



# The Future of Medicine

## “An Integrative Perspective of Precision Medicine”

Dr. A. Lawrence Cheng  
MD, CCFP(EM), MPH

# Faculty/Presenter Disclosure

- **Faculty:** Dr. A. Lawrence Cheng
- **Relationships with commercial interests in the past year:**
  - Medical Consultant – Molecular You

# Learning Objectives

- After completion of this presentation, participants will be able to:
  - Discuss a new paradigm in medicine that is moving from a disease centric approach to a systems biology, whole person approach.
  - Recognize the 4 P's of the new medicine: Predictive, Preventative, Personalized and Participatory
  - Understand the potential benefits and pitfalls for precision medicine with a balanced integrative perspective.
  - Understand the convergence of new technologies which are fueling this revolution in medicine

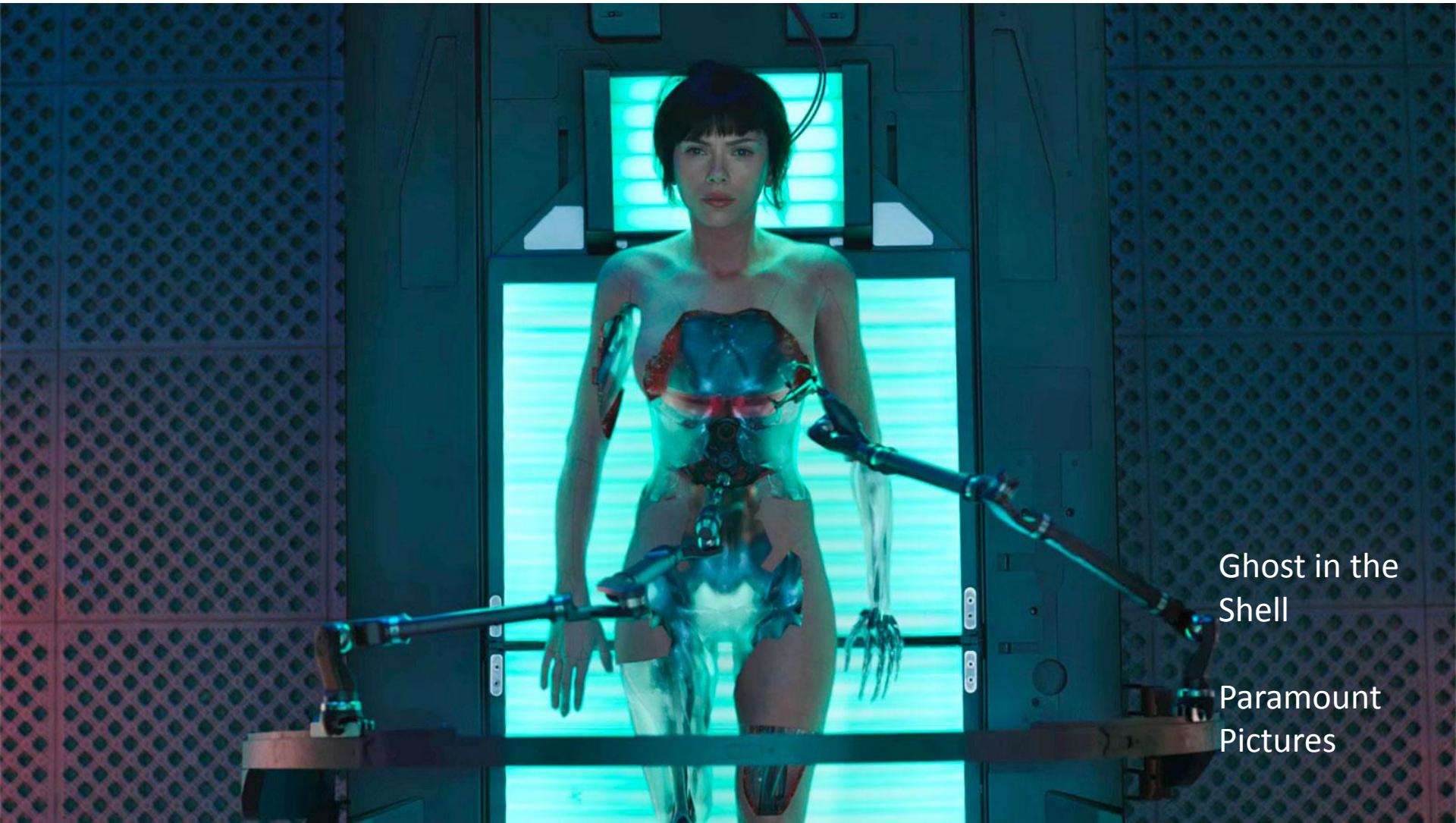
# Outline

- The Old Paradigm
- The New Medicine – 4 P's
- The Super-Convergence of Technology
- “Omics” Revolution
- The Democratization of Medicine
- A New Way of Thinking

Wall-E  
Pixar Pictures  
2008



Future of Humanity???



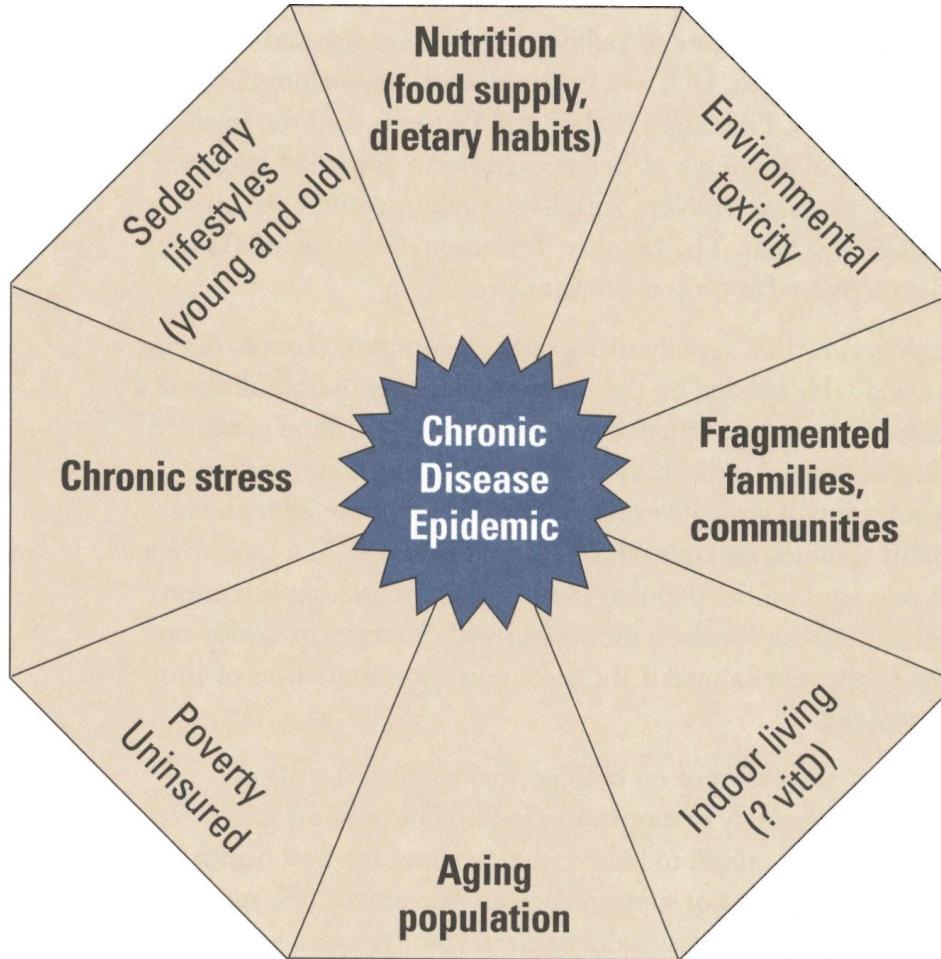
Ghost in the  
Shell

Paramount  
Pictures

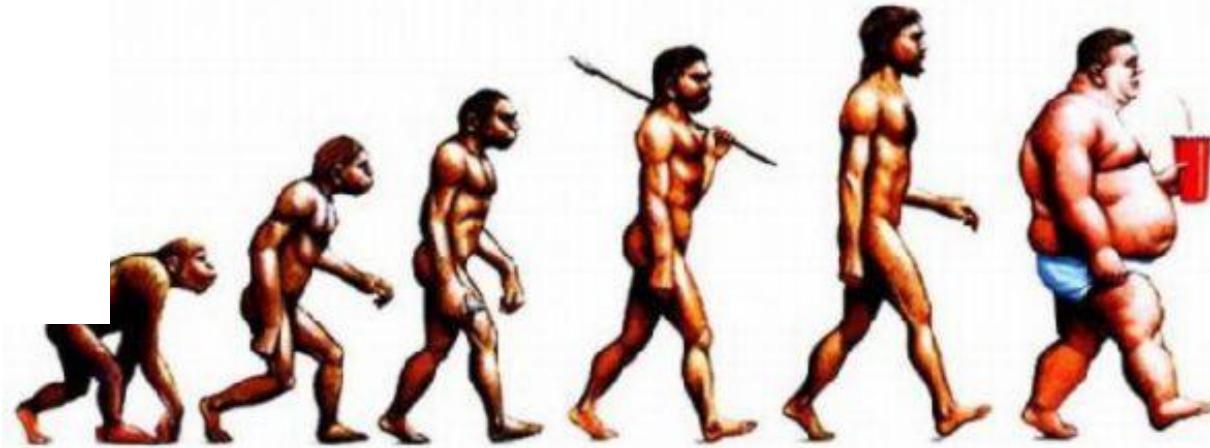
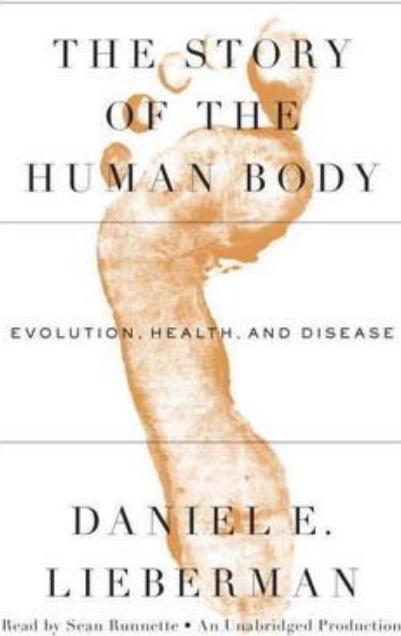
Embrace your Cyborg Destiny...



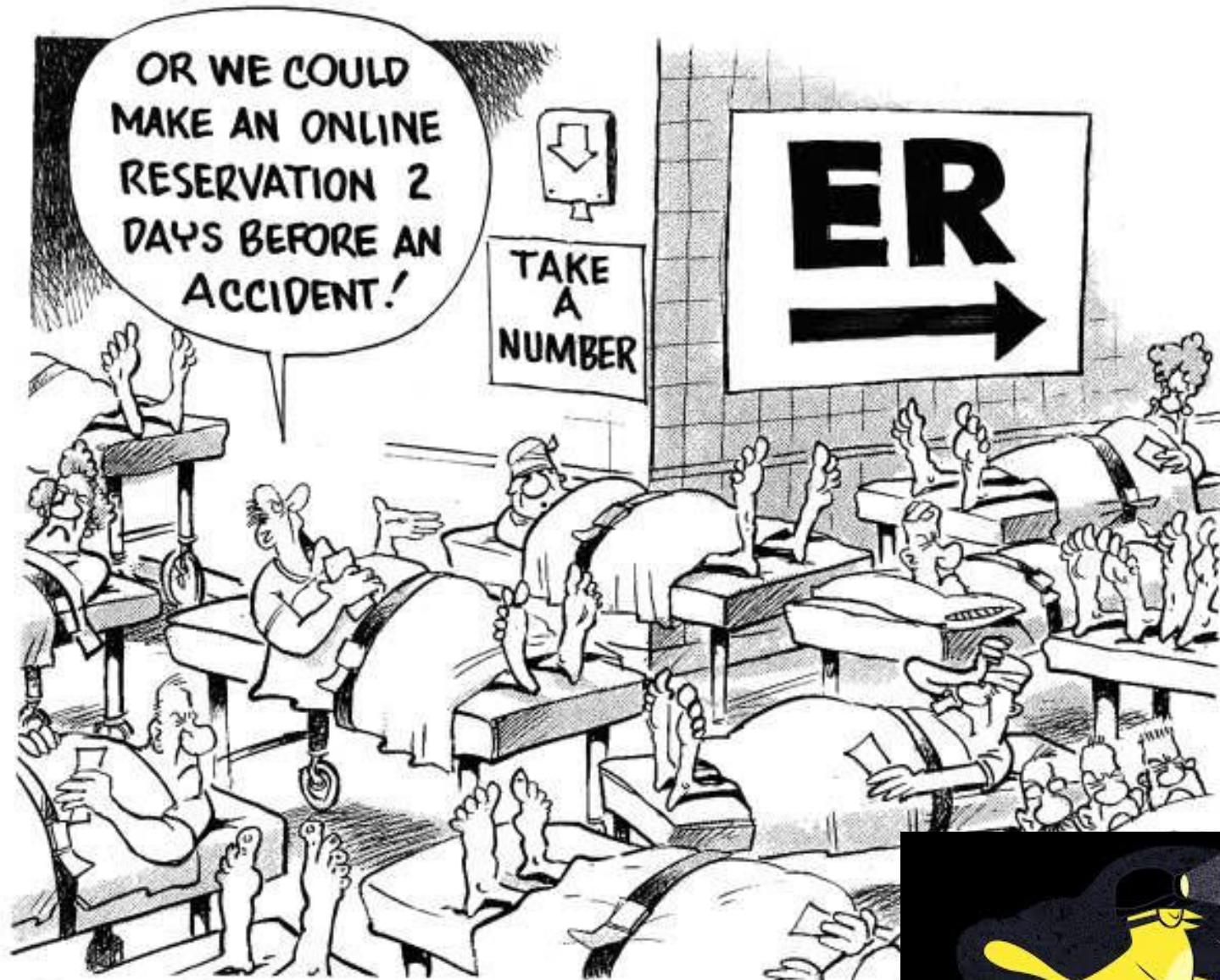
# The Epidemic of Chronic Disease



# Evolutionary Mismatch



<https://i2.wp.com/lifestylescience.eu/wp-content/uploads/2013/03/evolving-evolution14.jpg>



DAVE GRANLUND © [www.davegranolund.com](http://www.davegranolund.com)

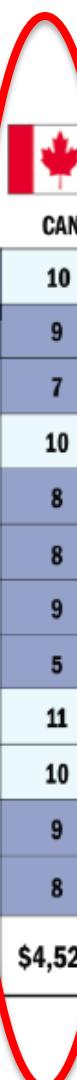
<http://www.politicalcartoons.com/cartoon/42a89a5e-c68e-4754-b798-d40a86e0cfa5.html>



# Disease Care System?



# Expensive AND Ineffective



	AUS	CAN	FRA	GER	NETH	NZ	NOR	SWE	SWIZ	UK	US
OVERALL RANKING (2013)	4	10	9	5	5	7	7	3	2	1	11
Quality Care	2	9	8	7	5	4	11	10	3	1	5
Effective Care	4	7	9	6	5	2	11	10	8	1	3
Safe Care	3	10	2	6	7	9	11	5	4	1	7
Coordinated Care	4	8	9	10	5	2	7	11	3	1	6
Patient-Centered Care	5	8	10	7	3	6	11	9	2	1	4
Access	8	9	11	2	4	7	6	4	2	1	9
Cost-Related Problem	9	5	10	4	8	6	3	1	7	1	11
Timeliness of Care	6	11	10	4	2	7	8	9	1	3	5
Efficiency	4	10	8	9	7	3	4	2	6	1	11
Equity	5	9	7	4	8	10	6	1	2	2	11
Healthy Lives	4	8	1	7	5	9	6	2	3	10	11
Health Expenditures/Capita, 2011**	\$3,800	\$4,522	\$4,118	\$4,495	\$5,099	\$3,182	\$5,669	\$3,925	\$5,643	\$3,405	\$8,508

The Commonwealth Fund, 2014

Acute care specialty

**Acute Care**

Primary care

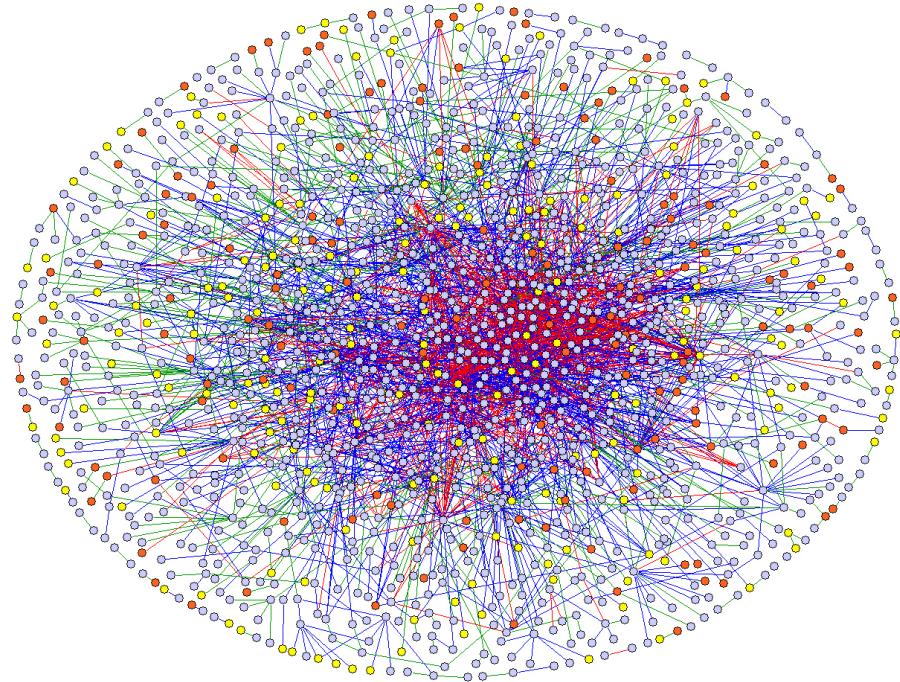
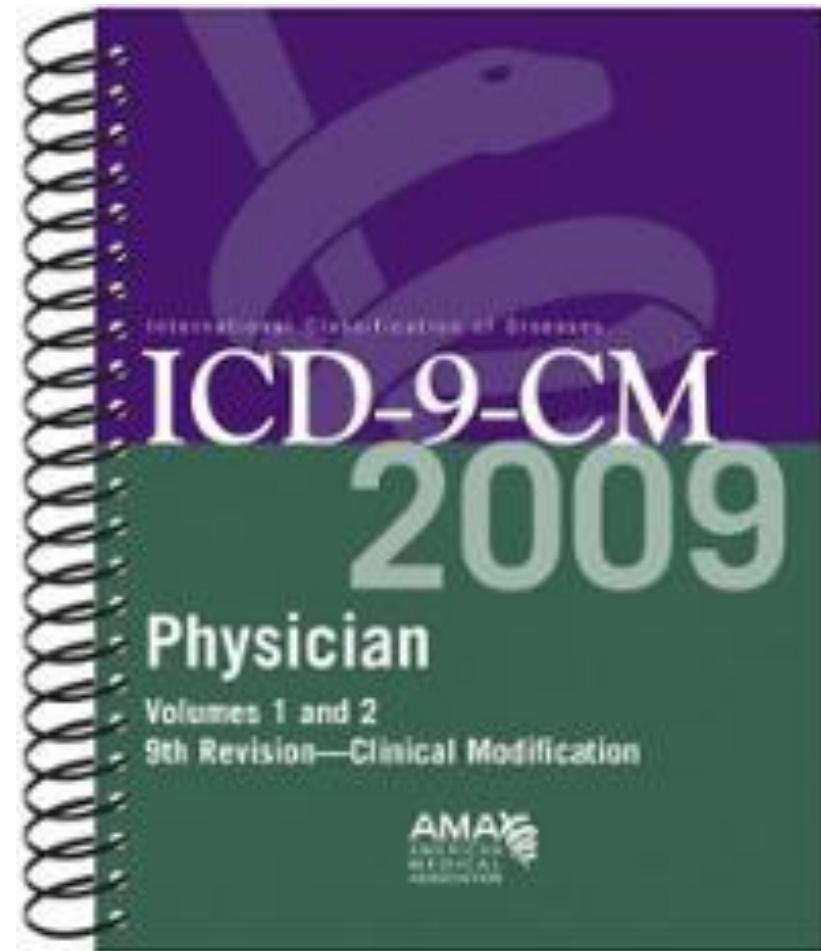
**Prevention**



-iology  
silos

Medicine organized by organ disease

# Do we have the right map?





# Systems biology and the future of medicine

Joseph Loscalzo<sup>1\*</sup> and Albert-Laszlo Barabasi<sup>1,2</sup>

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Volume 3, November/December 2011

## Outdated approach to defining Human Disease:

- Disease is defined by late manifestations in a dysfunctional organ system.
- Conventional disease paradigms generally neglect underlying pathobiological mechanisms.
- Conventional definitions of disease are excessively inclusive of the range of pathophenotypes.
- Disease is rarely (if ever) a simple consequence of an abnormality in a single gene product



CONNECT  
HEALTH

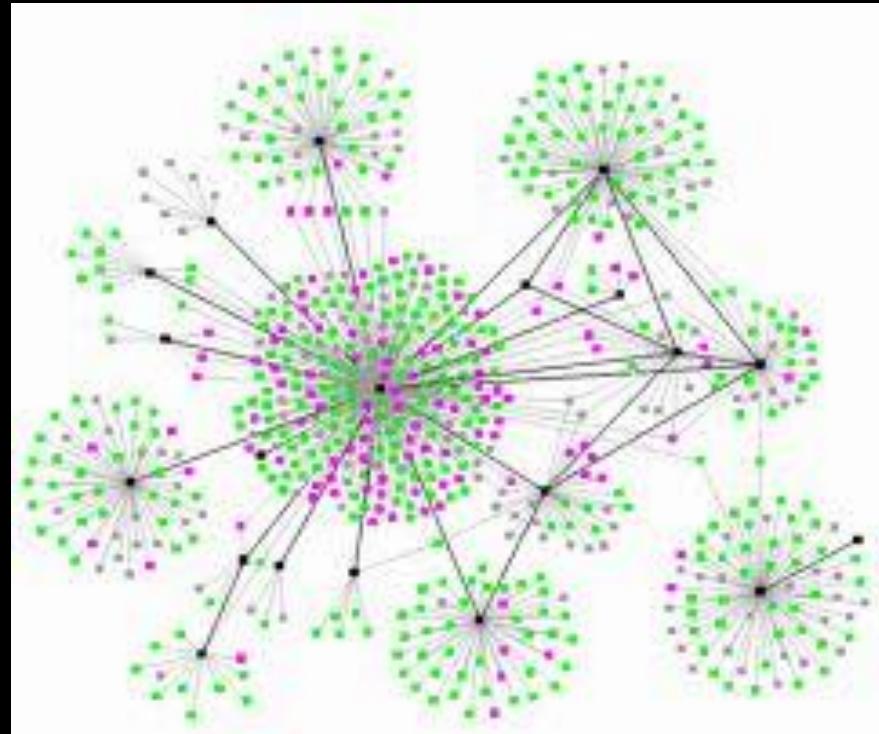
# Future of Medicine

“a move from a field of simple associations rooted in semi-empiric reductionism in search of a ‘cure’ for each disease to one that recognizes **the power of molecular networks** and systems upon which human biology is based.”

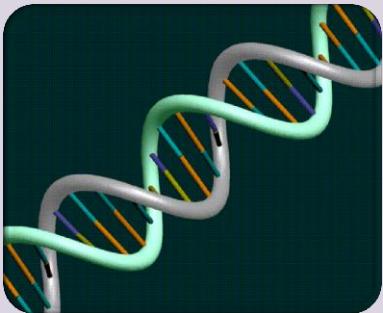
- Loscalzo J, Barabási AL. Systems biology and the future of medicine. Wiley Interdiscip Rev Syst Biol Med.2011;3(6):619-627.

“Biologic forms and functions are not simply determined by a genetic blueprint but are *emergent* properties of the entire epigenetic network.”

Fritjof Capra: The Hidden Connection



# The New Medicine – 4 P's



## Predictive

using  
genomics to  
determine the  
probability of  
a disease

## Preventive

knowing your  
individual risk  
profile  
motivates you  
to make  
changes

## Personalized

**targeted**  
and specific  
interventions  
and treatment

## Participatory

Empowered  
engagement in  
personal  
choices

4P

Medicine:<https://www.systemsbiology.org/research/p4-medicine/>

# Medicine for the average will be over!

$N = 10,000$

To

$N = 1$

Image:

[http://news.mit.edu/sites/mit.edu.newsoffice/files/images/2012/20120208160239-1\\_0.jpg](http://news.mit.edu/sites/mit.edu.newsoffice/files/images/2012/20120208160239-1_0.jpg)

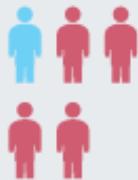


# Time for one-person trials

## IMPRECISION MEDICINE

For every person they 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



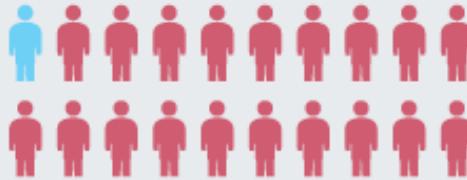
**2. NEXIUM** (esomeprazole)  
Heartburn



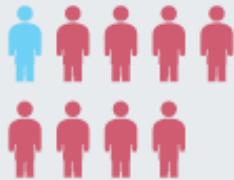
**3. HUMIRA** (adalimumab)  
Arthritis



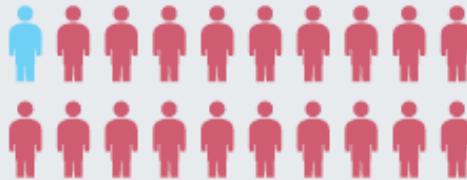
**4. CRESTOR** (rosuvastatin)  
High cholesterol



**5. CYMBALTA** (duloxetine)  
Depression



**6. ADVAIR DISKUS** (fluticasone propionate)  
Asthma



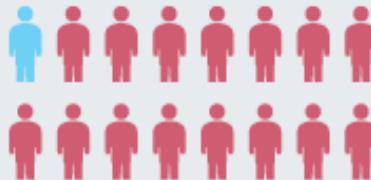
**7. ENBREL** (etanercept)  
Psoriasis



**8. REMICADE** (infliximab)  
Crohn's disease



**9. COPAXONE** (glatiramer acetate)  
Multiple sclerosis



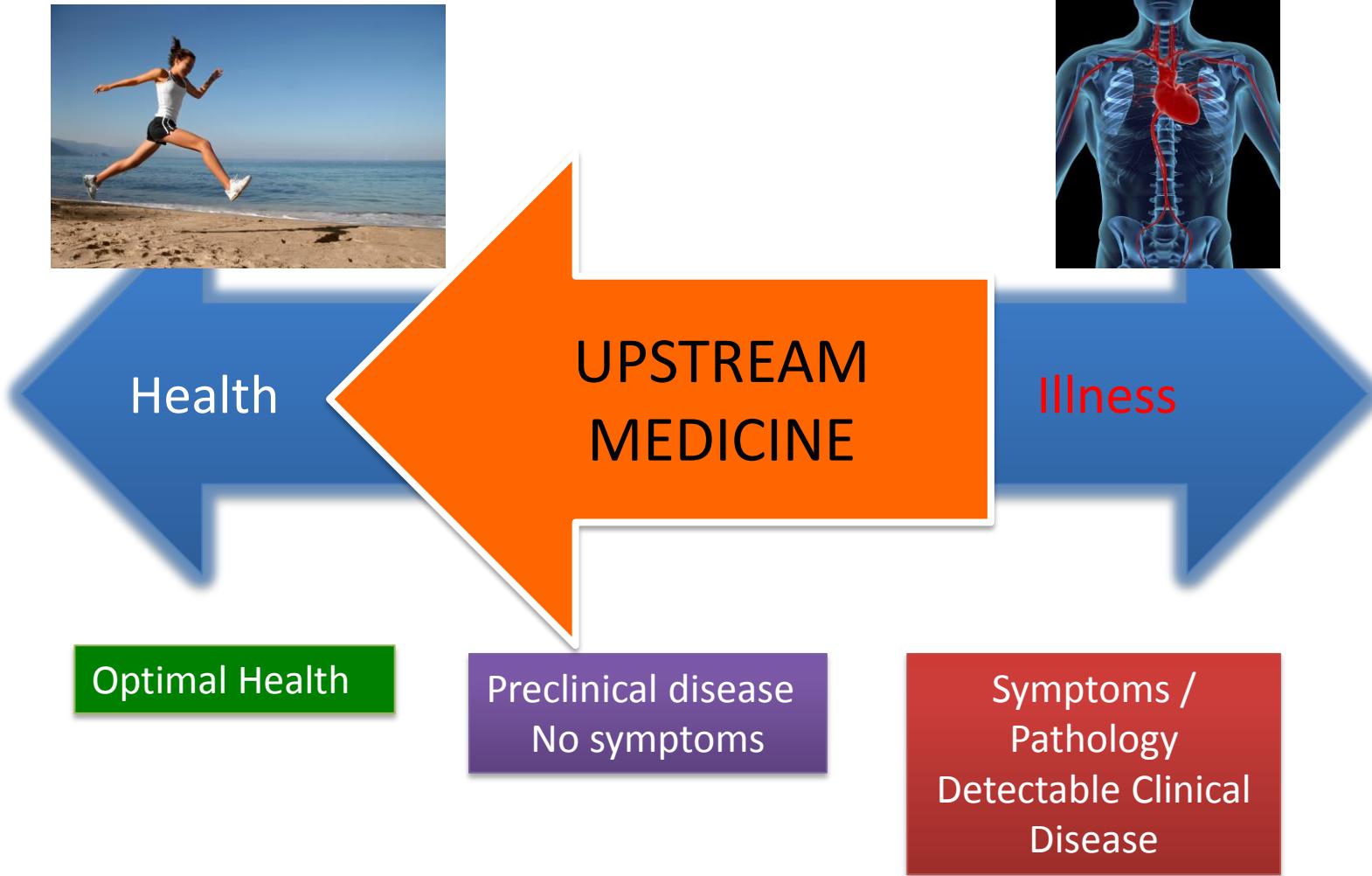
**10. NEULASTA** (pegfilgrastim)  
Neutropenia



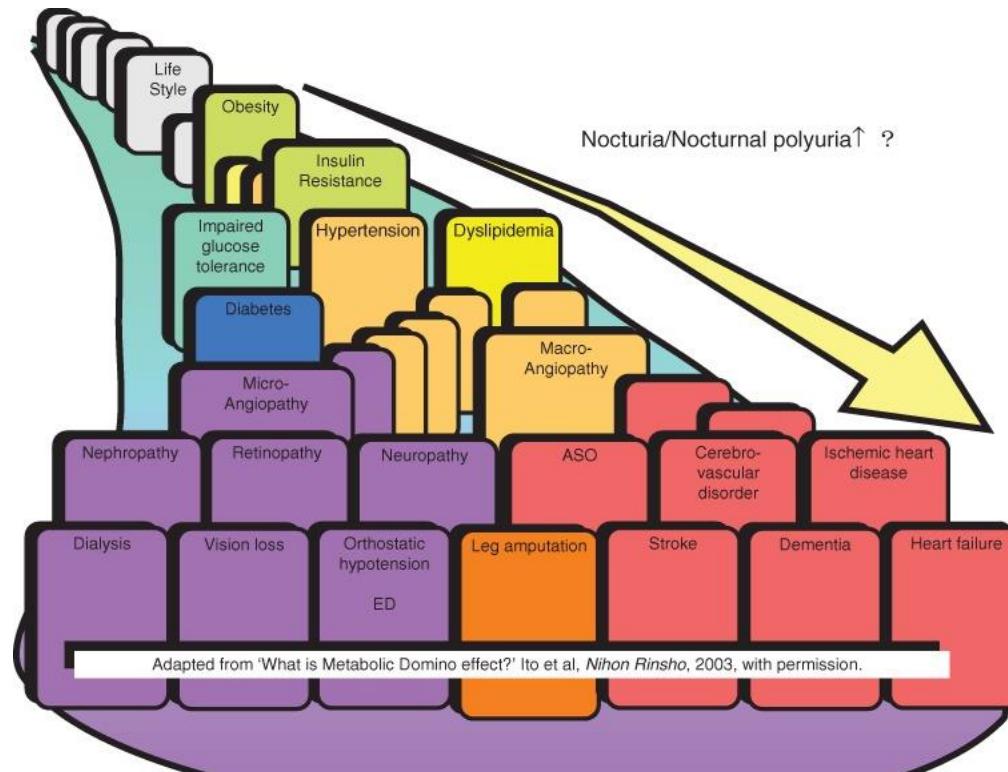
# Imprecision Medicine

Schork, Nicholas,  
Time for one-  
person trials.  
Nature, Vol 520.  
April 2015

# Health Continuum



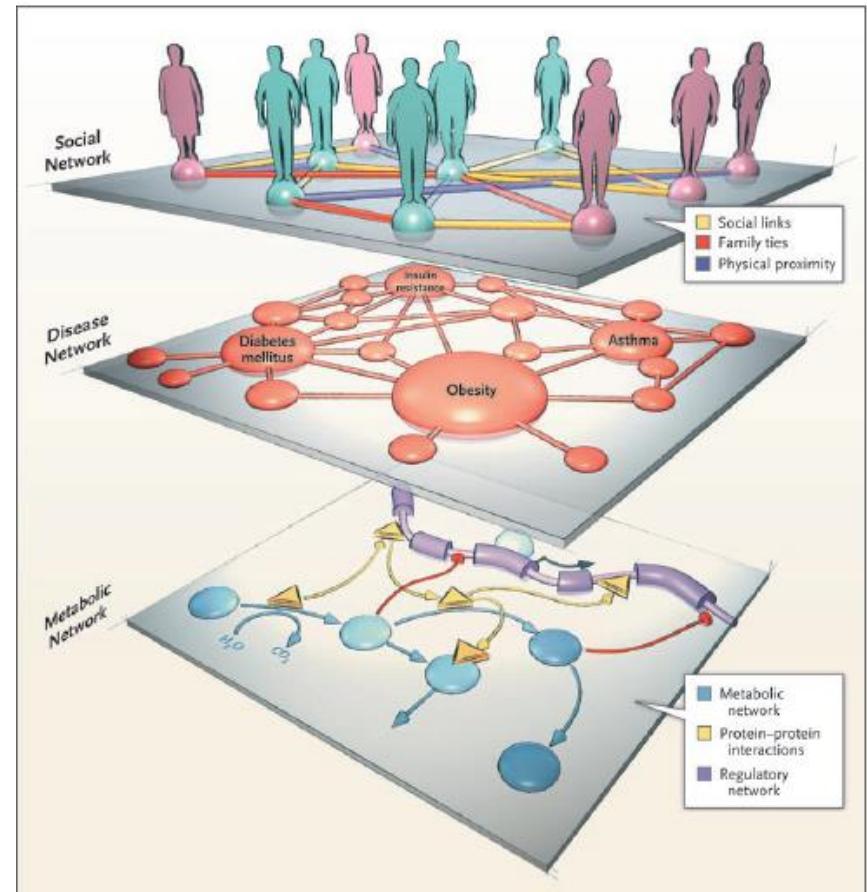
# Flow of events leading to chronic disease



Treating upstream rather than just downstream effects

# Network Medicine

- Although we often treat diseases separately, **most human diseases are not independent of each other.**



Barabasi, NEJM July 26, 2007

## REVIEW ARTICLE

MECHA  
Inflammation  
and Coronary Artery Disease

Göran K.

