People Unlimited

Super Longevity Weekend

November 15-17, 2019

Vitality In Aging: Precision Medicine Clinical Trials to Measure and Treat Aging

Brian M. Delaney, Director

James Watson, MD, Chief Medical Officer

Tara Smith, Clinical Trials Coordinator

Vitality in Aging (VIA) Research Group

Fort Lauderdale, Florida

Vitality In Aging (VIA)
Precision Medicine Clinical Trials

VIA Research Group
Founding Principle

- *Recover/maintain vitality as we age*
- *(= Recover/maintain health.)*
- *= "**Solve aging!**" –Bill Faloon*

Bill Faloon

Brian M. Delaney

Co-founders

Vitality in Aging (VIA) Research Group

Fort Lauderdale, Florida

Vitality In Aging (VIA)
Precision Medicine Clinical Trials

VIA Clinical Trials Mission Statement

"We are attempting to do today, for the study of aging, what the Framingham Heart Study did in 1948 for the study of heart disease and hypertension."

James Watson, MD

Brian M. Delaney
James Watson, MD
Principal Investigators
Vitality in Aging (VIA) Research Group
Fort Lauderdale, Florida

Funding/Donations

- Bill Faloon (primary sponsor)
- Many other individual donors
- Human Age Reversal Project 501(c)(3)
- Participant fee for some trials

Learning from History: The True Story of Franklin D. Roosevelt's Premature Death

(A major reason why the Framingham Heart Study was started)

- **1800s – early 1900s.** High blood pressure was NOT considered a "DISEASE" – no need for treatment.
- **1932.** Franklin D. Roosevelt – Only 50, not yet subject to the stresses of the presidency, yet already had high blood pressure (noted by his doctors).
- **1932-1945.** FDR's high blood pressure worsened. As president, he gradually developed signs of heart failure on X-ray and physical exam.
- **1945.** April 12, 1945 – FDR died of untreated high blood pressure, due to a major hemorrhagic (hypertensive) stroke. At the time of his death, his BP was 300/140mm Hg.

Brian M. Delaney

James Watson, MD

Principal Investigators
VIA Research Group

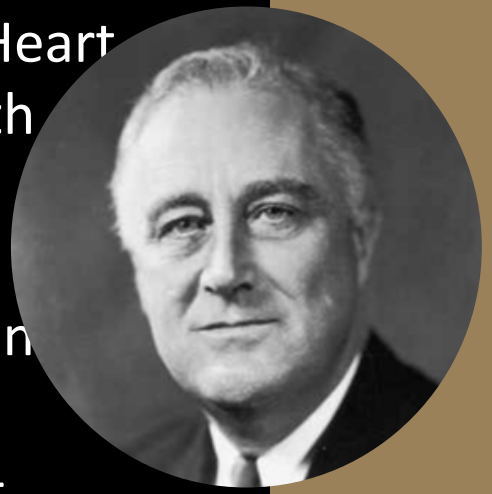
Learning from History: The True Story of Franklin D. Roosevelt's Premature Death

- Fact: FDR died prematurely at age 63 of hypertension – a condition his doctors thought was "*normal for his age*".
- Sequelae: As a result of FDR's premature death, doctors started to question conventional wisdom about HTN.
- Result: An epidemiologic, longitudinal study of heart disease and hypertension was started. FDR's death was a major reason why the **Framingham Heart Study** was proposed and funded.

Brian M. Delaney
James Watson, MD
Principal Investigators
VIA Research Group

Framingham Heart Study

Key Points About Framingham Heart Study



- Impetus for the Framingham Heart Study was the premature death FDR.
- Founded in 1948 by US Public Health Service with $500,000 in funding.
- Framingham, Massachusetts – chosen because it was “close to Boston” where researchers’ real jobs were (Boston University).
- Initial cohort of people – 5,278.

