"Individual, Consumer-Driven Care of the Future -- Taking Wellness One Step Further"

Closing Keynote Address

The World Congress 2nd Annual Leadership Conference

On Integrated Delivery Systems

San Diego, CA

May 7, 2014

Dr. Larry Smarr

Director, California Institute for Telecommunications and Information Technology

Harry E. Gruber Professor,

Dept. of Computer Science and Engineering

Jacobs School of Engineering, UCSD

http://lsmarr.calit2.net

Where I Believe We are Headed: Predictive, Personalized, Preventive, & Participatory Medicine

Newsweek

I am Lee Hood's Lab Rat!

A Doctor's Vision of the Future of Medicine

Leroy Hood
NEWSWEEK

From the magazine issue dated Jul 13, 2009



How Will the *Quantified Consumer* Be Integrated into Healthcare Systems?

www.newsweek.com/2009/06/26/a-doctor-s-vision-of-the-future-of-medicine.html

Early Adopting MDs Are Creating Partnerships with Their Quantified Patients

- **"The 100 participants will be guided on this 9-month journey by a coach and when necessary, be referred to their own health care practitioners."**
- **The data sets that will be evaluated include:**
  - **Self-Tracking Devices**
  - **Medical History, Traits, Lifestyle**
  - **Blood, Urine, Saliva**
  - **Gut Microbiome**
  - **Whole Genome Sequencing**



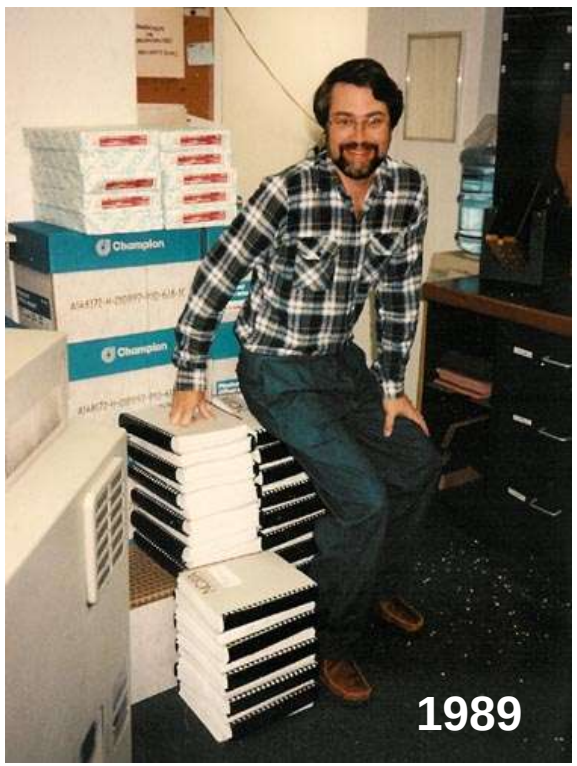
Will Grow to 1000, then 10,000

There are 8760 Hours in a Year
One of These Hours You Are With a Doctor…
The Other 8759 Hours Are Up to You!

https://pioneer100.systemsbiology.net/

My Decade Long Journey to Being a Quantified Self: I Arrived in La Jolla in 2000 After 20 Years in the Midwest

Age 41



Age 51



Age 61



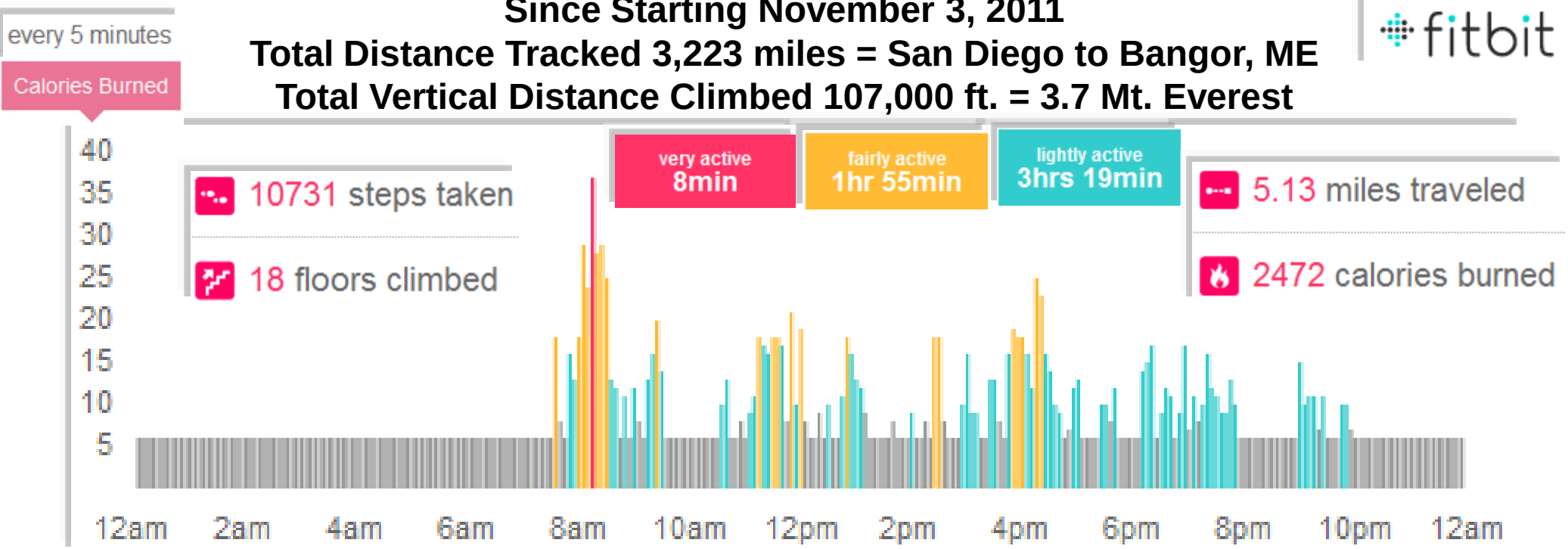
I Reversed My Body's Decline By Quantifying and Altering Nutrition, Exercise, Sleep, and Stress

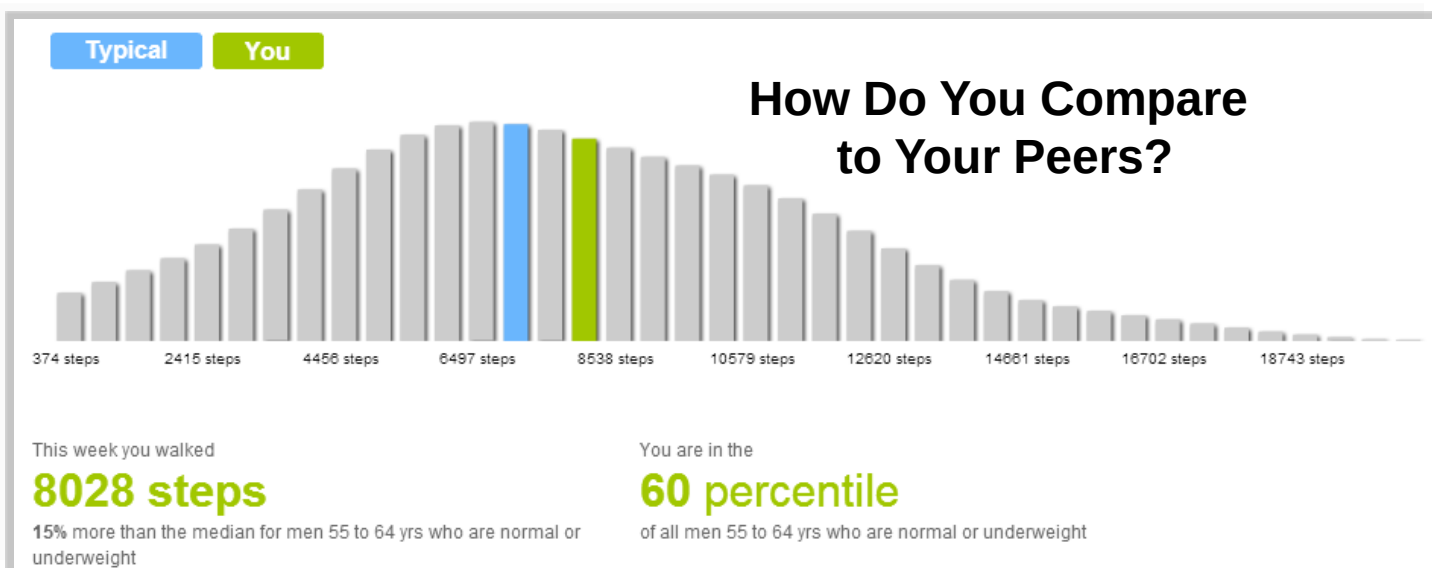
http://lsmarr.calit2.net/repository/LS_reading_recommendations_FiRe_2011.pdf

Wireless Monitoring
Helps Drive Exercise Goals

Since Starting November 3, 2011
Total Distance Tracked 3,223 miles = San Diego to Bangor, ME
Total Vertical Distance Climbed 107,000 ft. = 3.7 Mt. Everest

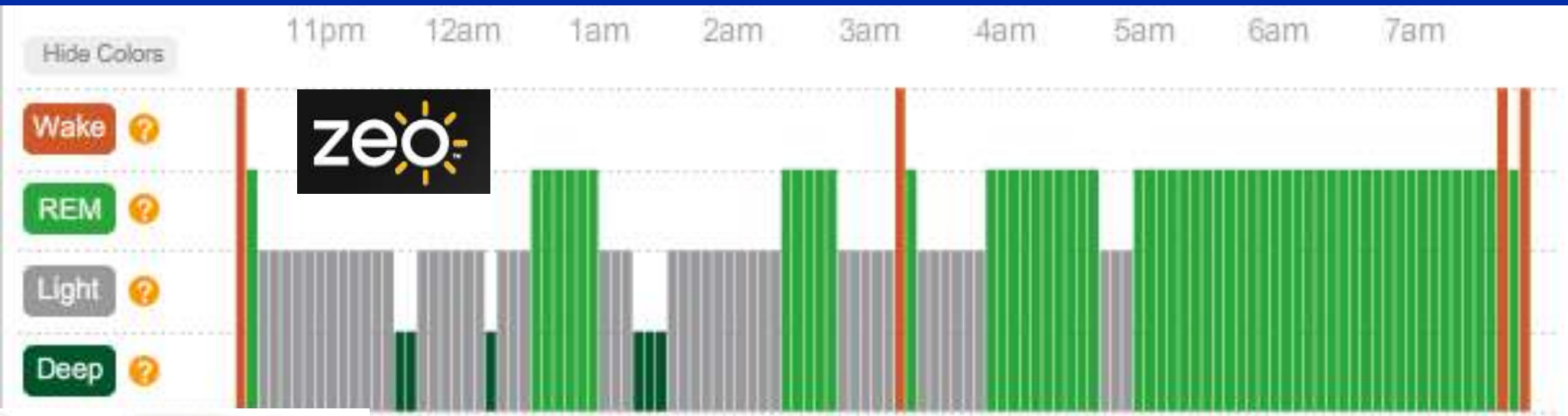
fitbit







Quantifying My Sleep Pattern Using a Zeo - Increased My Average to 8 Hours/Night

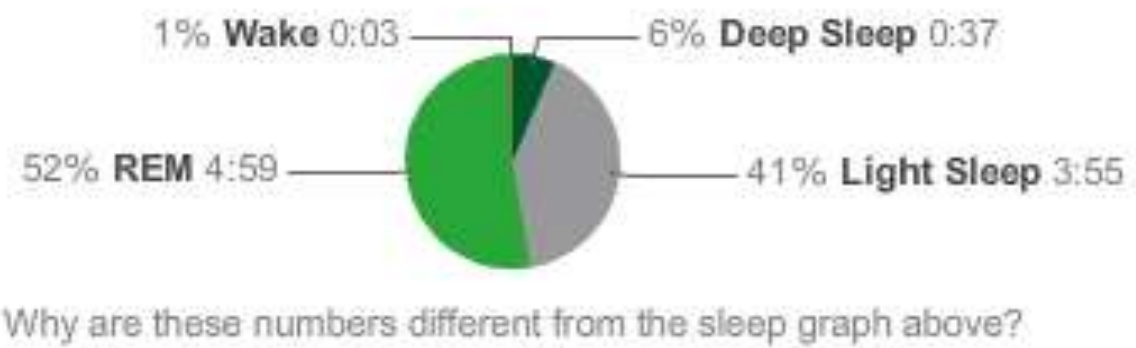




Stroke risk increased by sleeping less than six hours a night
-M. Ruiter, *Sleep* 2012