**R**ECENT RESEARCH HAS SHED LIGHT ON THE CAUSES OF CORONARY ARTERY DISEASE (CAD). Immune cells dominate early lesions and accelerate progression of the lesion in all major coronary syndromes. This review highlights the hypothesis of atherosclerotic CAD. It will review the evidence that CAD, like other diseases, is an inflammatory disease that requires metabolic risk factors to initiate, progress, and cause symptoms.

A decade ago, the treatment of hypertension was aimed at eliminating CAD by the end of the century. This hypothesis has needed revision. Cardiovascular diseases account for death globally within the next 15 years, particularly in developing countries and eastern Europe, and are the leading cause of death in the Western world.<sup>1</sup> Cardiovascular diseases are the most common cause of death in North America and are the second most common cause of death worldwide. We must therefore reassess our knowledge of cardiovascular disease and consider new strategies for prediction, prevention, and treatment.

## MAIN FEATURES OF ATHEROSCLEROTIC LESIONS

# Medicine by cause + mechanism

VS

# Symptoms + Diagnostic Label

Center for  
of Medi-  
l, Stock-  
r. Hans-  
edicine,  
ital, SE-  
goran.

very

Göran K. Hansson, M.D., Ph.D.  
N Engl J Med 2005; 352:1685-1695 [April 21, 2005](#)  
[DOI: 10.1056/NEJMra043430](https://doi.org/10.1056/NEJMra043430)

Doctors are men who prescribe medicines of which they know little, to cure diseases of which they know less, in human beings of whom they know nothing.

Voltaire

# High-Definition Medicine

Ali Torkamani,<sup>1,2,5,\*</sup> Kristian G. Andersen,<sup>1,3</sup> Steven R. Steinhubl,<sup>1,4</sup> and Eric J. Topol, MD<sup>1,4</sup>

<sup>1</sup>The Scripps Translational Science Institute, La Jolla, CA 92037, USA

<sup>2</sup>Department of Integrative Structural and Computational Biology, The Scripps Research Institute, La Jolla, CA 92037, USA

<sup>3</sup>Department of Immunology and Microbial Science, The Scripps Research Institute, La Jolla, CA 92037, USA

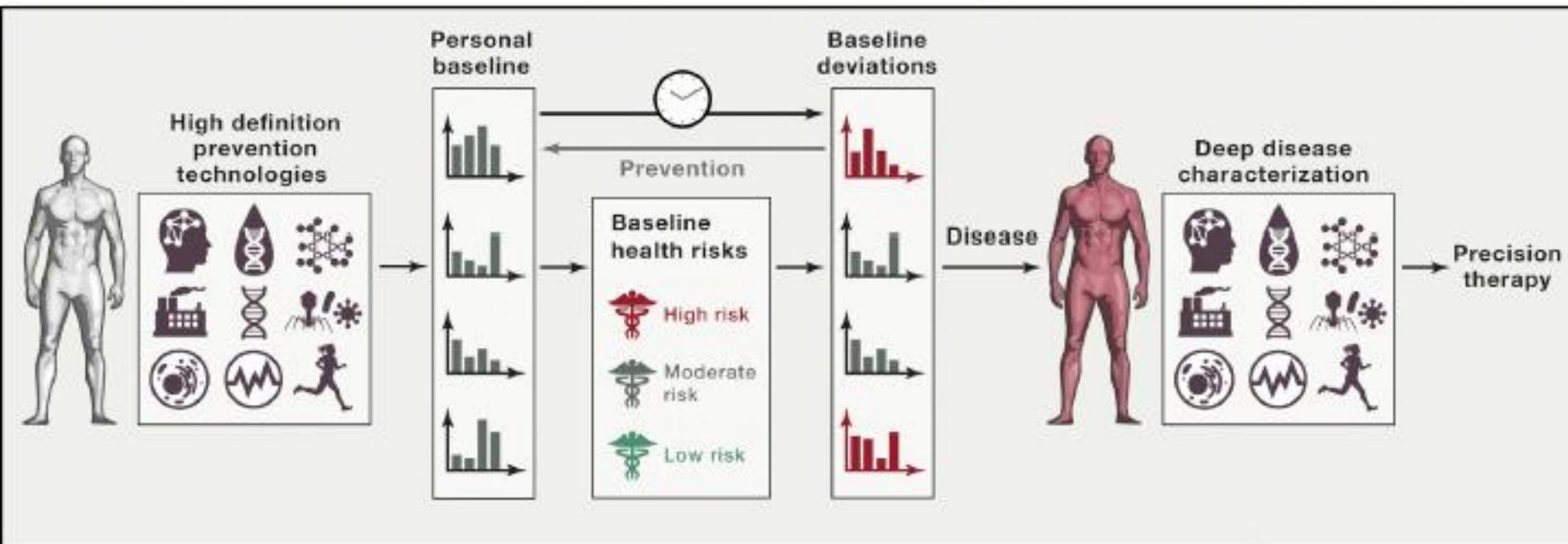
<sup>4</sup>Department of Molecular Medicine, The Scripps Research Institute, La Jolla, CA 92037, USA

<sup>5</sup>Lead Contact

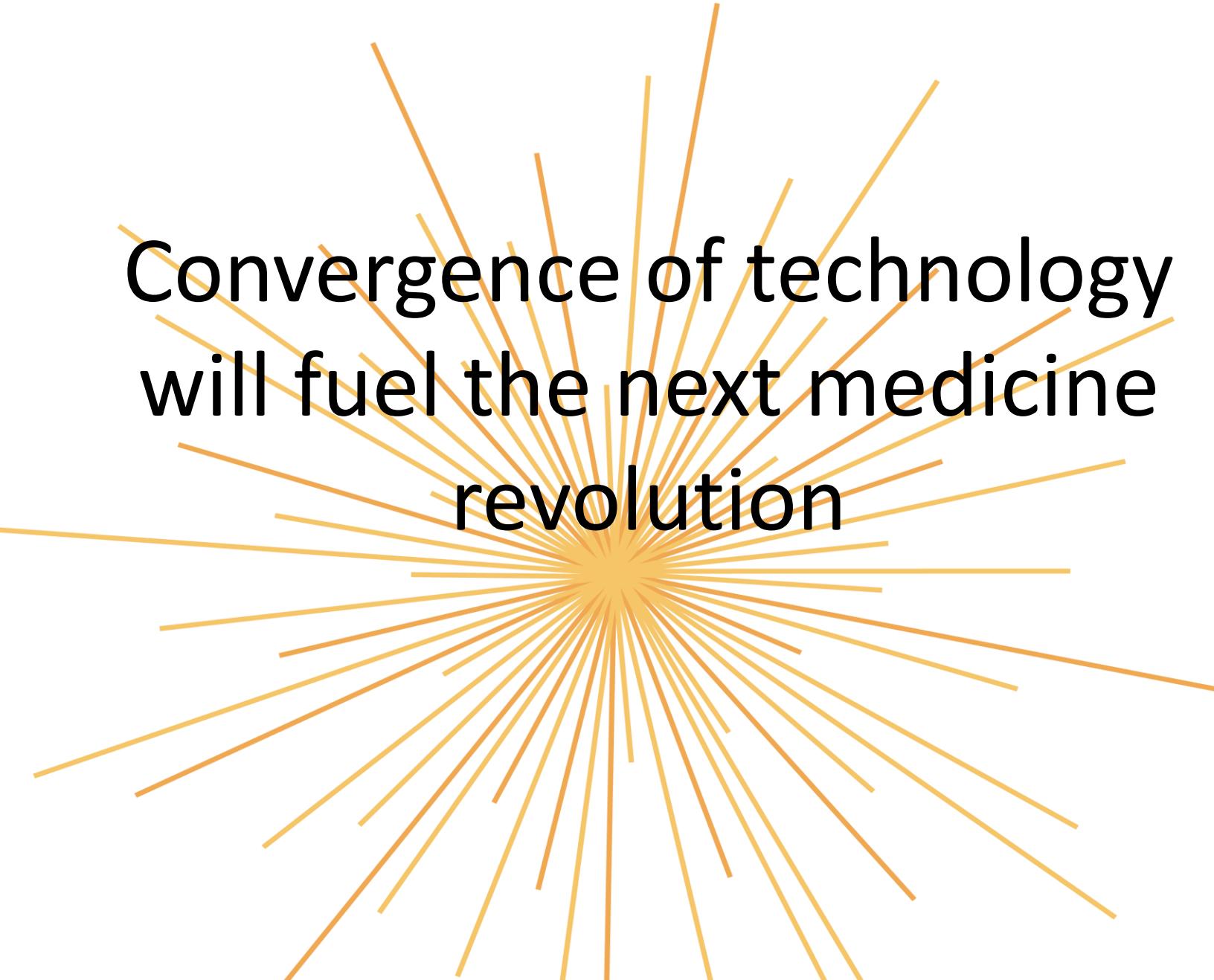
\*Correspondence: [atorkama@scripps.edu](mailto:atorkama@scripps.edu)

<http://dx.doi.org/10.1016/j.cell.2017.08.007>

The foundation for a new era of data-driven medicine has been set by recent technological advances that enable the assessment and management of human health at an unprecedented level of resolution—what we refer to as high-definition medicine. Our ability to assess human health in high definition is enabled, in part, by advances in DNA sequencing, physiological and environmental monitoring, advanced imaging, and behavioral tracking. Our ability to understand and act upon these observations at equally high precision is driven by advances in genome editing, cellular reprogramming, tissue engineering, and information technologies, especially artificial intelligence. In this review, we will examine the core disciplines that enable high-definition medicine and project how these technologies will alter the future of medicine.



High Definition Medicine



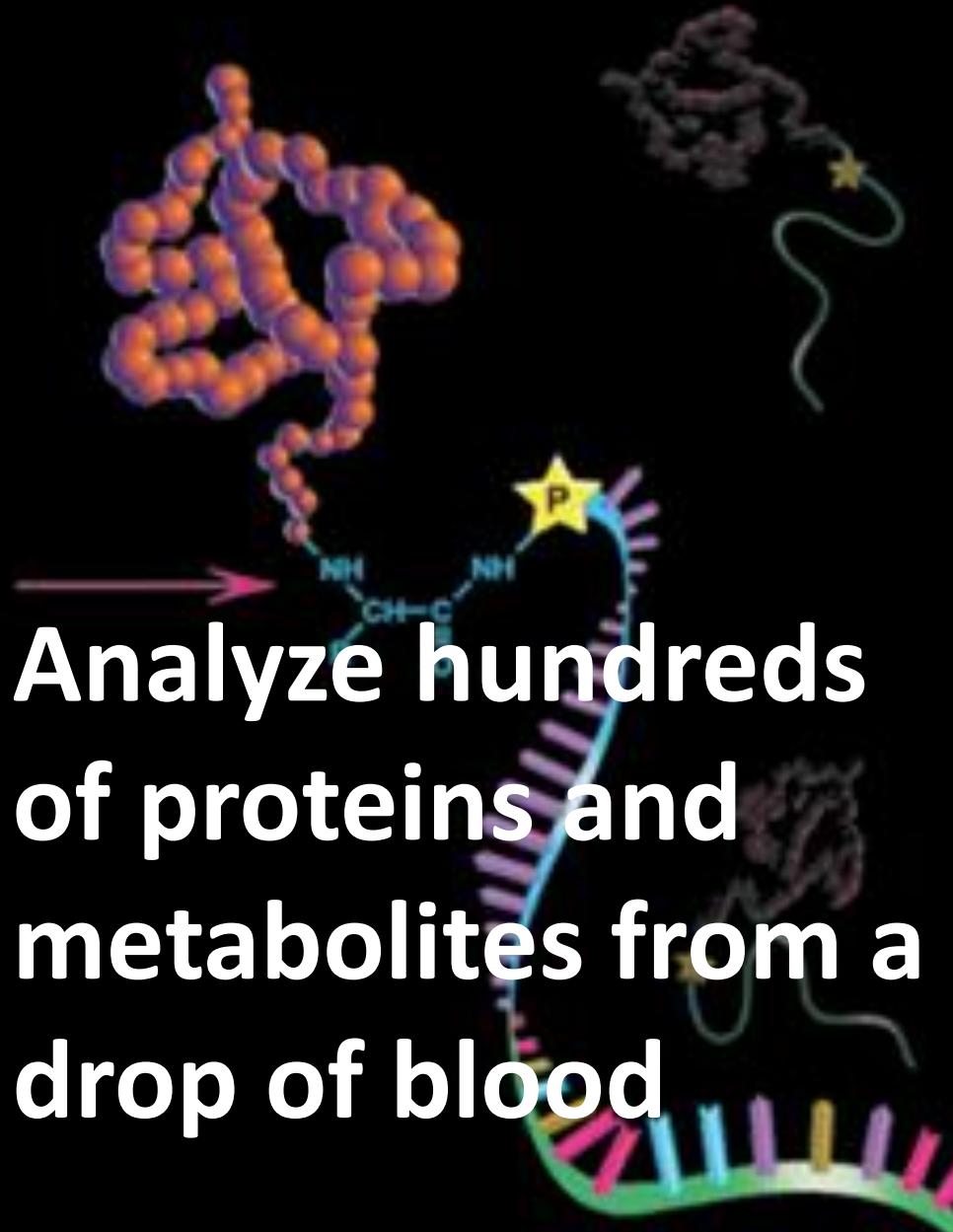
**Convergence of technology  
will fuel the next medicine  
revolution**



We can  
sequence  
your  
genome in  
a couple of  
hours...

Image:

<https://www.nhlbi.nih.gov/research/resources/nhlbi-precision-medicine-initiative/topmed/wgs>





We can describe the  
ecology of bacteria  
from your poop...



Computing power and data storage continues to increase...

[http://bits.blogs.nytimes.com/2013/01/08/  
amazons-known-unknowns/?\\_r=0](http://bits.blogs.nytimes.com/2013/01/08/amazons-known-unknowns/?_r=0)

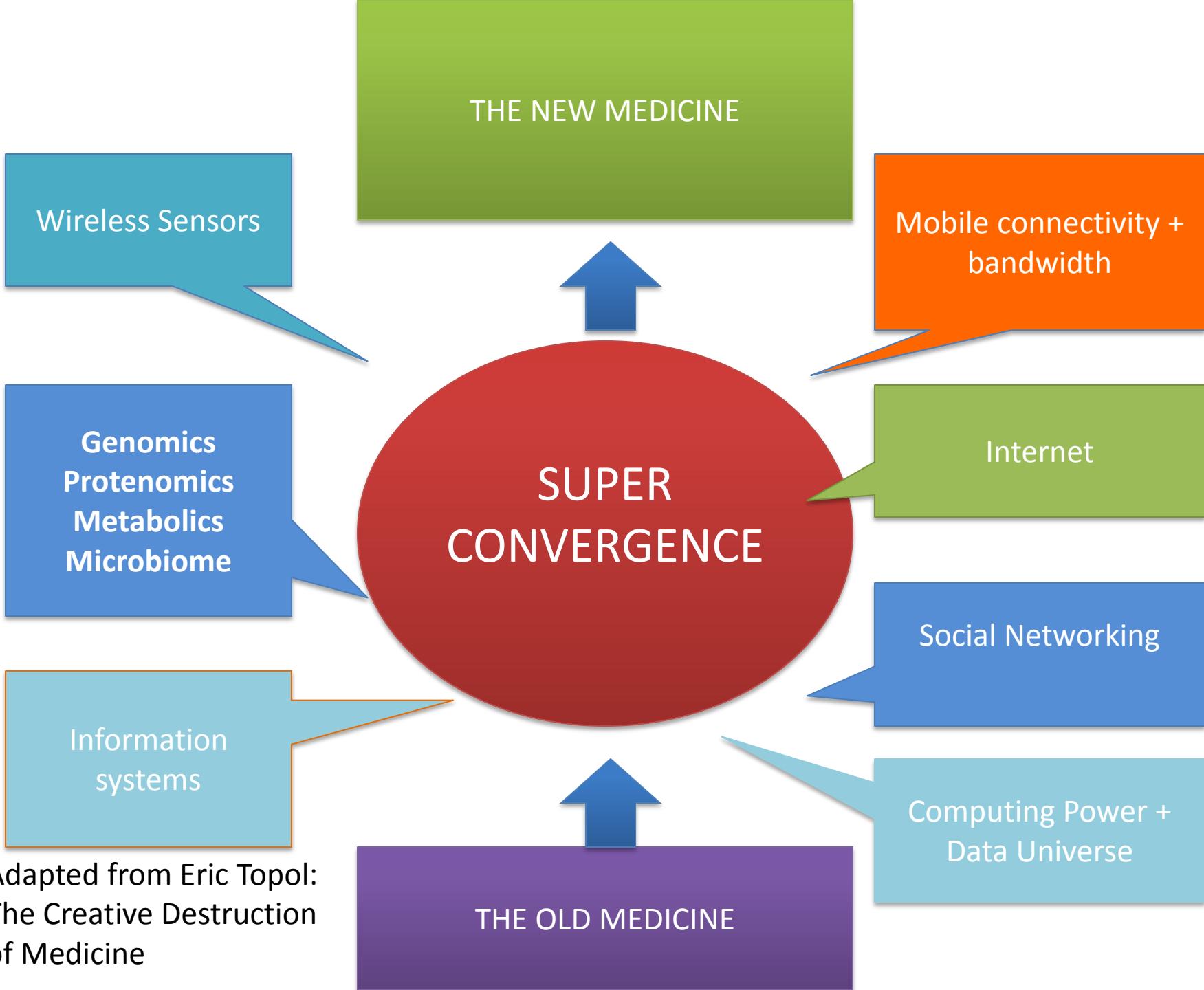
A dynamic, low-angle photograph of a male runner in motion, captured in a dark environment. He is wearing a dark athletic outfit. Several bright orange glowing cubes are attached to his body at various points: one on each arm, one on each leg, and two on his torso. Red lines connect these glowing points, suggesting a tracking or monitoring system. The runner's arms are extended forward, and his legs are in mid-stride. The background is dark and out of focus.

# Wearable technology that will track everything we do...

Image source: <http://nocamels.com/wp-content/uploads/2014/07/Ray-coverImage1-runner.jpg>



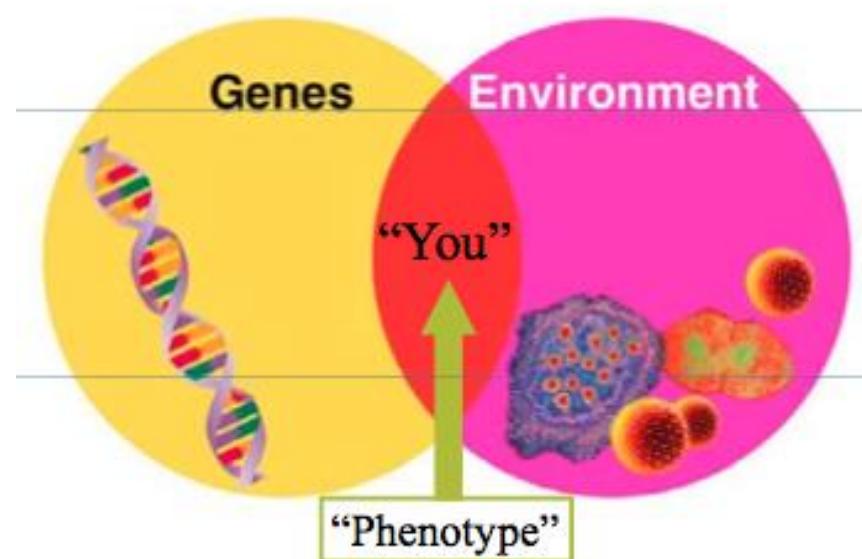
Internet, social media will allow us to connect and share our data...



# Epigenetics

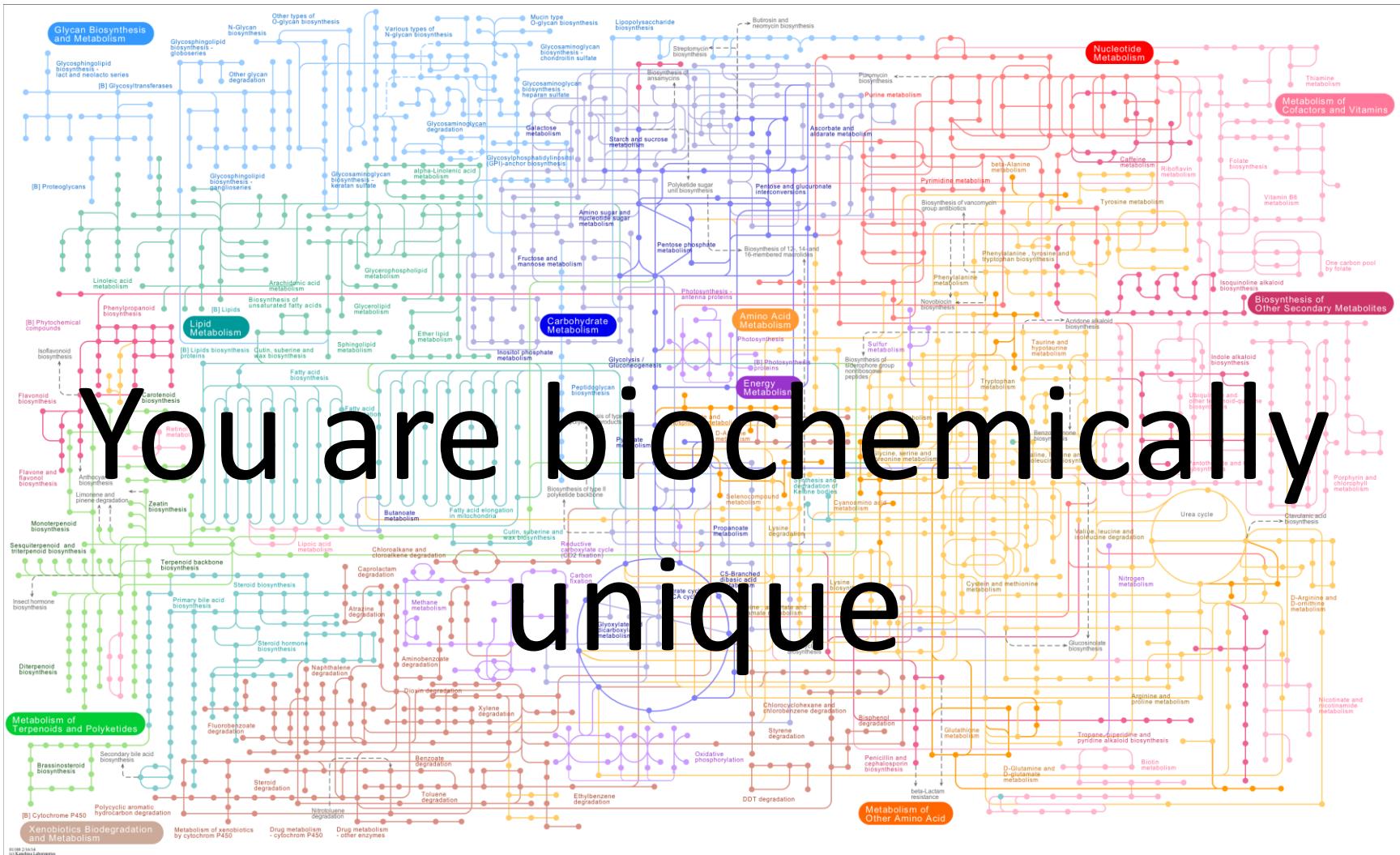
“our health and disease patterns...are not hardwired deterministically by our genes, but rather a consequence of the interaction of genetic uniqueness with environmental factors.”

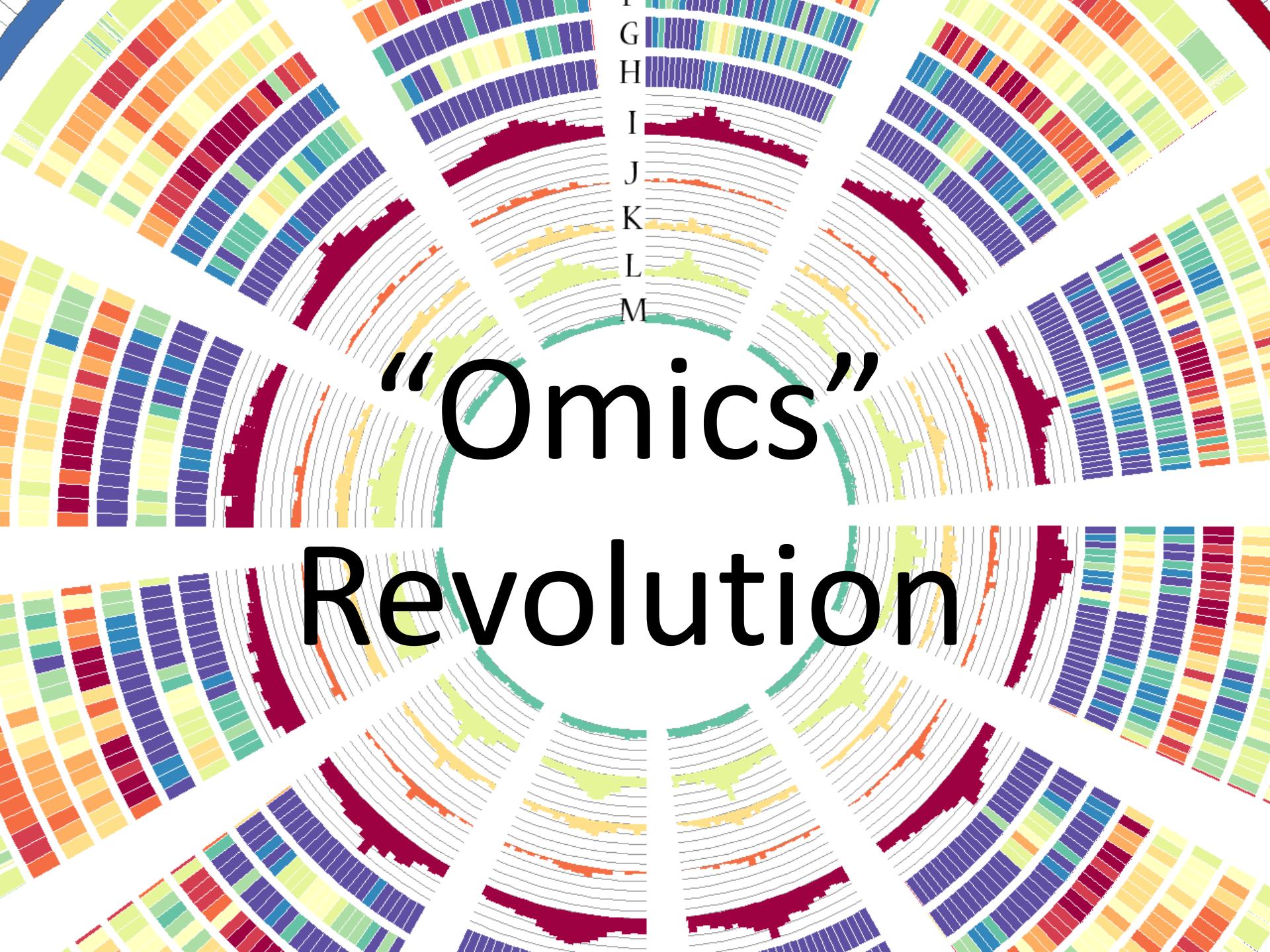
—Jeffrey Bland, PhD



CONNECT  
HEALTH

The image is a dense network diagram of biological pathways. It features a central purple circle labeled 'Central carbon metabolism' with arrows pointing to various metabolic routes. These routes include 'Fatty acid metabolism' (blue), 'Carbohydrate metabolism' (green), 'Amino acid metabolism' (orange), 'Nucleotide metabolism' (yellow), and 'Secondary metabolism' (pink). Specific pathways highlighted include 'Terpenoid backbone biosynthesis', 'Lipid metabolism', 'Chlorophyll and chlorophyllide degradation', 'Aromatic degradation', 'Methane metabolism', 'Aminobenzoate', 'Propanoate metabolism', 'Lysine degradation', 'Lysine biosynthesis', 'Cysteine and methionine metabolism', 'Glutathione biosynthesis', 'Nitrogen metabolism', 'Urea cycle', 'Cladoceran acid biosynthesis', 'D-Amino acid biosynthesis', and 'D-Arginine/D-Ornithine metabolism'. The diagram uses colored nodes and lines to represent different chemical species and their interactions.





# **“Omics” Revolution**

I  
G  
H  
I  
J  
K  
L  
M

# Molecular YOU...



**Proteomics**      **Transcriptomics**      **Genomics**      **Metabolomics**

Toxicogenomics      Archaeomics      Epigenomics  
Morphomics      Phosphoproteomics      Regulomics  
Kinomics      Alternatomics      Glycomics  
Behavioromics      Lipoproteomics      Secretomics  
Orfeomics      Lipidomics      Fluxomics  
Interactomics

“Care more particularly for  
the **individual** patient than  
for the special features of  
the disease.”

Sir William Osler



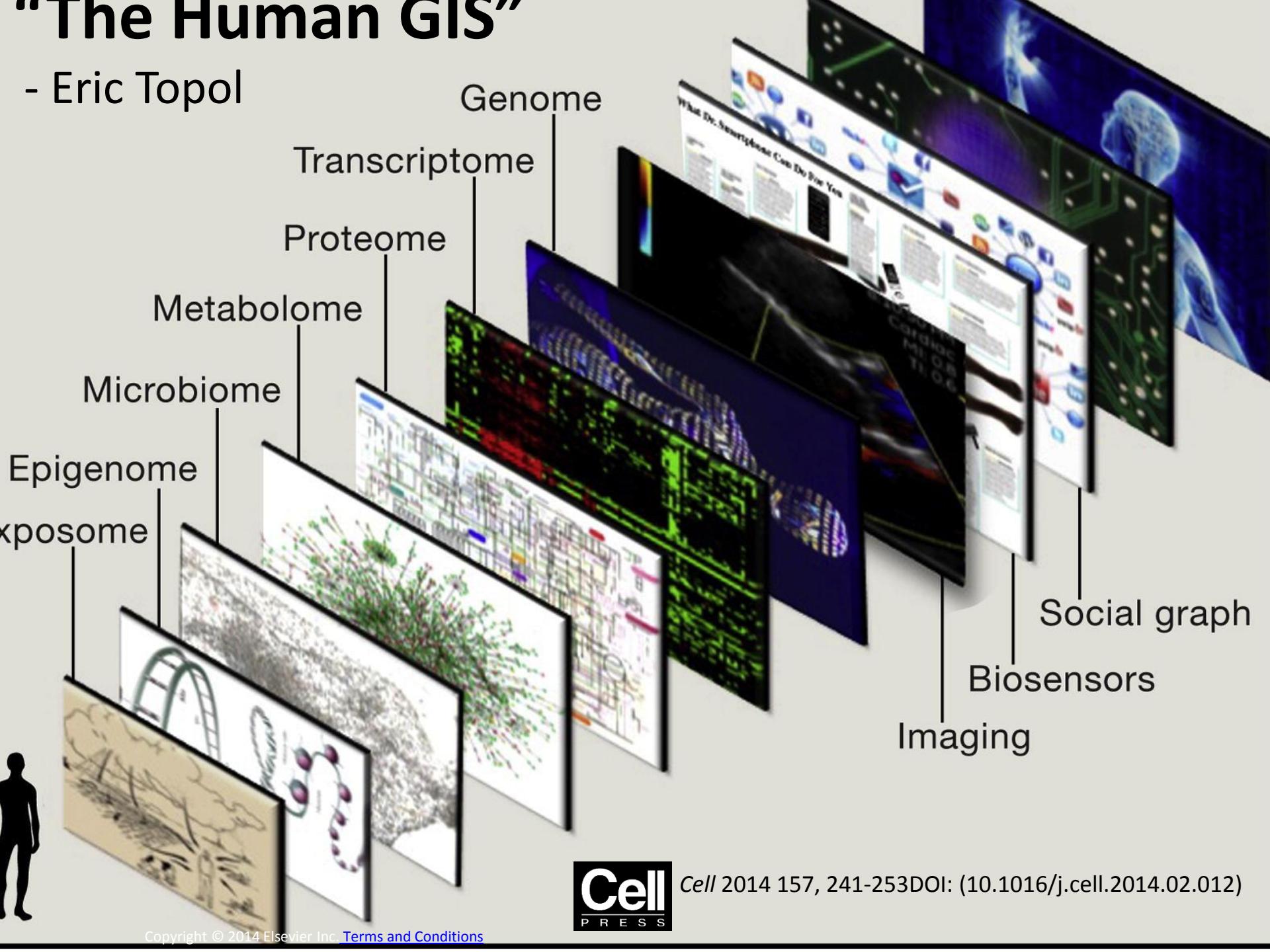
“Precision medicine is an emerging approach for disease treatment and prevention that takes into account **individual variability** in genes, environment and lifestyle for each person.”

