Change Your Genes – Change Your Life: Epigenetics of Longevity

Kenneth R. Pelletier, PhD, MD

Change Your Genes – Change Your Life
Epigenetics and Longevity

Kenneth R. Pelletier, PhD, MD

Clinical Professor of Medicine

Clinical Professor of Family & Community Medicine

Clinical Professor of Psychiatry

University of California School of Medicine,
San Francisco (UCSF Med)

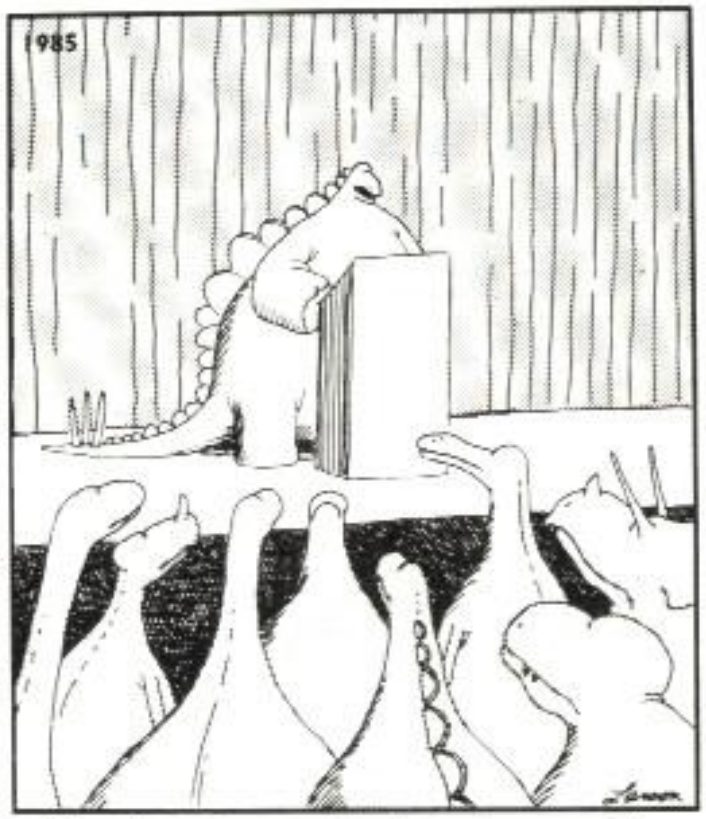
EPIGENETICS

GENETICS

This is how it works

Living to Be 100 and Beyond

Bessie Hedricks – Oldest Person in the USA living in Iowa at 116 on her birthday of November 7, 2022

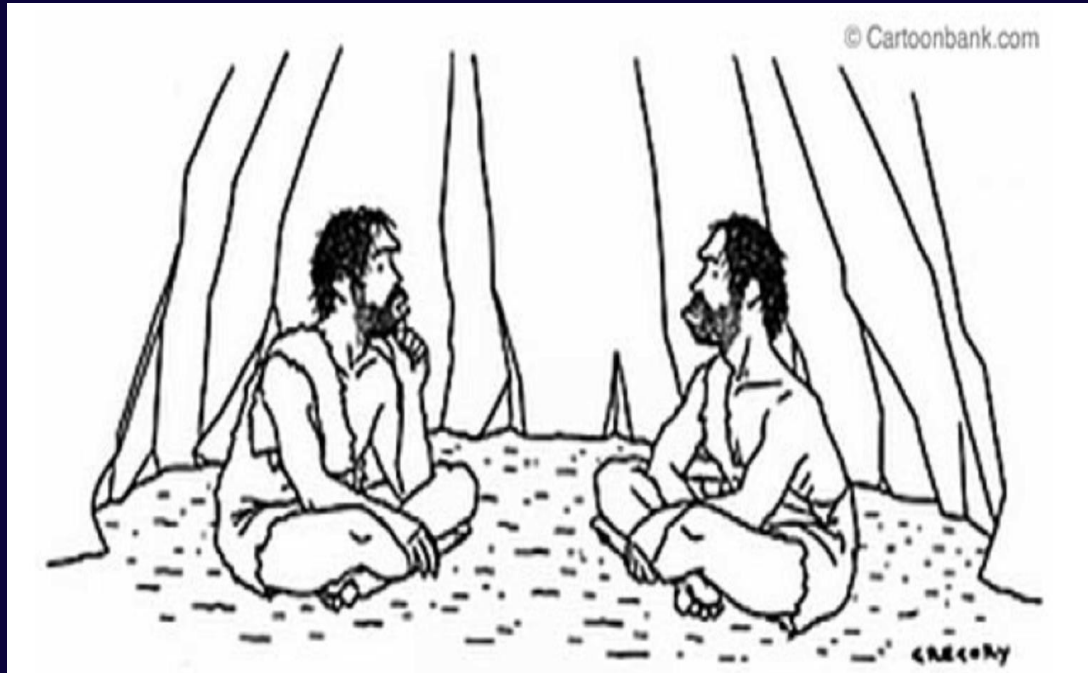


"The picture's pretty bleak, gentlemen. ... The world's climates are changing, the mammals are taking over, and we all have a brain about the size of a walnut."


Joe Klein:
The CIA's
Afghan Disaster
Yemen: The
New Center
Of Terror
Why the Recession
Hasn't Been Cool
To Teens
TIME
WHY
YOUR DNA
ISN'T YOUR
DESTINY
The new science of epigenetics
reveals how the choices you
make can change your genes
—and those of your kids
BY JOHN CLOUD

IDENTICAL TWINS and EPIGENETICS

- Dr Bert Vogelstein – Johns Hopkins University Medical School
- Longitudinal study in 2012, compared genomes of thousands of identical twins
- Focused on 24 major diseases over 15 years
- Parkinson's risk = 5%; CHD = 50% (random chance); and, Most Cancers = Less than 50%
- Whole genome sequencing could alert most individuals to an increased risk of only ONE disease on average
- Such sequencing can be misleading since each twin remains susceptible to all other diseases and not the same diseases as the twin

