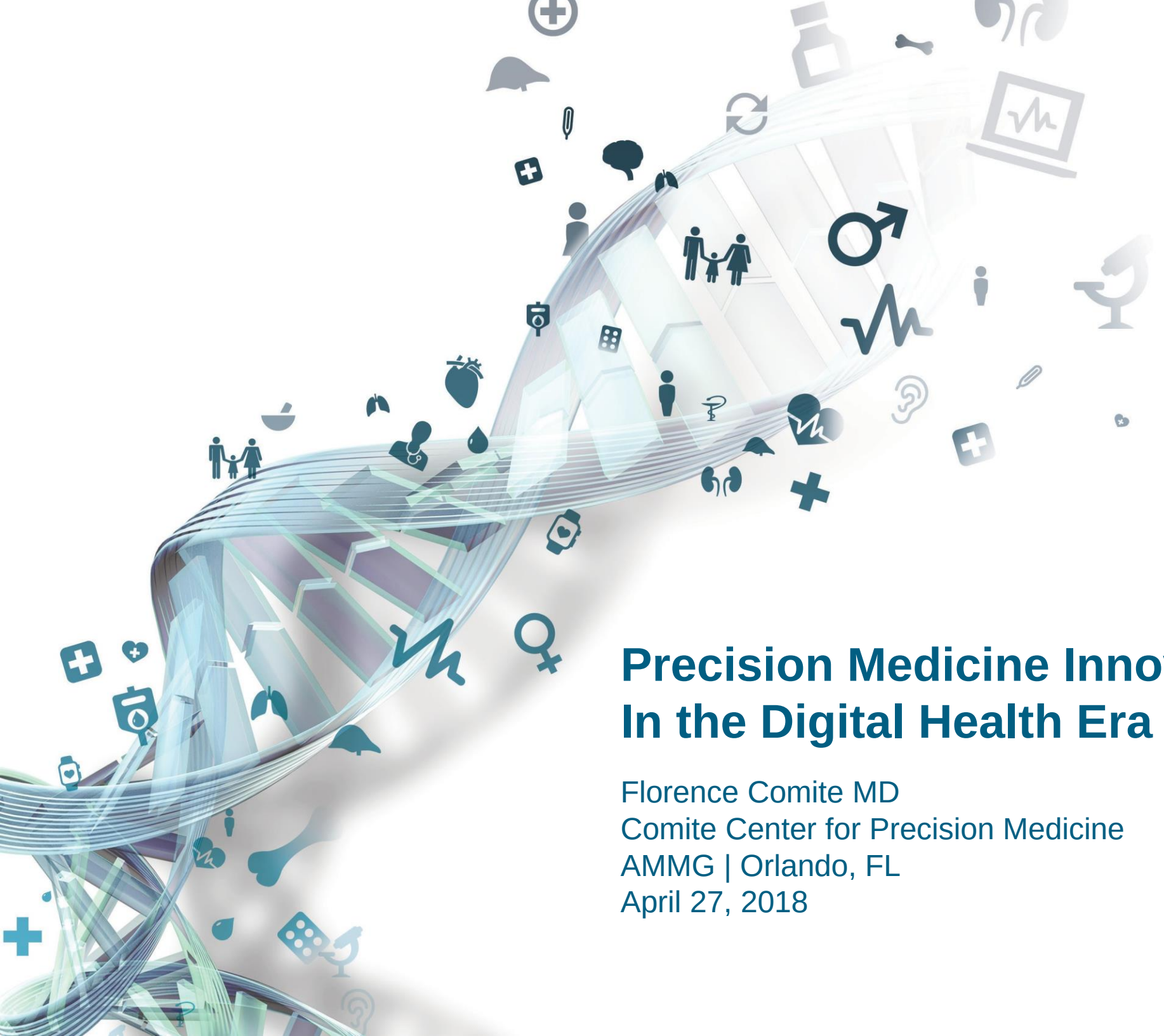
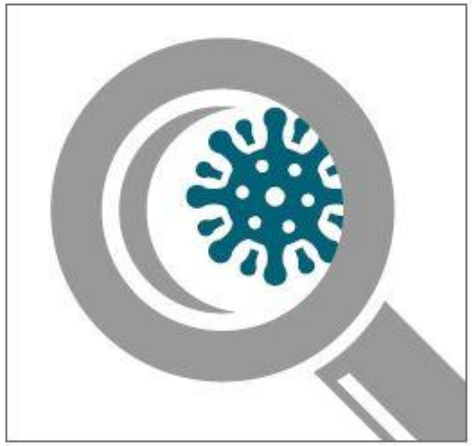


Precision Medicine Innovations In the Digital Health Era

Florence Comite MD
Comite Center for Precision Medicine
AMMG | Orlando, FL
April 27, 2018

What is Precision Medicine?



Detect

Detect disease decades before symptoms.



Predict

Predict risk-prone wiring, and the genetic “switches” that control expression.



Reverse

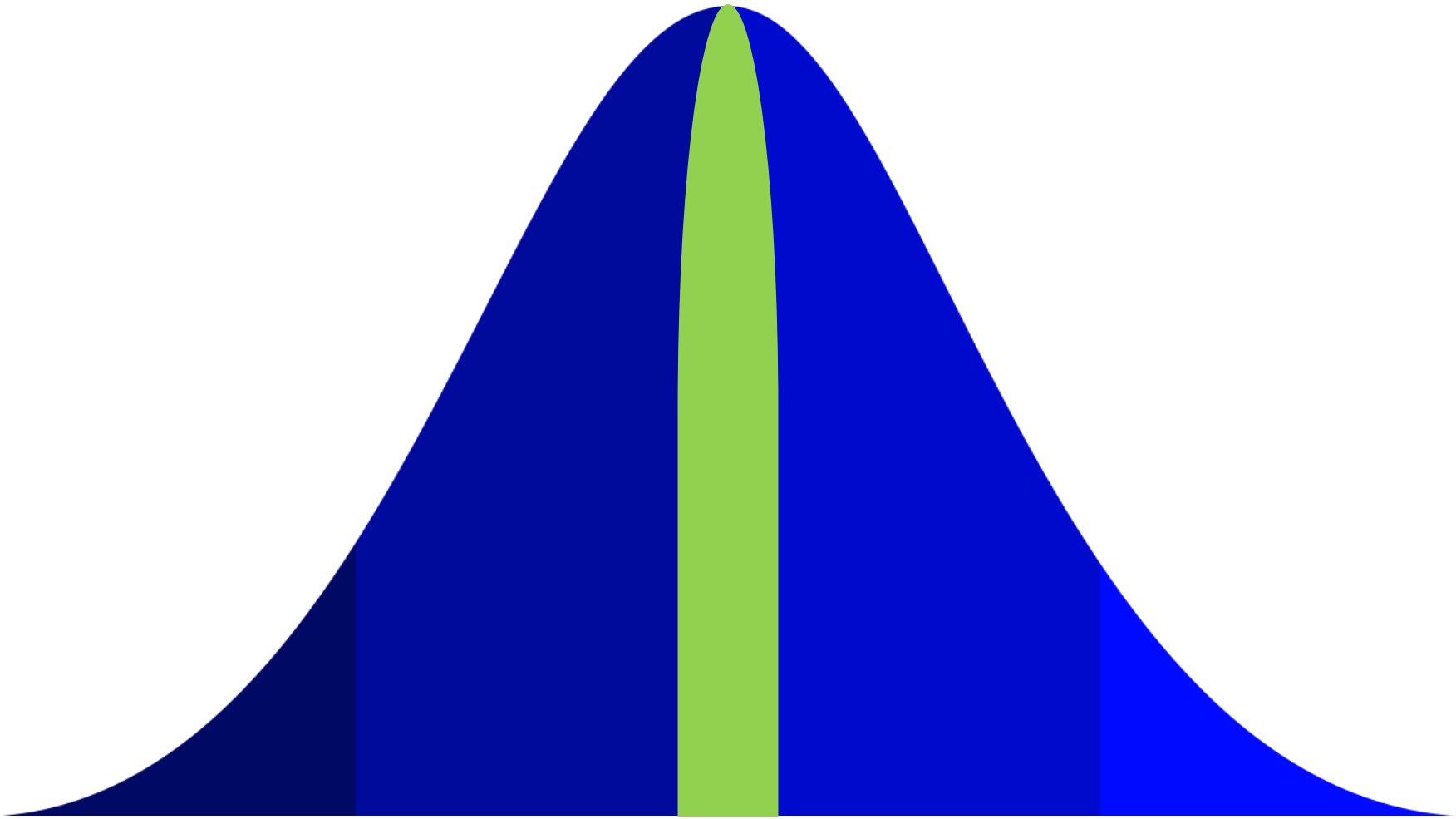
Reverse and prevent diseases of aging, with interventions personalized for you and you alone.



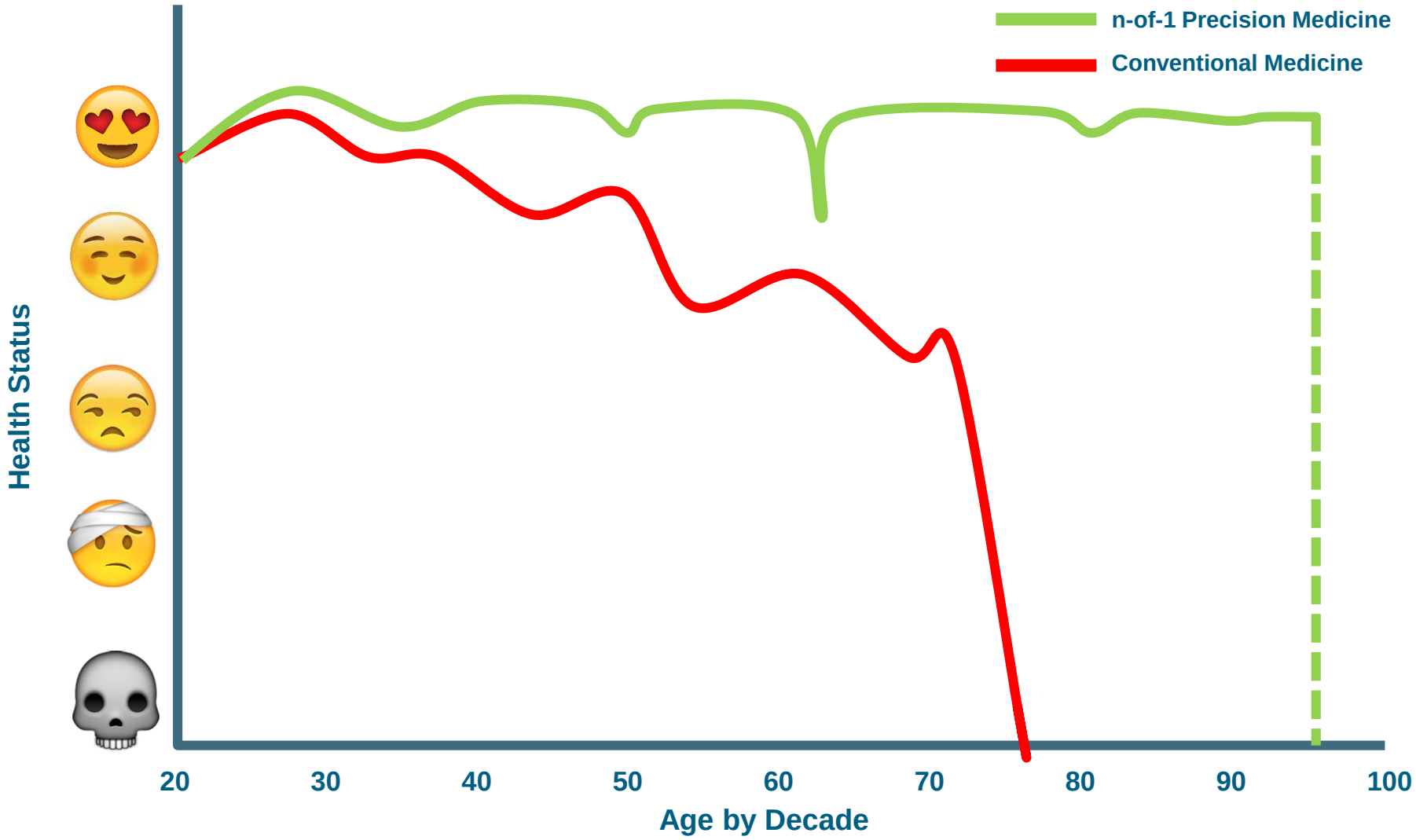
Own

Own your health destiny. Optimize your unique health trajectory and recapture health for life.