NIH

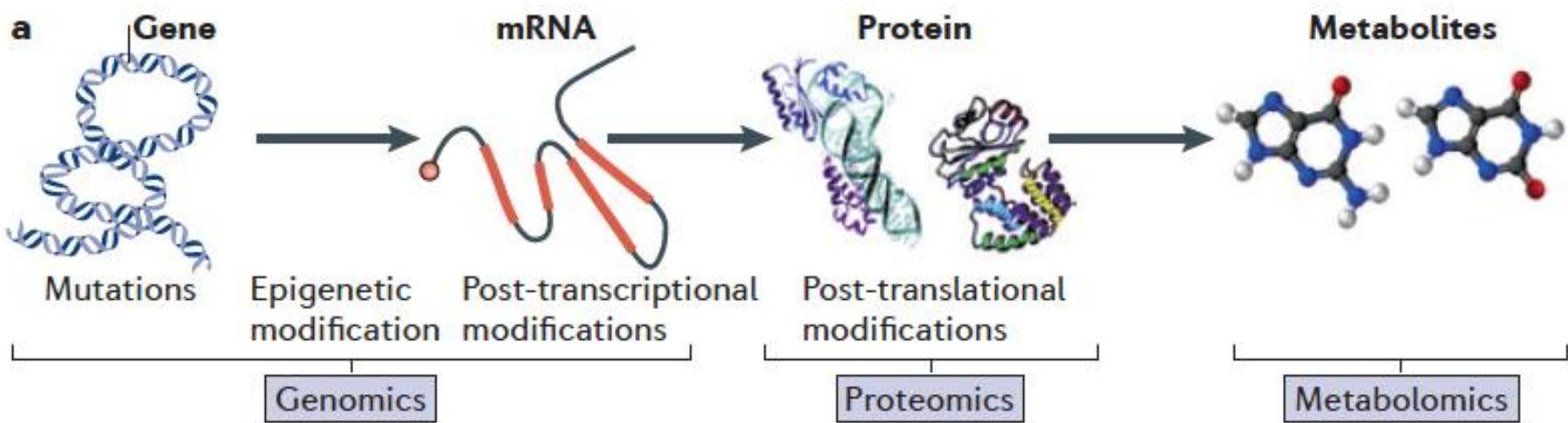
THE PRECISION MEDICINE INITIATIVE

# "The Human GIS"

- Eric Topol



# “Omics Cascade”



Patti G. et al. Nature Review Molecular Cell Biology 13, 263-269 (April 2012)

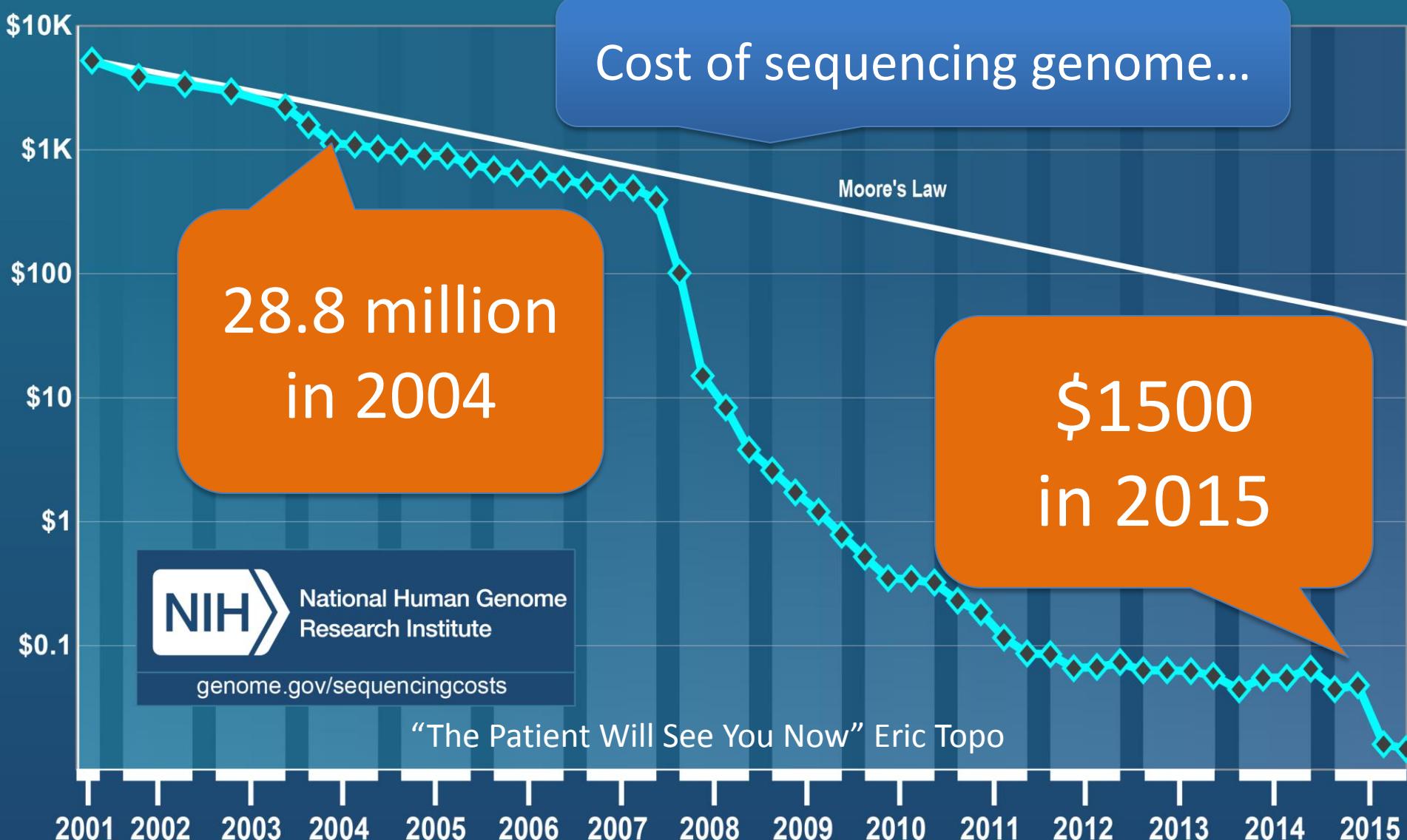
**Multiple evidence strands suggest that there may be as few as 19,000 human protein-coding genes.**

Ezkurdia I<sup>1</sup>, Juan D<sup>2</sup>, Rodriguez JM<sup>3</sup>, Frankish A<sup>4</sup>, Diekhans M<sup>5</sup>, Harrow J<sup>4</sup>, Vazquez J<sup>6</sup>, Valencia A<sup>7</sup>, Tress ML<sup>8</sup>.

DNA sequence of 6 billion A,C,T, G  
letters

98.5% of which does not code for  
genes

# *Cost per Raw Megabase of DNA Sequence*



# Genome sequencing Limitations

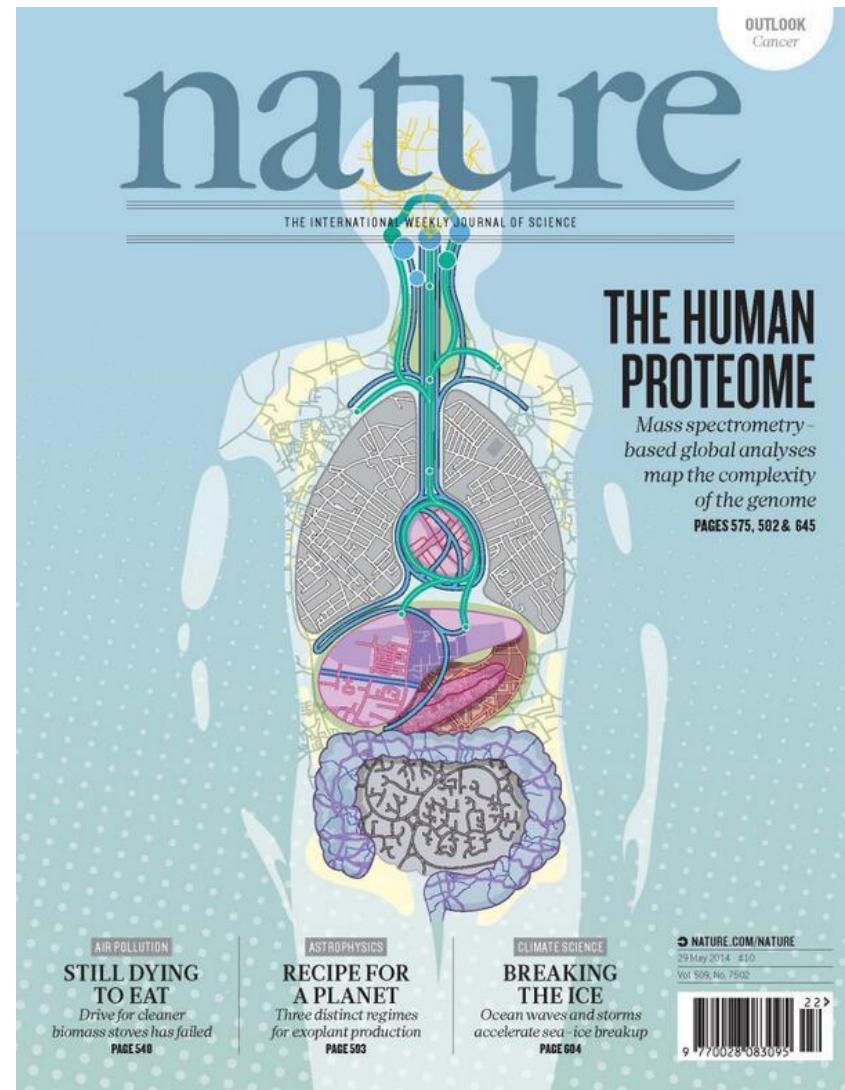
- We are all mosaics (our thirty seven trillion cells in our body do not have the same DNA.)
  - J. Lupski, “Genetics. Genome Mosaicism – One Human, Multiple Genomes.” Science 341 (2013):358-359
- Most variants will be of unknown significance (VUS)
- Does not look at all of the post translational modifications
- Exome – only 1.5% of entire DNA
- Most commercial tests only test for a portfolio of SNPs

Image: <http://2eof2j3oc7is20vt9q3g7tlo5xe.wpengine.netdna-cdn.com/wp-content/uploads/2013/10/genome-370x290.jpg>

# Proteomics

“Proteomic analysis refers to the systematic identification and quantification of the **complete complements of proteins** (proteome) of a biological system (cell, tissue, organ, biological fluid or organism) at a specific point in time”

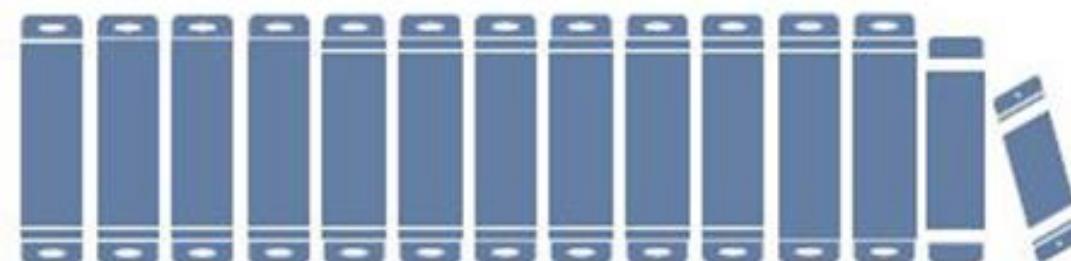
- [www.nature.com/subjects/proteomic-analysis](http://www.nature.com/subjects/proteomic-analysis)





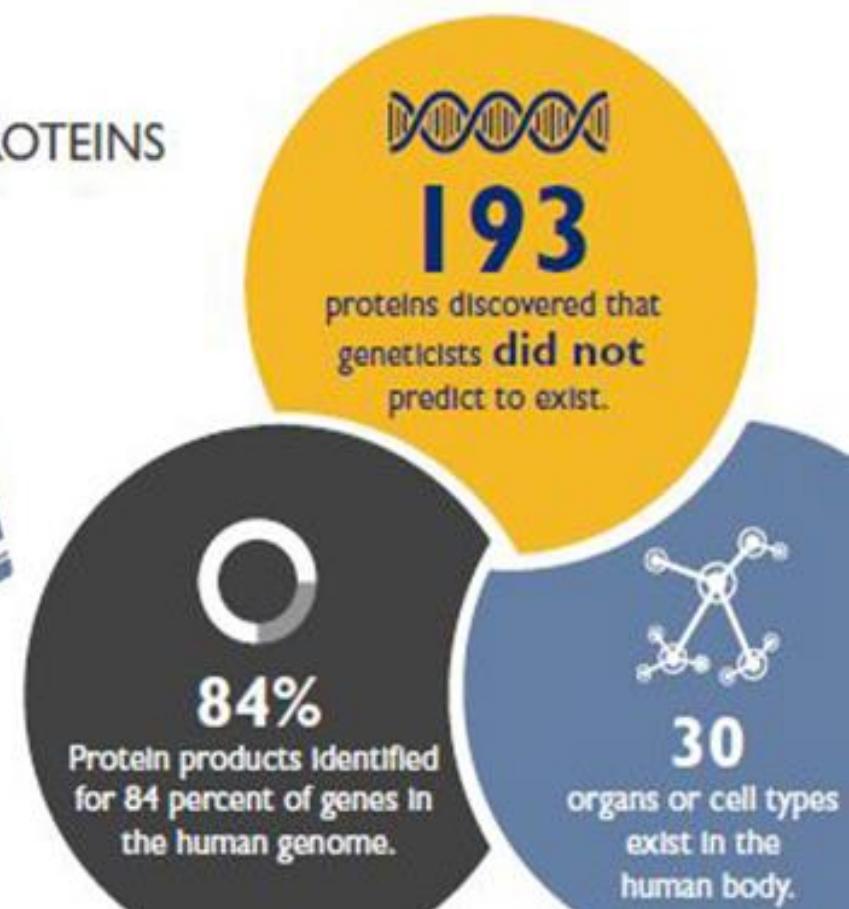
# HUMAN PROTEOME PROJECT

5 YEAR PROJECT TO CATALOG HUMAN PROTEINS



"You can think of the human body as a huge library where **each protein is a book**."

– Dr. Akhilesh Pandey

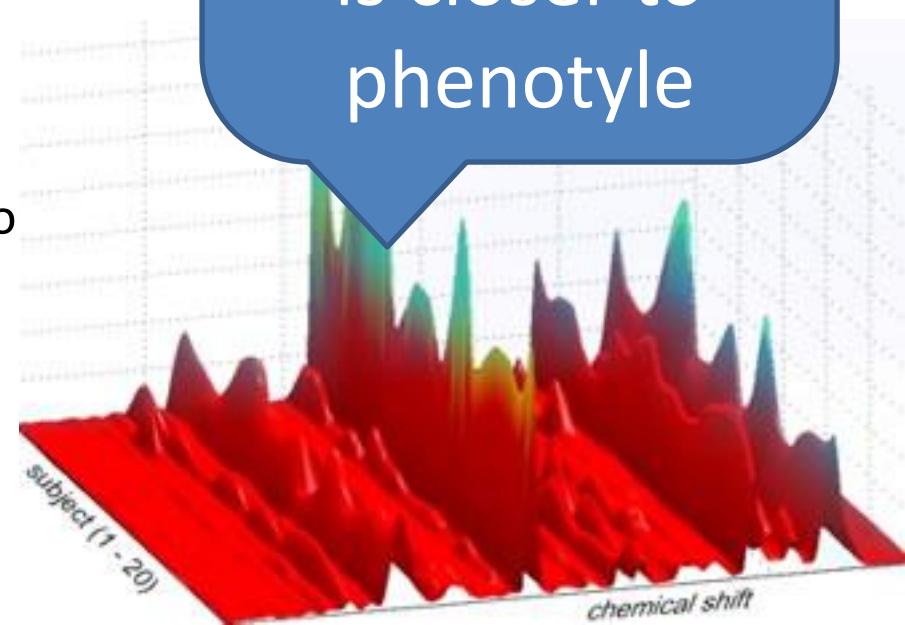


# Metabolomics

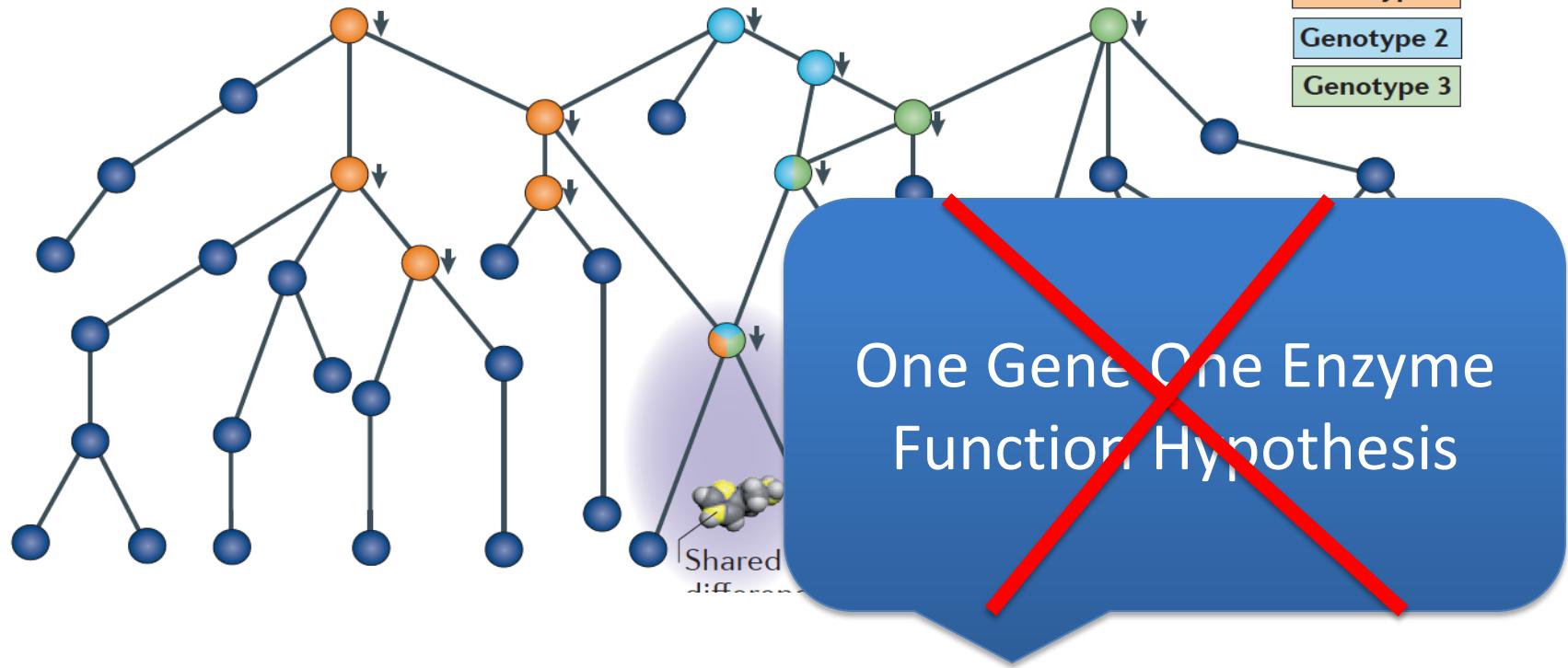
“Metabolites, the chemical entities that are transformed during metabolism, provides a **functional readout** of cellular biochemistry”

Direct signature of biochemical activity which is closer to phenotype

Patti G. et al. Nature Review Molecular Cell Bio  
269 (April 2012)



**b Theoretical metabolic pathway**



One gene can effect a multitude  
of different metabolic  
pathways...



We are mostly made  
of microbes!

There 10 x more  
bacterial cells than  
human cells in our  
bodies...

A dense field of various bacterial and viral particles against a teal background. The particles are rendered in shades of green, yellow, and orange, showing different morphologies such as spheres, rods, and viruses with spikes.

**Bacterial species contain  
more than 100 x more  
genes as our own human  
genome**

Creative Destruction of Medicine – Eric Topol

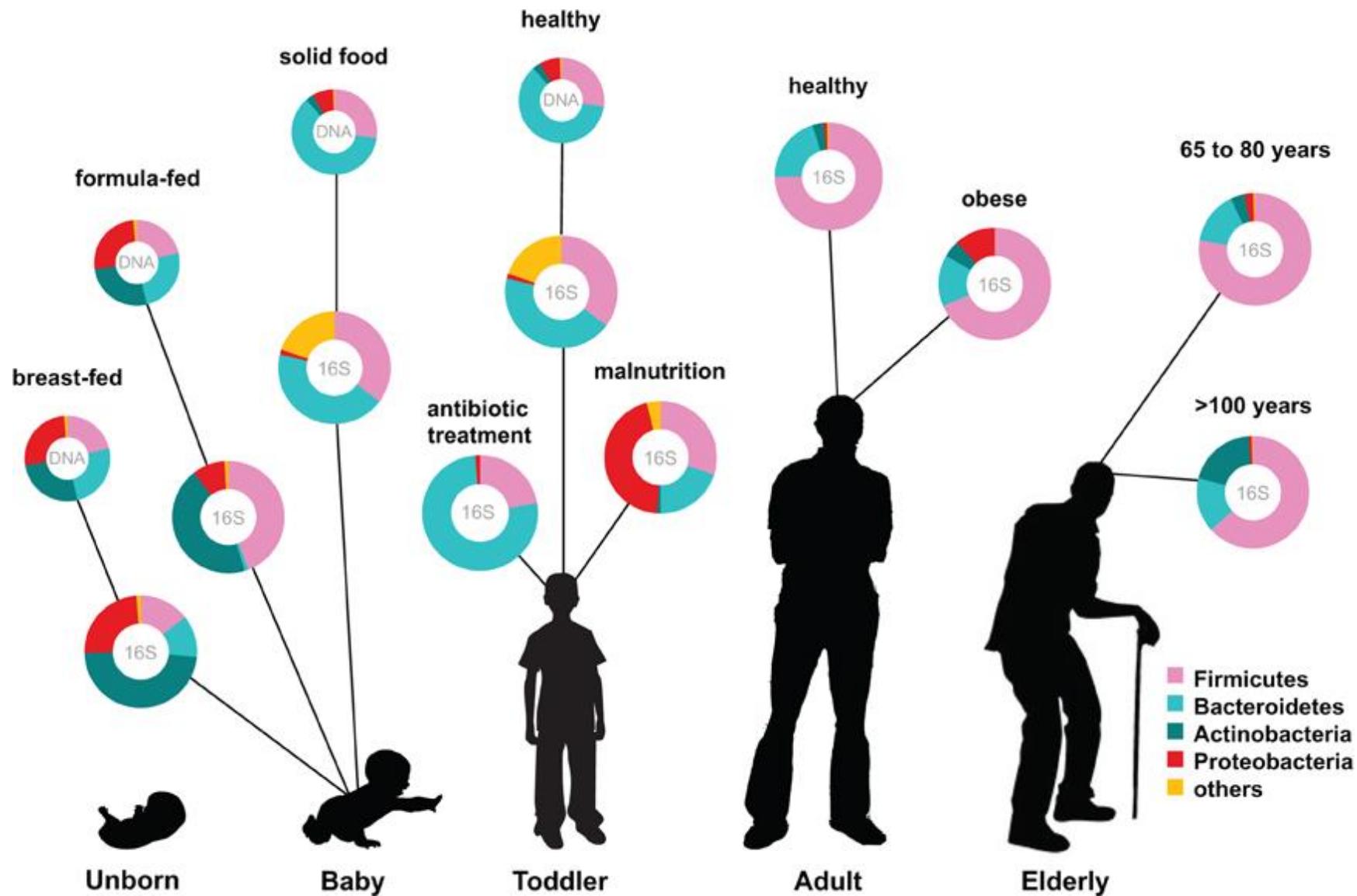


We are a  
walking  
“super-  
organism”

# Microbiome

## Your Inner Ecosystem.... The Ultimate Social Network

Scientific American  
Jennifer Ackerman Jun 12, 2012



Ottman N et al; The function of our microbiota: who is out there and what do they do? Front. Cell. Inf. Microbio 2:104



# Getting to know your gut microbiota

A huge quantity (hundreds of trillions) of bacteria and other microorganisms inhabit your intestines fulfilling key functions for your health and wellbeing

- Gut microbiota's weight can reach up to

1 to 2 Kg

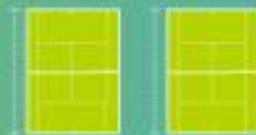


- 95% of our bacteria located in the **gastrointestinal (GI) tract**



- The GI tract surface is as big as 2 tennis courts

400 m<sup>2</sup>



- Bacteria are 10 to 50 times smaller than human cells



- In our body, microbes outnumber human cells by

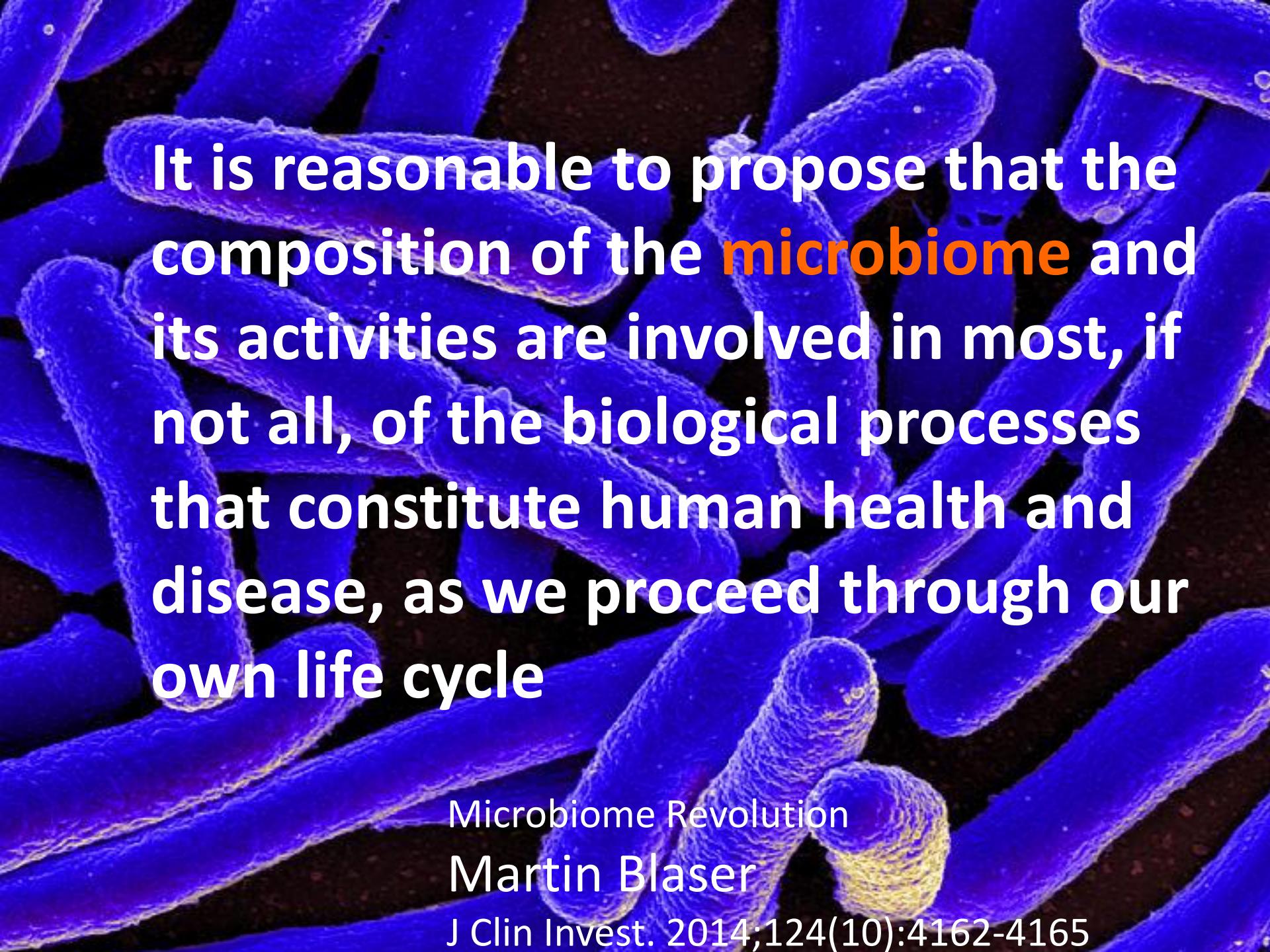
10:1



- Laid end to end, our body's bacteria would circle the Earth

2,5 times





It is reasonable to propose that the composition of the **microbiome** and its activities are involved in most, if not all, of the biological processes that constitute human health and disease, as we proceed through our own life cycle

Microbiome Revolution

Martin Blaser

J Clin Invest. 2014;124(10):4162-4165

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## The gut microbiota shapes intestinal immune responses during health and disease

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*June L. Round and Sarkis K. Mazmanian*

It is possible that alterations in the development or composition of the microbiota (known as dysbiosis) disturb the partnership between the microbiota and the human immune system, ultimately leading to altered immune responses that may underlie various human inflammatory disorders.