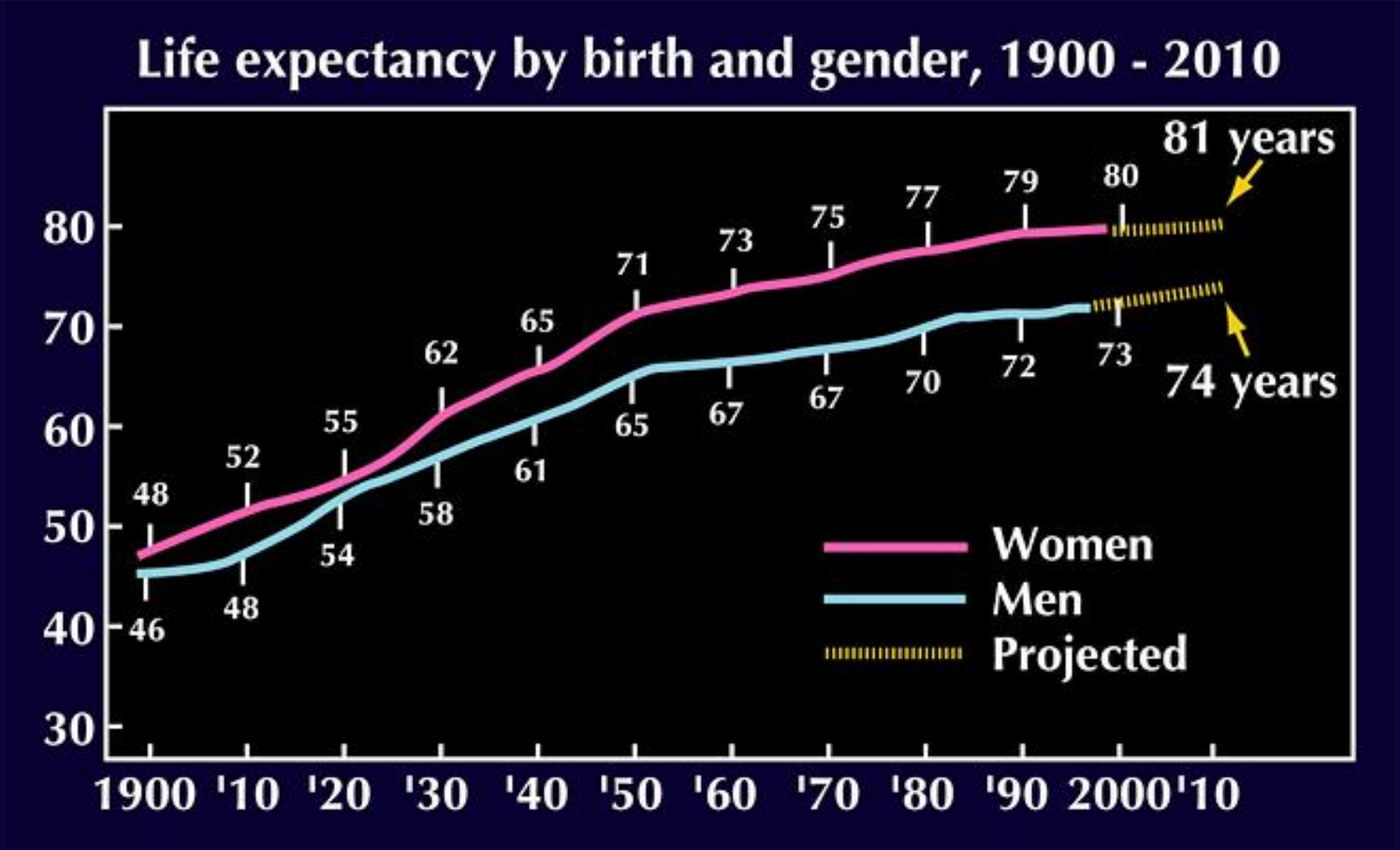


"Something's just not right—our air is clean, our water is pure, we all get plenty of exercise, everything we eat is organic and free-range, and yet nobody lives past thirty."

Single Nucleotide Polymorphisms: Common Genetic Variants SNPs

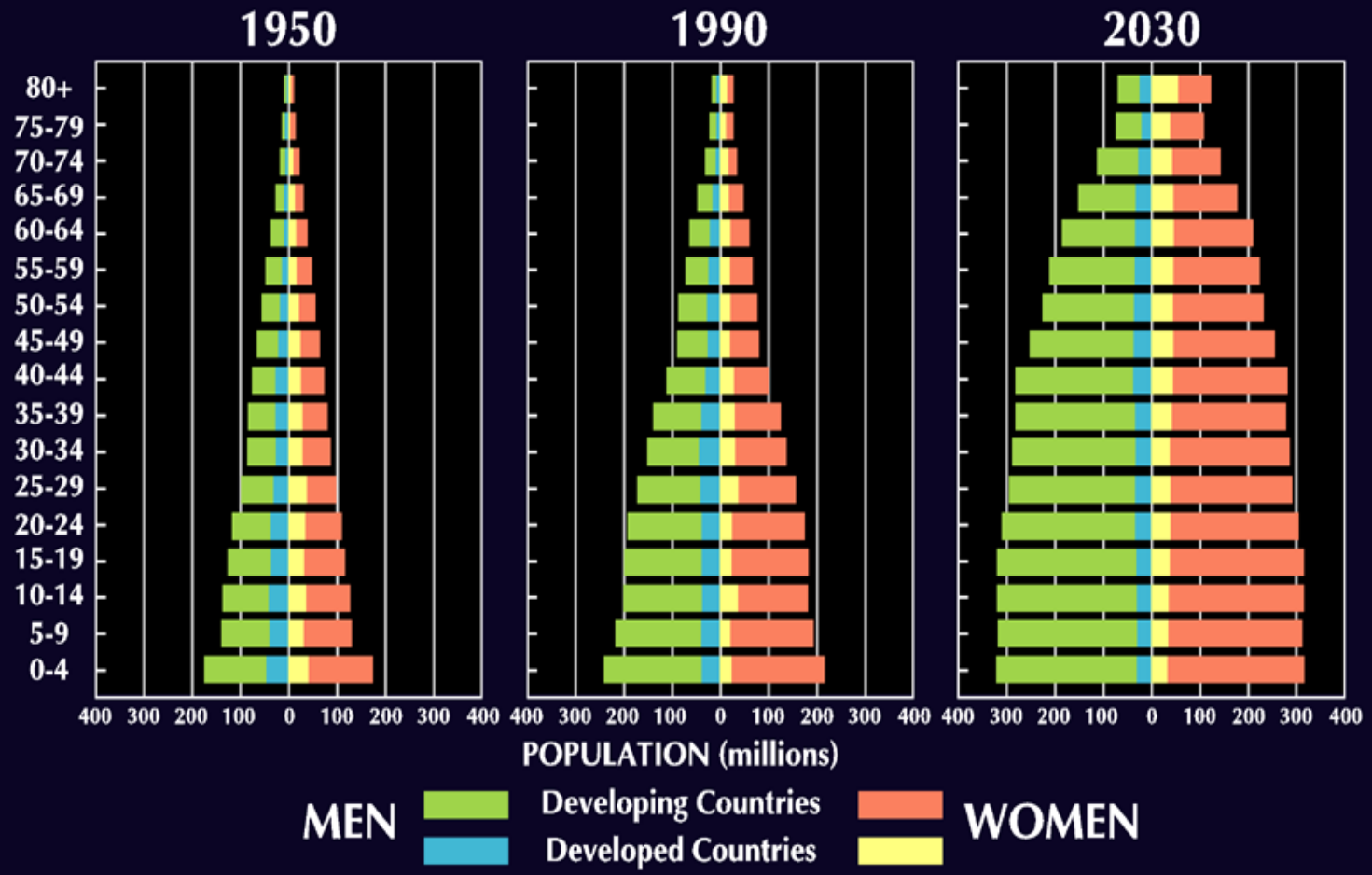
- SNPs act as a rheostat to express or suppress genetic predisposition
- Genetic Variation: Central to personalized medicine
- SNPs influence by diet/nutrition, stress/meditation, radiation, physical and psychosocial environment, Rxs, endocrine disruptors, and sense of purpose
- >3 million SNPs identified
- Estimated potential 10+ million SNPs in the human genome
- SNPedia: 83,452 Reference SNPs

HOW LONG WILL WE LIVE?



