“Deep Self - Quantifying the State of Your Body”

Invited Talk

NextMed / MMVR20

San Diego

February 21, 2013

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

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Abstract

The use of advanced IT technology to develop a detailed view of the state of one's body, along with its time rate of change, has made exponential progress in the last decade. During that time, the numbers by which I define my body's state has increased by one billion fold. I will describe how I have combined time series of over one hundred blood and stool variables with genomic sequencing of my human and microbial DNA and a variety of imaging modalities to simultaneously improve my health and discover previously unknown disease states. Currently, I am using advanced visualization technologies, which you can experience during the conference tour of Calit2, together with visual data analytics to decipher the complex interactions between the various components of my immune system and the human and microbial DNA present in my "superorganism" body.

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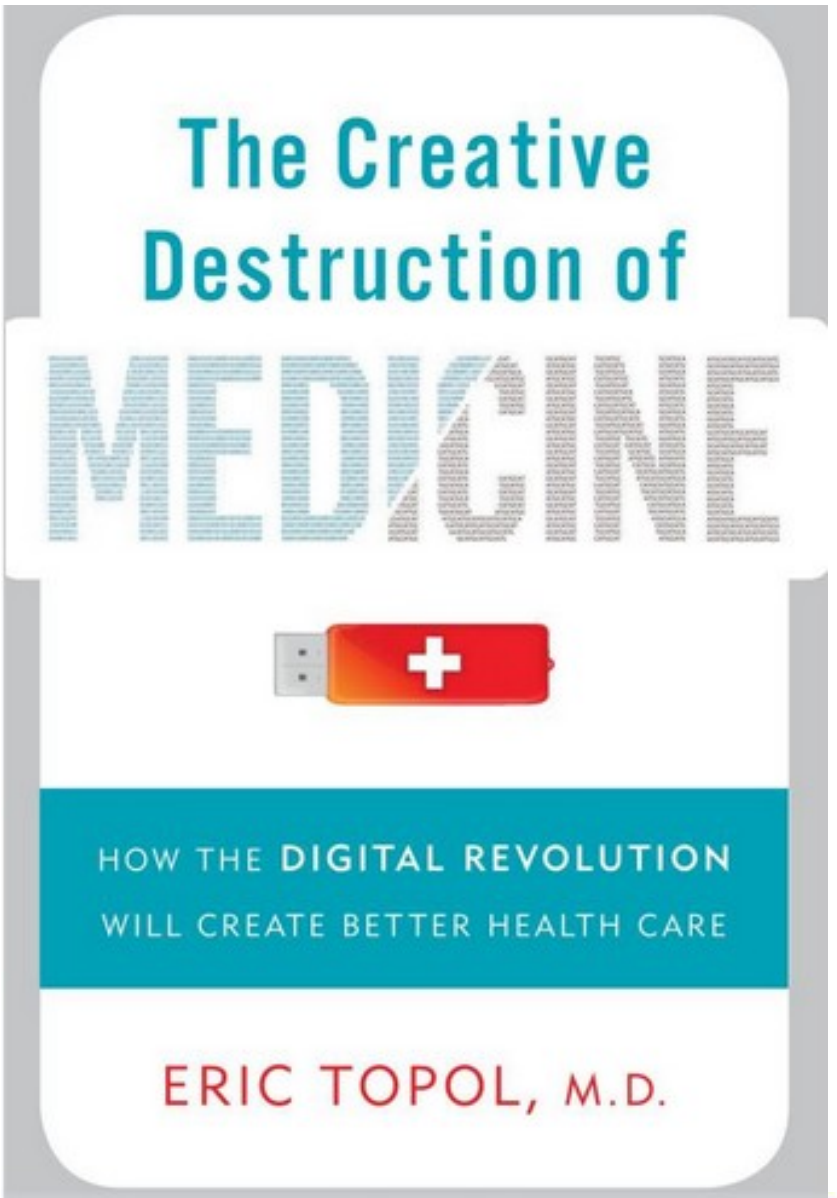
The Content of This Slide from 2001 Larry Smarr Calit2 Talk on Digitally Enabled Genomic Medicine

it²

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



July/August 2011



February 2012

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

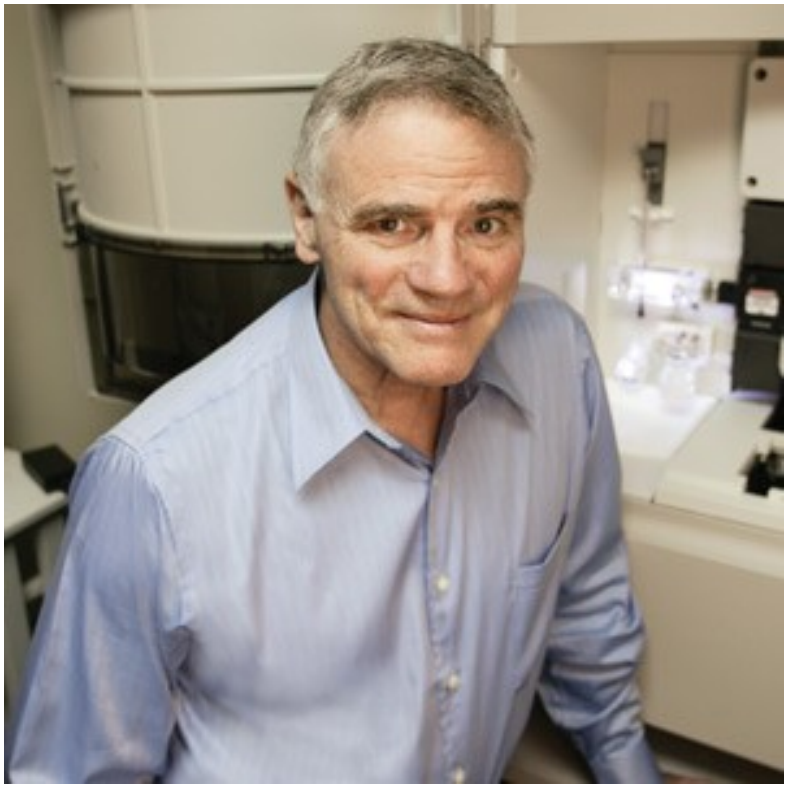
Newsweek

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



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

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I Arrived in La Jolla in 2000 After 20 Years in the Midwest and Decided to Move Against the Obesity Trend

Age 41



Age 51



Age 61



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

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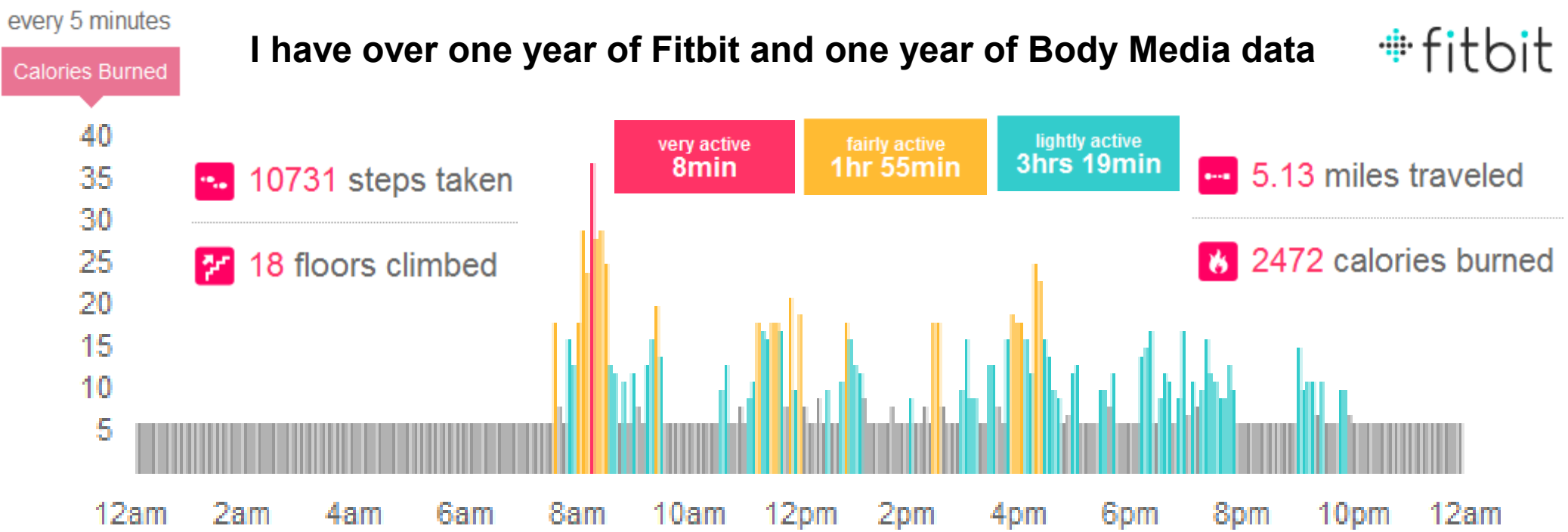
http://lsmarr.calit2.net/repository/LS_reading_recommendations_FiRe_2011.pdf

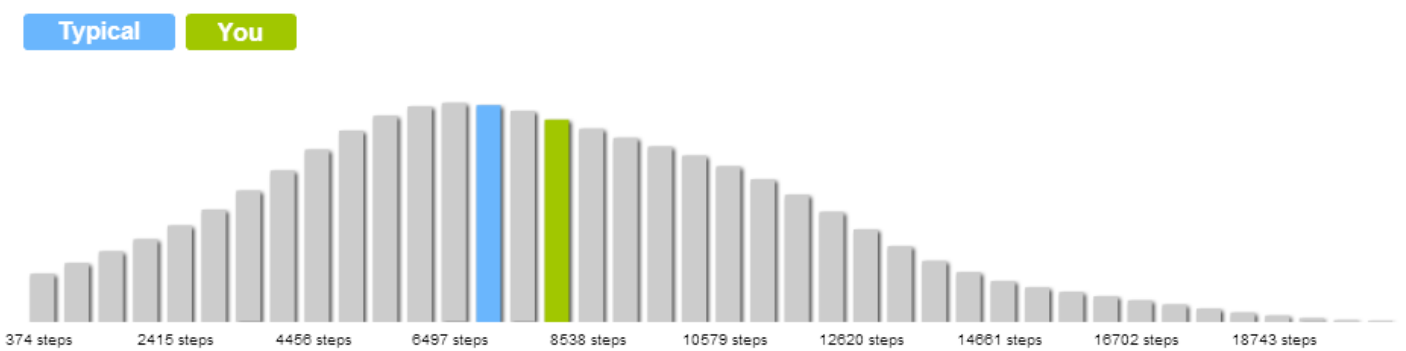
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Wireless Monitoring Helps Drive Exercise Goals

