The Digital Transformation of Healthcare

Guest Lecture

Professor Kevin Zhu's MBA Class

"Disruptive Technologies in Healthcare"

UCSD's Rady School

May 18, 2012

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

Follow me at http://lsmarr.calit2.net

Calit2 Has Been Had a Vision of "the Digital Transformation of Health" for a Decade

www.bodymedia.com



- **Next Step—Putting You On-Line!**
  - Wireless Internet Transmission
  - Key Metabolic and Physical Variables
  - Model -- Dozens of Processors and 60 Sensors / Actuators Inside of our Cars
- **Post-Genomic Individualized Medicine**
  - Combine
    - Genetic Code
    - Body Data Flow
  - Use Powerful AI Data Mining Techniques

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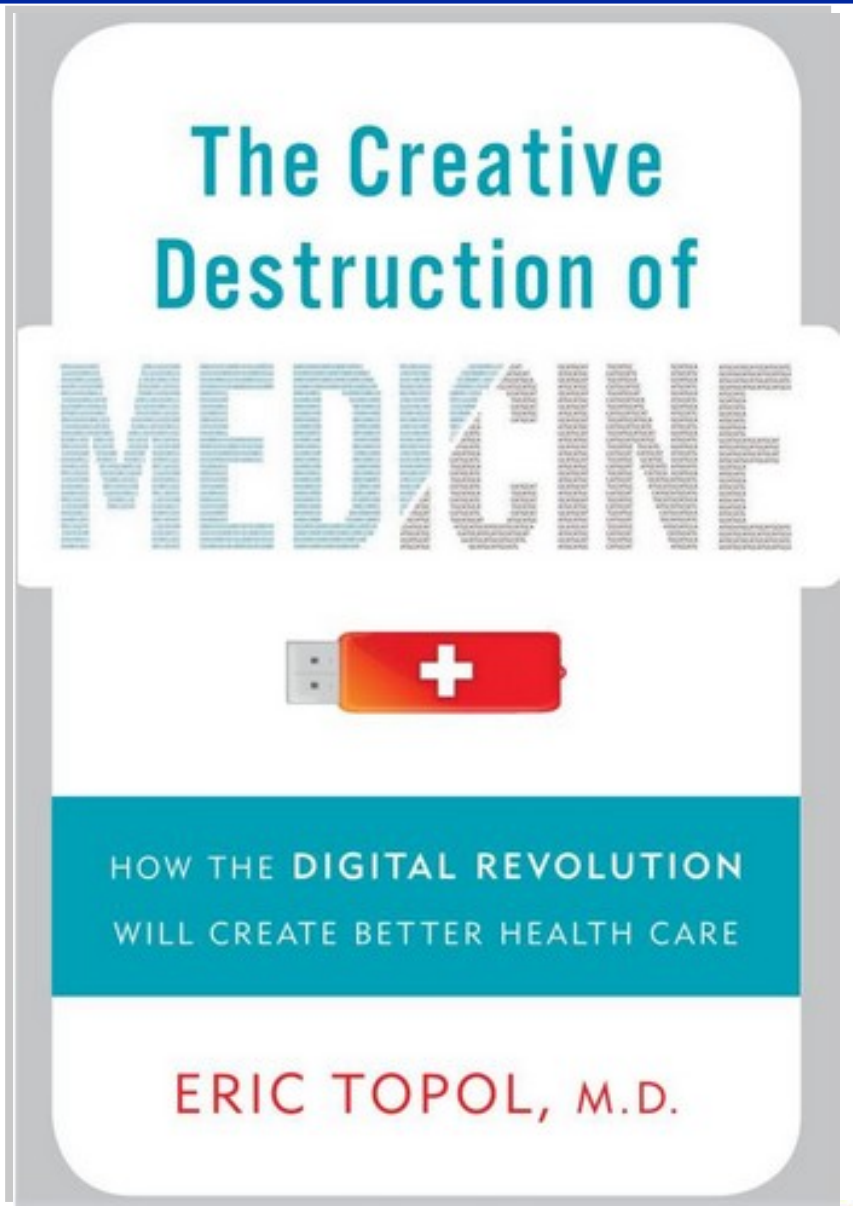
The Content of This Slide from 2001 Larry Smarr
Calit2 Talk on Digitally Enabled Genomic Medicine

it²

The Calit2 Vision of Digitally Enabled Genomic Medicine is an Emerging Reality



July/August 2011



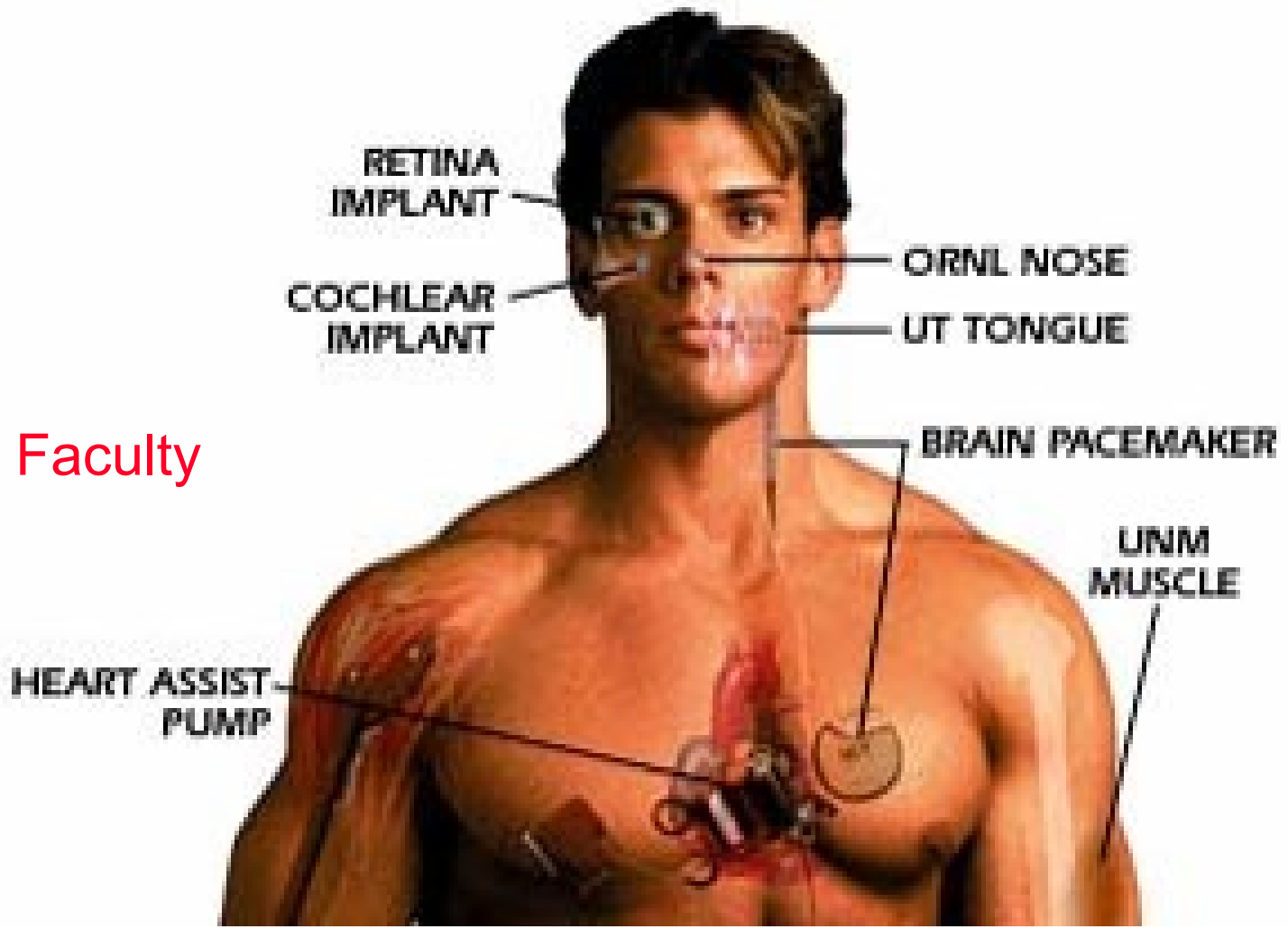
February 2012

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Lifechips--Merging Two Major Industries: Microelectronic Chips & Life Sciences

65 UCI Faculty



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lifechips
university of california, irvine
www.lifechips.org

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San Diego Has Become the National Center for Wireless Health



QUALCOMM Wireless Health

Gary & Mary West Wireless Health Institute™

CW PHS
Center For Wireless & Population Health Systems

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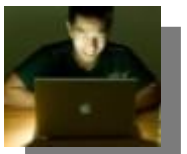
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CitiSense –New NSF Grant for Fine-Grained Environmental Sensing Using Cell Phones

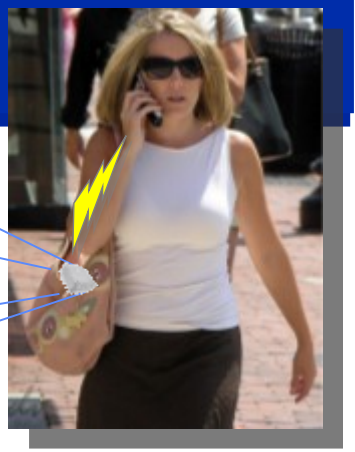




4oz
30 compounds









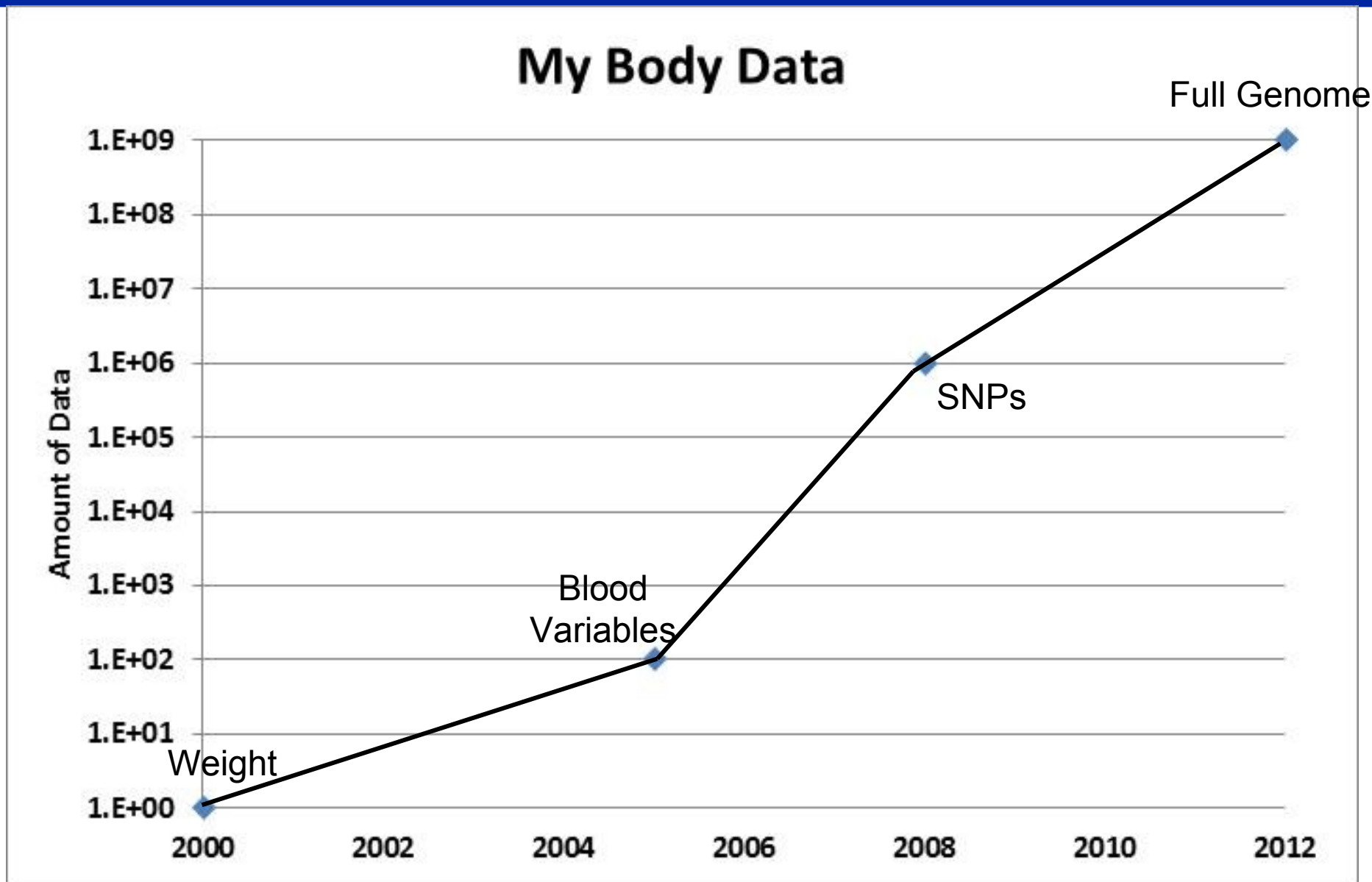




<u>CitiSense Team</u>
PI: Bill Griswold
Ingolf Krueger
Tajana Simunic Rosing
Sanjoy Dasgupta
Hovav Shacham
Kevin Patrick

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From One to a Billion Data Points Defining Me: The Exponential Rise in Body Data in Just One Decade!



