in retinal cells.

Old mice with damaged optic nerves regrew axons and reversed vision loss in a model of glaucoma.

"These results show that mammalian tissues retain a record of youthful information, encoded in part by DNA methylation, which can be accessed to improve tissue function and potentially reverse the effects of aging."

Lu, Y., Brommer, B., Tian, X. et al. Reprogramming to recover youthful epigenetic information and restore vision. Nature 588, 124–129 (2020). **https://doi.org/10.1038/s41586-020-2975-4**
https://www.nature.com/nature/volumes/588/tissues/7836

From Nature December 3, 2020



Created with **Biorender.com**

RESTORING VISION IN MICE VIA AXON REGENERATION

Retinal ganglion cells (RGCs) transmit visual information from the eye to the brain along projections called axons. Damage to the RGC axons prevents transmission of this information, leading to sight loss. Lu et al.2 report that treatment of damaged RGCs with a transcription-factor cocktail called OSK restores the cells to a youthful state, leading the axon regeneration and restoration of sight in mice.

https://www.nature.com/nature/volume/588/issue/7836

Year **2020** ended with an editorial published in **FORTUNE** magazine's annual investors guide that described **age-reversal** methods that had already been demonstrated in humans and animals. This FORTUNE article advocated for an "**Operation Warp Speed**" to reverse biological aging in people to avoid a "health care cost tsunami" as shown on the next three slides:

I responded to this "Operation Warp Speed" challenge by showing a video clip from a **1995** national television talk show where I advocated for society to initiate a revolution against pathological aging.

Fortune Magazine December 30, 2020

"CRACKING THE CODE OF BIOLOGICAL AGING COULD SOLVE AMERICA'S HEALTH CARE CRISIS"

"The most exciting oportunity for such an improvement in health productivity is to understand the biology of aging." —Eli Dourado

https://fortune.com/2020/12/30/anti-aging-research-health-care-spending-biden/

Fortune Magazine December 30, 2020

MAINSTREAM RECOGNITION OF THE NEED TO REVERSE THE AGING PROCESS

"Without treatments to slow or reverse aspects of biological aging, an aging population means we are in for a health care cost tsunami."

"With such treatments, Americans would experience more healthy, productive years of life." —Eli Dourado

https://fortune.com/2020/12/30/anti-aging-research-health-care-spending-biden/

Fortune Magazine December 30, 2020

FORTUNE MAGAZINE'S CONCLUSION:

"Why not Launch an Operation Warp Speed for Biological Aging?" — Eli Dourado

http://www.sciencedaily.com/releases/2020/01/200108160338.htm

https://fortune.com/2020/12/30/anti-aging-research-health-care-spending-biden/

The next slide describes a **January 2020** study where the *C-elegans* lab model lifespan was extended the **human** equivalent of over **400 years**. This breakthrough occurred in response to modulating just two cell pathways (**mTOR** and **insulin** signaling). This study received international media coverage as it demonstrated the potential for radically extended lifespans using technologies evolving today.

Science Daily January 8, 2020

PATHWAYS THAT EXTEND LIFESPAN BY 500% IDENTIFIED

"Scientists have identified synergistic cellular pathways for longevity that amplify lifespan fivefold in *C.*

elegans, a nematode worm used as a model in aging research."

"The increase in lifespan would be the equivalent of a human living for **400** or **500 years**, according to one of the scientists."

Jianfeng Lan, Jarod A. Rollins, Xiao Zang, Di Wu, Lina Zou, Zi Wang, Chang Ye, Zixing Wu, Pankaj Kapahi, Aric N. Rogers, Di Chen. Translational Regulation of Nonautonomus Mitichondrial Stress Response Promotes Longevity. Cell Reports, 2019;28(4): 1050 DOI: 10.1016/j.celrep.2019.06.078

The next slide summarizes interventions that people are self-experimenting with today to counteract multiple mechanisms of pathological aging.

Moving forward to **January 2021**, a study using a simple **CRISPR** editing technique more than doubled lifespan of progeroid mice.

FROM THE WALL STREET JOURNAL JAN. 7, 2021

CRISPR Gene-editing Treatment "... mice with progeria that got the gene-editing treatment lived more than twice as long as the untreated mice."

https://www.wsj.com/articles/crispr-genev-editing-treatment-could-point-way-to-fix-for-deadly-aging-disease-11609950054

FROM THE WALL STREET JOURNAL JAN. 7, 2021

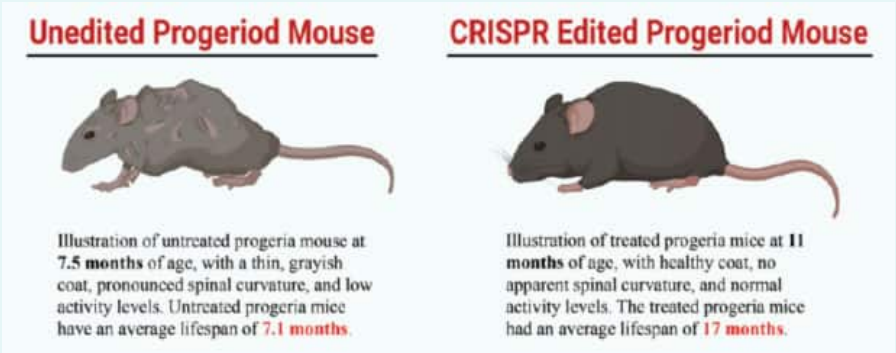
CRISPR Gene-editing Treatment "Could Point Way to Fix for Deadly Aging Disease."