I have over one year of Fitbit and one year of Body Media data

fitbit







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This week you walked

8028 steps

15% more than the median for men 55 to 64 yrs who are normal or underweight

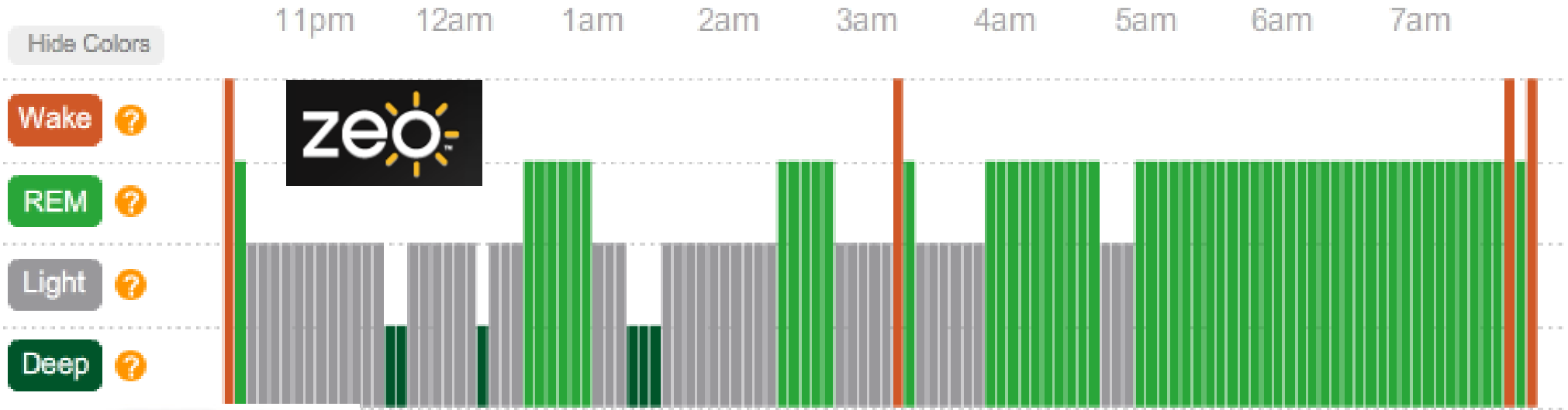
You are in the

60 percentile

of all men 55 to 64 yrs who are normal or underweight

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

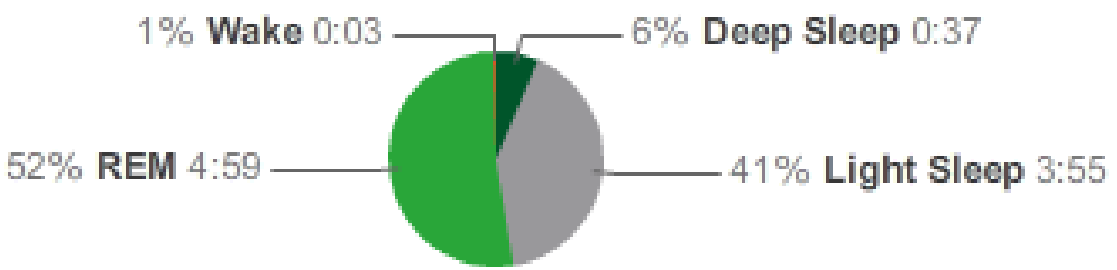




Stroke risk increased by sleeping less than six hours a night
-M. Ruiter, *Sleep* 2012

Total Z: 9 hr 31 min

Time to Z: 0 hr 2 min



Why are these numbers different from the sleep graph above?

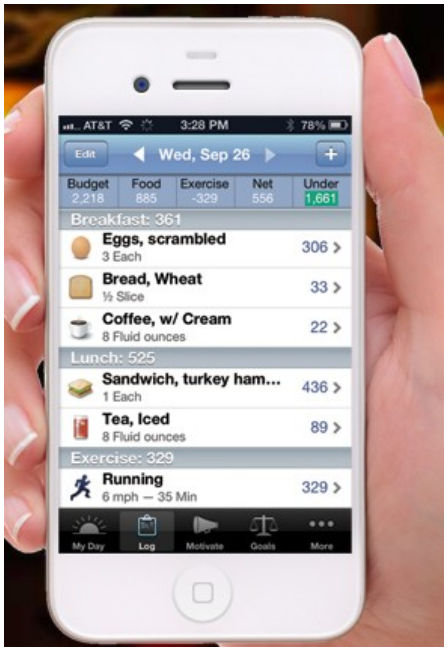
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REM is Normally 20% of Sleep
Mine is Between 45-65% of Sleep

An Infant Typically Has 50% REM

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Challenge-Develop Standards to Enable MashUps of Personal Sensor Data Across Private Clouds



Lose It-
Calories Ingested



Body Media-
Calories Burned



Withing/iPhone-
Blood Pressure





EM Wave PC-
Stress



Azumio-Heart Rate



Zeo-Sleep

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From Measuring Macro-Variables to Measuring Your Internal Variables

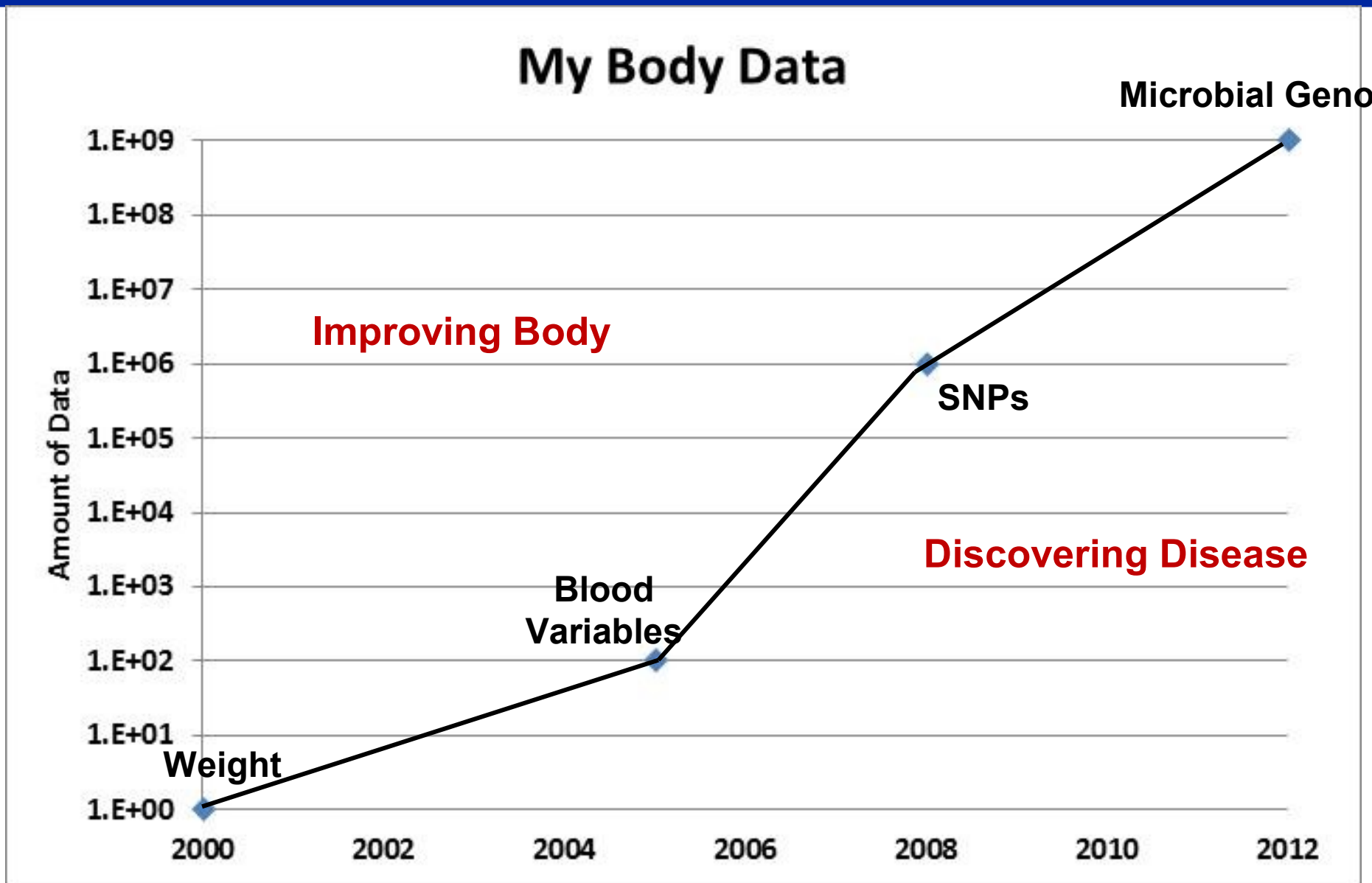


www.technologyreview.com/biomedicine/39636

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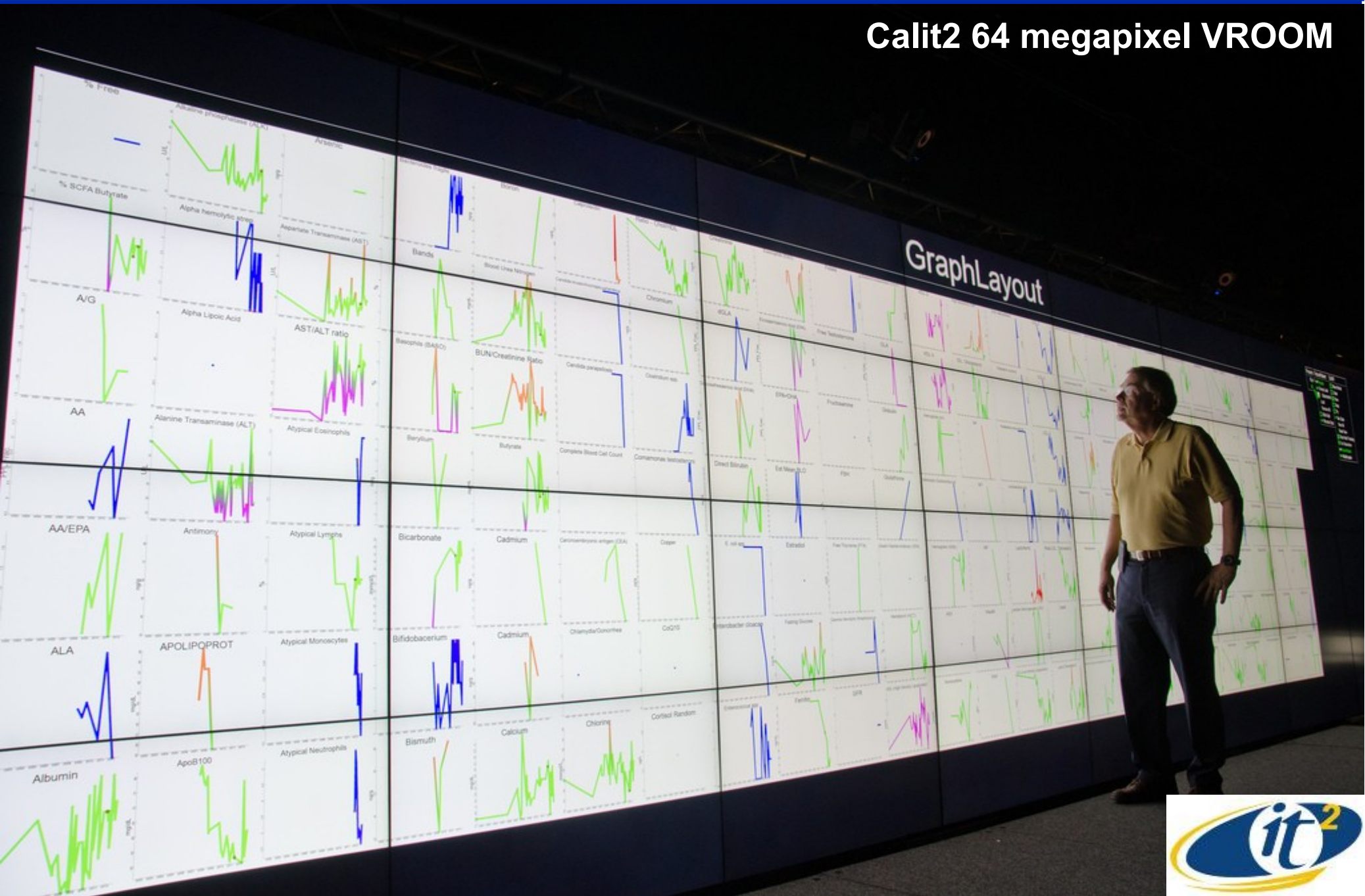
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From One to a Billion Data Points Defining Me: The Exponential Rise in Body Data in Just One Decade!