Total Z: 9 hr 31 min

Time to Z: 0 hr 2 min



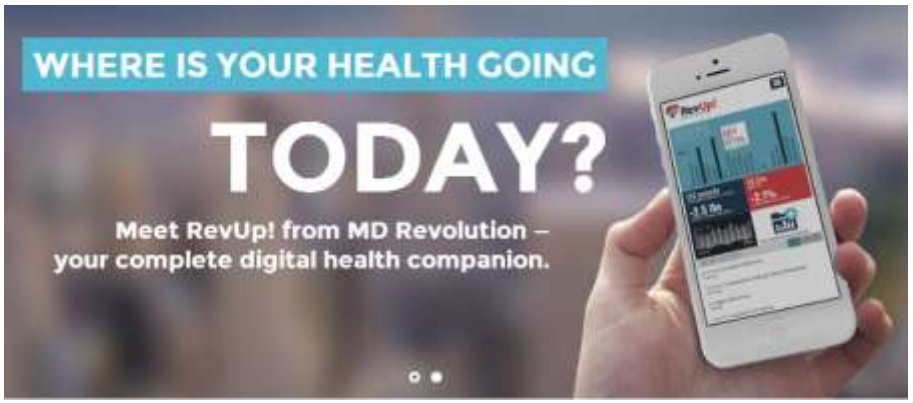
I Recorded Over 700 Nights

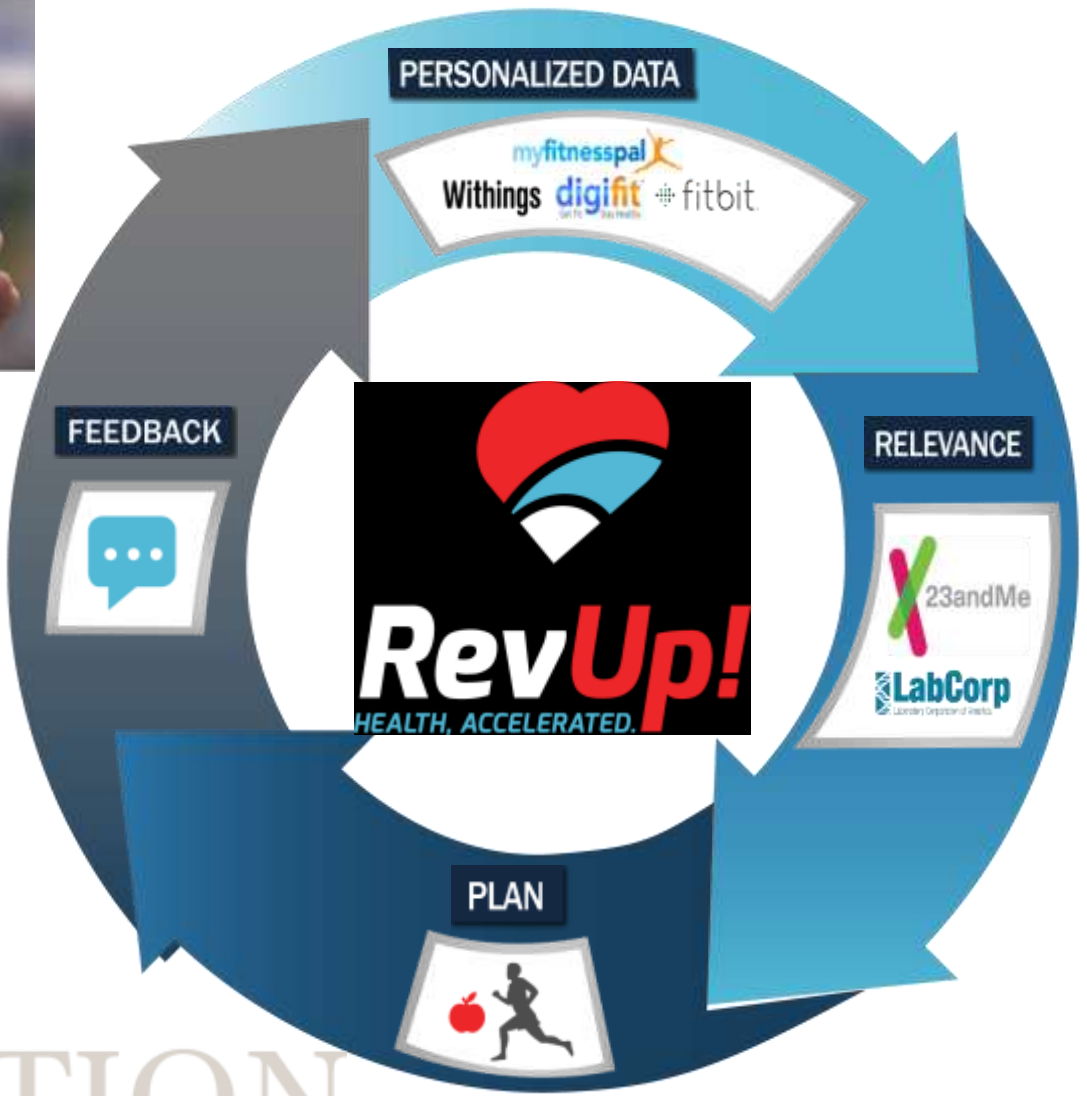
REM is Normally 20% of Sleep

Mine is Between 45-65% of Sleep

An Infant Typically Has 50% REM

MDRevolution's RevUp! Integrates a Variety of Sensors & Then Completes the Behavior Feedback Loop

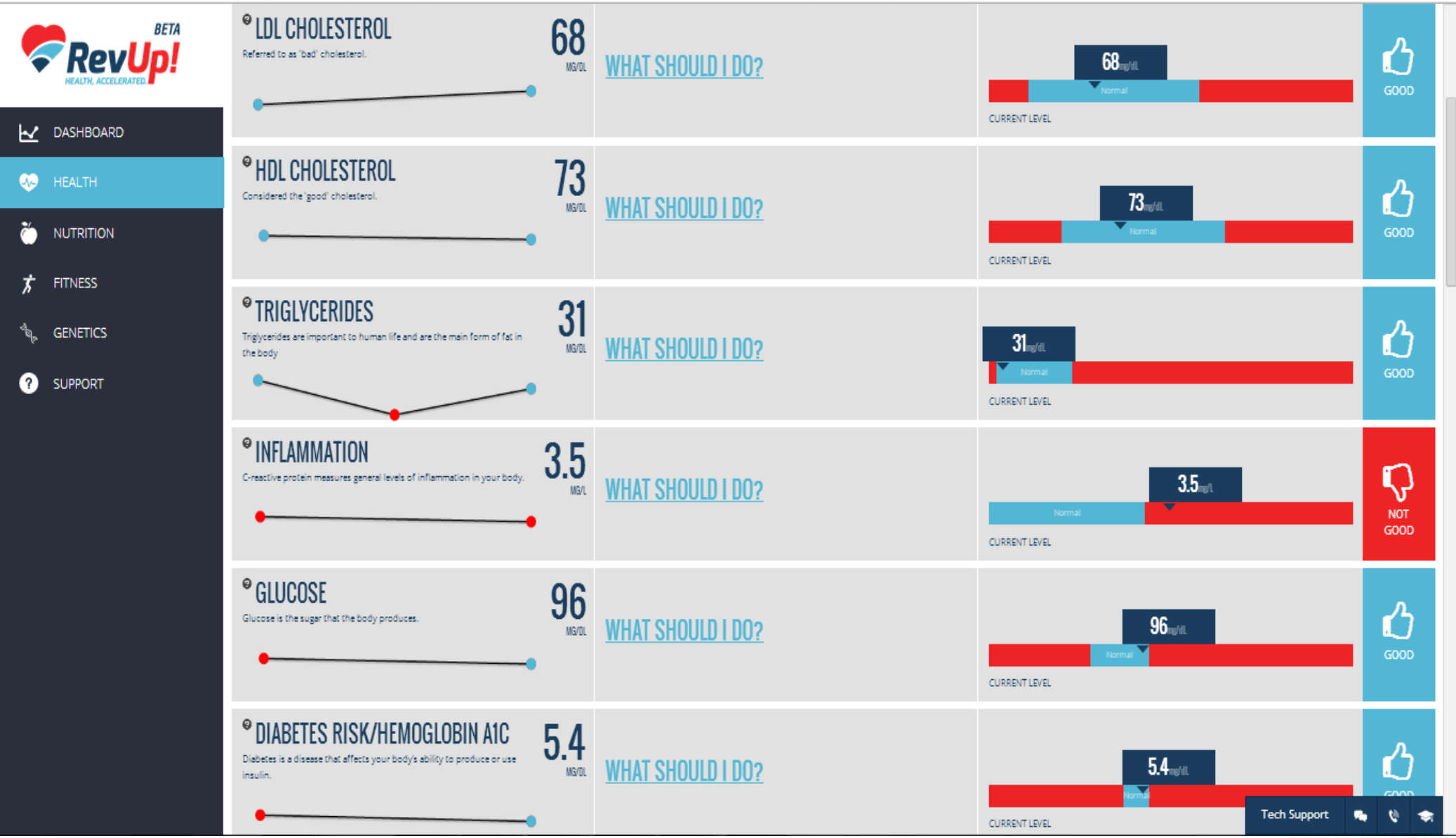




MD REVOLUTION

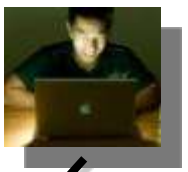
Source: Samir Damani, MD Revolution

MDRevolution's RevUp!
Also Integrates Blood Variables and Genetics



CitiSense –UCSD NSF Grant for Fine-Grained "Exposome" Sensing Using Cell Phones





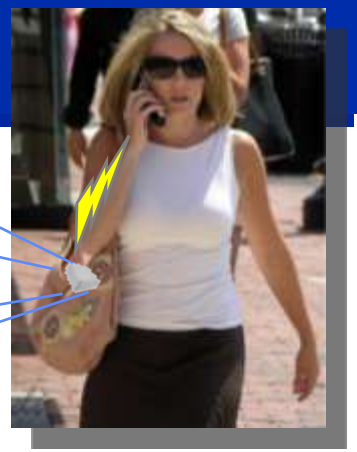
4oz
30 compounds

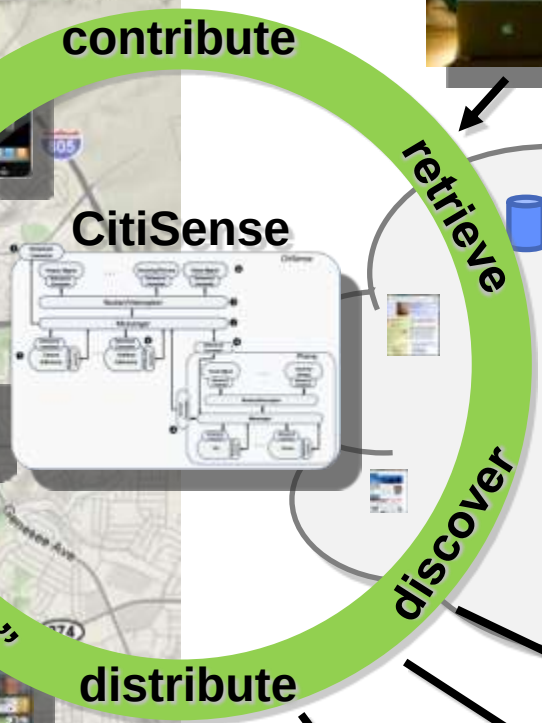


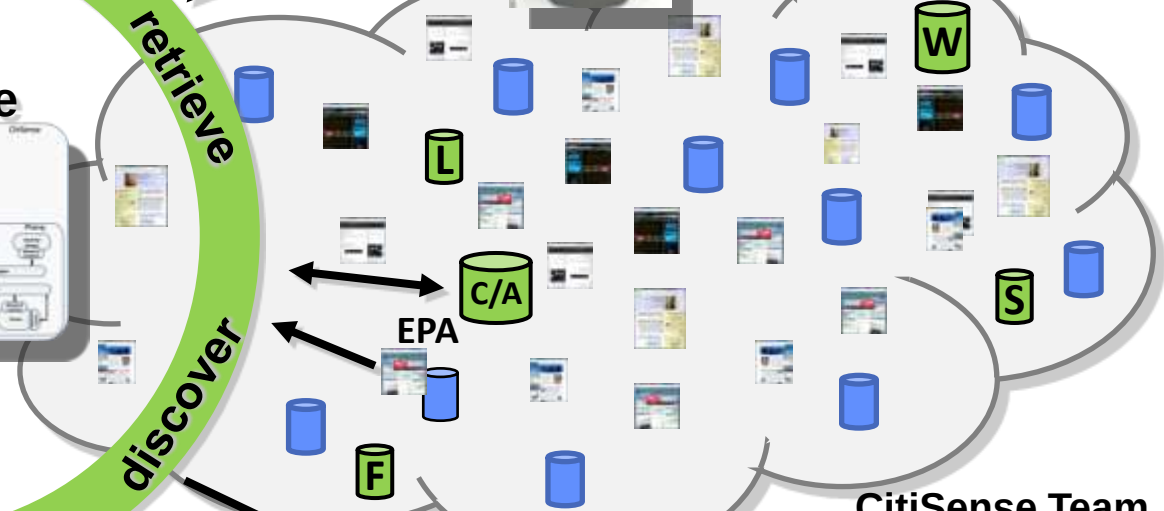
Seacoast Sci.