# Diseases influenced by microbial metabolism

Gut Brain

Asthma  
/Atopy

Cardiovascular

Colon Cancer

Biliary Disease

Altered drug  
metabolism

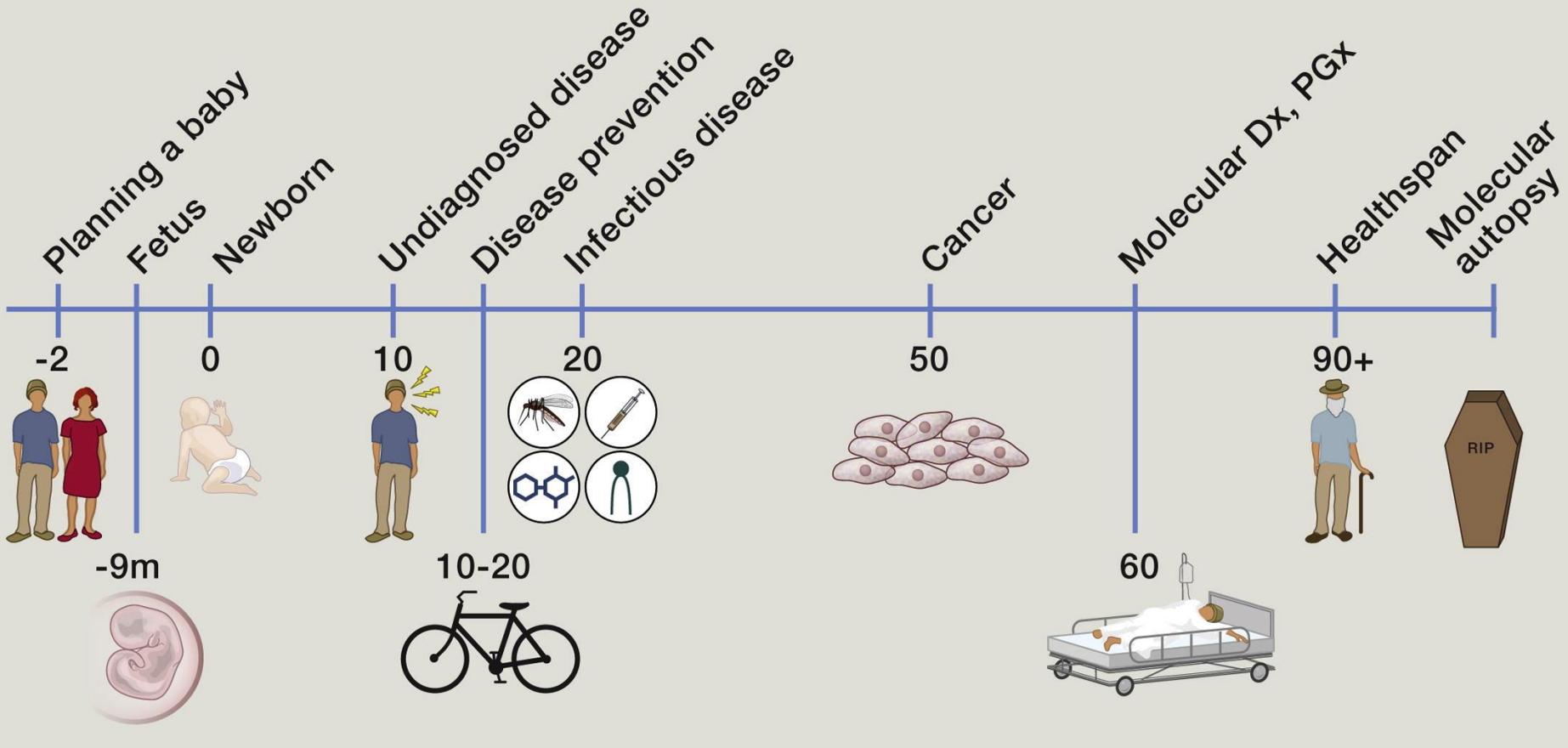
Peripheral  
Vascular Disease

Obesity / Metabolic  
Syndrome

Inflammatory Bowel  
Disease

# Individualized genomic medicine

From prewomb to tomb



Cell 2014 157, 241-253DOI: (10.1016/j.cell.2014.02.012)

# Diagnostic sequencing for rare, undiagnosed diseases

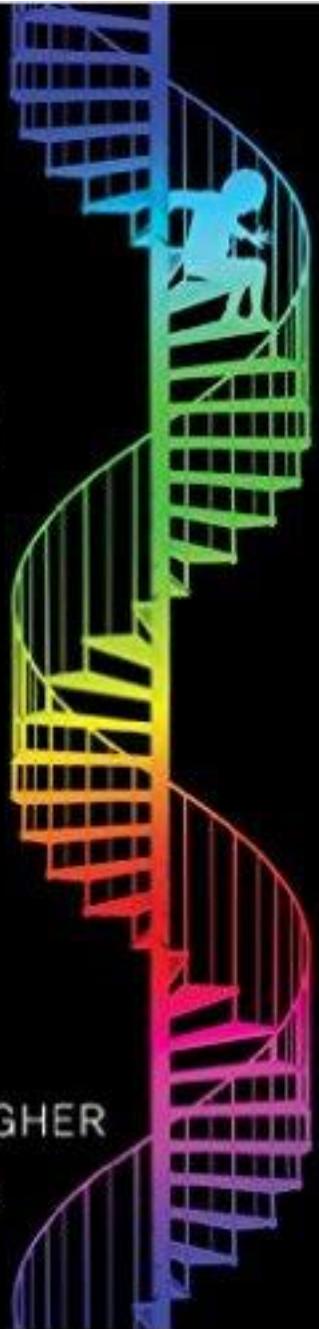
- Now possible to use sequencing to understand the molecular diagnosis of an unknown condition.
- Success rate ranges from 25 – 50%
- Nic Volker story

# One in a Billion

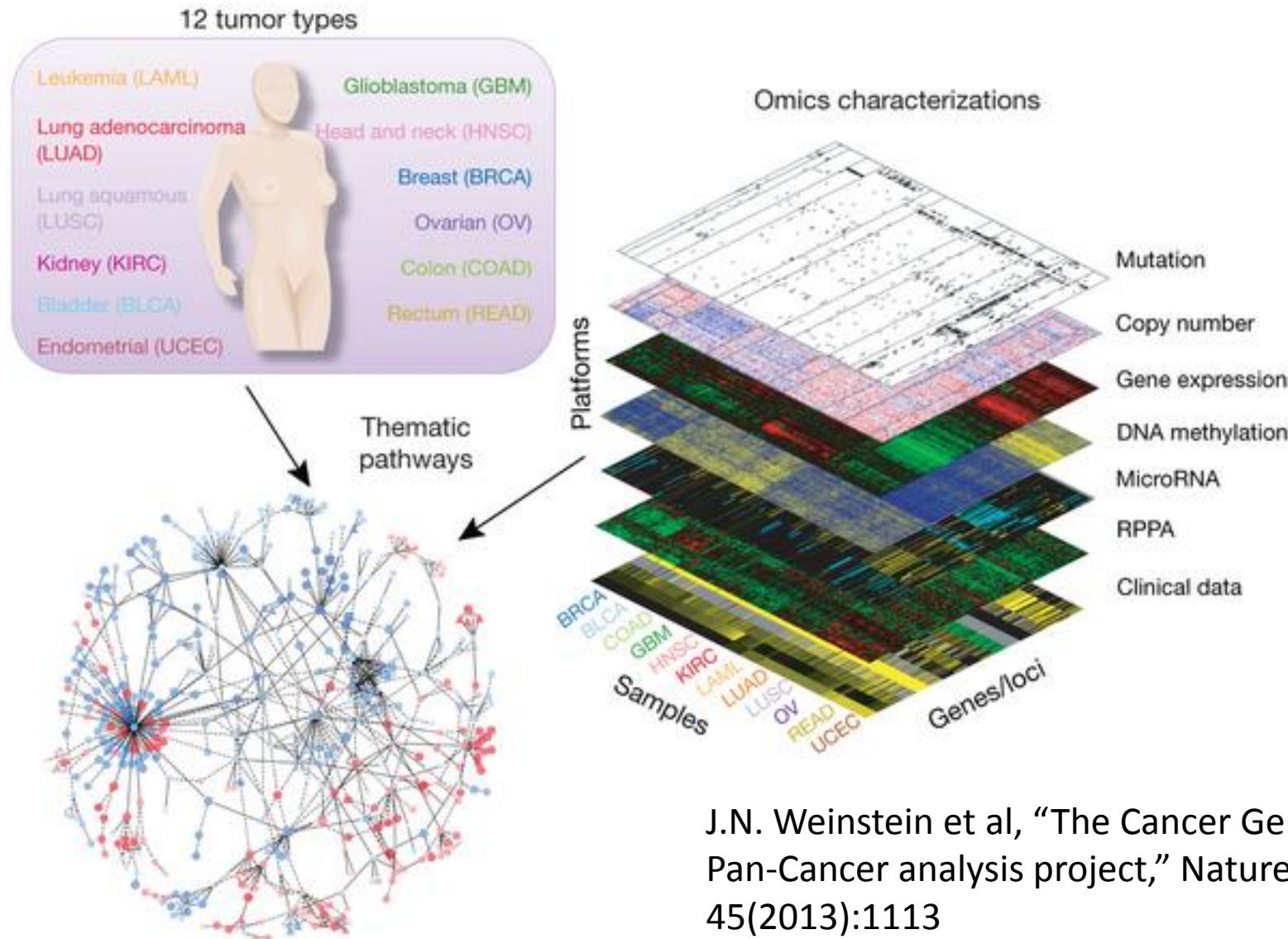
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The Story of Nic Volker  
and the Dawn of  
Genomic Medicine

MARK JOHNSON  
and KATHLEEN GALLAGHER  
Winners of the Pulitzer Prize



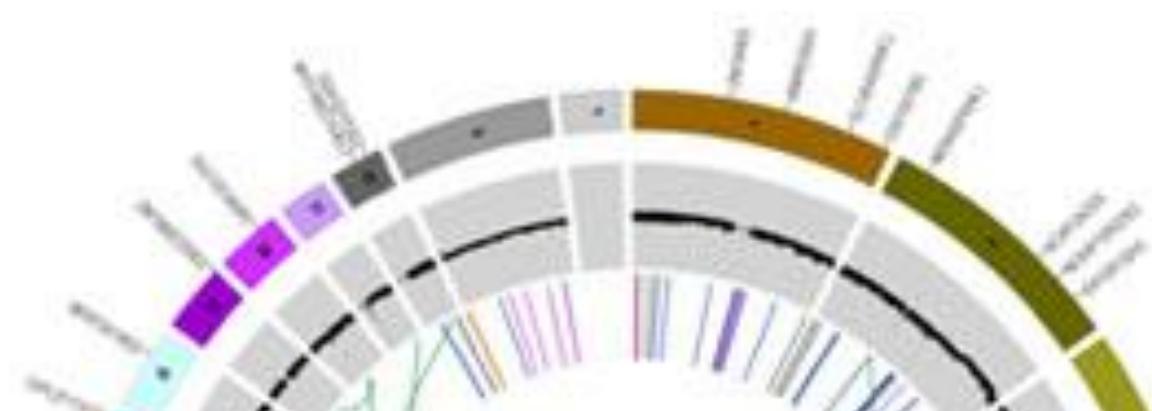
# Cancer Genomics



# Cancer Genomics

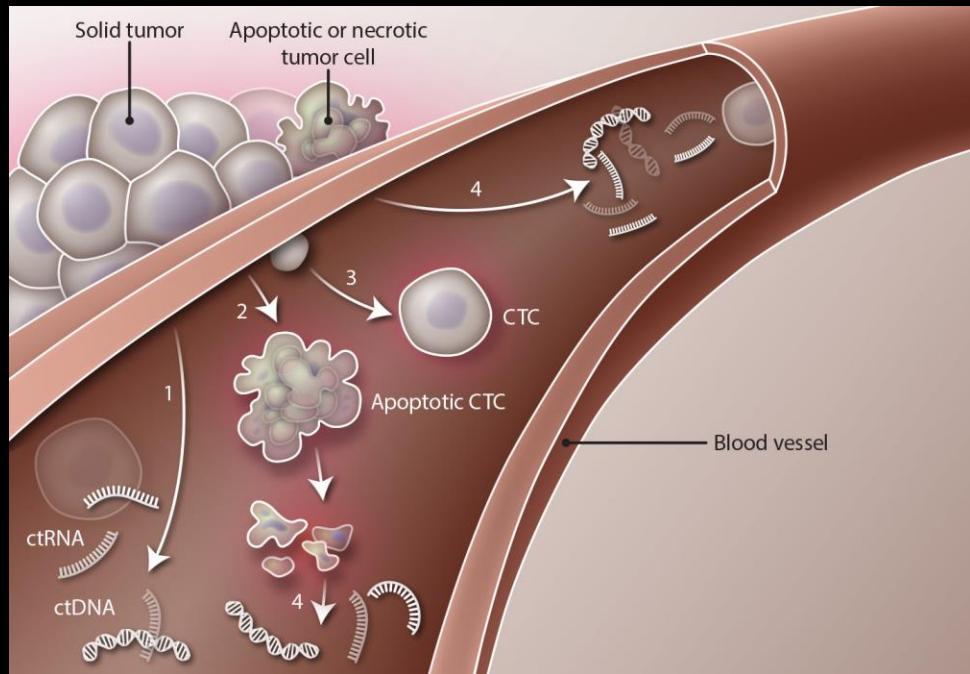
“Cancer can longer be treated as a single disease...the nature of a person’s cancer once manifest is defined by genomic, epignomic, and genetic expression patterns that are **individual and unique**.”

- Dr. Jeffrey Bland
- [https://www.functionalmedicine.org/files/library/IFM-Omics-Series-Part4.pdf?utm\\_source=IFM&utm\\_medium=website&utm\\_campaign=page](https://www.functionalmedicine.org/files/library/IFM-Omics-Series-Part4.pdf?utm_source=IFM&utm_medium=website&utm_campaign=page)

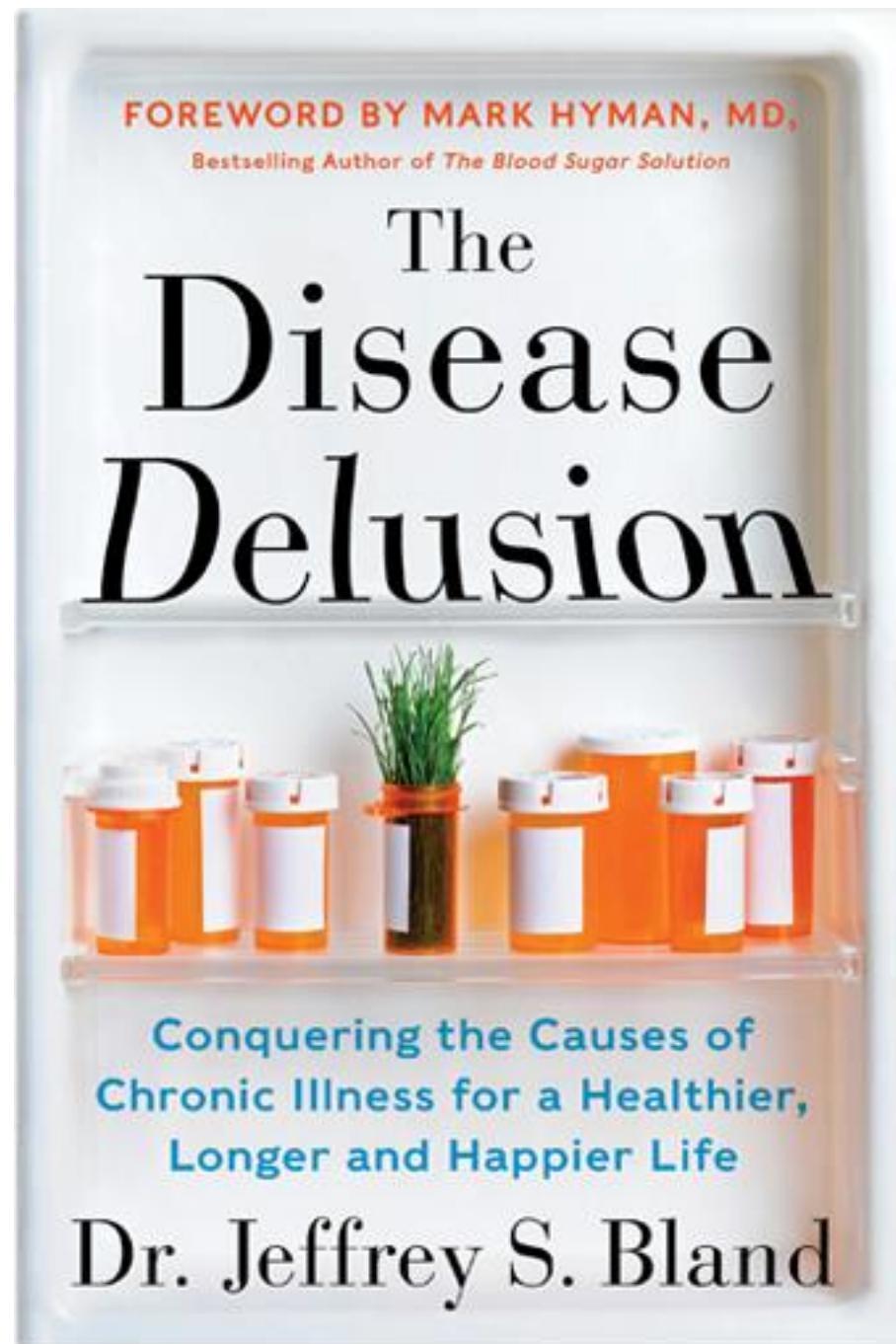


# Cancer Genomics

- Diagnostic biomarkers for early detection
- Liquid biopsies
- Matching targeted therapies
- Preventing toxicities
- Tracking and prognostics



“Diseases  
Don’t  
Exist”



# Molecular Diagnosis

Under  
stan

cular  
cular

Type II Diabetes is an umbrella term for a variety underlying problems of glucose metabolism :

- Insulin resistance
- Islet cell problems
- Defective insulin transporter
- Defective ion channel
- Abnormal adrenergic receptor
- Etc.

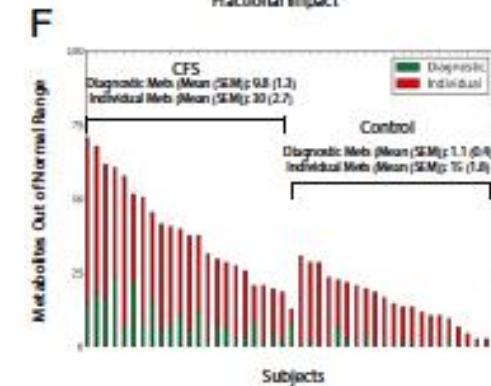
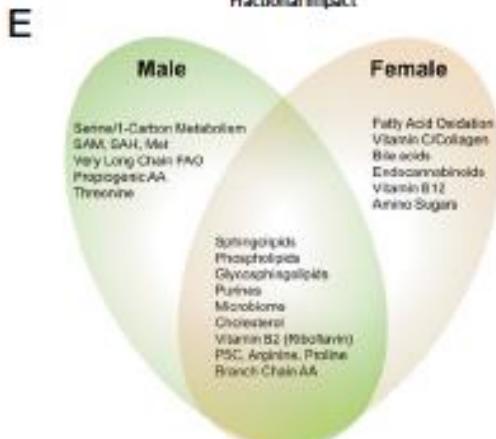
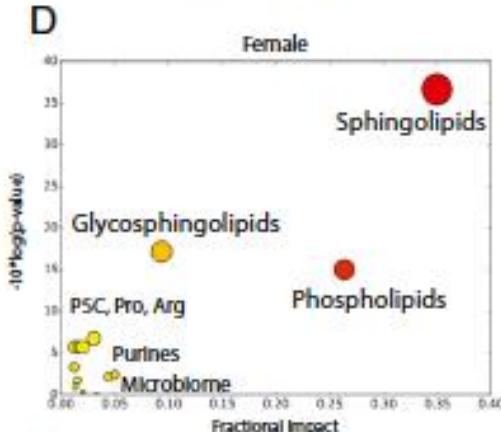
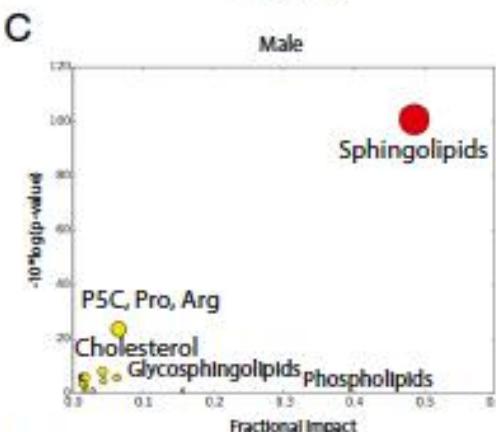
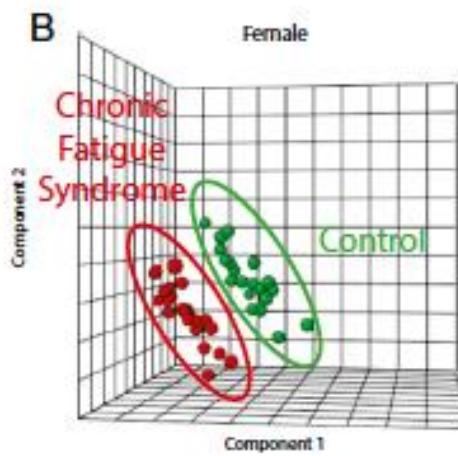
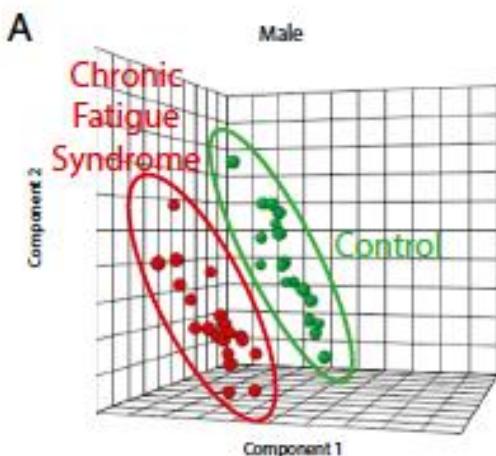
# Better understanding of Complex Chronic Disease

## Metabolic features of chronic fatigue syndrome

Robert K. Naviaux<sup>a,b,c,d,1</sup>, Jane C. Naviaux<sup>a,e</sup>, Kefeng Li<sup>a,b</sup>, A. Taylor Bright<sup>a,b</sup>, William A. Alaynick<sup>a,b</sup>, Lin Wang<sup>a,b</sup>, Asha Baxter<sup>f</sup>, Neil Nathan<sup>f,2</sup>, Wayne Anderson<sup>f</sup>, and Eric Gordon<sup>f</sup>

<sup>a</sup>The Mitochondrial and Metabolic Disease Center, University of California, San Diego School of Medicine, San Diego, CA 92103-8467; <sup>b</sup>Department of Medicine, University of California, San Diego School of Medicine, San Diego, CA 92103-8467; <sup>c</sup>Department of Pediatrics, University of California, San Diego School of Medicine, San Diego, CA 92103-8467; <sup>d</sup>Department of Pathology, University of California, San Diego School of Medicine, San Diego, CA 92103-8467; <sup>e</sup>Department of Neurosciences, University of California, San Diego School of Medicine, San Diego, CA 92103-8467; and <sup>f</sup>Gordon Medical Associates, Santa Rosa, CA 95403

Edited by Ronald W. Davis, Stanford University School of Medicine, Stanford, CA, and approved July 13, 2016 (received for review May 11, 2016)



# Metabolomics as a Tool for Discovery of Biomarkers of Autism Spectrum Disorder in the Blood Plasma of Children

Paul R. West<sup>1\*</sup>, David G. Amaral<sup>2</sup>, Preeti Bais<sup>3</sup>, Alan M. Smith<sup>1</sup>, Laura A. Egnash<sup>1</sup>, Mark E. Ross<sup>1</sup>, Jessica A. Palmer<sup>1</sup>, Burr R. Fontaine<sup>1</sup>, Kevin R. Conard<sup>1</sup>, Blythe A. Corbett<sup>4</sup>, Gabriela G. Cezar<sup>1✉</sup>, Elizabeth L. R. Donley<sup>1</sup>, Robert E. Burrier<sup>1</sup>

**1** Stemina Biomarker Discovery, Madison, Wisconsin, United States of America, **2** The M.I.N.D. Institute and Department of Psychiatry and Behavioral Sciences, University of California Davis, Davis, California, United States of America, **3** The Jackson Laboratory for Genomic medicine, University of Connecticut Health Center, Farmington, Connecticut, United States of America, **4** Department of Psychiatry, Psychology and Kennedy Center, Vanderbilt University, Nashville, Tennessee, United States of America

# Better early detection of disease

FULL PAPER

BJC

British Journal of Cancer (2016) 115, 848–857 | doi: 10.1038/bjc.2016.243

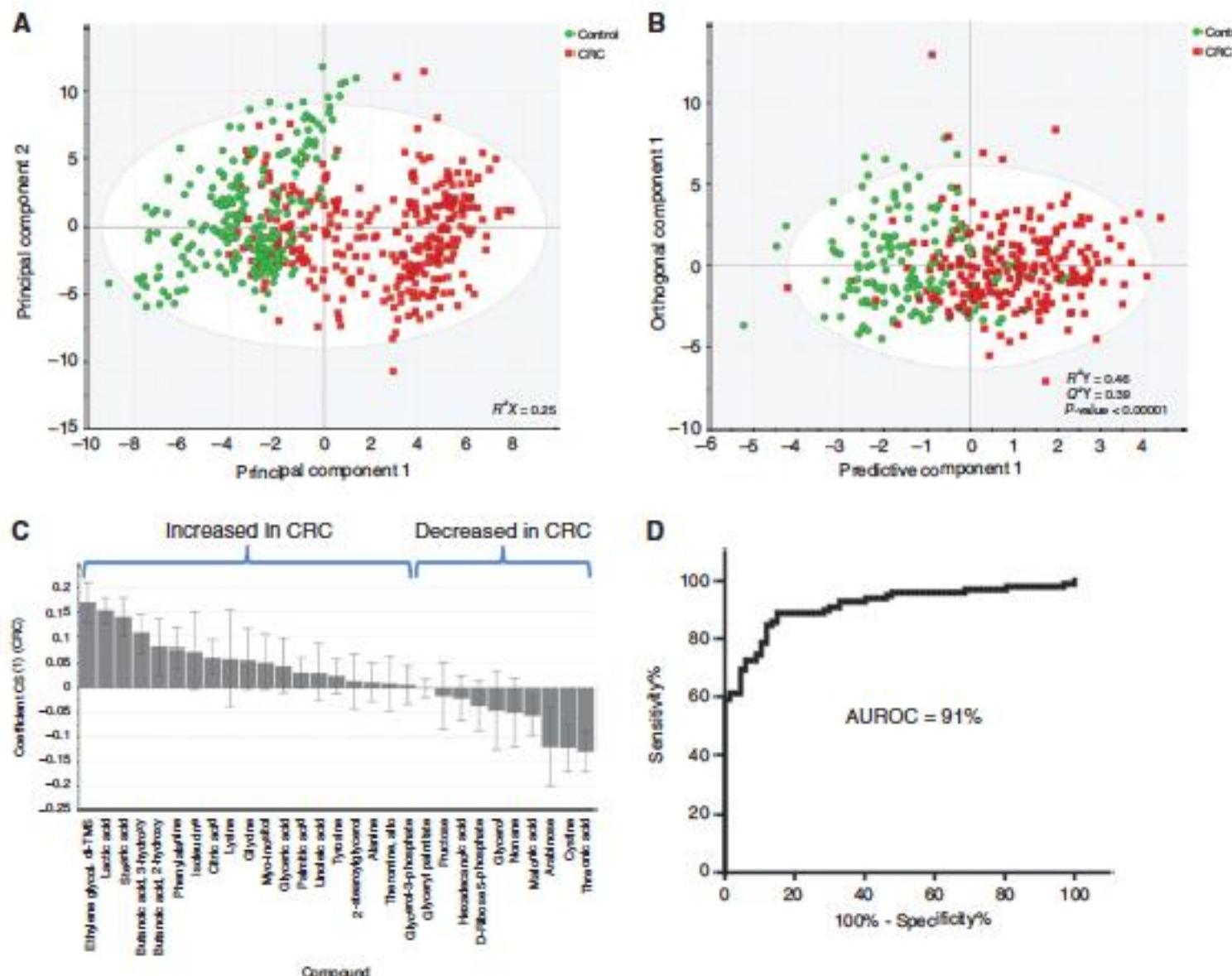
Keywords: colorectal adenocarcinoma; metabolomics profiling; mass spectrometry; cancer biomarker

## A validated metabolomic signature for colorectal cancer: exploration of the clinical value of metabolomics

Farshad Farshidfar<sup>1,2</sup>, Aalim M Weljie<sup>3,4</sup>, Karen A Kopciuk<sup>5,6</sup>, Robert Hilsden<sup>7,8</sup>, S Elizabeth McGregor<sup>2,6</sup>, W Donald Buie<sup>1</sup>, Anthony MacLean<sup>1</sup>, Hans J Vogel<sup>3</sup> and Oliver F Bathe<sup>\*,1,2</sup>

<sup>1</sup>Department of Surgery, University of Calgary, Calgary, AB, Canada; <sup>2</sup>Department of Oncology, University of Calgary, Calgary, AB, Canada; <sup>3</sup>Department of Biological Sciences, University of Calgary, Calgary, AB, Canada; <sup>4</sup>Institute for Translational Medicine and Therapeutics, University of Pennsylvania, Philadelphia, PA, USA; <sup>5</sup>Department of Mathematics and Statistics, University of Calgary, Calgary, AB, Canada; <sup>6</sup>Cancer Epidemiology and Prevention Research, Alberta Health Services, Calgary, AB, Canada;

<sup>7</sup>Department of Medicine, University of Calgary, Calgary, AB, Canada and <sup>8</sup>Forzani and MacPhail Colon Cancer Screening Centre, Alberta Health Services, Calgary, AB, Canada



Metabolomic signature of CRC patients is distinct from disease free controls

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY  
© 2016 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION  
PUBLISHED BY ELSEVIER

VOL. 68, NO. 25, 2016  
ISSN 0735-1097/\$36.00  
<http://dx.doi.org/10.1016/j.jacc.2016.09.972>

## FOCUS SEMINAR: GENETICS

### STATE-OF-THE-ART REVIEW

# The Emerging Role of Metabolomics in the Diagnosis and Prognosis of Cardiovascular Disease

John R. Ussher, PhD,<sup>a,b</sup> Sammy Elmariah, MD, MPH,<sup>c</sup> Robert E. Gerszten, MD,<sup>d</sup> Jason R.B. Dyck, PhD<sup>a</sup>



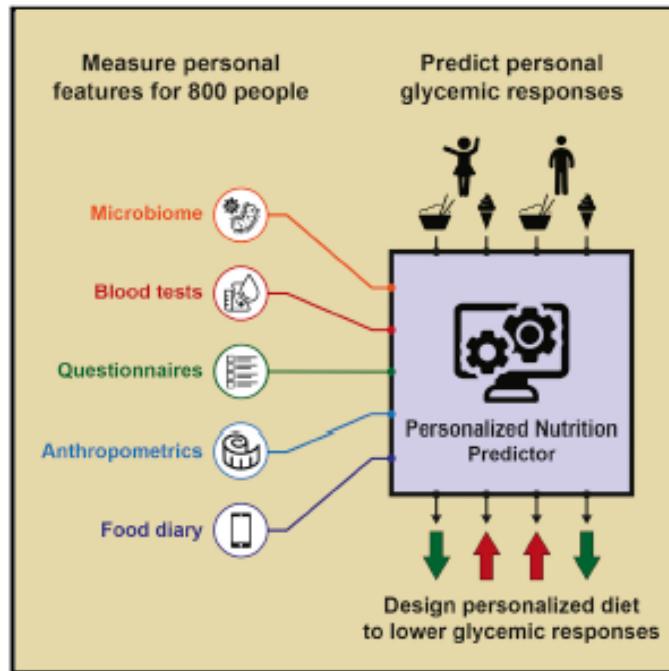


# Personalized Therapeutics

<http://www.wizardhealth.co/wp-content/uploads/2016/12/naslovprecizna-c.jpg>

# 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

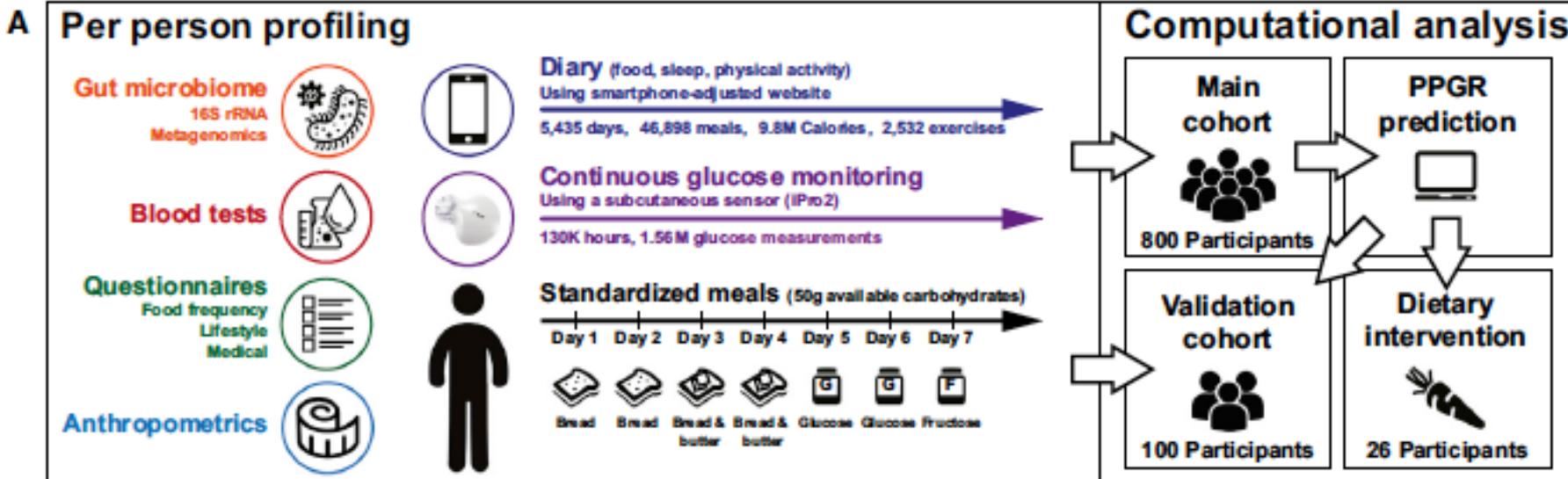
People eating identical meals present high variability in post-meal blood glucose response. Personalized diets created with the help of an accurate predictor of blood glucose response that integrates parameters such as dietary habits, physical activity, and gut microbiota may successfully lower post-meal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

## Highlights

- High interpersonal variability in post-meal glucose observed in an 800-person cohort
- Using personal and microbiome features enables accurate glucose response prediction
- Prediction is accurate and superior to common practice in an independent cohort
- Short-term personalized dietary interventions successfully lower post-meal glucose

One size does  
not fit all...

# Personalized Nutrition by Prediction of Glycemic Responses



- high interpersonal variability in post-meal glucose (800 person cohort)
- using personal and microbiome features enables accurate glucose response prediction
- short-term personalized dietary interventions successfully lower post-meal glucose

Sci Transl Med. 2010 May 26; 2(33): 33ra37.

