Creating Health: Applying the Science of Lifestyle Medicine

Mark Pettus MD

- Week 1: Epigenetics and Health: How well do you fit into your genes?
- Week 2: Inflammation: The bad gift that keeps giving
- Week 3: Metabolic Health: How to become a member of this exclusive club.
- Week 4: Circadian Rhythms and Health: Riding the rhythms of life

OSHER LIFELONG LEARNING INSTITUTE

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For the Joy of Learning!

1

Epigenetics and Health
How well do you fit into your genes?

Mark Pettus MD
Associate Professor of Medicine
University of Massachusetts Medical School

September 23, 2022

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Disclosures

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The Health Edge

TRANSLATING THE SCIENCE OF SELF-CARE

HOME BERKSHIRE HOLISTIC WEIGHT LOSS HEALTH PROGRAM EFFORTLESS WEIGHT LOSS HYPNOSIS EXCELLENT REVIEW ARTICLES
JOHN BAGNULO PHD, MPH JOURNEY TO HEALTH MARK C. PETTUS MD MEN'S HEALTH FORUM OLLI 2019 AND 2020 OLLI 2022 FALL PROGRAM

www.thehealthedgepodcast.com

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Learning Objectives

- Participant will understand the implication of epigenetics i.e., how lifestyle-environment influence healthspan and longevity.
- Participant will understand some examples of nutrigenomics i.e., how food influences changes in our gene expression patterns and overall health.
- Participant will understand how social connection-bonding alters epigenetic patterns and health throughout the life continuum.

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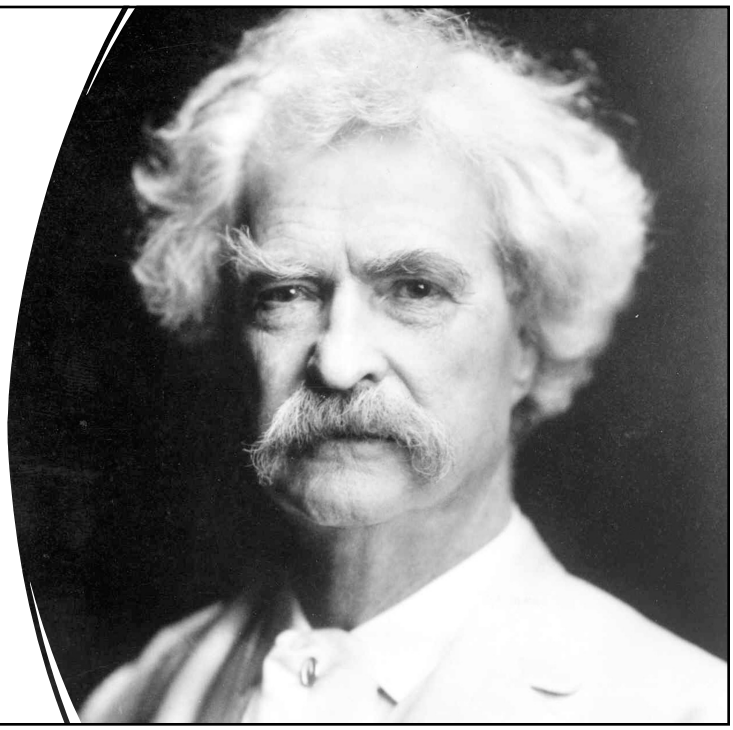
"It's not what we don't know that gets us into trouble, it's what we know that ain't so"

Mark Twain



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So what do we know that ain't so?

You are not a prisoner of your DNA

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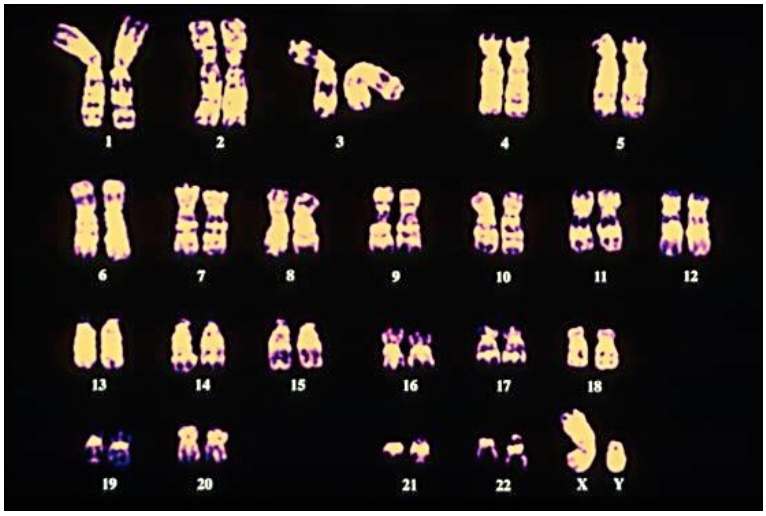
Your "Book of Life" in 23 Chapters