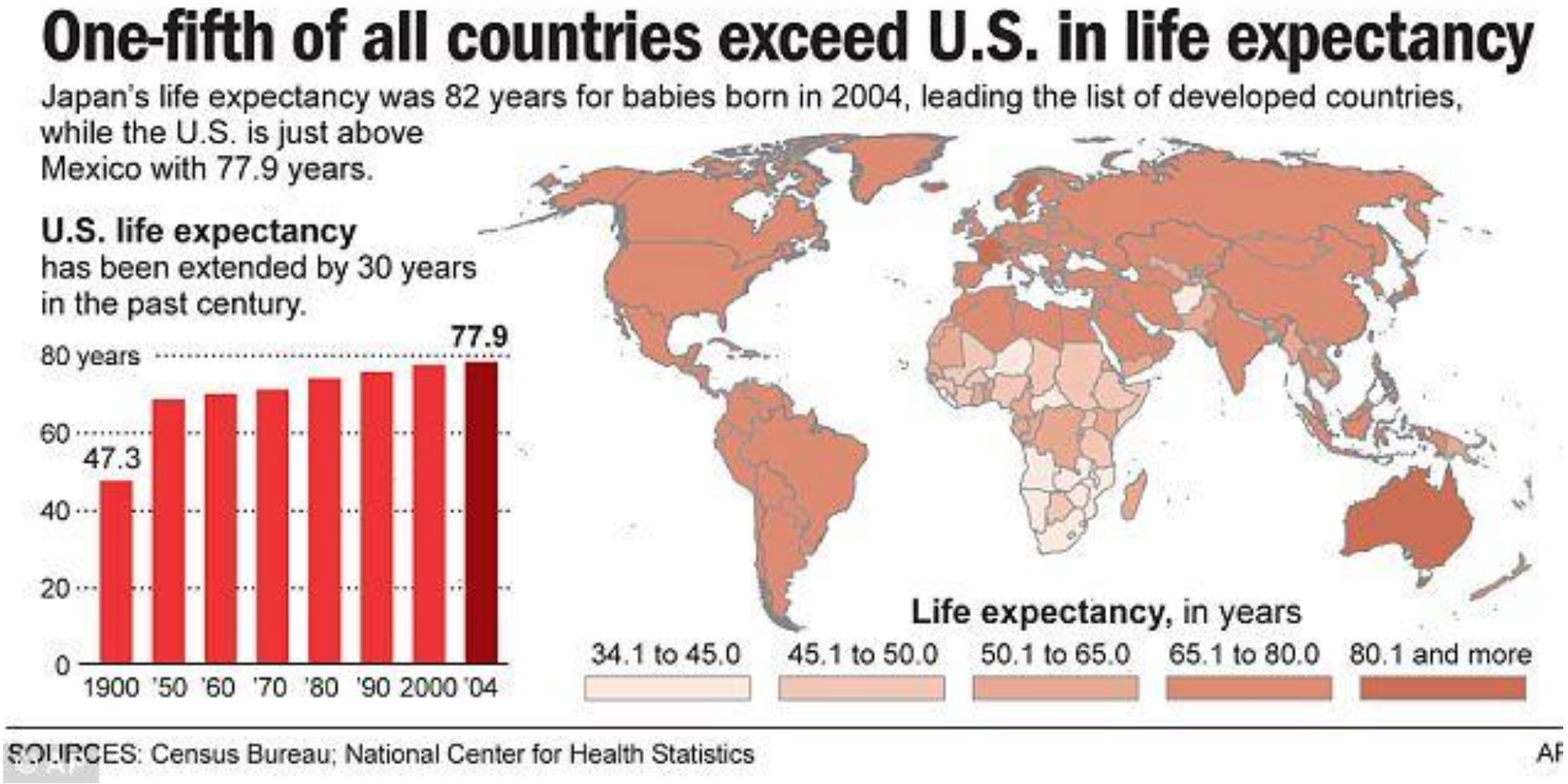
Why It Matters: There is NO Normal



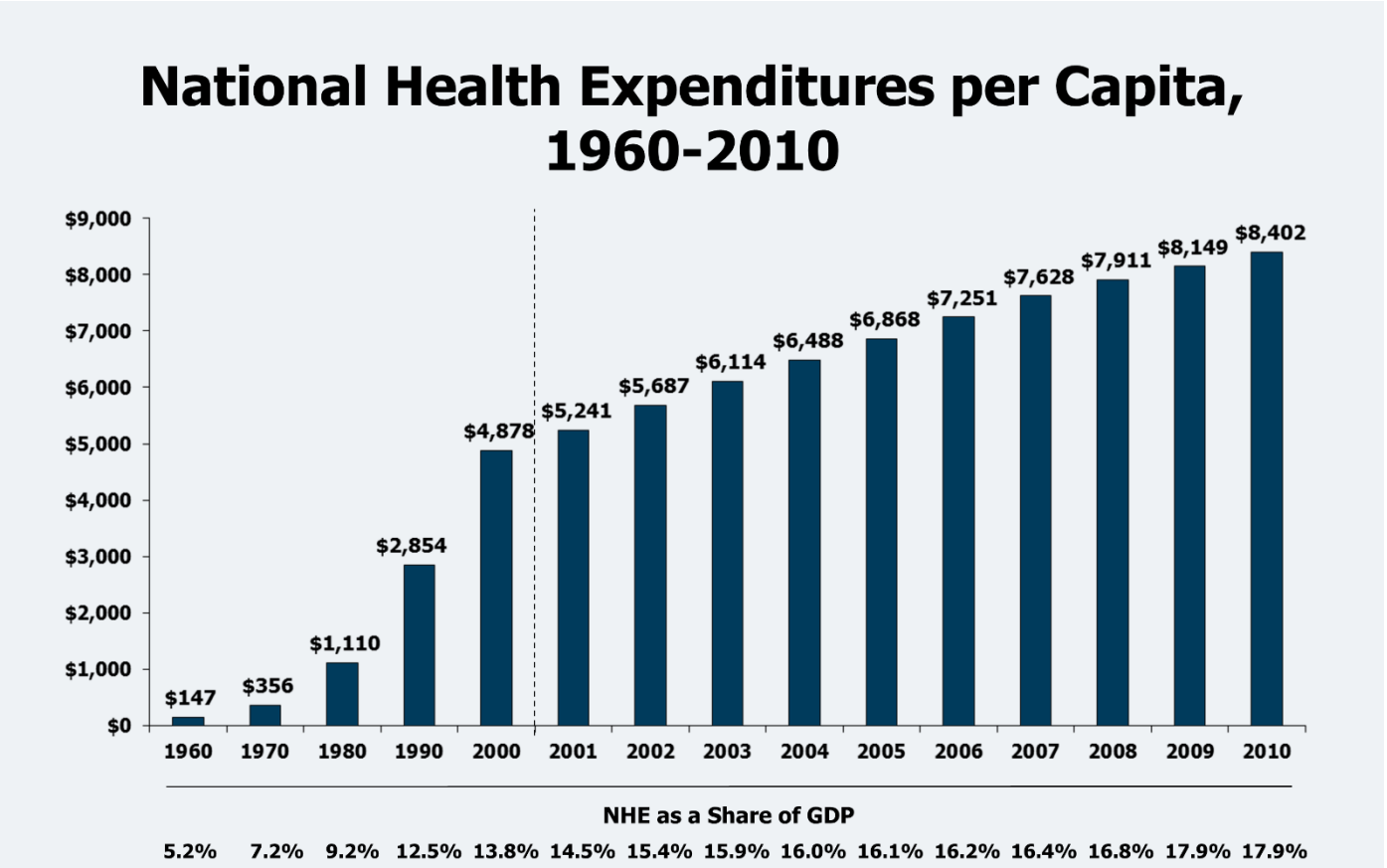
The Promise: A Health Span to Match Your Lifespan



Why We Need It: Longevity Crisis



Why We Need It: Living Longer in Poor Health



Notes: According to CMS, population is the U.S. Bureau of the Census resident-based population, less armed forces overseas.

Source: Centers for Medicare and Medicaid Services, Office of the Actuary, National Health Statistics Group, at http://www.cms.hhs.gov/NationalHealthExpendData/ (see Historical; NHE summary including share of GDP, CY 1960-2010; file nhegdp10.zip).

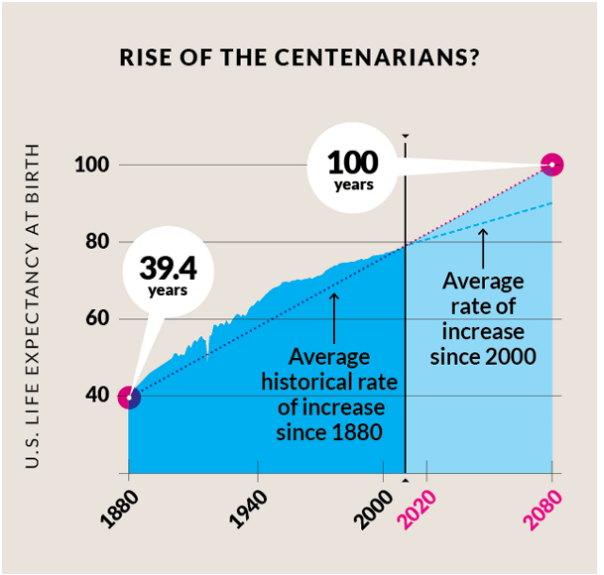
THE HENRY J. KAISER FAMILY FOUNDATION

~~Wealth~~ *Health* to Last a Lifetime



Fred Lamprey, 90, WWII pilot still flying







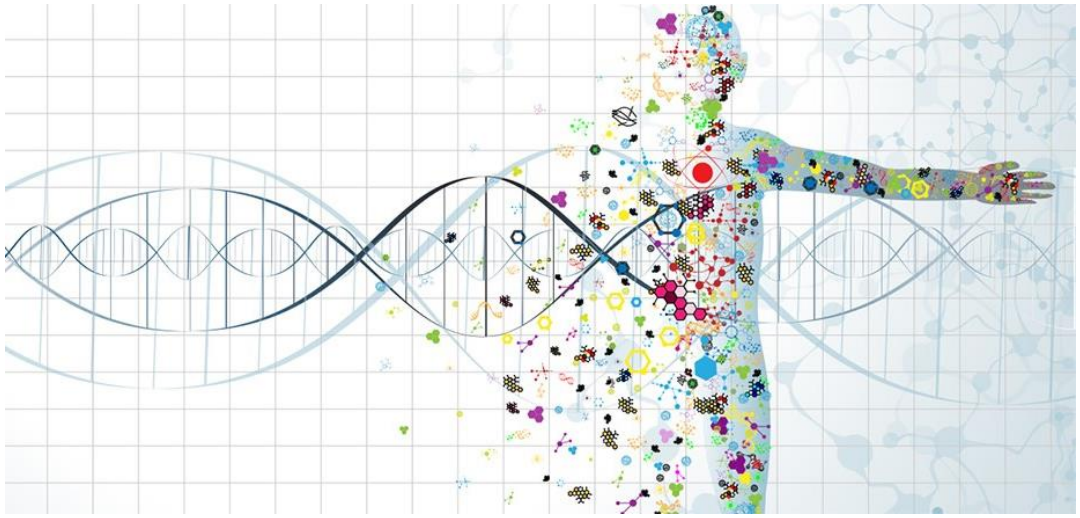
Hildegund Buerkle, 83, world record sprinter

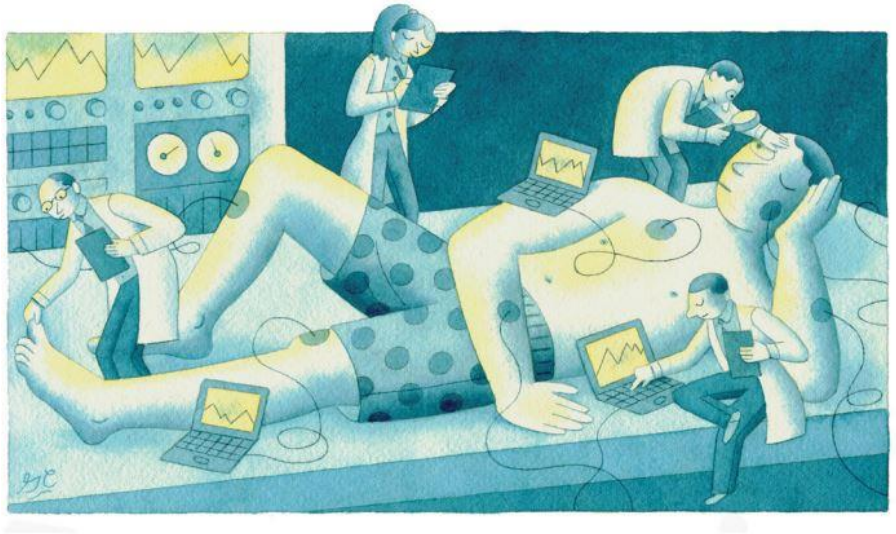


Bette Calman, 87, world renowned yogi

The Precision Medicine *Omics* Revolution Has Arrived







Time for one-person trials

Precision medicine requires a different type of clinical trial that focuses on individual, not average, responses to therapy, says **Nicholas J. Schork**.

One Size Fits One



IMPRECISION MEDICINE

For every person they do help (blue), the ten highest-grossing drugs in the United States fail to improve the conditions of between 3 and 24 people (red).