Source: US National Center for Health Statistics

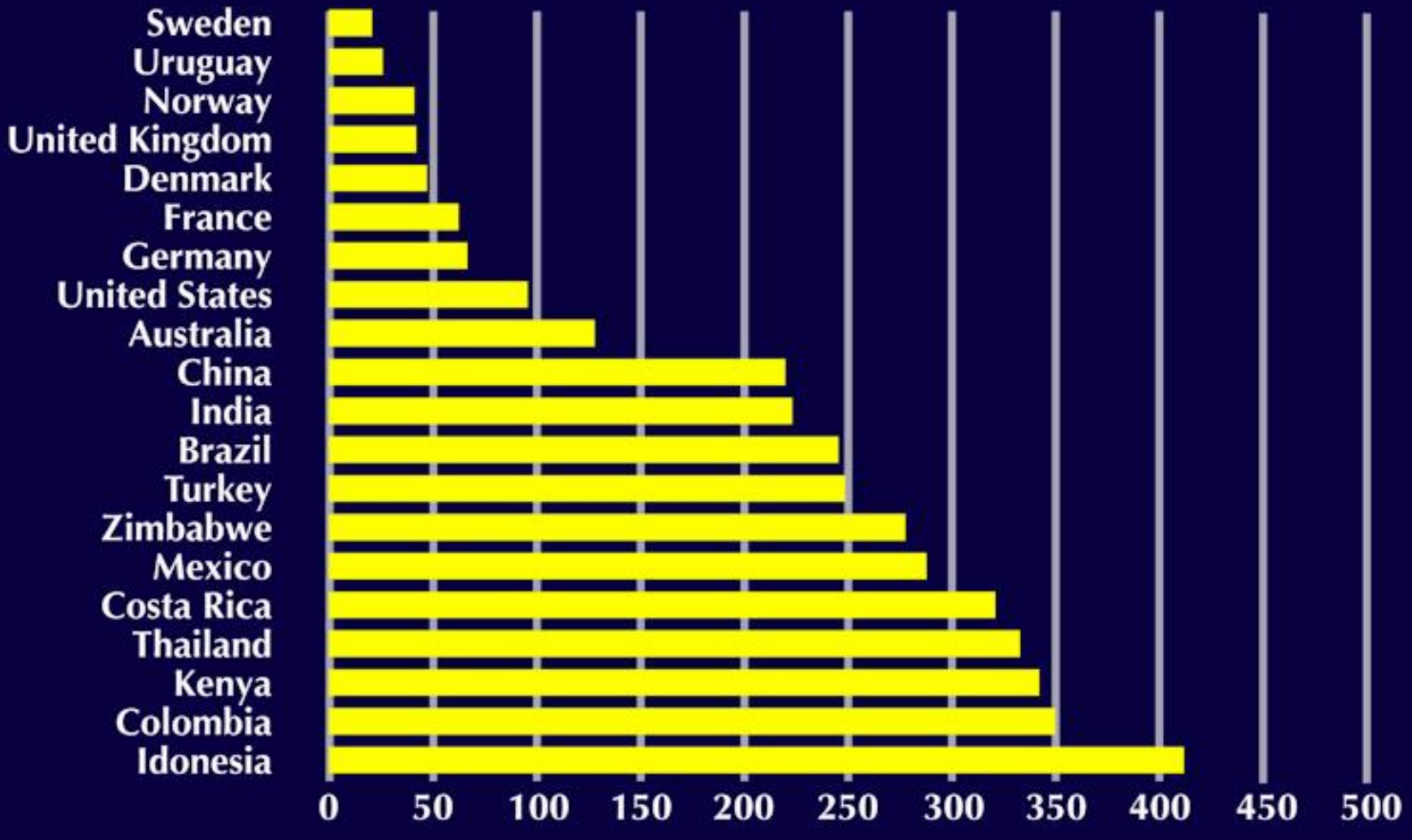
GRAYING of PLANET EARTH

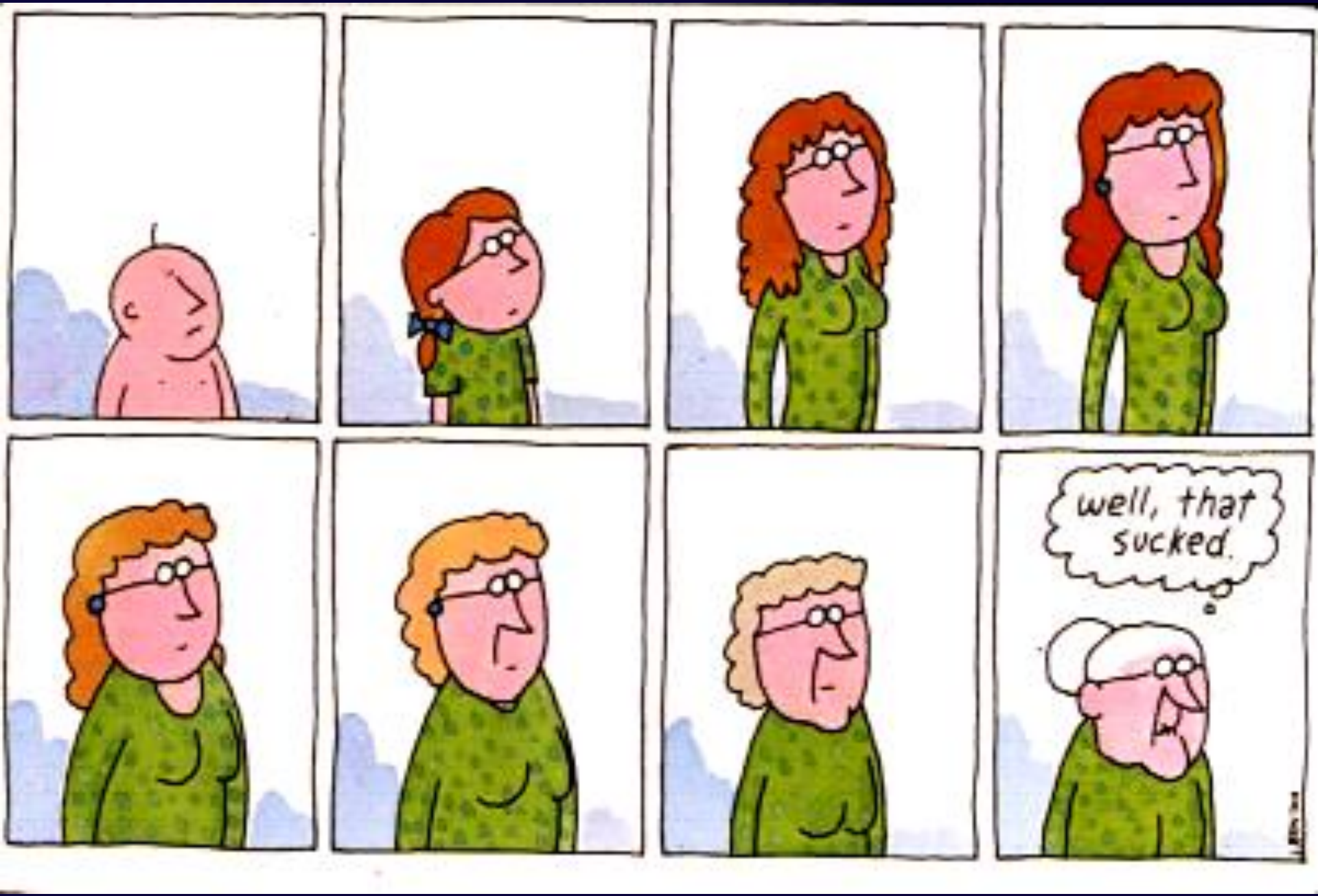


National Academy of Sciences, 5/2001. "Data Needs for an Aging World", F. Thomas Juster, Institute for Social Research, University of Michigan, Ann Arbor

EA8077.13

Percent Increase in Elderly (> 65) Population: 1990 to 2025




well, that sucked.