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I am the Digitally-Enabled "Patient of the Future": Measuring the State of Your Body and "Tuning" It

Age 51





Age 61

I Arrived in La Jolla in 2000 After 20 Years in the Midwest and Discovered I was Pre-Diabetic.

I Reversed My Body's Decline By Altering Nutrition and Exercise

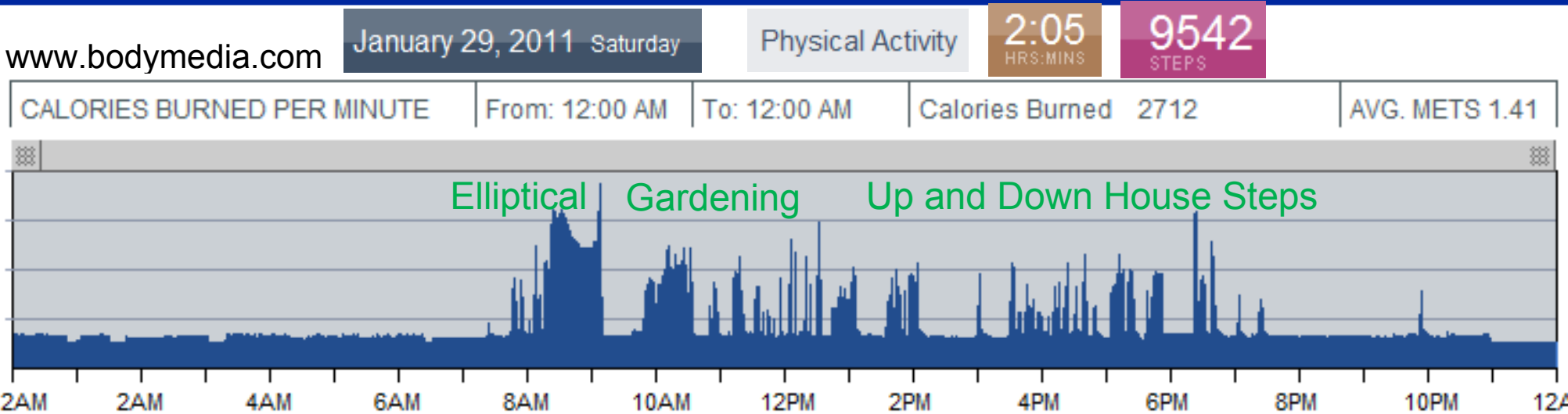
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"LifeChip" Wireless Monitoring Helps Drive Exercise Goals

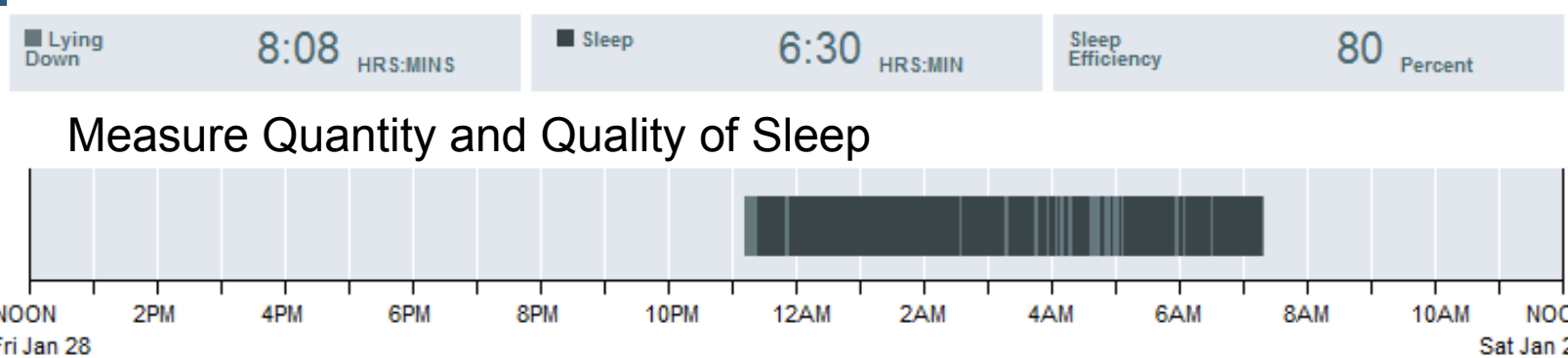
BODYMEDIA® Know your Body. Change your life

www.bodymedia.com





25 Week Average:
2473 Calories Burned/Day
1:19 hr Physical Activity/Day (>3 METs)
6887 Steps/Day (~3.4 Miles)

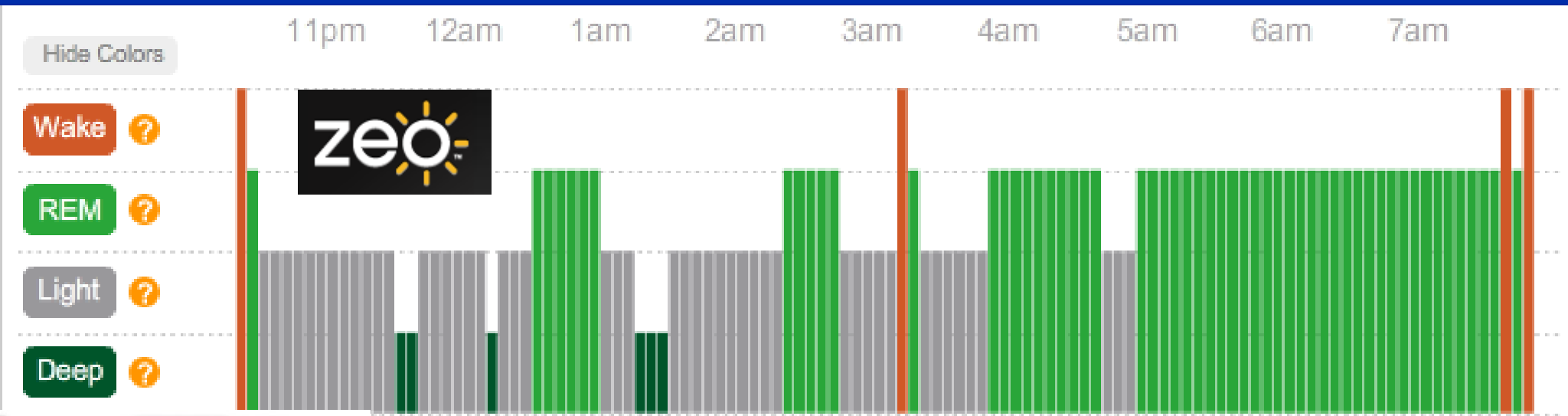


25 Week Ave: 6:51 hrs with 81% Efficiency

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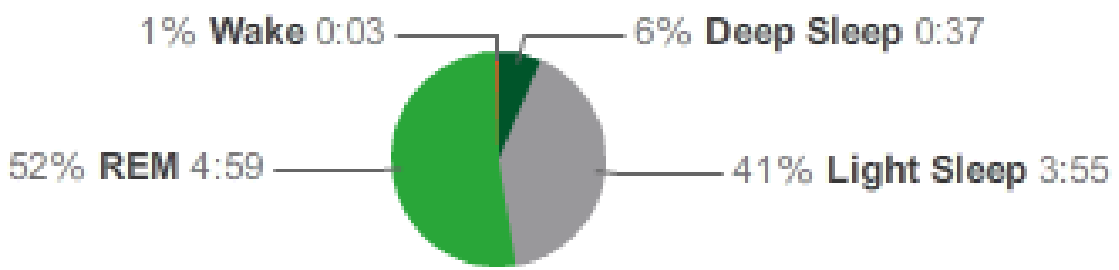
Quantifying My Sleep Pattern Using a Zeo "LifeChip" - Surprisingly About Half My Sleep is REM!





Total Z: 9 hr 31 min

Time to Z: 0 hr 2 min



Why are these numbers different from the sleep graph above?

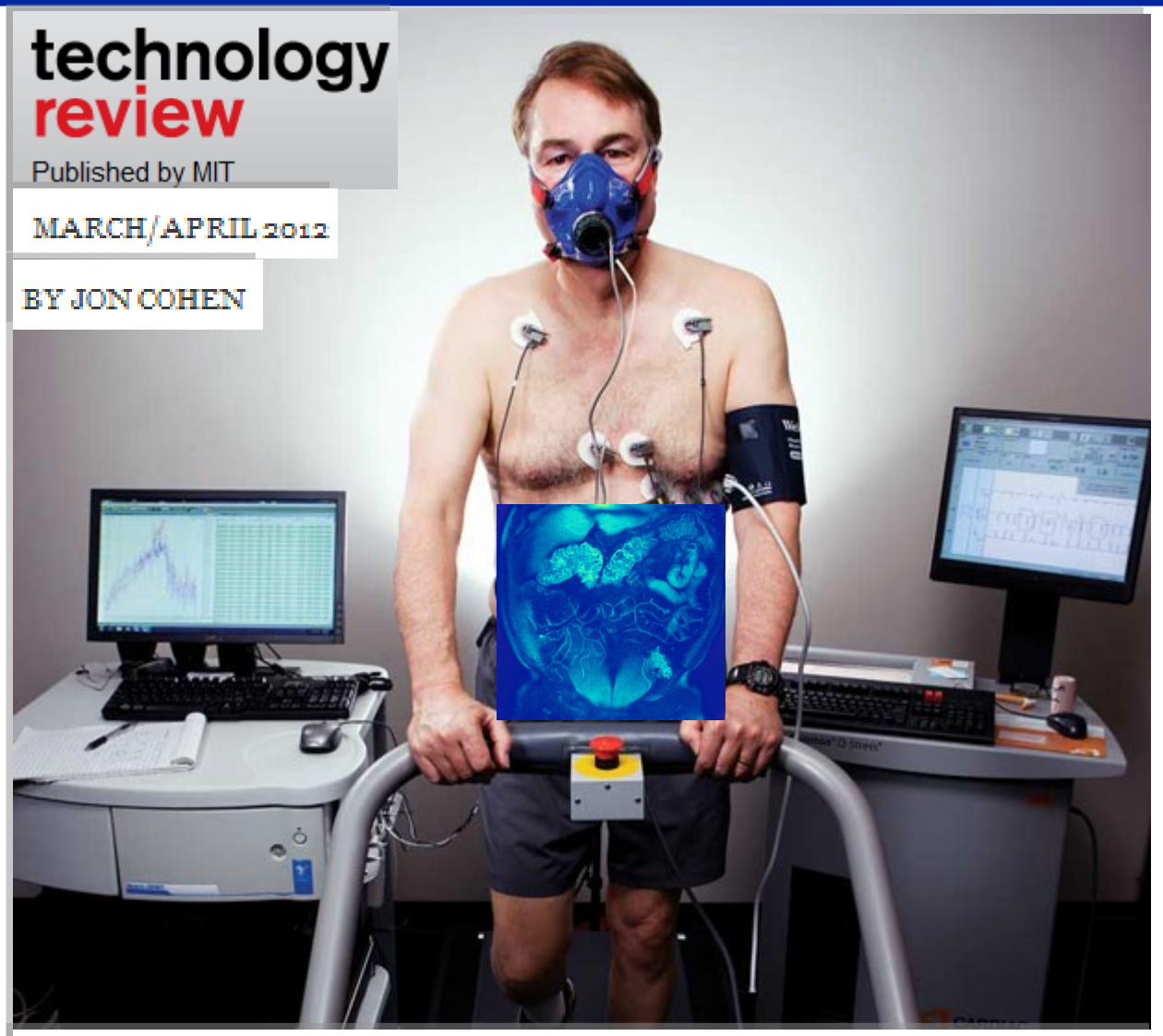
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REM is Normally 20% of Sleep
Mine is Between 45-65% of Sleep