Median lifespan of CRISPR-treated mice was 510 days compared to 215 days for the unedited group. If this model of progeria applies to humans, children with progeria might live into their forties or later.

https://www.wsj.com/articles/crispr-genev-editing-treatment-could-point-way-to-fix-for-deadly-aging-disease-11609950054

Progeria is a genetic disease that causes accelerated aging in afflicted people. Death usually occurs between ages 12-20 with debilitating degenerative changes emerging in early life. Not only did the CRISPR-edited progeroid mice live much longer, but they remained free of the degenerative changes far longer.

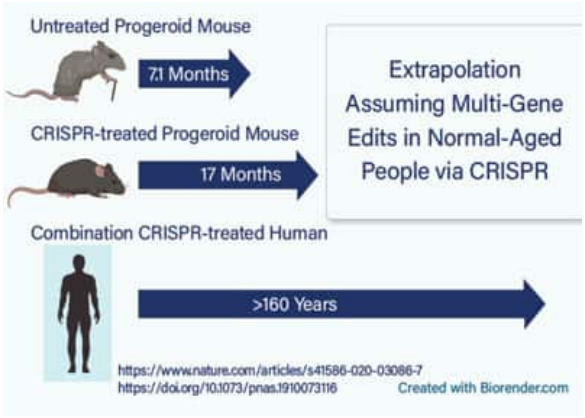
CRISPR GENE-EDITING TREATMENT



Created with **Biorender.com**

https://www.wsj.com/articles/crispr-gene-editing-treatment-could-apoint-way-to-fix-for-deadly-aging-disease-11609950054

Under the optimistic extrapolation that combination CRISPR gene editing therapy might enable normal aged people to benefit, I created a chart showing what the human lifespan potential could be if combination CRISPR produced these same benefits.



Not all our advisors agreed with this optimistic extrapolation, but I pointed out that a single dose of combination **CRISPR** treatment was shown in **November 2019** to reverse multiple effects of aging in mice as shown on the following slide:

PNAS November 19, 2019

RESULTS FROM A SINGLE DOSE COMBINATION GENE THERAPY:

1. 58% increased function after heart failure
2. 38% reduction in vascular disease marker
3. 75% reduction in kidney atrophy
4. Complete reversal of obesity and diabetes

Noah Davidsohn, Matthew Pezone, Andyna Vernet, Amanda Graveline, Daniel Oliver, Shimyn Slomovic, Sukanya Punthambaker, Xiaoming Sun, Ronglih Liao, Joseph V. Bonventre, and Gerorge M. Church.

PNAS November 19, 2019 116(47) 23505-23511; **https://doi.org/10.1073/pnas.1910073116**

On the same day the **CRISPR** study on progeroid mice was published (Jan 6, 2021), another study more relevant to normal **aging** found the CRISPR edit of just one senescence-accelerating gene (KAT7) increased lifespan by **25%** in mice. The CRISPR-treated mice also had improvements in overall **appearance** and **grip strength**.

Science Translational Medicine AAAS January 6, 2021

"A GENOME-WIDE CRISPR-BASED SCREEN IDENTIFIES KAT7 AS A DRIVER OF CELLULAR SENESCENCE"

KAT7 gene is significant driver of cell senescence. Targeting KAT7 using CRISPR enabled:

1. 25% extended lifespan in normal aged mice.[1]
2. Improved overall appearance and grip strength.[1]

Mice and humans share virtually the same set of genes though in slightly different forms.[2]

1. **https://science mag.org/content/13/575/eabd2655/tab.pdf**
2. **https://www.genome.gov/10001345/importance-of-mouse-genome**

I then presented another optimistic extrapolation that if this simple single-gene edit works in people the same way as mice, our average lifespan might increase to **98 years** (from the pathetically short 77-78 years today).

The January 22, 2021 issue of a prestigious international business newspaper (***Financial Times***) described aging as a "**disease**" and talked about **anti-aging** therapies this century that could prove as transformative as **antibiotics** were in the last century.

Life Extension has fought a **42-year** war to persuade the public (and government) to recognize **aging as a disease** that future treatments might eradicate. It's finally going mainstream!