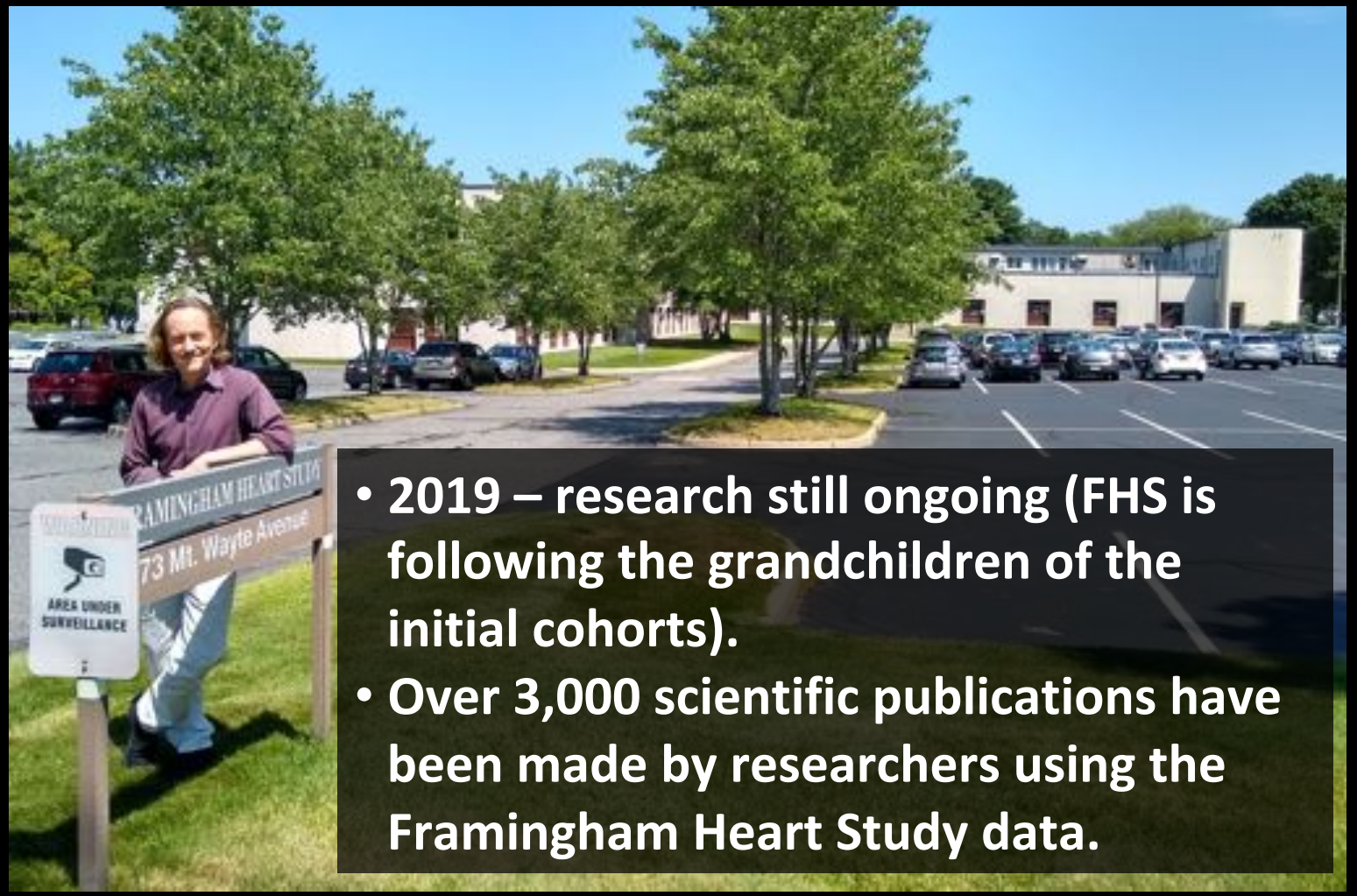
Brian M. Delaney

James Watson, MD

Principal Investigators
VIA Research Group

Framingham Heart Study

Key Points About Framingham Heart Study



- 2019 – research still ongoing (FHS is following the grandchildren of the initial cohorts).
- Over 3,000 scientific publications have been made by researchers using the Framingham Heart Study data.

Brian M. Delaney

James Watson, MD

Principal Investigators
VIA Research Group

Analogy: The similarities between FDR's death in 1945 and death from age-related dz today

HTN/Heart Disease vs. Aging/Age-Related Diseases

- FDR died prematurely of treatable HTN
- HTN not recognized as a disease in 1945
- 1945 – cause of HTN not well understood
- 1950s – Progress begins (diuretics) for Tx HTN that lengthen life

- 2019 – Millions die prematurely of age-related disease
- 2019 – Aging not recognized as a disease by FDA and the medical establishment
- 2019 – Molecular cause(s) of aging not well understood
- 2019 – Scientists are finally starting to discover drugs for Tx aging that may ↑ health span and lengthen life

VIA VITALITY IN AGING

Brian M. Delaney
James Watson, MD
Principal Investigators
VIA Research Group

Analogy: Framingham Heart Study and the Vitality In Aging Longitudinal Study

For the study of aging, the Vitality In Aging (VIA) Longitudinal Study seeks to do what the Framingham Heart Study did for our scientific understanding of heart disease and hypertension.

Brian M. Delaney

James Watson, MD

Principal Investigators
VIA Research Group

Aging Science: Where Were We 10 Years Ago?

(. . . in our understanding and treatment options for aging)

- **2009.** **WHO** (and **FDA, EMA, etc.)** did not recognize "aging" as a disease. No ICD-9 code for "aging" or for arthritis, OA, etc. *as* "age-related diseases".
- **2009.** Few reliable ways of quantitatively and precisely measuring biological age available.
- **2009.** Manhattan Beach Summit on Aging, California
  - Team of aging researchers and others convened in CA.
  - Conclusion: No validated method to reverse aging in humans had been scientifically proven in 2009*.

* Note: Calorie restriction has long been shown to increase healthspan, but only *slows* aging… it does not *reverse* aging. (And, not fun....)

2009

Brian M. Delaney

James Watson, MD

Principal Investigators
VIA Research Group

Aging Science: Where Were We 10 Years Ago?

(. . . in our understanding and treatment options for aging)

Manhattan Beach Summit
November 2009

2009

NO *Validated Method to Reverse Aging in Humans*

Brian M. Delaney

James Watson, MD

Principal Investigators
VIA Research Group

Aging Science: Milestones in Last 10 Years

- **2012.** Epigenetic “DNA methylation clocks” invented that precisely measure age (Horvath and Hannum DNAm Clocks).
- **2013.** Reliable method of calculating biological age (BA) – 9 blood biomarkers mathematically combined (Levine BA Calculator).
- **2015.** First senolytic drug/supplements discovered (dasatinib, quercetin).

2009 – 2018

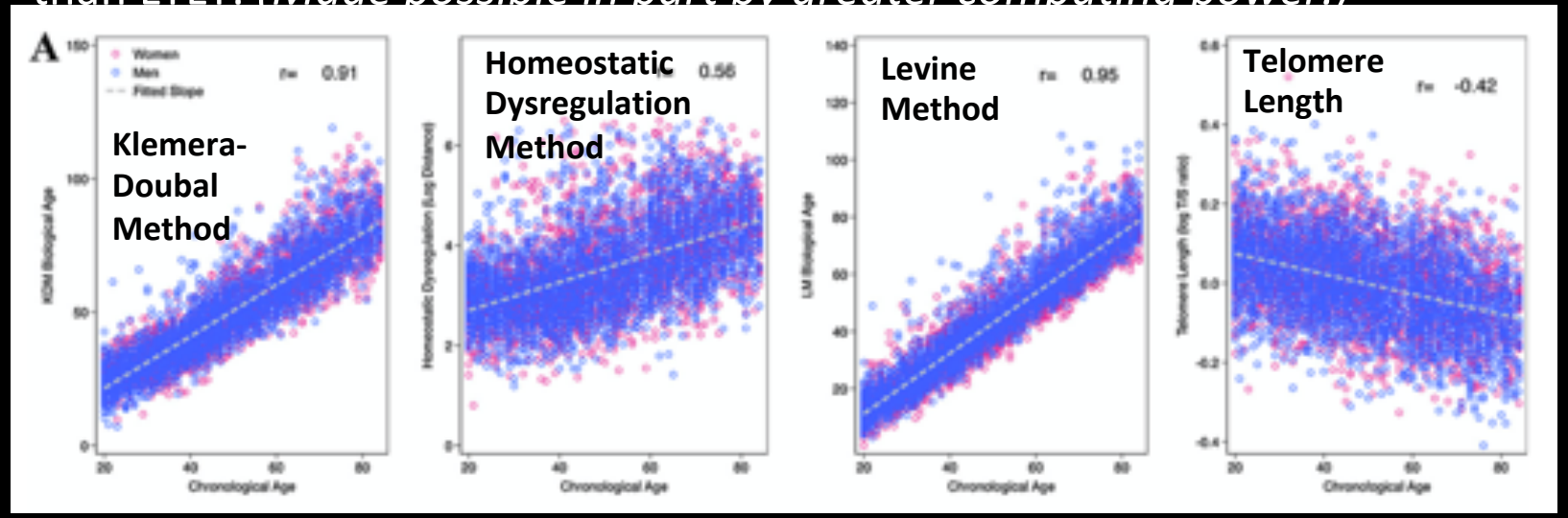
Brian M. Delaney
James Watson, MD
Principal Investigators
VIA Research Group

Aging Science: Very Recent Milestones

Discoveries Made in the Last 12 Months

- **2018.** Second generation epigenetic "DNA methylation clocks" developed that measure biological age (PhenoAge clock) and correlate with Levine BA Calculator (i.e. biological age calculated based on blood biomarkers & SBP).