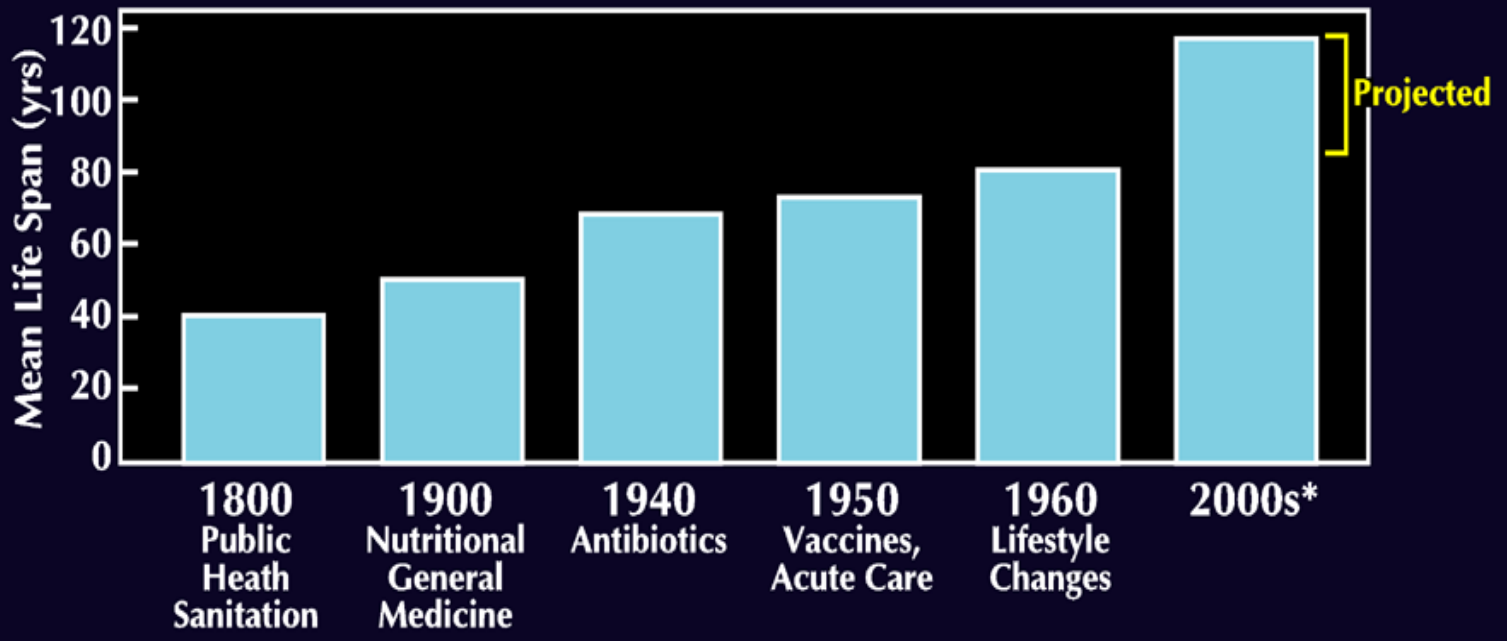
85 - And - Older Population

Year	Number	Percentage of US Population
1900	122,000	0.2%
1990	3,021,000	1.2%
2000	4,333,000	1.6%
2010	5,969,000	2.0%
2020	6,959,000	2.1%
2030	8,843,000	2.5%
2040	13,840,000	3.7%
2050	18,893,000	4.8%

1960 - 1994

- The total population grew 45%
- The number of those 65 and over grew 100 percent
- The number of those 85 and over grew 274 percent