Intel MSP

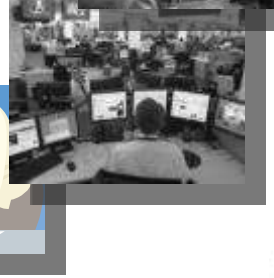












CitiSense Team
PI: Bill Griswold
Ingolf Krueger
Tajana Simunic Rosing
Sanjoy Dasgupta
Hovav Shacham
Kevin Patrick

CW PHS
CENTER FOR WIRELESS & POPULATION HEALTH SYSTEMS

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Consumer Self Measurement is Exploding Totally Outside of the Medical Complex

From the First San Francisco QS Meetup in 2008
To 116 Cities in 37 Countries in Four Years



Groups	Members	Interested	Cities	Countrie
157	27,814	7,373	116	37

The Self-Monitoring Business Has Reached Market Takeoff

- **MyFitnessPal**
  - 40 Million Users
  - Aug 2013 Raised $18M Series A, Led by Kleiner Perkins
- **Fitbit**
  - Has Raised ~$70M
- **BodyMedia Was Bought by Jawbone**
  - For ~$100M
- **Zeo Sleep Monitor**
  - Closed Down in 2013

More Mergers Likely as the Shakeout Continues

mHealth Technology Progression



Mobile Health Market Projected to be $30B-$60B by 2015

Source: Rick Valencia, Qualcomm Life

QUALCOMM LIFE
a Qualcomm company

UC San Diego

UC Irvine
University of California, Irvine

Health Data Exploration Project

Project Director: Kevin Patrick, MD, MS
Professor, Family and Preventive Medicine, UCSD
Director, Center for Wireless and Population Health Systems, Calit2

Project Co-Director, Jerry Sheehan, MA
Chief of Staff, Calit2

Investigators

Matthew Bietz, PhD, Project Scientist, UC Irvine
Judith Gregory, PhD, Adjunct Professor, UC Irvine
Scout Calvert, PhD, Project Scientist, UC Irvine
Ramesh Rao, PhD, Director, Calit2/UCSD

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Robert Wood Johnson Foundation



Personal Data for the Public Good

New Opportunities to Enrich Understanding of Individual and Population Health

FINAL REPORT OF THE HEALTH DATA EXPLORATION PROJECT
FEBRUARY 2013

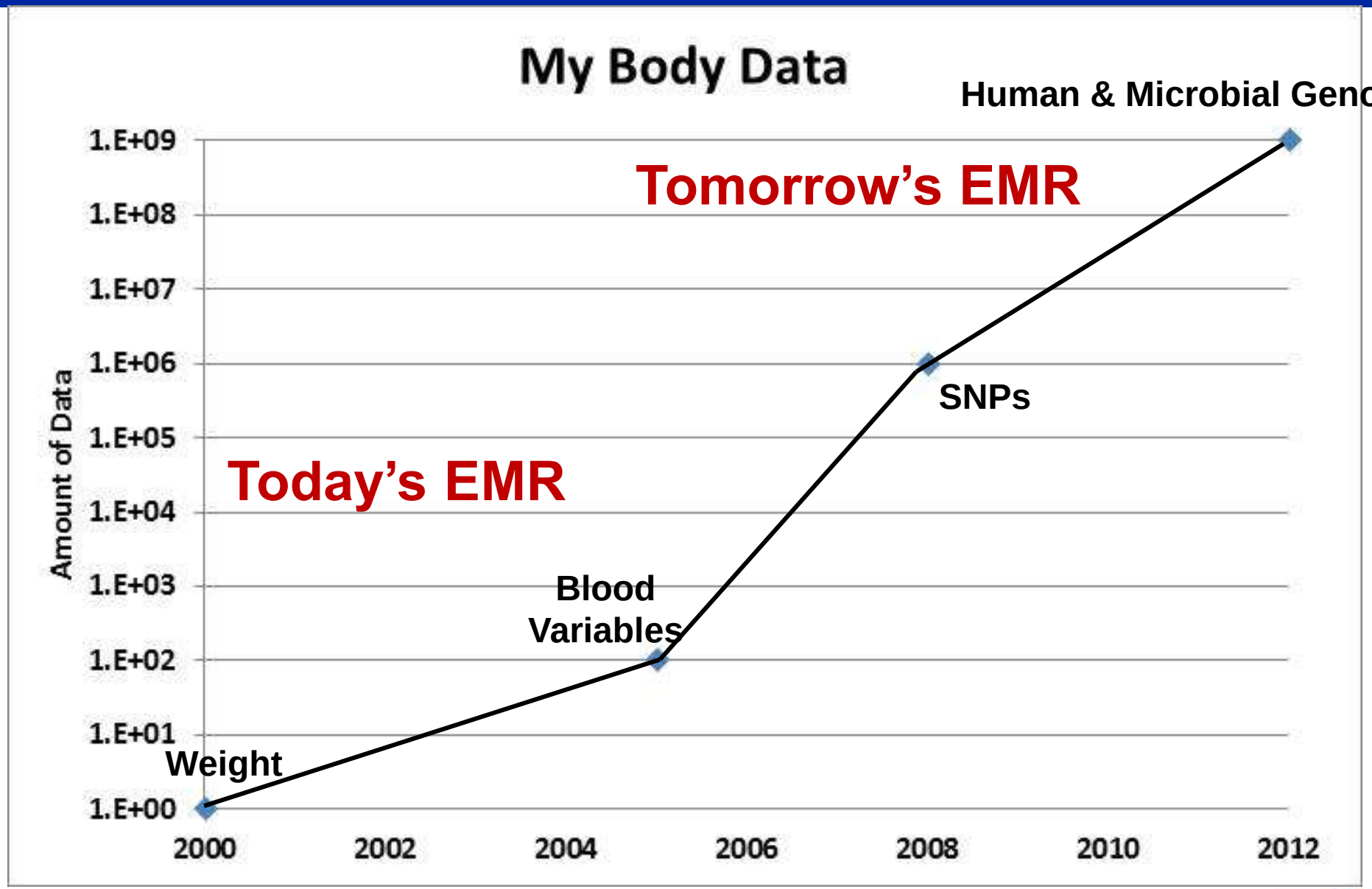
Health Data Exploration project

From Measuring Macro-Variables to Measuring My Internal Variables – What Did I Learn?

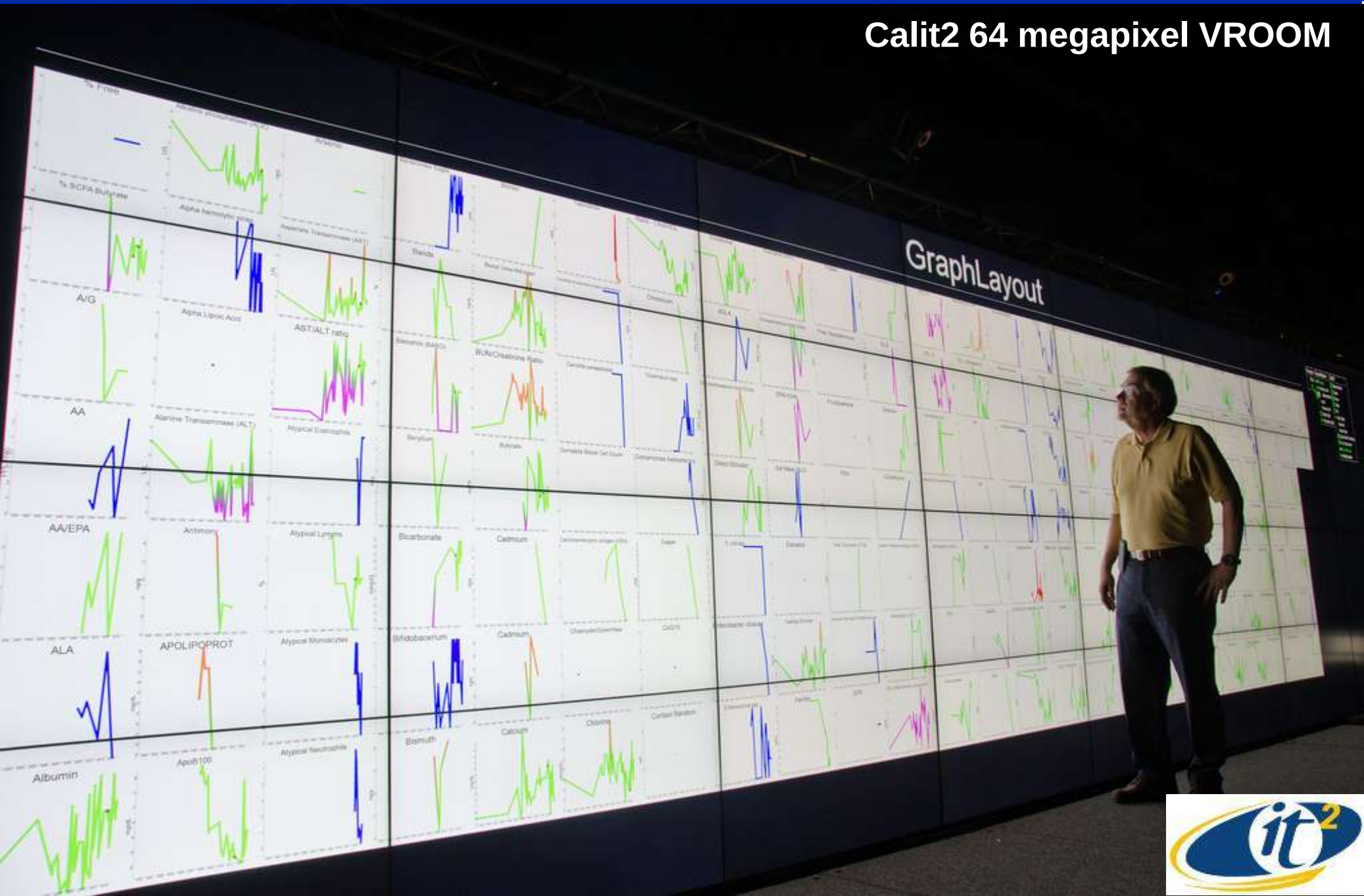


www.technologyreview.com/biomedicine/39636

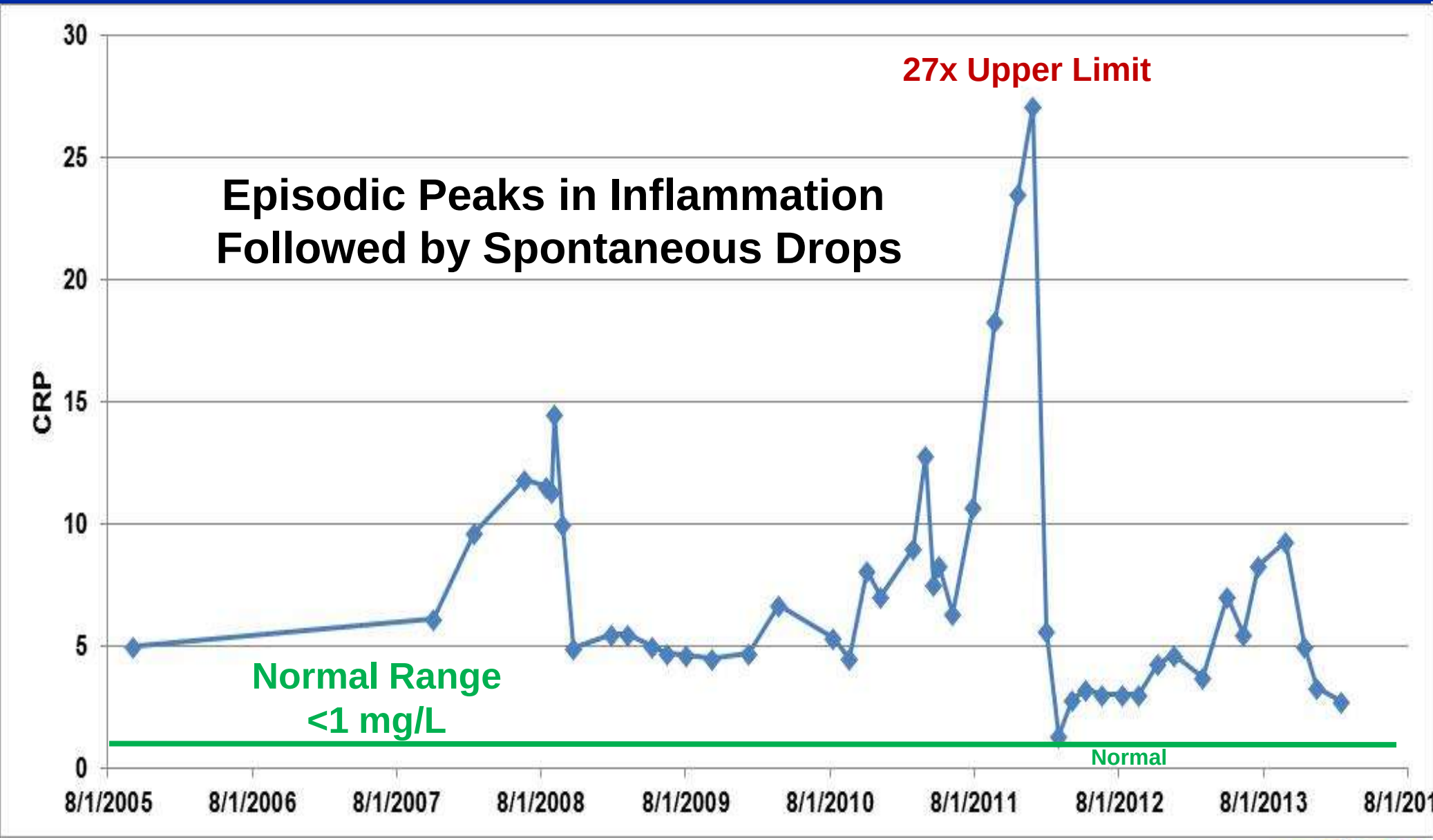
From One to One Billion Data Points Defining Me: *Big Data* Coming to the Electronic Medical Record (EMR)