As reported in the Financial Times AAAS January 22, 2021

"AGING IS LIKE A DISEASE"

The 21st century could see anti-aging therapies that are as important to people as antibiotics were in the past century. undergo a radical change.

https://www.ft.com/contentd6d3cad8-f6e14a3c-b0cb-2b1afdeb95a0

On **February 20, 2021**, ***Web*MD** published an editorial titled **"Is there a Cure for Aging?"** and described groups that are seeking to **reverse engineer** our biological clock to "***prevent death itself***."

***Web*MD** then described species like the "immortal jellyfish" and lobsters that seemingly live forever (if not eaten first).

WebMD February 20, 2021

"IS THERE A CURE FOR AGING?"

An article published on WebMD.com describes billions of dollars of investor money that seek to significantly improve human biology.

WebMD describes heroic efforts being made to eliminate lethal diseases and prevent death in people.

The WebMD website published a moving graph showing that by around year 2065, life expectancy potential of people might approach 900 years.

https://www.webmd.com/healthy-aging/story/is-there-a-cure-for-aging

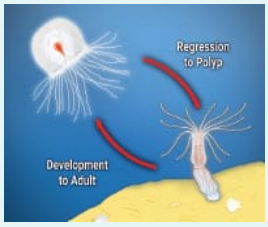
WebMD February 20, 2021

ANIMALS THAT APPEAR TO LIVE INDEFINITELY

The *Turritopsis dohrnii* jellyfish may be immortal according to some scientists. It can renew its own life indefinitely by transforming back to an infantile stage if it becomes damaged, starved, sick or old.

Lobsters (if not eaten first) produce a youthful enzyme that has some scientists speculating if there may be an upper limit to its longevity potential.

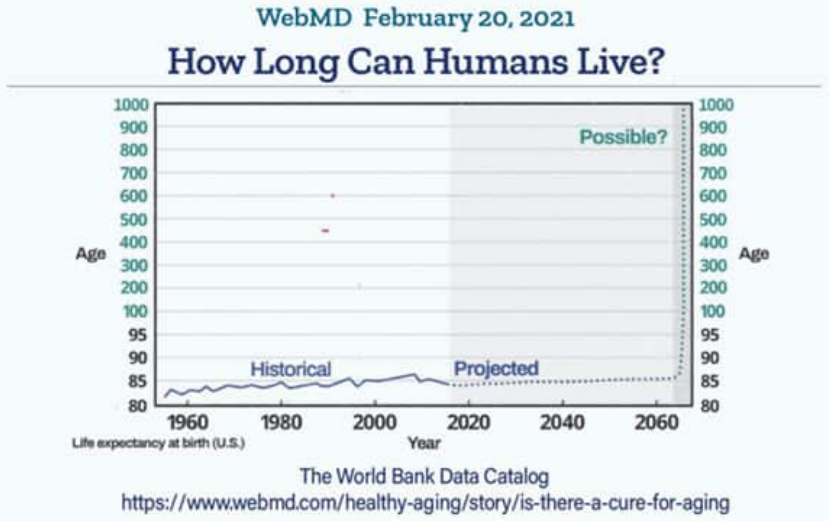
https://www.webmd.com/healthy-aging/story/is-there-a-cure-for-aging



Created with **Biorender.com**

What surprised me was a moving graph published by ***Web*MD** showing human lifespan potential of over **900 years** occurring around year **2065**. I made it clear this chart did not come from an age reversal research group, but ***Web*MD** itself:

On **March 2, 2021**, another **CRISPR** study was announced where it significantly reduced cholesterol and triglyceride levels in mice. The significance of this finding is that it may be possible to optimize artery-clogging lipids in people without the need for statin and other drugs commonly used today.



Science Alert March 2, 2021

CRISPR MAY ELIMINATE NEEED FOR DRUGS

Single CRISPR injection reduces cholesterol up to 57% in mice.

"In addition to the cholesterol reduction, the experiment produced a 29.4% decrease in triglycerides..." —Peter Dockrell

https://www.sciencealert.com/experimental-crispr-treatment-cuts-cholesterol-in-mice-by-up-to-57-in-single-shot

A few days later (March 8, 2021), the **Nobel Prize in Chemistry** was awarded to two scientists working to engineer humans to be disease resistant.

The **FDA** approved the first study in human history of an anti-aging drug (metformin) in **2015**. This was the first time the FDA approved a clinical trial that targets markers of human "aging" as a clinical end point.

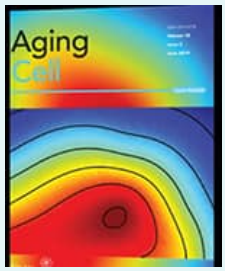
In early **2021**, the FDA approved two additional clinical trials where **metformin** will be studied to see if measures of age-delay and age reversal occur in **older people**.