ACTUAL and PROJECTED CHANGES in LIFE EXPECTANCY

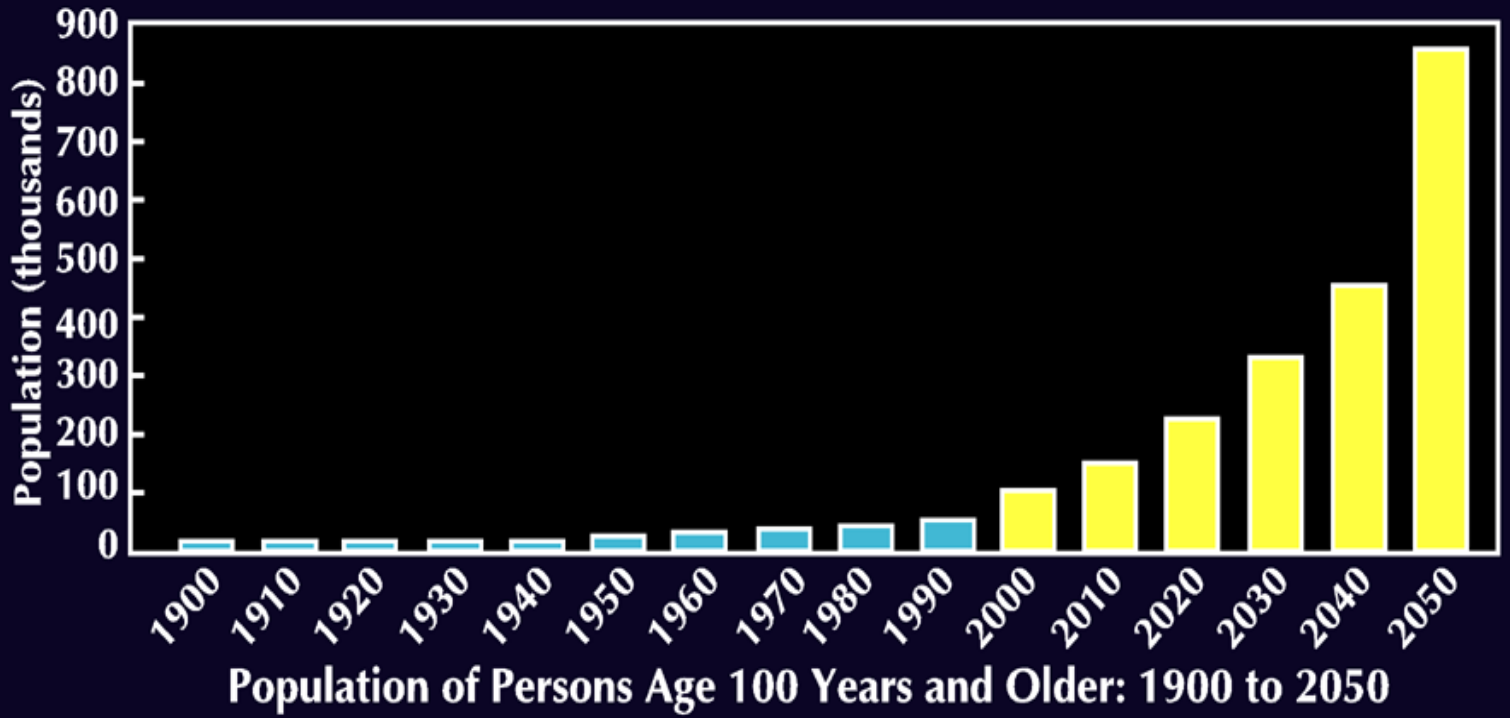


*Projections include the use of drugs that prolong life, antioxidants, hormones, gene therapy, lifestyle / preventive medicine, and integrative medicine innovations.

Christine K. Cassell, Geriatrics, January 2001, Vol 56, Number 1

EA8077.11

POPULATION of CENTENARIANS (> 100) 1900 to 2050



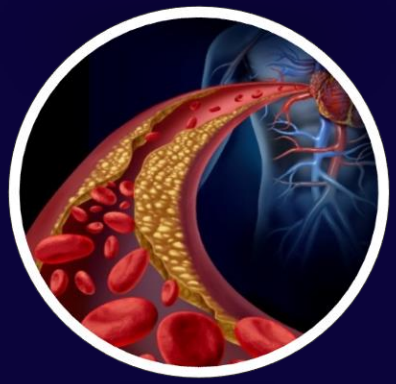
Adapted from Krach CA and Velkoff VA. U.S. Bureau of the Census (Series T23-199 RV) Centenarians in the United States. USGPO: Washington, DC, 2001.

EAB077.12


DIPLÔME
LE LIVRE GUINNESS DES RECORDS
TITULAIRE
RECORD
DATE
Jeanne Calment

Epigenetics: A Tripartite Assay

=



=

=

Oceans of BioHacks
“Here Dwell Dragons”

Literally thousands of promises and perils with Longevity Biohacks

- Senolytic Pharmacology - Metformin; Rapamycin; NAD (precursors of NR and NWN); Fisetin; EGCG; Resveratrol; Omega-3 c DHA and EPA; Astralagus; Taurine; Curcumin; MICROBIOME (Pre and Post Biotics); DGMs; and Biotelemetry
- Biohacks - Intermittent Fasting (1938); Hayflick Limit of 120 (1960s); Stem Cells "Banking"; Klotho (Platelet Factor 4 - PF4) - Antiaging hormone injections; Alzheimer's Slowing/Reversing (Bredesen); GLP Inhibitors - Ozempic and Wegovy); DNA Repair; CRISPR Editing, "Young Blood" Transfusions (Thiel); Medical Grade Hyperbaric Oxygen - Aviv Clinic c Shai Efrati in Israel; Cryonic Freezing/Cold Water Immersion (Wim Hof); and MEDITERRANEAN DIET
- Epigenetic Assays - David Sinclair (Harvard c "Chemical Cocktail); Inside Tracker; Horvath's Clock (UCLA); Telomeres (Blackburn at UCSF Med); Function Health (Hyman); Church (Harvard); OneGevity (Thorne); Viome (Partnership with CVS); AI/CHAT GPT; and, Bryan Johnson - “My ultimate goal? Don’t die!”


I GOT ONE OF THOSE DNA KITS. TURNS OUT I'M 85% WATER, 8% DIRT AND 7% DOG PEE.
-S-
WRITER & ARTIST
SCOTT NICKEL
MAD
MADMAG.COM

The Nobel Prize in Physiology or Medicine 2009

"for the discovery of how chromosomes are protected by telomeres"