An Infant Typically
Has 50% REM

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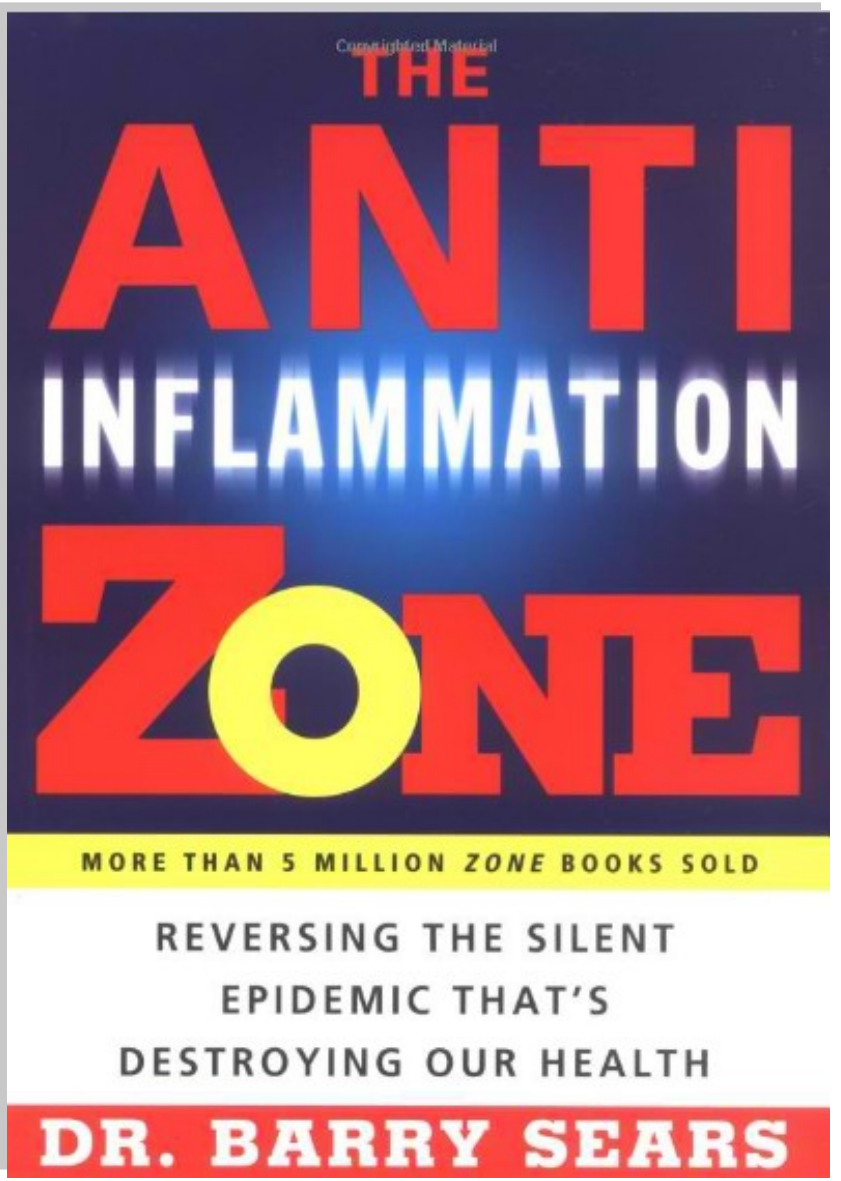
From Measuring Macro-Variables to Measuring Your Internal Variables



www.technologyreview.com/biomedicine/39636

Tracking and Reducing Inflammation is Critical to Your Health



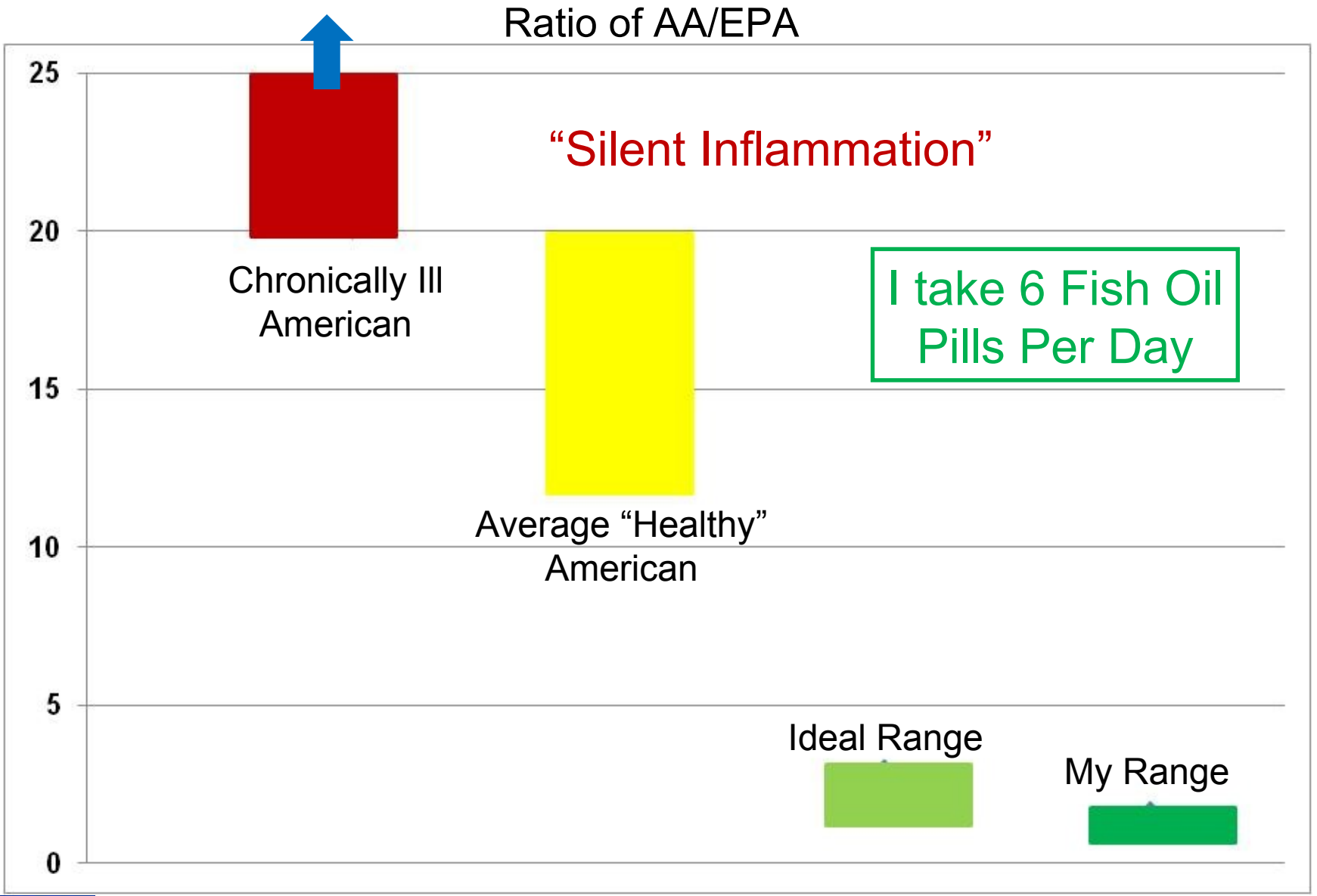


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I Have Greatly Lowered My Body's Inflammation From Food By Increasing Omega-3s



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Range Source: Barry Sears
My Tests by www.yourfuturehealth.com

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My Quarterly Blood Tests In Addition to Lipids: Only One Was Far Beyond Normal Limits

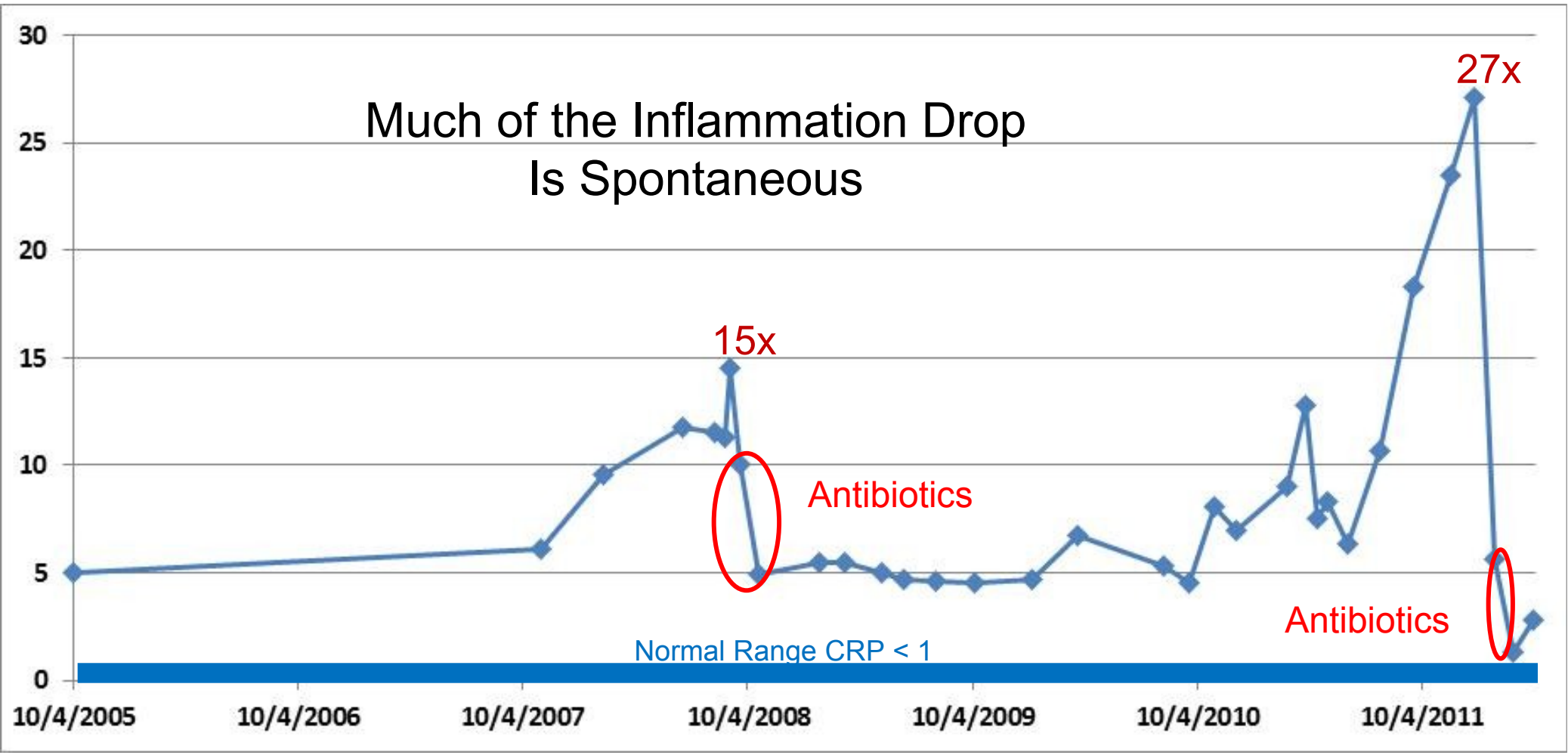
- **Electrolytes**
  - Sodium, Potassium, Calcium, Magnesium, Phosphorus, Boron, Chlorine, CO_2
- **Micronutrients**
  - Arsenic, Chromium, Cobalt, Copper, Iron, Manganese, Molybdenum, Selenium, Zinc
- **Blood Sugar Cycle**
  - Glucose, Insulin, A1C Hemoglobin
- **Cardio Risk**
  - Complex Reactive Protein
  - Homocysteine
- **Kidneys**
  - Bun, Creatinine, Uric Acid
- **Protein**
  - Total Protein, Albumin, Globulin
- **Liver**
  - GGTP, SGOT, SGPT, LDH, Total Direct Bilirubin, Alkaline Phosphatase
- **Thyroid**
  - T3 Uptake, T4, Free Thyroxine Index, FT4, 2nd Gen TSH
- **Blood Cells**
  - Complete Blood Cell Count
  - Red Blood Cell Subtypes
  - White Blood Cell Subtypes
- **Cancer Screen**
  - CEA, Total PSA, % Free PSA
  - CA-19-9
- **Vitamins & Antioxidant Screen**
  - Vit D, E; Selenium, ALA, coQ10, Glutathione, Total Antioxidant Fn.