1. ABILIFY (aripiprazole)
Schizophrenia



2. NEXIUM (esomeprazole)
Heartburn



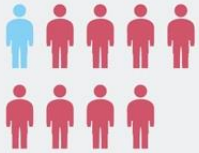
3. HUMIRA (adalimumab)
Arthritis



4. CRESTOR (rosuvastatin)
High cholesterol



5. CYMBALTA (duloxetine)
Depression



6. ADVAIR DISKUS (fluticasone propionate)
Asthma



7. ENBREL (etanercept)
Psoriasis



8. REMICADE (infliximab)
Crohn's disease



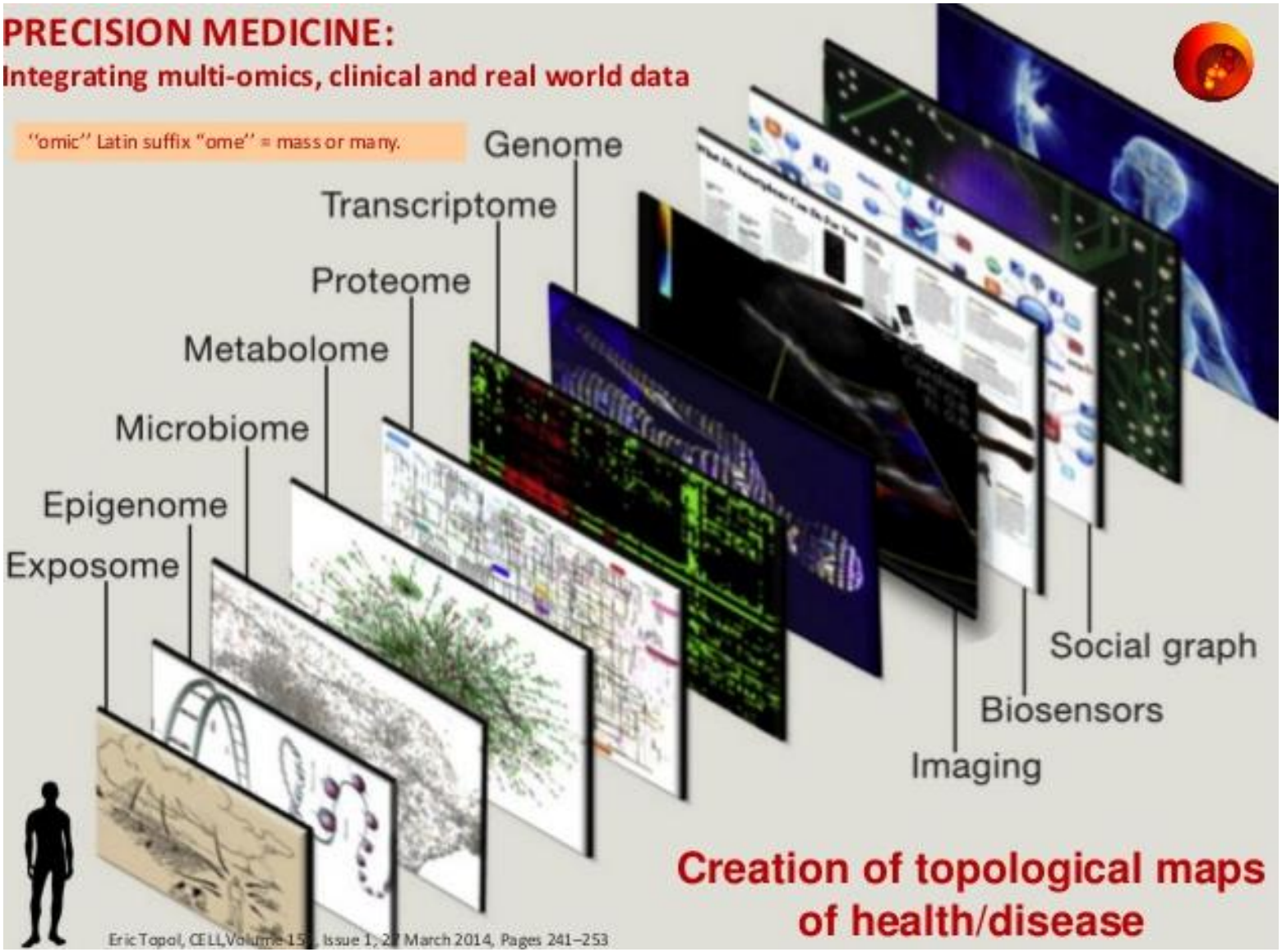
9. COPAXONE (glatiramer acetate)
Multiple sclerosis



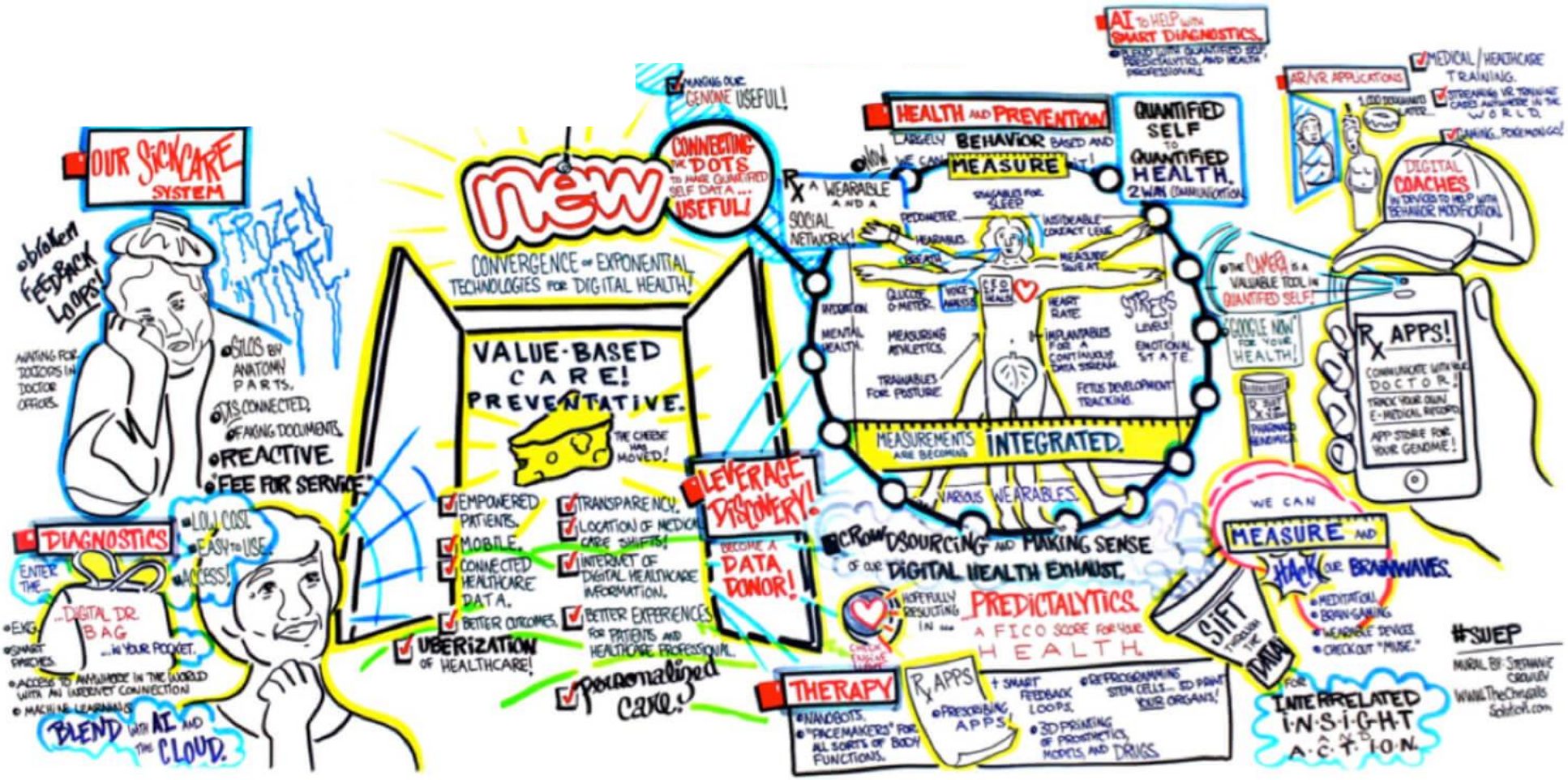
10. NEULASTA (pegfilgrastim)
Neutropenia



Omics Technologies: Mapping the Patient Journey

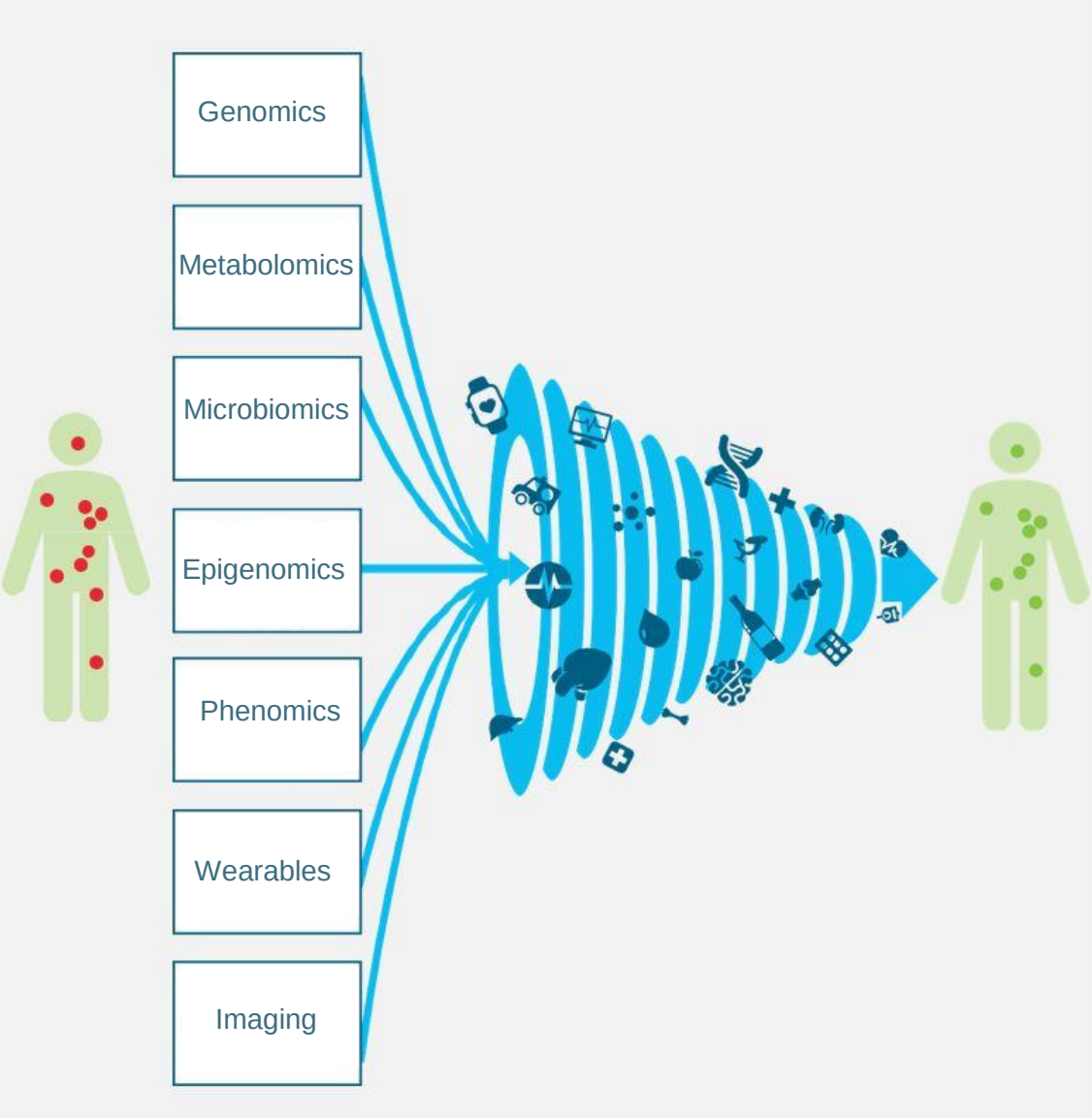


The Problem: Lots of Noise, Minimal Signals, No Integration



Singularityhub.com

The Solution: Precision Medicine



What Do I Know About Precision Medicine & Omics?