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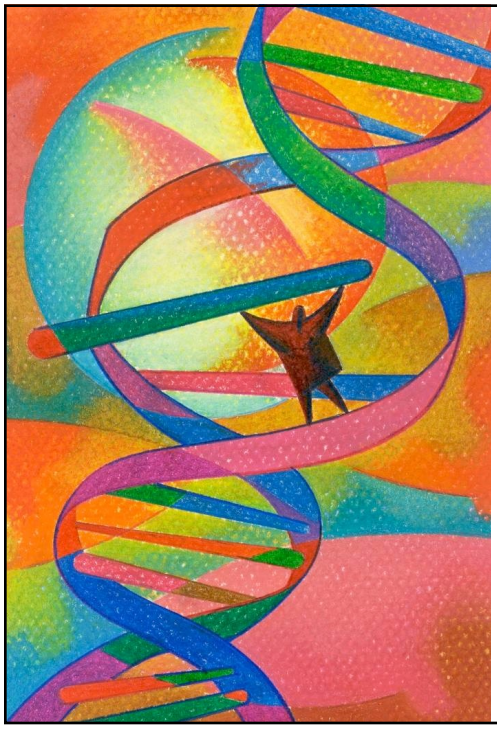

The Emerging Evidence

- All health and disease are byproducts of complex *individualized* gene-environment interactions that may go back more than a generation before conception and continue throughout our lives.
- Your DNA i.e., your "Book of Life" has a Stone Age imperative, not often compatible with 21st century environmental inputs.
- This incompatibility creates a disrupted metabolic trajectory that forms the basis of chronic complex disease.
- Through ***proven lifestyle medicine interventions***, our gene expression patterns can be transformed to promote optimal function and health.
- Re-writing ones Book of Life remains possible throughout the age continuum by aligning one's environmental inputs with that which one's Book of Life are best suited for.

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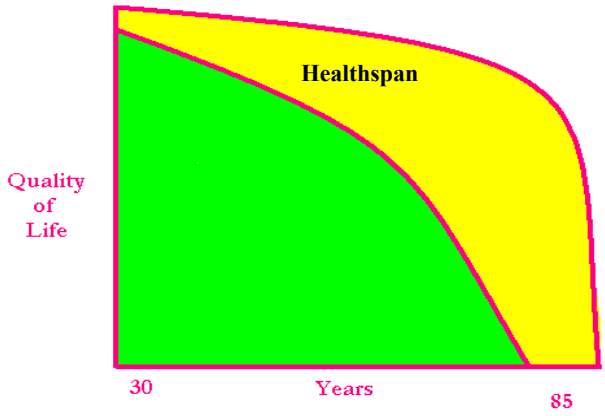
Healthspan and Longevity

SPECIAL ARTICLE ARCHIVE

Aging, Natural Death, and the Compression of Morbidity

James F. Fries, M.D.

N Engl J Med 1980; 303:130-135 | July 17, 1980



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"Only 8% of what contributes to longevity can be traced to genetics. Over 90% of what contributes to longevity and healthy aging is lifestyle."