- **2019.** New, more accurate mathematical methods of calculating biological age with multiple blood biomarkers. All 3 new methods more accurate than LTLT. *(Made possible in part by greater computing power.)*



2018 – 2019

Brian M. Delaney

James Watson, MD

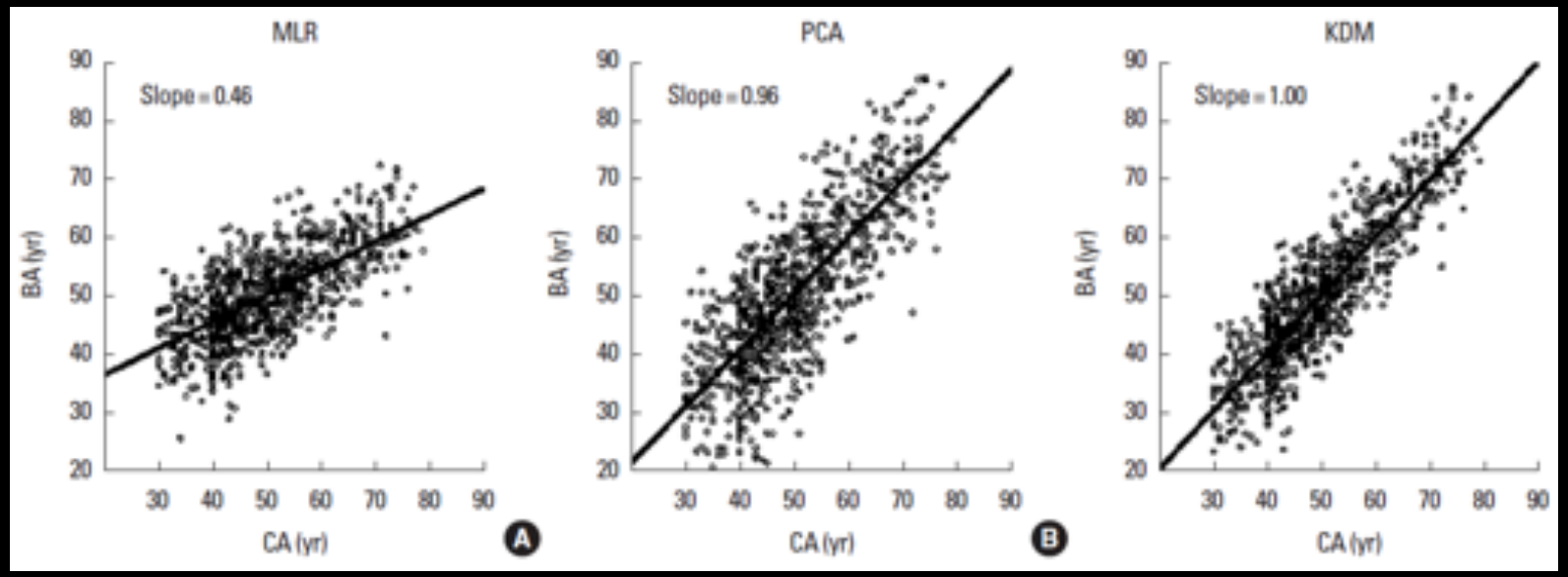
Principal Investigators
VIA Research Group

Reference: Hastings WJ, Shalev I, Belsky DW, Comparability of biological aging measures in the National Health and Nutrition Examination Study, 1999-2002, *Psychoneuroendocrinology* 2019; Aug;106:171-178.

Aging Science: Very Recent Milestones

Discoveries Made in the Last 12 Months

- **2019.** Old method of combining biomarkers (multiple linear regression) shown to be less accurate than newer mathematical methods (Klemera-Doubal method, Principal Components Analysis)



Reference: Jee H, Selection of a set of biomarkers and comparisons of biological age estimation models for Korean men. *J Exerc Rehabil.* 2019 Feb; 15(1): 31–36.