Photo: Gerbil, Licensed by Attribution Share Alike 3.0

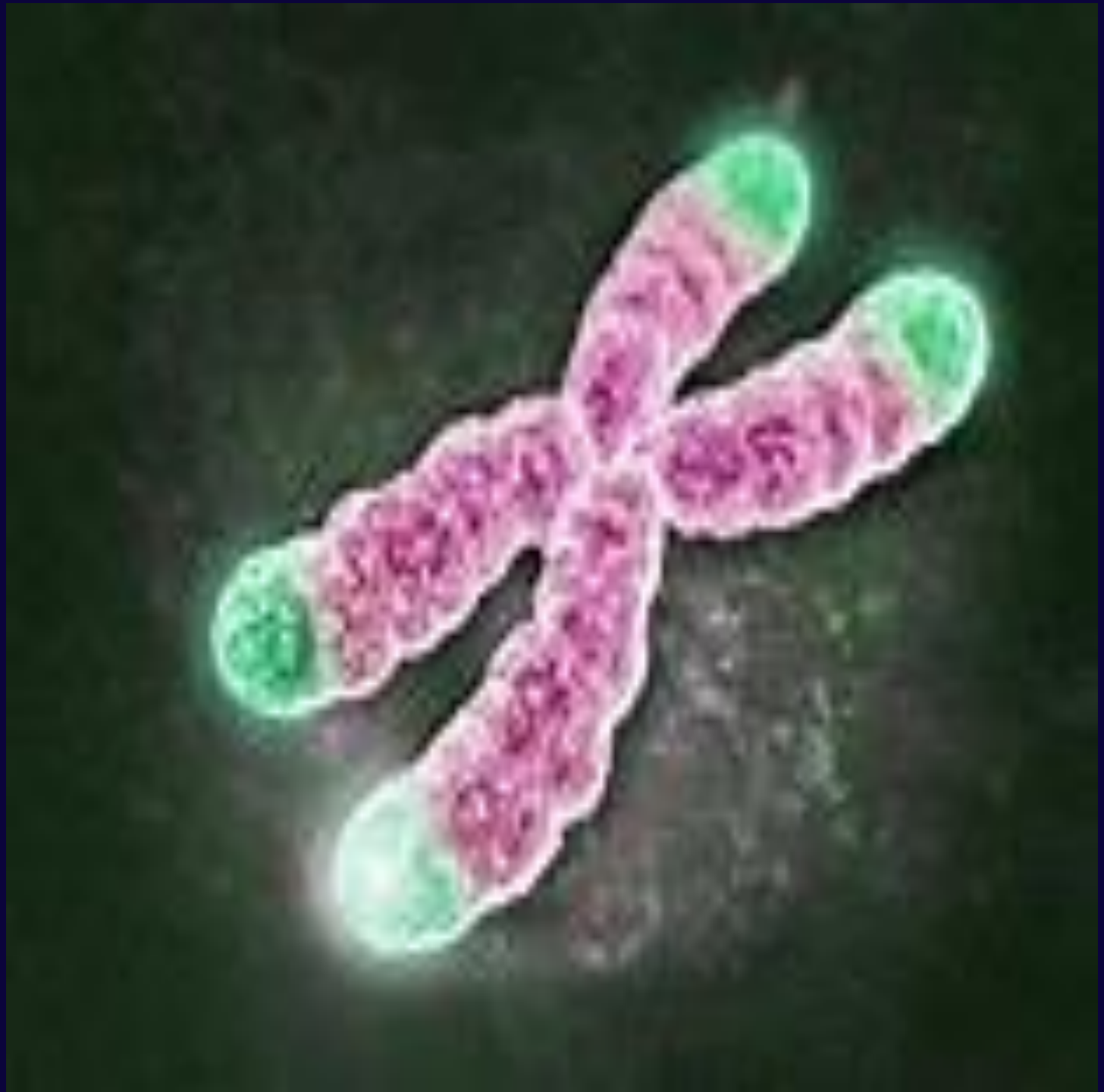
Elizabeth H. Blackburn

Photo: Gerbil, Licensed by Attribution Share Alike 3.0

Carol W. Greider

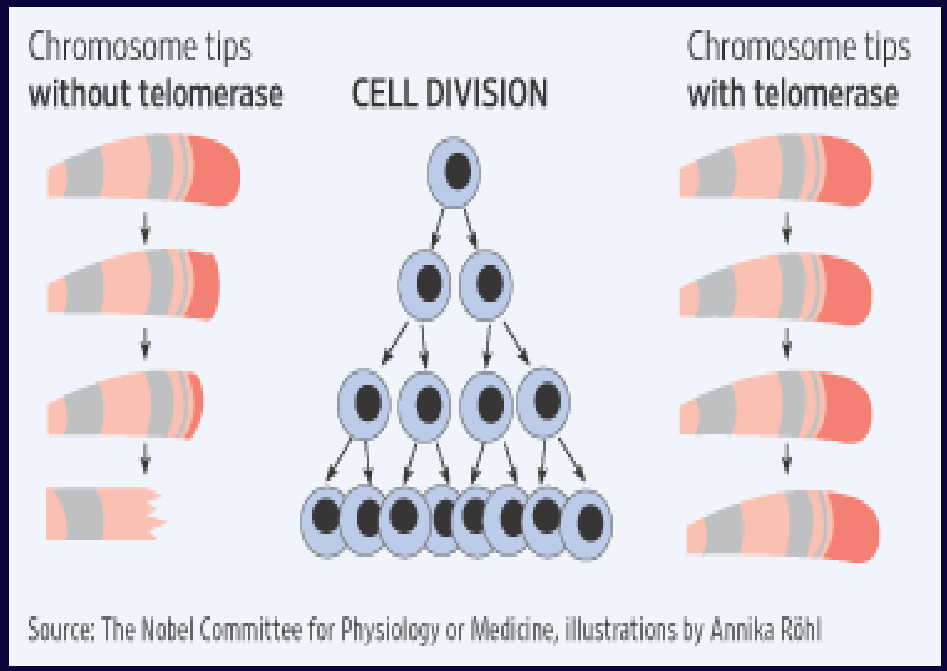
Photo © Harvard Medical School

Jack W. Szostak



Protective Caps

- Without telomerase, chromosomes fray over time and cells eventually stop dividing.



The Connection Between Telomeres and Aging

Telomere length is one of the most critical biomarkers for human aging and in the early diagnosis of age-related diseases

- In any living organism, aging is the result of the decrease in the number and/or function of cells
- Every time cells replicate, telomeres shorten until they reach a point where the cells can no longer divide properly
- Cells with such short telomeres usually become senescent or enter apoptosis, and eventually die
- Therefore, telomere length is a crucial biomarker providing insight into understanding organismal aging

Telomere Theory of Aging

- A decrease in telomerase activity precedes telomere shortening and introduction of telomerase into normal human cells extends life-span.

  Bodnar et al. Science 1998 Jan 16;279(5349:349-52

- On the cellular level, senescence, chromosome stability, and cell viability are regulated by the telomeres and their associated proteins, deoxyribonucleic acid-protein complexes located at both ends of eukaryotic chromosomes.

  Blasco Nature Reviews Genetics 6, 611-622 (August 2005)

- Shortening of the telomeres has been shown to be associated with increased mortality rate from age related diseases. Individuals with shorter telomeres had a mortality twice that of those with longer telomeres.

  Cawthon et al Lancet 2003; 361: 3933-95

Obama in 2008

Obama in 2012

1860 Abraham Lincoln 1865

Lifestyle Changes May Lengthen Telomeres

A small UCSF pilot study shows for the first time that changes in diet, exercise, stress management and social support can result in longer telomeres, the parts of chromosomes that affect aging.

Here are some lifestyle changes undertaken by study participants:

Diet:

High in whole foods, plant-based protein, fruits, vegetables; Low in fat (10% of calories) and refined carbohydrates

Exercise:

Moderate aerobic exercise – walking 30 minutes per day for six days a week

Stress Management:

Gentle, yoga-based stretching or meditation for 60 minutes daily

Social Support

REF: Lin J, Epel ES, Blackburn E. Telomeres and lifestyle factors: roles in cellular aging. Mutat Res 2012; 730: 85–89.