Eric Verdin MD
President and CEO, Buck Institute

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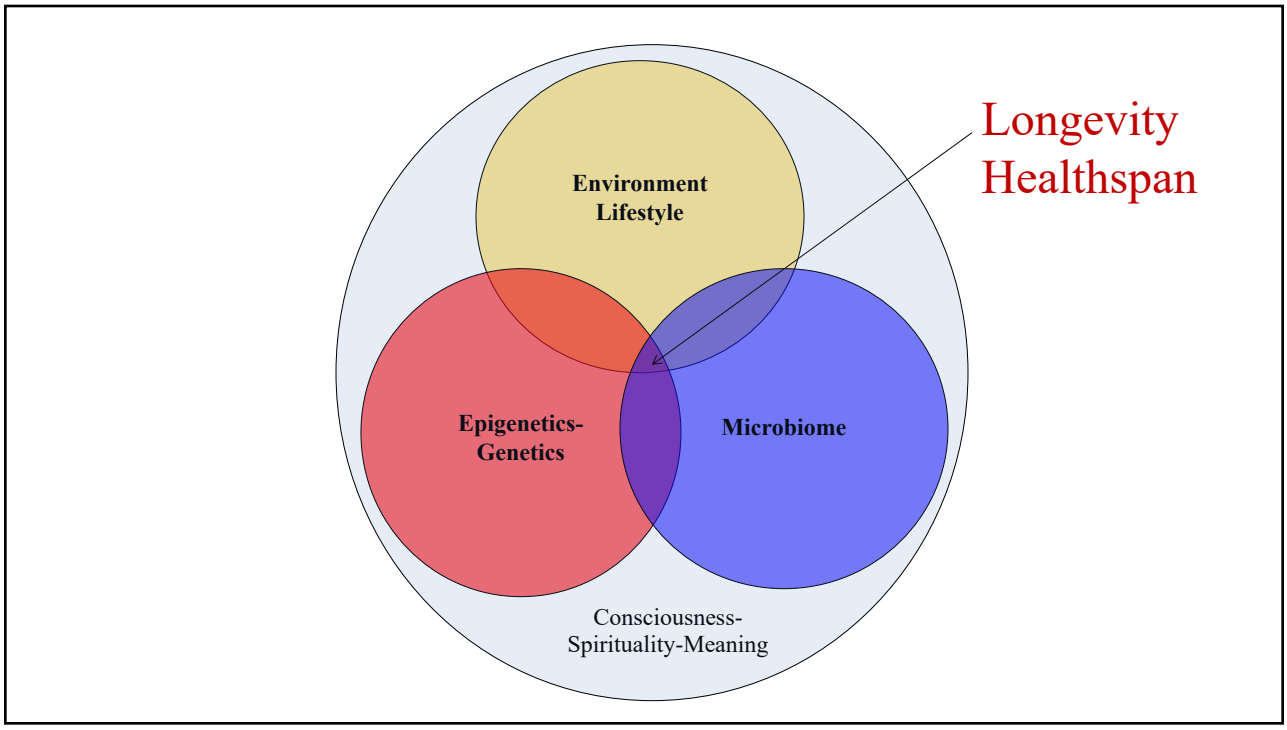

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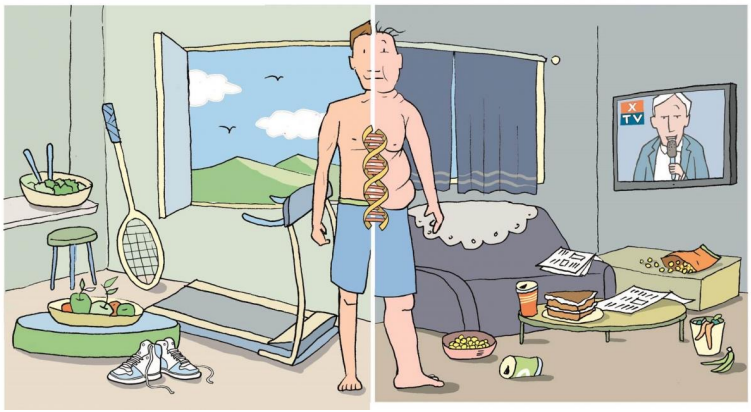
Epigenetics:

A life with many possibilities.