I reminded the group that when metformin was combined with **DHEA** and growth hormone for one year, markers of **human aging** were reversed **2.5 years** as measured by the Horvath Epigenetic Clock.

I mentioned that **metformin** had been listed as an **anti-aging drug in *Life Extension Magazine*®** in **1995**:

Aging Cell September 2019

THYMIC AGE REVERSAL DEMONSTRATED IN 2019

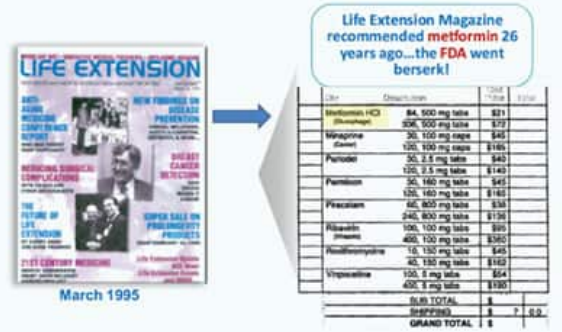


Study conducted by Dr. Greg Fahy in collaboration with researchers from Stanford University and UCLA used individualized doses of:

- Human growth hormone
- DHEA
- Metformin

Study subjects also provided with daily vitamin D3 and zinc.

Reversal of epigenetic aging and immunosenescent trends in humans, GM Fahy, RT Brooke, JP Watson, Z Good… - Aging Cell, 2019



I next provided some updates on **rapamycin** and how people can participate in a clinical trial that will measure aging parameters in people over a 12-month period receiving two different weekly doses of rapamycin:

Data on **senolytics** continue to validate their potential efficacy including enhancing **kidney function** in mice.

April 2021

MTOR INHIBITION WITH RAPAMYCIN IMPROVES ALZHEIMER'S IN MOUSE MODEL OF DISEASE

Effects of rapamycin in mouse model of **Alzheimer's**:

- Improved cerebrovascular function (better than non-Alzeimer's mice)
- Reduction of *beta-amyloid* in brain cortex
- Reversed memory deficits

mTOR Attenuation with Rapamycin Reverses Neurovascular Uncoupling and Memory Deficits in Mice Modeling Alzheimer's Disease. Candice E. Van Skike, Stacy A. Hussong, Stephen F. Hernandez, Andy Q. Banh, Nicholas DeRosa, Veronica Galvan Journal of Neuroscience 12 May 2021, 41 (19) 4305-4320; DOI: 10.1523/JNEUROSCI.2144-20.2021. PMID 33888602.

From ClinicalTrials.gov June 18, 2021

RAPAMYCIN HUMAN STUDY RECEIVES $485,000 FUNDING

- Randomized, placebo-controlled trial into the safety/efficacy of rapamycin in reducing clinical measures of aging in older population.
- Two differing doses: 5 mg or 10 mg of rapamycin one time a week or a placebo.
- Primary Outcome Measure: Changes in visceral fat as measured by (DXA) scan.
- Secondary Outcomes: Range of clinical measures, e.g., bone density, blood tests, etc.
- 20 people enrolled at $360 each (original cost before donations was $1,200).

Principal investigators: James Watson, M.D. and Sajad Zalzala, M.D. Sponsor: AgelessRx Collaborator: University of California, Los Angeles To enroll log on to: **https://wwwagelessrx.com/pearl**

My next slide was a discovery at the **Buck Institute** on a way to measure the effects of **senolytics**. This research has been transferred to **Tufts University** where our **Age Reversal Network** (**www.age-reversal.net**) will assist in identifying suitable human study subjects.

May 19, 2021

MORE THAN 50% OF AMERICANS OVER AGE 75 ARE BELIEVED TO HAVE KIDNEY DISEASE[1]

Senolytic Enhances Kidney Regeneration in Mice Senolytic treatment with ABT-263:

- Reduced senescent cell numbers
- Restored regenerative profile in aged mouse kidney
- Improved kidney function[2]

1. https://www.kidney.org/news/monthly/wkd_aging
2. Mylonas KJ, O'Sullivan ED, Humphries D, Baird DP, Docherty MH, Neely SA, Krimpenfort PJ, Melk A, Schmitt R, Ferreira-Gonzalez S, Forbes SJ, Hughes J, Ferenbach DA. Cellular senescence inhibits renal regeneration after injury in mice, with senolytic treatment promoting repair. Sci Transl Med. 2021 May 19;13(594):eabb0203. doi: 10.1126/scitranslmed.abb0203. PMID: 34011625.

June 1, 2021

BUCK INSTITUTE ANNOUNCES NON-INVASIVE TEST TO MEASURE SENOLYTIC EFFICACY

- Precise measure of senescent cell destruction demonstrated in cell culture and mice.