2018 – 2019

Brian M. Delaney

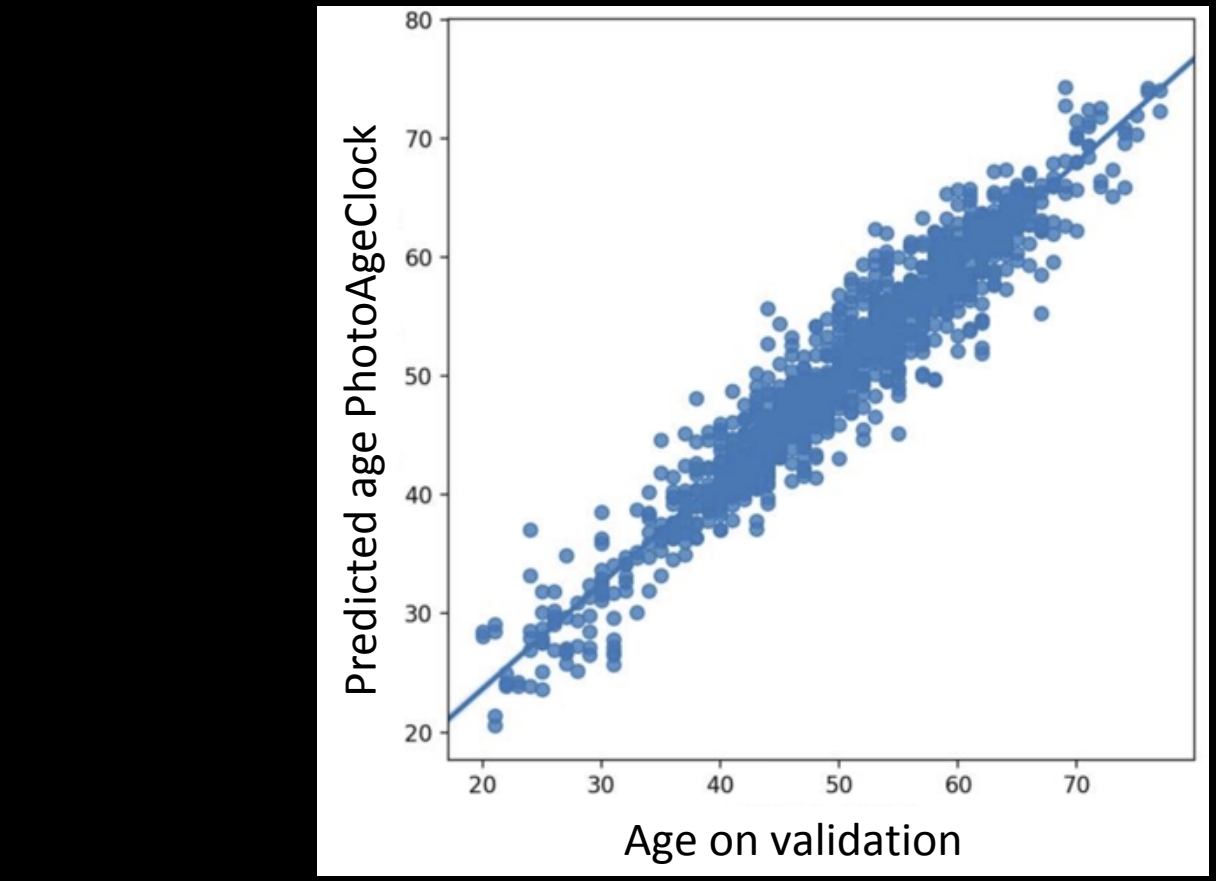
James Watson, MD

Principal Investigators
VIA Research Group

Aging Science: Very Recent Milestones

Discoveries Made in the Last 12 Months

- **2018. PhotoAgeClock** developed; relies solely on photographs of eye corners from facial images. MAE 2.3 years. Not AI, but machine learning. (More accurate than Horvath's original DNAm clock.)



Bobrov E et al., PhotoAgeClock: deep learning algorithms for development of non-invasive visual biomarkers of aging, *Aging (Albany NY)*, 2018 Nov; 10(11): 3249–3259.

2018 – 2019

Brian M. Delaney

James Watson, MD

Principal Investigators
VIA Research Group

Aging Science: Very Recent Milestones

Discoveries/Progress Made in the Last 12 Months

- **2019.** 1st in humans clinical trial of senolytic compounds, dasatinib (D) + quercetin (Q) shown to be safe in patients with severe idiopathic pulmonary fibrosis (IPF) [1]

  D + Q = ↑ distance on 6-minute walk test in IPF patients

- **2019.** 1st clinical trial (pilot study) reported showing epigenetic age (DNAm) reversal with cocktail of drugs/supplements (hGH, Metformin, DHEA) [2]

  Immune boosting cocktail: 1 year → 2.5 year younger DNAm age

- **2019.** World Health Org. announces that the new ICD-11 codes will include diagnosis code modifier for identifying diseases as being "age-related"

  ICD-11 code (modifier) for "age-related disease": XT9T

2019

Brian M. Delaney

James Watson, MD

Principal Investigators
VIA Research Group

[1] Justice JN, et al., Senolytics in idiopathic pulmonary fibrosis: Results from a first-in-human, open-label, pilot study, *EBioMedicine*, 2019 Feb;40:554-563.

Aging Science Today:
Multiple Promising Interventions

VIA VITALITY IN AGING

STAC (Sirtuin) activators

Senolytics

mTOR inhibitors

NAD⁺ & NAD⁺/NADH ratio restoration

Immune Restoration

AMPK activators

2019

DNA Editing CRISPR-Cas9

Heterochronic parabiosis mimetics

Mitochondrial Compounds

RNA editing ADAR-assisted

Stem cell & exosome therapies

Brian M. Delaney

James Watson, MD

Principal Investigators
VIA Research Group

Aging Biotechnology Today: More than 12 Companies Targeting "Aging" as a Disease

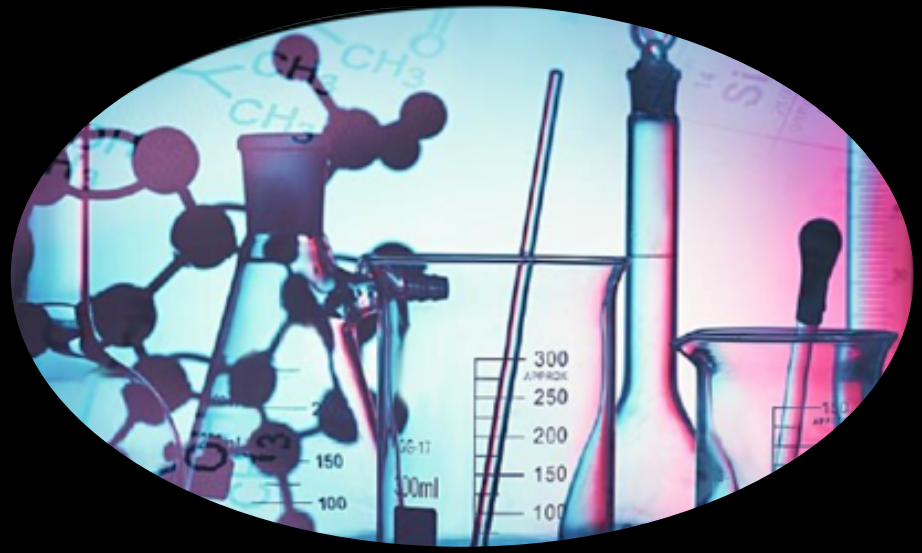
Unity Biotechnology

Life Biosciences

Veritas Genetics

Oisín Biotechnologies

Calico



2019

Intervene Immune

InSilico

Cobar

Senolytic Therapeutics

Continuum Biosciences

Cleara Biotech

Selphagy Therapeutics

Nebula Genomics

Brian M. Delaney
James Watson, MD
Principal Investigators
VIA Research Group

Purpose: VIA Research Studies:
Measuring & Treating Aging like a Dz

We are not the only ones doing this!

Nir Barzilai, Ph.D., Albert Einstein College of Medicine
Metformin Advocate
TAME Trial Author

David Sinclair, Ph.D.
Harvard Medical School
NMN Advocate
Co-founder, Life Biosciences

VIA
Clinical
Trials

Brian M. Delaney
James Watson, MD
Principal Investigators
VIA Research Group

1st ***VIA*** Clinical Trial:

VIA Longitudinal Study:

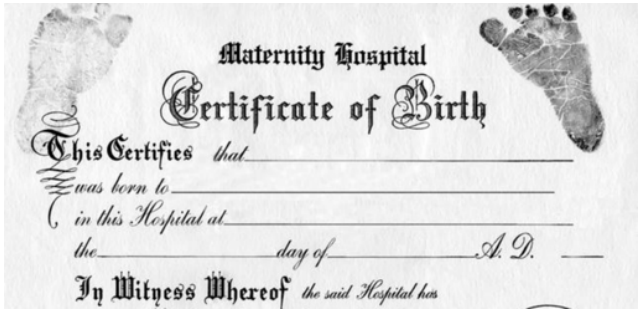
Measuring Aging with Precision Medicine

"Before we can treat aging, we must first accurately measure aging without having to wait for the person to 1st die of aging."
(Hope not to have to rely on mortality as endpoint.)