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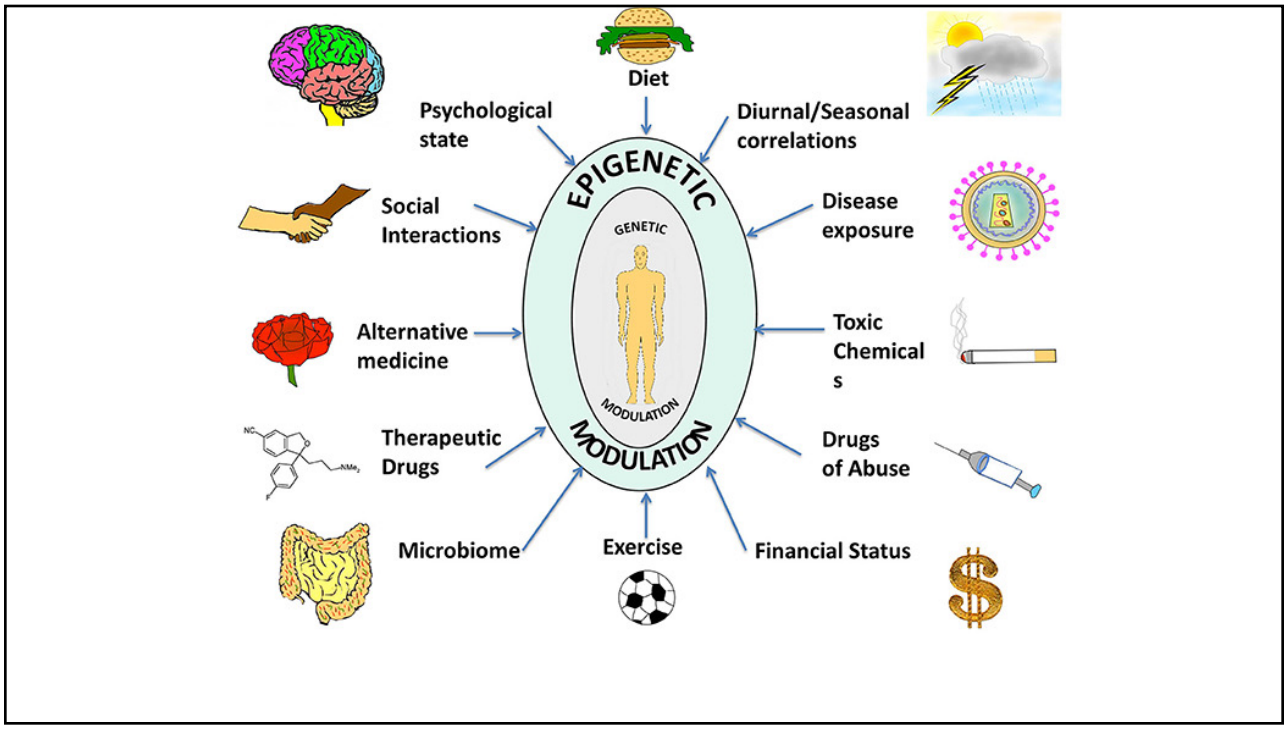

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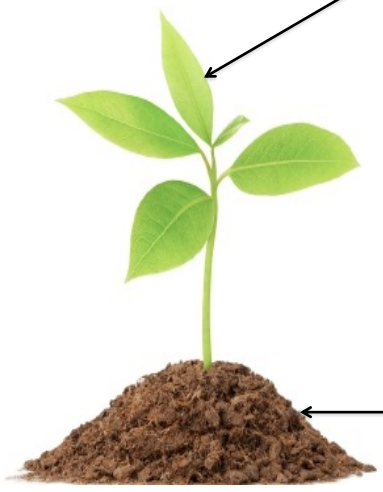
Integrative Medicine



Disease (how things appear)
Pre-diabetes, Diabetes, Obesity, Metabolic Syndrome,
Heart Disease, Stroke, Depression, Autoimmunity,
Alzheimer's, Cancer, Fibromyalgia, Chronic fatigue

Core Metabolic Imbalances (what drives them)
Inflammation
High Insulin Levels
Circadian Cycle Disruption

Root Causes (what are their origins)
Genetic-Epigenetic-Lifestyle
Nutrition Movement Stress Response
Environmental toxins Sleep Social Connection Trauma
Conflict Management Mindfulness
Meaning in Work, Love, Play
Socioeconomics

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Health as a byproduct of gene-environmental compatibility