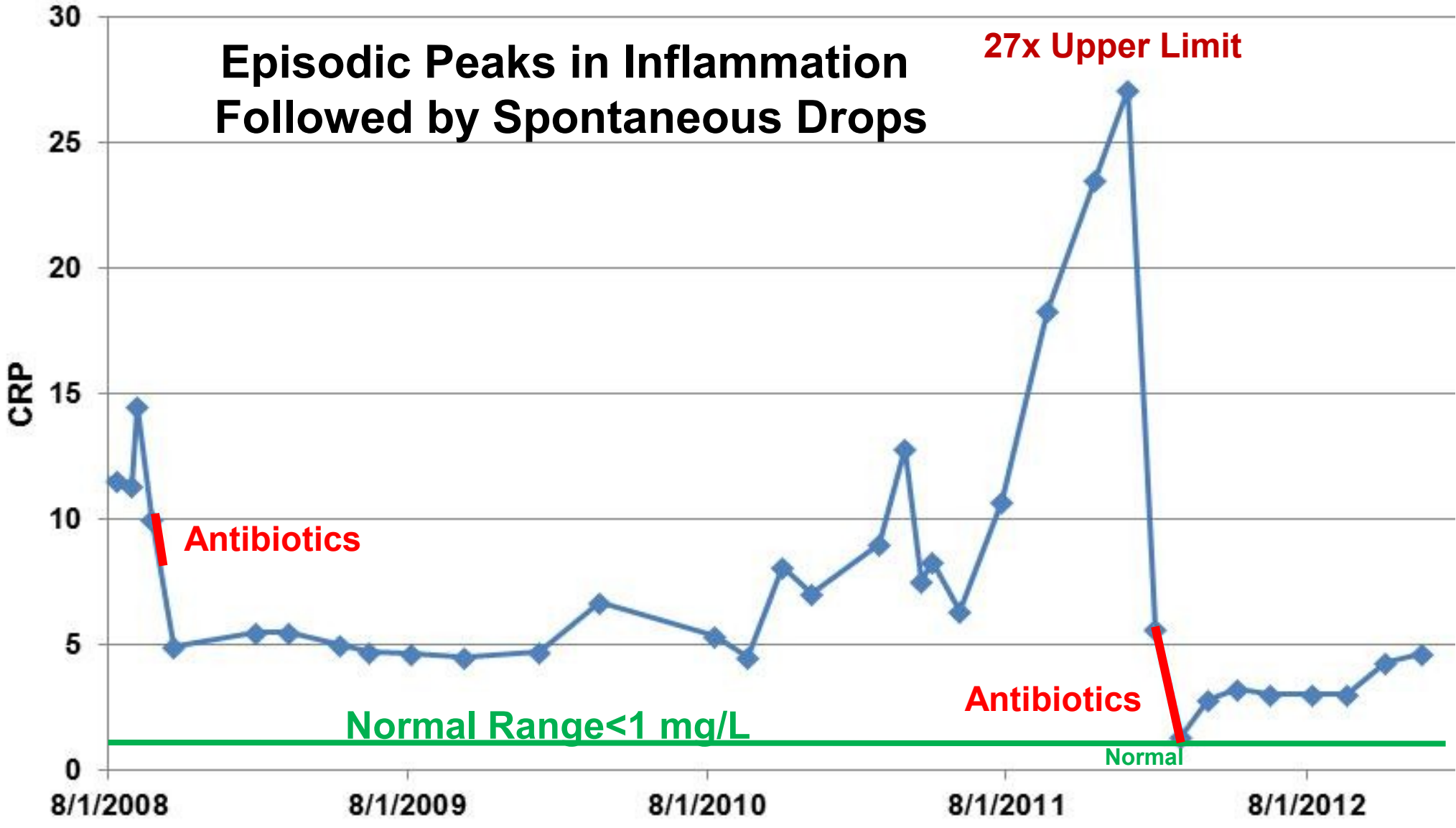


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Visualizing Time Series of 150 LS Blood and Stool Variables, Each Over 5 Years



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

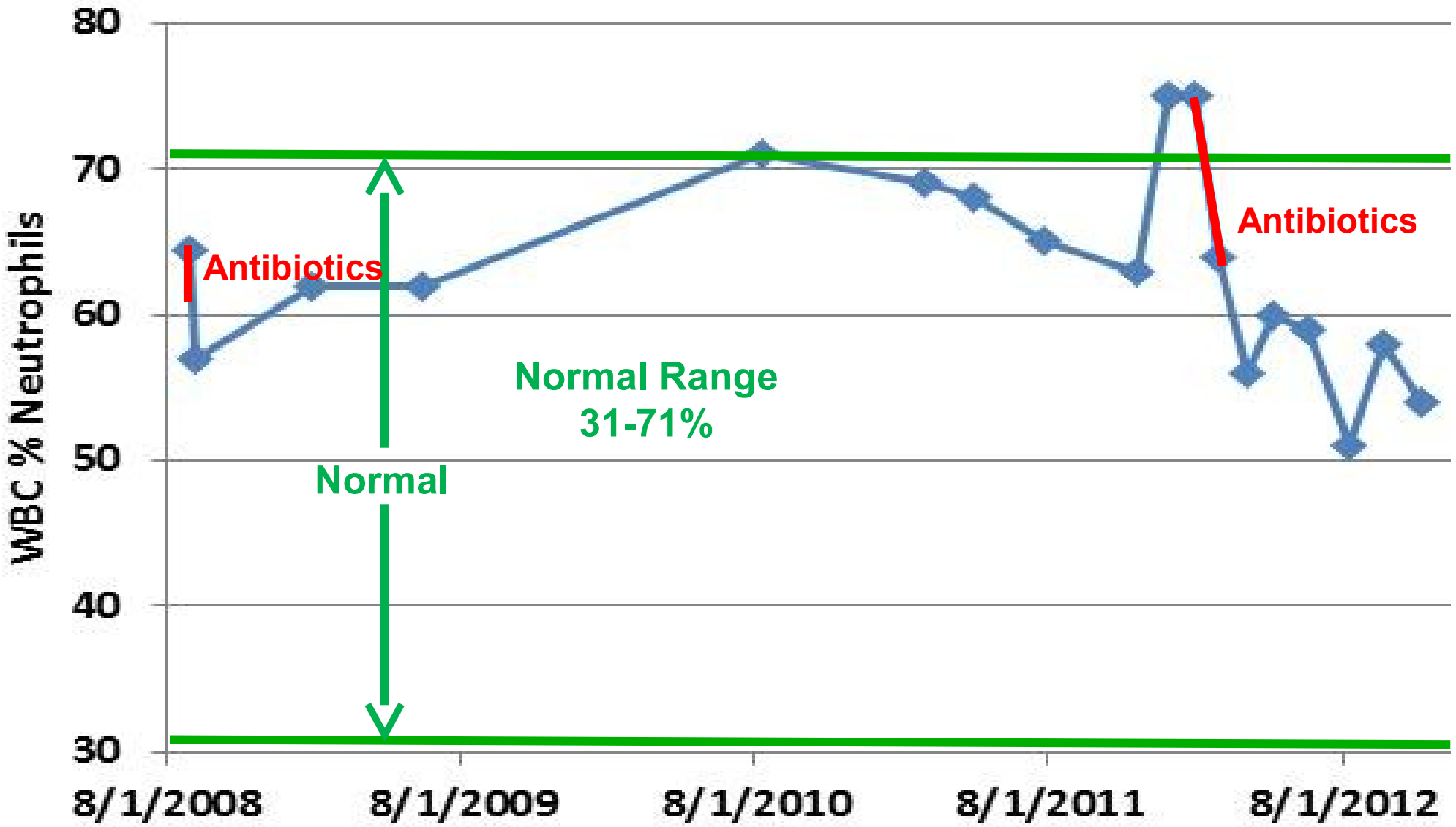


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Complex Reactive Protein (CRP) is a Blood Biomarker for Detecting Presence of Inflammation

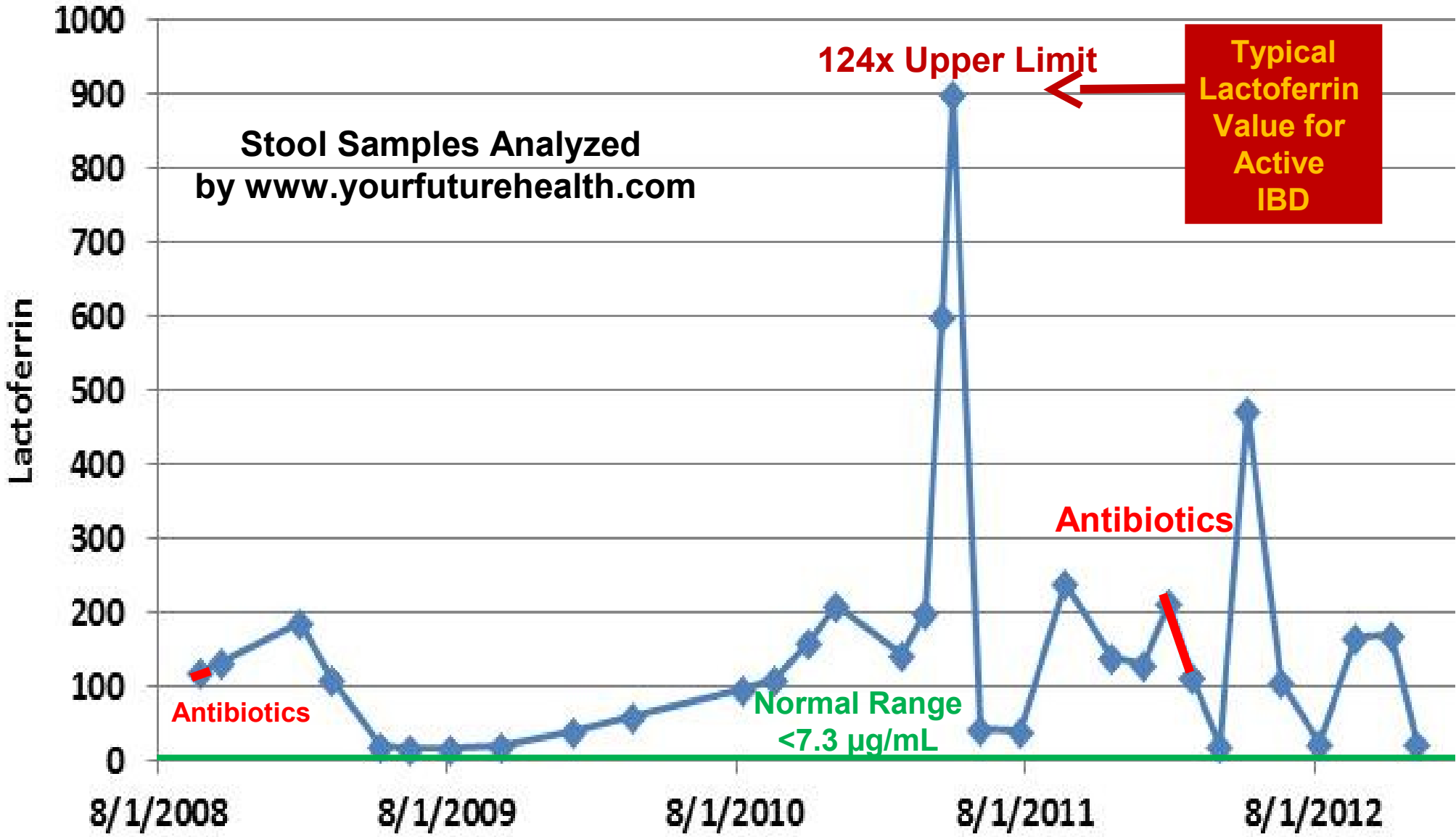
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"Killer White Blood Cells" –Neutrophils – Were Out of Range When CRP Peaked