- USDA funding full-time research at Tufts University to make this available to humans.
- Age Reversal Network will assist to develop this test of senolytic therapy efficacy for upcoming clinical trials. (September 8, 2021)
- When available, this test will enable precise dosing of senolytic drugs and nutrients.

https://www.cell-metabolism/pdf/S15504131(21)00115-7.pdf

On **June 26, 2021**, the first **human** trial using **CRISPR** gene therapy was shown to reduce serum levels of a misfolding protein (transthyretin) in a form of a disease called **amyloidosis**.

On **July 6, 2021**, *Popular Mechanics* announced that the U.S. military is studying the **NAD⁺** precursor **nicotinamide riboside** to improve human performance.

From Fierce Biotech June 26, 2021

FIRST HUMAN TRIAL USING CRISPR

- Transthyretin amyloidosis is caused by the accumulation of misfolded transthyretin proteins.
- Misfolded transthyretin amyloid proteins build up and cause heart failure and other diseases.
- If left untreated death occurs in 2 to 5 years.

CRISPER/Cas9 gene editing reduced serum levels of transthyretin, a key biomarker for the disease, by 87% in humans.

(Standard care therapy typically reduces transthyretin by 80%.)

This is the first time gene editing has been proven to work in humans, which "opens up a whole new area of therapies for patients that wasn't there."

https://www.fiercebiotech.com/biotech/first-human-trial-results- intellia-shows-world-gene-editing-has-arrived

I reminded the audience that most of them had been using **nicotinamide riboside** for many years based on publications in *Life Extension Magazine®*.

From Popular Mechanics July 6, 2021

"THE U.S. MILITARY IS TESTING A PILL THAT COULD DELAY AGING"

- U.S. Special Operations Command Investing more money in anti-aging clinical trials.
- Trial to start soon of "anti-aging pill"
- NAD⁺ precursor being tested to enable "improved human performance…like Increased endurance and faster recovery from injury."

"Reduced levels of NAD+ are linked to aging and numerous diseases, including mitochondrial dysfunction, inflammation and a variety of associated diseases. These levels decline as humans age and remain depleted during disease states."

https://www.popularmechanics.com/science/health/a36905562/usmilitary-testing-anti-aging-pill/

I concluded this portion of my presentation by showing the cover of the **September 2021** issue of **Prevention** magazine.

Life Extension Magazine November 2014

NAD+ RESTORATION TURNED REAL 7 YEARS AGO

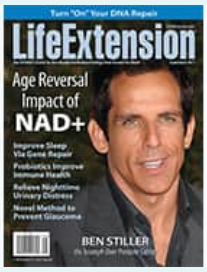
- Since **2001 Life Extension** has sought ways to restore **NAD⁺**.
- **NAD⁺** helps turn "off" degenerative processes.

- Proven methods to boost **NAD+** became available in circa **2014**

Life Extension Magazine September 2017

NAD+ SHARPLY PLUMMETS WITH AGE

- At age 50, we have 50% less cell NAD+ than at age 20.
- By age 80, NAD+ levels Drop by as much as 98%.



The significance of this is that for decades, **Prevention** had been critical of attempts to slow biological aging. In those early days, Prevention viewed aging as a natural process that should not be interfered with.

The September 2021 article in **Prevention** favorably described research on everything we have been studying. I complimented **Prevention** and others for waking up to the fact that there are methods beyond healthy lifestyles that may extend healthy lifespans.

The next segment of my presentation moved on to what people can do now to slow aging and reduce disease risk.

Prevention Magazine September 2021

PREVENTION MAGAZINE FAVORABLY DESCRIBES:

- Intermittent Fasting
- Metformin
- DNA methylation testing
- Sirtuin activation
- Young plasma transfer
- Senolytic drugs

One of my focuses was on the benefits of **intermittent fasting**. The most popular way people are doing this today is **fasting** (nothing but water, black coffee, or tea) for about 16 hours most days and consume a reasonable number of calories during an eight-hour period.

The benefits are enormous, including boosting **AMPK**, turning down excess **mTOR** and enabling a cellular housekeeping process to occur known as **autophagy**.

Stated succinctly, **autophagy** enables **cellular housekeeping** to occur.

If one does not take a break from constantly ingesting calories, cells never get a chance to remove cellular waste products that accumulate.

Those unable to fast often rely on **AMPK activating** compounds and/or those that directly suppress **excess mTOR**.

From the New England Journal of Medicine Dec. 26, 2019

EFFECTS OF INTERMITTANT FASTING ON HEALTH, AGING, AND DISEASE

Animal models show consistent robust benefits of **intermittent fasting**:

- Suppresses inflammation
- Reduces obesity and type II diabetes
- Protects against cardiovascular disease
- Lowers risk of neurodegenerative disorders
- Reduces cancer incidence

https://nejm.org/doi/full/10.1056/NEJMra1905136

Nature Research October 27, 2020

"INTERMITTENT FASTING FROM DAWN TO SUNSET FOR 4 CONSECUTIVE WEEKS INDUCES ANTICANCER SERUM PROTEOME RESPONSE & IMPROVES METABOLIC SYNDROME."