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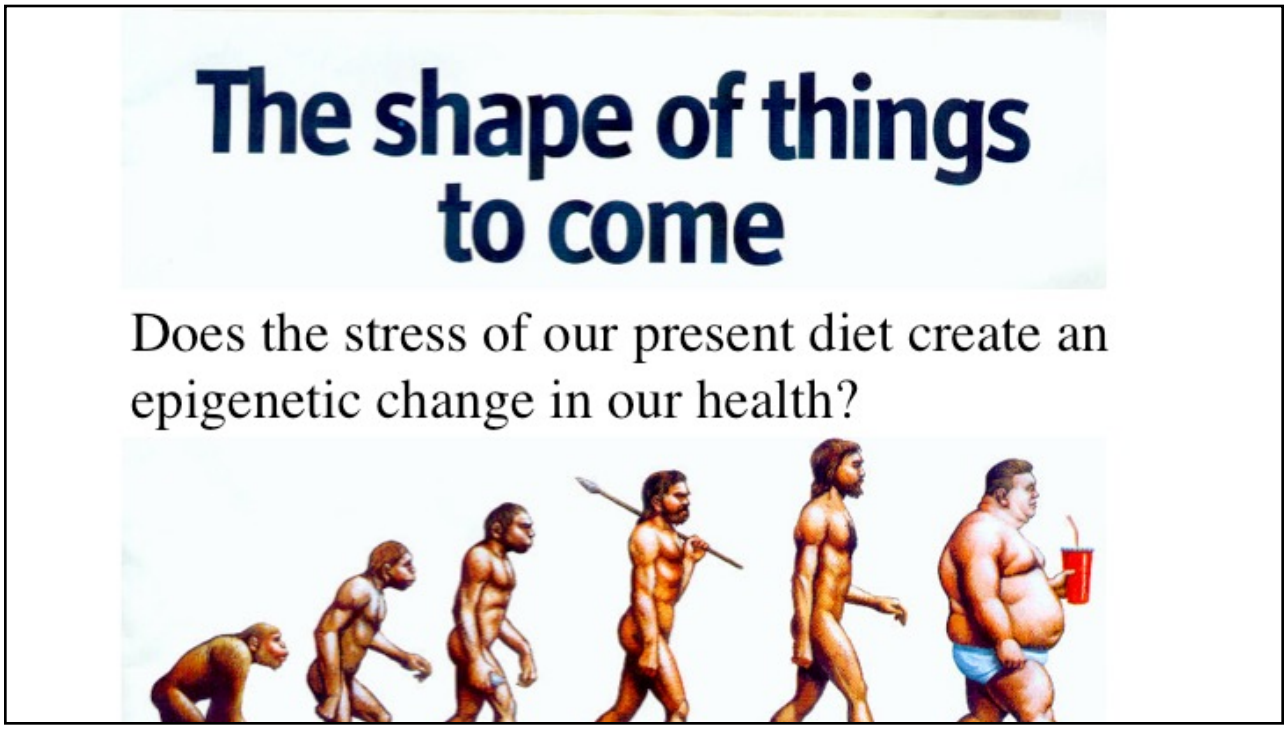
The shape of things to come
Does the stress of our present diet create an epigenetic change in our health?

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An Ancient Design For Survival in Modern Times

…our design has maintained many of the Stone Age imperatives, but life in the fast lane has not.

Then	Now
•Fight-flight	•Anxiety, PTSD, depression
•Energy conservation	•Metabolic Syndrome
•Immunity	•Autoimmunity and allergy
•Promotion of clotting	•Heart attack and stroke

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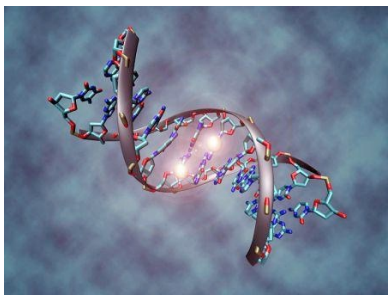
Representative Clinical Conditions Suggested to Have Epigenetic Origins

- Obesity
- Type 2 DM and Metabolic Syndrome
- Coronary artery disease
- Autoimmune Diseases
- Cancer
- Allergic Disorders
- Depression
- Neurologic: Alzheimer's, PD, ALS, Autism



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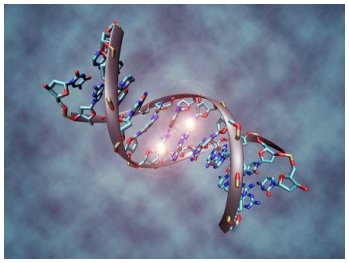
Lifestyle-Behavioral Factors Shown to Have Health-Promoting Epigenetic Influences

- Plant-based, unprocessed foods
- Movement
- Mindfulness practices
- Bonding-social connection
- Reduction in Environmental Toxin exposure
- Microbiome diversity
- Natural environments
- Purpose-meaning



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Epigenetics in Primates

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Epigenetics in Primates

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From Robert Sapolsky PhD

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Robert Sapolsky PhD Stanford

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Robert Sapolsky PhD Stanford

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From Robert Sapolsky PhD

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Junk Food Monkeys

- Much heavier with more body fat
- Metabolic Syndrome
- Insulin resistant with elevated fasting and post-prandial insulin levels
- Increased TGAs
- Move a lot less
- Socialized and play less
- High Infertility
- Die younger

From Robert Sapolsky PhD

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Epigenetics in humans

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Effects of Traditional and Western Environments on Prevalence of Type 2 Diabetes in Pima Indians in Mexico and the U.S.

Leslie O. Schulz, PHD[1], Peter H. Bennett, MB, FRCP[2], Eric Ravussin, PHD[3], Judith R. Kidd, PHD[4], Kenneth K. Kidd, PHD[4], Julian Esparza, MS[5] and Mauro E. Valencia, PHD[5]

CONCLUSIONS—The much lower prevalence of type 2 diabetes and obesity in the Pima Indians in Mexico than in the U.S. indicates that even in populations genetically prone to these conditions, their development is determined mostly by environmental circumstances, thereby suggesting that type 2 diabetes is largely preventable. This study provides compelling evidence that changes in lifestyle associated with Westernization play a major role in the global epidemic of type 2 diabetes.