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High Values of Lactoferrin (Shed from Neutrophils) From Stool Sample Suggested Inflammation in Colon

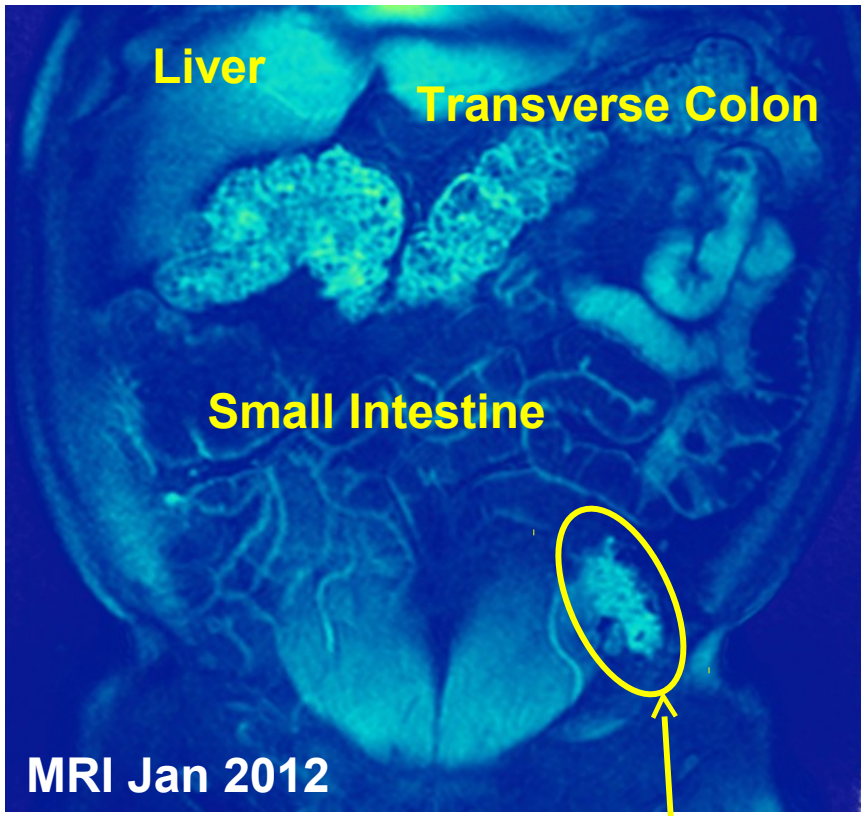


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Lactoferrin is a Sensitive and Specific Biomarker for Detecting Presence of Inflammatory Bowel Disease (IBD)

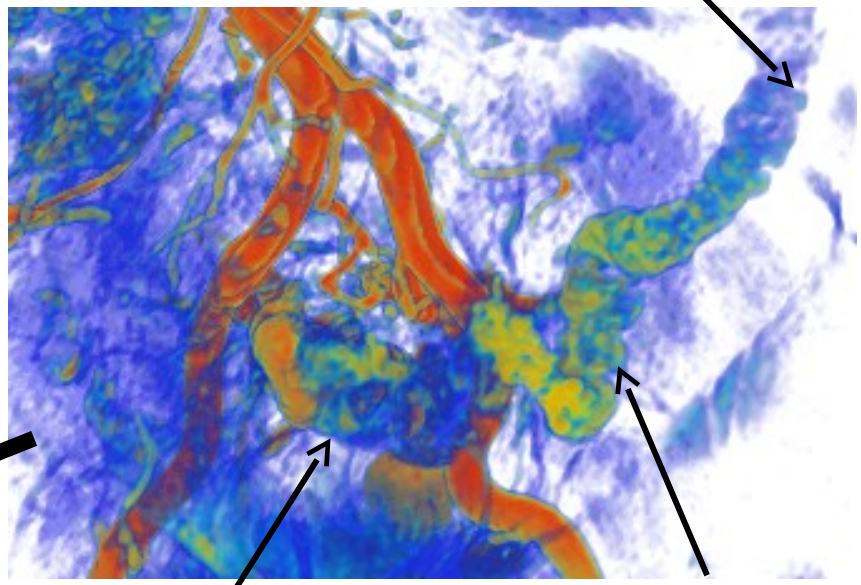
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Confirming the IBD (Crohn's) Hypothesis: Finding the "Smoking Gun" with MRI Imaging



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

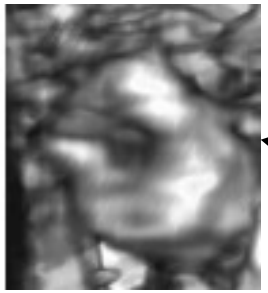
Descending Colon



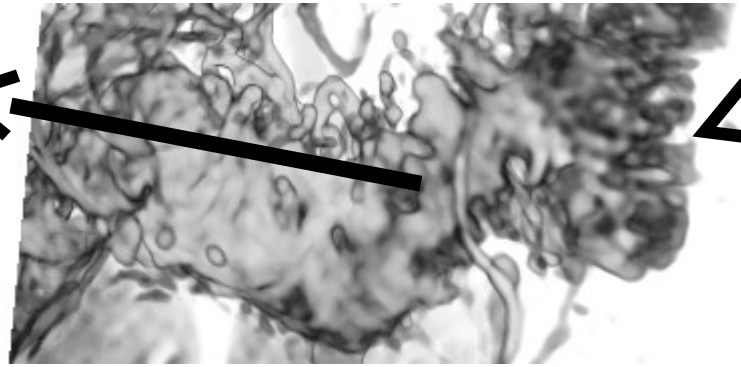
Major Kink

Sigmoid Colon
Threading Iliac Arteries

Cross Section



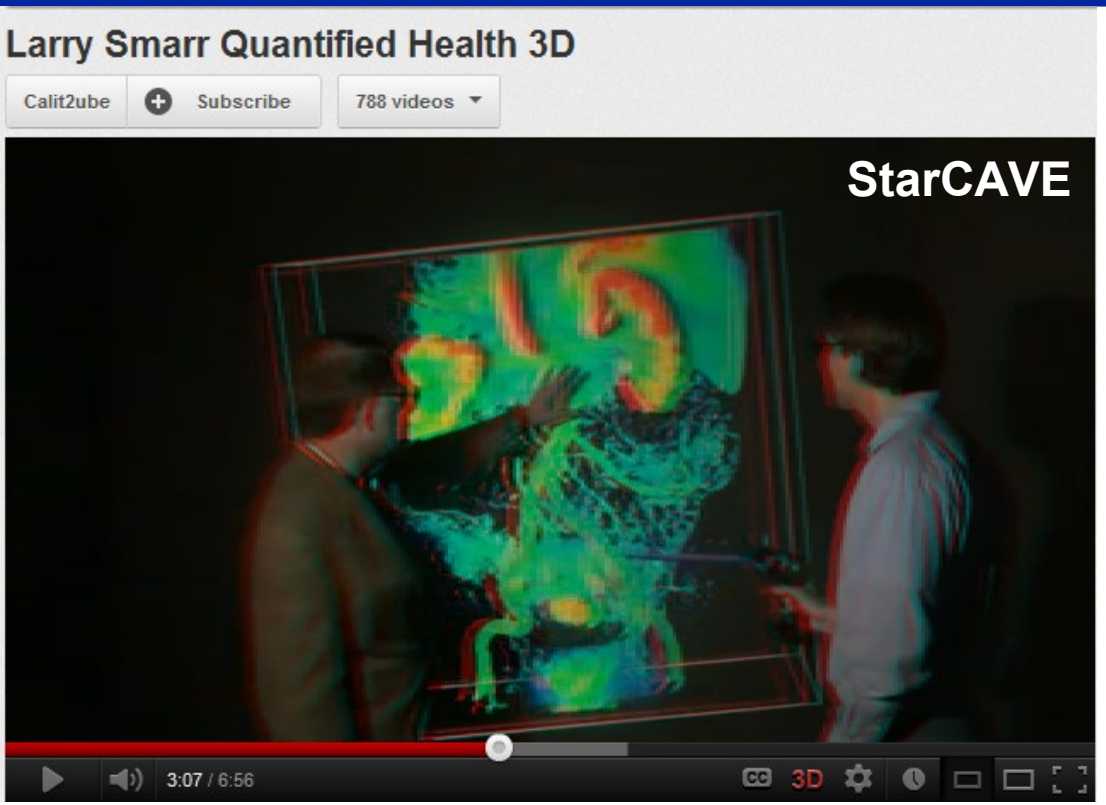
Diseased Sigmoid Colon



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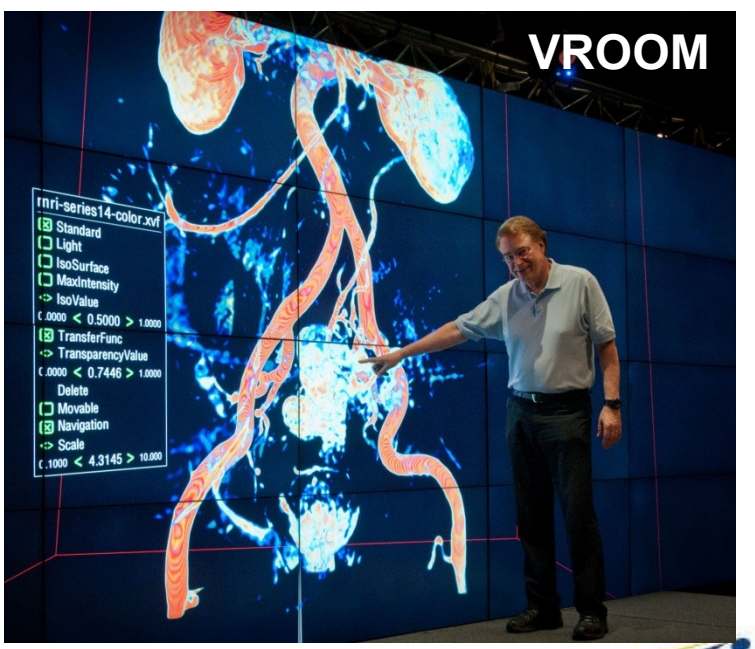
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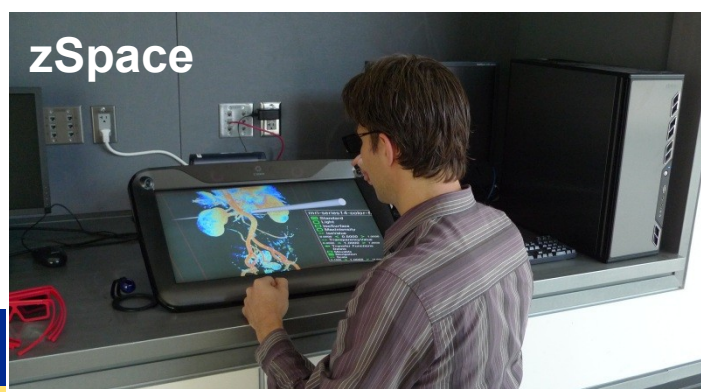
Interactively Exploring My Body With Calit2 Virtual Reality Facilities



www.youtube.com/watch?v=9c4DtJ_L_Ps







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Photo & CalVR software Courtesy of Jurgen Schulze, Calit2

Connecting Colonoscopy "Inside View" With MRI "Outside View"



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LS Colon Images and Colonoscopy Video On Calit2 Director's Colony OptIPortable Wall

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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!