No eating/drinking from dawn to dusk… 14-15 hours each day:

- **7.25 pounds** of **weight loss**
- **8.8 mmHg** reduction in **blood pressure**
- Significant increase in **tumor suppressor/anticancer proteins**
- Significant decrease in several **tumor promoter/pro-cancer** proteins
- Increasing a protein called **calreticulin** (by around **16 times**)
- Calreticulin enhances **IgG response** to a **SARS-CoV** spike protein

Scientific Reports,(2020)10:18341 https://doi.org/10.1038/s41598-020-73767-w
https://creativecommons.org/licenses/by/4.0/legalcode

In addition to fasting, I advocated for the audience to consume a **Mediterranean diet** and showed several slides about healthy foods people should consume and toxic ones to avoid.

The first two slides in the next column show the remarkable reductions in **mortaltiy** in those who adhere more to a **Mediterrean diet**.

I showed three of the many ***Life Extension***® magazines that have long advocated for readers to follow a **Mediterrean diet**.

My presentations include photos and descriptions of dead **billionaires** who are missing the super-longevity boat. In the example below, I mention an individual who died of a **heart attack** at the early age of **57**. Was he having comprehensive **blood tests** and taking corrective actions? I don't know, but too many people fail to test for proven causes of cardiovascular disease.

From the British Journal of Nutrition

"MEDITERRANEAN DIET AND MORTALITY IN THE ELDERLY: A PROSPECTIVE COHORT STUDY AND META-ANALYSIS"

"In the multi-variable model, high adherence to the **Mediterranean diet** was associated with **25% lower risk of death** as compared with the lowest category."

Published online by Cambridge University Press: 30 August 2018
https://www.cambridge.org/core/journals/british-journal-of-nutrition/article/mediterranean-diet-and-mortality-in-the-elderly-a-prospective-cohort-study-and-a-metaanalysis/F2D6B083AA187849477112DB77820521

American Heart Association June 30, 2021

MEDITERRANEAN DIET SCORE, DIETARY PATTERNS AND RISK OF SUDDEN CARDIAC DEATH

Study of **21,000** people over **9.8** years reveals:

- Diet high in fried foods, organ meats and processed meats regularly had a **46%** ***higher*** risk of **sudden cardiac death** compared to those with least adherence.
- Those who most closely followed the traditional **Mediterranean diet** had a **26%** ***lower*** risk of sudden cardiac death than those with the least adherence to this eating style.

Mediterranean diet defined as high in vegetables and whole grains, low intake of meat, high intake of marine omega-3s.

Originally published 30 June 2021 **https://doi.org/10.1161/JAHA.120.019158**

Journal of the American Heart Association

MEDITERRANEAN DIET HEALTHY FOODS

More fruits, vegetables, and whole grains, and less dairy & meat than typical western diet.

Heart disease mortality has plummeted by **68%** since **1969**, but that statistic means nothing if you are part of the group still dying from heart disease.

WHO MISSED THE LONGEVITY BOAT?

Baron Benjamin de Rothschild (1963-2021)

Expiration date: Jan. 15, 2021

Net worth >$1.5 billion

Heir to a French banking fortune, died of a heart attack at age 57 on January 15, 2021.

He oversaw the Edmond de Rothschild empire, which has stakes in banks in France and Switzerland, owns restaurants, hotels, and vineyards in Argentina, New Zealand, South Africa, Spain and France.

https://www.Forbes.com/profiles/benjamin-de-rothschild

Perhaps the easiest way of slashing **heart attack** risk is to have an at-home **Omega-3 Index** test and target a level above **6.8%.**

REDUCTION IN HEART DISEASE MORTALITY IN THE UNITED STATES

Age-standardized **death rate** from **heart disease** per 100,000 people dropped:

From: **520** in **1969**

To: **167** in **2014**

68% decline over 45 years

Weir HK, Anderson RN, Coleman King SM, Soman A, Thompson TD, Hong Y, et al. Heart Disease and Cancer Deaths — Trends and Projections in the United States, 1969–2020. Prev Chronic Dis 2016;13:160211. DOI: **http://dx.doi.org/10.5888/pcd13.160211**external icon

Two recent published studies substantiate the benefit of achieving a *higher* **Omega-3 Index** score.

Life Extension Magazine August 2020

The **Omega-3 Index** is a blood test that measures the **percent** of omega-3 fatty acids in red blood cells.

Red blood cell **EPA/DHA** content is a good measure of sustained omega-3 status.

You want your **Omega-3 Index** score to be **> 6.8%**.

Typical Japanese Omega-3 Index is > **8.0%**. That may correlate with **5 year** *longer* life expectancy in **Japan**.