Lifestyle Choices Offset Dementia Risk Genes (2019)

Two studies: 1) Rotterdam from the University Medical Center in Rotterdam, Netherlands; and, 2) UK Biobank in England

- Median follow up was 14.1 years in Rotterdam and 8 years in the UK
- Rotterdam analyzed data from 6,300 individuals 55 and older – People at low APOE risk, the risk of dementia with an “unfavorable lifestyle” was higher than those with a “favorable” lifestyle
- UK Biobank assessed 196,383 individuals which used a polygenic risk score including APOE. Stronger genetic predisposition and older age had higher dementia incidence - irrespective of modifiable risk profile
- Differences in methodology, baseline, measures created somewhat contradictory results

Ref: Licher S, et al. “Genetic predisposition, modifiable risk-factor profile and long-term dementia risk in the general population”. Nat Medicine 2019; DOI:10.1038/s41591-019-0547-7

"You don't look anything like the long haired, skinny kid I married 25 years ago. I need a DNA sample to make sure it's still you."

Telomere Length & Long-term Endurance Exercise Affects on Biological Aging

Telomeres are potential markers of cellular age
They are associated with physical aging

Test Groups

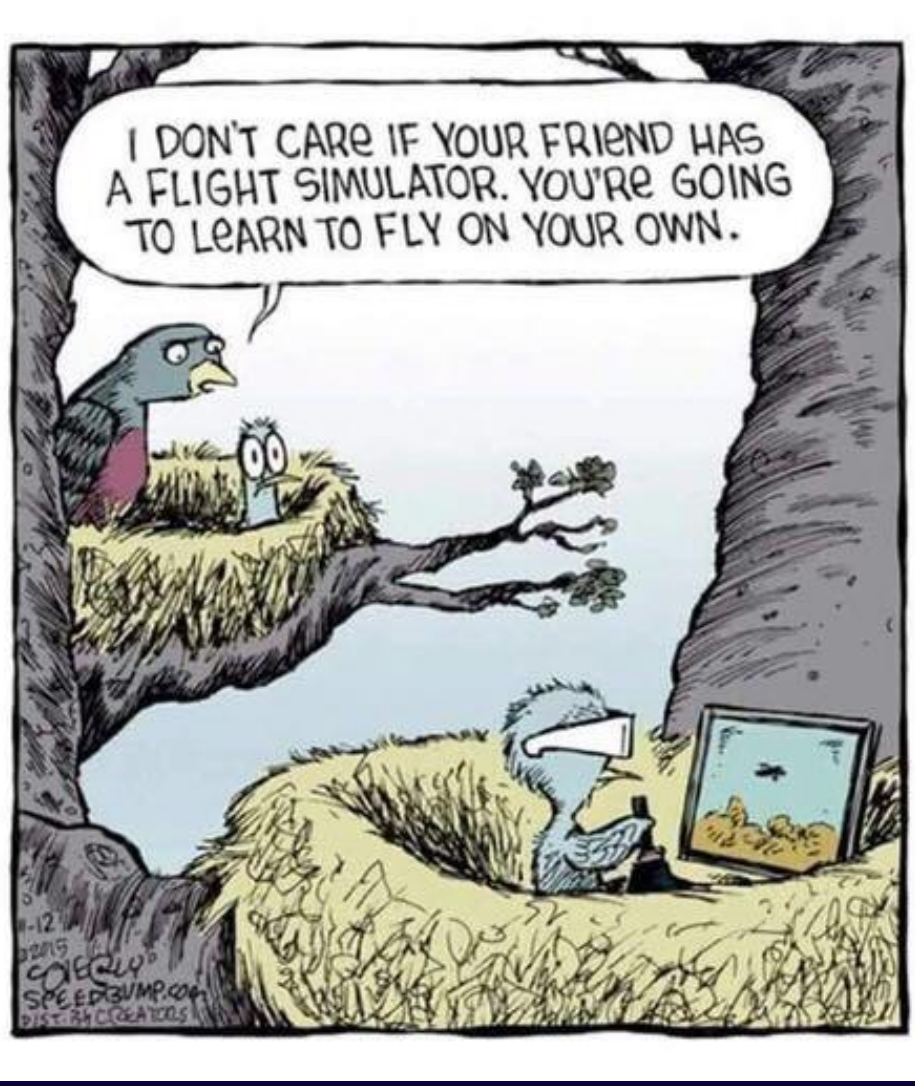
- 10 men (22-27 yrs) and 10 men (66-77 yrs)
- 5 Cross Country Birkenbeiner Racers + 5 Recreationally active participants from each group

Results

1. Older athletes had longer telomere length compared with older recreational
2. Younger athletes telomere length was not different from young non-athletes
3. Among the athletes there was a strong correlation b/n VO2 max and Telomeres
4. Corresponding association among non-athletes was relatively weak

Long-term endurance exercise training may provide a protective effect on telomere length in the older people

REF: Journals.plos.org; Osthus, Nauman et al; 2012


I DON'T CARE IF YOUR FRIEND HAS A FLIGHT SIMULATOR. YOU'RE GOING TO LEARN TO FLY ON YOUR OWN.

Telomere TLC:
Healthy Aging Begins with Protecting Your Telomeres

Slow Telomere Shortening

- ✓ Meditate
- ✓ Eat a healthy diet
  - Omega-3 fatty acids
  - Antioxidants
  - Vitamin D
  - Intermittent Fasting
  - Caloric & Portion Reduction
- ✓ Mediterranean/Pescatarian
- ✓ Exercise - Interval Training
- ✓ Be Happy/Altruistic

Speed Telomere Shortening

- Obesity
- Psychological Stress
- Radiation/Petrochemicals
- Smoking/Air Quality
- Pollution/Toxins/Herbicides
- Lifestyle Diseases
- Oxidative Stress/CRP

Conclusion

"Adopting multiple healthy lifestyle behaviors is protective … there are things you can do to protect your brain to reduce the risk of cognitive decline as you age."

Ref: Licher S, et al. "Genetic predisposition, modifiable risk-factor profile and long-term dementia risk in the general population". Nat Medicine 2019; DOI:10.1038/S41591-019-0547-7

Alzheimer's Blood Test Detection (2019)

Study focused on 158 adults over age 50 who were "cognitively normal" at the Washington University School of Medicine, St Louis

- Used mass spectrometry to measure: 1) Amyloid Beta 42; and 2) Amyloid Beta 40. Ratio of these 2 forms goes down as amyloid deposits in the brain goes up.
- Underwent PET scan which correlated 88% of the time with blood draw
- Added: 1) Age over 65 (risk doubles every 5 years after 65); 2) APOE4 (raises risk 3-5 times); and, 3) Gender (2 of 3 Alzheimer's pts are female)
- Age and APOE4 raised accuracy of blood test to 94%

Ref: Rushlau K. "Blood test may identify Alzheimer's symptoms before they arise". Integrative Practitioner, August 15, 2019

“Be careful reading books about health.
You might die of a misprint.”