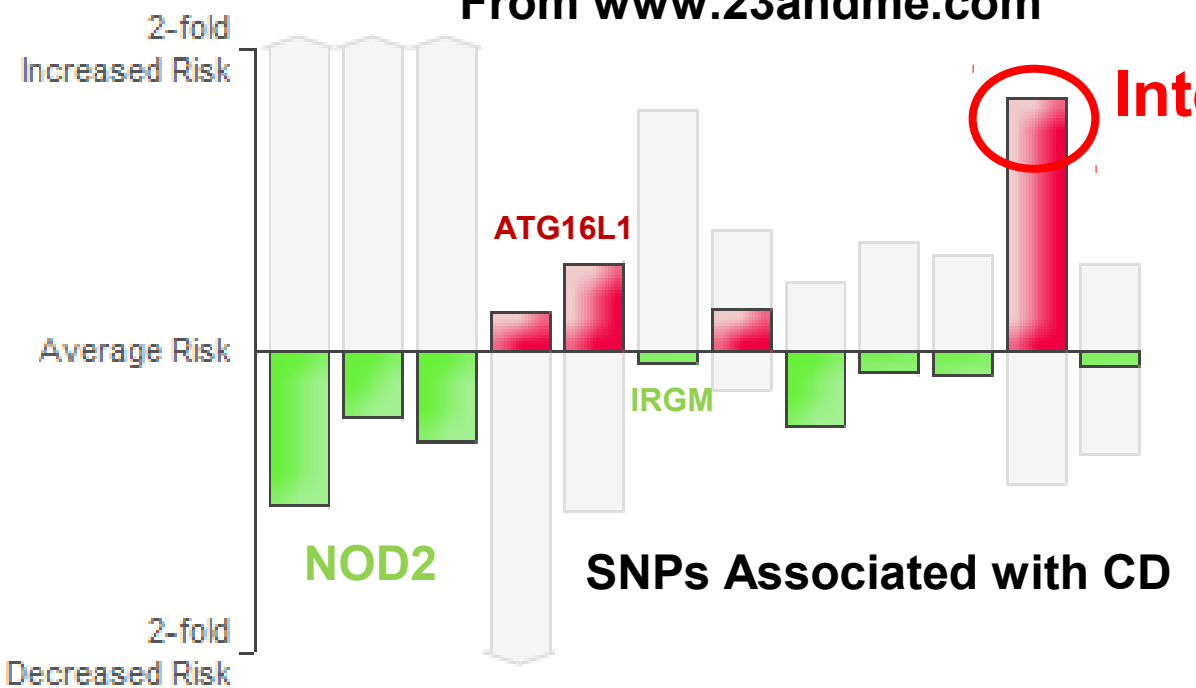
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Paul B. Eckburg & David A. Relman
Clin Infect Dis. 44:256-262 (2007)

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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

Now Comparing 163 Known IBD SNPs with 23andme SNP Chip

News and Views

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

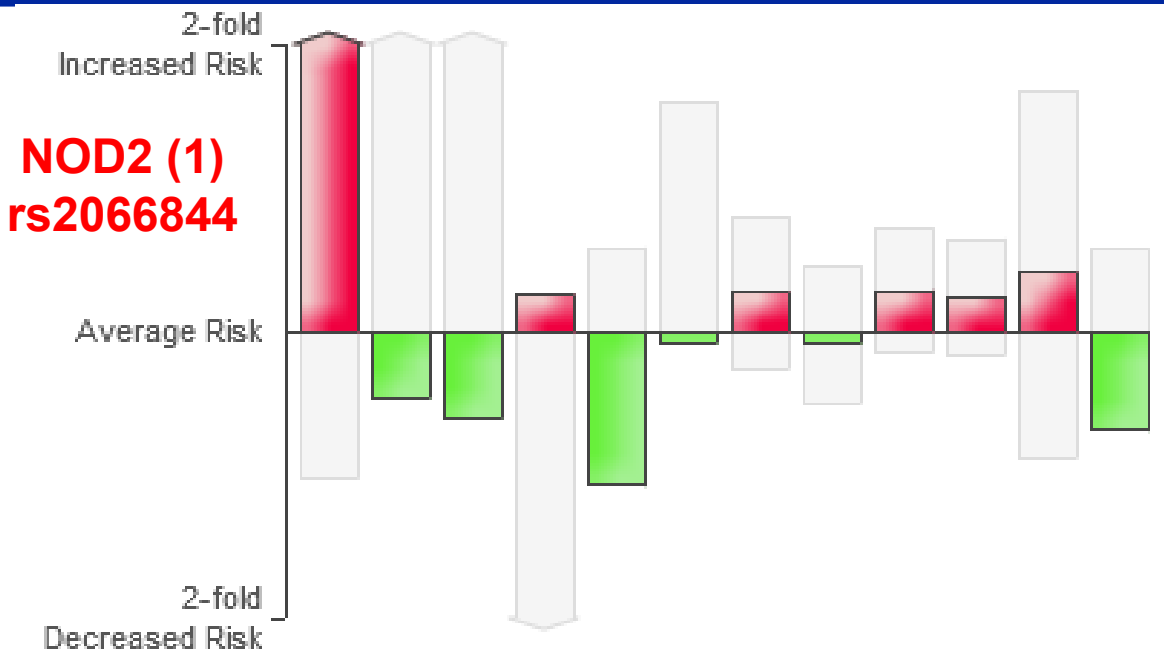
IL-23: a master regulator in Crohn disease

Markus F Neurath[1]

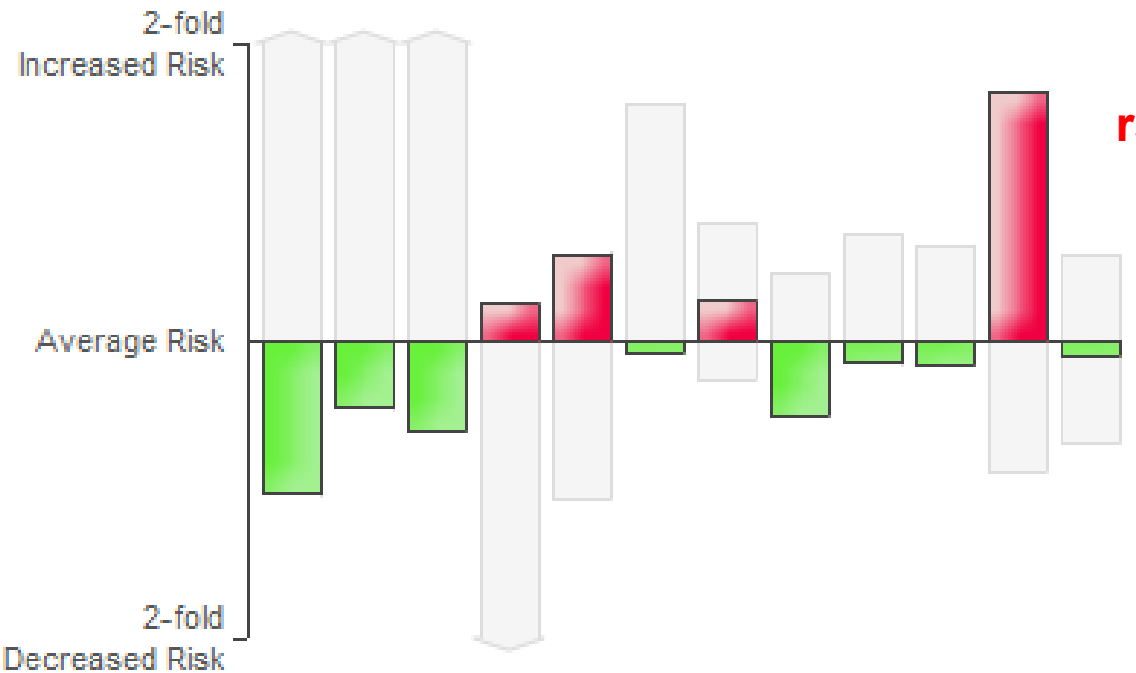
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Crohn's May be a Related Set of Diseases Driven by Different SNPs



Female
CD Onset
At 20-Years Old



Il-23R
rs1004819

Me-Male
CD Onset
At 60-Years Old

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Imagine Crowdsourcing 23andme SNPs For Even a Small Portion of Crohnology!