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I Track Over 100 Blood Variables Over Time

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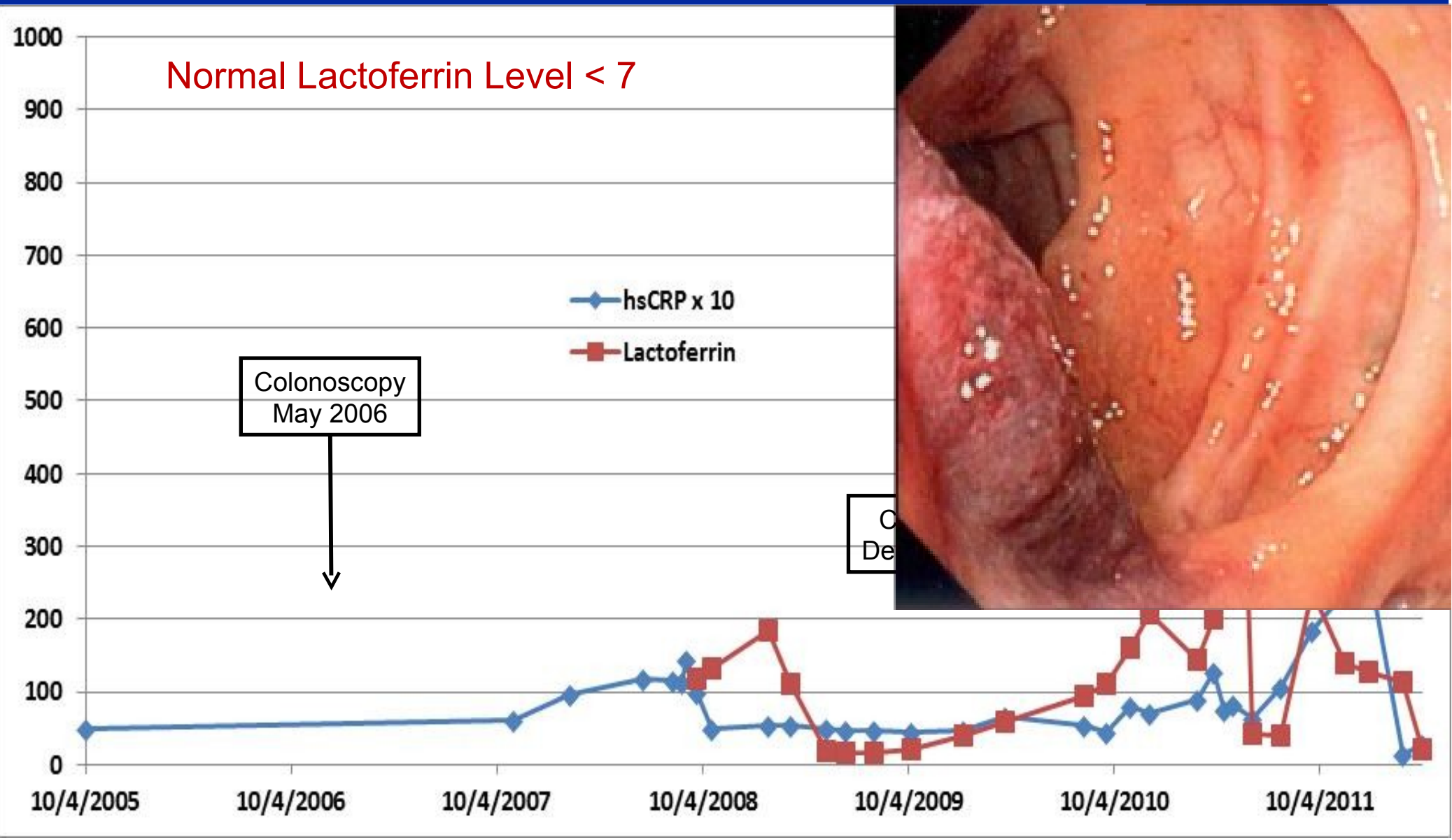
Natural Anti-Inflammation Can Be Much Larger Effect Than Antibiotic-Induced Inflammation Remission



Demonstrates Value of Fine-Grained Time Series

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Frequent Stool Analysis Reveals Lactoferrin Spike to Active Crohn's Disease (CD) Level

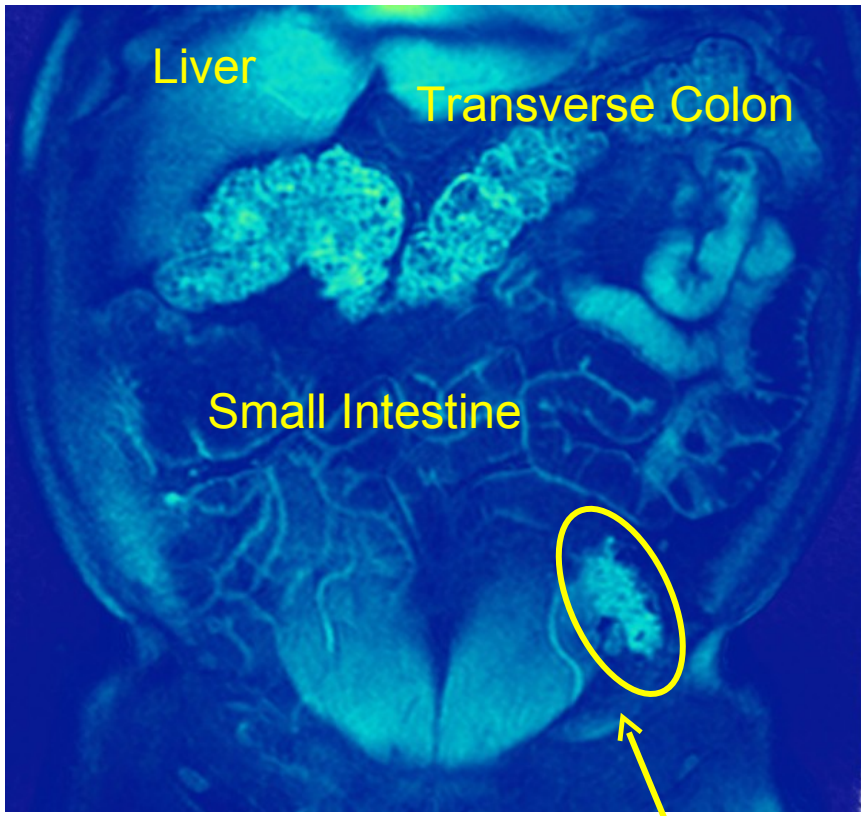


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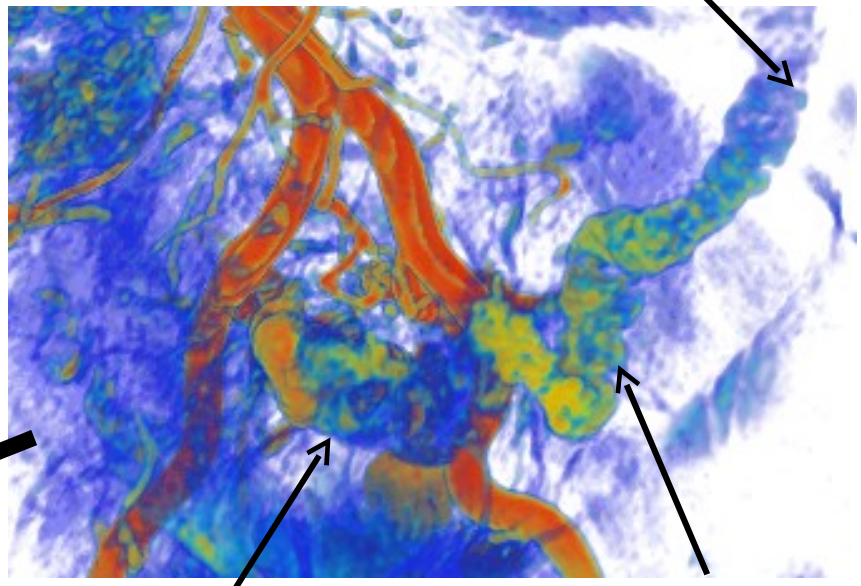
Colonoscopy and Biopsies
Support CD Diagnosis

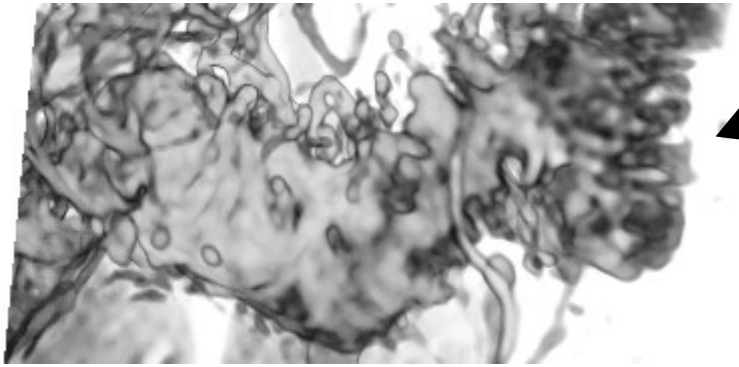
it²

Confirming the Crohn's Hypothesis: Finding the "Smoking Gun" with MRI Imaging



I Obtained the MRI Slices
From UCSD Medical Services
and Converted to Interactive 3D
Working With
Calit2 Staff & DeskVOX Software