Visualizing 5-10 Year Time Series of 150 Blood & Stool Variables Led Me to Discover a Chronic Disease

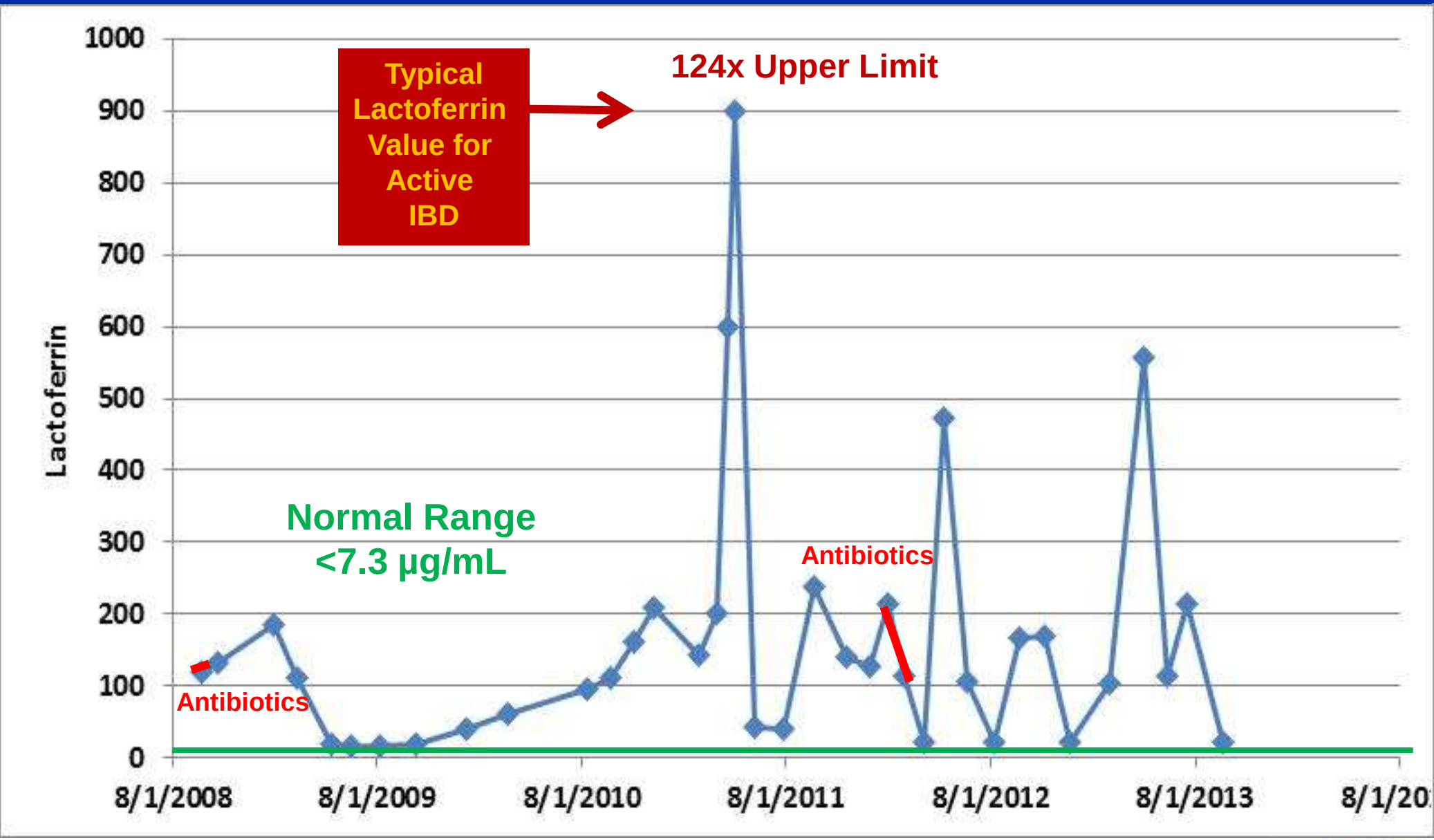


Only One of My Blood Measurements Was Far Out of Range--Indicating Chronic Inflammation



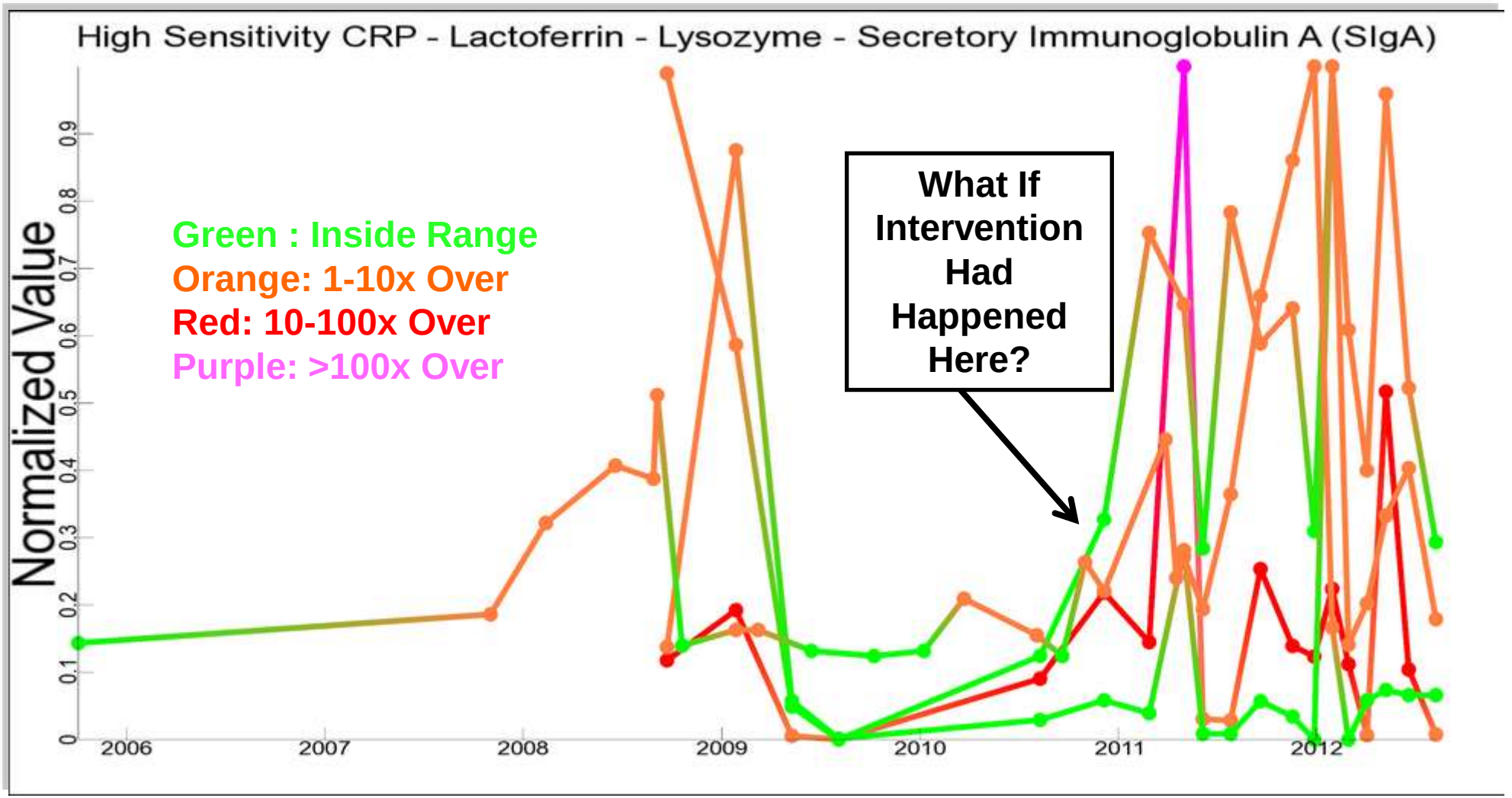
Complex Reactive Protein (CRP) is a Blood Biomarker for Detecting Presence of Inflammation

But by Using Stool Analysis Time Series, I Discovered I Had Episodically Excursions of My Immune System



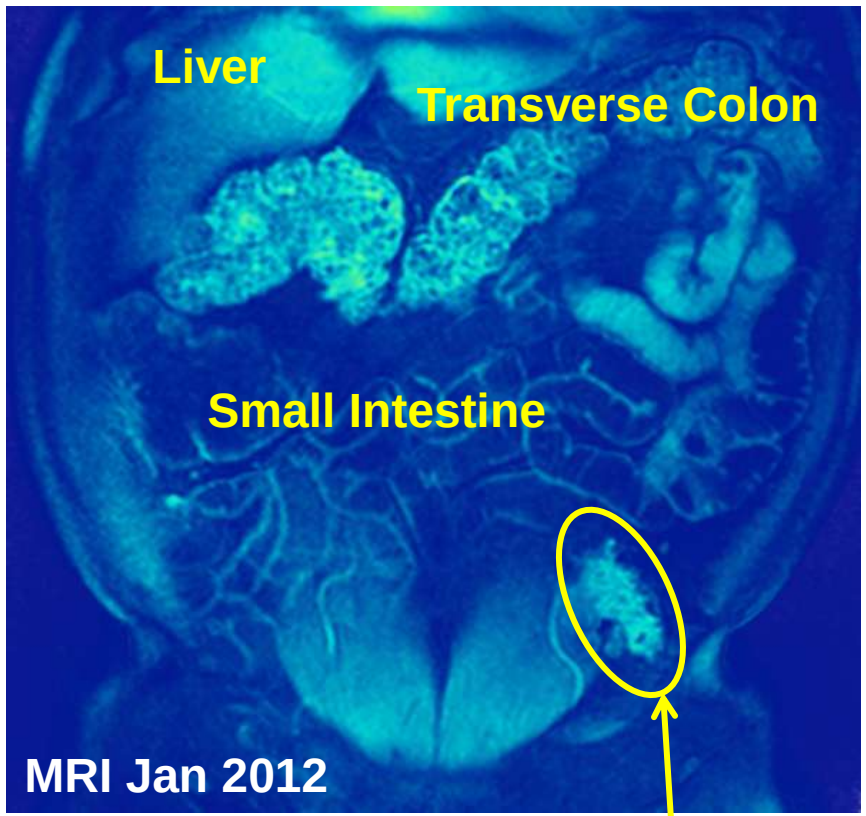
Lactoferrin is a Protein Shed from Neutrophils -
An Immune System Antibacterial that Sequesters Iron

Putting Multiple Immunological Biomarker Time Series Together, Reveals Major Immune Dysfunction