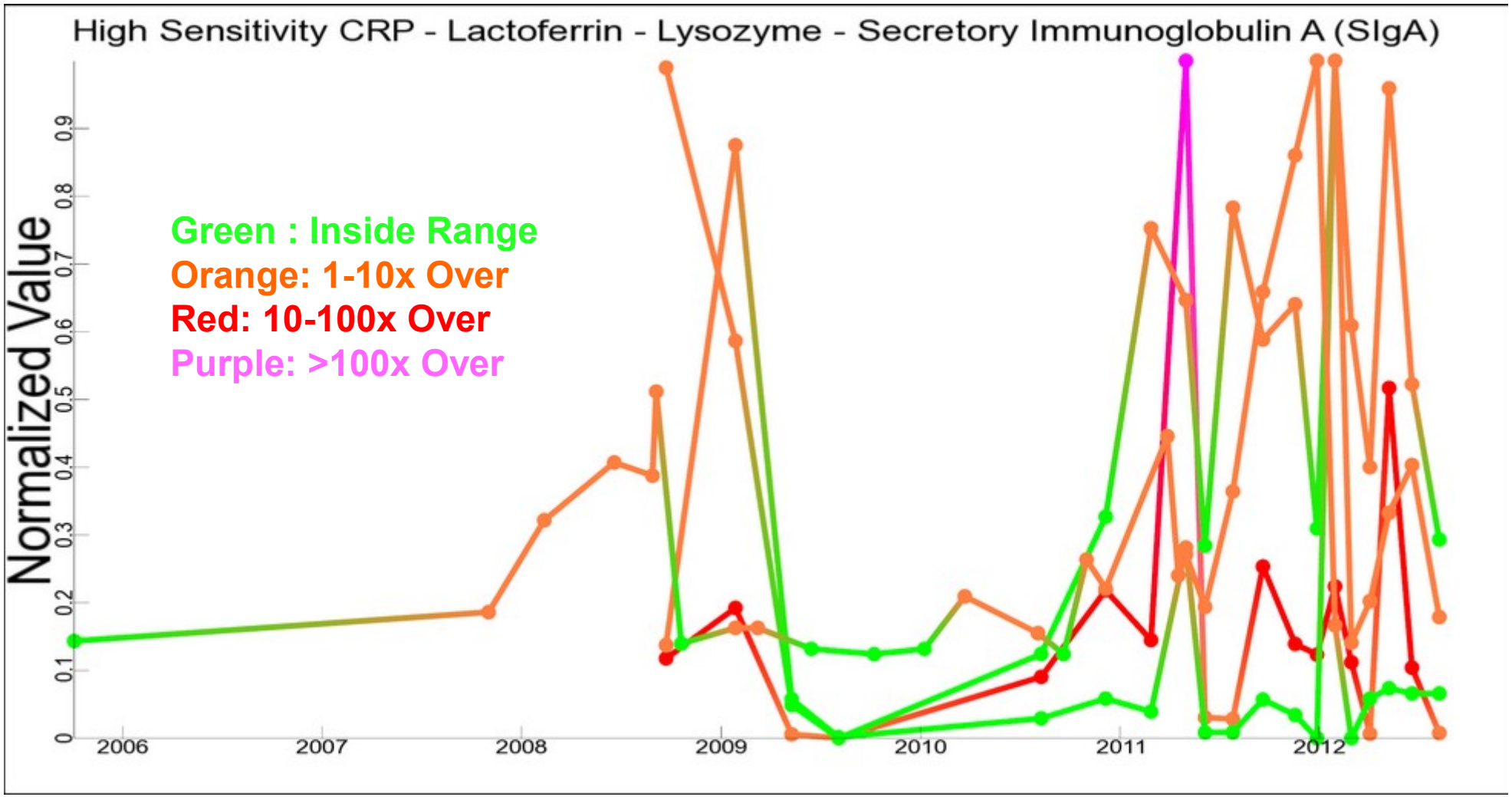


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www.crohnology.com

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



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Source: Calit2 Future Health Expedition Team

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Four Immune Biomarkers Over Time Compared with Four Signs/Symptoms



Here Immune biomarkers are normalized 0 to 1, with 1 being the highest value in five years

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Source: Photo of Calit2 64-megapixel VROOM

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Microbes are 90% of Your Cells-So I Set Out to Determine My Gut Microbes & Their Time Variation



Shipped Stool Sample
December 28, 2011

I Received
a Disk Drive April 3, 2012
With 35 GB FASTQ Files

Weizhong Li, UCSD
NGS Pipeline:
230M Reads
Only 0.2% Human

Required 1/2 cpu-yr at SDSC
Per Person Analyzed!

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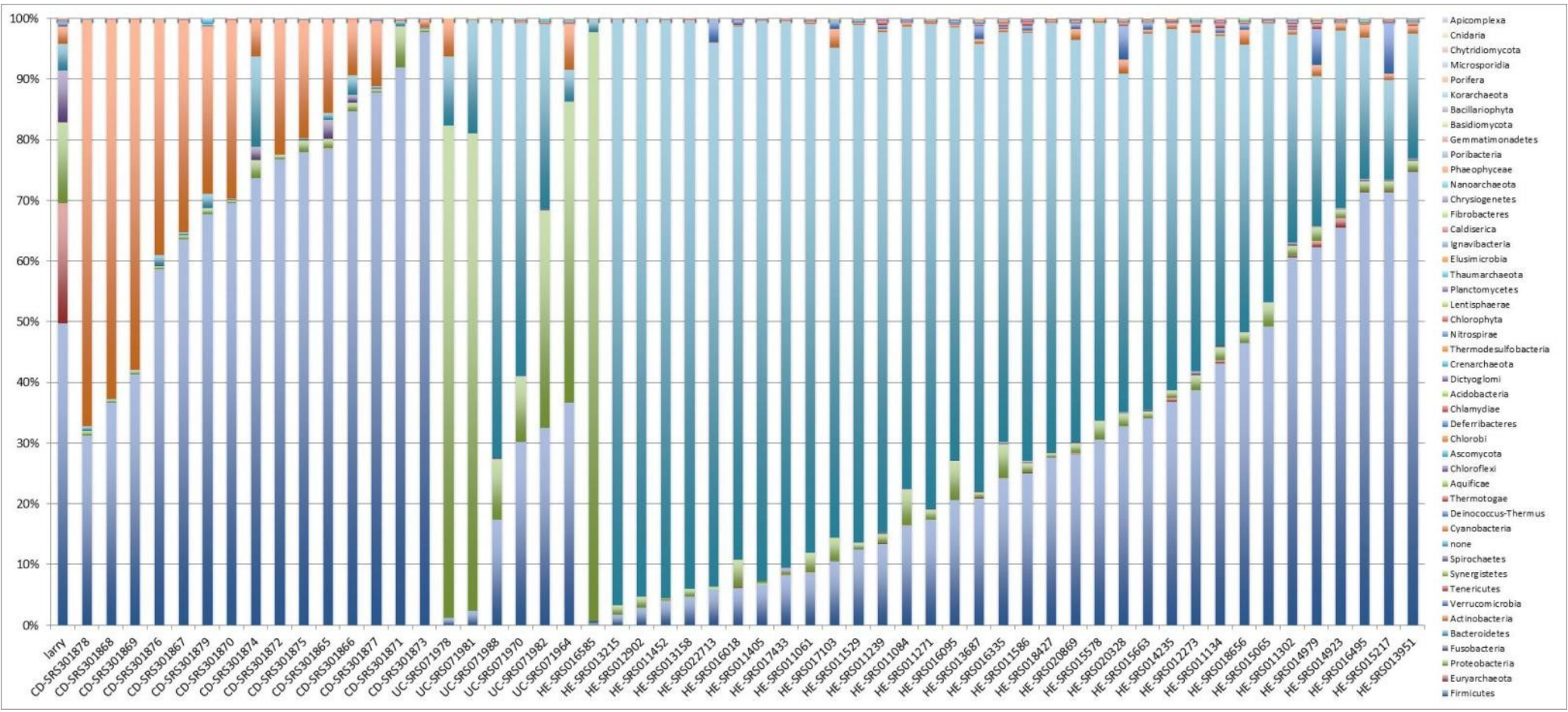
UC San Diego
HEALTH SCIENCES

J. Craig Venter
INSTITUTE

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Phyla Gut Microbial Abundance: LS, Crohn's, UC, and Healthy Subjects

Source: Weizhong Li, UCSD; Calit2 FuturePatient Expedition



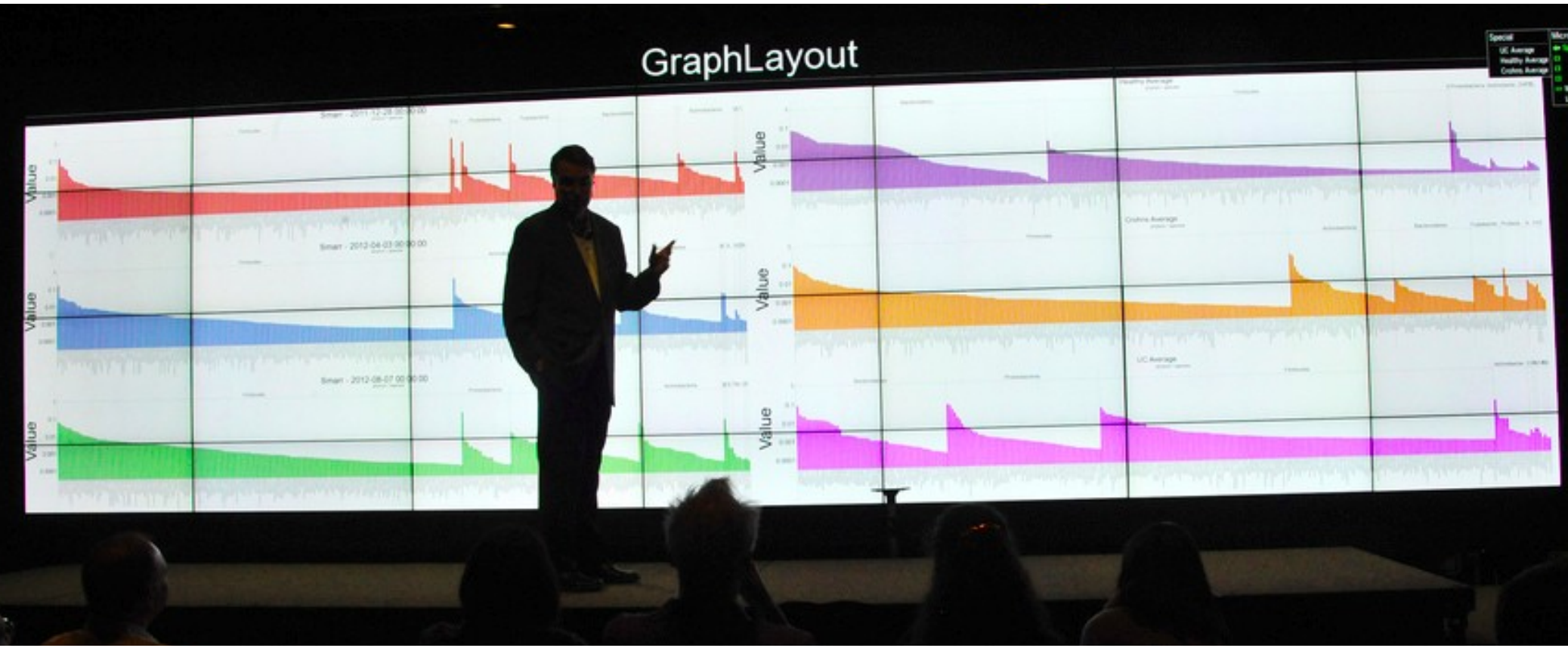
LS **Crohn's** **Ulcerative Colitis** **Healthy**