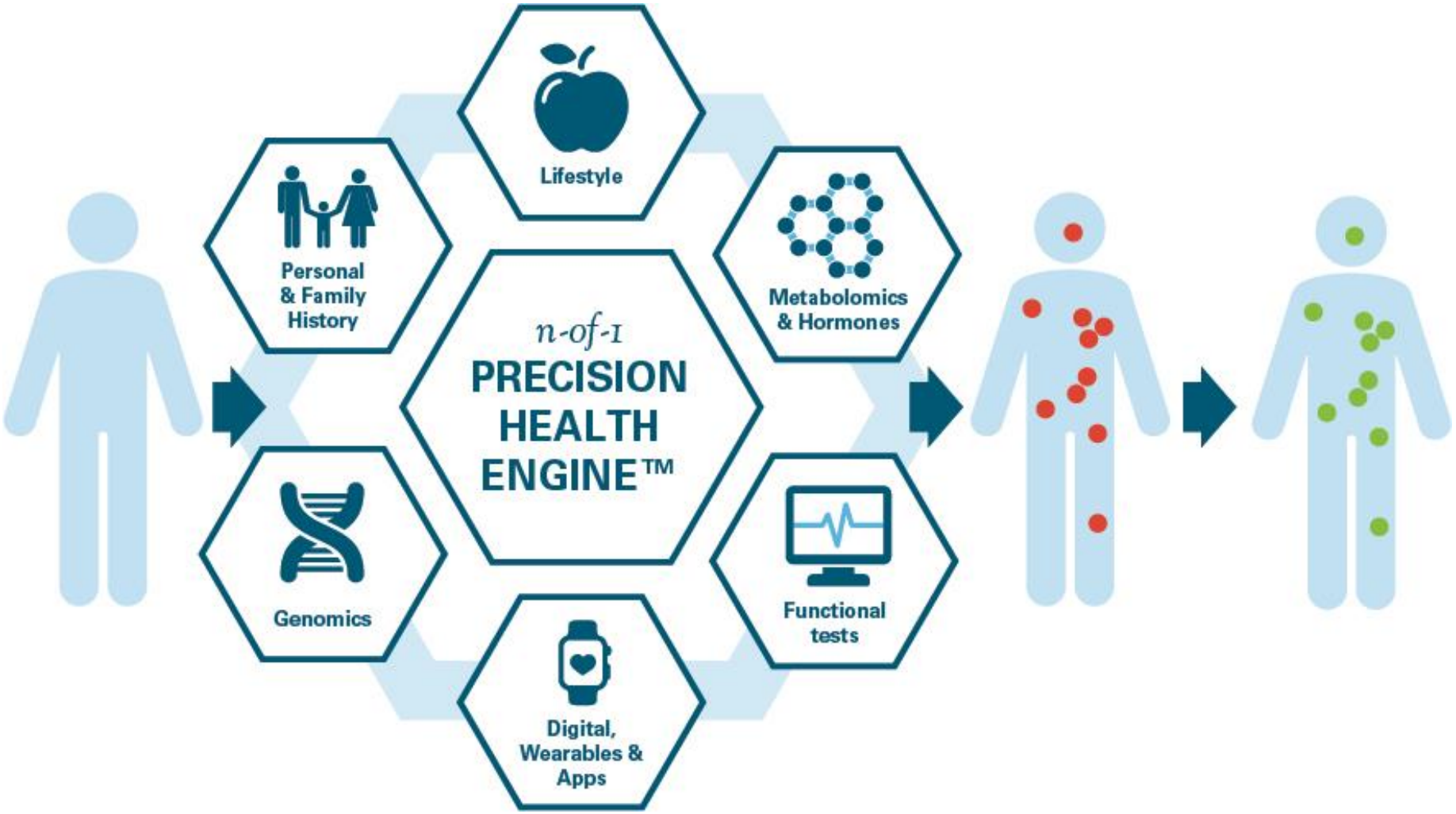








Precision Medicine in Action: Making Omics Data Actionable



Integrate, Interpret, Intervene!



The Revealing Power of Precision Medicine



Complaint: Slowing Down
Key Finding: Hashimoto's Thyroiditis



Complaint: Diabetes?
Key Finding: No diabetes; visceral fat



Complaint: Slow workout recovery
Key Finding: Prediabetes



Complaint: Fainting episodes & dehydration
Key Finding: Silent myocardial infraction (heart attack)



Complaint: Can't improve running time
Key Finding: Sarcopenia (muscle wasting) & stress fractures



Complaint: Poor diet
Key Finding: Prostate cancer



Complaint: Feeling lousy
Key Finding: Diabetes



Complaint: Low libido
Key Finding: Osteoporosis



Complaint: Obesity
Key Finding: Sleep disorder

Precision Medicine Detects Risks You Can't See



Meet Dr. Greg, a 45-years-young health conscious surgeon who looks great and does everything right.

- Prediabetes
- Low free testosterone
- Elevated homocysteine; low B vitamins
- Family history of DVT, pulmonary emboli, heart disease, hyperlipidemia
- MTHFR

Precision Medicine Predicts Risks that Compromise Longevity



"My doctor told me my lab work is 'normal'! Why don't I feel optimal?"

- JB, 62 yo

What Lies Beneath: Advanced Lipid Tests

A standard lipid panel will show you this …

Test Name	Units	Result and Risk Category		
		Optimal	Moderate	High
Lipid Panel				
CHOLESTEROL,TOTAL	mg/dL	145		
TRIGLYCERIDES	mg/dL	66		
HDL CHOLESTEROL	mg/dL	43		
LDL CHOL,CALCULATED	mg/dL	89		
CHOLESTEROL/HDL RATIO	calc	3.4		
NON-HDL CHOLESTEROL	mg/dL	102		

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CHOLESTEROL/HDL RATIO	calc	3.4		
NON-HDL CHOLESTEROL	mg/dL	102		

But what about this?

Lipoprotein Subfractions				
LDL PARTICLE NUMBER	nmol/L		1534	
LDL SMALL	nmol/L			242
LDL MEDIUM	nmol/L			334
HDL LARGE	nmol/L			4932

What Lies Beneath: Advanced Lipid Tests

A standard lipid panel will show you this …

Test Name	Units	Result and Risk Category		
		Optimal	Moderate	High
Lipid Panel				
CHOLESTEROL,TOTAL	mg/dL	145		
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LDL CHOL,CALCULATED	mg/dL	89		
CHOLESTEROL/HDL RATIO	calc	3.4		
NON-HDL CHOLESTEROL	mg/dL	102		

Or this?

Inflammation				
FIBRINOGEN ANTIGEN	mg/dL			419 H
LP PLA2 (PLAC®)	ng/mL	146		

What Lies Beneath: Advanced Lipid Tests

A standard lipid panel will show you this …

Test Name	Units	Result and Risk Category		
		Optimal	Moderate	High
Lipid Panel				
CHOLESTEROL,TOTAL	mg/dL	145		
TRIGLYCERIDES	mg/dL	66		
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LDL CHOL,CALCULATED	mg/dL	89		
CHOLESTEROL/HDL RATIO	calc	3.4		
NON-HDL CHOLESTEROL	mg/dL	102		

Or this?

Genetic Cardiovascular Markers

CARDIO IQ(TM) 9P21 GENO	
rs10757278	gg
rs1333049	cc

Feed Your Genes, Turn Off Cardiovascular Disease Risk

PLOS ONE



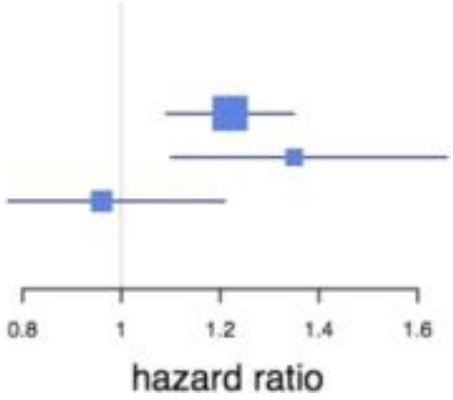
The Effect of Chromosome 9p21 Variants on Cardiovascular Disease May Be Modified by Dietary Intake: Evidence from a Case/Control and a Prospective Study

Ron Do[1], Changchun Xie[2,3], Xiaohe Zhang[2], Satu Männistö[4], Kennet Harald[4], Shofiqul Islam[2,3], Swneke D. Bailey[1], Sumathy Rangarajan[2], Matthew J. McQueen[2], Rafael Diaz[5], Liu Lisheng[6], Xingyu Wang[7], Kaisa Silander[4,8], Leena Peltonen[4,8†], Salim Yusuf[2], Veikko Salomaa[4], James C. Engert[1,9,10*], Sonia S. Anand[2,3*], on behalf of the INTERHEART investigators

Prudent diet

Group	n	n case	HR	CI	p
Low	12314	678	1.22	1.09–1.35	0.0003
Medium	3526	189	1.35	1.10–1.66	0.0041
High	3289	147	0.96	0.77–1.21	0.73

Test of homogeneity: p=0.0011



Your Genes are Not Your Destiny

The Atlantic

13 Anonymous Genetic Superheroes Walk Among Us

Or do they?



Wong Campion/ Reuters

ED YONG

APR 11, 2016 | SCIENCE

"These people, unbeknownst to them, **carry genes that all but guarantee that they'll get fatal diseases.** And yet, somehow, **they're completely healthy**. They might carry other genes that mitigate their risk. Or perhaps, **some aspect of their diet, lifestyle, or environment shields them** from their harmful inheritance."

BB, 66 yo female superhero

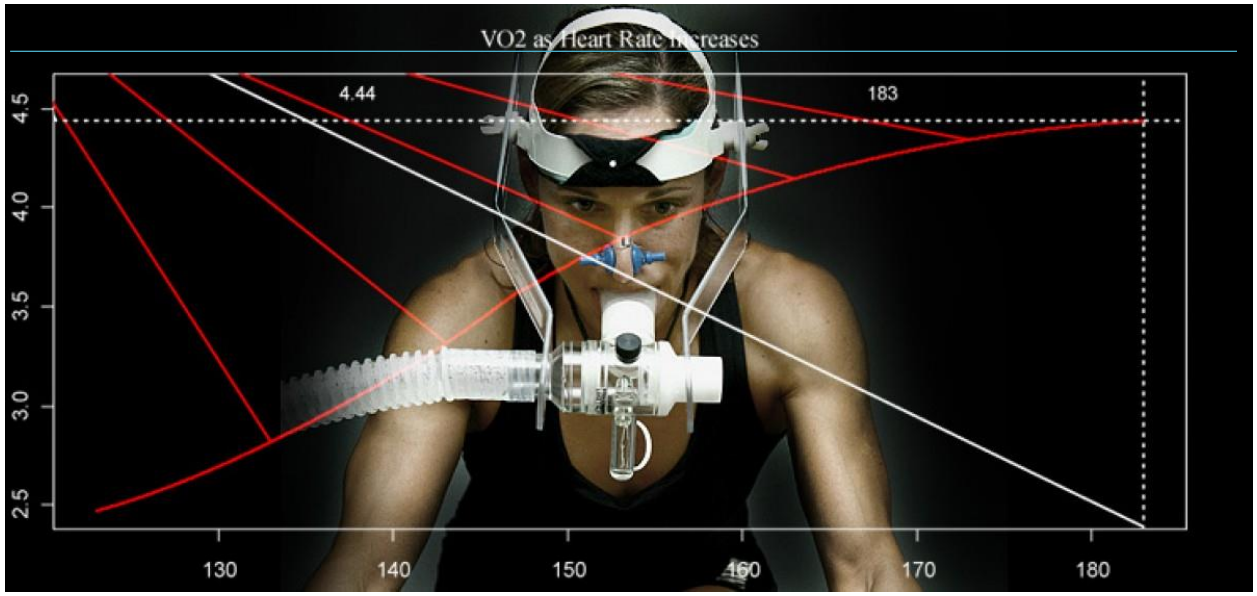
Clinically Significant Findings				
Variant	Interpretation	Associated Condition	Mode of Inheritance	Zygosity
LRRK2 c.6055G>A (p.Gly2019Ser)	Pathogenic	LRRK2-Related Parkinson Disease	Autosomal Dominant	Heterozygous

ER, 75 yo male superhero

Clinically Significant Findings				
Variant	Interpretation	Associated Condition	Mode of Inheritance	Zygosity
LRRK2 c.6055G>A (p.Gly2019Ser)	Pathogenic	LRRK2-Related Parkinson Disease	Autosomal Dominant	Heterozygous

MU: Gold Star for Functional Fitness

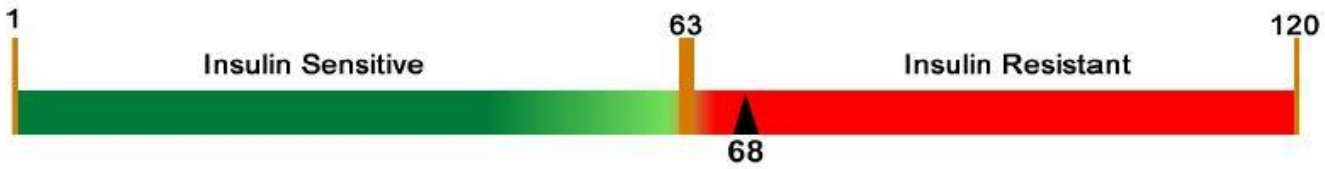
Age	44 years
Speed, Incline	5 mph, 7.5%
Predicted VO2Max	28.9 ml/kg/min
Actual VO2Max	**43.2** ml/kg/min