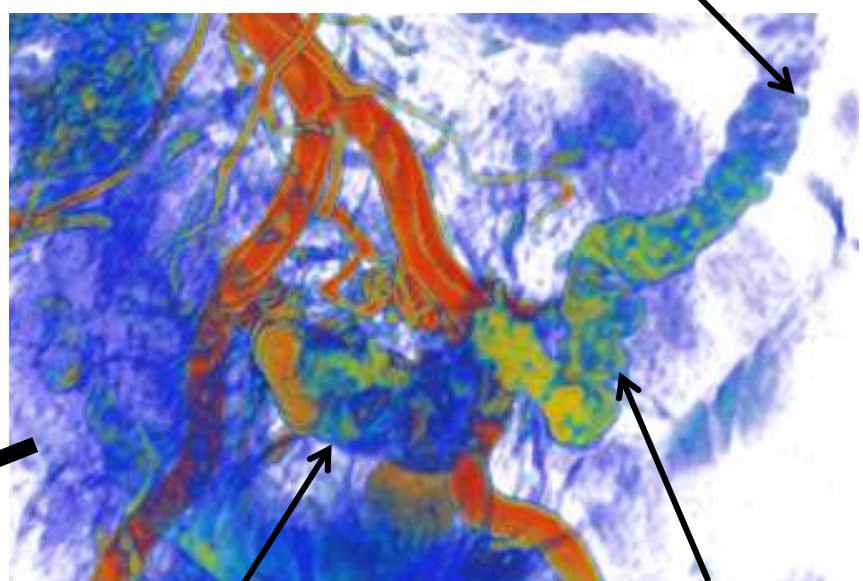


Source: Calit2 Future Health Expedition Team

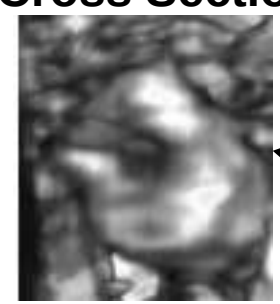
Confirming the IBD Hypothesis: Finding the "Smoking Gun" with MRI Imaging



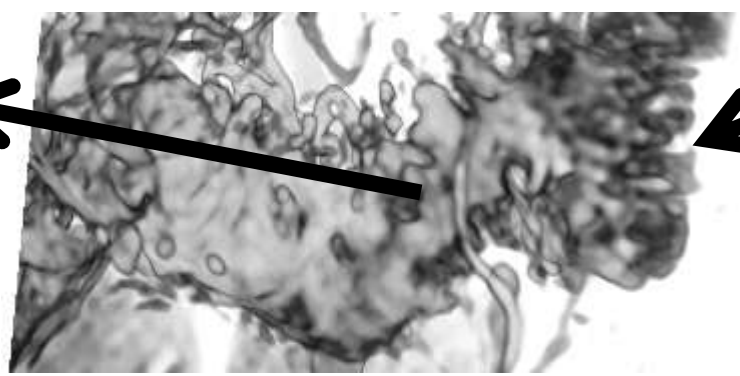
I Obtained the MRI Slices From UCSD Medical Services and Calit2 Staff Converted Data to an Interactive 3D "Video Game"



Cross Section



Diseased Sigmoid Colon



I Asked Myself
Why Did I Have an Autoimmune Disease like IBD?

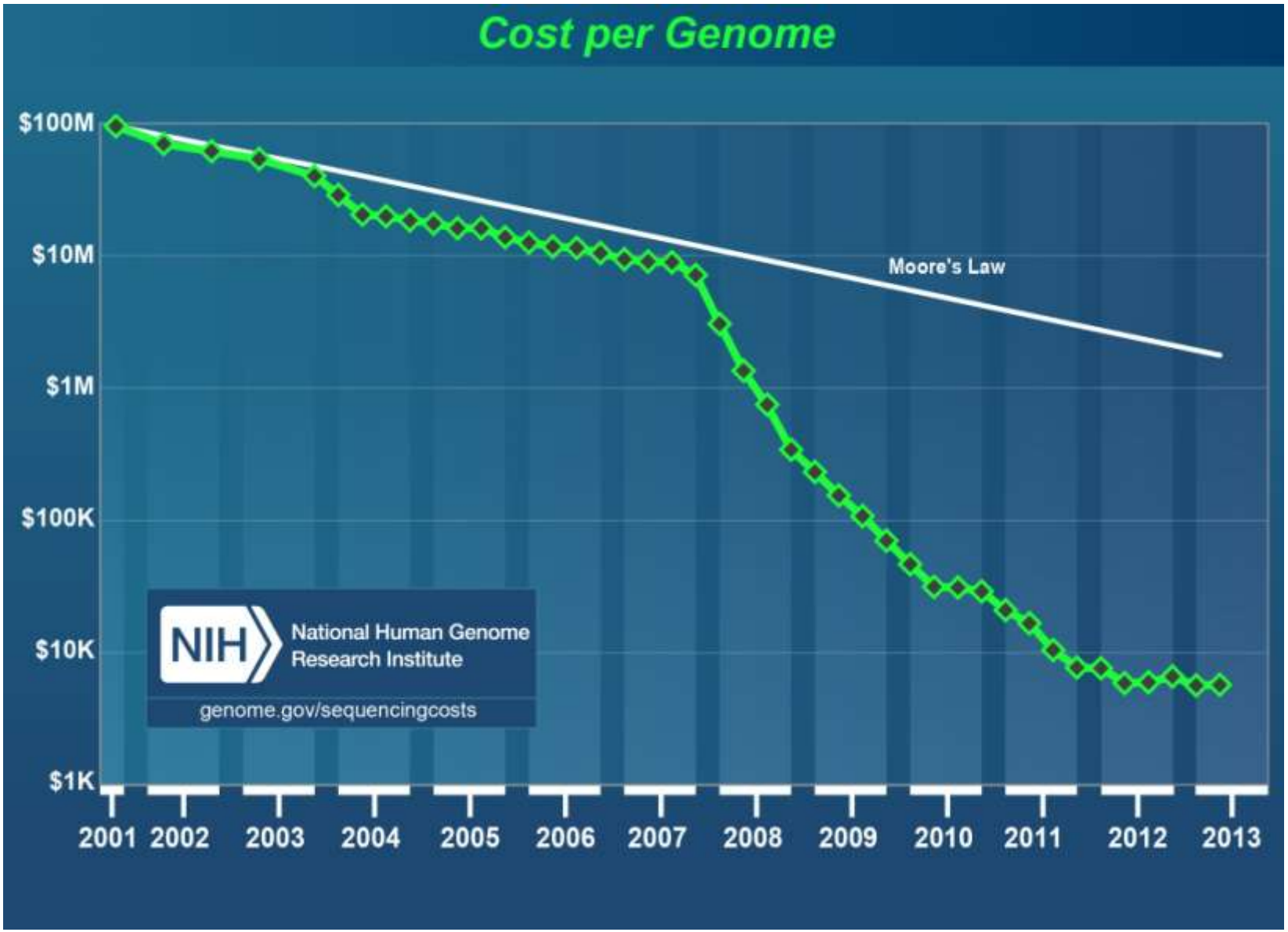
Despite decades of research,
the etiology of Crohn's disease
remains unknown.
Its pathogenesis may involve
a complex interplay between
host genetics,
immune dysfunction,
and microbial or environmental factors.

--The Role of Microbes in Crohn's Disease

So I Set Out to Quantify All Three!

Paul B. Eckburg & David A. Relman
Clin Infect Dis. 44:256-262 (2007)

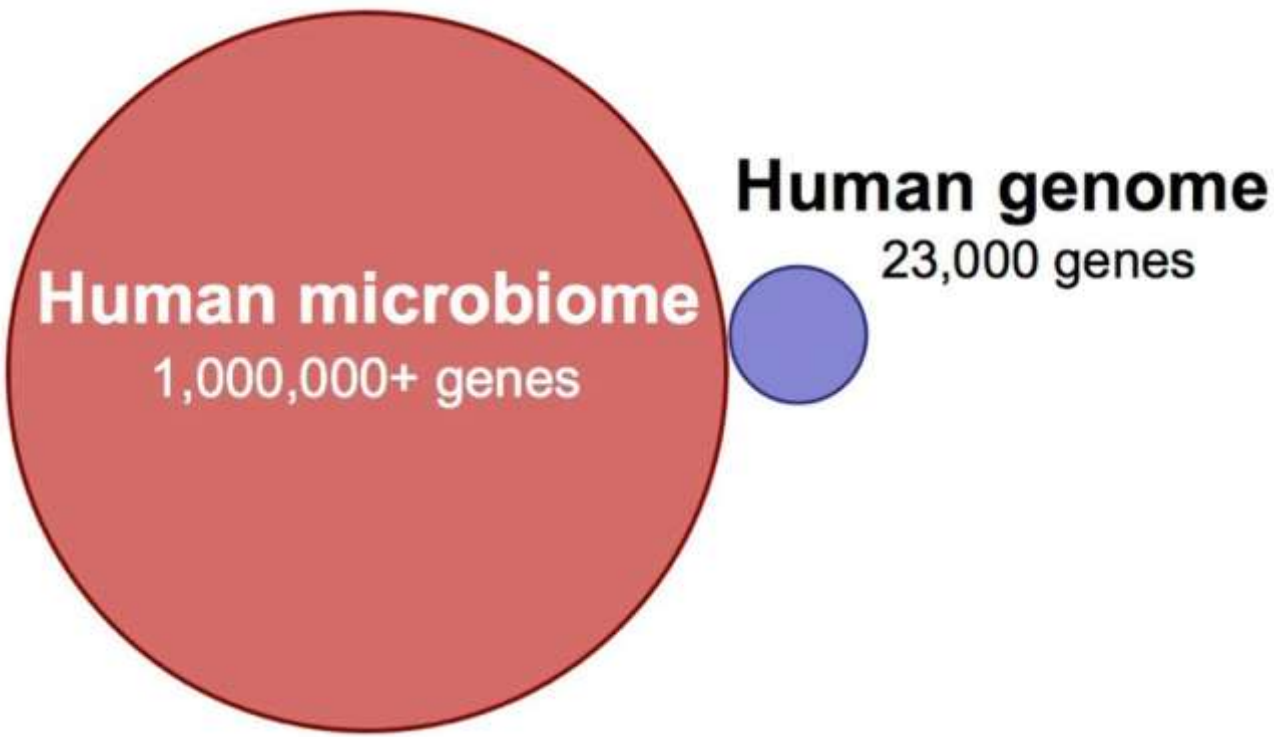
The Cost of Sequencing a Human Genome Has Fallen Over 10,000x in the Last Ten Years!



This Has Enabled Sequencing of Both Human and Microbial Genomes

Healthcare Must Include a Vast Amount of Microbial Information That is Not in Today's Medicine

Your Body Has 10 Times As Many Microbe Cells As Human Cells



99% of Your DNA Genes Are in Microbe Cells Not Human Cells

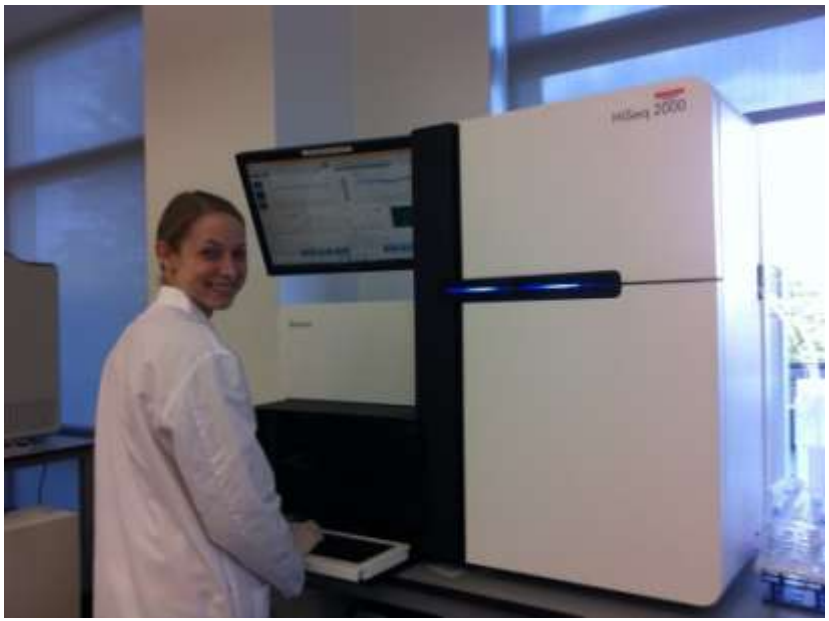
Inclusion of the Microbiome Will Radically Change Medicine

J. Craig Venter™ INSTITUTE

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To Map Out the Dynamics of My Microbiome Ecology I Partnered with the J. Craig Venter Institute

- **JCVI Did Metagenomic Sequencing on Seven of My Stool Samples Over 1.5 Years**
- **Sequencing on Illumina HiSeq 2000**
  - **Generated 200 Million 100bp Reads**
- **JCVI Lab Manager, Genomic Medicine**
  - **Manolito Torralba**
- **IRB PI Karen Nelson**
  - **President JCVI**