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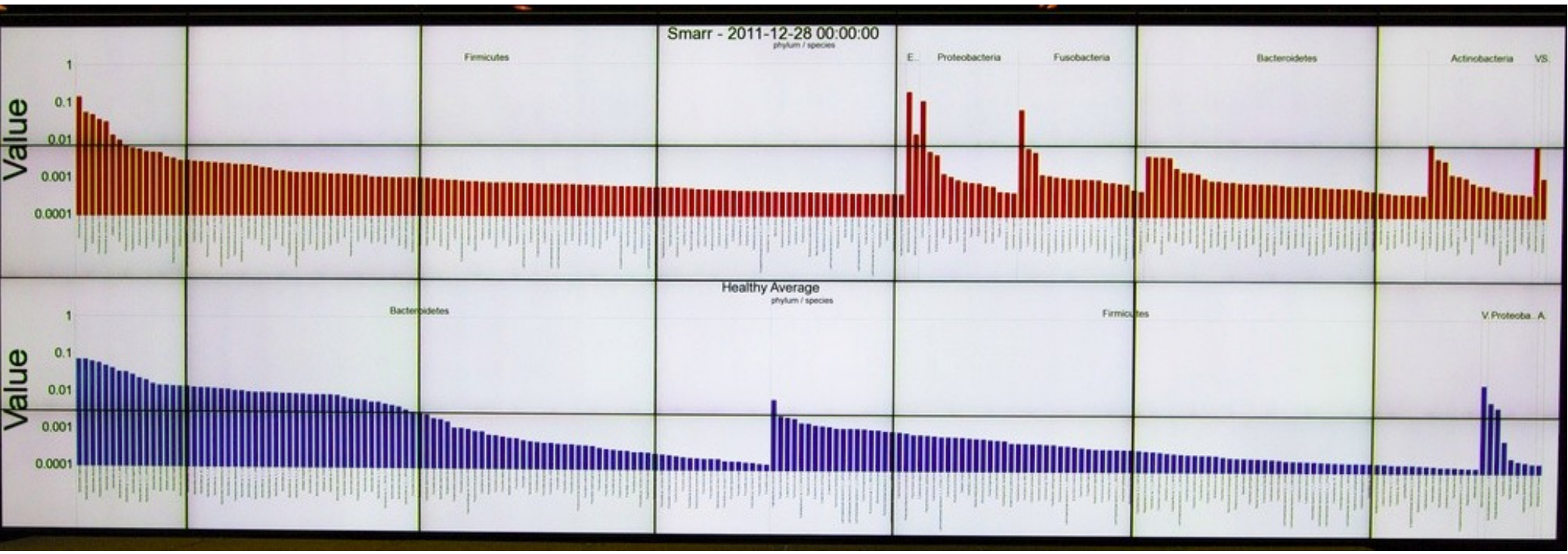
Toward Noninvasive Microbial Ecology Diagnostics

it²

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



LS Gut Microbe Species 12/28/11 (red) compared to Average of 35 Healthy Subjects (blue)



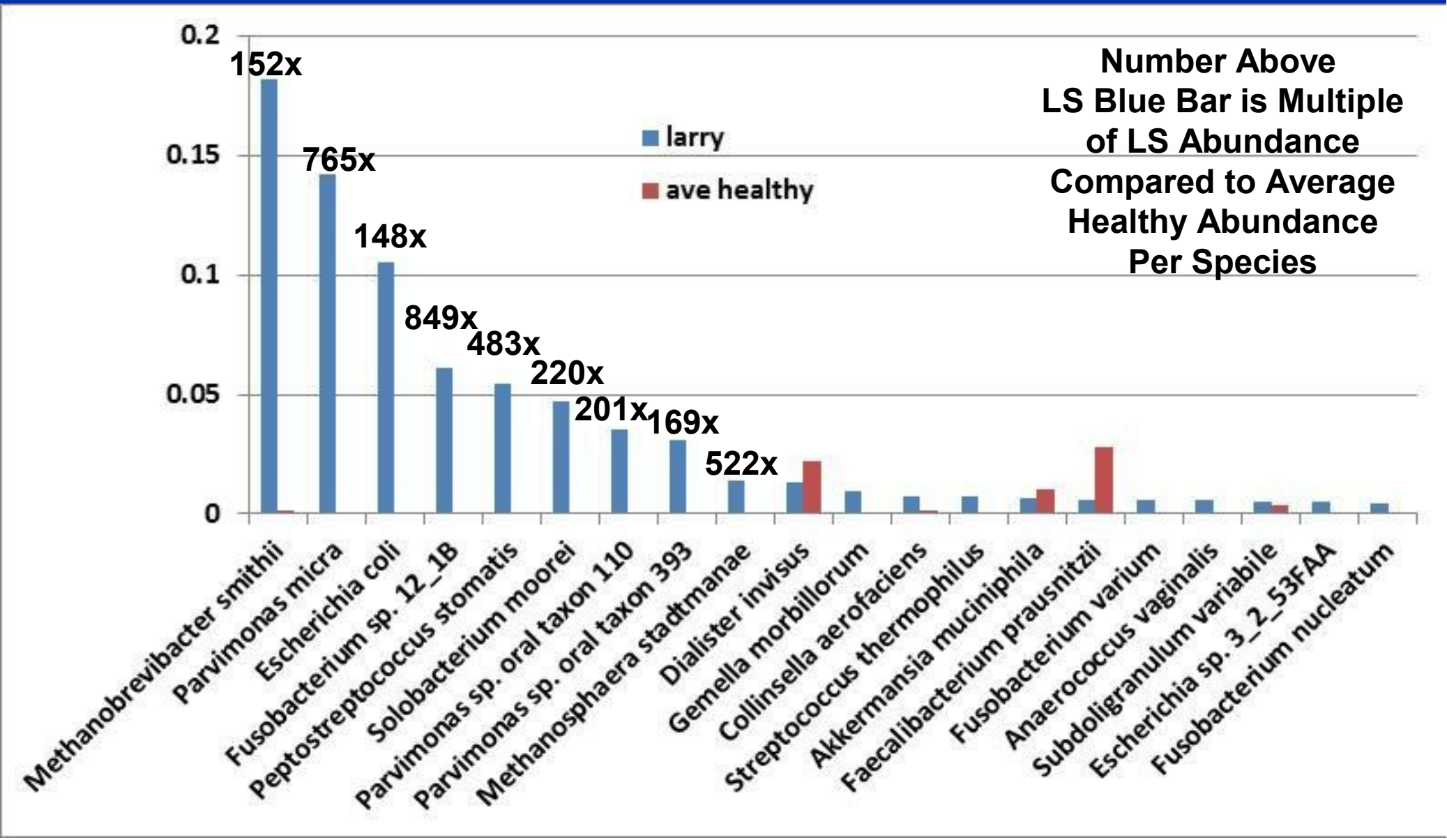
Derived from metagenomic sequencing of LS stool sample.
Each species is a bar,
height is logarithmic abundance,
species are divided into microbial phyla

Source: Photo of Calit2 64-megapixel VROOM

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Top 20 Most Abundant Microbial Species In LS vs. Average Healthy Subject



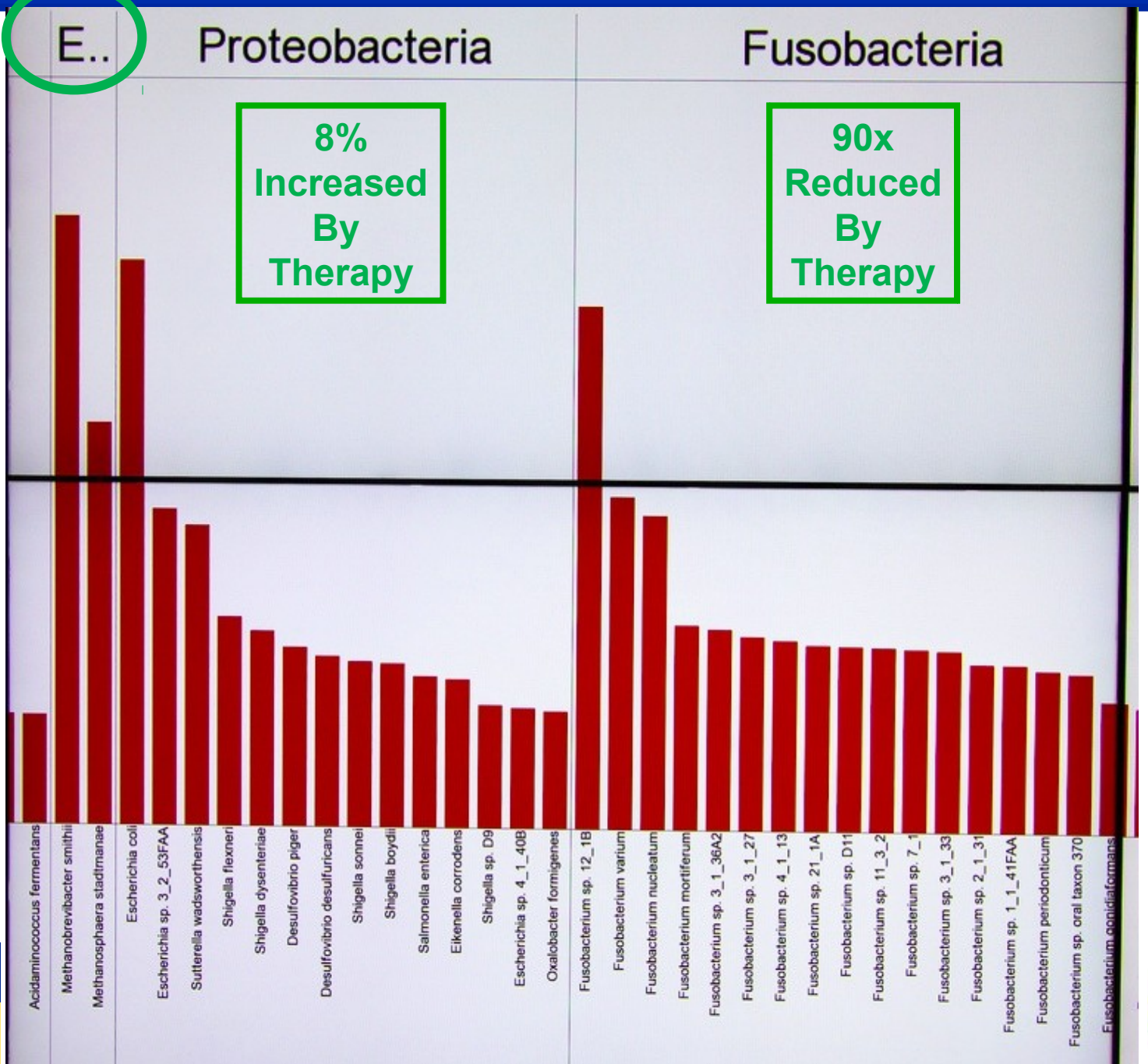
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Source: Sequencing JCVI; Analysis Weizhong Li, UCSD
LS December 28, 2011 Stool Sample

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Closeup of Uncommon LS Microbes 12/28/11 Stool Sample

45x Reduced By Therapy

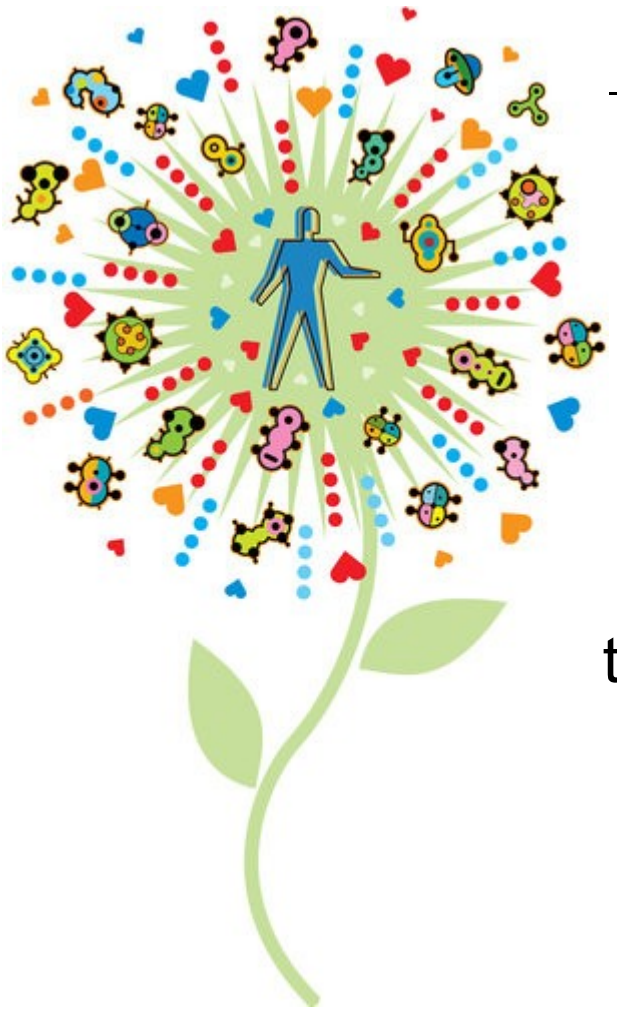


Two separate research teams have found strikingly high concentrations of *Fusobacterium* in tumor samples collected from colorectal cancer patients. October 18, 2011

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From War 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."