Sigmoid Colon
Threading Iliac Arteries

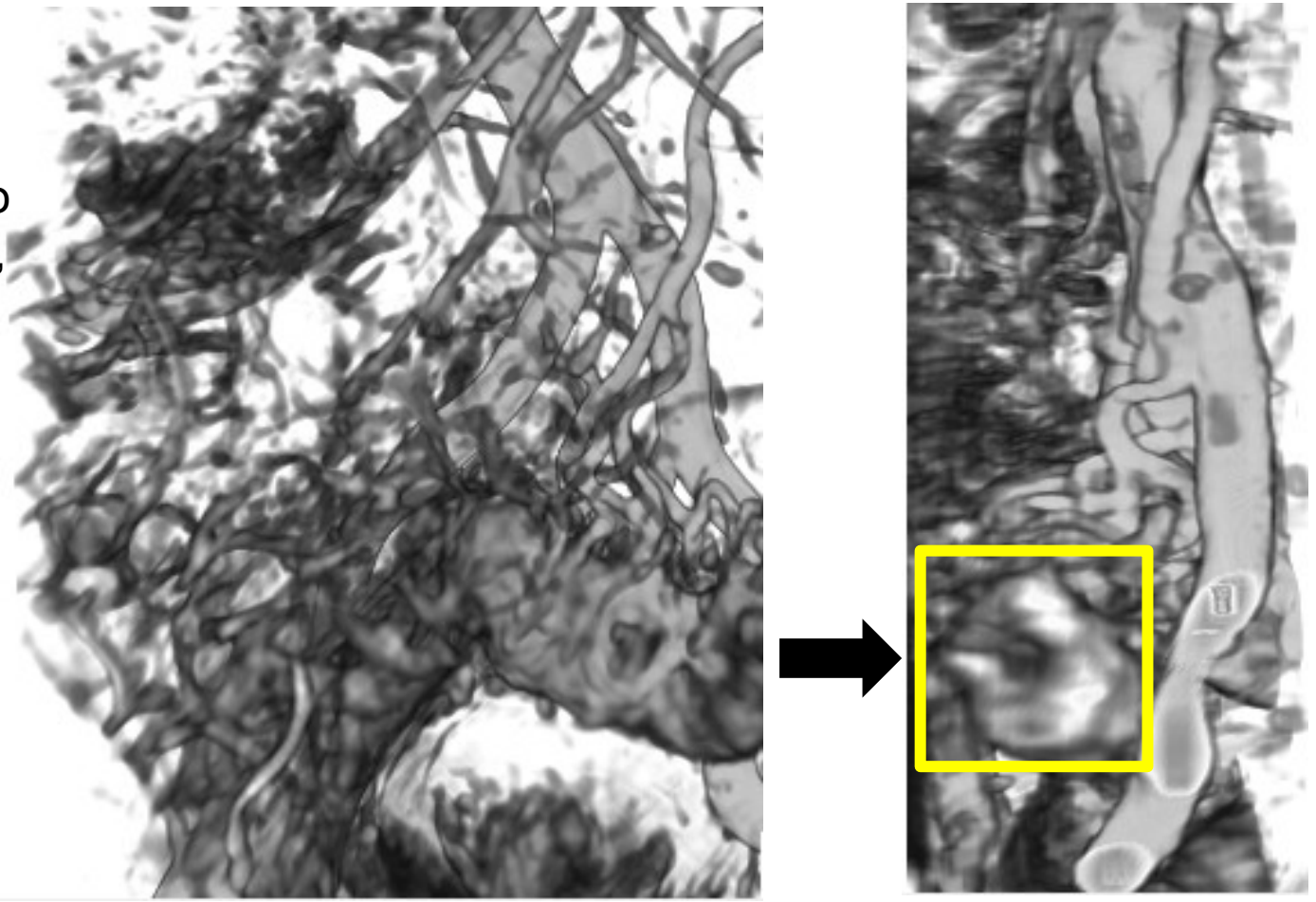
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LS Sigmoid Colon Cross Sections Showing Inflamed Wall

Jan 2012 MRI Enterography report: “long segment wall thickening in the proximal and mid portions of the sigmoid colon, extending over a segment of approximately 16 cm, with suggestion of intramural sinus tracts.

Ulcerative Colitis is Restricted to the Mucosa, while Crohn's Disease Affects the Whole Bowel Wall

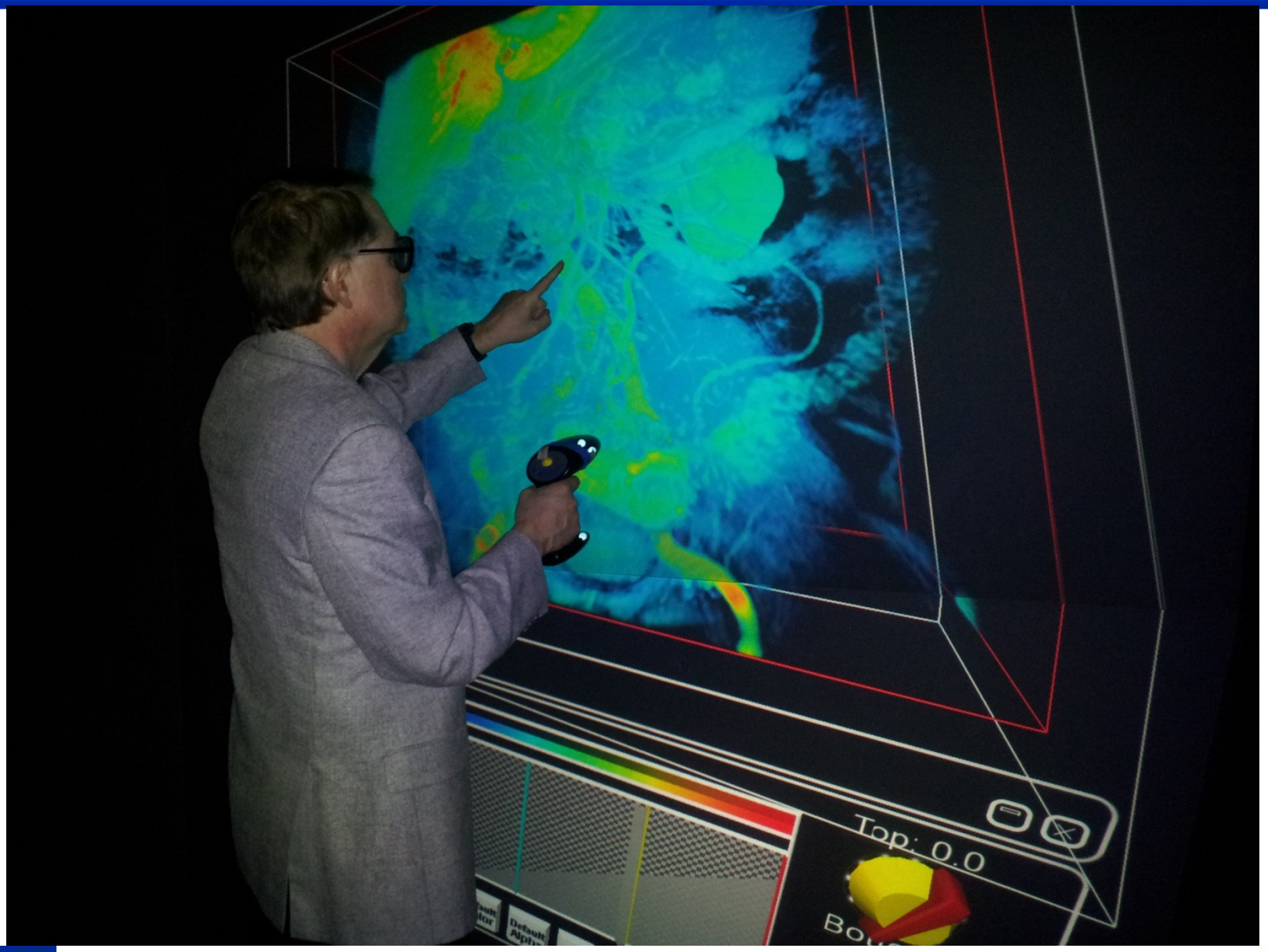


Note Thickness of Wall - Normal is 3mm (like a Balloon)

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Source: L Smarr Using Calit2’s Jurgen Schultz Software

Exploring My Internal Organs in the Calit2 Virtual Reality CAVE Using DeskVOX Software



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Photo & DeskVOX Software Courtesy of Jurgen Schulze, Calit2

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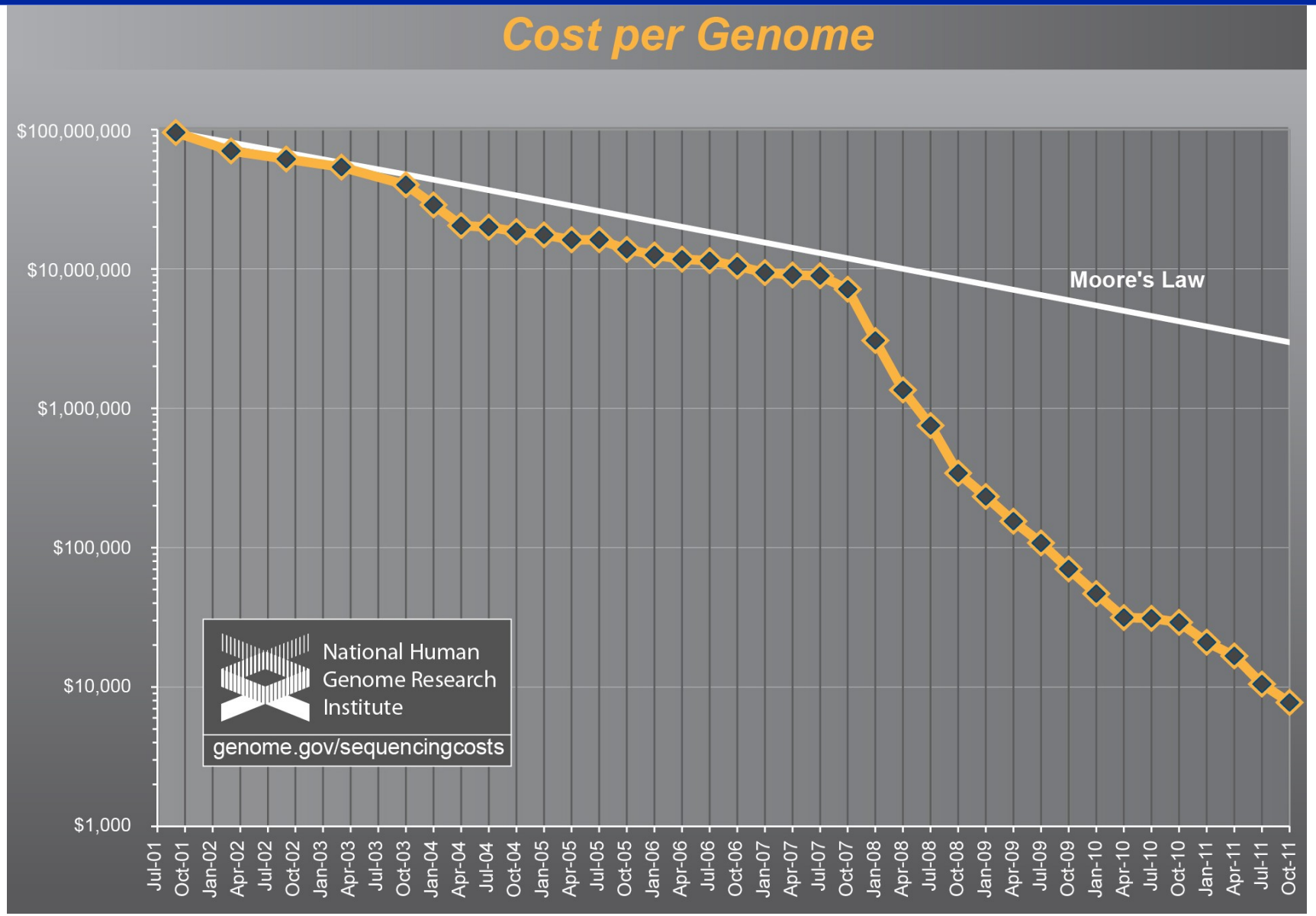
Autoimmune Diseases
Effect 5-8% of Americans

- **Crohn's Disease**
- **Ulcerative Colitis**
- **Rheumatoid Arthritis**
- **Multiple Sclerosis**
- **Psoriasis**
- **Type 1 Diabetes,**
- **Ankylosing Spondylitis**
- **Lupus Erythematosus**
- **Plus Over 70 Others**

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*
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!