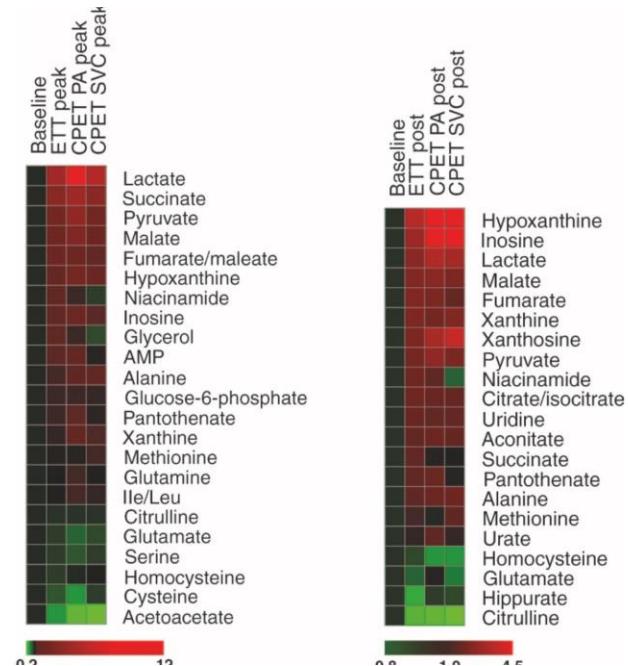
doi: [10.1126/scitranslmed.3001006](https://doi.org/10.1126/scitranslmed.3001006)

## Metabolic Signatures of Exercise in Human Plasma

Gregory D. Lewis,<sup>1,2,3,4,\*</sup> Laurie Farrell,<sup>1</sup> Malissa J. Wood,<sup>1</sup> Maryann Martinovic,<sup>1</sup> Zoltan Arany,<sup>5</sup> Glenn C Rowe,<sup>5</sup> Amanda Souza,<sup>4</sup> Susan Cheng,<sup>1,6,7</sup> Elizabeth L. McCabe,<sup>6</sup> Elaine Yang,<sup>4</sup> Xu Shi,<sup>4</sup> Rahul Deo,<sup>1,8</sup> Frederick P. Roth,<sup>8</sup> Aarti Asnani,<sup>1,2</sup> Eugene P. Rhee,<sup>4,9</sup> David M. Systrom,<sup>10</sup> Marc J. Semigran,<sup>1</sup> Ramachandran S. Vasan,<sup>6,11,12</sup> Steven A. Carr,<sup>4</sup> Thomas J. Wang,<sup>1,6</sup> Marc S. Sabatine,<sup>3,7</sup> Clary B. Clish,<sup>4</sup> and Robert E. Gerszten<sup>1,2,3,4,\*</sup>

[Author information ►](#) [Copyright and License information ►](#)

Metabolic profiling can provide us with signatures of exercise performance and will help us determine optimal levels of exercise



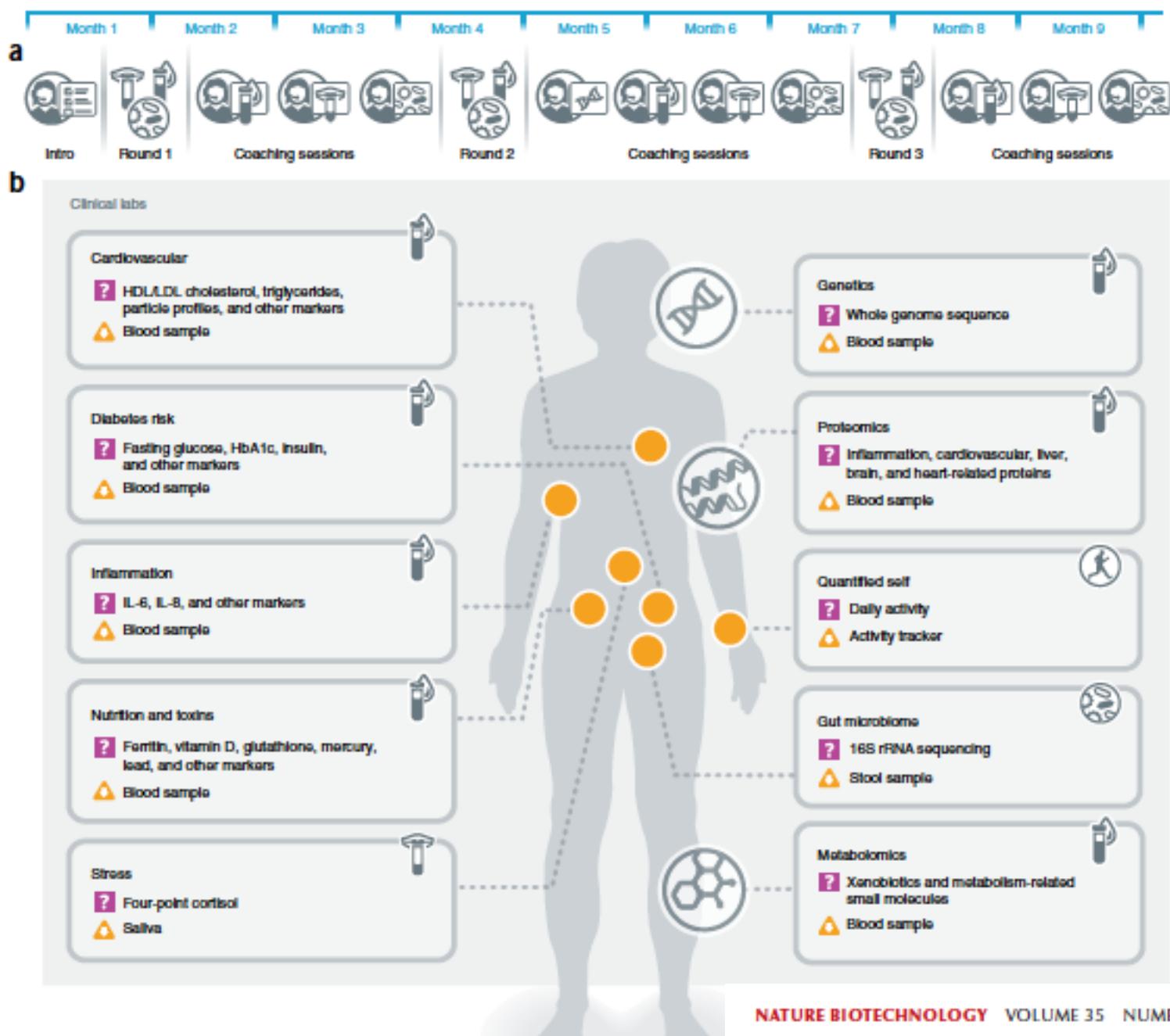
# Scientific Wellness

nature  
biotechnology

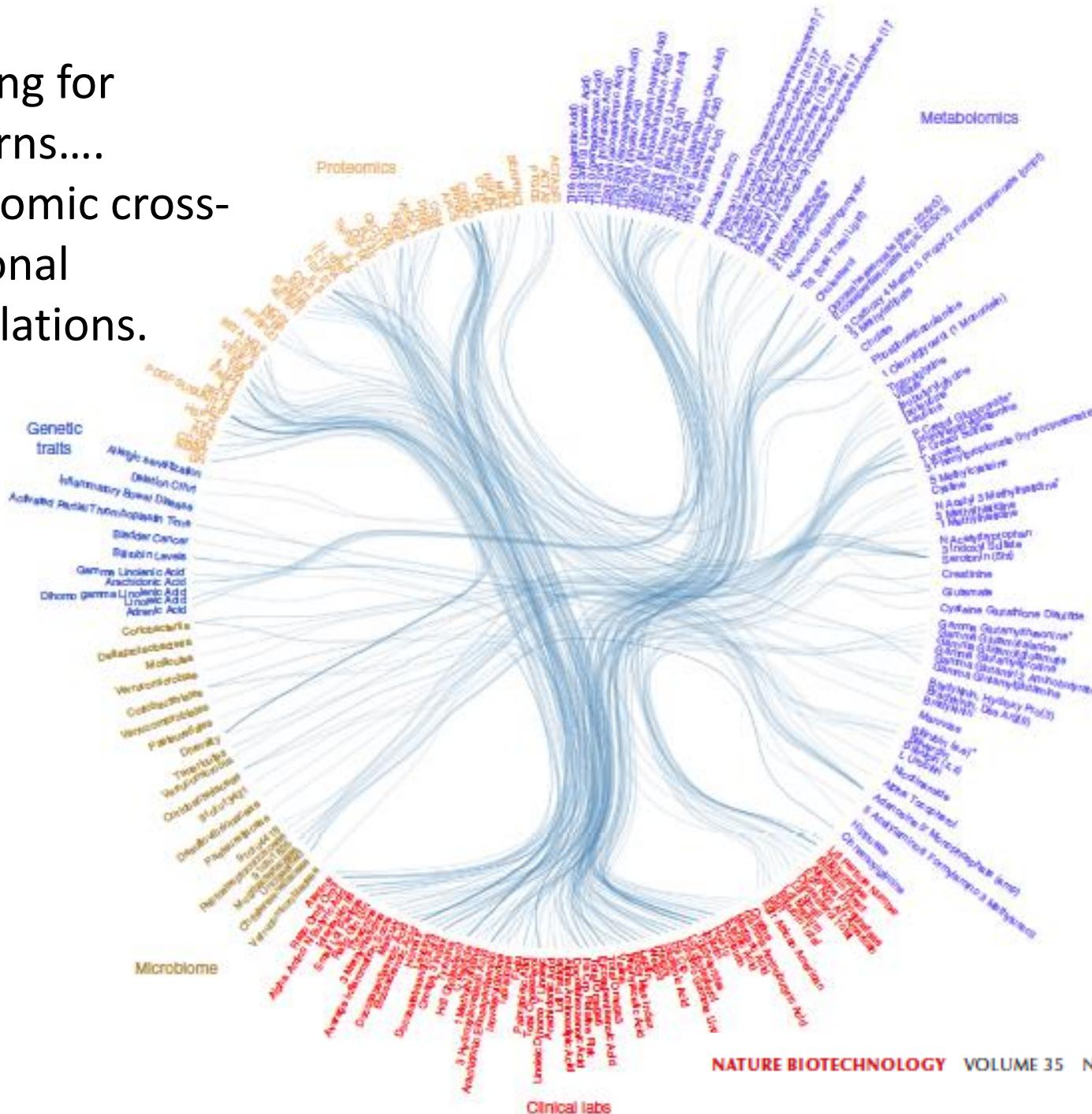
ARTICLES

A wellness study of 108 individuals using personal, dense, dynamic data clouds

Nathan D Price<sup>1,2,6,7</sup>, Andrew T Magis<sup>2,6</sup>, John C Earls<sup>2,6</sup>, Gustavo Glusman<sup>1</sup> , Roie Levy<sup>1</sup>, Christopher Lausted<sup>1</sup>, Daniel T McDonald<sup>1,5</sup>, Ulrike Kusebauch<sup>1</sup>, Christopher L Moss<sup>1</sup>, Yong Zhou<sup>1</sup>, Shizhen Qin<sup>1</sup>, Robert L Moritz<sup>1</sup> , Kristin Brogaard<sup>2</sup>, Gilbert S Omenn<sup>1,3</sup>, Jennifer C Lovejoy<sup>1,2</sup> & Leroy Hood<sup>1,4,7</sup>



Looking for  
patterns....  
Inter-omic cross-  
sectional  
Correlations.



# Pharmacogenomics



Image:

[https://www.promedica.org/Public%20Documents/images/pill\\_dna2.jpg](https://www.promedica.org/Public%20Documents/images/pill_dna2.jpg)

“There is **no** such thing as an  
**idiosyncratic drug reaction**; merely  
our **own ignorance** of important  
underlying mechanisms”

Rachel Tyndale  
“Pharmacogenomics and the Changing Face of Medicine”  
Presented at IFM Symposium 2015

# Pharmacogenomics

- Absorption / metabolism / binding / transport / excretion is **genetically determined**
- “At **least a third** of the money that is spent on prescription drugs is **wasted...**”
- “This is because a substantial proportion of patients are prescribed medications that are at an individual level **either ineffective or dangerous**”
  - Harper, Topol, “Pharmacogenomics in Clinical Practice and Drug Development,” Nature Biotechnology 30, No. 11 (2012); 1117-1124

# Adverse Drug Reactions

**Table 1**

**Percentage using prescription medication, by sex and selected characteristics, household population aged 6 to 79, Canada, 2007 to 2011**

	%
Total	40.5
Age group	
6 to 14 <sup>†</sup>	11.7
15 to 24	26.2 <sup>*</sup>
25 to 44	28.0 <sup>*</sup>
45 to 64	55.1 <sup>*</sup>
65 to 79	82.1 <sup>*</sup>

82% of all adults age 65 – 79 take at least one prescription medication.



Review | April 15, 1998

# **Incidence of Adverse Drug Reactions in Hospitalized Patients**

## **A Meta-analysis of Prospective Studies**

Jason Lazarou, MSc; Bruce H. Pomeranz, MD, PhD; Paul N. Corey, PhD

*JAMA*. 1998;279(15):1200-1205. doi:10.1001/jama.279.15.1200.

Estimated 100,000 deaths in 1994 /  
6<sup>th</sup> leading cause of death in US

# Response rates to drug therapy

Therapeutic area	Efficacy rate (%)
Alzheimer's	30
Analgesics (Cox-2)	80
Asthma	60
Cardiac Arrhythmias	60
Depression (SSRI)	62
Diabetes	57
HCV	47
Incontinence	40
Migraine (acute)	52
Migraine (prophylaxis)	50
Oncology	25
Osteoporosis	48
Rheumatoid arthritis	50
Schizophrenia	60

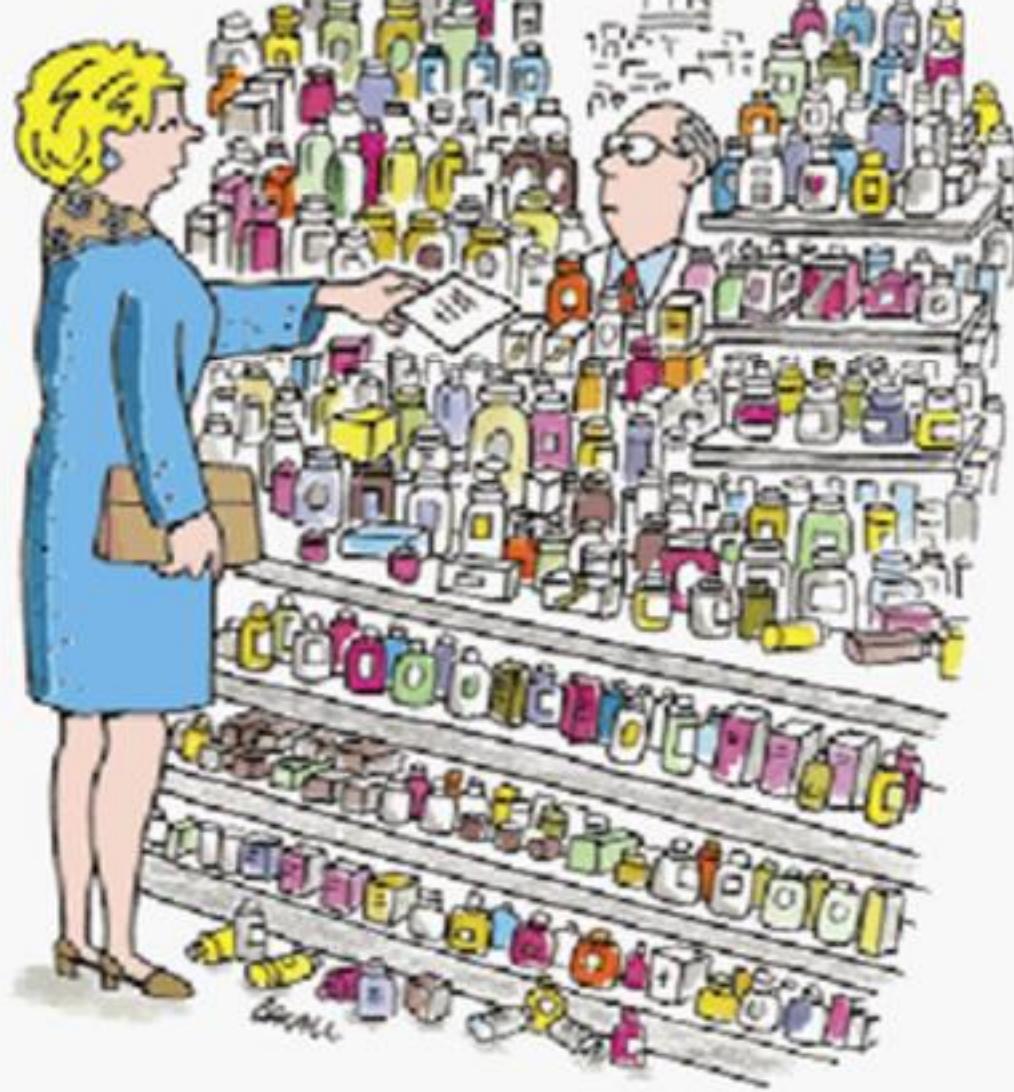
Efficacy rates range from 25% to 80% but most are LESS than 60%

# Pronounced DNA – Drug Effects

Drug + Condition	Comment
Lithium	Efficacy in Han Chinese
Interferon $\alpha$	Efficacy to cure
Carbamazepine	Stevens-Johnson Syndrome
Simvastatin	Severe muscle inflammation
Flucloxacillin for infections	Liver toxicity



A.R. Harper and E. J. Topol, "Pharmacogenomics in Clinical Practice and Drug Development," Nature Biotechnology 30, no. 11(2012):1117-1124



"Here's my sequence..."

*New Yorker, 2000*

# Digital YOU

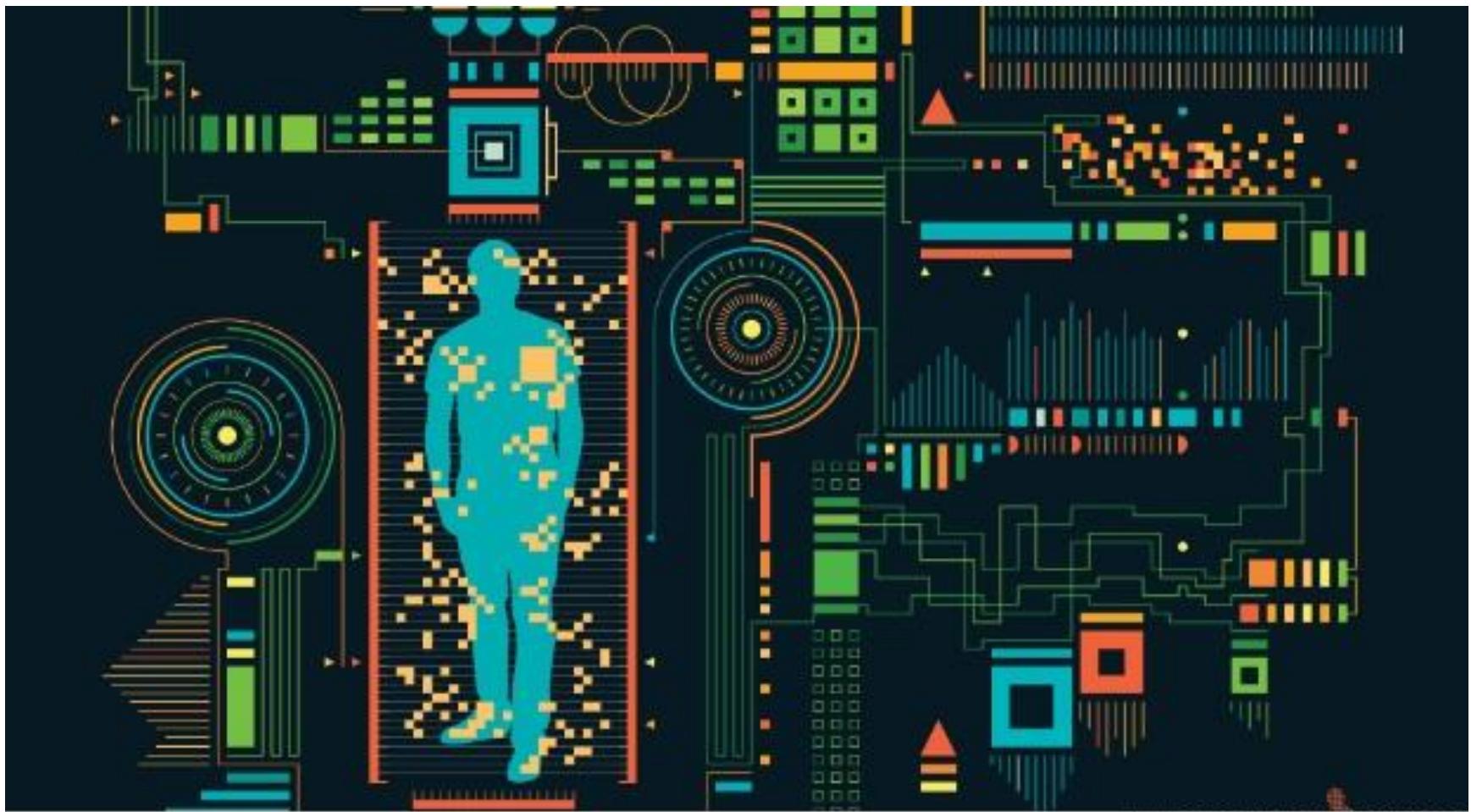
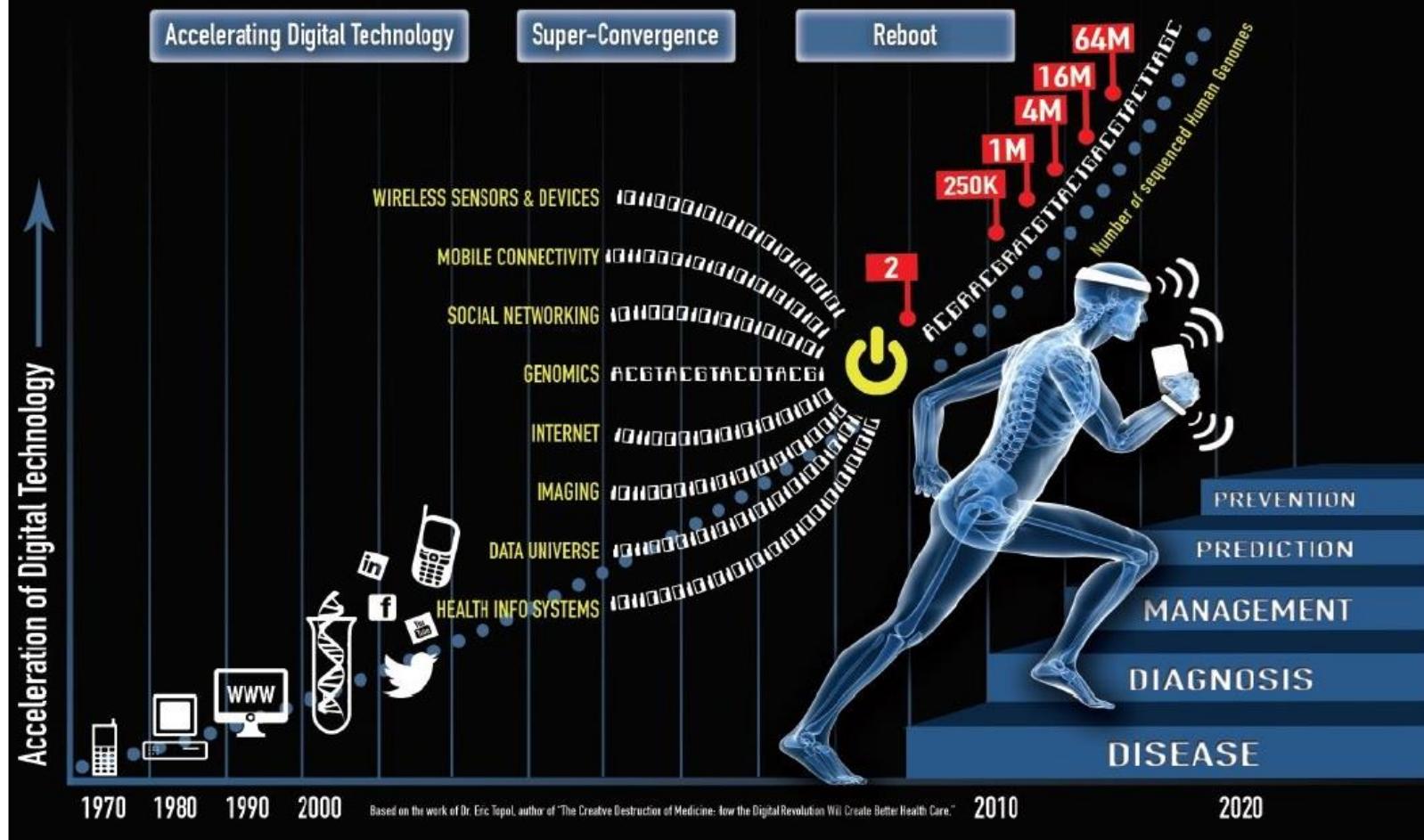


ILLUSTRATION: ERIC FROMMELT

<https://sites.google.com/site/quantifiedself777/>

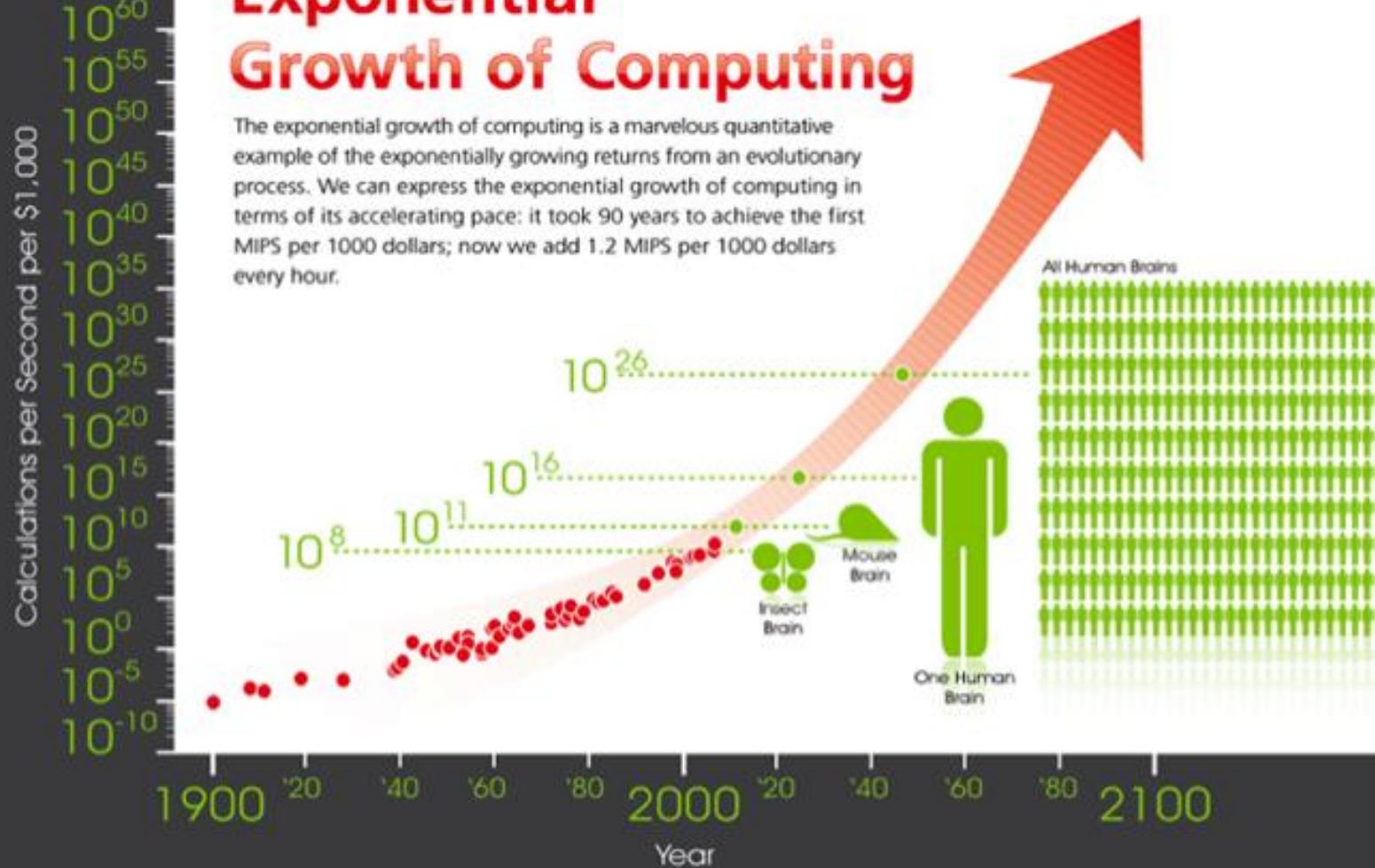
# DIGITAL HEALTH

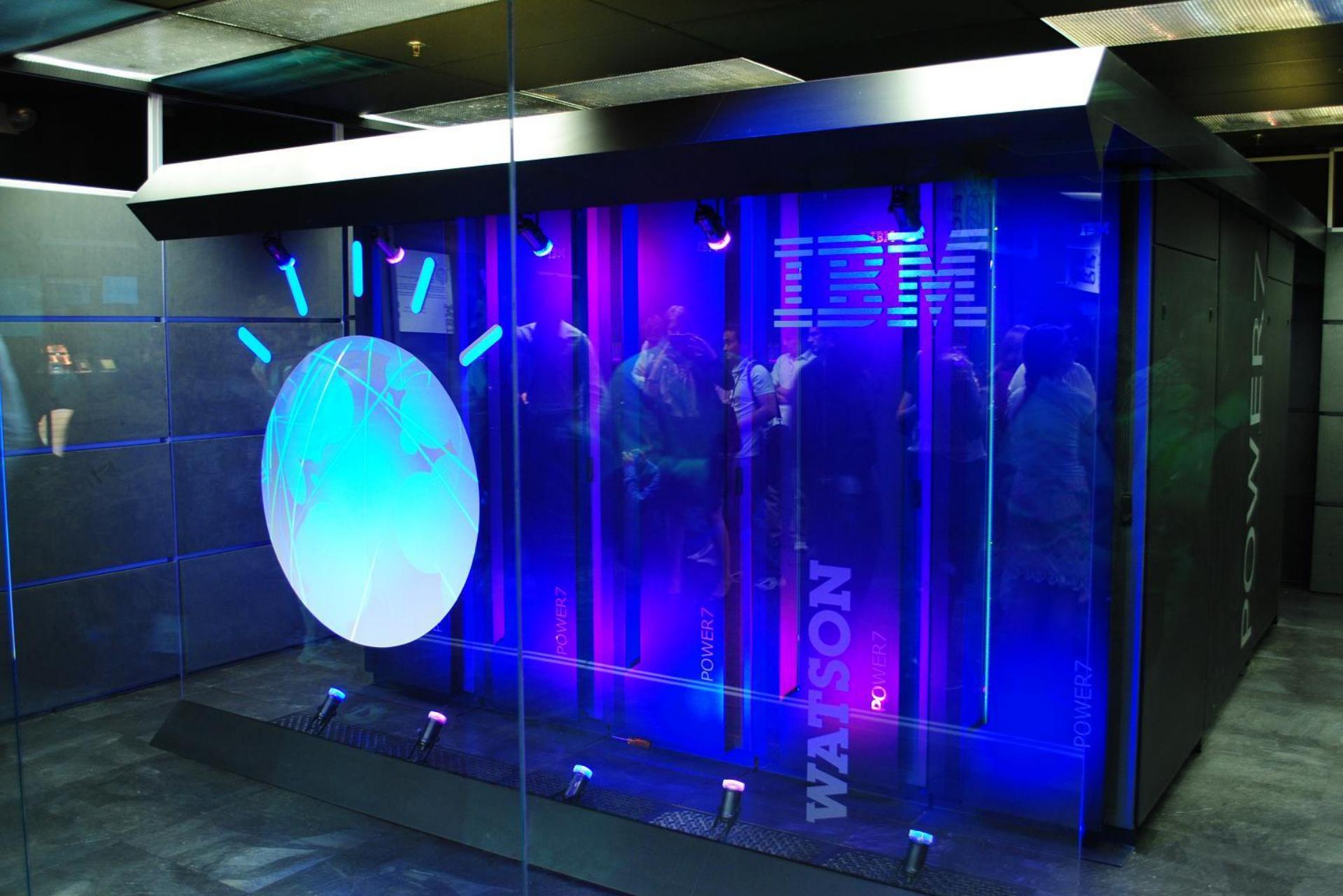
## 6 CHARACTERS REBOOTING MEDICINE AND HEALTH O, 1, A, C, G, T



# Exponential Growth of Computing

The exponential growth of computing is a marvelous quantitative example of the exponentially growing returns from an evolutionary process. We can express the exponential growth of computing in terms of its accelerating pace: it took 90 years to achieve the first MIPS per 1000 dollars; now we add 1.2 MIPS per 1000 dollars every hour.





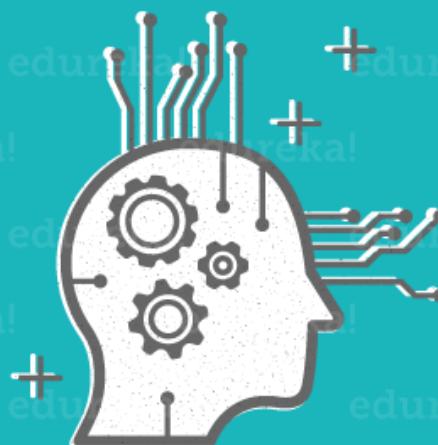
Ai and Medicine: Rise of the Machines....

# What is Deep Learning?

edureka!