Prevalence of type 2 DM 5 times higher in Arizona Pima's compared to Mexican Pima's.

Diabetes Care August 2006 vol. 29 no. 8 1866-1871

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TSUNAMI: THE POLITICS OF RELIEF
Newsweek
Diet & Genes
The New Science of Nutrition and Aging
HEALTH FOR LIFE
With Harvard Medical School

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Nutritional Epigenetics

- Randy Jirtle PhD
- Relationship between nutrition, methylation and gene expression
- Protection against BPA toxicity in nutrient-methylation models

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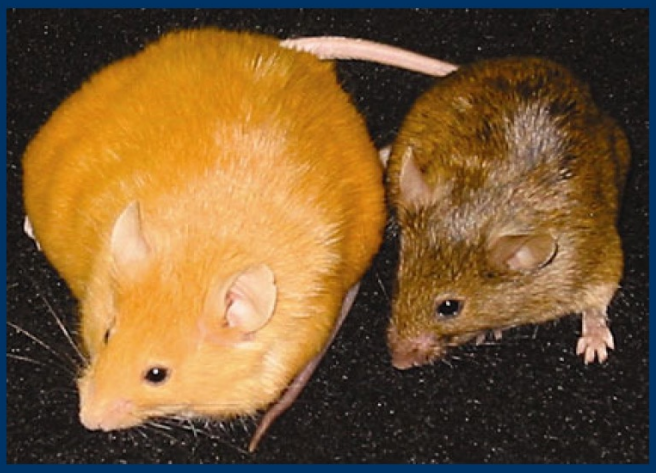
Epigenetics: Feeding Your Genes



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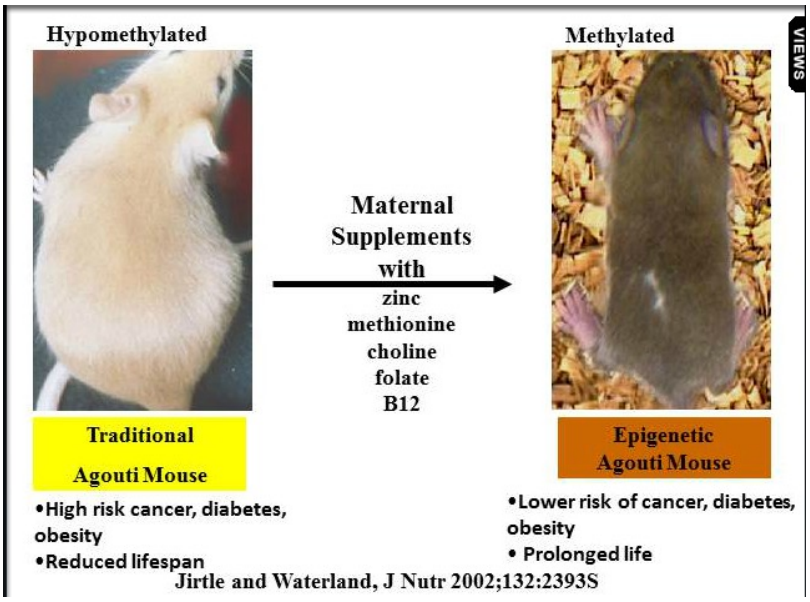
Hypomethylated
Methylated
VIEWS
Maternal Supplements with
zinc
methionine
choline
folate
B12
Traditional Agouti Mouse
Epigenetic Agouti Mouse
•High risk cancer, diabetes, obesity
•Reduced lifespan
•Lower risk of cancer, diabetes, obesity
• Prolonged life
Jirtle and Waterland, J Nutr 2002;132:2393S

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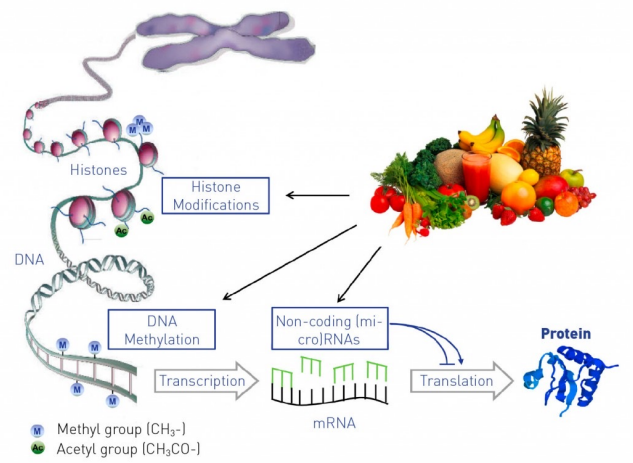
TIME
WHY YOUR DNA ISN'T YOUR DESTINY
The new science of epigenetics reveals how the choices you make can change your genes —and those of your kids
BY JOHN CLOUD