Sick at the Cellular Level

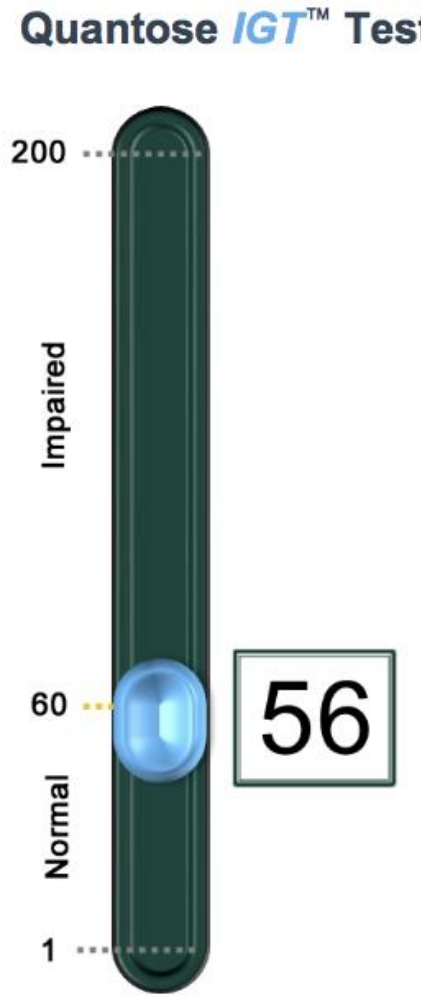
Biomarkers	6.24.16	1.19.17	
Glucose, Fasting	92	84	↓
Hemoglobin A1C	5.5	5.2	↓
Glucose, Mean Blood	119	108	↓
Insulin, Total	4.6	4.9	↑



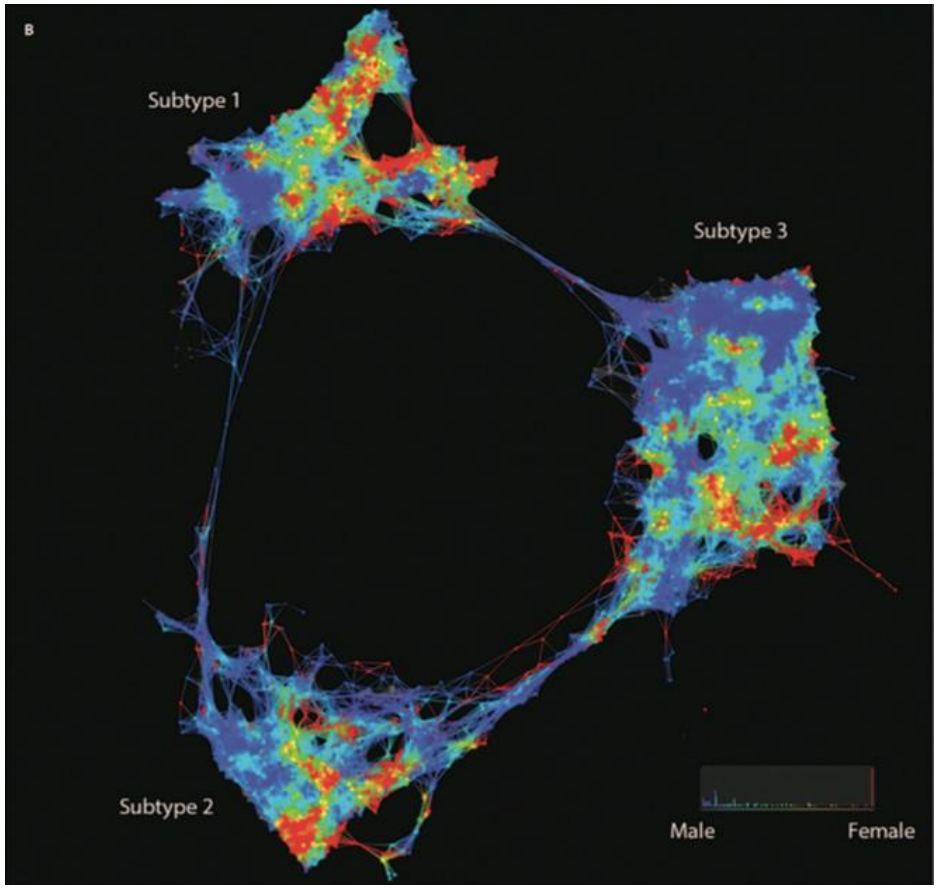


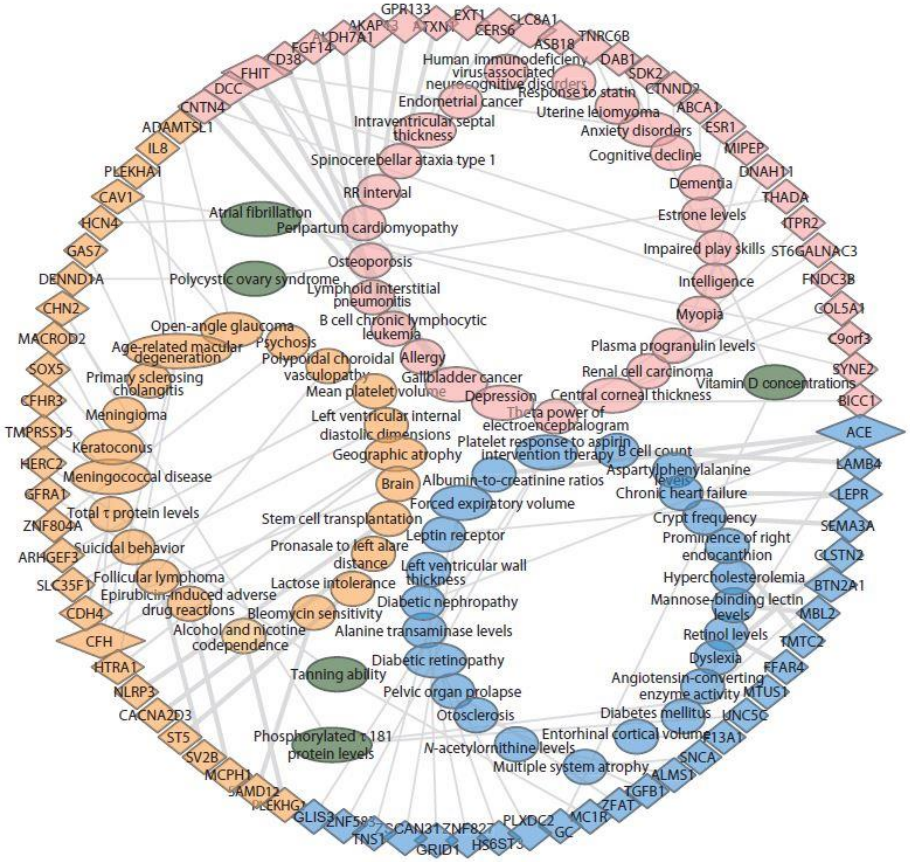
Metabolite	Result	Units	Reference Interval
Insulin	5.8	µu/mL	3.13 - 21.3
AHB	7.39	µg/mL	1.92 - 7.37
LGPC	23.1	µg/mL	7.60 - 25.4
Oleic Acid	84.2	µg/mL	25.9 - 114

The reference intervals were established using 456 non-diabetic subjects at risk for diabetes (IFG, IGT, and/or FINDRISC score >12).



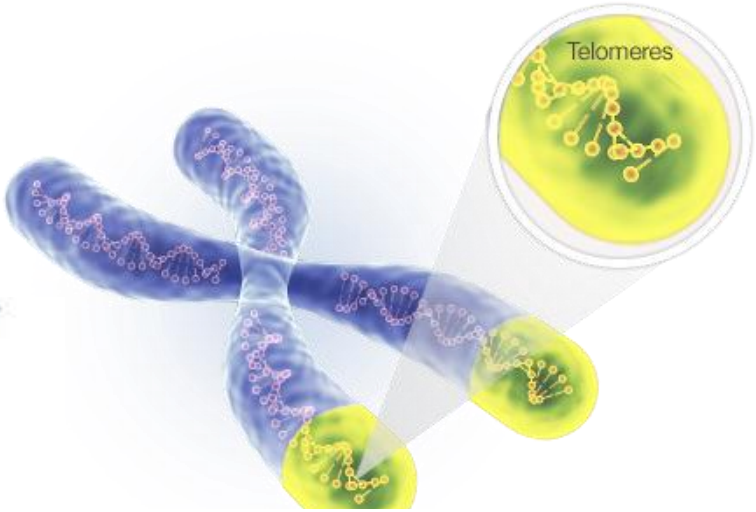
Reversing a Type 2 Diabetic Trajectory, Precisely

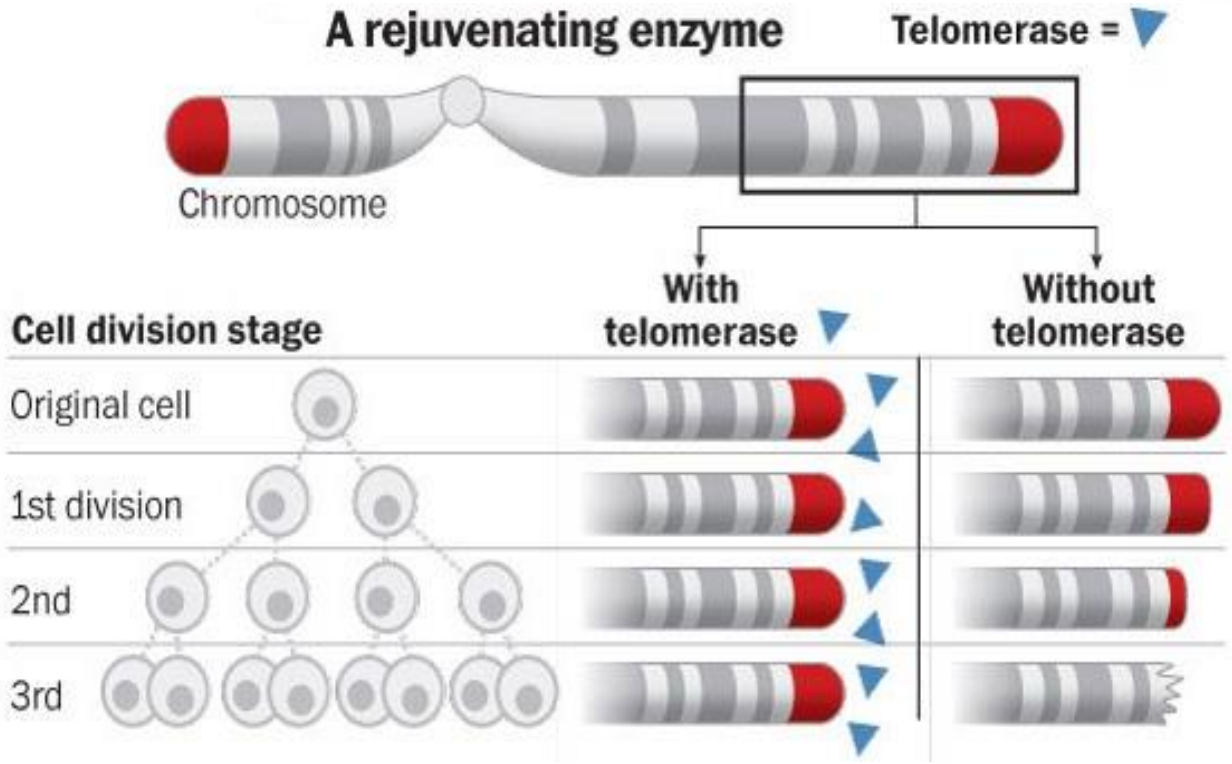




Li L, Cheng WY, Glicksberg BS, Gottesman O, Tamler R, Chen R, Bottinger EP, Dudley JT. Identification of type 2 diabetes subgroups through topological analysis of patient similarity. Sci Transl Med. 2015 Oct 28