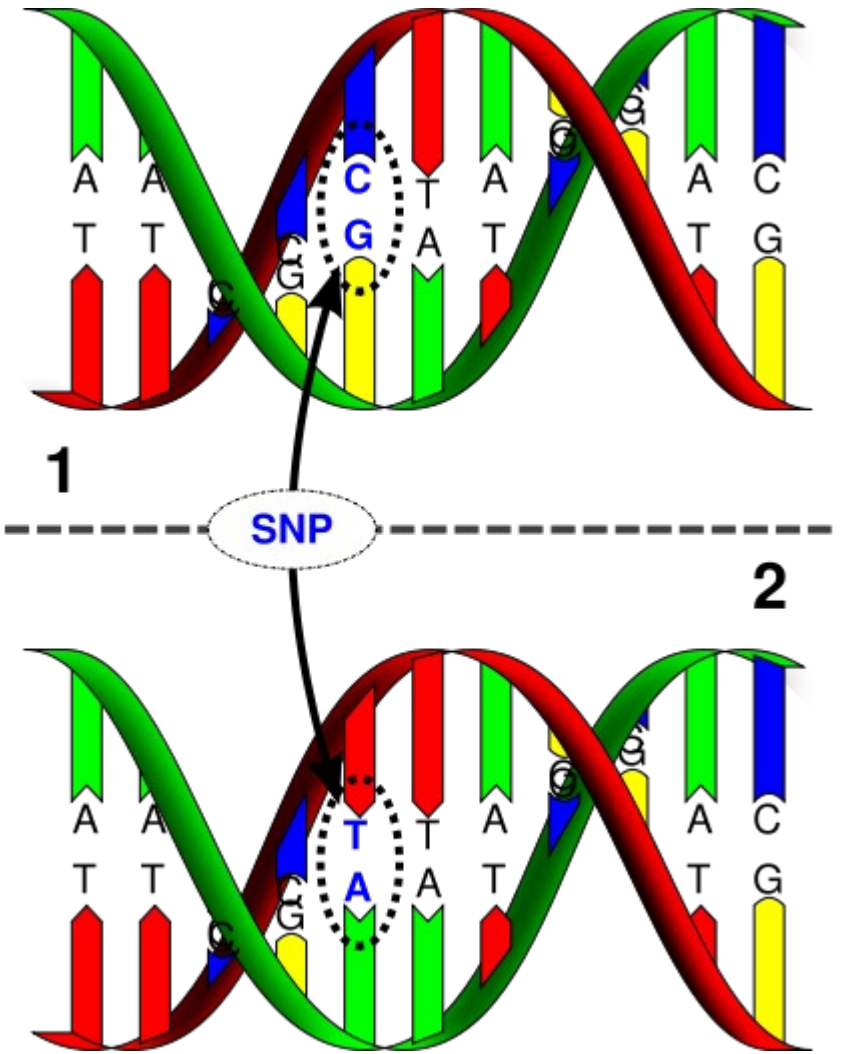
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This Has Enabled Sequencing of
Both Human and Microbial Genomes

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Single Nucleotide Polymorphisms (SNPs) Make Up About 90% of All Human Genetic Variation

Person A



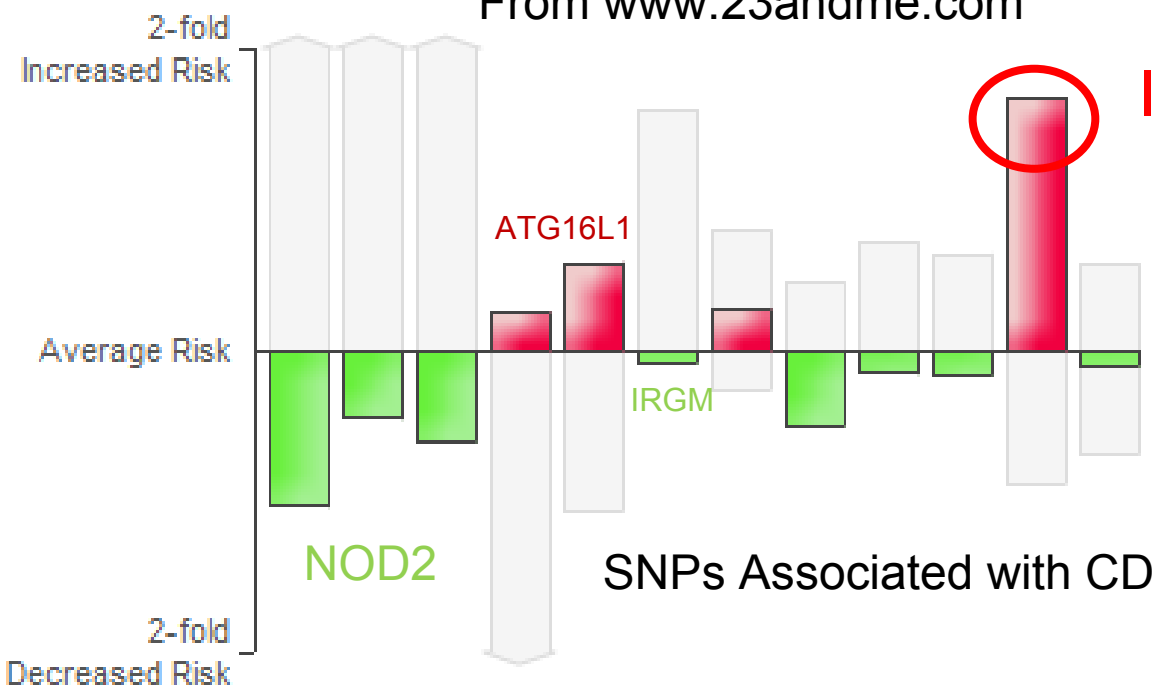
Person B

SNPs Occur Every 100 to 300 Bases Along Human DNA

www.23andme.com Tracks One Million SNPs

I Wondered if Crohn's is an Autoimmune Disease, Did I Have a Personal Genomic Polymorphism?

From www.23andme.com



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

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]

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I Have Been Accepted by PGP and Spoke at GET 2012: My Full Genome Will Be Sequenced This Year

World DNA Day: April 25, 2012

GET Genomes Environments Traits CONFERENCE

Personal Genome Project

Posted 06.01.08 | NOVA scienceNOW

The Personal Genome Project, spearheaded by George Church of Harvard's Center for Computational Genetics, aims to recruit 100,000 people willing to offer up their DNA and personal life histories. It's all in an effort to further knowledge of human genetics and why we get—or don't get—diseases.

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www.personalgenomes.org

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From 10,000 Human Genomes Sequenced in 2011 to 1 Million by 2015 Out of Less Than 5,000 sq. ft.!

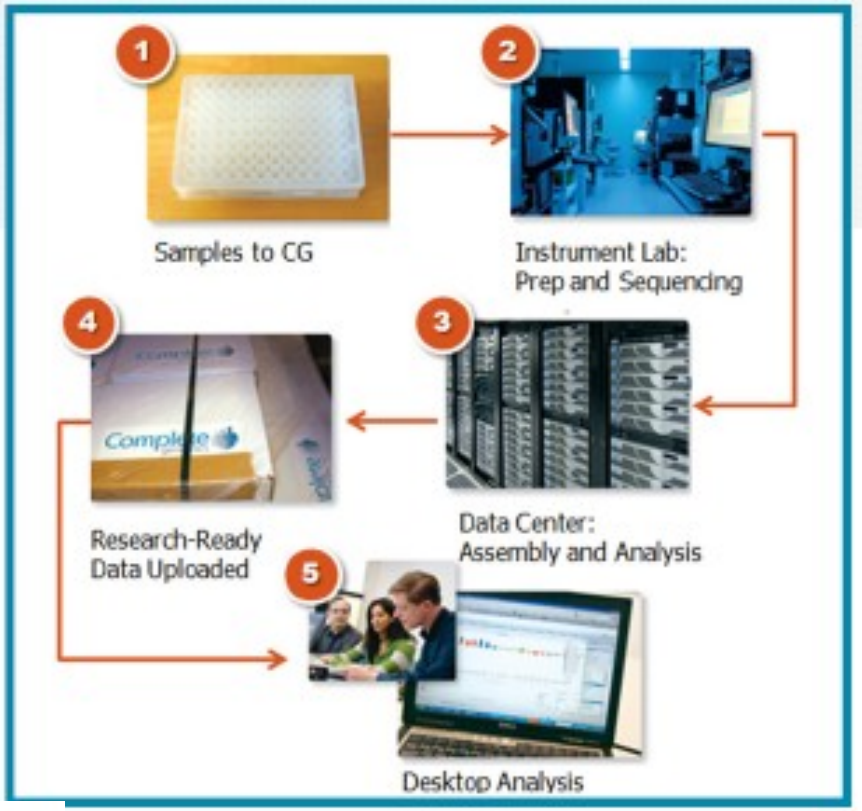
Proprietary Sequencing Technology

Designed and Optimized for Whole Human Genome Sequencing **Quality**, **Cost** and **Scale**



Outsourced Business Model

A Turnkey Service Enabling Customers to **Outsource** WGS – Samples In, **Research Ready Data** Out



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Complete genomics

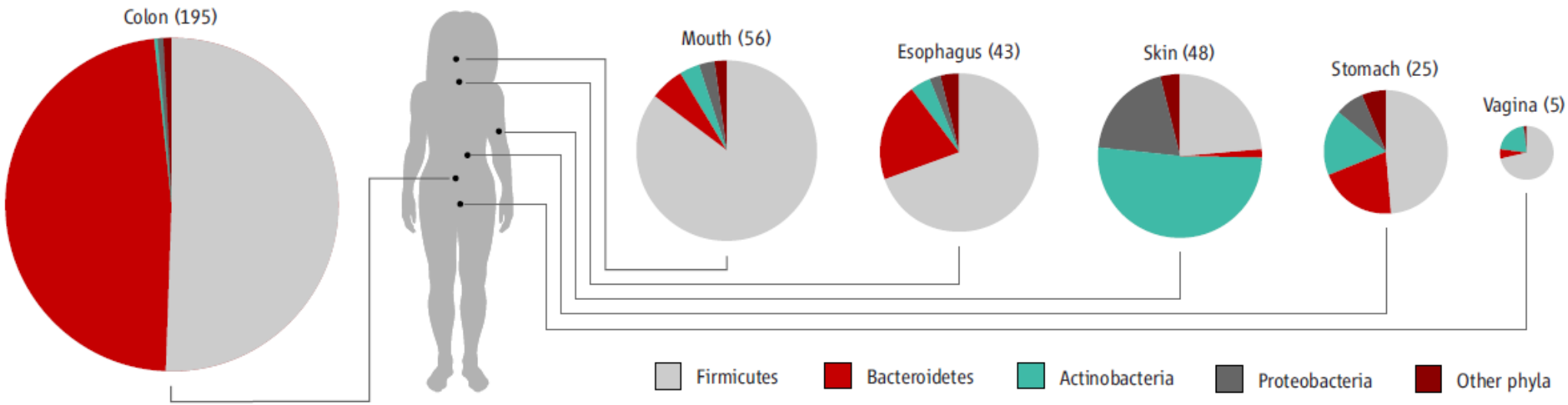
4 Million Newborns / Year in U.S.

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You are a Superorganism:
Your Body Has Ten Microbes for Every Human Cell!

Human Microbiome Project

The NIH Common Fund
WE ACCELERATE DISCOVERY.



Firmicutes Are the Dominant Phyla
in the Human Microbiome

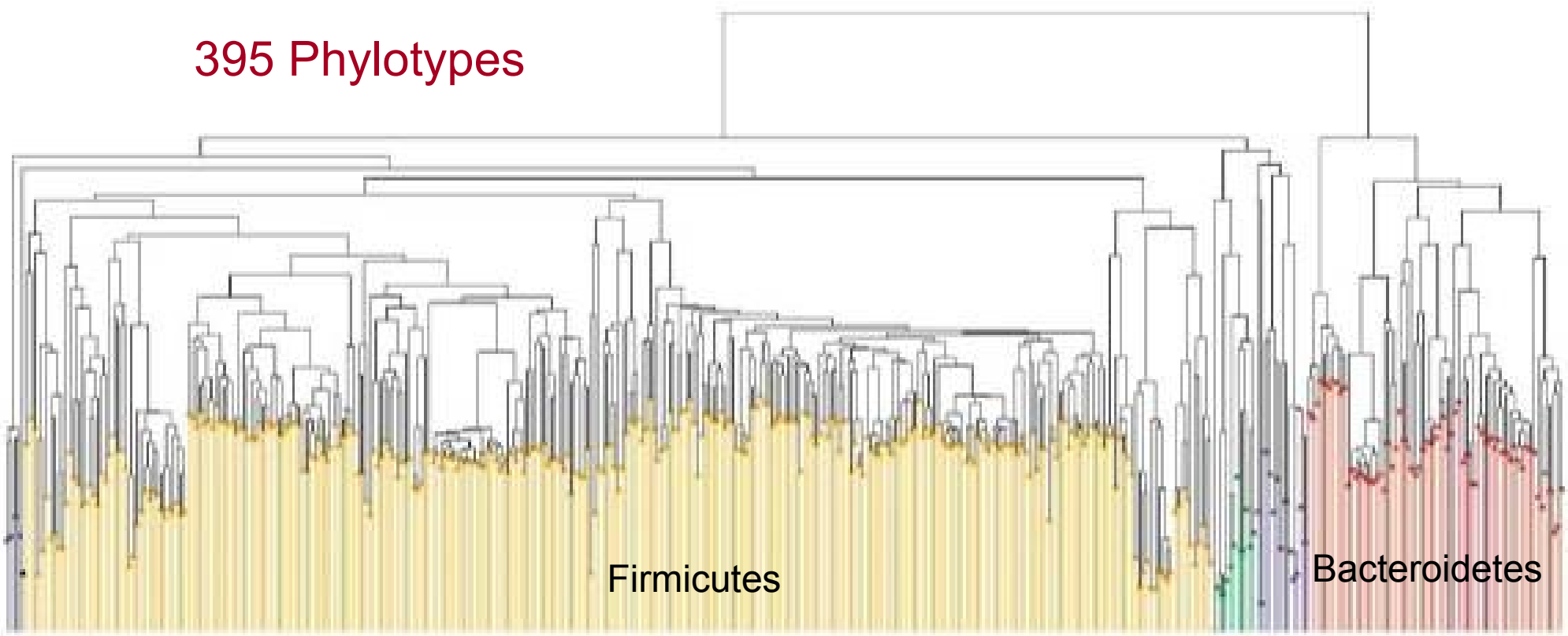
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Science v.330, p. 1619 (2010)

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The Gut Microbiome Has Been Mapped in the Last Five Years Using Genome Sequencing

"A majority of the bacterial sequences corresponded to uncultivated species and novel microorganisms."