Mark Twain

First Age Reversal in a Mammal

Telomerase reactivation reverse tissue degeneration in aged telomerase-deficient mice

- Telomerase Activation was used to change old mice to young adults
- Brain, spleen and reproductive organs were all rejuvenated;
- Resulting in increased neurons and new viable sperm cells
- Sense of smell returned
- None of the mice developed cancer

REF: 2011 DePinho et al


I DEMAND A DNA TEST!

TREM2 and Alzheimer's (2019)

Genetic markers of higher TREM2 levels are protective from research at the Washington University School of Medicine, St Louis

- TREM2 is a protein that may help microglia cells clear excessive amounts of brain amyloid and tau
- Detected in the CSF of 813 older adults
- Increased levels of TREM2 reduced Alzheimer's risk and delayed the age of onset. Lower levels increased the risk.
- Target TREM2 directly or another part of the pathway governed by the gene MS4A4A

Ref: Deming Y, et al. "The MSA gene cluster is a key modulator of soluble TREM2 and Alzheimer disease risk." Science Translational Medicine 2019;DOI: 10.1126/scitranslmed.aau229

"If I'd known I was going to live this long, I'd have taken better care of myself" –

Eubie Blake, 96 years old

MEDITATION and EPIGENETICS

Numerous studies indicating positive impact on epigenetics biomarkers

- A 2008 study by Benson and Liberman at Harvard Medical School analyzed 22,000 genes and found changes in genes that upregulate energy metabolism as well as suppression of NF-kB which plays a role in inflammation, stress, trauma, and cancer.
- Replicated this study in 2013 with 26 long time practitioners of he relaxation response after a single 20 minute practice session compared to 26 who had never used that technique. Outcomes documented positive epigenetic changes in immune function, energy metabolism, insulin secretion, mitochondrial activation, and repair of telomeres.
- At the UCSF School of Medicine a 2008 study focused on prostate cancer. Participants were 31 men with a low risk form of prostate cancer who elected to decline immediate surgery, hormonal therapy, or radiation. Intervention was a three month program of a low fat, plant based diet and stress management. At the end of the 3 month intervention, these practices had decreased the expression of the genes associated with prostate cancer.


DALAI LAMA'S BIRTHDAY PARTY
WOW, NOTHING! JUST WHAT I ALWAYS WANTED!

FROM INNER SPACE to OUTER SPACE NASA “Twins” Study (2018)

- In 2018, Astronaut Scott Kelly set a record for the longest solo spaceflight in history at 340 straight days in space
- Researchers compared his genetic profile to his identical twin (Mark) who is also a NASA astronaut but remained on Earth during those 340 days
- During that time in space, Scott manifested “space genes” which were changed in their expression including his immune system, DNA repair, bone formation, hypoxia, telomeres had increased in length, and he had increased in height by over 2 inches
- Shorty after his return his height changed back to normal and 93% of his DNA expression normalized
- However … that means that 7% of his gene expression remained changed and “may remain that way permanently”
- In posting a Twitter, Scott quipped: “What? My DNA changed by 7%! Who knew? This could be good news! I no longer have to call Scott my identical twin brother anymore.”

REF: CBS Denver (13 March 2018)

“Divine Dozen” – Longevity Factors

- Mediterranean Diet – Fish but little or no red meat or poultry
- Smoking – Non processed tobacco products and no inhalation
- Physical Activity – Daily farming and/or fishing not in a gym
- Strong Psychosocial Bonds – No person is an island, domestic and farm animals
- Old Age is Respected – Head of the family and makes major decisions
- Sexually Active – Touching, hugging, and intercourse into 80s and 90s

"I generally avoid temptation unless I can't resist it!"

Mae West (1936)

“Divine Dozen” – Longevity Factors

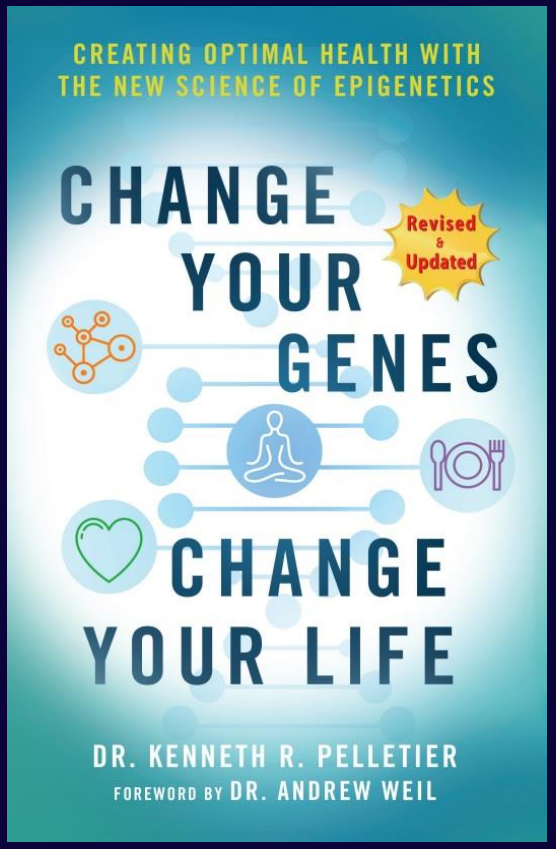
- No Fear of Death – Disability and “being a burden” is an issue
- Alcohol consumption – More than “moderate” but with meals
- Sound/Clean/”Organic” Environment – Little to no pollution/toxins
- Appropriate Primary Medical Care – Includes “alternative” therapies
- Genetic and Epigenetic Influences – Lifestyle and gene interacting
- Meditation/Prayer/Introspection – Have a philosophy of life = Wisdom

"Health nuts are going to feel stupid someday, lying in the hospital dying of nothing!"

Redd Foxx

Epigenetics – What is Known

- Tripartate Assay: Genetic, Blood (CBC), and Microbiome
- Genes predict probabilities not certainties
- Biomarkers of health not disease prediction
- Monogenic/Fully Penetrant - Applications of single gene = single disease is very limited
- Genes work within complex genetic and environmental matrices
- Human base is @ 21,000 genes – DNA for protein coding is only 5% of this entire genome = “Dark Genome”
- Genes are turned on or off like a rheostat
- Gene expression changes – What we do matters!
- Majority of genetic expression governed by beliefs and lifestyle choices
- Neanderthal genes are alive and well – Stress Responses



drpelletier.com


That's all
for now
folks!
Bugs!

Saturday 8:30am – 9:30am

Plenary: Change Your Genes - Change Your Life: Epigenetics of Longevity

Please scan this QR code on you mobile

or tablet device to access the session feedback survey

Plenary: Change Your Genes - Change You r Life: Epigenerics of Longevity