Yet **53%** of **Life Extension** supporters have less-than-optimal **omega-3** status as shown on slide below:

December 2018

OMEGA-3-INDEX AND RISK OF DEATH

People with **omega-3** RBC scores > **6.8%** compared with those < **4.2%**:

39% lower risk for **cardiovascular** disease

34% lower risk of **death** from *any* cause

(Subjects average age 66 and followed over 7 years)

Higher **Omega-3 Index** associated with reduced risks because of:

- Lowering of **triglycerides, blood pressure, platelet aggregation, heart rate**
- Lower markers of **inflammation** and **arterial plaque** vulnerability
- Reduced rate of telomere rate attrition

Journal of Clinical Lipidology (2018) 12, 718-727.

June 16, 2021

HIGHER OMEGA-3 BLOOD SCORE = NEARLY 5 YEARS INCREASED LIFE EXPECTANCY

- Predictive model for correlation/association from Framingham Offspring Cohort (n=2,240)
- Baseline omega-3 index score and relevant covariates evaluated over **11-year** follow-up.
- Standard risk adjustments: age, sex, total cholesterol, HDL cholesterol, hypertension treatment, systolic blood pressure, smoking status, prevalent diabetes.
- Extensive **validation** process to account for confounding risk factors.

Analysis reveals red blood cell **omega-3 index** over **6.8%** in people is associated with **4.7 years** additional **life expectancy** compared with **omega-3 index** under **4.2%**.

The American Journal of Clinical Nutrition, ngab195. **https://doi.org/10.1093/ajcn/nqab195**

The **Omega-3 Index** is available from several labs. Those who want to order from Life Extension can do so by calling **1-800-208-3444** or logging on to: **www.LifeExtension.com/blood**

Life Extension July 27, 2021

OMEGA-3 INDEX SCORES IN LIFE EXTENSION SUPPORTERS

53.7% have Omega-3 Index scores < 6.8%

- Only 1,300 mg of added EPA/DHA from fish/supplements moves Omega-3 Index from < 4.2% to > 6.8%.
- Plant derived omega-3 precursors (ALA) not shown to achieve these robust EPA/DHA increases.
- Omega-3 Index at-home test costs $74.25—May save $$$ on fish oil supplements.

Omega-3 Index test available at: **www.LifeExtension.com/blood**

Journal of Clinical Lipidology (2018) 12, 718-727.

I finish my presentation with a transhumanist update including a study published in the ***New England Journal of Medicine*** in **July 2021** where a brain implant into a stroke-paralyzed patient enabled the patient to translate words from their brain on to a computer screen.

This finding advances the concept of the brain/cloud interface where the human brain might merge with the Cloud and achieve limitless self-improvements according to futurist **Ray Kurzweil**.

New England Journal of Medicine July 14, 2021

"BRAIN IMPLANT LETS MAN SPEAK AFTER BEING SILENT FOR MORE THAN A DECADE"

New England Journal of Medicine study shows brain implant in a stroke paralyzed (15 years) patient enabled brain signals to be translated into words on a computer screen.

Comment by expert on brain-computer interfacing: "Human Brain/Cloud Interface technologies will empower us to preserve crucial brain information, interface our brain directly with the cloud, positively impact learning, and provide data for the study of consciousness. This technology is not distant in the future, as many believe."—Nuno R.B. Martins, Ph.D (July 28, 2021)

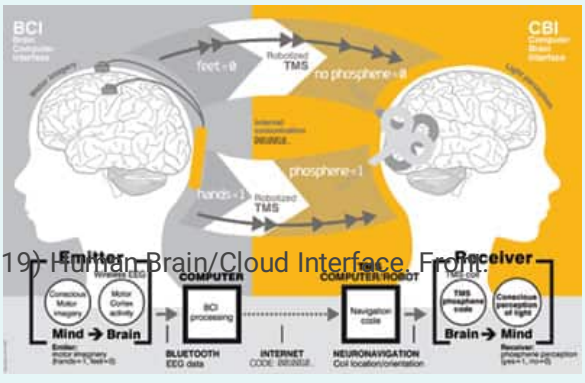
https://www.nejm.org/doi/full/10.1056/NEJMoa2027540

https://www.wsj.com/articles/brain-implant-lets-man-speak-after-being-silent-for-more-than-a-decade-11626296422

I showed the group an announcement made on **July 30, 2021** where **Elon Musk** has raised an additional **$205 million** to develop brain implants that can directly communicate with phones and computers.

Frontiers in Neuroscience March 20, 2019

HUMAN BRAIN/ CLOUD INTERFACE



Human brains could be connected to the internet in"the next few decades" scientists predict.