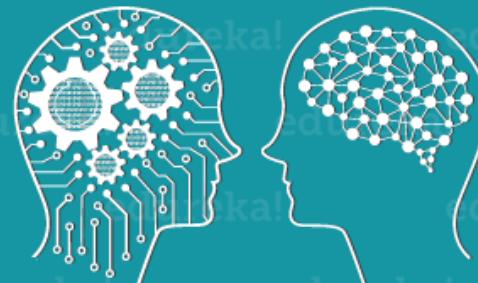
## ARTIFICIAL INTELLIGENCE

Engineering of making Intelligent  
Machines and Programs



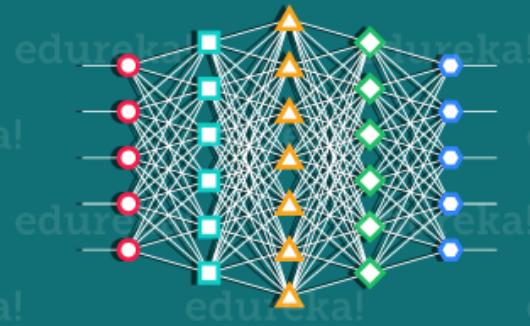
## MACHINE LEARNING

Ability to learn without being  
explicitly programmed



## DEEP LEARNING

Learning based on Deep  
Neural Network



1950's

1960's

1970's

1980's

1990's

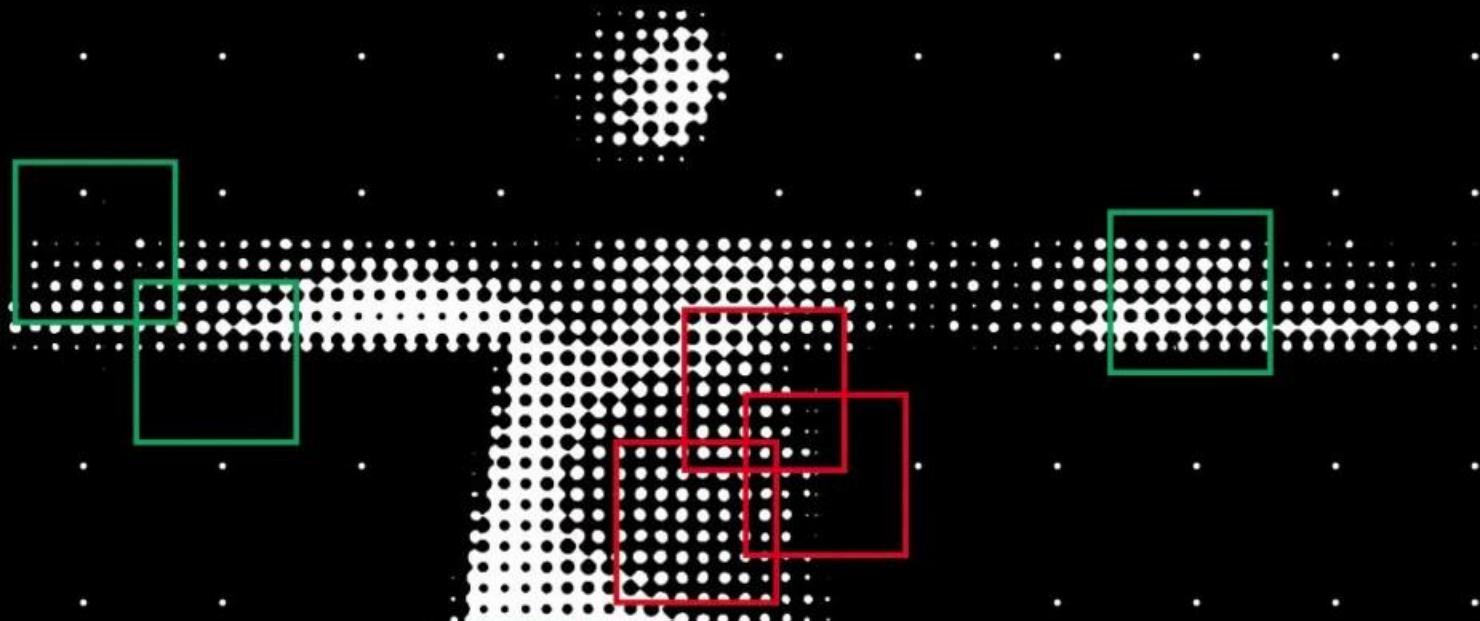
2000's

2006's

2010's

2012's

2017's

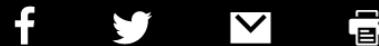


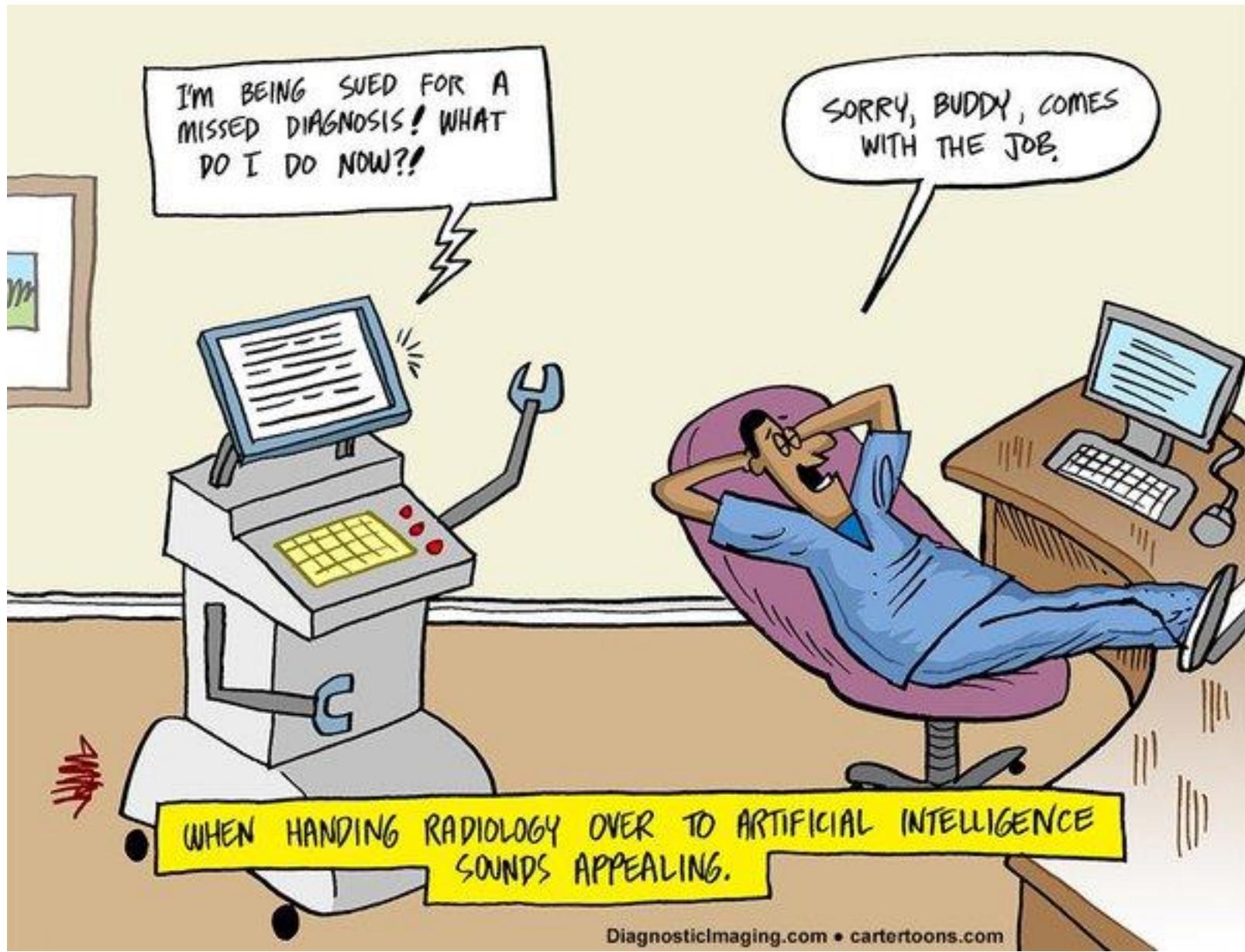
ANNALS OF MEDICINE APRIL 3, 2017 ISSUE

# A.I. VERSUS M.D.

*What happens when diagnosis is automated?*

By Siddhartha Mukherjee





<http://medicalfuturist.com/the-future-of-radiology-and-ai/>

- “It’s just completely obvious that in five years deep learning is going to do better than radiologists,” he went on. “It *might* be ten years. I said this at a hospital. It did not go down too well.”
  - Geofrey Hinton – Computer Scientist / University of Toronto
  - <https://www.newyorker.com/magazine/2017/04/03/ai-versus-md>



## LESIONS LEARNT

*Artificial intelligence powers detection  
of skin cancer from images* PAGES 36 & 115

## LETTER

doi:10.1038/nature21056

# Dermatologist-level classification of skin cancer with deep neural networks

Andre Esteva<sup>1\*</sup>, Brett Kuprel<sup>1\*</sup>, Roberto A. Novoa<sup>2,3</sup>, Justin Ko<sup>2</sup>, Susan M. Swetter<sup>2,4</sup>, Helen M. Blau<sup>5</sup> & Sebastian Thrun<sup>6</sup>

# Deep Learning at Chest Radiography: Automated Classification of Pulmonary Tuberculosis by Using Convolutional Neural Networks<sup>1</sup>

## Purpose:

To evaluate the efficacy of deep convolutional neural networks (DCNNs) for detecting tuberculosis (TB) on chest radiographs.

## Materials and Methods:

Four deidentified HIPAA-compliant datasets were used in this study that were exempted from review by the institutional review board, which consisted of 1007 posteroanterior chest radiographs. The datasets were split into training (68.0%), validation (17.1%), and test (14.9%). Two different DCNNs, AlexNet and GoogLeNet, were used to classify the images as having manifestations of pulmonary TB or as healthy. Both untrained and pretrained networks on ImageNet were used, and augmentation with multiple preprocessing techniques. Ensembles were performed on the best-performing algorithms. For cases where the classifiers were in disagreement, an independent board-certified cardiothoracic radiologist blindly interpreted the images to evaluate a potential radiologist-augmented workflow. Receiver operating characteristic curves and areas under the curve (AUCs) were used to assess model performance by using the DeLong method for statistical comparison of receiver operating characteristic curves.

## Results:

The best-performing classifier had an AUC of 0.99, which was an ensemble of the AlexNet and GoogLeNet DCNNs. The AUCs of the pretrained models were greater than that of the untrained models ( $P < .001$ ). Augmenting the dataset further increased accuracy ( $P$  values for AlexNet and GoogLeNet were .03 and .02, respectively). The DCNNs had disagreement in 13 of the 150 test cases, which were blindly reviewed by a cardiothoracic radiologist, who correctly interpreted all 13 cases (100%). This radiologist-augmented approach resulted in a sensitivity of 97.3% and specificity 100%.

## Conclusion:

Deep learning with DCNNs can accurately classify TB at chest radiography with an AUC of 0.99. A radiologist-augmented approach for cases where there was disagreement among the classifiers further improved accuracy.

Deep learning with DCNNs can accurately classify TB at chest radiography with an AUC of 0.99. A radiologist-augmented approach for cases where there was disagreement among the classifiers further improved accuracy.

<http://pubs.rsna.org/doi/abs/10.1148/radiol.2017162326>



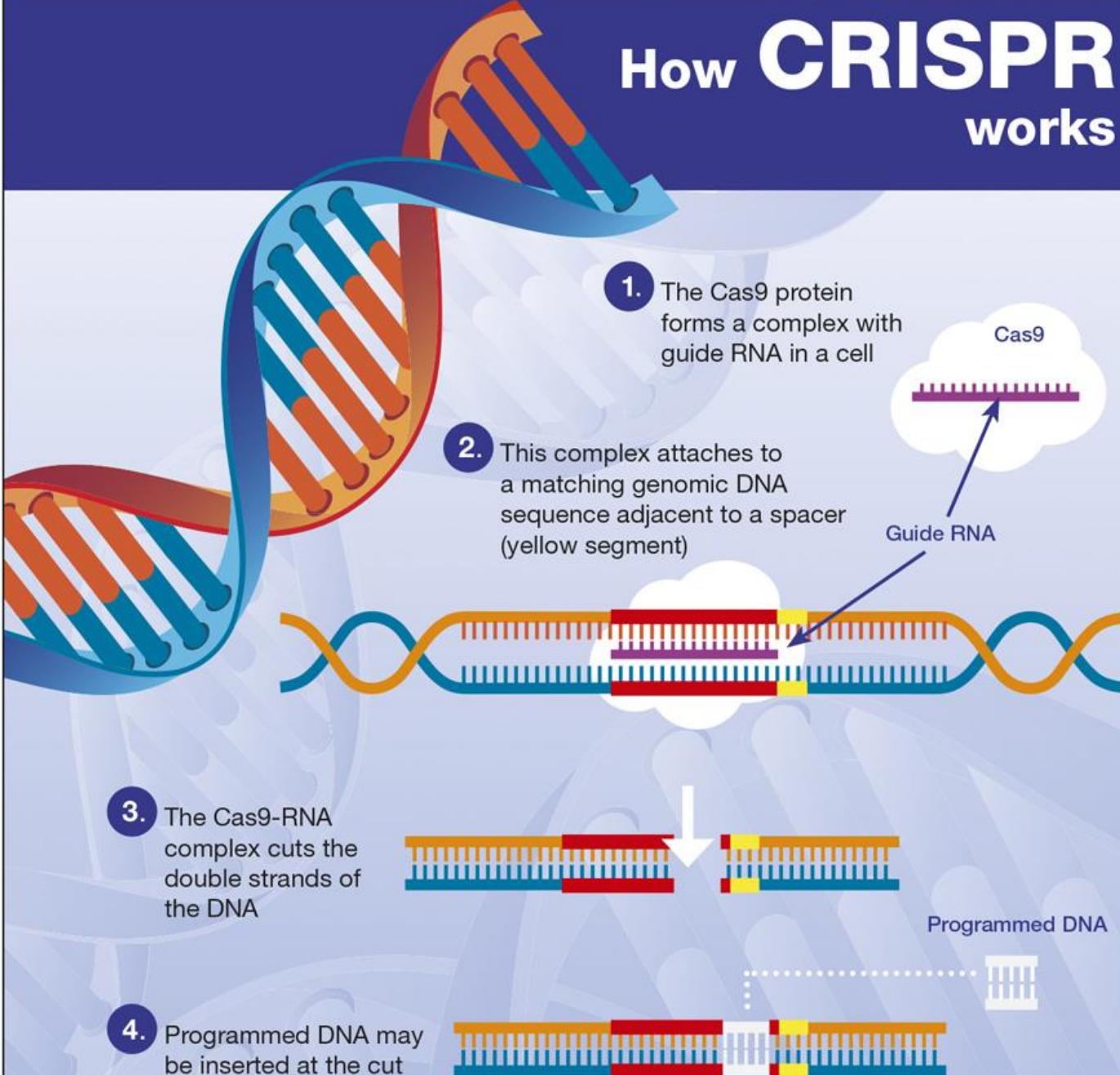
**Rewriting Life**

## First Human Embryos Edited in U.S.

Researchers have demonstrated they can efficiently improve the DNA of human embryos.

by Steve Connor    July 26, 2017

# How CRISPR works



<https://www.cambridge.org/core/services/aop-file-manager/file/582df76221b559de0536a2c2>

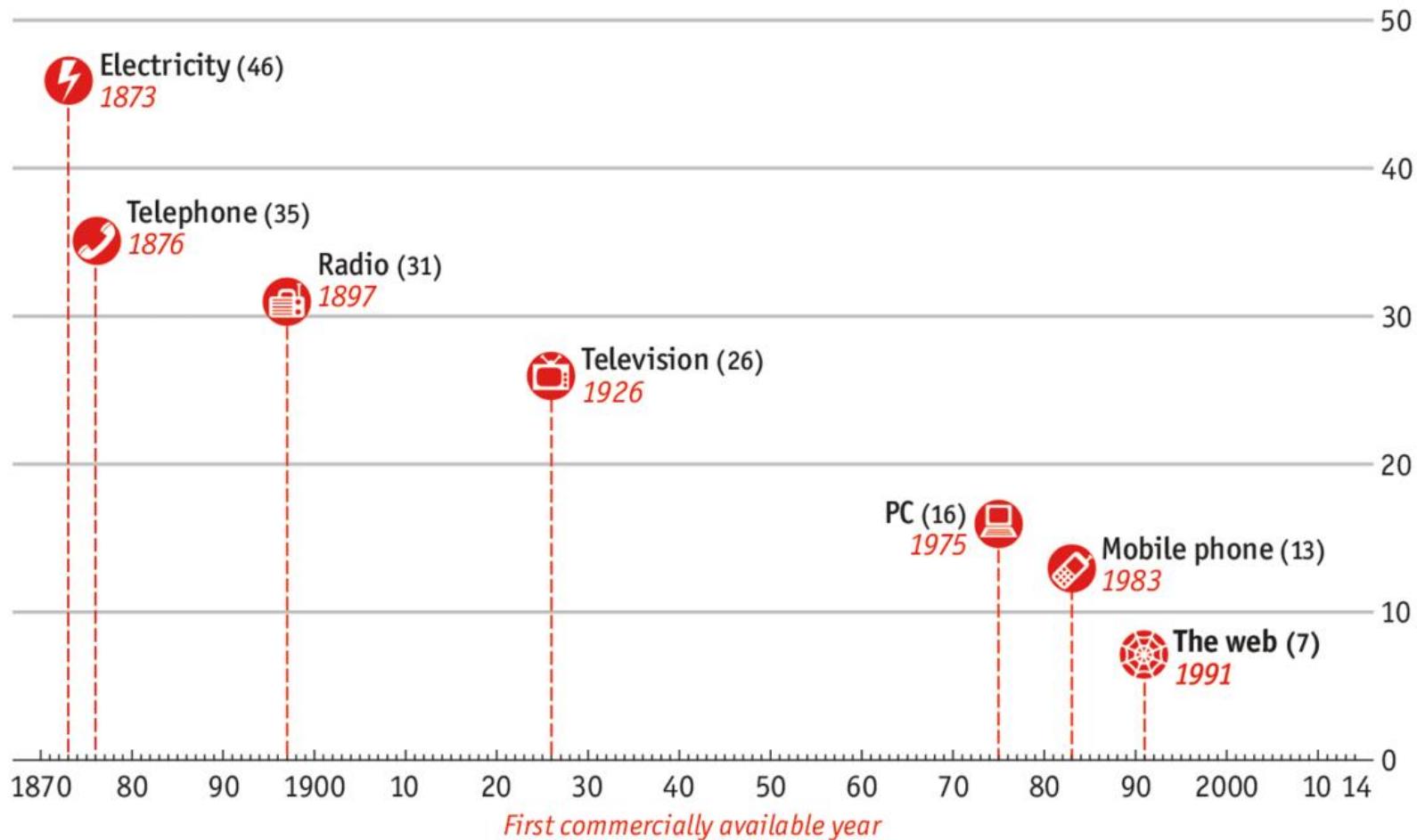
# Medicine will be revolutionized by the Internet of Things (IOT)



A world of interconnected, sensor laden devices and objects...

## Technology adoption

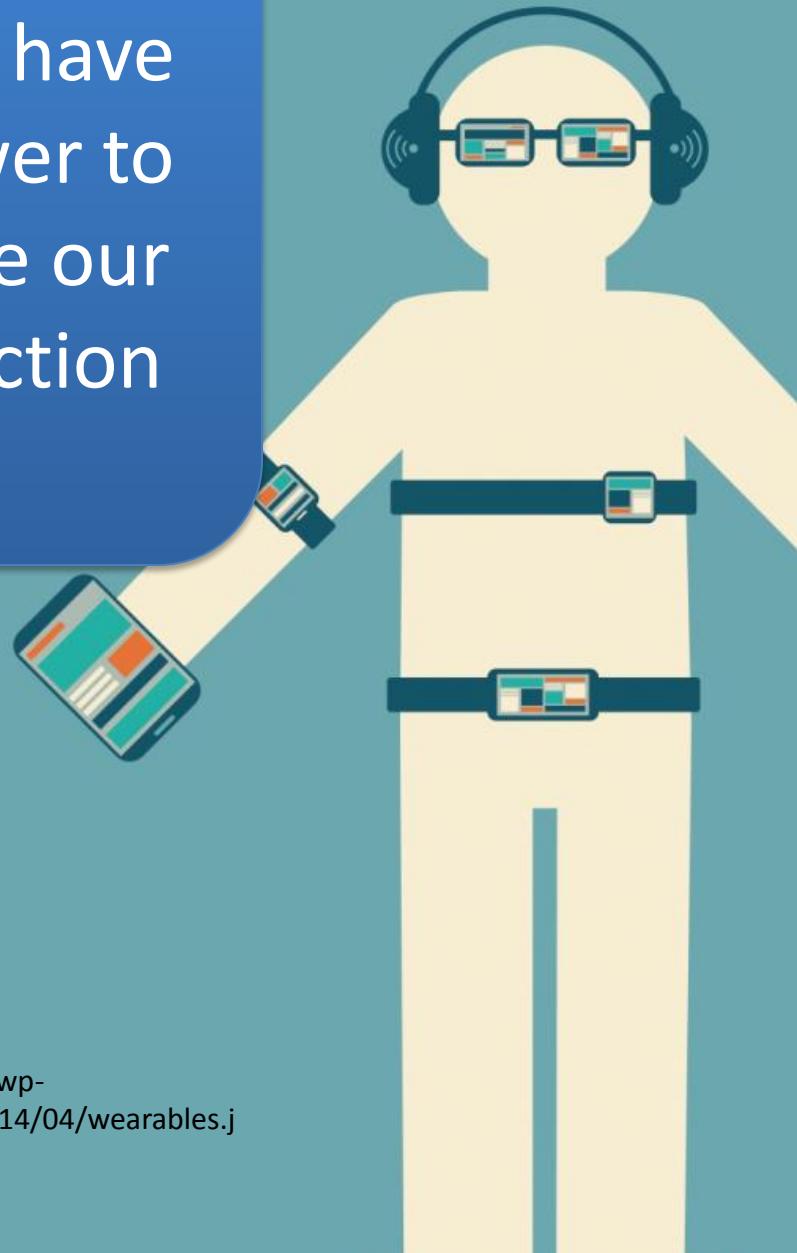
Years until used by one-quarter of American population



Source: Singularity.com

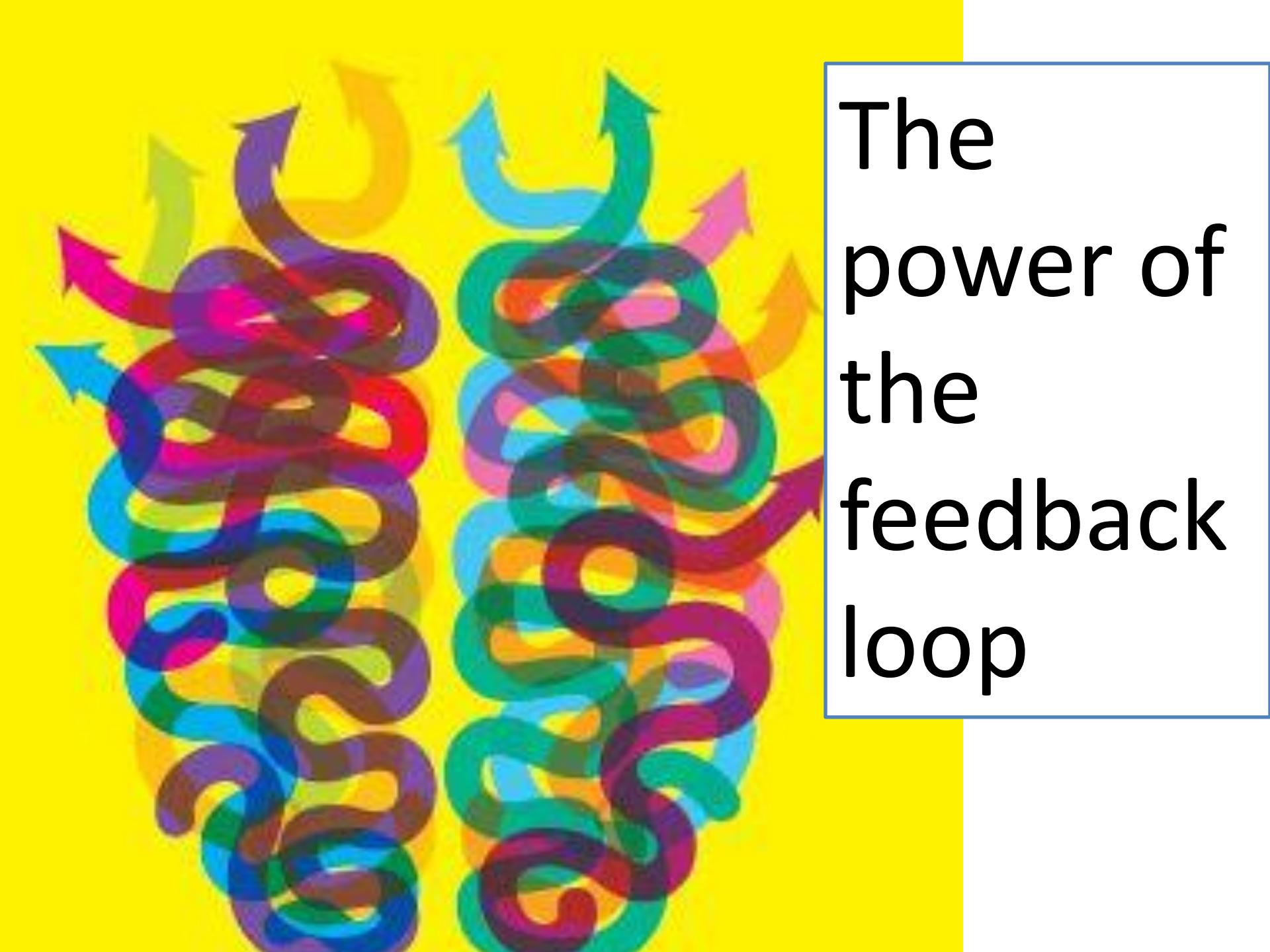
Economist.com/graphicdetail

Sensors have  
the power to  
measure our  
every action



...as self-regulating  
organisms, we can  
profoundly change  
our behaviour once  
we are provided  
with relevant data...

Wired Magazine  
The Feedback Loop Thomas Goetz  
July 2010



The  
power of  
the  
feedback  
loop

# A New Species

HOMO  
DISTRACTUS

(William Powers –  
Hamlet's Blackberry)

Image: [http://whatsnext.nuance.com/wp-content/uploads/homo\\_distractus.jpg](http://whatsnext.nuance.com/wp-content/uploads/homo_distractus.jpg)

A horizontal row of black silhouettes of various people of different ages, ethnicities, and genders, standing side-by-side against a white background.

# The democratization of medicine

# Asymmetry of information flow in medicine is over...



Nothing about me...  
without me

THE PATIENTS KNOW MORE ABOUT  
THEIR DISEASES THAN ME. I MUST  
GET FASTER MODEM, HIGHER  
SPEED INTERNET ACCESS THAN

THEM



Image:

<https://tanyaznamenskaya.files.wordpress.com/2015/09/patienteducation.jpg>

## **Inviting Patients to Read Their Doctors' Notes: A Quasi-experimental Study and a Look Ahead**

Tom Delbanco, MD\*; Jan Walker, RN, MBA\*; Sigall K. Bell, MD; Jonathan D. D...  
Nadine Farag, MS; Henry J. Feldman, MD; Roanne Meilla, MPH; Long Ngo, Ph...  
Neha Trivedi, BS; Elisabeth Vodicka, BA; and Suzanne G. Lev...

**Open patient records.**

- Majority reported an increased sense of control, greater understanding of their medical issues
- Improved recall of their plans for care
- Better preparation for future visits
- Few patients reported being confused, worried or offended by what they read
- Did not increase the workload for doctors



# Viewing Laboratory Test Results Online: Patients' Actions and Reactions

Kate Christensen & Valerie M. Sue

Research | Vol. 5, 2013 | October 3, 2013

*Conclusion: This study demonstrates that patients who view their lab test results online overwhelmingly react **with positive** rather than negative emotions.*

“It’s a simple stress test – I do your blood work, send it to the lab...and never get back to you with the results.”



*“It’s a simple stress test—I do your blood work, send it to the lab,  
and never get back to you with the results.”*

CN  
COLLECTION

D. Sipress, New Yorker, accessed: <http://imgc-cn.artprintimages.com/images/P-473-488-90/67/6740/EC7Z100Z/posters/david-sipress-it-s-a-simple-stress-test-i-do-your-blood-work-send-it-to-the-lab-and-n.jpg>



## Could ePatient Networks Become the Superdoctors of the Future?

As technology allows patients to pool their knowledge, can the collective experience of the sick create better care?



There's something seriously wrong with a health care system that makes patients wait a month or more just to get a doctor's appointment. Fed up with this information bottleneck all too common in the U.S., a new breed of ePatients is crowdsourcing treatment databases online and using mobile technology to access and share health information.

"People are recognizing that they can and need to take an active role in managing their health instead of just sitting by and going to doctor's appointments," says Sean Ahrens, a leader of the ePatient movement who was diagnosed with the inflammatory condition known as Crohn's disease at age 12. His startup, Healthy Labs, launched a site called Crohnology last year that lets people with Crohn's and ulcerative colitis record and share treatments--including medications, dietary changes, even alternative medicine--in a structured database.

# Social Networks

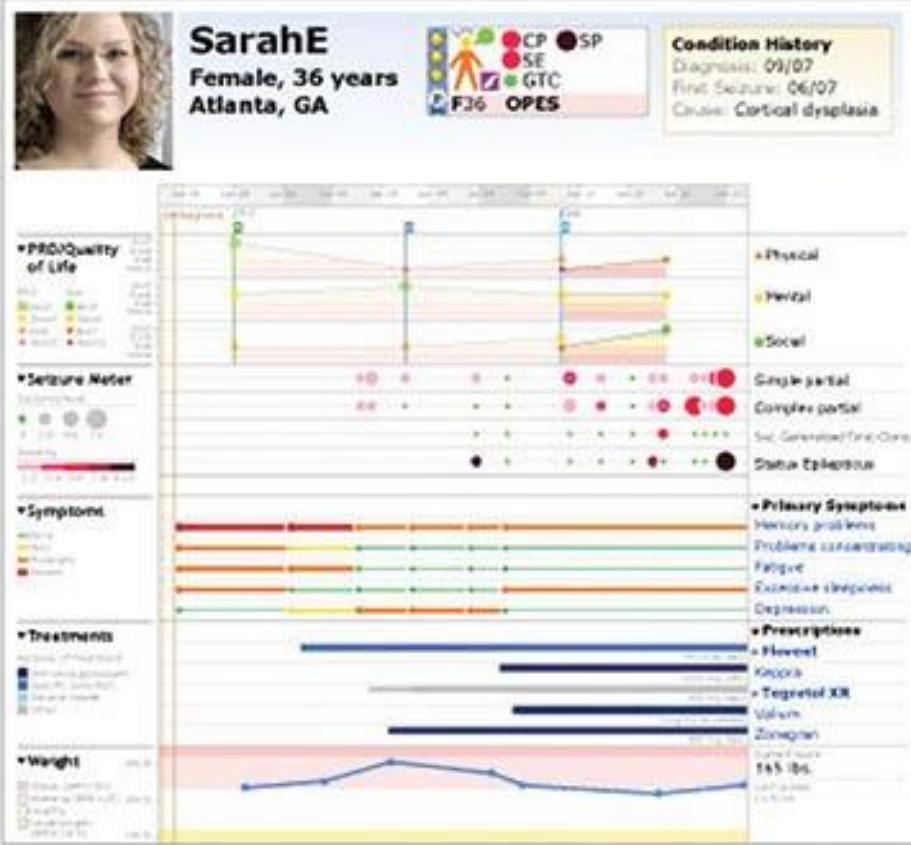


<https://www.patientslikeme.com>

# patientslikeMe®

Join a free online community  
for patients with epilepsy.

## Share Your Health Profile

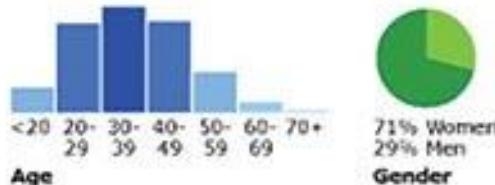


## Find Patients Like You



You can search by epilepsy type, seizure type, symptoms, gender and age to more easily connect with patients like you.