Telomere Biology: Aging in Reverse

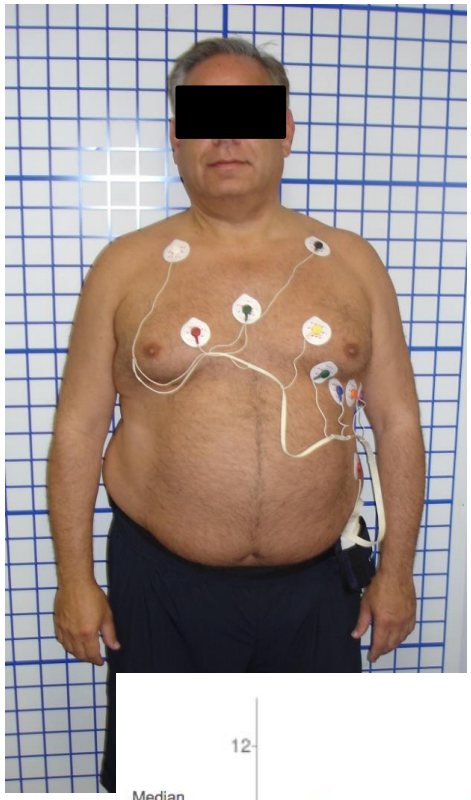






Astragalus Root

MF: Reversing the Clock, Year After Year

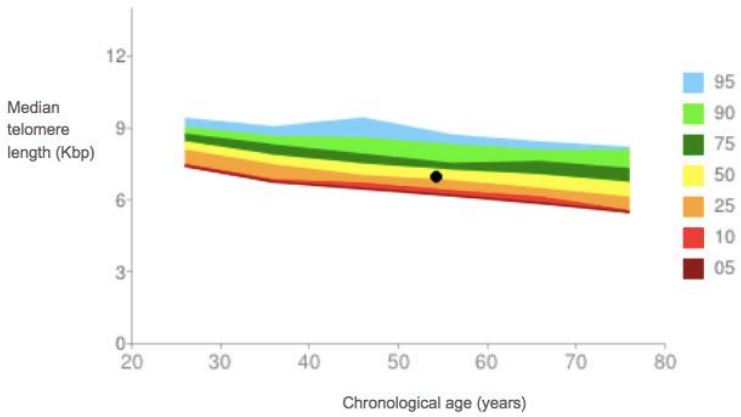


2009
Biological
Age

56.8

Chronological
Age

54.8 years



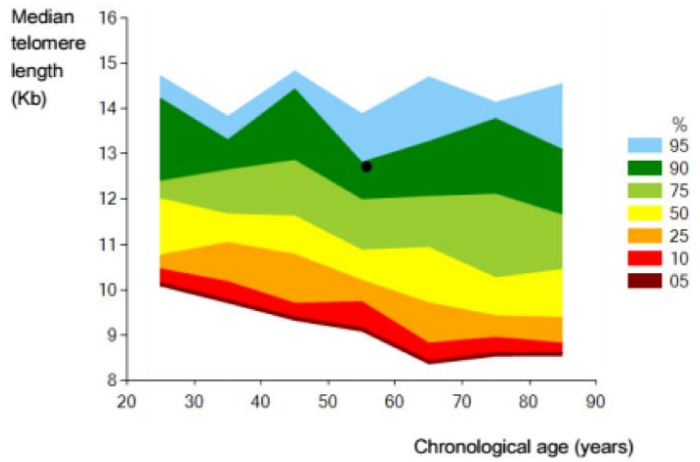


2010
Biological
Age

52.6

Chronological
Age

56.2 years

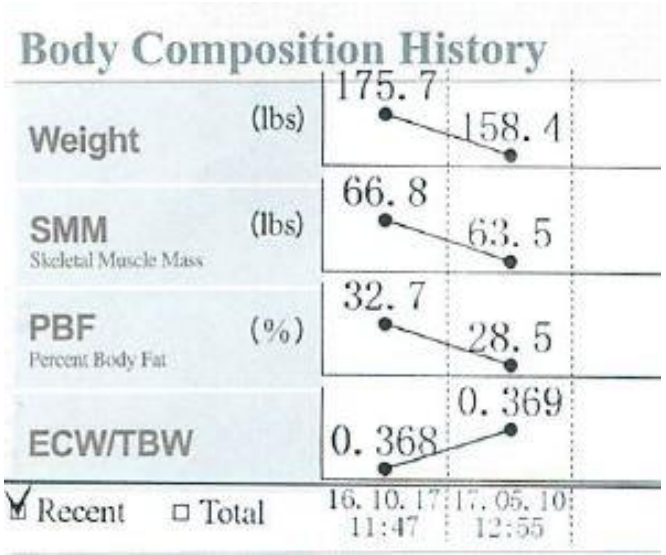


AN: Burning Fat & Building Muscle with Peptides





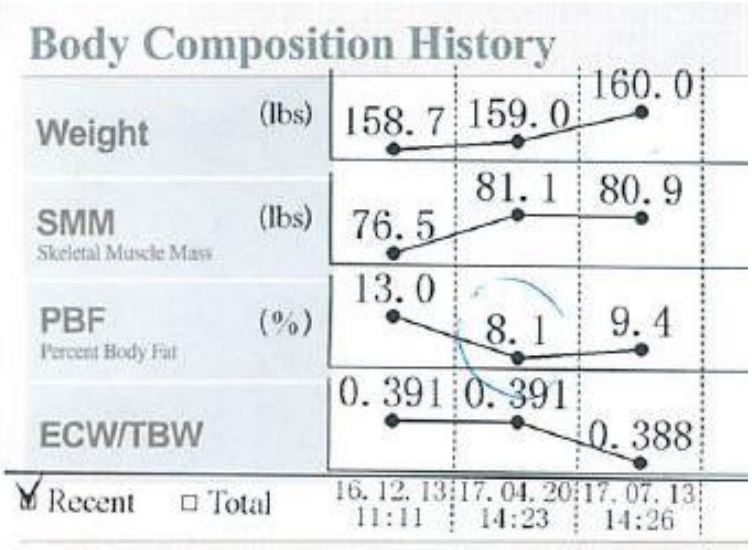
AN, 43 yy female
7 months
Lost 17.3 lbs
Reduced body fat by 4.2%

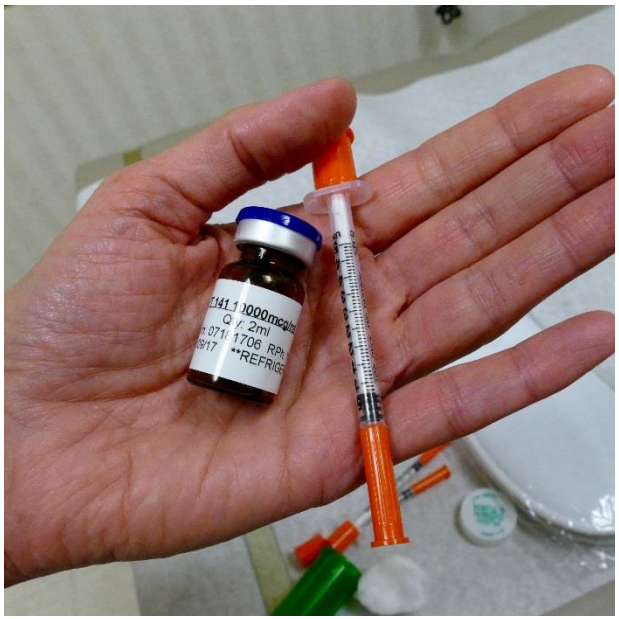


Rx: n=1 Prime Peptides
(CJC 1295 & Ipamorelin blend)
Inject 0.1 cc (10 units), 5x weekly

DH: Envy of the Fitness Community at 75 Years Young







DH, 75 yy male
7 months
Gained 4.4 lbs lean muscle
Reduced body fat by 3.6%

Rx: n=1 Prime Peptides (CJC 1295 & Ipamorelin blend)
Inject 0.1 cc (10 units), 5x weekly

JH: Body Re-composition on T Therapy





T cream Rx:
04.16 2 mg qd to10.16 3 mg qd

	Baseline 03.04.16	6-8 wks 09.08.16	6-12 mos 01.09.17
Total T	24	84	190
Free T	0.9	5.6	23.9
LH	<0.2	8.2	7.6
FSH	<0.7	8.1	5.6

BODY COMPOSITION	Baseline 04.12.16	12 mos 04.19.17
Total Weight (lbs)	165.5	134.1
Lean Body Mass (lbs)	94	101.6
Body Fat (lbs)	66.5	32.4

PW: 2 Month Intervention, Drastic Body Re-composition

InBody **December 2016**

[InBody770]

ID	Height	Age	Gender	Test Date / Time
4088923401	5ft. 11. 5in.	53	Male	2016.12.15. 12:43

Body Composition Analysis

	Values	Total Body Water	Lean Body Mass	Weight
Intracellular Water (lbs)	71. 0	112. 7	154. 3	192. 2
Extracellular Water (lbs)	41. 7			
Dry Lean Mass (lbs)	41. 7			
Body Fat Mass (lbs)	37. 9			

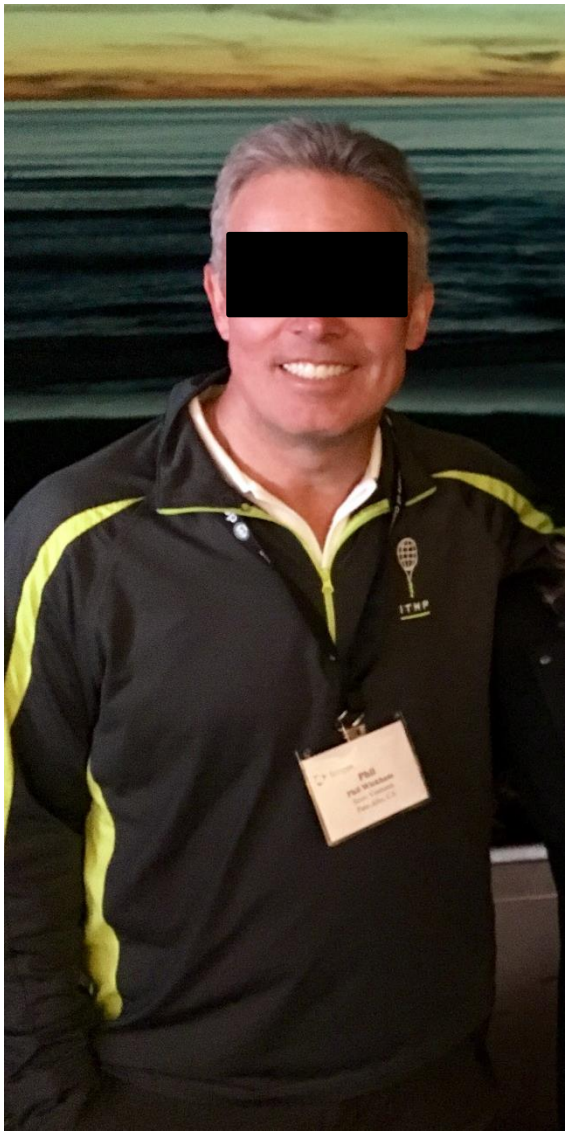
InBody **February 2017**

[InBody770]

ID	Height	Age	Gender	Test Date / Time
4088923401	5ft. 11. 5in.	53	Male	2017.02.20. 16:26

Body Composition Analysis

	Values	Total Body Water	Lean Body Mass	Weight
Intracellular Water (lbs)	74. 7	119. 7	164. 2	196. 8
Extracellular Water (lbs)	45. 0			
Dry Lean Mass (lbs)	44. 5			
Body Fat Mass (lbs)	32. 6			



Whole Genome Sequencing: A Mutation That Protects!

Clinically Significant Findings				
Variant	**Interpretation**	**Associated Condition**	**Mode of Inheritance**	**Zygosity**
AMPD1 c.133C>T (p.Gln45Ter)	Pathogenic	Myoadenylate Deaminase Deficiency	Autosomal Recessive	Homozygous

"A deficiency in AMPD is the **most prevalent genetic disease in humans**, the number of people heterozygous approaching 10% of Caucasian.

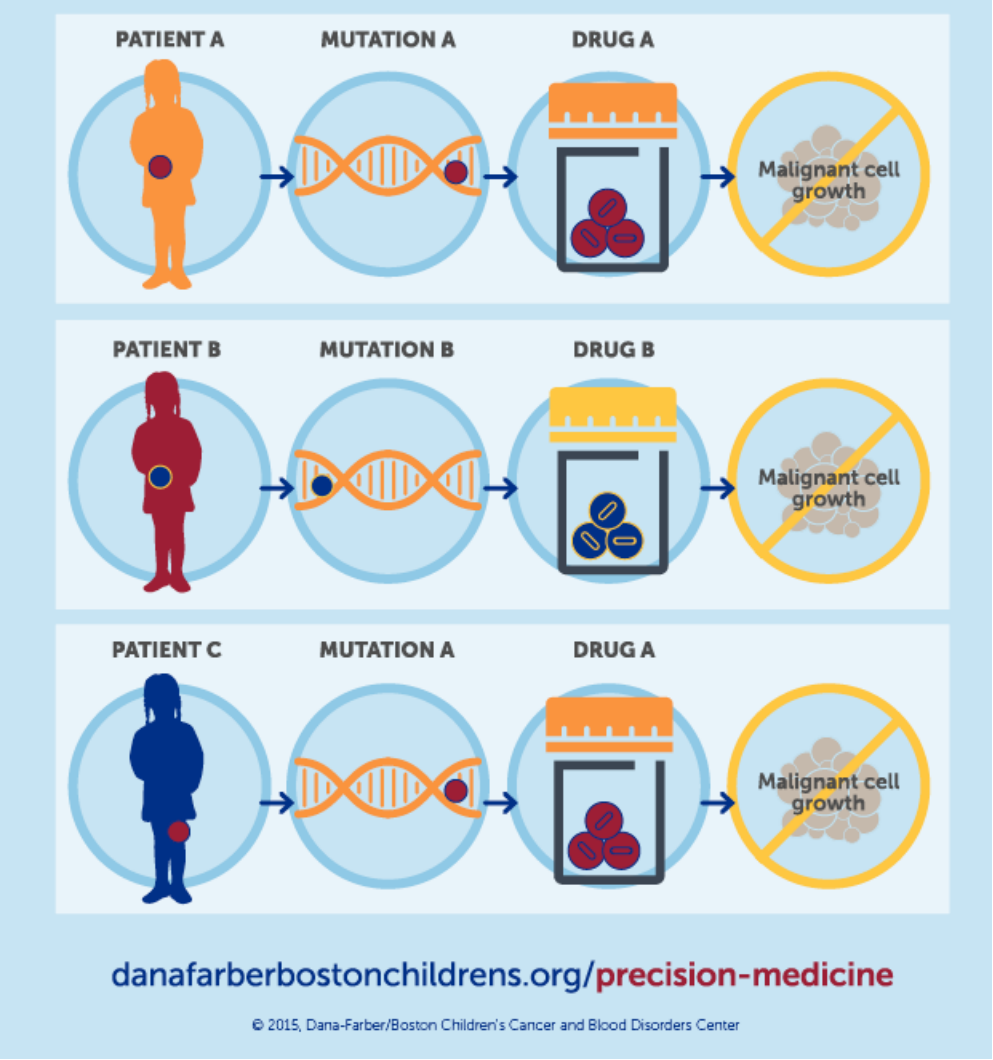
"Interestingly, **a mutation in a least one AMPD allele** appears to confer a **protective effect** on individuals at risk for one of the most prevalent diseases of industrialized nations, **congestive heart failure**."