Martins NRB, Angelica A, Chakravarthy K, Svidinenko Y, Boehm FJ, Opris I, Lebedev MA,

Swan M, Garan SA, Rosenfeld JV, Hogg T and Freitas RA Jr (2019) Human–Brain/Cloud Interface. Front. Neurosci. 13:112. doi: 10.3389/fnins.2019.00112

https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0105225

Conscious Brain-to-Brain Communication in Humans Using Non-Invasive Technologies

Carles Grau,Romuald Ginhoux, Alejandro Riera,Thanh Lam Nguyen, Hubert Chauvat, Giulio Ruffini

RAY KUZWEIL'S EXIT PLAN TO IMMORTALITY

- Survive until year 2045
- Singularity enables neocortex to merge with cloud-based artificial intelligence
- Neocortex/AI enters limitless self-improvement cycles.

Result is superintelligence that advances our abilities to incomprehensive levels.

And for skeptics who cannot comprehend the magnitude of this, I went back to **1903** when the first heavier-than-air flight made headline news around the world, but virtually no one at the time envisioned flying buses.

CNBC July 30, 2021

ELON MUSK'S BRAIN COMPUTER STARTUP RAISES $205 MILLION FROM GOOGLE VENTURES AND OTHERS

- Neuralink is trying to develop high-bandwidth brain implants that can communicate with phones and computers
- Total investment in the company now stands at $363 million.

https:// www.cnbc.com/2021/07/30/elon-musks-neuralink-backed-by-google-ventures-peter-thiel-sam-altman.html

A mere 54 years after the **Wright Brothers**, intercontinental air travel became routine.

I analogized the rapid pace of science further with the Mars Rover that has a flying helicopter that is controlled remotely from earth.

Getting back to **cellular reprogramming**, I analogized what may happen if the biomedical sciences advance as quickly as aviation did.

I summarized how quickly we are rewriting the **rules of biology** with the following slide:

SCIENTIFIC BREAKTHROUGHS AND SUBSEQUENT ADVANCES

- **1903** First "Flying Machine" travels **120 feet** at Kitty Hawk
- **2021** Robot + helicopter travel **140 million** miles to Mars

- **2011** Cells from **100-year-old human** fully **rejuvenated***
- **2022** Autologous iPSC studied for systemic rejuvenation

* **https://pubmed.ncbi.nlm.nih.gov/22056670/**

Our Mission!

Surging numbers of **elderly** Americans are suffering and causing astronomical medical outlays.

CELLULAR REPROGRAMMINGREWRITING THE RULES OF BIOLOGY

- Time-honored doctrine of biology was that the fate of cells was irreversibly determined, and that rejuvenation was impossible.
- Starting in 2006, **cell reprogramming** demonstarted cellular rejuvenation.
- Rejuvenation achieved in cells from very old **humans** (2011).
- Research underway to rejuvenate whole organisms (including humans).
- The "impossible" was achieved overnight via **cellular reprogramming**.

https://pubmed.ncbi.nlm.nih.gov/33627519

The best solution is to delay and reverse degenerative changes that occur in aged people. Even modest success will improve quality and quantity of life while averting a healthcare cost crisis.

I want to welcome a record number of new supporters who have joined our **Life Extension** community.

Some want to read everything they can in the **anti-aging** field while others mainly seek access to high-quality **dietary supplements**.

Every time you purchase a **nutrient formula** or **blood test** from **Life Extension**, you support scientists on the cutting edge of regenerative medicine **research**.

Those who want to receive **free** email updates about research findings, scientific conferences, and clinical trials should enroll at:

www.age-reversal.net

Annual RAADfest Conference

RAADfest is a non-profit scientific conference that I help to financially subsidize. It enables people to stay informed and connect with many of the best doctors, scientists and thought leaders in the field.

RAADfest 2022 will be held live in **San Diego**, California on October 6-9, 2022, taking proper precautions to make it safe and enjoyable.

The registration is affordable at $620 and this includes organic meals so the entire group can stay together and interact.

To learn more and reserve your place, and to see RAADfest's comprehensive safety and cancellation policies log on to:

www.Raadfest.com

In Summary...

It is a personal privilege to interact with and fund scientists on the front lines of regenerative medicine research.

My objective is to save as many human lives as possible including our own.

For those seeking to **delay aging** today, the article on page 18 of this month's isssue describes how eating a particular food group can add many healthy years to your **life expectancy**.

Welcome to our fantastic voyage!

For longer life,

William Faloon

Related Lab Testing

- **Research-Use Iron Panel Blood Test**
- **Exosome/yFFP Study Panel**
- **Pro7 Advanced Nutrigenomic Panel Cheek Swab**

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Spread the word to LE customers

Learn More

STRESS AND BURNOUT STUDY

Feeling Frazzled? Is stress keeping you up at night?

Learn More and Apply

†2022 Consumer Satisfaction, Rated #1 Catalog/Internet Brand.
Ratings based on results of the 2022 ConsumerLab.com Survey of Supplement Users.
More information at www.consumerlab.com/survey.

These statements have not been evaluated by the Food and Drug Administration.
These products are not intended to diagnose, treat, cure, or prevent any disease.