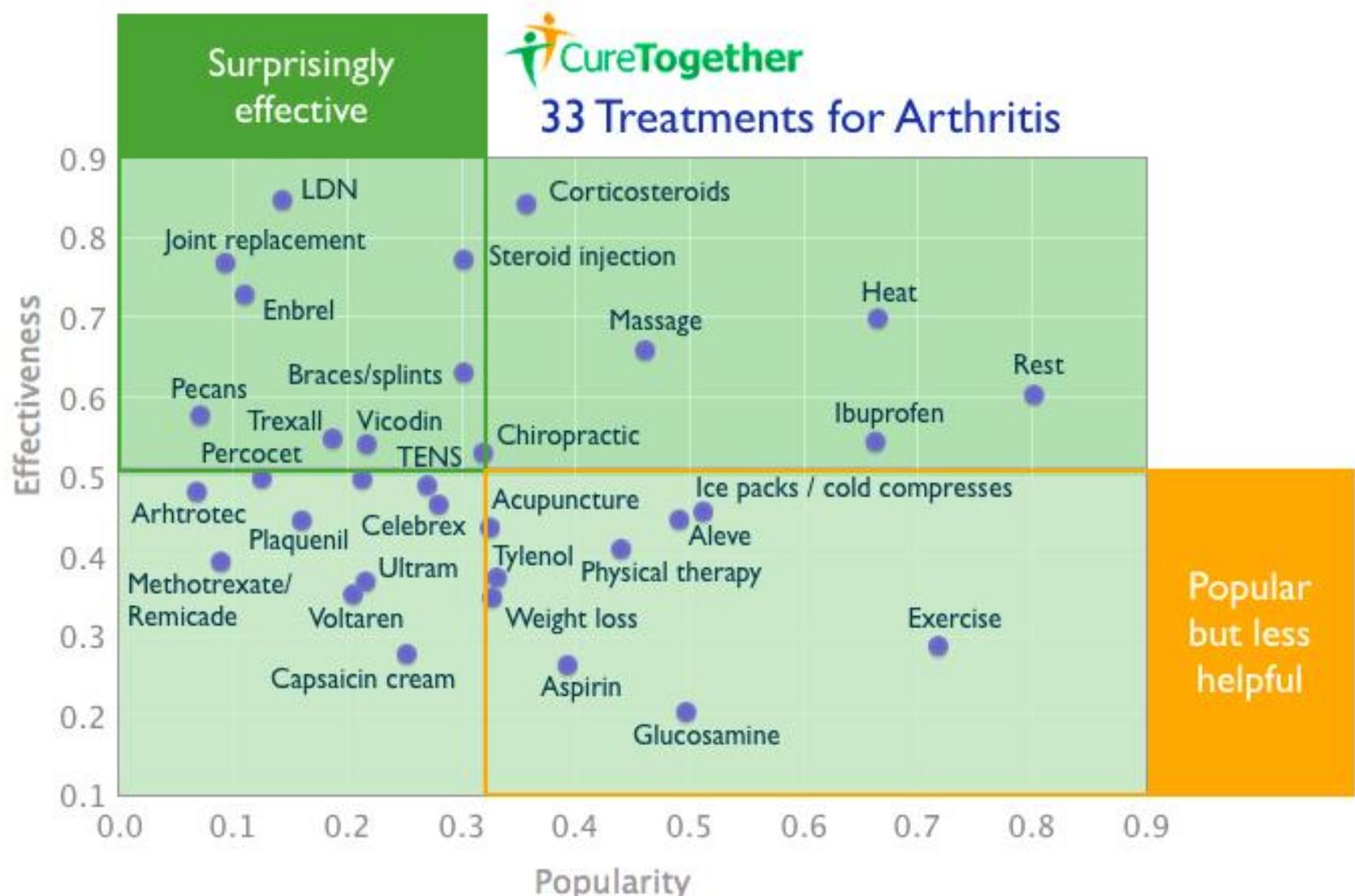
2,354 total patients



The issues that are most important to our patients:



Learn From Real World Patient Experiences



“the idea of going down to  
your doctor’s office is going  
to feel as foreign as going to  
the video store”

Anita Hamilton –”Could ePatient Networks Become the Superdoctors of the Future? – Fast Company:  
<http://www.fastcoexist.com/1680617/could-epatient-networks-become-the-superdoctors-of-the-future>

# Virtual Visits

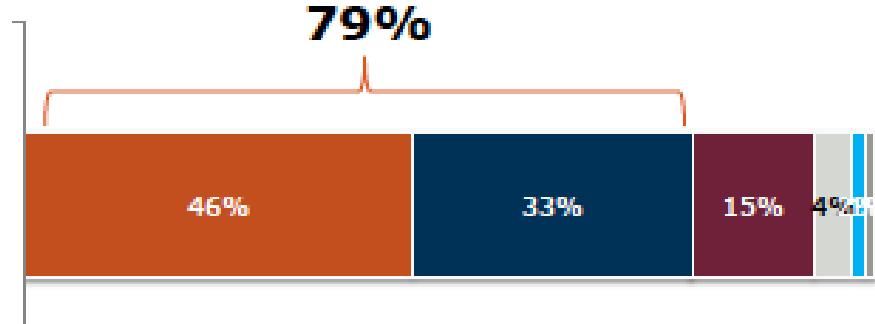
- Kaiser Permanente
  - 8000 doctors
  - 3.4 million members
  - Virtual visits increased from 4.1 million visits in 2011 to 10.5 million in 2012
  - **Projected to exceed 20 million virtual visits by 2016**

70% of surveyed patients preferred virtual visits...

(Cisco study: “The idea of the virtual Doctor visits is Growing on Us” Fierce Health IT, March 7, 2013)

## Attitudes on Virtual Visit Experience

The quality of care I receive from an online visit with a doctor is the same as in an in-person visit.



**patient login**

forgot your password?

**start a visit**[home](#)[for patients](#)[for dermatologists](#)[conditions](#)[our dermatologists](#)[about us](#)[events](#)

September is Head Lice Prevention Month

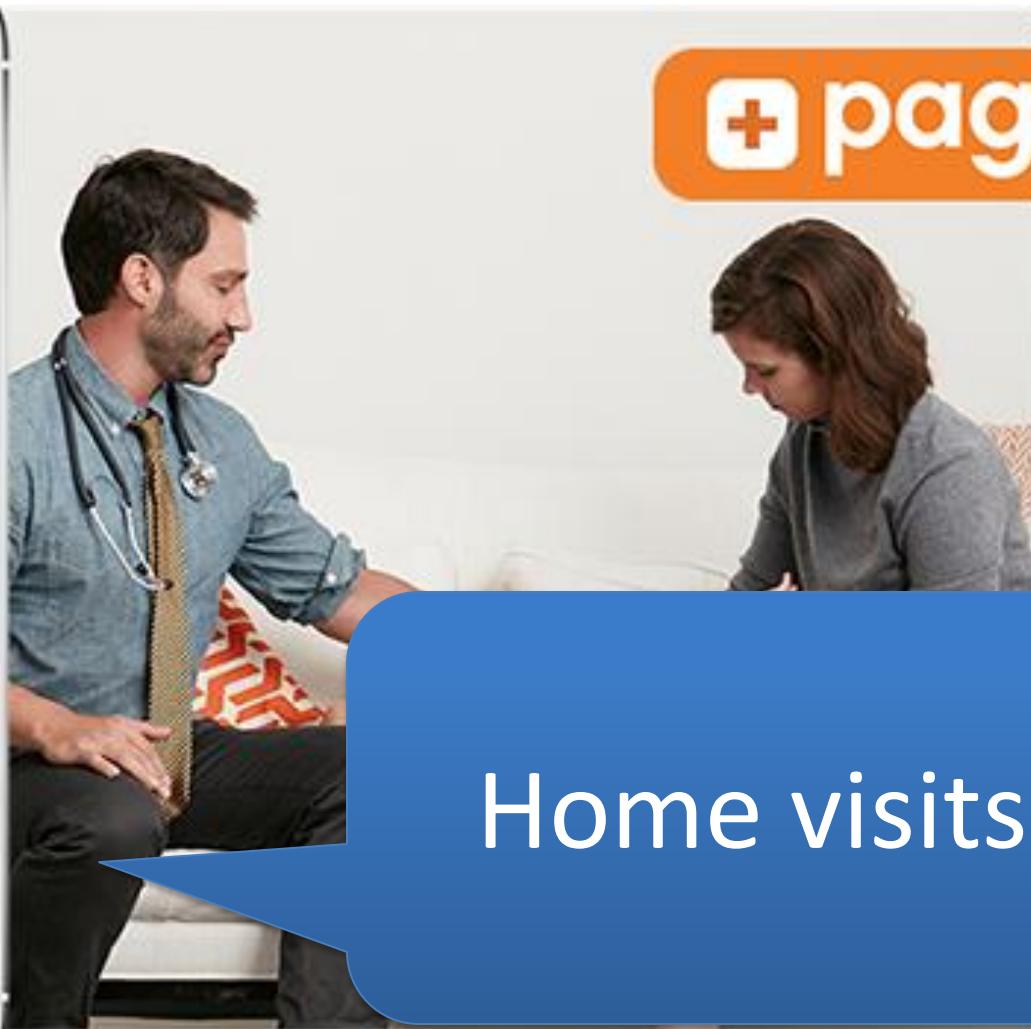
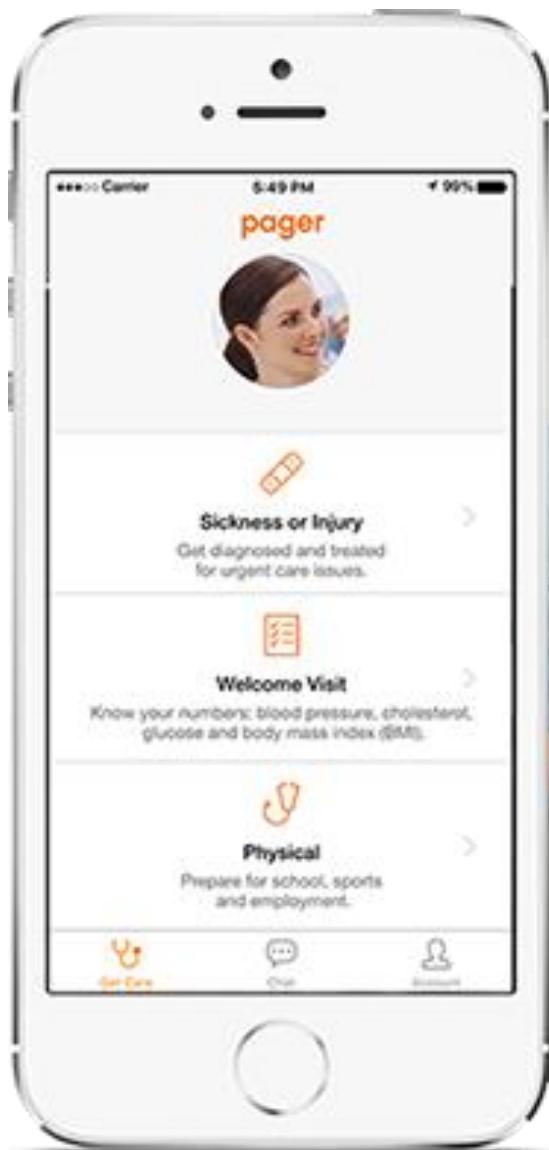
<https://www.dermatologistoncall.com>

## THE DOCTOR WILL SEE YOU NOW

Instant access to board-certified dermatologists.  
A few digital photos are all it takes to get started  
in your quest for a lifetime of healthy skin.

**get started now**

My smartphone Doctor will  
see me now....

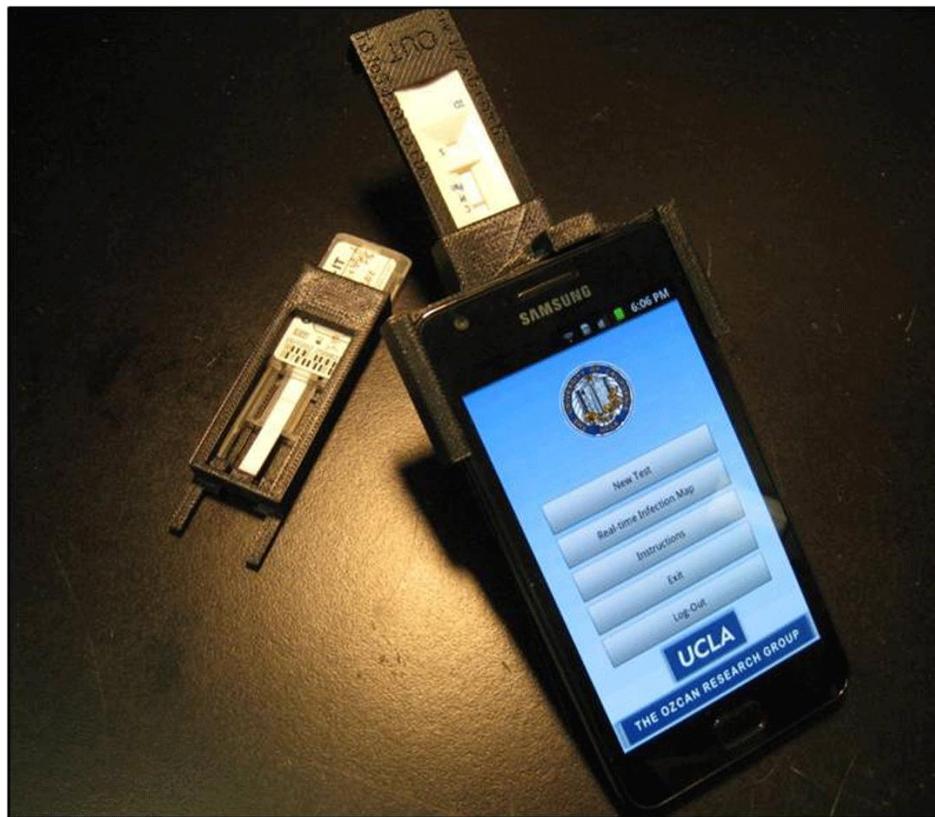


Home visits!

<https://pager.com>

- “I deeply believe it has to be a basic human right for everybody to have access to the kind of testing infrastructure that can tell you about these conditions in time for you to do something about it.”
  - Elizabeth Holmes, CEO of Theranos

# Lab on a Chip



SOUNDING BOARD

## Precision Medicine — Personalized, Problematic, and Promising

J. Larry Jameson, M.D., Ph.D., and Dan L. Longo, M.D.

N ENGL J MED 372;23 NEJM.ORG JUNE 4, 2015

- “Perhaps the most daunting challenge for precision medicine is to **manage the complexity** associated with the progressively refined nosology (classification) of disease.”

## VIEWPOINT

## Will Precision Medicine Improve Population Health?

Muth J. Khourey, MD,  
PhD  
Office of Public Health  
Genomics, Centers for  
Disease Control and  
Prevention, Atlanta, Georgia.

Sandro Galea, MD,  
DrPH  
Boston University  
School of Public Health,  
Boston, Massachusetts.

**Announcement** of the precision medicine initiative has led to a variety of responses, ranging from enthusiastic expectations<sup>1</sup> to explicit skepticism,<sup>2</sup> about potential health benefits, limitations, and return on investment. This Viewpoint discusses whether precision medicine is unlikely or likely to improve population health, aiming to forge a consensus that bridges disparate perspectives on the issue. The potential of precision medicine to improve the health of individuals or small groups of individuals is not addressed here because it involves a different question with different metrics.

### Precision Medicine Is Unlikely to Improve Population Health

There are 3 fundamental reasons why precision medicine might not improve the health of populations. First, disease pathogenesis, especially for common noncommunicable diseases, is extraordinarily complex. Abundant evidence has demonstrated this for the association between the multiplicity of specific genes and conditions, including obesity, hypertension, or certain cancers. Additionally, it is known that genetic associations have, in most instances, small effect sizes in contrast with more robust contributions of behavioral and social factors.

Second, a central promise of precision medicine is the identification of predictors of disease that can help guide interventions. This may prove to be the case for some diseases, especially cancer, but is unlikely to be the case for most other complex diseases. The challenge arises from the mathematical foundations of genetic epidemiology. Although large population studies can identify associations between genotypes and phenotypes, resulting associations have limited capacity to predict phenotype in individuals, which is the ultimate goal of precision medicine. It would take substantially stronger associations—several orders of magnitude greater than have been identified so far—to provide sufficient evidence to improve disease prediction in individuals.

Third, an assumed potential benefit of precision medicine (predicated on accurate and meaningful risk prediction) is that disease in the population can be avoided or forestalled by large numbers of individuals who, when provided with accurate risk prediction, will change their behavior to mitigate their personal risk. Although this may seem intuitively plausible, current data suggest that individuals do not change their behavior much even when they become aware of being in a high-risk group.<sup>3</sup>

Overemphasis on precision medicine by the scientific community and health systems could pose a challenge to the health of populations for other reasons.

First, the United States faces extraordinary challenges to the health of its population. Over the past 30 years, the United States has fallen behind other high-income peer nations in health attainment on many metrics, including life expectancy and infant mortality, and there are persistent gaps in health outcomes by income and race/ethnicity.<sup>4</sup> The solution to these challenges is probably not an increased focus on the individual, but rather involves focusing on the social, economic, and structural drivers of population health that are ubiquitous and inevitably linked to health achievement as a country. The centrality of the precision medicine effort to the US national health research agenda may distract from efforts to remedy the foundational causes of ill health such as poverty, obesity, and education. Without addressing these causes, there will be little, if any, success in reversing the trends of poor achievement in US population health.

Second, precision medicine could (and to some extent has) led to a shift from which projects are funded by health research agencies. Funding for grants with a population health or public health goal has declined over the past 10 years at the National Institutes of Health, whereas funding for -omic research has increased substantially. This shift in funding may lead to an emerging generation of health scientists who see the world through an individualist lens and may not engage in factors that can improve the health of populations.

Third, the promise of precision medicine may lead to other promises such as the recently announced cancer “moonshot,” which may echo previous efforts that have not lived up to expectations. The hype, which could become unrealized health benefits, could lead to disillusionment in the goals of health science, with potentially lasting consequences affecting public confidence and investment in medical research.

**Precision Medicine Can Improve Population Health**  
By contrast, there are 3 fundamental reasons that advances in precision medicine might improve population health. First, population health could improve by applying complementary individual and public health approaches to health care and disease prevention. A focus on the wider environmental and social determinants of health is of great importance in addressing health inequities. However, pitting the health of individuals against the health of populations risks widening an unnecessary divide between medicine and public health. Population health planning requires directing efficient use of resources toward those most at risk. Stratification of populations into risk groups for multiple chronic diseases could provide more efficient and effective prevention and treatment strategies and

# Will Precision Medicine Improve Population Health?

## Unlikely:

1. Disease pathogenesis for non-communicable diseases is extraordinarily complex
2. Genetic associations in most instances have small effect sizes in contrast to behavioural and social factors
3. Behaviour change is difficult even with sufficient data.

Corresponding Author: Muth J. Khourey, MD, PhD, Office of Public Health Genomics, Centers for Disease Control and Prevention, 1600 Clifton Rd, Atlanta, GA 30333 (muk@cdc.gov).

jama.com

JAMA | October 4, 2016 | Volume 316, Number 13

1357

# Will Precision Medicine Improve Population Health?

JAMA October 4, 2016 Volume 316, Number 13

Precision Medicine can improve population health:

1. Population health could improve by complementary individual and public health approaches to disease prevention.
2. Genetically targeted approaches to health has demonstrated benefit (newborn screening)
3. Not limited to genes, drugs and disease – powerful tools for precision public health (better infectious disease identification etc.)

---

Muin J. Khouri, MD,  
PhD  
Office of Public Health  
Genomics, Centers for  
Disease Control and  
Prevention, Atlanta,  
Georgia.

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Sandro Galea, MD,  
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# Will Precision Medicine Improve Population Health?

JAMA October 4, 2016 Volume 316, Number 13

Muin J. Khoury, MD,  
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Disease Control and  
Prevention, Atlanta,  
Georgia.

Sandro Galea, MD,  
DrPH  
Boston University  
School of Public Health,  
Boston, Massachusetts.

## The major challenge:

- how to use emerging information from multiple levels from reductionist molecular markers to holistic macrolevel risk factors (behaviour, environment, policies) – to develop a better understanding of the determinants of health.
- Even with millions of bits of data collected from individuals, it may well be that population-level interventions affecting housing, nutrition, poverty, access to resources and education may have more benefit on health than individualized interventions
- Combination of approaches will be required...

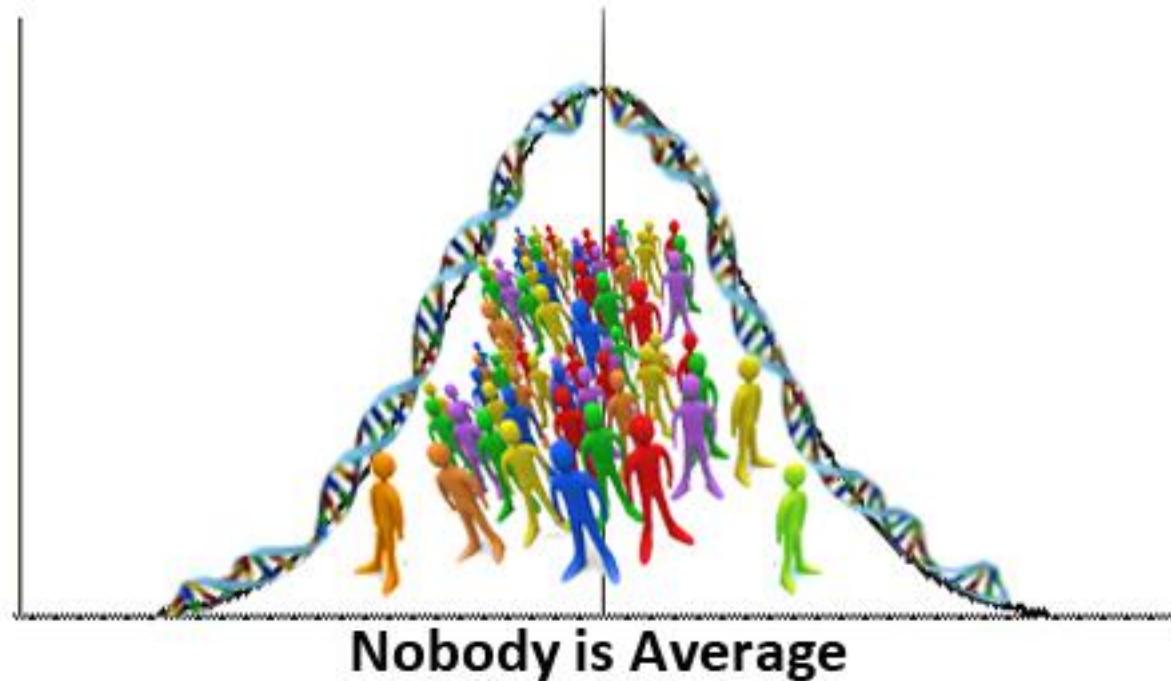


## Genomics and Health Impact Blog

[Home](#)[About this Blog](#)[Archives](#)[Authors](#)

Nobody is average but what to do about it? The challenge of individualized disease prevention based on genomics

Posted on July 2, 2014 by Muin J Khoury, Director, Office of Public Health Genomics, Centers for Disease Control and Prevention



Nobody is Average but what do to about it?

SEPTEMBER 22, 2014

# TIME

## Never Offline.

The Apple Watch is just the start.  
How wearable tech will change  
your life—like it or not

BY LEV GROSSMAN  
AND MATT VELLA

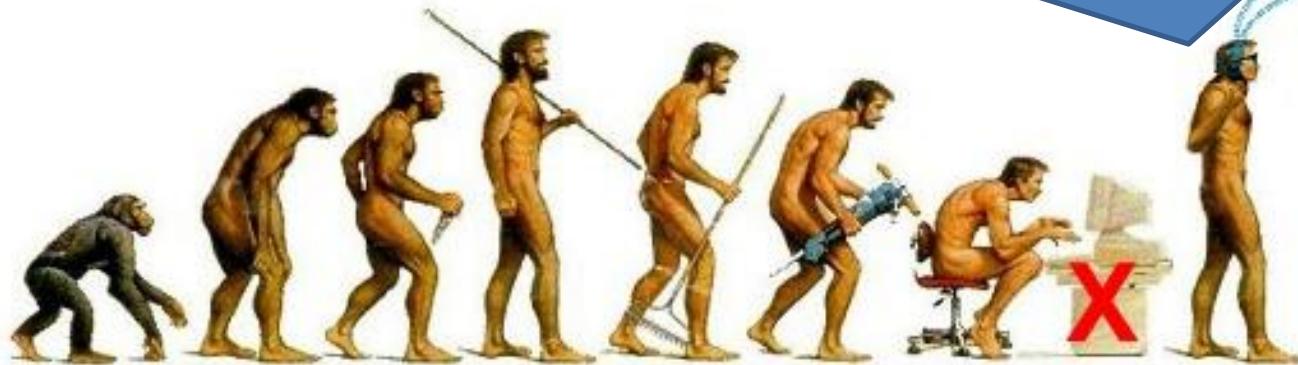


time.com

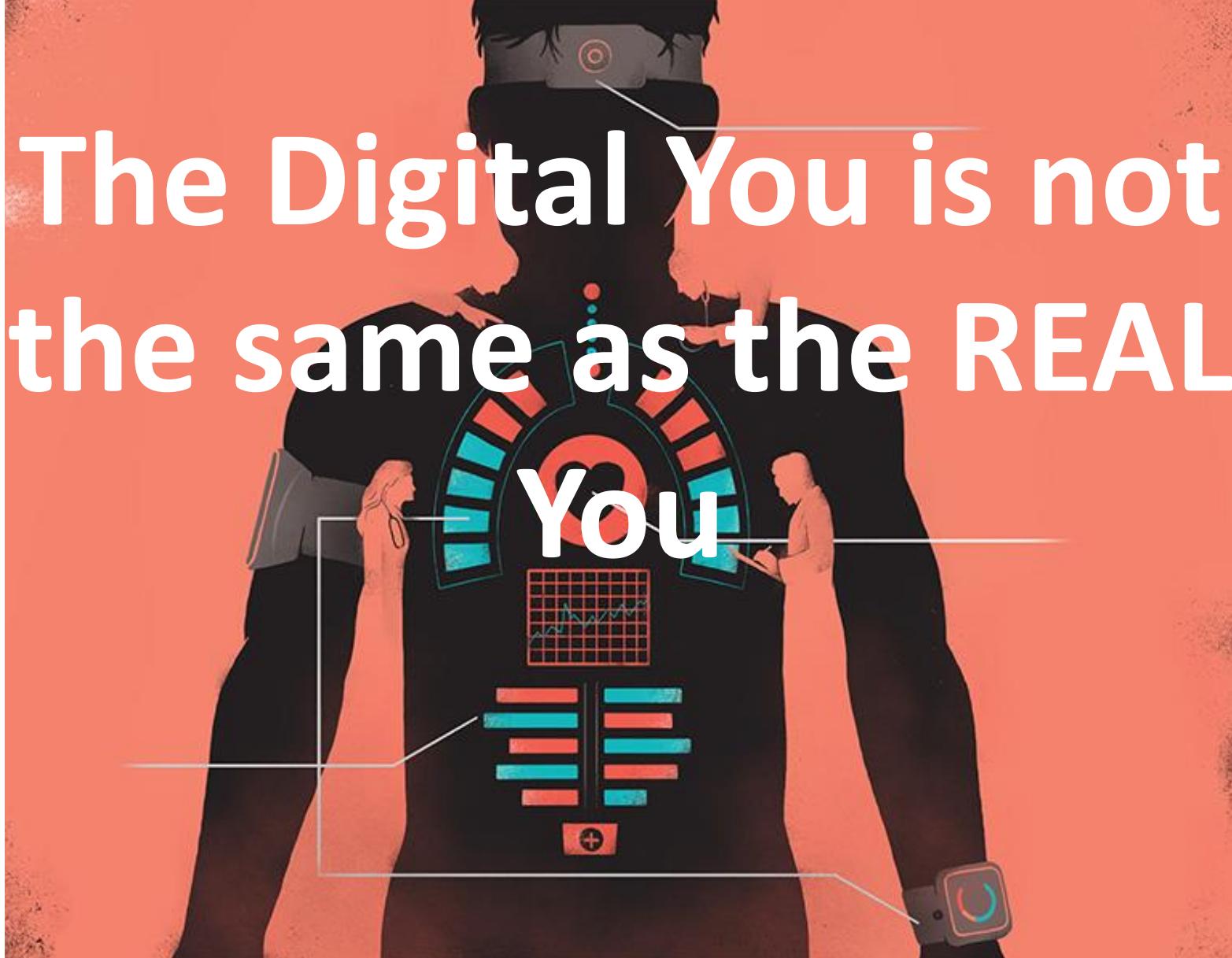
Is this really  
good thing??

“Eventually we won’t need a doctor...Machine learning makes a better Dr. House than Dr. House”

Vinod Kholsa



*“Homo sapiens have had it, Homo digitus\* is the future”*



The Digital You is not  
the same as the REAL  
You

“It is more important to  
know what **sort of person**  
**has a disease** than to know  
what sort of disease a  
person has.”

Hippocrates



**HEALTH** | CASES

# Not on the Doctor's Checklist, but Touch Matters

DANIELLE OFRI and M.D. AUG. 2, 2010

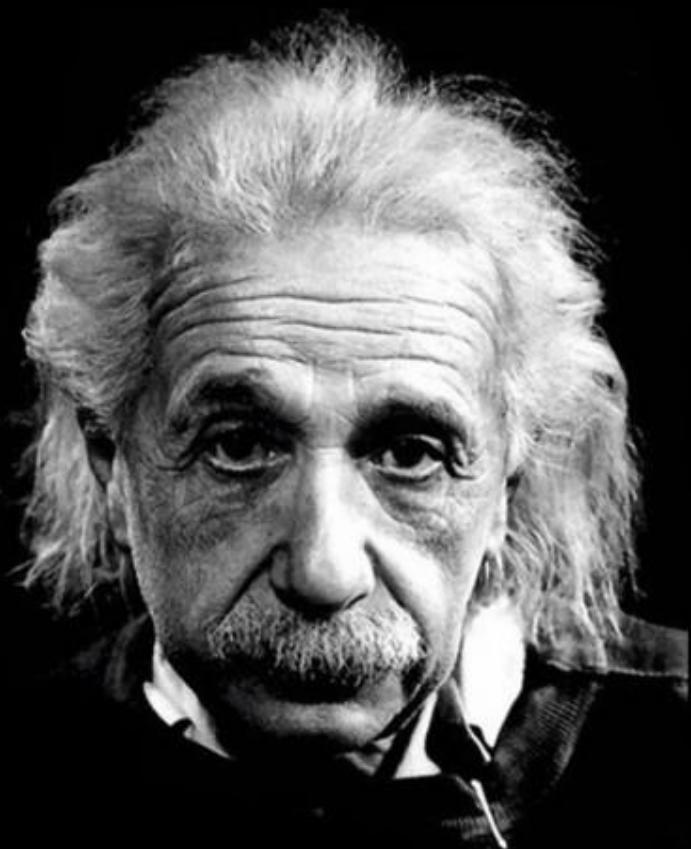
[http://www.nytimes.com/2010/08/03/health/03case.html?\\_r=0](http://www.nytimes.com/2010/08/03/health/03case.html?_r=0)



# Digital Dystopia

- Risk of hacked individualized information – genomics, biosensor info (legislation still very far behind)
- A world of Cyberchondriacs???
- Ethical dilemmas – prenatal screening
- Privacy? / Security of genetic data?
- Genetic discrimination by insurance and employers??

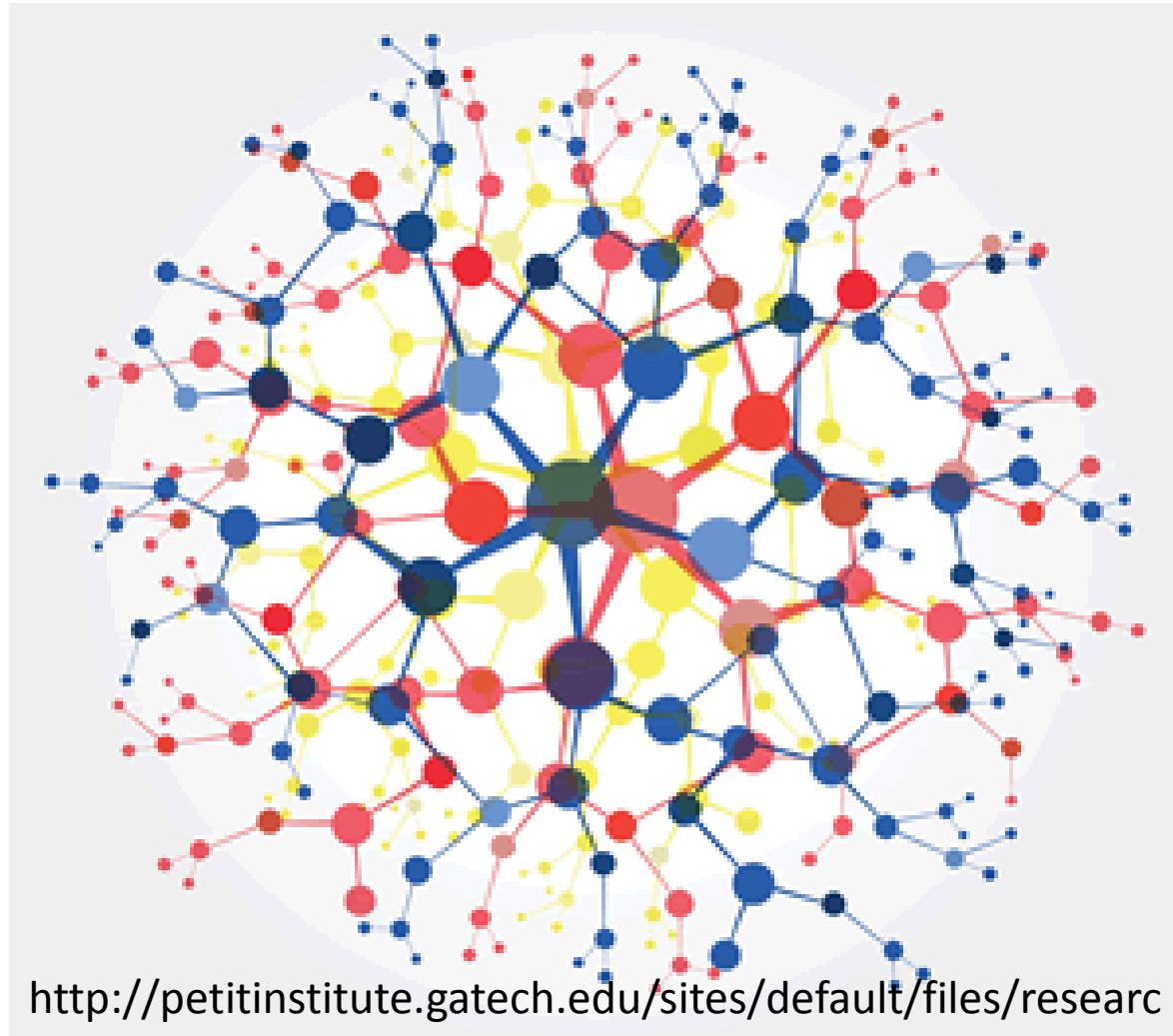
We need to change  
our thinking...



We can't solve problems  
by using the same kind  
of thinking we used  
when we created them.