Illumina HiSeq 2000 at JCVI



Manolito Torralba, JCVI



Karen Nelson, JCVI

J. Craig Venter INSTITUTE

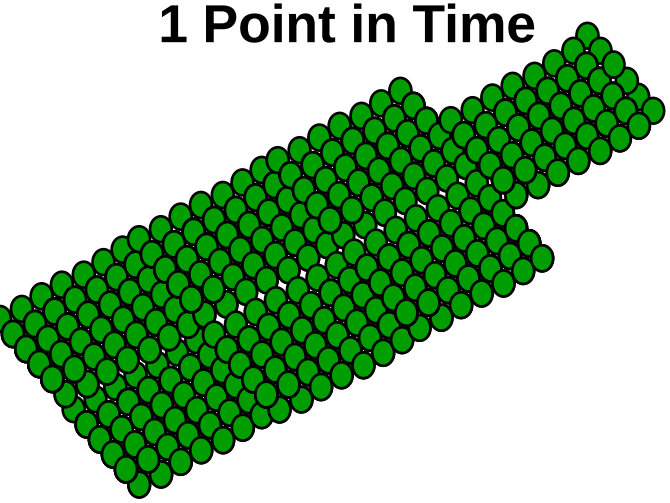
it²

We Downloaded Additional Gut Microbiomes from NIH HMP For Comparative Analysis

From Sequences to Bacterial Species Relative Abundance Required 25 CPU-Years at San Diego Supercomputer Center

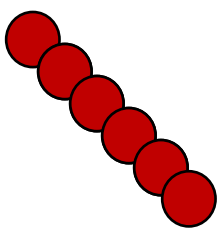
"Healthy" Individuals

250 Subjects
1 Point in Time



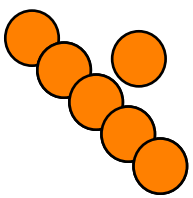
Larry Smarr

6 Points in Time

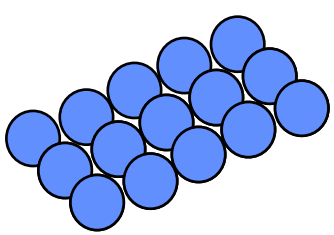


IBD Patients

2 Ulcerative Colitis Patients,
6 Points in Time



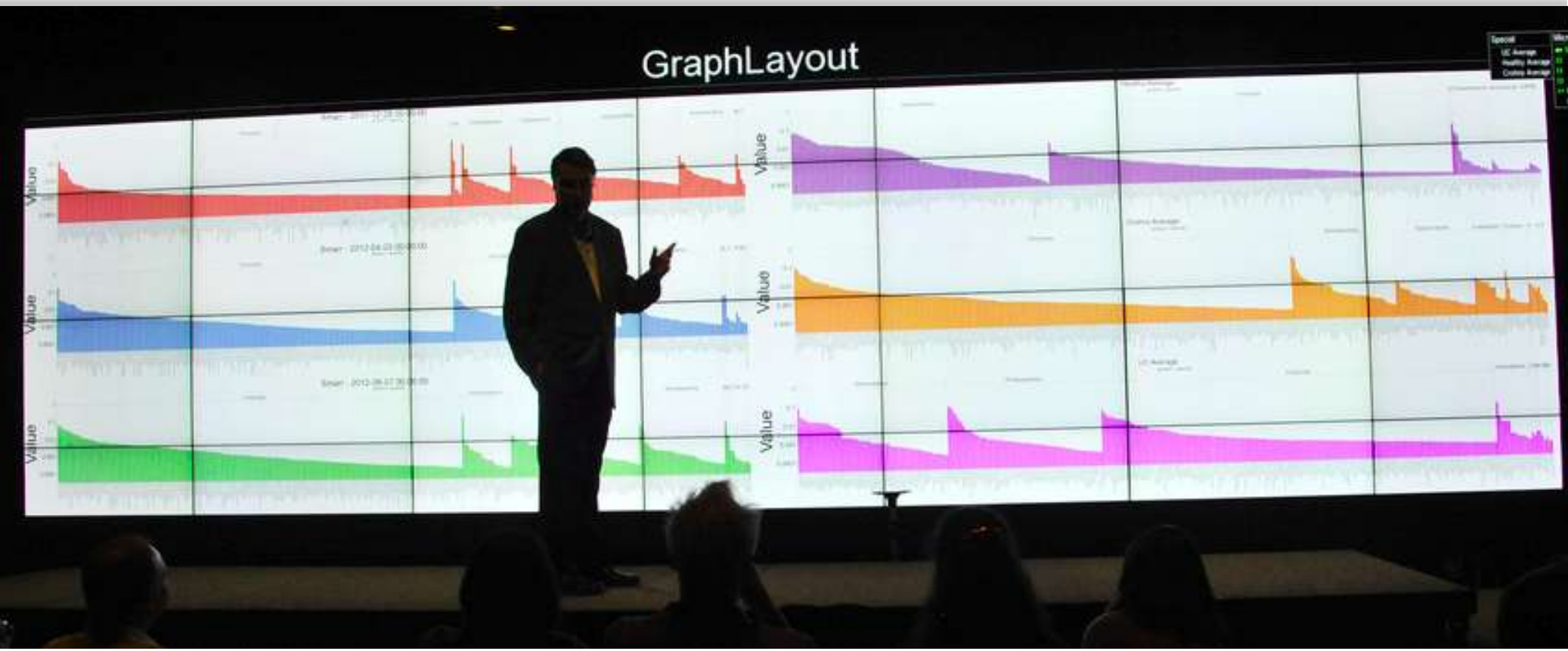
5 Ileal Crohn's Patients,
3 Points in Time



Total of 27 Billion Reads
Or 2.7 Trillion Bases

Source: Jerry Sheehan, Calit2
Weizhong Li, Sitao Wu, CRBS, UCSD

Using Supercomputing Allows Comparison of the Relative Abundance of 200 Gut Microbe Species

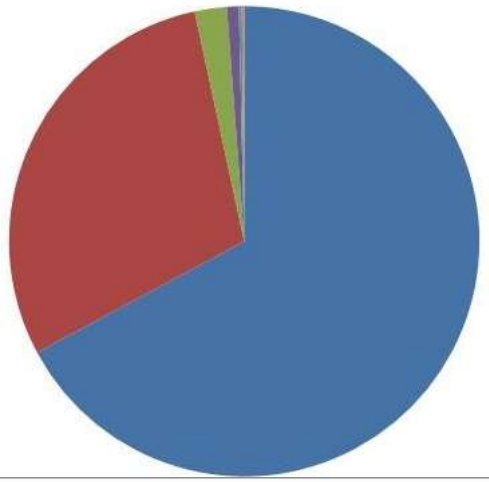


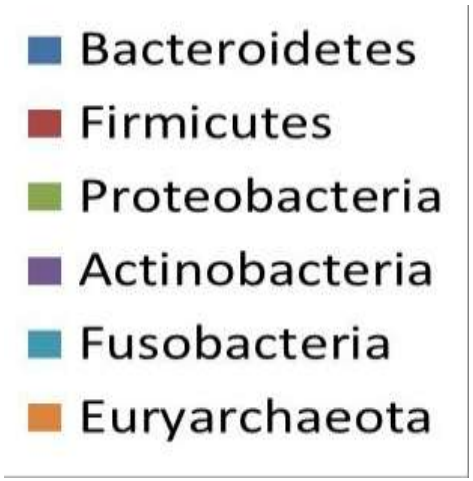
Comparing 3 LS Time Snapshots (Left)
with Healthy, Crohn's, UC (Right Top to Bottom)

Calit2 VROOM-FuturePatient Expedition

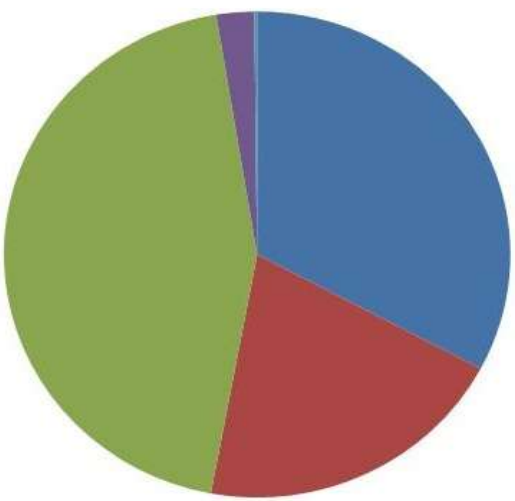
We Found Major Shifts in Microbial Ecology Between Healthy and Two Forms of IBD