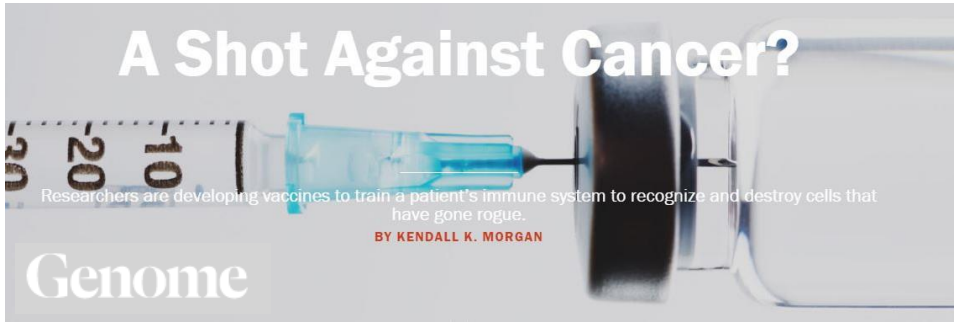


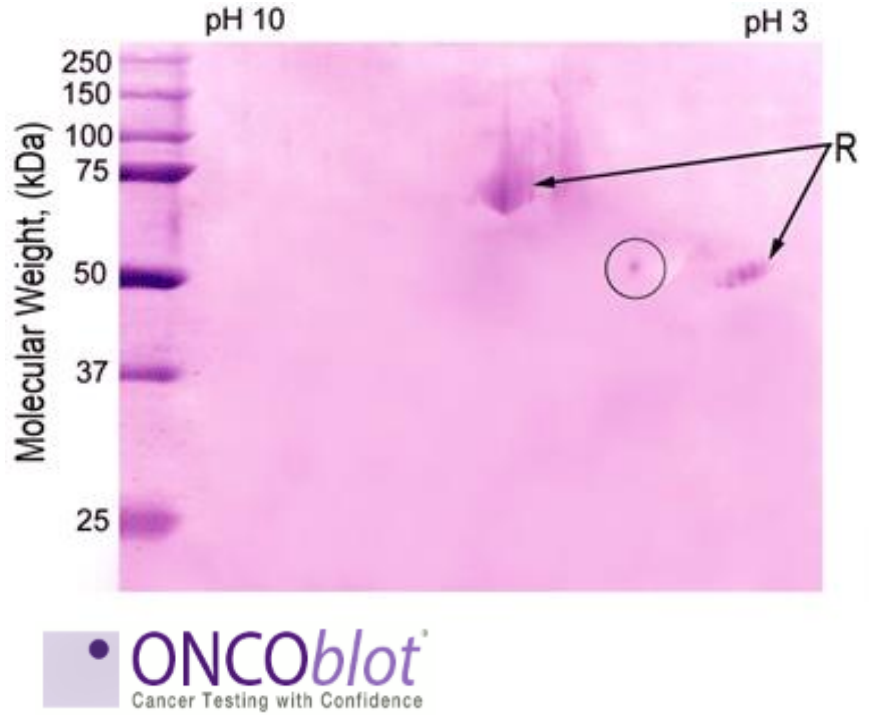
A Novel Bipartite Intronic Splicing Enhancer Promotes the Inclusion of a Mini-exon in the AMP Deaminase 1 Gene*

Thomas Genetta‡, Hiroko Morisaki§¶, Takayuki Morisaki§ and Edward W. Holmes‖**

Cancer: New Ways to Detect, Predict, Reverse







ONCOblot to Detect & Reverse Stage 0 Cancer

ONCOblot® TEST RESULTS

ENOX2 proteins evident: Yes X No

ENOX2	Molecular Weight (kDa)	Isoelectric Point (pH)	Tissue of Origin
Protein 1	64	4.6	Breast

Test Description: The ONCOblot® blood serum test reveals the presence of cancer-specific ENOX2 proteins to verify the tissue of origin of cancers as early as stage 0, identify the origin of metastasized cancers of unknown primary, and confirm cancer recurrence. Its utility for ENOX2 detection in the general population for cancer has not been determined. The ONCOblot® test results are provided to medical professionals for interpretation and are not intended to replace current standards of care.

JH, 44 yo Female, ENOX2 protein markers detected stage 0 breast cancer.

TT, 50 yo Female, ENOX2 protein markers detected stage 0 uterine cancer.

ONCOblot® TEST RESULTS

ENOX2 proteins evident: Yes X No

ENOX2	Molecular Weight (kDa)	Isoelectric Point (pH)	Tissue of Origin
Protein 1	63	4.4	Not in data base

Test Description: The ONCOblot® blood serum test reveals the presence of cancer-specific ENOX2 proteins to verify the tissue of origin of cancers as early as stage 0, identify the origin of metastasized cancers of unknown primary, and confirm cancer recurrence. Its utility for ENOX2 detection in the general population for cancer has not been determined. The ONCOblot® test results are provided to medical professionals for interpretation and are not intended to replace current standards of care.

ONCOblot® TEST RESULTS

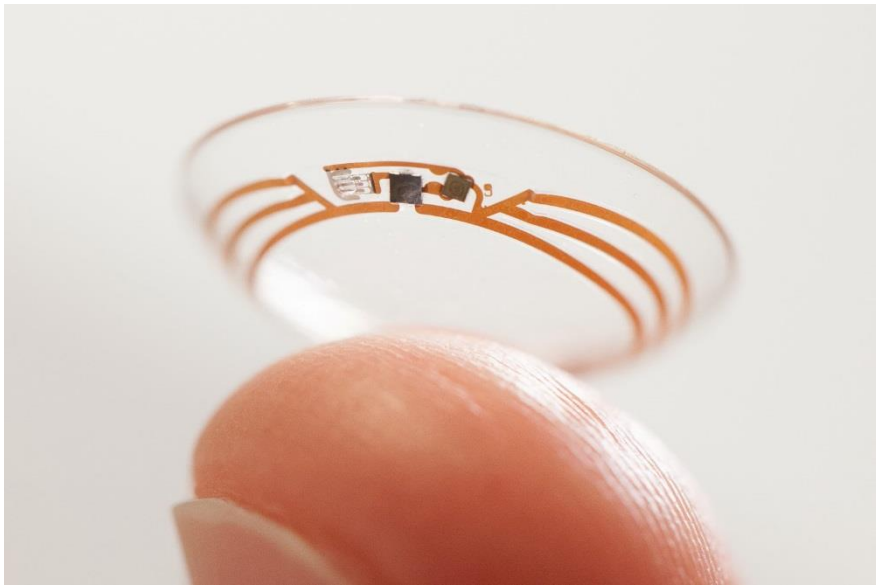
ENOX2 proteins evident: Yes X No

ENOX2	Molecular Weight (kDa)	Isoelectric Point (pH)	Tissue of Origin
Protein 1	80	5.3	Prostate

Test Description: The ONCOblot® blood serum test reveals the presence of cancer-specific ENOX2 proteins to verify the tissue of origin of cancers as early as stage 0, identify the origin of metastasized cancers of unknown primary, and confirm cancer recurrence. Its utility for ENOX2 detection in the general population for cancer has not been determined. The ONCOblot® test results are provided to medical professionals for interpretation and are not intended to replace current standards of care.

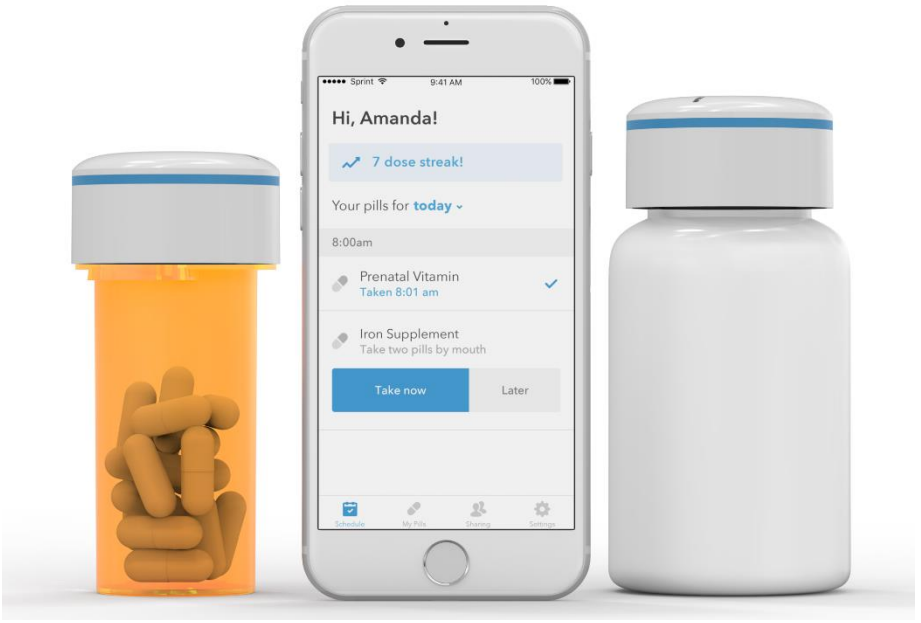
MF, 58 yo male, ENOX2 protein markers detected stage 0 prostate cancer.