<https://stcutcher.files.wordpress.com/2015/03/distributed-captive-solaris-smarter-thinking-1024x612.jpg?w=948&h=566>

# Disease centric to a systems biology, whole person approach



# New Operating System for 21<sup>st</sup> Century Medicine

“**Functional medicine** represents an **operational system** that focuses on the underlying causes of disease from a **systems biology** perspective that engages the patient and practitioner in a **therapeutic partnership**”

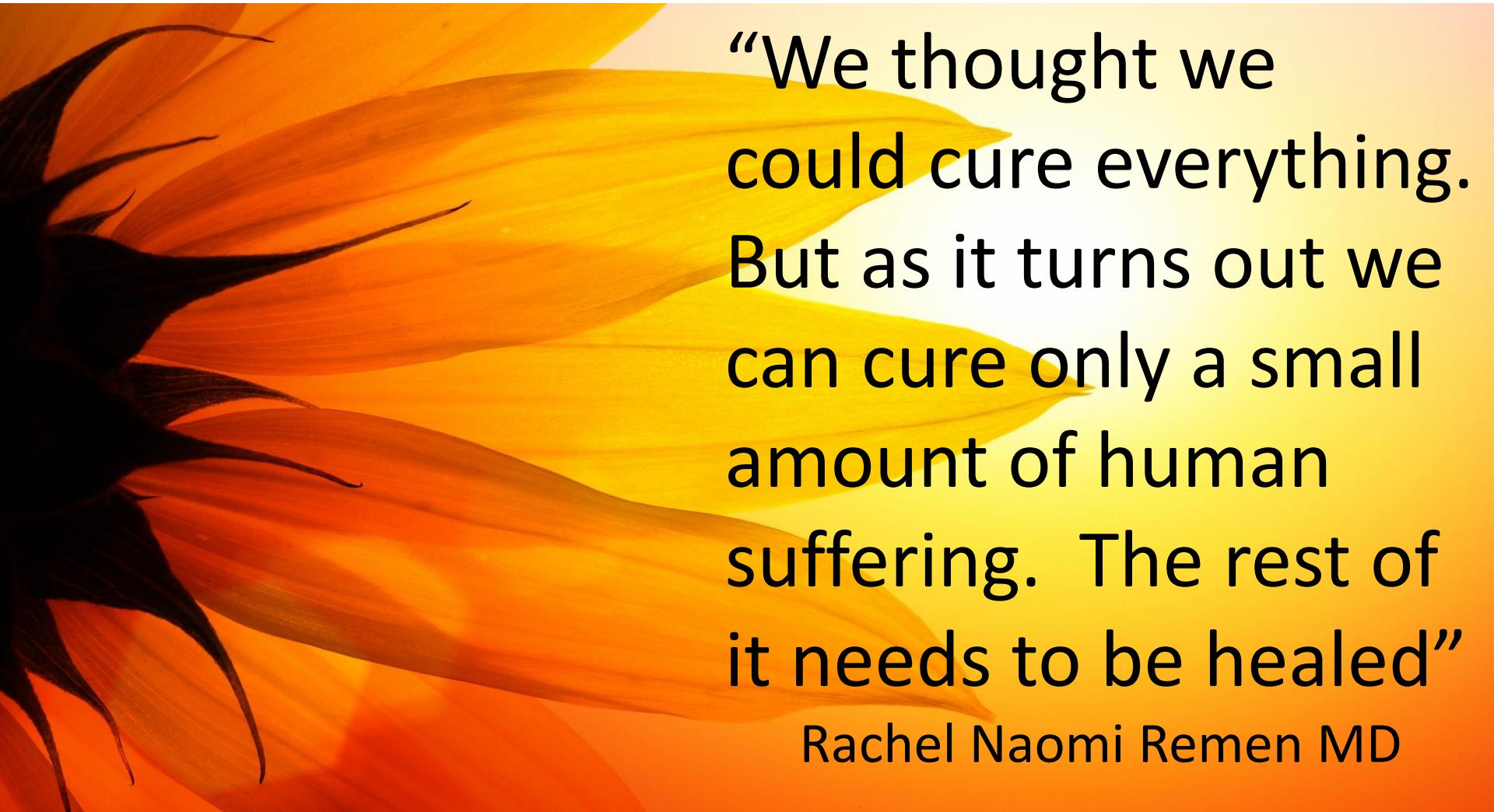
- Institute of Functional Medicine:  
Jones DS, Bland JS, Quinn S. What is functional medicine? In: Institute for Functional Medicine et al, eds. Textbook of Functional Medicine. Federal Way, WA: Institute for Functional Medicine; 2010:5-14.

# Future of Medicine Evolution or Revolution

“...we have rejected the wisdom of ancient medicine, failing to recognize the interconnected web not only between, mind, body, spirit but also between individual, community , and planet.”

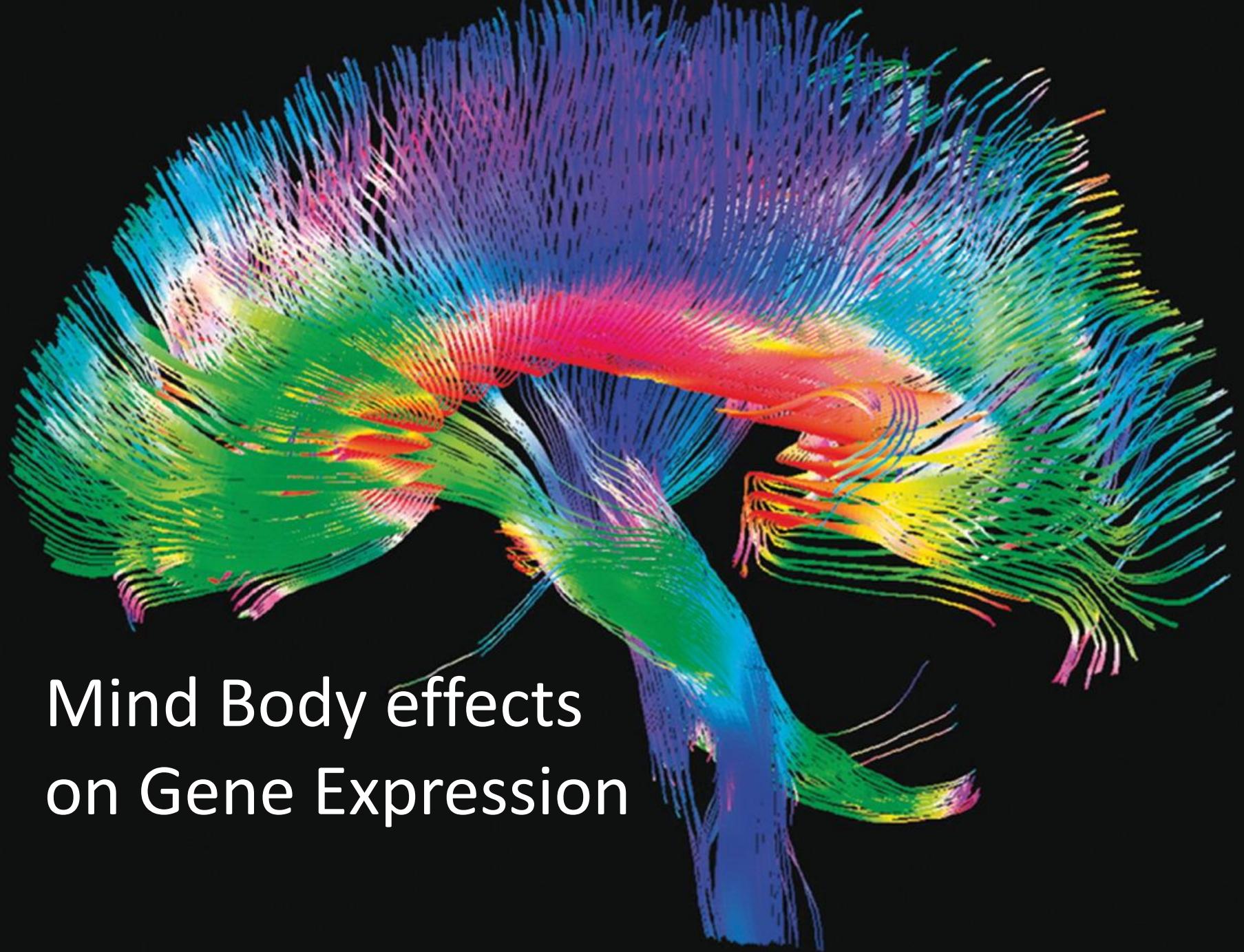
Michael Finkelstein MD: Future of Medicine: Evolution or Revolution ([http://www.huffingtonpost.com/michael-finkelstein-md/the-future-of-medicine-evolution-or-revolution\\_b\\_8993128.html](http://www.huffingtonpost.com/michael-finkelstein-md/the-future-of-medicine-evolution-or-revolution_b_8993128.html))

# Healing

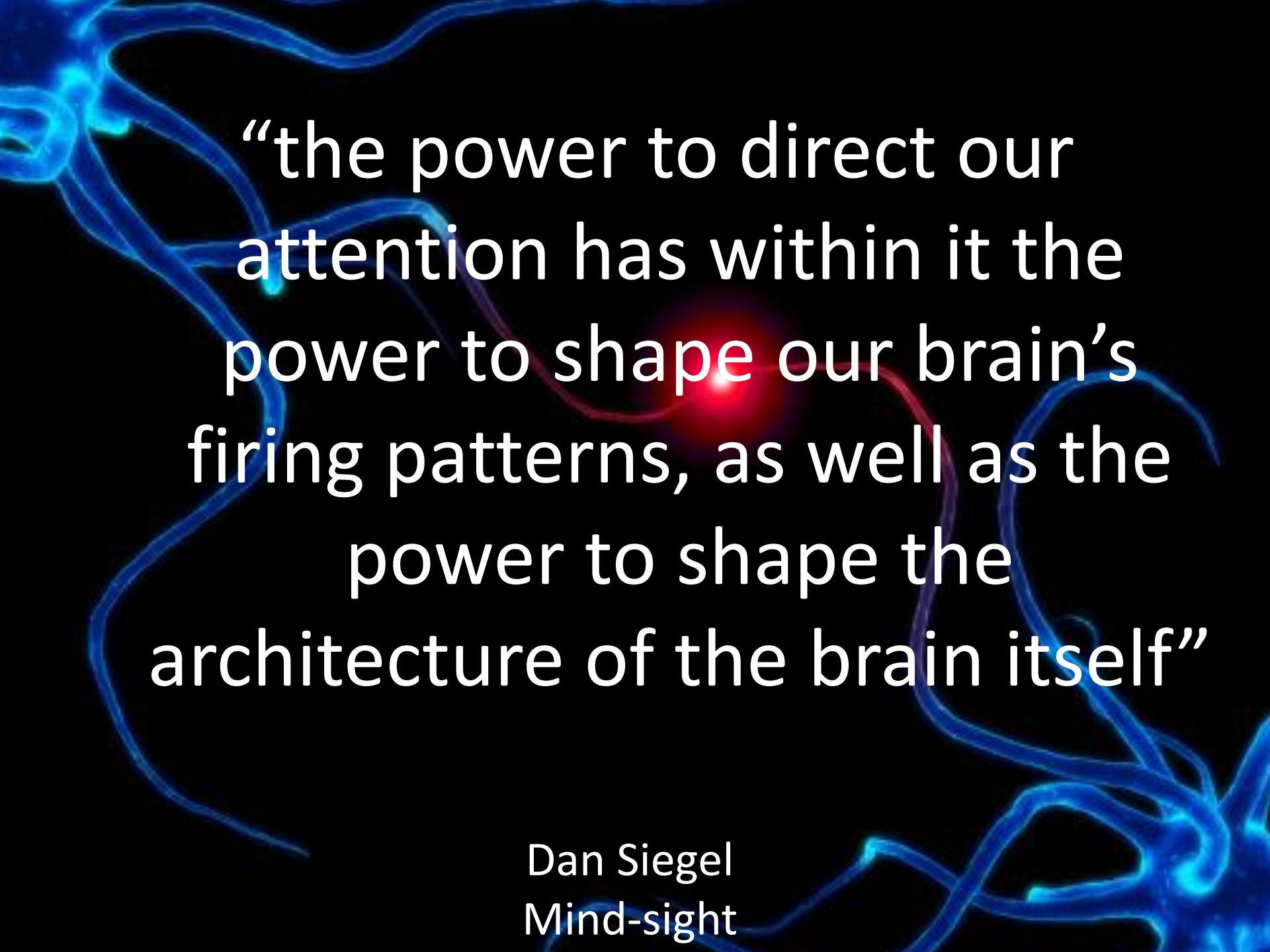


“We thought we could cure everything. But as it turns out we can cure only a small amount of human suffering. The rest of it needs to be healed”

Rachel Naomi Remen MD



Mind Body effects  
on Gene Expression



“the power to direct our attention has within it the power to shape our brain’s firing patterns, as well as the power to shape the architecture of the brain itself”

Dan Siegel  
Mind-sight

**“**

**NEUROPLASTICITY PROVIDES US WITH  
A BRAIN THAT CAN ADAPT NOT ONLY  
TO CHANGES INFILCTED BY DAMAGE,  
BUT ALLOWS ADAPTATION TO ANY AND  
ALL EXPERIENCES AND CHANGES WE  
MAY ENCOUNTER...**

STRESS

# Mindfulness Can Literally Change Your Brain

by Christina Congleton, Britta K. Hölzel, and Sara W. Lazar

JANUARY 08, 2015

Neuroscientists have also shown that practicing mindfulness affects brain areas related to perception, body awareness, pain tolerance, emotion regulation, introspection, complex thinking, and sense of self.

<https://hbr.org/2015/01/mindfulness-can-literally-change-your-brain>



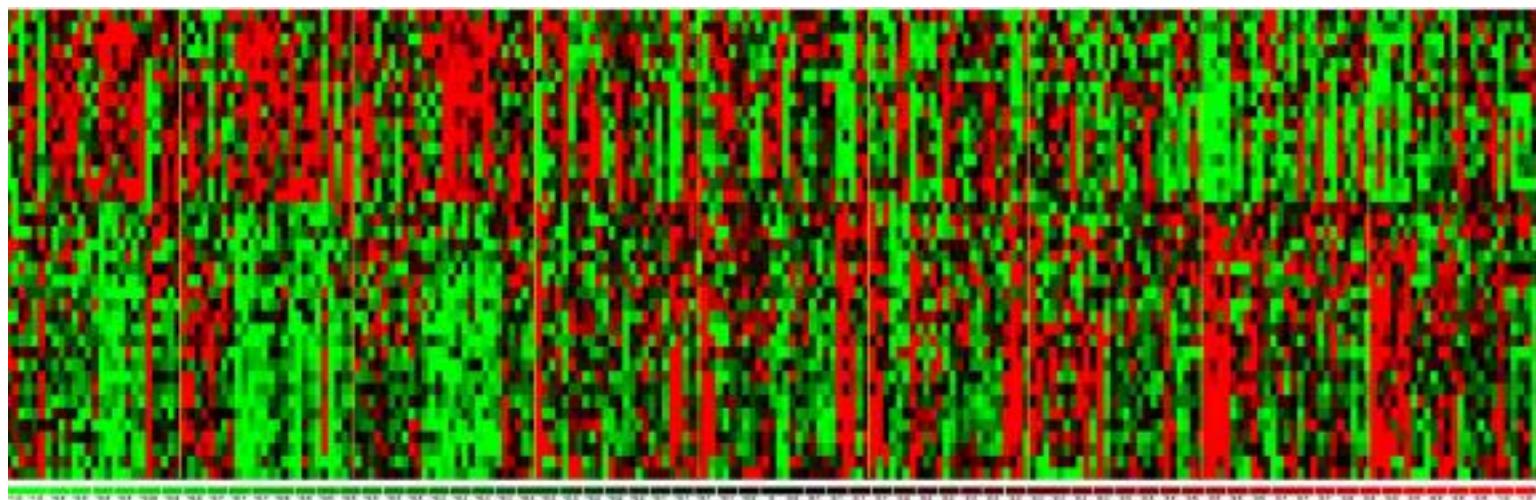
<https://www.wired.com/2006/02/dalai/>

# Mind-body genomics

---

## Relaxation Response Induces Temporal Transcriptome Changes in Energy Metabolism, Insulin Secretion and Inflammatory Pathways

Manoj K. Bhasin<sup>1,4,5\*</sup>, Jeffery A. Dusek<sup>6\*</sup>, Bei-Hung Chang<sup>7,8\*</sup>, Marie G. Joseph<sup>5</sup>, John W. Denninger<sup>1,2</sup>, Gregory L. Fricchione<sup>1,2</sup>, Herbert Benson<sup>1,3†</sup>, Towia A. Libermann<sup>1,4,5\*†</sup>



Bhasin MK, Dusek JA, Chang B-H, Joseph MG, Denninger JW, et al. (2013) Relaxation Response Induces Temporal Transcriptome Changes in Energy Metabolism, Insulin Secretion and Inflammatory Pathways. PLoS ONE 8(5): e62817. doi:10.1371/journal.pone.0062817

# Methods

- 26 subjects – no previous experience with relaxation-response practices
  - 8 weekly sessions (mindfulness meditation, mantra, breathwork)
  - 20 minute audio CD practice daily
- 26 subjects – with 4 – 20 years or experience (meditation, yoga, repetitive prayer)
- Blood samples for gene translation collected
  - Before 20 minute session
  - Immediately after
  - 15 minutes after completion

# Results

- Rapid changes in gene translation (in minutes) are induced
- Genes linked:
  - Energy metabolism
  - Mitochondrial function
  - Oxidation reduction
  - Insulin secretion
  - Down regulation of NF-KB (inflammation)

# Genomic Stability

- Long term practice up-regulated pathways associated with:
  - Genomic stability
    - Telomere packing, maintenance



# **Neuroprotective effects of yoga practice: age-, experience-, and frequency-dependent plasticity**

*Chantal Villemure<sup>1,2\*†</sup>, Marta Čeko<sup>1,3†</sup>, Valerie A. Cotton<sup>1,3</sup> and M. Catherine Bushnell<sup>1,2,4</sup>*

<sup>1</sup> National Center for Complementary and Integrative Health, National Institutes of Health, Bethesda, MD, USA, <sup>2</sup> Faculty of Dentistry, McGill University, Montreal, QC, Canada, <sup>3</sup> Integrated Program in Neuroscience, McGill University, Montreal, QC, Canada, <sup>4</sup> Department of Anesthesia, McGill University, Montreal, QC, Canada

- Yogis had larger brain volume in:
  - somatosensory cortex (mental map of the body)
  - Superior parietal cortex (directing attention)
  - Visual cortex
  - Hippocampus (dampening stress)
  - Precuneus / posterior cingulate cortex (concept of self)

# Genomic Counter-Stress Changes Induced by the Relaxation Response

Jeffery A. Dusek<sup>1,2,3,6\*</sup>, Hasan H. Otu<sup>3,4\*</sup>, Ann L. Wohlhueter<sup>1</sup>, Manoj Bhasin<sup>3,4</sup>, Luiz F. Zerbini<sup>3,4</sup>, Marie G. Joseph<sup>4</sup>, Herbert Benson<sup>1,3,5\*</sup>, Towia A. Libermann<sup>3,4\*</sup>

- It is becoming increasingly clear that **psychosocial stress** can manifest as system-wide perturbations of cellular processes, generally **increasing oxidative stress** and promoting a **pro-inflammatory milieu**

Dusek JA, Otu HH, Wohlhueter AL, Bhasin M, Zerbini LF, Joseph MG, et al. (2008) Genomic Counter-Stress Changes Induced by the Relaxation Response. PLoS ONE 3(7): e2576. doi:10.1371/journal.pone.0002576

# Gratitude and the brain

- Gratitude and generosity go hand in hand at a psychological and neurobiological level
- Increase brain activity in anterior cingulate cortex and medial prefrontal cortex (feelings of reward, moral cognition, fairness..)

## Neural correlates of gratitude

Glenn R. Fox\*, Jonas Kaplan, Hanna Damasio and Antonio Damasio

Department of Psychology, Brain and Creativity Institute, University of Southern California, Los Angeles, CA, USA



Photo:<http://nymag.com/scienceofus/2016/01/how-expressing-gratitude-change-your-brain.html>

## The Emerging Field of Human Social Genomics

**George M. Slavich<sup>1</sup> and Steven W. Cole<sup>1,2</sup>**

<sup>1</sup>Cousins Center for Psychoneuroimmunology and Department of Psychiatry and Biobehavioral Sciences, University of California, Los Angeles, and <sup>2</sup>Department of Medicine, Division of Hematology-Oncology, UCLA Molecular Biology Institute, Jonsson Comprehensive Cancer Center, and UCLA AIDS Institute, University of California, Los Angeles

Clinical Psychological Science  
1(3) 331–348

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DOI: [10.1177/2167702613478594](https://doi.org/10.1177/2167702613478594)  
<http://cpx.sagepub.com>



Love + Connection matters...

“Genes influence behavior,  
we reckon, but not the other  
way around.”

Slavich G, Cole, S. The Emerging Field of Human Social Genomics, Clinical Psychological Science 1(3) 331-348, 2013

# Subjective experience

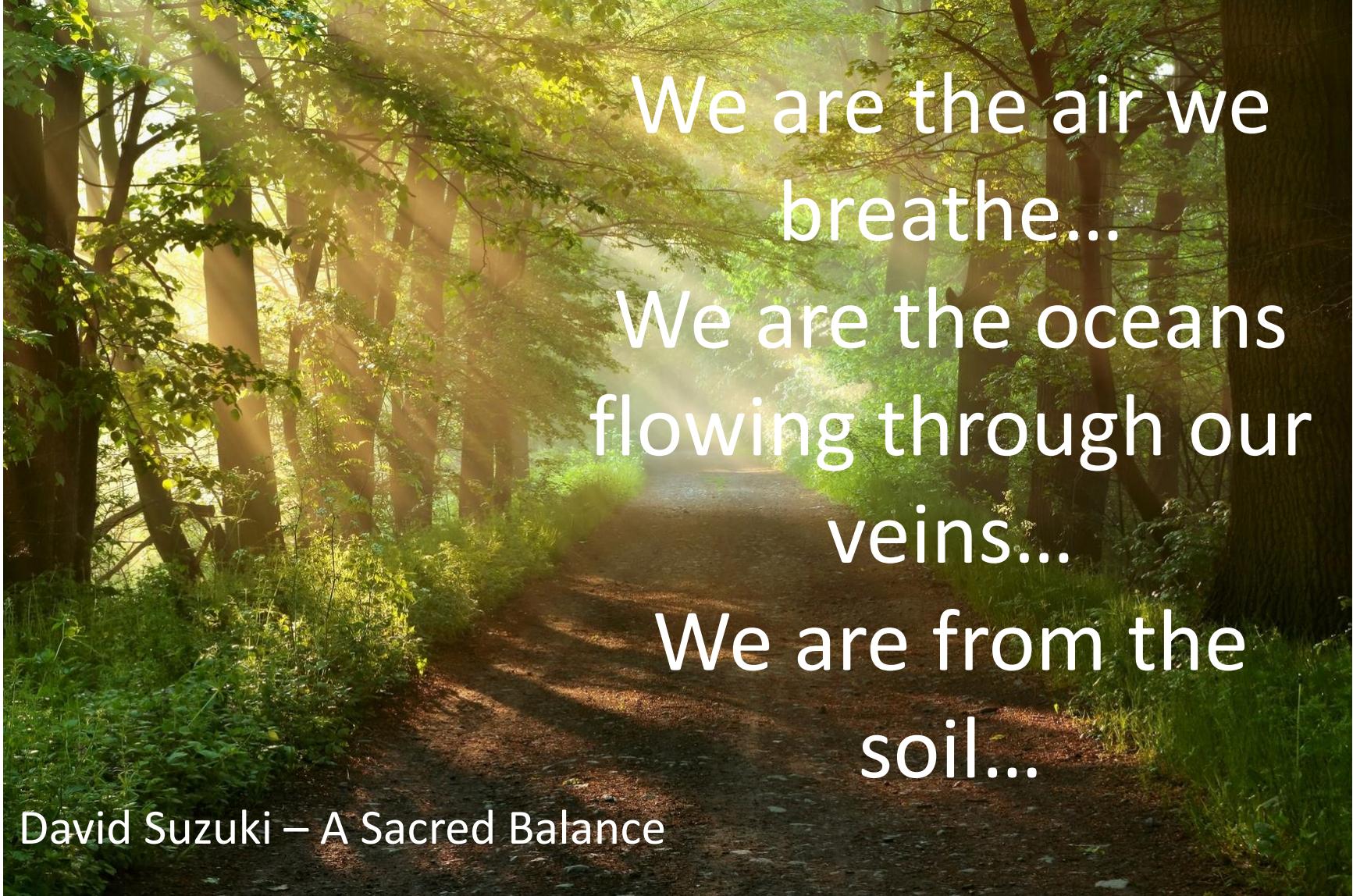
- “Moreover, it appears that these effects are often more strongly tied to **people’s subjective perceptions** of their surrounding social environment (e.g. feeling lonely) than to “objective features of those environments (e.g. being single)

Slavich G, Cole, S. The Emerging Field of Human Social Genomics, Clinical Psychological Science 1(3) 331-348, 2013

# Expanding Identity

“cultivating our capacity to sense energy and information flow helps us **expand** the “self” beyond the boundaries of our body and reveals the fundamental truth that we are indeed part of an interconnected world.”

Daniel Siegel



We are the air we  
breathe...

We are the oceans  
flowing through our  
veins...

We are from the  
soil...

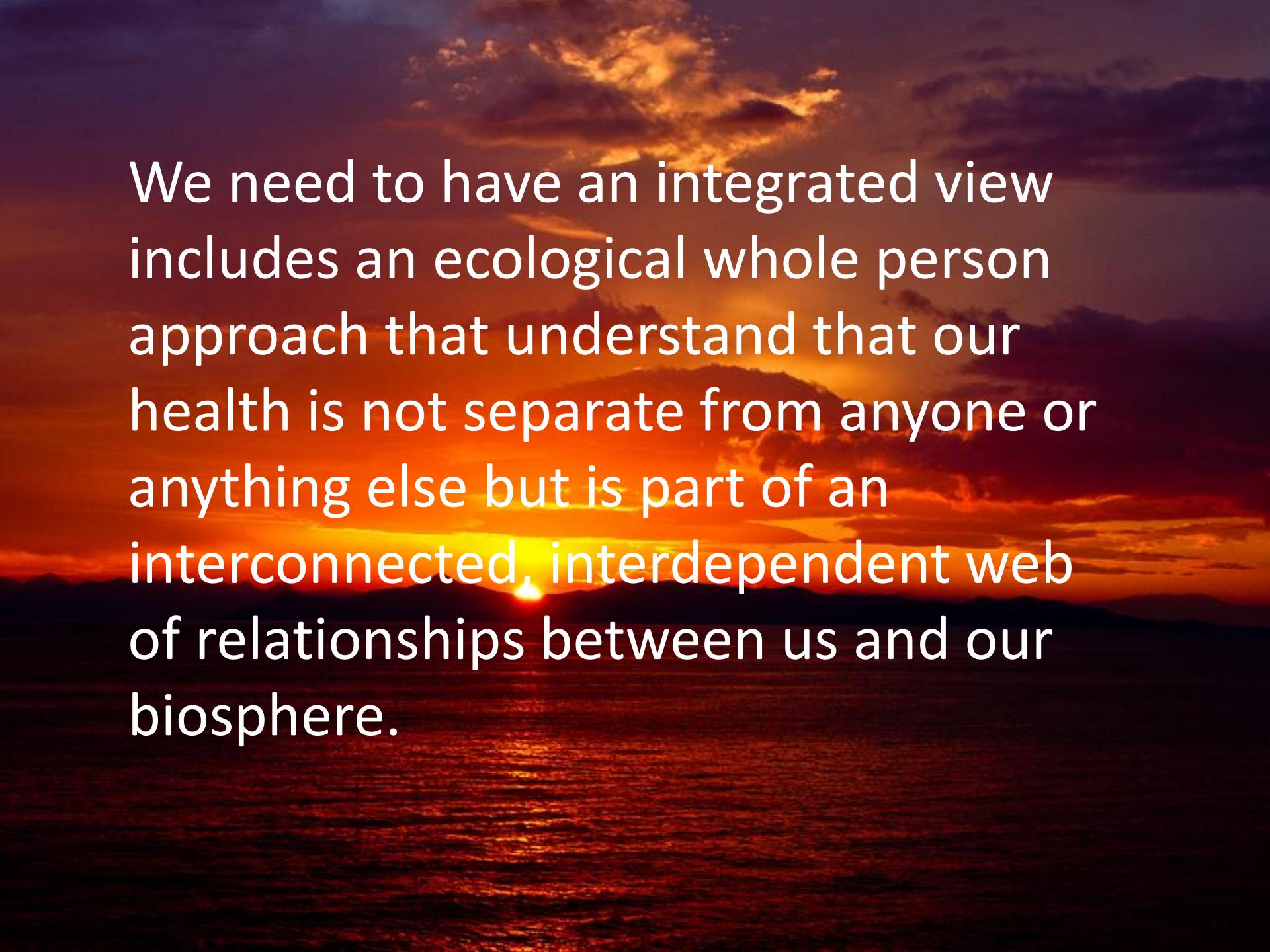
David Suzuki – A Sacred Balance



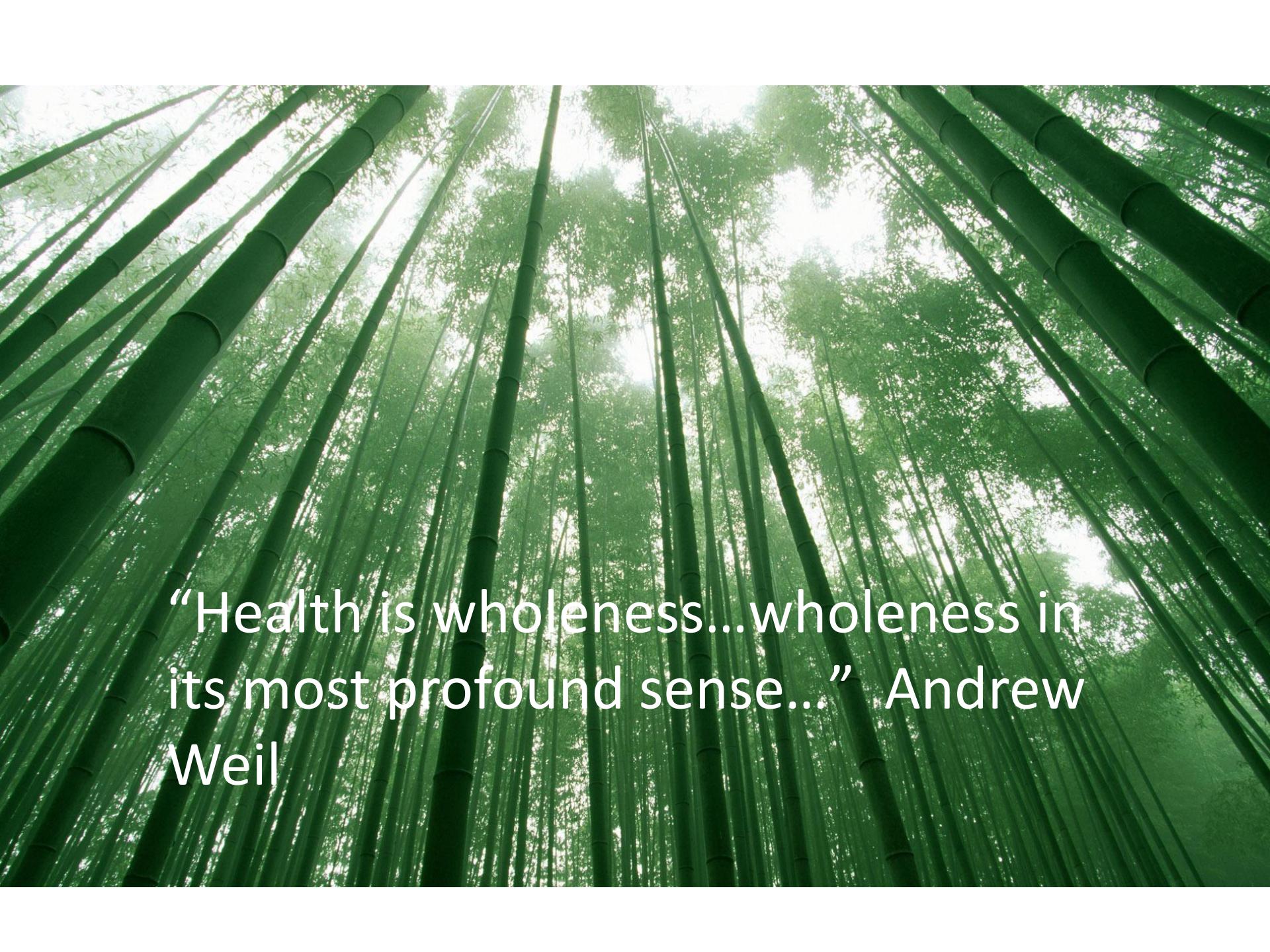
Our Health is not separate  
from our Planet's Health

# Call to Action

We need to ensure that we don't over rely on technology and forget the person. We need to resist the temptation to continue the reductionist paradigm and think that everything can be understood by zeros and ones.

A photograph of a sunset or sunrise over a body of water, likely a lake or sea. The sky is filled with dramatic, orange and yellow clouds, with the sun partially visible on the horizon. In the distance, dark silhouettes of mountains are visible against the bright sky.

We need to have an integrated view  
includes an ecological whole person  
approach that understand that our  
health is not separate from anyone or  
anything else but is part of an  
interconnected, interdependent web  
of relationships between us and our  
biosphere.

A photograph of a bamboo forest from a low angle, looking up. The bamboo stalks are numerous, thin, and light green, creating a dense, vertical pattern that reaches towards a bright, overexposed sky.

“Health is wholeness...wholeness in  
its most profound sense...” Andrew  
Weil