Histones
Histone Modifications
DNA
DNA Methylation
Non-coding (mi-cro)RNAs
Transcription
Translation
Protein
mRNA
Methyl group (CH3-)
Acetyl group (CH3CO-)

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Different carbohydrates produce unique genomic responses

high glycemic carbs

62 genes up-regulated
linked to oxidative stress,
Cytokine mediated immunity and
Interleukin pathways

low glycemic carbs

71 genes down-regulated
regulating insulin signaling
and adipocyte cell size
Improved insulin index

Source: Kallio et al. Am J Clin Nutr;2007:851:1417-27

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Brain Derived Neurotropic Factor (BDNF)

- Exercise
- Caloric Restriction
- Meditation
- Curcumin
- Green tea
- Coffee
- DHA
- Intermittent Fasting/TRE
- Probiotics

→ BDNF ←

- SAD
- Stress
- Inflammation
- Insulin resistance
- Circadian Disruption
- Sedentary states
- Social Isolation

Bredesen. *AGING*, June 2016, Vol. 8 No.6

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Environmental Programming of Gene Activity- Bonding

Glucocorticoid Receptor Gene

Traumatic Childhood Events

- ↓ GR Gene
- ↓ GR Receptors
- ↑ Stress Response

Bonding

- ↑ GR Gene
- ↑ GR Receptors
- ↓ Stress Response

McGowan PO, Sasaki A, D'Alessio AC, Dymov S, Labonte B, Szyf M, Turecki G, Meaney MJ. Epigenetic regulation of the glucocorticoid receptor in human brain associates with childhood abuse. Nat Neurosci. 2009;12(3):342-348.

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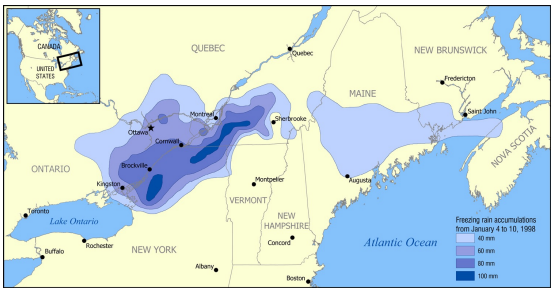
RESEARCH ARTICLE VIEWS SHA

DNA Methylation Signatures Triggered by Prenatal Maternal Stress Exposure to a Natural Disaster: Project Ice Storm

Lei Cao-Lei, Renaud Massart, Matthew J. Suderman, Ziv Machnes, Guillaume Elgbeili, David P. Laplante, Moshe Szyf, Suzanne King

Published: September 19, 2014 • DOI: 10.1371/journal.pone.0107653



Conclusions

"These data provide first evidence in humans supporting the conclusion that PNMS results in a lasting, broad, and functionally organized DNA methylation signature in several tissues in offspring. We can infer that the epigenetic effects found in Project Ice Storm are due to objective levels of hardship experienced by the pregnant women."

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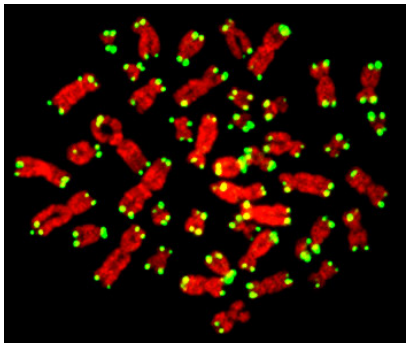
Effect of comprehensive lifestyle changes on telomerase activity and telomere length in men with biopsy-proven low-risk prostate cancer: 5-year follow-up of a descriptive pilot study

Prof Dean Ornish, MD, Jue Lin, PhD, Prof June M Chan, PhD, Elissa Epel, PhD, Colleen Kemp, RN, Prof Gerdi Weidner, PhD, Ruth Marlin, MD, Steven J Frenda, MA, Mark Jesus M Magbanua, PhD, Jennifer Daubenmier, PhD, Ivette Estay, PhD, Nancy K Hills, PhD, Nita Chainani-Wu, DMD, Prof Peter R Carroll, MD, Prof Elizabeth H Blackburn, PhD