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DIY Systems Biology - Toward P4 Healthcare

Perspective

Over 1000 Downloads So Far

Quantifying your body: A how-to guide from a systems biology perspective

Larry Smarr

University of California, San Diego, CA, USA

Download pdfs from Journal:

http://onlinelibrary.wiley.com/doi/10.1002/biot.201100495/full



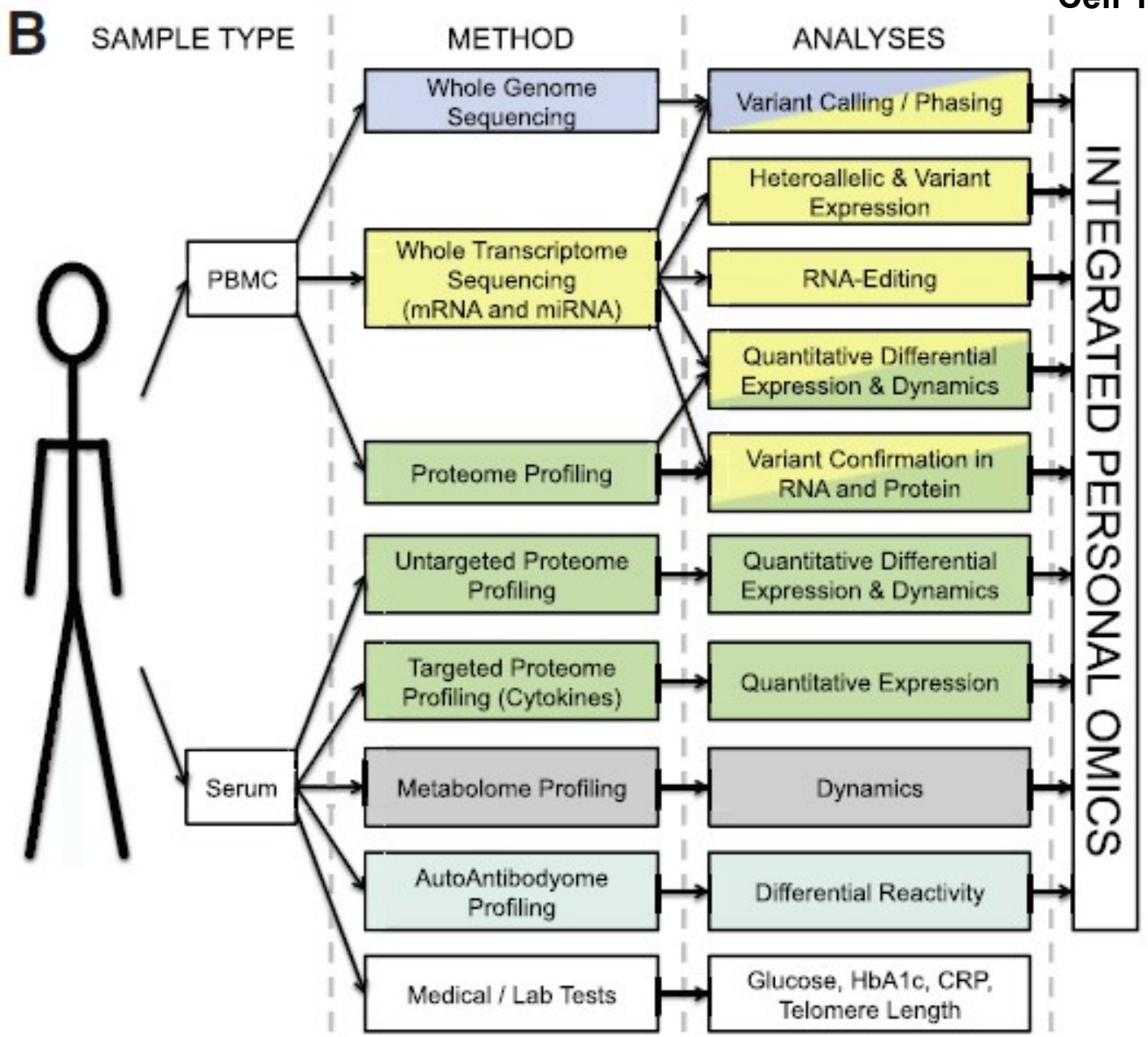
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Biotechnol. J. 2012, 7, 980–991

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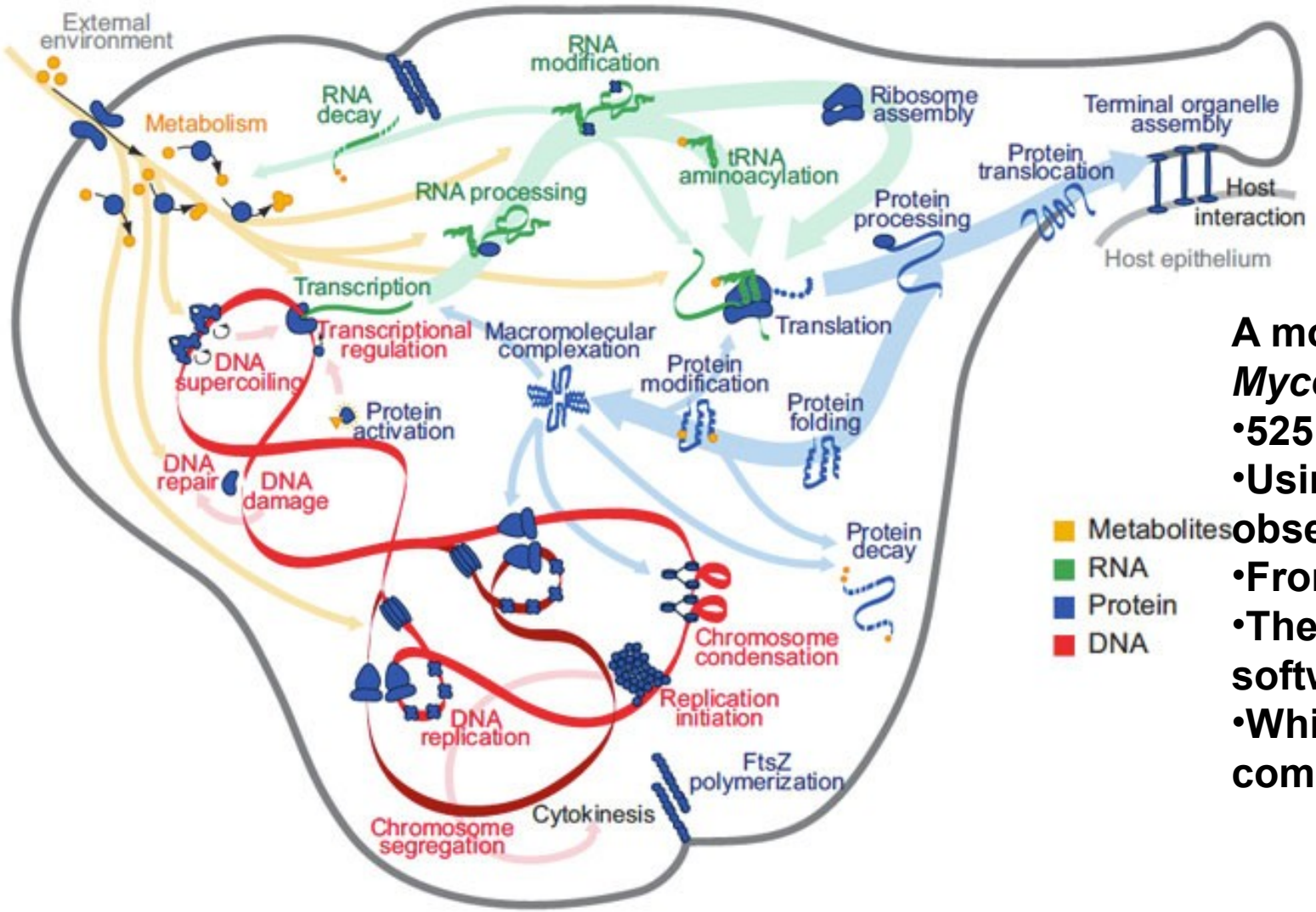
Integrative Personal Omics Profiling Reveals Details of Clinical Onset of Viruses and Diabetes

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**

“A Whole-Cell Computational Model Predicts Phenotype from Genotype”



Cell

Cell *150*, 389–401, July 20, 2012

A model of *Mycoplasma genitalium,*

- **525 genes**
- **Using 1,900 experimental observations**
- **From 900 studies,**
- **They created the software model,**
- **Which requires 128 computers to run**

Jonathan R. Karr,[1,4] Jayodita C. Sanghvi,[2,4] Derek N. Macklin,[2] Miriam V. Gutschow,[2] Jared M. Jacobs,[2] Benjamin Bolival, Jr.,[2] Nacyra Assad-Garcia,[3] John I. Glass,[3] and Markus W. Covert[2,*]

[1]Graduate Program in Biophysics

[2]Department of Bioengineering

Stanford University, Stanford, CA 94305, USA

[3]J. Craig Venter Institute, Rockville, MD 20850, USA

Early Attempts at Modeling the Systems Biology of the Gut Microbiome and the Human Immune System

Trends in Biotechnology June 2011, Vol. 29, No. 6

Prospects for systems biology and modeling of the gut microbiome

Fredrik H. Karlsson, Intawat Nookaew, Dina Petranovic and Jens Nielsen

Department of Chemical and Biological Engineering, Chalmers University of Technology, Kemivägen 10, SE-412 96 Göteborg, Sweden

2012 IEEE 26th International Parallel and Distributed Processing Symposium

High-Performance Interaction-Based Simulation of Gut Immunopathologies with ENteric Immunity SImulator (ENISI)

Keith Bisset*, Md. Maksudul Alam*, Josep Bassaganya-Riera*, Adria Carbo*, Stephen Eubank*, Raquel Hontecillas*, Stefan Hoops*, Yongguo Mei*, Katherine Wendelsdorf*, Dawen Xie*, Jae-Seung Yeom*†, and Madhav Marathe*†

**Virginia Bioinformatics Institute*

†Department of Computer Science

Virginia Tech, Blacksburg VA 24061

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A Vision for Healthcare in the Coming Decades

Using this data, the planetary computer will be able to build a computational model of your body and compare your sensor stream with millions of others. Besides providing early detection of internal changes that could lead to disease, cloud-powered voice-recognition wellness coaches could provide continual personalized support on lifestyle choices, potentially staving off disease and making health care affordable for everyone.

ESSAY
An Evolution Toward a Programmable Universe
By LARRY SMARR
Published: December 5, 2011

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The New York Times

Science

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