James Watson, MD
Principal investigator
VIA Research Group

Chronological vs. Biological Age

- **Chronological age** – birth certificate, driver's license, etc.



- **Biological age (BA)** – No standard, accepted definition of BA
  Example: measuring "decline of function"

VIA: Next Generation Clinical Trials to Measure Aging

Brian M. Delaney
James Watson, MD
Principal Investigators
VIA Research Group

How to Measure Biological Age (BA)?

Functional Aging (impact on daily life)

- Cognitive Function
- Physical Function
- Mood
- Mental Health

Phenotypic Aging (phenotypes that change)

- Body Composition
- Energetics
- Homeostatic Mechanisms
- Brain health

Biological Aging (root mechanisms)

- Molecular damage
- Defective repair
- Energy exhaustion
- Signal/noise reduction

Luigi Ferrucci, MD, PhD, Morgan Levine, Pei-Lun Kuo, and Eleanor M. Simonsick, Time and the Metrics of Aging, *Circ Res,* 2018 Sep 14; 123(7): 740–744.

VIA: Next Generation Clinical Trials to Measure Aging

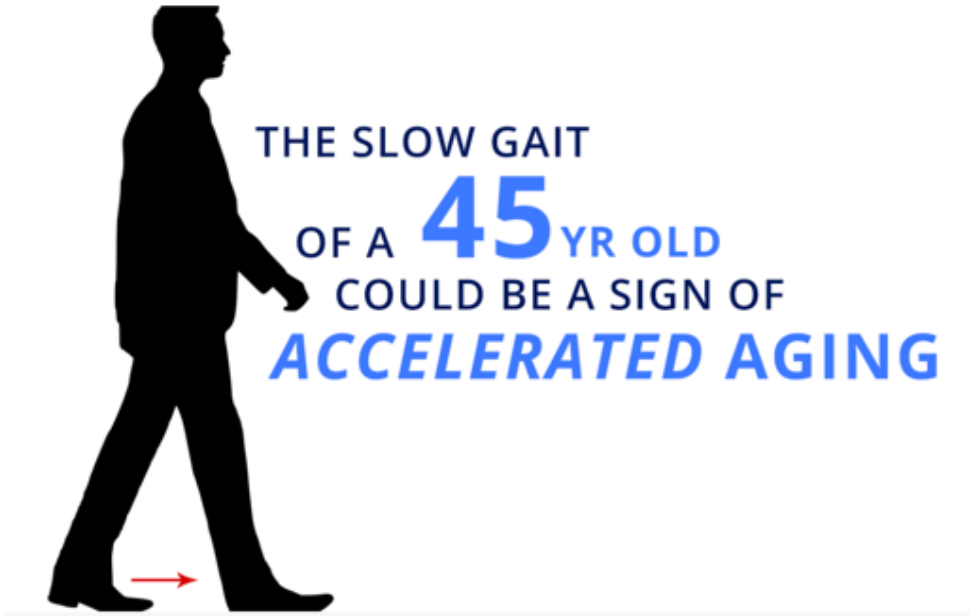
Brian M. Delaney

James Watson, MD

Principal Investigators
VIA Research Group

Older, established methods of measuring “true” or biological age (BA)

- **Oldest Method of Measuring BA:** *Measure “Decline in Function” (aka “Functional Measurement”)* Ex: measuring “gait speed”



- Recent study, October, 2019
- Ref: JAMA Network Open
- Studied 904 people aged 45
- “Slow walkers” had:
  - ↓ brain volume
  - ↓ cortical thickness
  - ↓ brain surface area
  - ↑ white matter lesions associated with small vessel disease

VIA: Next Generation Clinical Trials to Measure Aging

Brian M. Delaney
James Watson, MD
Principal Investigators
VIA Research Group

Ref: Rasmussen L, et al. Association of Neurocognitive and Physical Function with Gait Speed in Midlife, *JAMA*, Oct. 11, 2019.

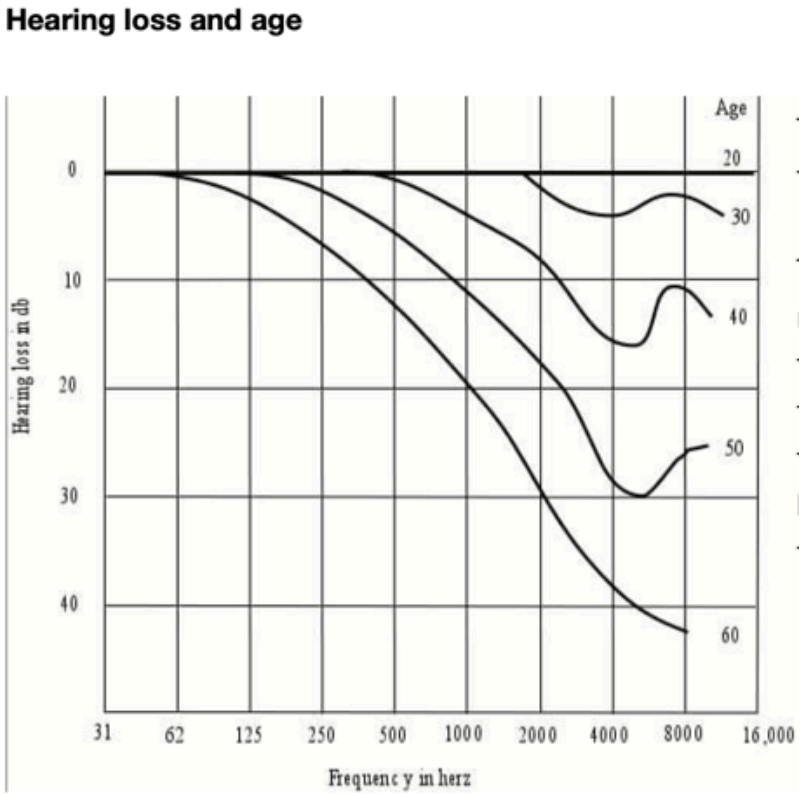
Older, established methods of measuring “true” or biological age (BA)

- **Example of a commonly used “decline in function measurement” of aging**

  Ex: Presbycusis (aka age-related hearing loss)

  High frequencies are the first to go (or to “arrive”, falsely: tinnitus)