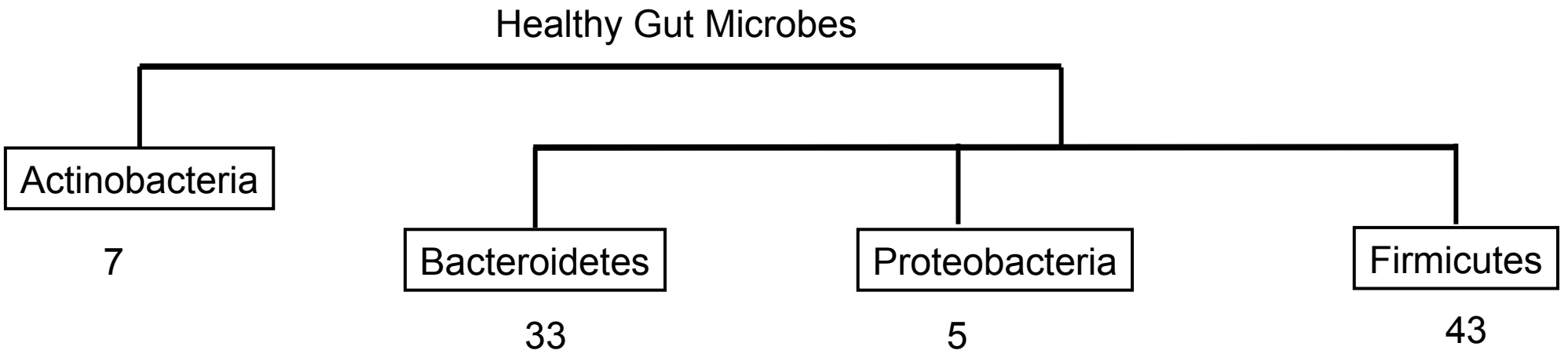


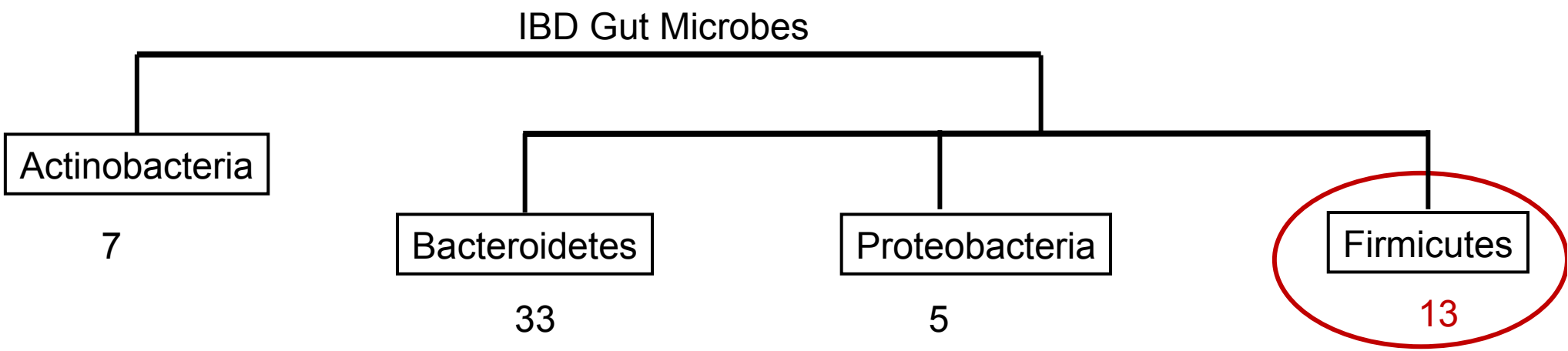
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"Diversity of the Human Intestinal Microbial Flora"
Paul B. Eckburg, et al *Science* 308, 1635-8 (2005)

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Crohn's Disease Patients Have Number of Firmicute Gut Microbe Species Reduced by Over 2/3!





The Missing Firmicutes Inhibit Pro-Inflammation

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Manichanh, et al, *Gut* 2006;55:205–211

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Next Step: Use Microarray to Measure Time Series of Microbial Diversity

www.secondgenome.com

SECOND GENOME
THE MICROBIOME COMPANY



LBL's Gary Andersen and his PhyloChip

"Second Genome has developed a sensitive, flexible and robust platform for the identification of microbiome-based signatures for the rapid identification of microbial gut health biomarkers."

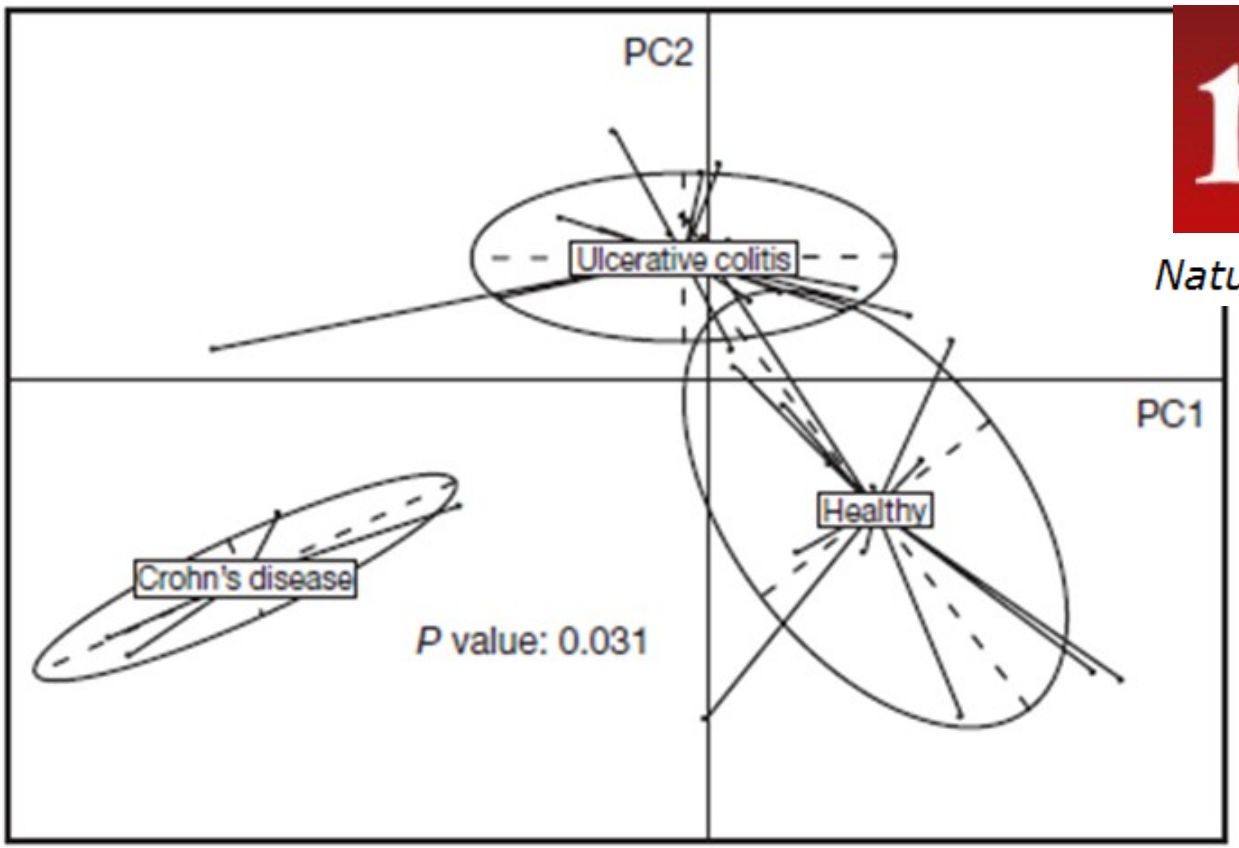
DNA microarray that can identify, within hours, over 50,000 different microbes



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Microbial Metagenomics Can Diagnose Disease States



nature

Nature **464**, 59-65 (4 March 2010)

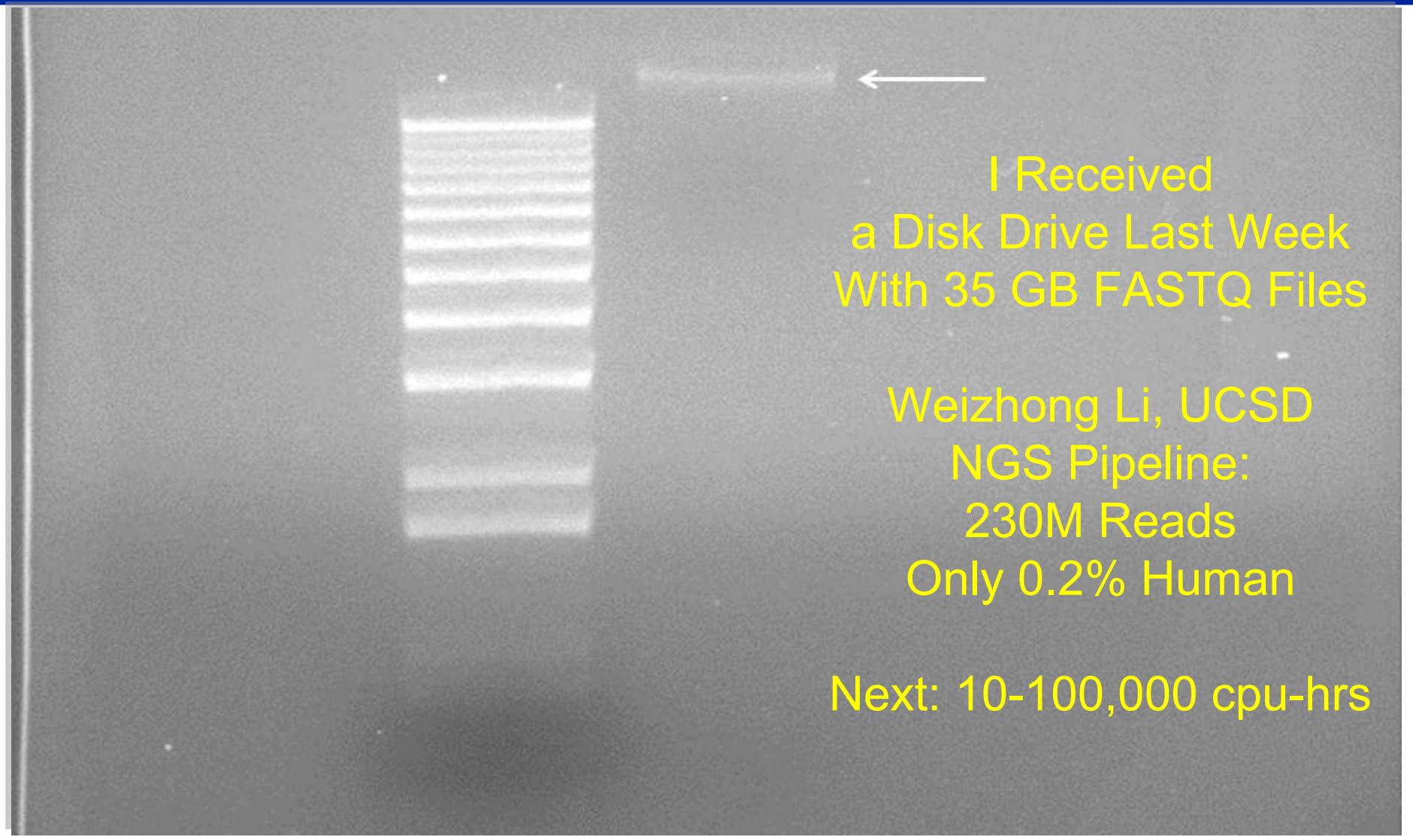
IBD Patients Harbored, on Average, *25% Fewer Microbial Genes* than the Individuals Not Suffering from IBD.