Digital Health: The Patient Will See You Now

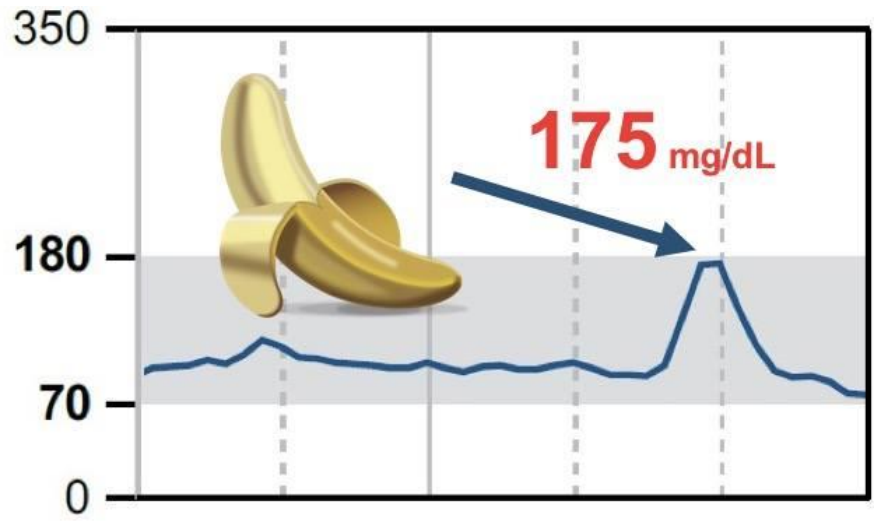




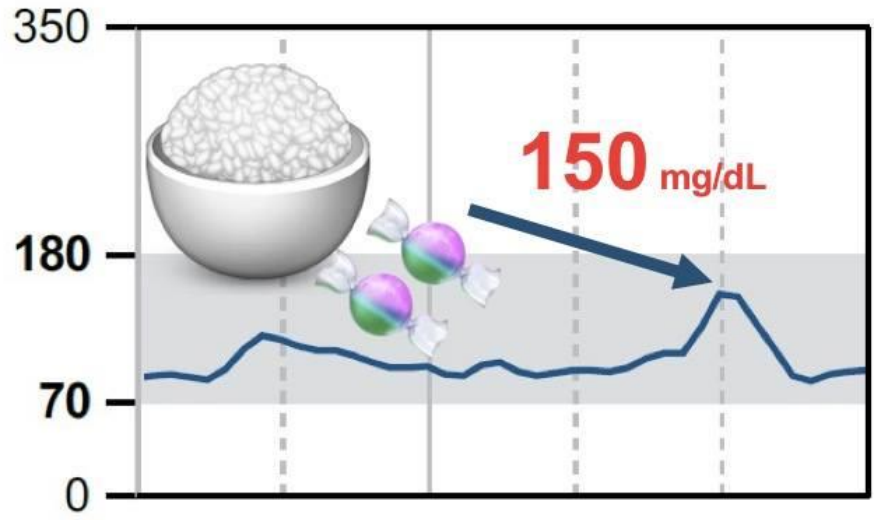




FCG: Freaky Fructose Findings









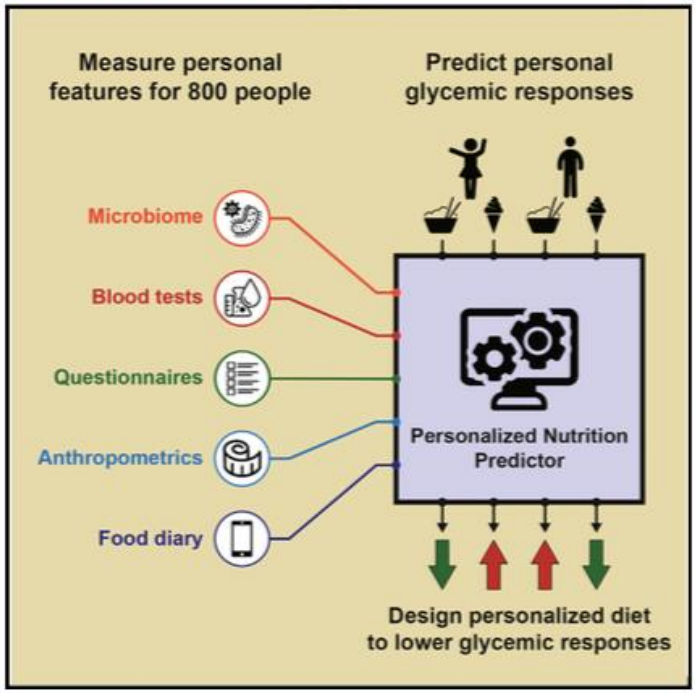
Do You Know Your Carb Type?

Article

Cell

Personalized Nutrition by Prediction of Glycemic Responses

Graphical Abstract



Authors

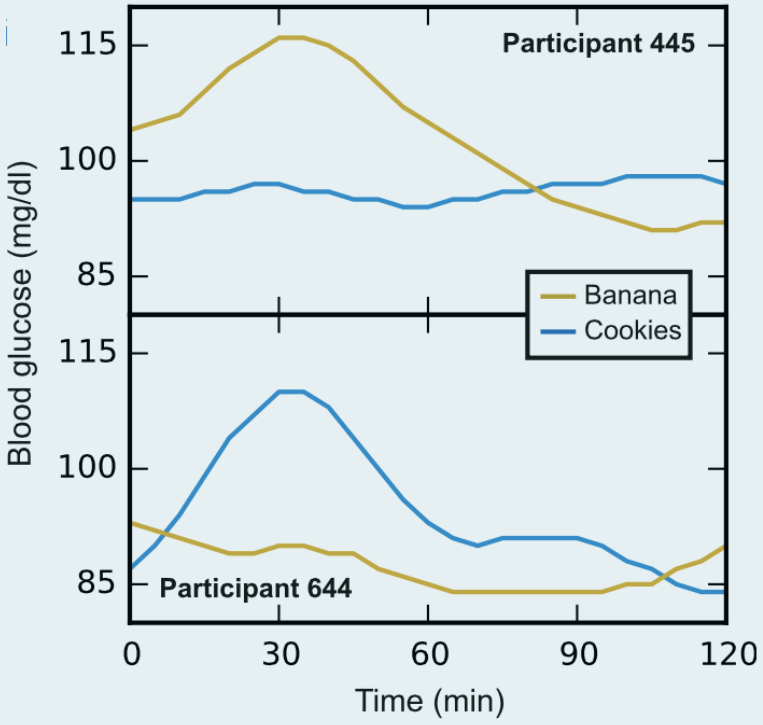
David Zeevi, Tal Korem, Niv Zmora, ..., Zamir Halpern, Eran Elinav, Eran Segal

Correspondence

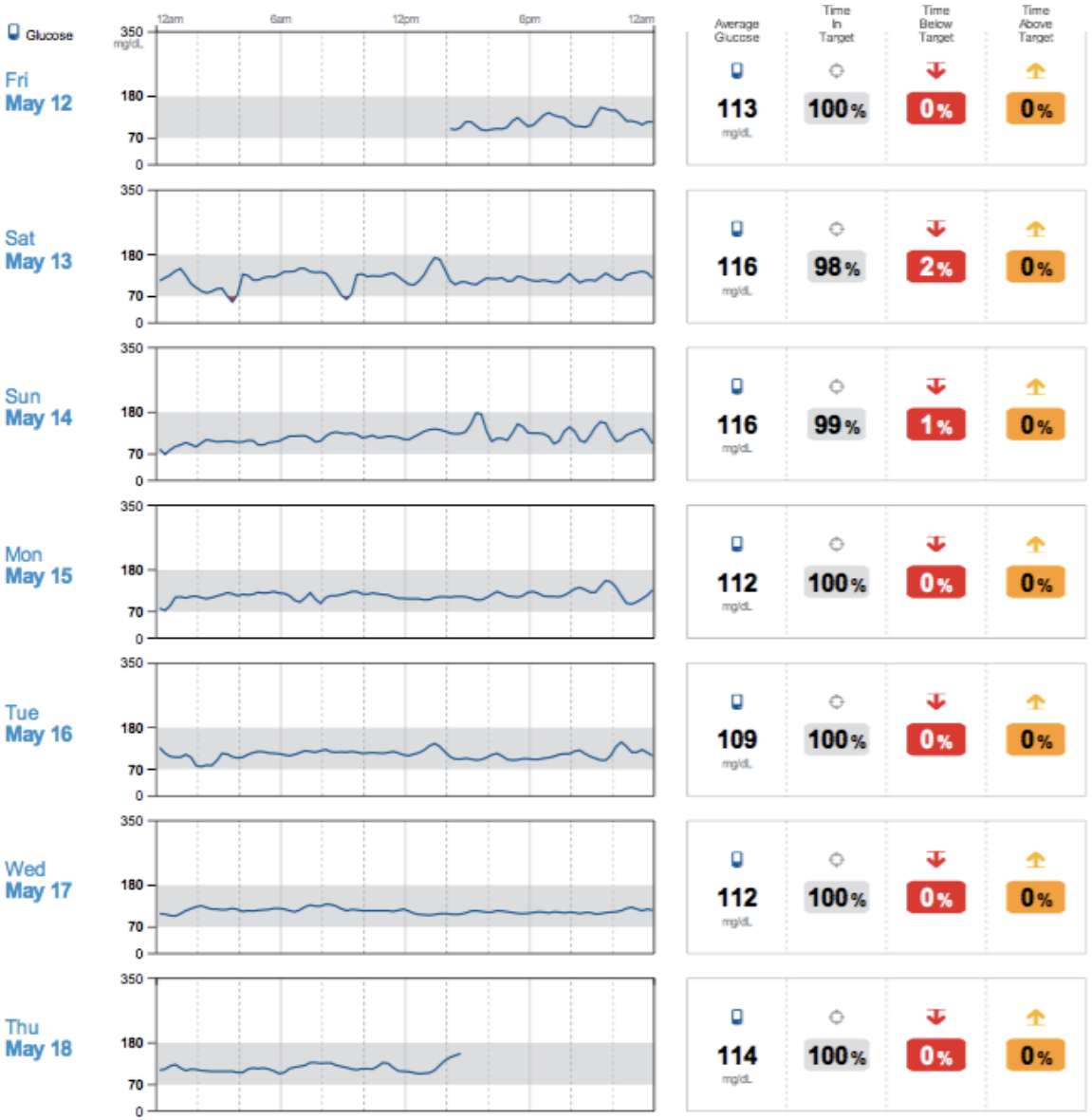
eran.elinav@weizmann.ac.il (E.E.), eran.segal@weizmann.ac.il (E.S.)

In Brief

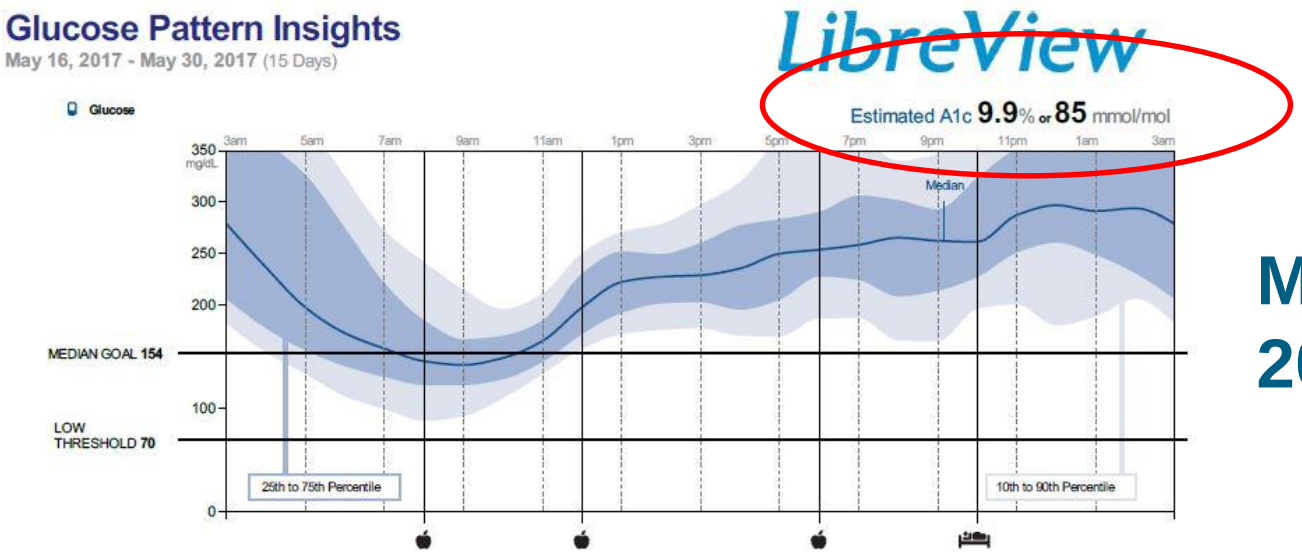
People eating identical meals present high variability in post-meal blood glucose response. Personalized diets created with the help of an accurate predictor of blood glucose response that integrates parameters such as dietary habits, physical activity, and gut microbiota may successfully lower post-meal blood glucose and its long-term metabolic consequences.



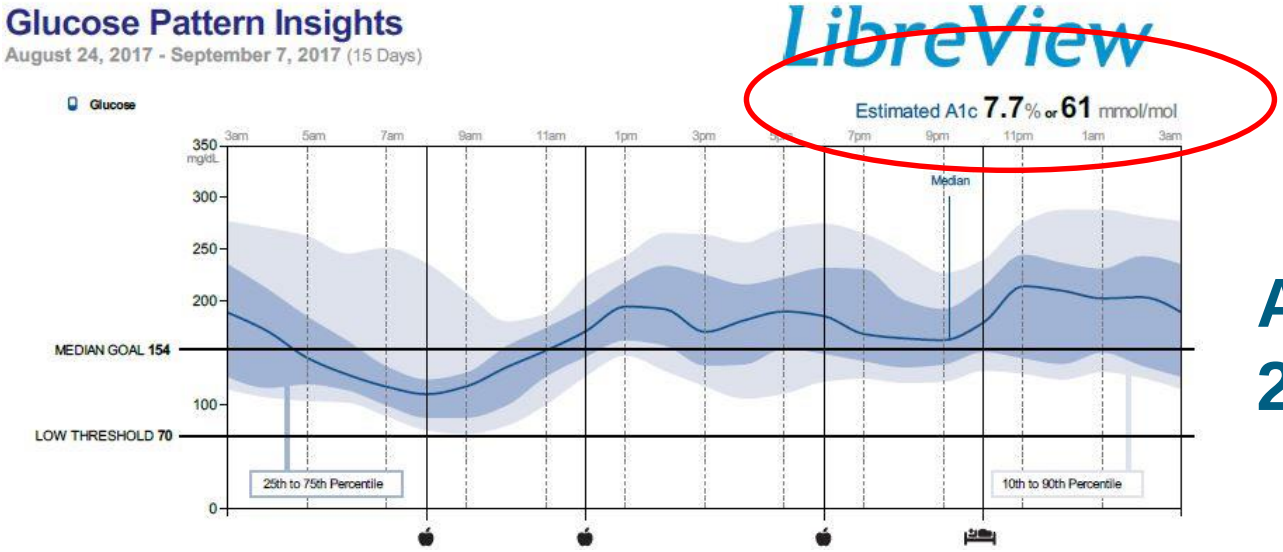
FC: Steady & Elevated; Resistant to Triggers



SL: Reversing Diabetes, in Real Time



May 2017



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Thank you

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