Published: 17 September 2013



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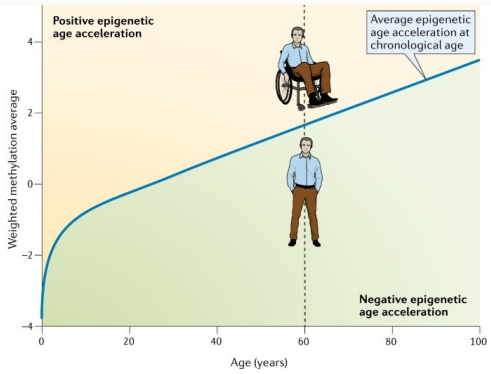
Review Article | Published: 11 April 2018

EPIGENETICS

DNA methylation-based biomarkers and the epigenetic clock theory of ageing

Steve Horvath & Kenneth Raj



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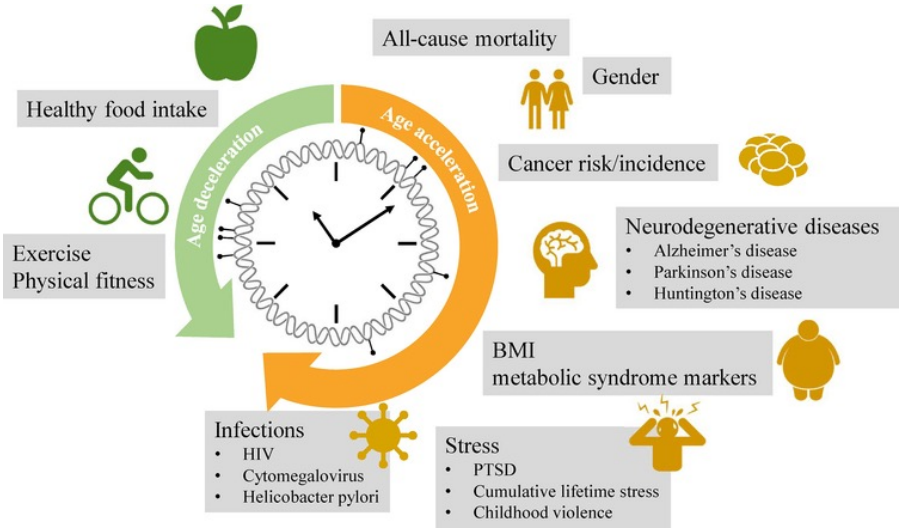

Back to the future: Epigenetic clock plasticity towards healthy aging
•January 2018 Mechanisms of Ageing and Development DOI:10.1016/j.mad.2018.01.002

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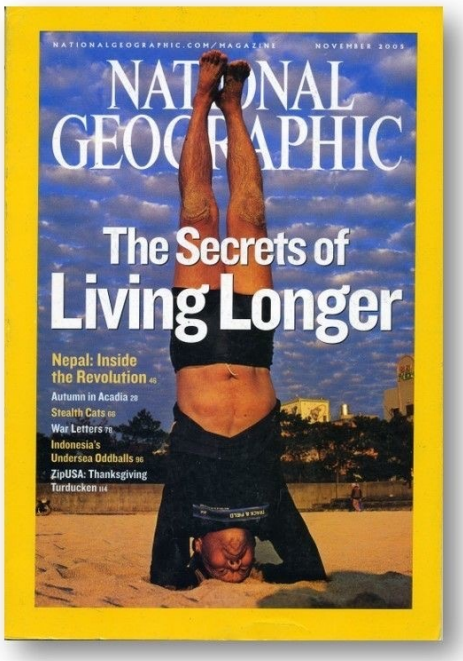

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FAMILY FIRST
Invest time with family & add up to 6 years to your life.
PLANT SLANT
Put less meat & more plants on your plate.
WINE @ FIVE
Enjoy a glass of wine with good friends each day.
80% RULE
Eat mindfully & stop when 80% full.
MOVE NATURALLY
Find ways to move more! You'll burn calories without thinking about it.
PURPOSE
Wake up with purpose each day to add up to 7 years to your life.
RIGHT TRIBE
Surround yourself with people who support positive behaviors.
DOWN SHIFT
Reverse disease by finding a stress relieving strategy that works for you.
BELONG
Belong to a faith-based community, & attend services 4 times a month to add 4–14 years to your lifespan.
POWER 9®
Live longer by applying these principles from the people who have lived longest!

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