Ave. Healthy

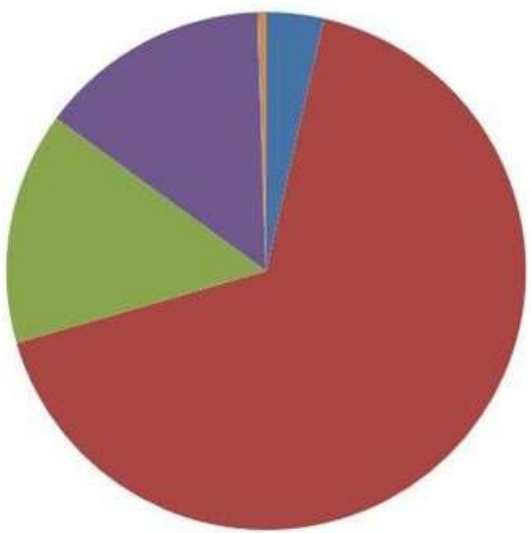




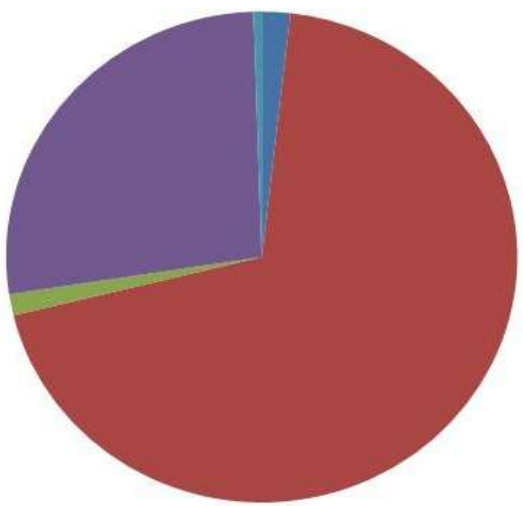
Ave. Ulcerative Colitis



LS Apr 2012



Ave. Crohn's



Explosion of Proteobacteria

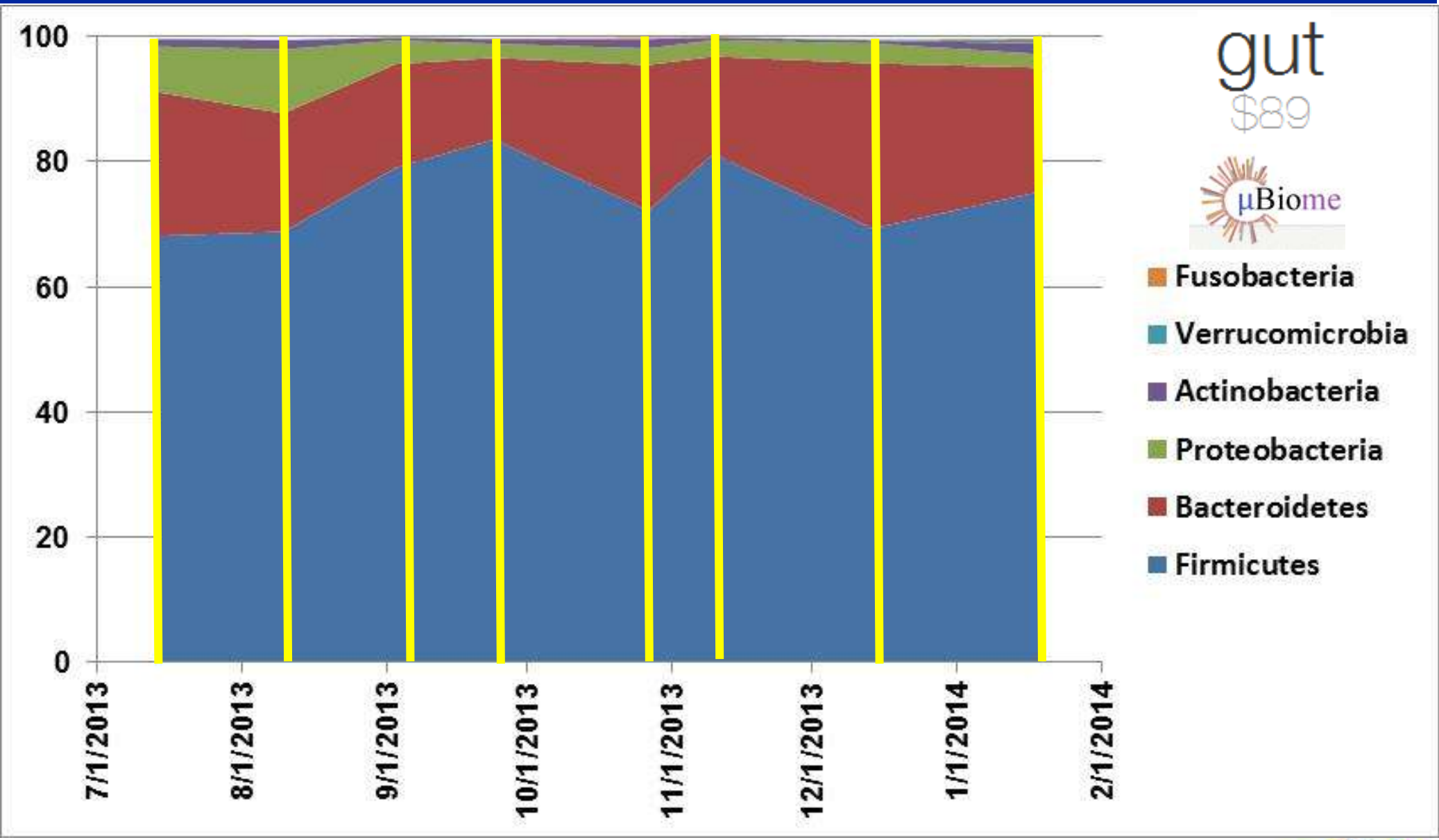
On the IBD Spectrum

Collapse of Bacteroidetes

Toward Microbiome Disease Diagnosis

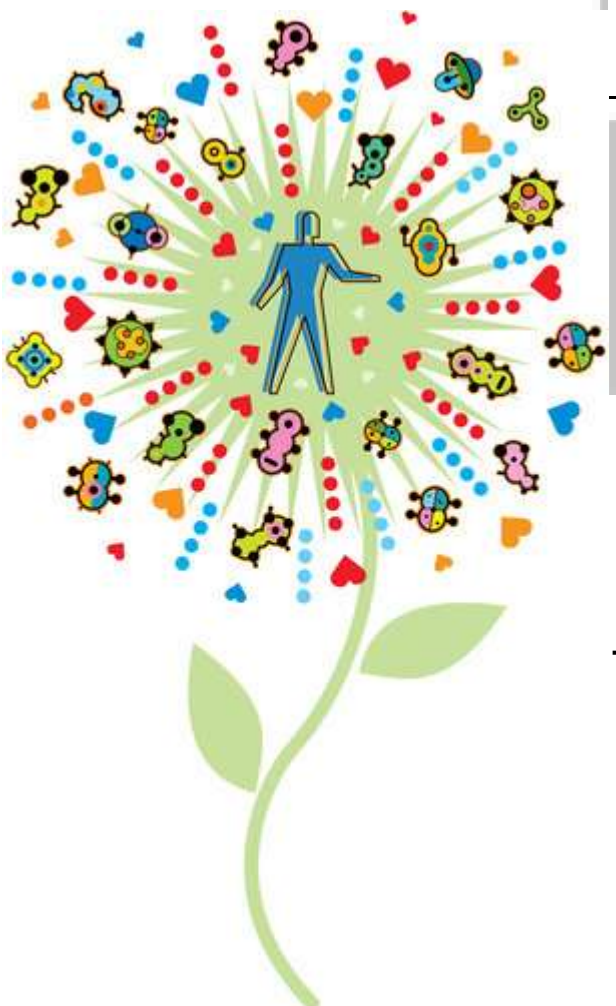


Inexpensive Consumer 16S Time Series of Microbiome Allows Similar Analysis Through Ubiome



Data source: LS (Yellow Lines Stool Samples); Sequencing and Analysis Ubiome

From a War Metaphor to Gardening



The New York Times

Science

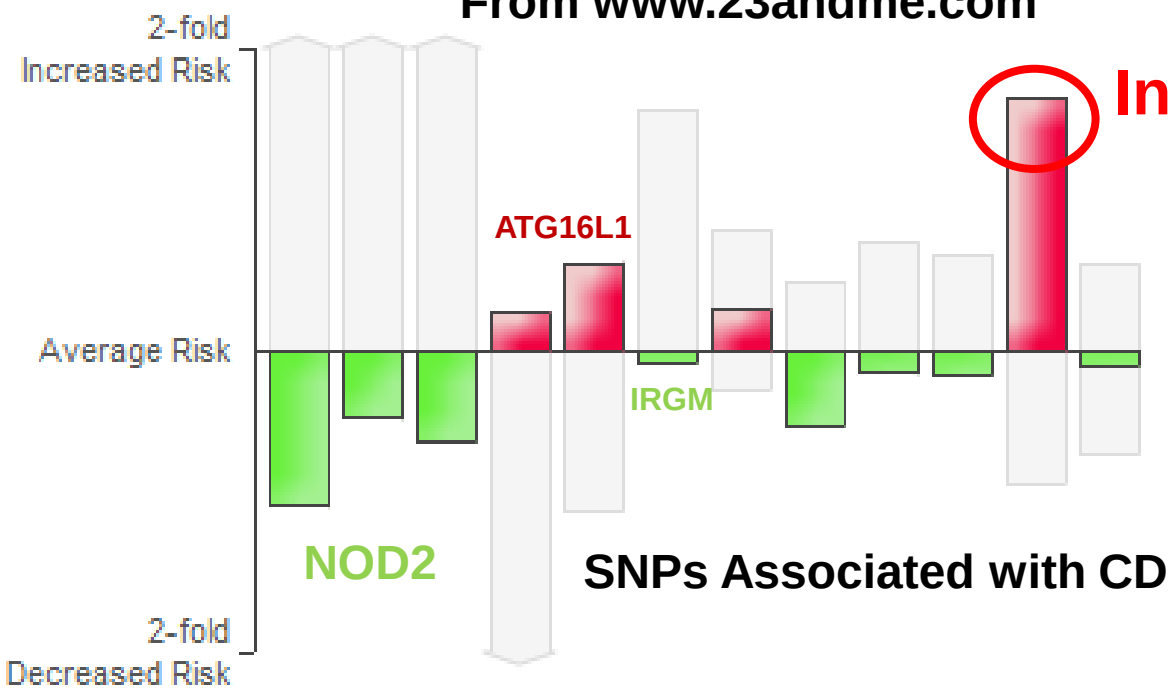
Tending the Body's Microbial Garden

By CARL ZIMMER
Published: June 18, 2012

"I would like to lose the language of warfare,"
said Julie Segre, a senior investigator at
the National Human Genome Research Institute.
"It does a disservice to all the bacteria
that have co-evolved with us
and are maintaining the health of our bodies."

I Found I Had One of the Earliest Known SNPs Associated with Crohn's Disease

From www.23andme.com



Polymorphism in Interleukin-23 Receptor Gene — 80% Higher Risk of Pro-inflammatory Immune Response rs1004819

A Genome-Wide Association Study Identifies *IL23R* as an Inflammatory Bowel Disease Gene

Richard H. Düerr, *et al.*
Science **314**, 1461 (2006)

News and Views

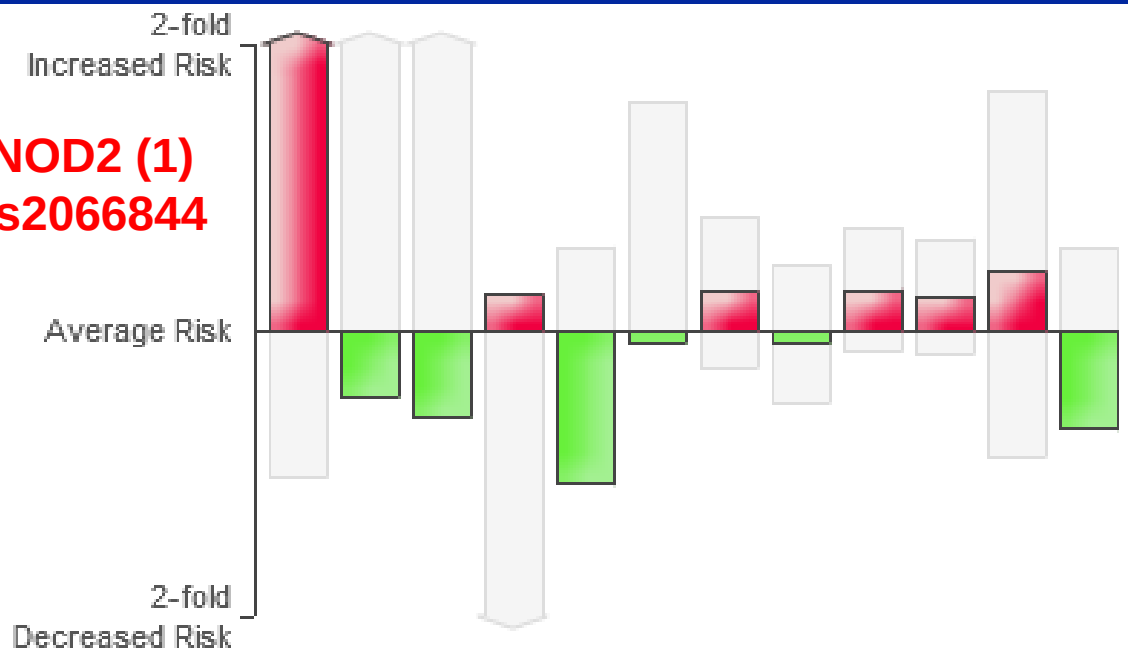
Nature Medicine **13**, 26 - 28 (2007)
doi:10.1038/nm0107-26

IL-23: a master regulator in Crohn disease

Markus F Neurath[1]

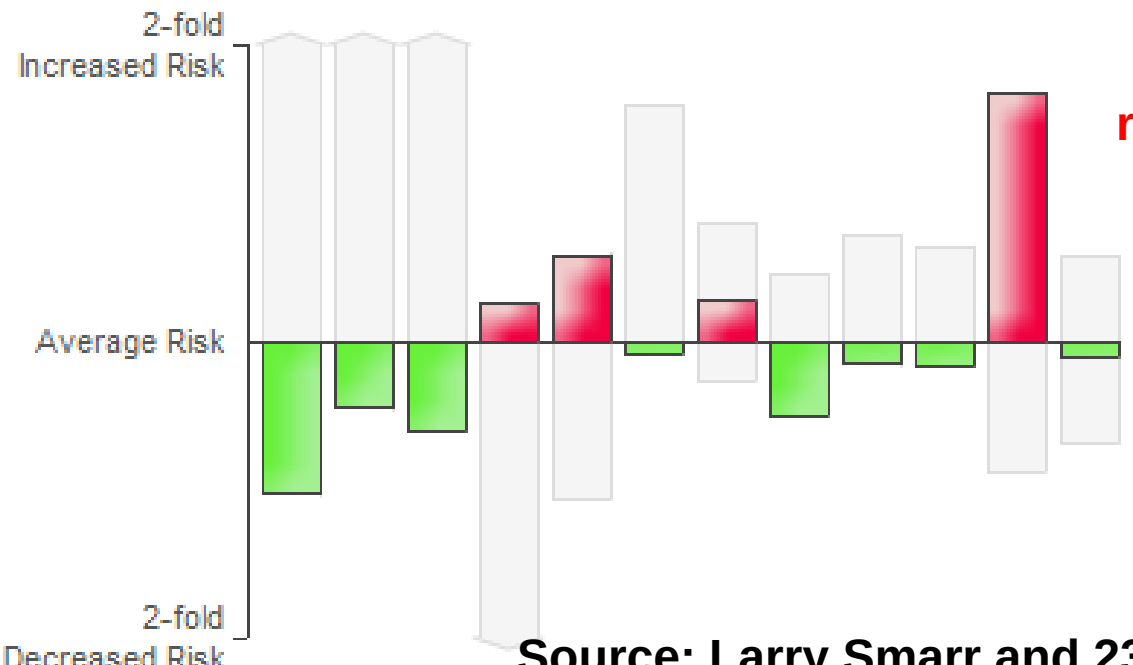
There Is Likely a Correlation Between CD SNPs and Where and When the Disease Manifests