Audiogram Test



VIA: Next Generation Clinical Trials to Measure Aging

Brian M. Delaney

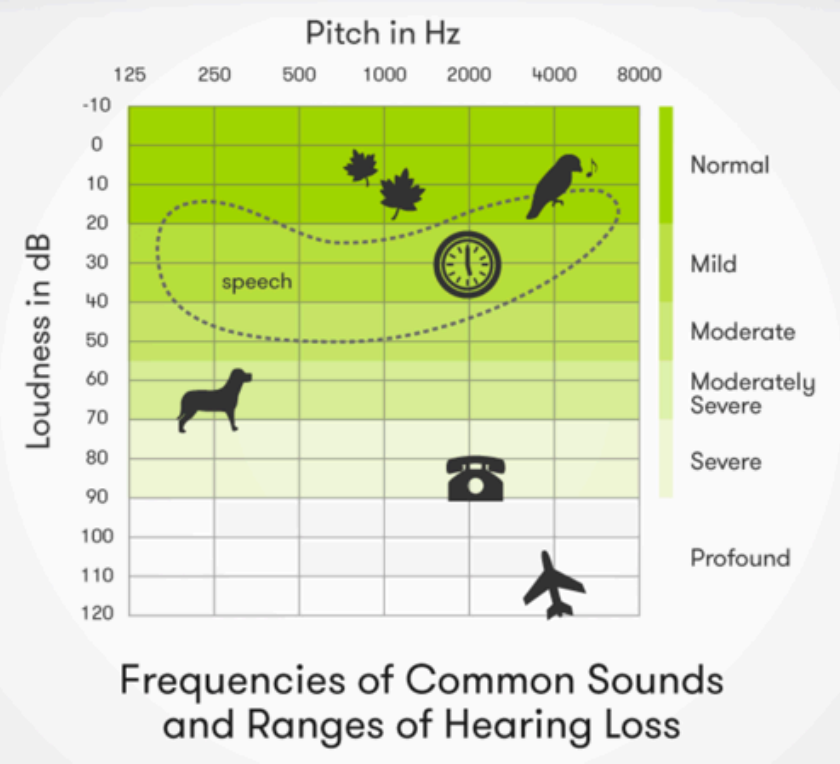
James Watson, MD

Principal Investigators
VIA Research Group

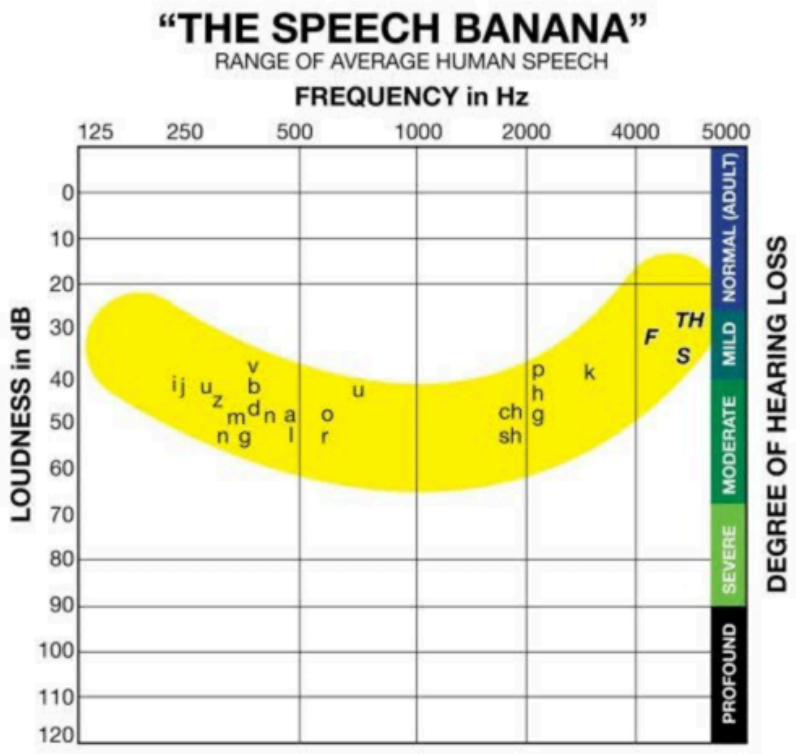
Problems with “decline in function” measurements of biological age (BA)

- **No defined “standard decline” –** wide variation of normal (variance)

  Example: decline in hearing. *(Pilots’ hearing: nothing to do with age.)*



Ex: Different sounds lost @ different BA



Ex: “F”, “TH”, and “S” sounds lost 1st with aging

VIA: Next Generation Clinical Trials to Measure Aging

Brian M. Delaney

James Watson, MD

Principal Investigators
VIA Research Group

Despite problems with measure of functional age, *cannot eliminate functional tests* (in the absence of mortality data.)

- **PhotoAgeClock** and many newer clocks validated against CA. That isn't exactly what's needed.
- Need test of **BA** to be able to test effects of interventions (with waiting for mortality data).
- Can't escape need for either 1) **mortality data**, or 2) **improved tests of functional age**.

VIA: Next Generation Clinical Trials to Measure Aging

Brian M. Delaney
James Watson, MD
Principal Investigators
VIA Research Group

Hence, need better toolbox

1. Cohort of **meticulous** individuals who can make decade- or even **decades**-long commitment to a **demanding** observational study.
2. Tissue samples stored long-term for later "back-testing" using new tests as they are developed.
3. Interventional trials to see whether direct modulation of putative testable pathways alters aging in some way. (Though main purpose here is safety.)

VIA: Next Generation Clinical Trials to Measure Aging

Brian M. Delaney
James Watson, MD
Principal Investigators
VIA Research Group

Brian M. Delaney
James Watson, MD
Principal Investigators
Vitality in Aging (VIA)
Research Group
Fort Lauderdale, Florida

3 VIA Clinical Trials*

1. **The VIA Longitudinal Study**
   N = 1,000
2. **The VIA Tissue Biorepository**
   N = 1,000
3. **THE VIA Interventions Trial**
   N = 30-50

*IRB Committee Supervising VIA Clinical Trials:
Institute for Regenerative and Cellular Medicine,
Santa Monica, CA

VIA Longitudinal Study

"Framingham Heart Study of Aging"

VIA Longitudinal Study – Key Points

- Size: N = 1,000 volunteers. Males and females.
- Study design: Epidemiological long-term study, like the Framingham Heart Study.
- Funding: 70% funded by Bill Faloon (rest participant contributions to cost).
- Eligibility: Anyone aged 20-90 can join.
- Treatment: Self-selected interventions (may follow Interventions protocol or any other if desired).

VIA: Next Generation Clinical Trials for Measuring Aging

Brian M. Delaney

James Watson, MD

Principal Investigators
VIA Research Group

Vitality In Aging Longitudinal Study

(*Or . . . perhaps more than 1000)*

- Enrollment drive at RAADfest, Oct. 3–6
- Expected 50 or so enrollees
- Planned for 100 to be safe

- Enrolled 260
- Had to turn people away

Next enrollment drive already “oversubscribed”

Need to expand to underserved communities, achieve diversity. Mobile medical unit needed.