Figure 4 | Bacterial species abundance differentiates IBD patients and healthy individuals. Principal component analysis with health status as

A human gut microbial gene catalogue established by metagenomic sequencing

Junjie Qin[1]*, Ruiqiang Li[1]*, Jeroen Raes[2,3], Manimozhiyan Arumugam[2], Kristoffer Solvsten Burgdorf[4],

First Stage of Metagenomic Sequencing of My Gut Microbiome at J. Craig Venter Institute



Gel Image of Extract from Smarr Sample-Next is Library Construction

Manny Torralba, Project Lead - Human Genomic Medicine
J Craig Venter Institute

January 25, 2012

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

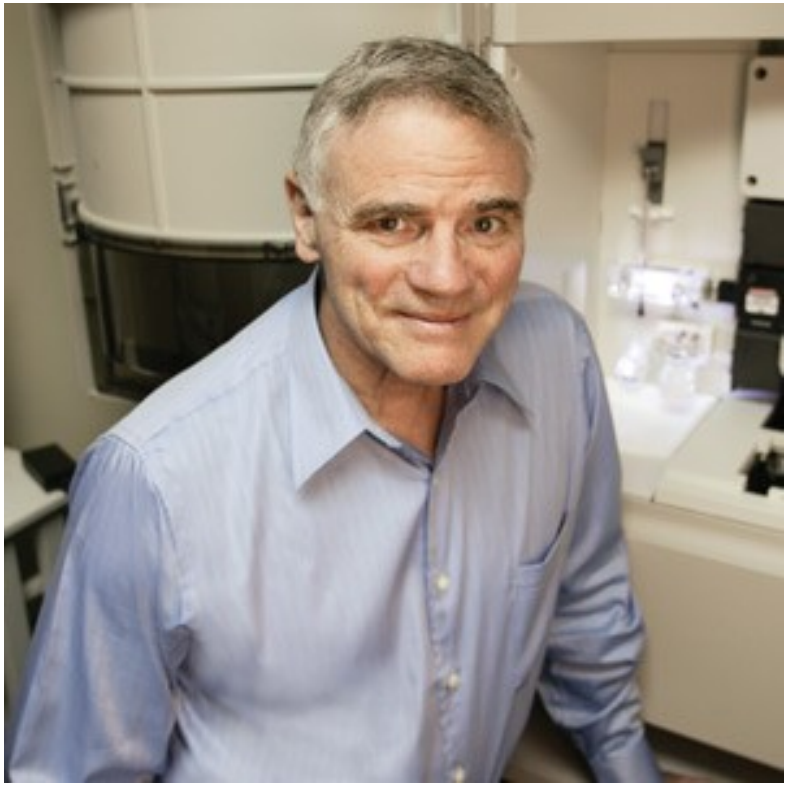
Newsweek

I am Leroy Hood's Lab Rat!

A Doctor's Vision of the Future of Medicine

Leroy Hood
NEWSWEEK

From the magazine issue dated Jul 13, 2009



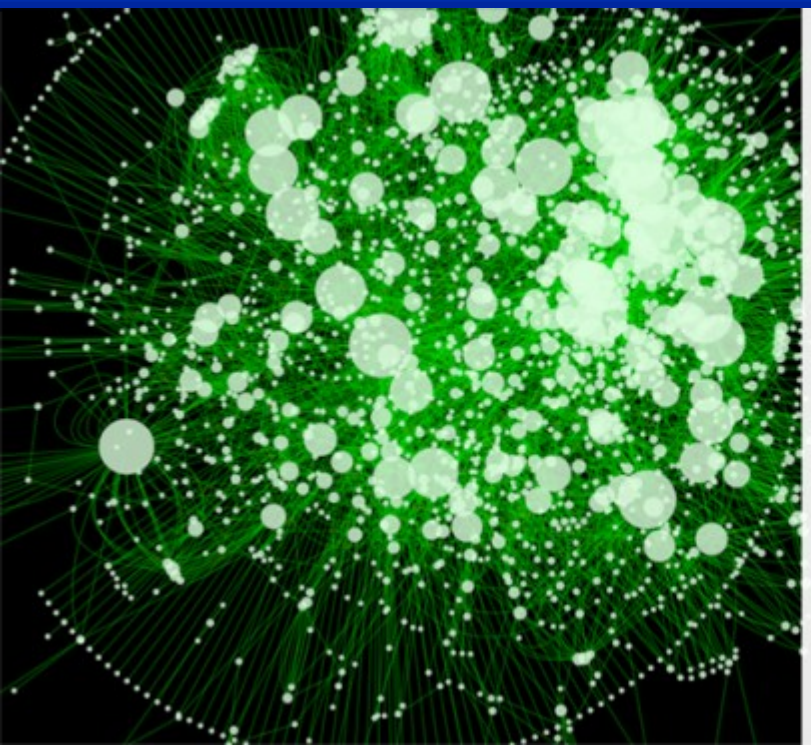
Using a "LifeChip"
Quantify ~2500 Blood Proteins,
50 Each from 50 Organs or Cell Types
from a Single Drop of Blood
To Create a Time Series

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

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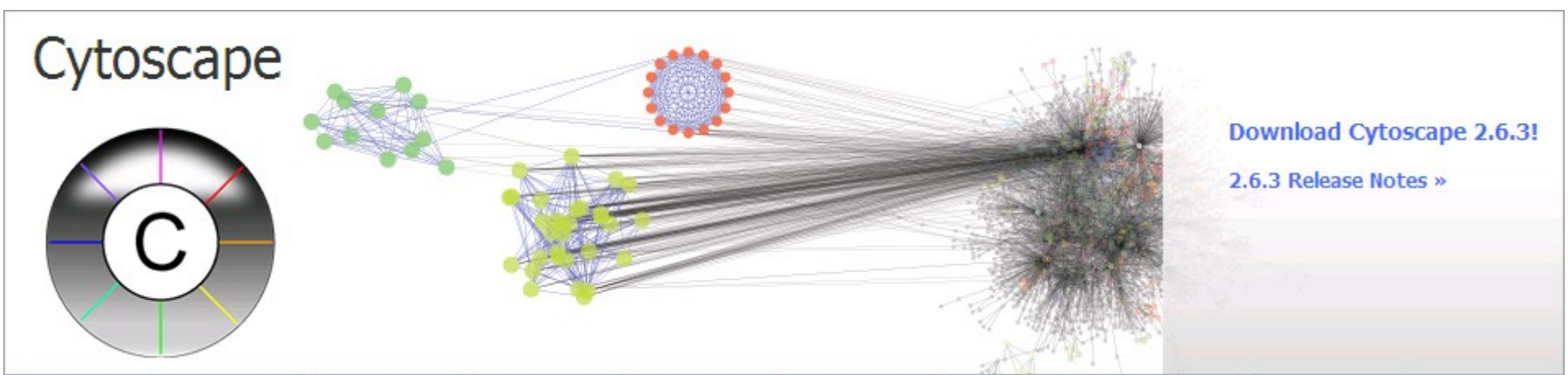
Integrating Systems Biology Data: Cytoscape



Cytoscape

An Open Source Platform for Network Analysis and Visualization

- **OPEN SOURCE Java Platform for Integration of Systems Biology Data**
- **Layout and Query of Interaction Networks (Physical And Genetic)**
- **Visual and Programmatic Integration of Molecular State Data (Attributes)**



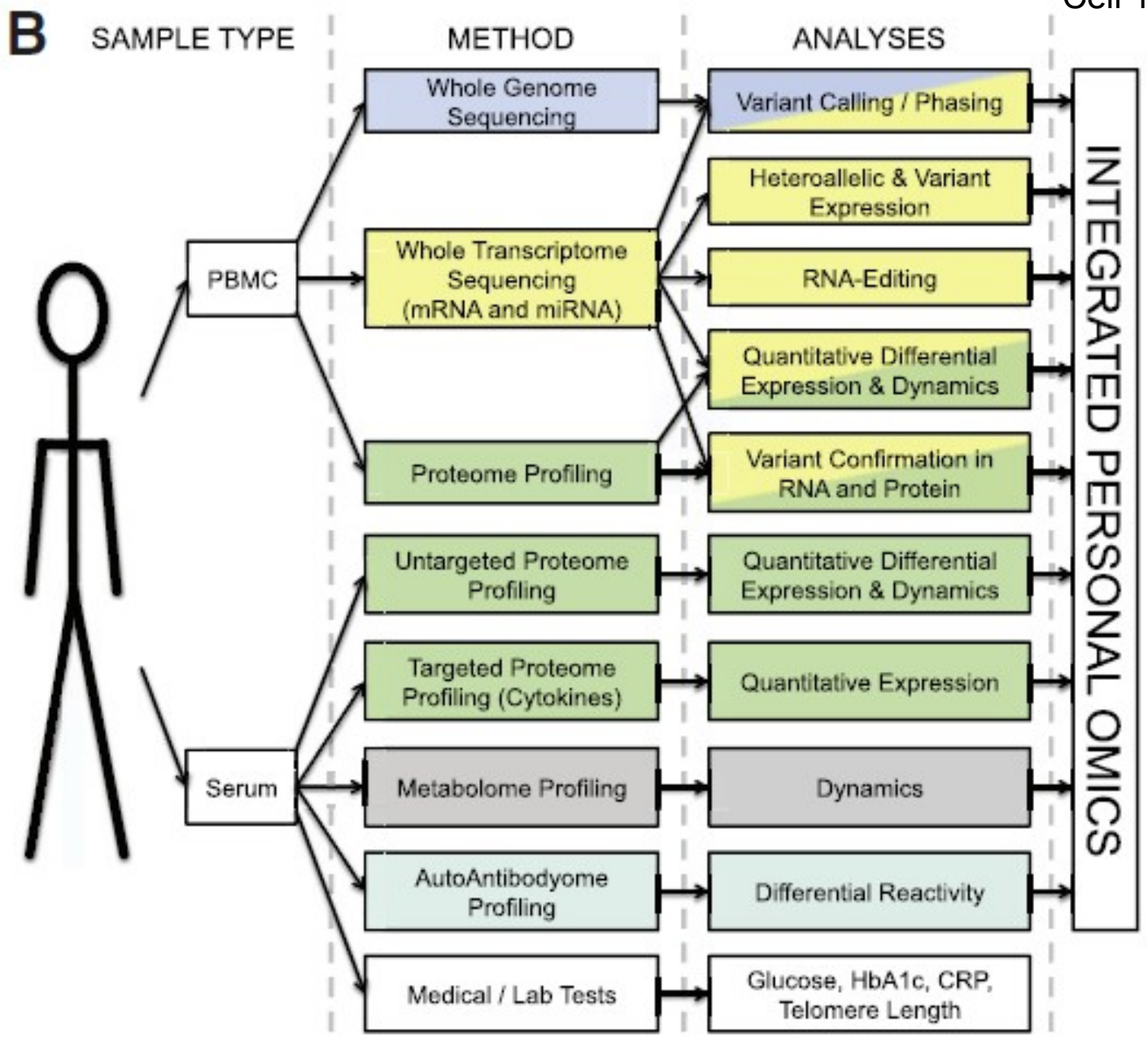
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www.cytoscape.org

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Integrative Personal Omics Profiling: What I am Doing, But 1000 Times the Data!

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**