Subject with Ileal Crohn's



Female
CD Onset
At 20-Years Old

Subject with Colon Crohn's



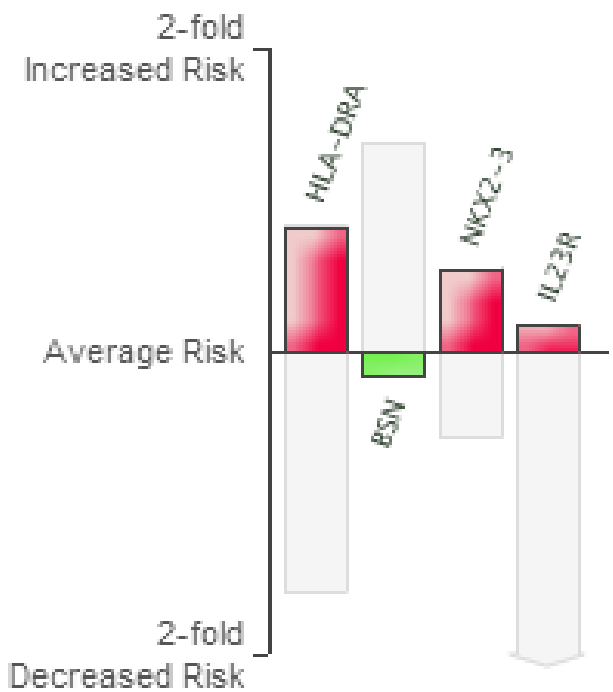
Me-Male
CD Onset
At 60-Years Old

Source: Larry Smarr and 23andme

I Also Had an Increased Risk for Ulcerative Colitis, But a SNP that is Also Associated with Colonic CD



I Have a 33% Increased Risk for Ulcerative Colitis HLA-DRA (rs2395185)

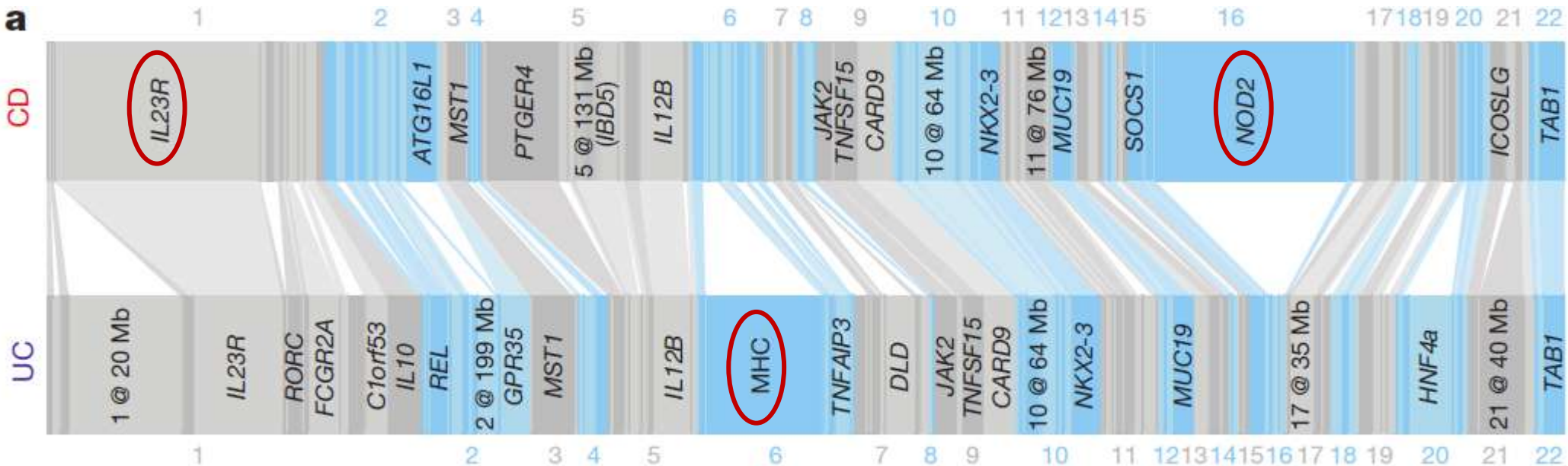


I Have the Same Level of HLA-DRA Increased Risk as Another Male Who Has Had Ulcerative Colitis for 20 Years

"Our results suggest that at least for the SNPs investigated [including HLA-DRA], colonic CD and UC have common genetic basis."
-Waterman, et al., IBD 17, 1936-42 (2011)

So IBD May be Stratified by a Personalized Combination of the 163 Known SNPs Associated with IBD

The Current Division of IBD Into Crohn's Disease and Ulcerative Colitis May Turn Out to be Superseded by a More Accurate Human Genetic Stratification



- The width of the bar is proportional to the variance explained by that locus
- Bars are connected together if they are identified as being associated with both phenotypes
- Loci are labelled if they explain more than 1% of the total variance explained by all loci

"Host–microbe interactions have shaped the genetic architecture of inflammatory bowel disease," Jostins, et al. Nature 491, 119-124 (2012)

Crowdsourcing of Patients Is Creating Huge Population-Wide Knowledge Bases

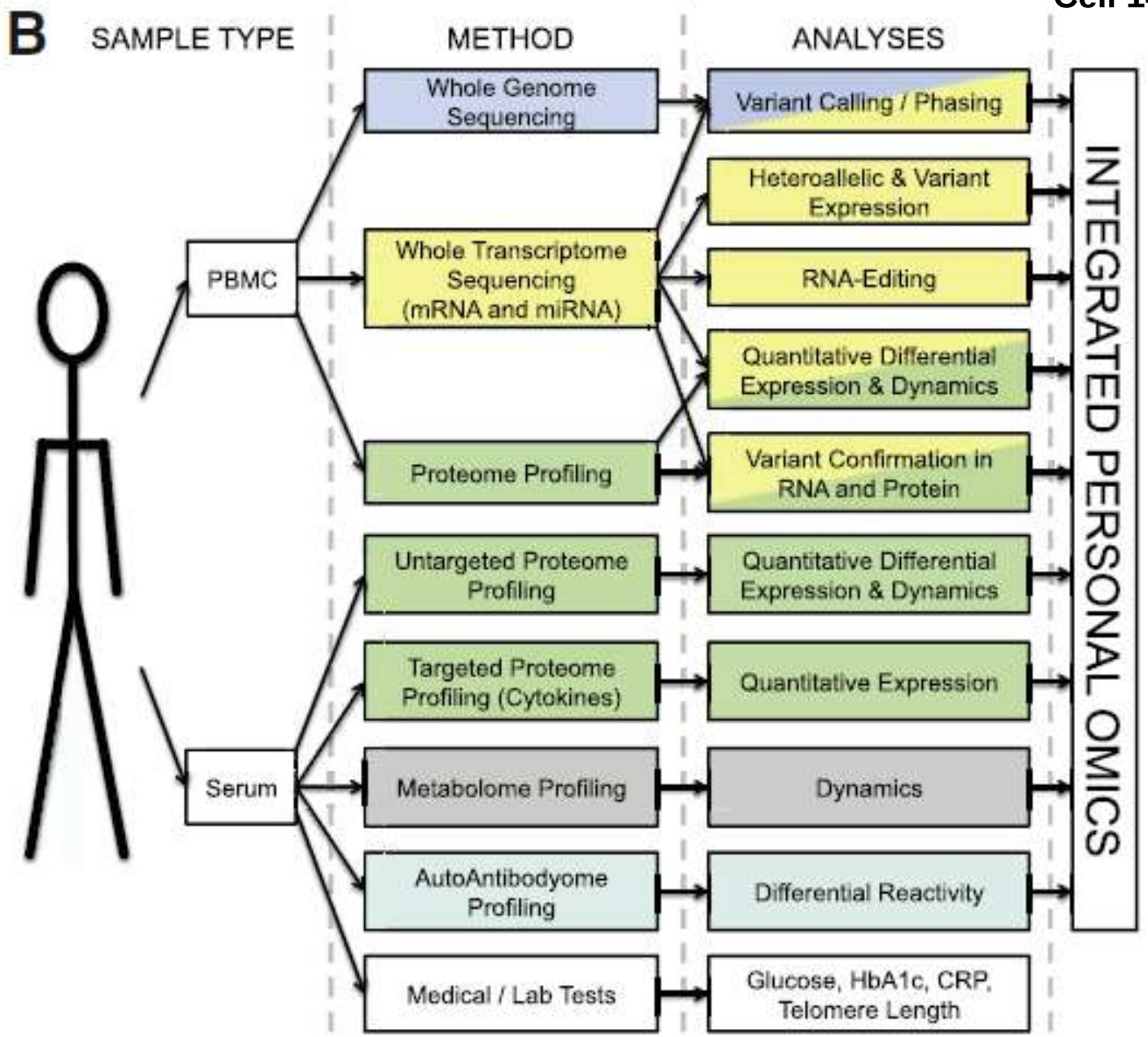
- **Currently 300,000 23andme Members**
  - **Growing Rapidly to One Million**
- **IBD Affects ~1/300 Americans**
  - **Implies ~3000 IBD Subjects**
  - **Detailed IBD Survey to Members for Phenotyping**
- **Enables Internal Genome-Wide Association Studies (GWAS)**

- **Also Working with Crohnology (Sean Ahrens)**
  - **Encouraging His >5000 Crohn's Members to Use 23andme**
  - **Combine SNPs with Detailed Phenotyping and Drug Impacts**



Integrative Personal Omics Profiling By Creating Time Series of Omics

Cell 148, 1293–1307, March 16, 2012



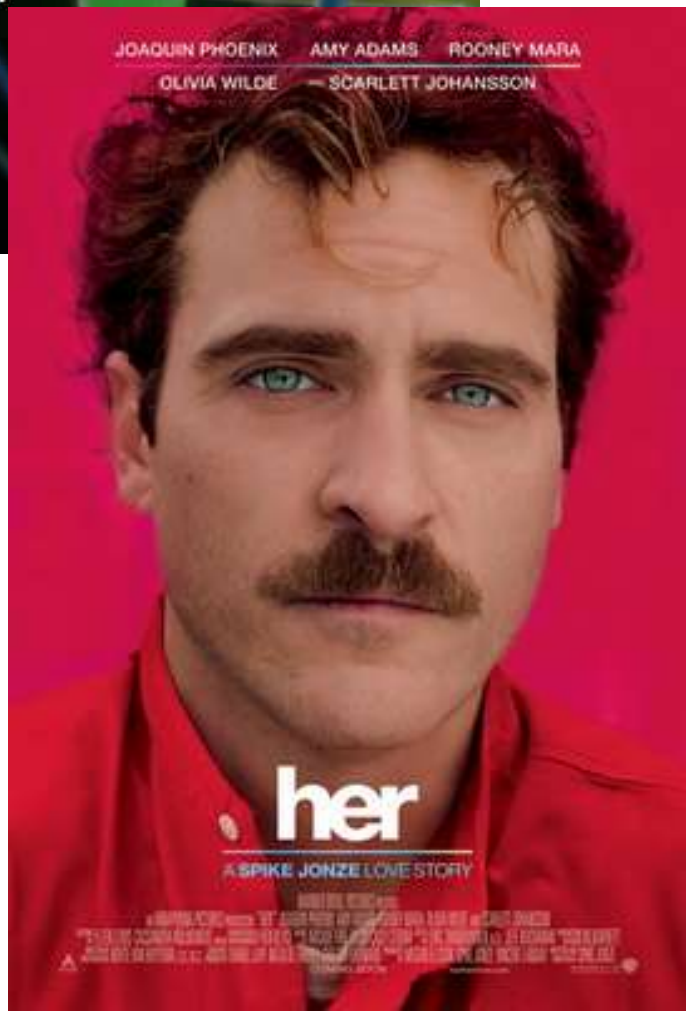
- **Michael Snyder, Chair of Genomics Stanford Univ.**
- **Genome 140x Coverage**
- **Blood Tests 20 Times in 14 Months**
  - **tracked nearly 20,000 distinct transcripts coding for 12,000 genes**
  - **measured the relative levels of more than 6,000 proteins and 1,000 metabolites in Snyder's blood**

Deep Learning Will Provide Personalized Assistants to Coach Us to Wellness

What Is Watson?

Watson is a cognitive technology *that processes information more like a human than a computer—by understanding natural language, generating hypotheses based on evidence and learning as it goes.*

Where Medicine Coaching is Now



Where Wellness Coaching is Going

The Looming Disruption In Integrated Healthcare Delivery Systems

- **Citizens Create Vast Datasets Outside of EMRs**
- **Post-“Watson” Personalized Coaches**
- **Doctors Must Partner with Super-Informed Patients**
- **From Pharmaceuticals to Medicinal Foods**
- **From Treating Sickness to Maintaining Wellness**

Thanks to Our Great Team!

UCSD Metagenomics Team

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Karen Nelson
Shibu Yooseph
Manolito Torralba

Calit2@UCSD Future Patient Team

Jerry Sheehan
Tom DeFanti
Kevin Patrick
Jurgen Schulze
Andrew Prudhomme
Philip Weber
Fred Raab
Joe Keefe
Ernesto Ramirez



SDSC Team

Michael Norman
Mahidhar Tatineni
Robert Sinkovits

UCSD Health Sciences Team

William J. Sandborn
Elisabeth Evans
John Chang
Brigid Boland
David Brenner