VIA: Next Generation Clinical Trials for Measuring Aging

Brian M. Delaney

James Watson, MD

Principal Investigators
VIA Research Group

Vitality In Aging Longitudinal Study

(*Beyond 1000)*

Coming soon . . . .

VIA: Next Generation Clinical Trials for Measuring Aging

Brian M. Delaney

James Watson, MD

Principal Investigators
VIA Research Group

Vitality In Aging Longitudinal Study

Purpose and Objectives

- **Biomarker validation** – Validate old and new biomarkers
- **Biomarker discovery** – Ex: PhotoAge biomarkers (machine learning)
- **Gene Discovery** – What SNPs are linked to “age acceleration” or “age deceleration”
- **Epigenetic Discovery** – what epigenetic factors cause “age acceleration” or “age deceleration”
- **Lifestyle Factors** – Discover what lifestyle factors alter aging rates
- **Anti-aging supplements?** – Discover what supplements alter aging rates
- **Anti-aging drugs** – Discover FDA-approved drugs for effects on aging

VIA: Next Generation Clinical Trials for Measuring Aging

Brian M. Delaney

James Watson, MD

Principal Investigators
VIA Research Group

Vitality In Aging Longitudinal Study

Tests That Will Be Done on All Participants

1. **Blood biomarkers.** Levine Biological Age Calculator used to calculate biological age using 9 blood biomarkers: Albumin, Creatinine, Glucose, C-reactive protein (CRP) % lymphocytes, Mean cell volume (MCV), red cell distribution width (RDW), alkaline phosphatase, & WBC.
2. **Physical function tests – *AgeMeter*™**

- auditory reaction time,
- highest audible pitch
- vibrotactile sensitivity
- visual reaction time
- visual movement time
- muscle speed and coordination
- lung forced vital capacity (FVC)
- forced expiratory volume (FEV_1)
- decision reaction time
- decision movement time,
- memory tests
- blood oxygen saturation.

VIA: Next Generation Clinical Trials for Measuring Aging

Brian M. Delaney

James Watson, MD

Principal Investigators
VIA Research Group

Vitality In Aging Longitudinal Study

Tests That Will Be Done on all participants

3. **Physiologic Testing.** Systolic BP, Diastolic BP, pulse pressure, 6-minute walk test, Hand grip testing, 30 second chair-to-standing test, 4 memory tests (MMSE, etc.).

4. **Body Composition testing.** **Seca™ bioimpedance device used to** measure % body fat, visceral fat, lean body mass, resistance, reactance, and body hydration, and Phase angle.

5. **Heart Rate Variability (HRV) testing.** All volunteers will undergo testing and analysis to measure autonomic aging, and psychophysiologic stress (RMSSD, SDNN, HF, LF, HF/LF, VLF, ULF, and non-linear analysis.

VIA: Next Generation Clinical Trials for Measuring Aging

Brian M. Delaney

James Watson, MD

Principal Investigators
VIA Research Group

VIA Longitudinal Study Optional Tests

Additional, *Optional* Tests

Whole genome sequencing. All volunteers will have the chance to undergo high fidelity complete genome sequencing (30X coverage) of their entire DNA (genes, pseudogenes, noncoding DNA, etc.).

Participation in Harvard's PGP mandatory. (Degree of participation up to study participant.)

VIA: Next Generation Clinical Trials for Measuring Aging

Brian M. Delaney

James Watson, MD

Principal Investigators
VIA Research Group

VIA Longitudinal Study Optional Tests

Additional, *Optional* Tests

1. **Epigenetic (DNAm) Clock testing** – some volunteers will undergo DNA methylation clock testing with PhenoAge, SkinAge, and GrimAge DNAm clocks
2. **Telomere Length testing (LTLT)** – some volunteers will undergo leukocyte telomere length testing with ***FlowFISH*** method (more accurate than other methods)
3. **Cellular Senescence Tests*** – this requires a skin and fat biopsy, then special tissue stains for β-galactosidase, p16INK4a, and other markers of cellular senescence
4. **DEXA scan**** – this is a low dose X-ray test - measures bone density, body fat, lean body mass (muscle), and visceral fat (more accurate than Bioimpedance testing)
5. **NAD+ testing** – this is an experimental, non-validated test of NAD+ levels

* This require tissue biopsy (skin and fat). They will be done only on individuals who agree to have skin and fat biopsies.

** This requires exposure to X-ray radiation

VIA: Next Generation Clinical Trials for Measuring Aging

Brian M. Delaney

James Watson, MD

Principal Investigators
VIA Research Group

VIA Longitudinal Study Optional Tests

Additional, *Optional* Tests

6. **Neural-derived exosome testing** – volunteers will undergo exosome testing w/blood-derived neural exosomes that predict Alzheimer's risk with 100% accuracy
7. **Total body MRI testing** – most accurate measure of visceral fat and lean body mass. Can also be useful for screening for brain aging, prostate CA, breast CA
8. **Cardiac stress testing –** Will be done to screen high risk pts for heart dz
9. **Novel Vitamin K measurement (VitaK Innovation in Life Science)** – measures Vitamin K using an in vitro diagnostic system
10. **CT Angiogram + Coronary Artery Calcium testing** – will be done for those whose cardiac stress testing is abnormal or who are at high risk
11. **Carotid intimal thickness testing (CIMT) –** will be done on those who are at high risk for stroke, based on Framingham Risk Score
12. **Arterial Stiffness testing (VitaK StiffnoGraph)** – best test of endothelial aging, nitric oxide (eNOS), and endothelial health (better than FMD of brachial artery)

VIA: Next Generation Clinical Trials for Measuring Aging

Brian M. Delaney
James Watson, MD
Principal Investigators
VIA Research Group

Standing on the Shoulders of Giants

- **1945** – FHS
- **1965** – Honolulu Heart Program (Honolulu Asia Aging Study, Multiethnic Cohort Study)
- **1971** – NHANES
- **1972** – Dunedin
- **1998** – InCHIANTI (Invecchiare in Chianti)
- **2006** – Newcastle 85+ Study
- *(Many, many others focused on age-associated illness: ERFC, etc.)*

In Good Company!

Brian M. Delaney

James Watson, MD

Principal Investigators
VIA Research Group

Honolulu Heart Program (HHP)/ Honolulu Asia Aging Study (HAAS)

Proc Natl Acad Sci U S A. 2008 Sep 16; 105(37): 13987–13992.
Published online 2008 Sep 2.

Landmark discovery

FOXO3A genotype is strongly associated with human longevity

Bradley J. Willcox, Timothy A. Donlon, Qimei He, Randi Chen, John S. Grove, Katsuhiko Yano, Kamal H. Masaki, D. Craig Willcox, Beatriz Rodriguez, and J. David Curb

Brian M. Delaney
James Watson, MD
Principal Investigators
VIA Research Group

VIA Tissue Biorepository

IRB-approved Tissue Bank

What is a Tissue Bank?

- Samples of blood, skin, saliva, etc. stored at -80 °C
- All donors have signed consent to bank/share tissue
- Donors are “de-identified”
- Samples linked to de-identified health information, blood biomarkers, and functional/physiological tests of donors

Why a Tissue Bank?

- Tissue can be legally shared with researchers who obtain IRB approval for a study and permission from tissue bank
- New discoveries can be made by many researchers
- New tests can be “back-tested” with stored samples of blood

VIA Tissue Biorepository Tissue Bank for sharing samples

Brian M. Delaney

James Watson, MD

Principal Investigators
VIA Research Group

VIA Interventions Trial

IRB-approved Clinical Trial to “Treat” Aging

What is the VIA Interventions Trial?

- **Size**: N = 30 volunteers. Males and females.
- **Study design** - Phase I (safety) trial.
- **Funding**: 100% funded by donations. IRB approved.
- **Who can join?** - Volunteers that have already signed up for the VIA Longitudinal Study and can be compliant.
- **Exclusion**: Volunteers that have major lifestyle factors known to accelerate aging (smoking, obesity, sedentary lifestyle, drug use, etc.).

VIA: 1st Clinical Trial for Treating Aging

Brian M. Delaney

James Watson, MD

Principal Investigators
VIA Research Group

VIA Interventions Trial

IRB-approved Clinical Trial to “Treat” Aging

Q: What Compounds are being used in the VIA Interventions Trial?

- **Cocktail** – supplements and FDA-approved drugs are being combined, based on proven longevity testing in animals
- **Off-label use** – All of the FDA-approved drugs are being used “off label” to treat aging
- **Molecular Pathways Targeted** – Both calorie restriction (CR) and CR-independent pathways are being targeted

VIA: 1st Clinical Trial for Treating Aging

Brian M. Delaney

James Watson, MD

Principal Investigators
VIA Research Group

VIA Interventions Trial Compounds

- **Foundation** – Selection based on the proven science of calorie restriction
- **Compounds Selection** – we selected at least one compound to target each known aging pathway:
  - CR pathways aging – 6 pathways
  - Non-CR pathways of aging – 4 pathways
- **Safety**- all compounds proven to be safe alone, but have not been tested in combinations like this
- **4 FDA-approved drugs** – being "repurposed"
- **9 Supplements** – all proven to be effective in animal models of aging or inflammation

VIA: 1st Clinical Trial for Treating Aging

Brian M. Delaney
James Watson, MD
Principal Investigators
VIA Research Group

VIA Interventions Trial Compounds

Both Drugs and Supplements will be used to cover all Aging Pathways

Calorie Restriction Mimetics

- Metformin
- Rapamycin
- Gynostemma p.
- Nicotinamide Riboside (NR)
- β-lapachone
- Pterostilbene

Non-CR Pathway Compounds

- Glucosamine
- Omega-3 fatty acids
- Dasatinib
- Quercetin
- Fisetin

VIA: 1st Clinical Trial for Treating Aging

We don't care if it is a drug or a supplement
We only care that the compound works and is safe

Brian M. Delaney
James Watson, MD
Principal Investigators
VIA Research Group

VIA Interventions Trial Compounds

Compound	Safe in Humans	Mechanism of action	Effect on Healthspan and Lifespan in Animals & effect on All Cause Mortality in Humans (ACMH)
Glucosamine	yes	↑autophagy	↑ healthspan and lifespan no data on ACMH
Metformin	yes	↑ AMPK	↑ healthspan and lifespan ↓ ACMH by 20-32%
Gynostemma p.	yes	↑ AMPK	↑ lifespan, no data on healthspan no data on ACMH
Rapamycin	yes	↓ mTOR	↑ healthspan and lifespan ↓ cancer by 40% & 56%
Betaine	yes	↓ inflammation	no data on lifespan/healthspan, non data on ACMH
NR	yes	↑ NAD^+	↑ healthspan and lifespan no data on ACMH
β-lapachone	yes	↑ NAD^+/NADH ratio	↑ healthspan and lifespan no data on ACMH
Pterostilbene	yes	↑ SIRT1	no data on ↑lifespan & healthspan no data on ACMH
Omega-3 FAs	safe	↓ inflammation &	↓ telomere shortening ↓ ACMH by 6-19%
Dasatinib	yes	↓ senescent cells	↑ lifespan/healthspan w/quercetin no data on ACMH
Quercetin	yes	↓ senescent cells	↑ lifespan/healthspan w/dasatinib no data on ACMH
Fisetin	yes	↓ senescent cells	no data on ↑lifespan & healthspan no data on ACMH

VIA: 1st Clinical Trial for Treating Aging

Brian M. Delaney
James Watson, MD
Principal Investigators
VIA Research Group

Why not stem cells, MSCs, exosomes, other "new biologics" / "living medicine"?!

- **Might overwhelm the effects of all the other interventions!**
- **Budget limitations (study)** – Prices for exosomes are coming down, but are still high. Most stem cell treatments expensive.
- **Budget limitations (individuals)** – If we show relatively inexpensive drugs and supplements can help people, many people who want the treatments will be able to afford them.
- **VIA Longitudinal Study will nonetheless shed light on stem cells/exosomes** – With large enough cohort of life-extension enthusiasts, can expect to have enough people paying for stem cell/ exosome therapy *on their own* that, over time, conclusions about safety and efficacy can be drawn.
- **More intervention trials planned!** – Because we are excited about regenerative and cellular medicine, already planning and seeking funding for a study with exosomes. Other studies will follow.

VIA: 1st Clinical Trial for Treating Aging

Brian M. Delaney

James Watson, MD

Principal Investigators
VIA Research Group

Vitality In Aging Clinical Trials

Summary & Conclusions

3 IRB-approved clinical trials

- **Study #1**: 1,000-person epidemiological study of aging for 10 years with whole genome testing, epigenetic clock testing, blood biomarker biological age testing with Levine BA method, KDM method, and PCA methods, telomere testing, functional biomarker tests annual exams, etc.
- **Study #2**: Tissue biorepository with de-identified samples of blood, tissue, etc. – for sharing with academic researchers studying aging.
- **Study #3**: 30-person Interventions trial using cocktail of 12 supplements and drugs already proven to affect aging in animal models.

VIA VITALITY IN AGING

Precision Medicine Clinical Trials to Accurately Measure Biological Age and Treat Aging

Vitality In Aging (VIA) Clinical Trials

VitalityInAging.org

Info@VitalityInAging.org

Precision Medicine Clinical Trials to Accurately Measure Biological Age and Treat Aging