"Integrating Healthcare Informatics, Imaging, and Systems Biology-A Personal Example"

Plenary Lecture

2nd IEEE Conference on Healthcare Informatics, Imaging, & Systems Biology

Calit2@UCSD

September 27, 2012

Dr. Larry Smarr

Director, California Institute for Telecommunications and Information Technology

Harry E. Gruber Professor,

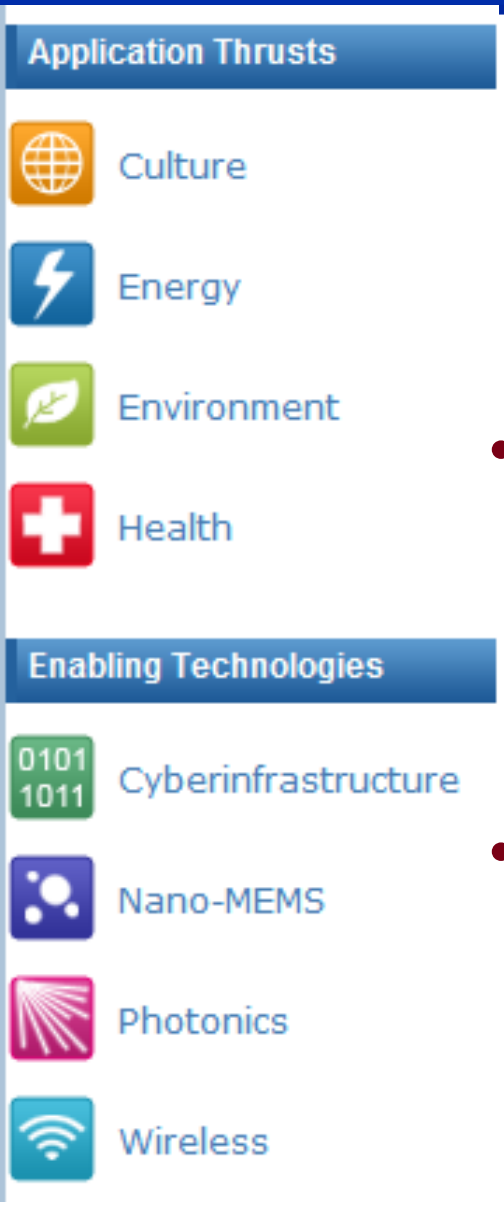
Dept. of Computer Science and Engineering

Jacobs School of Engineering, UCSD

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The Ten Year
Calit2 Path Forward



- **Ten-Year Vision of Digital Transformation**
  - **Affiliated Academic Units**
  - **Calit2 News and Videos**
- **This Talk Focuses in on:**
  - **The Digital Transformation of Health**

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www.calit2.net/research/index.php

it²

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

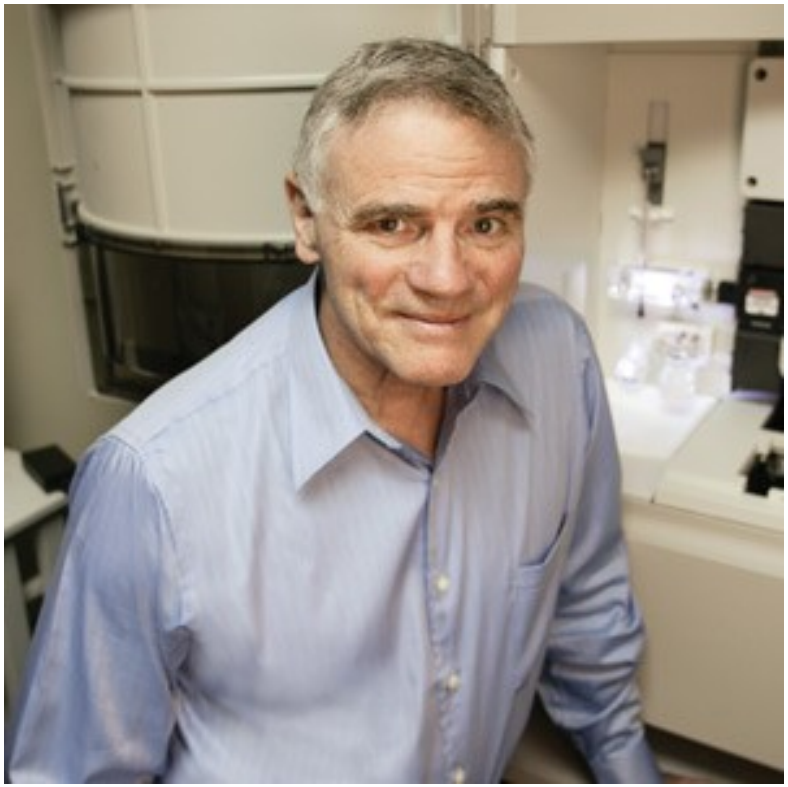
Newsweek

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

it²

Invited Paper for Focus Issue of Biotechnology Journal, Edited by Profs. Leroy Hood and Charles Auffray.

Perspective

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

Larry Smarr

University of California, San Diego, CA, USA

Download Pdfs from my Portal:

http://lsmarr.calit2.net/repository/Biotech_J._LS_published_article.pdf

http://lsmarr.calit2.net/repository/Biotech_J._Supporting_Info_published.pdf



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Biotechnol. J. 2012, 7, 980–991

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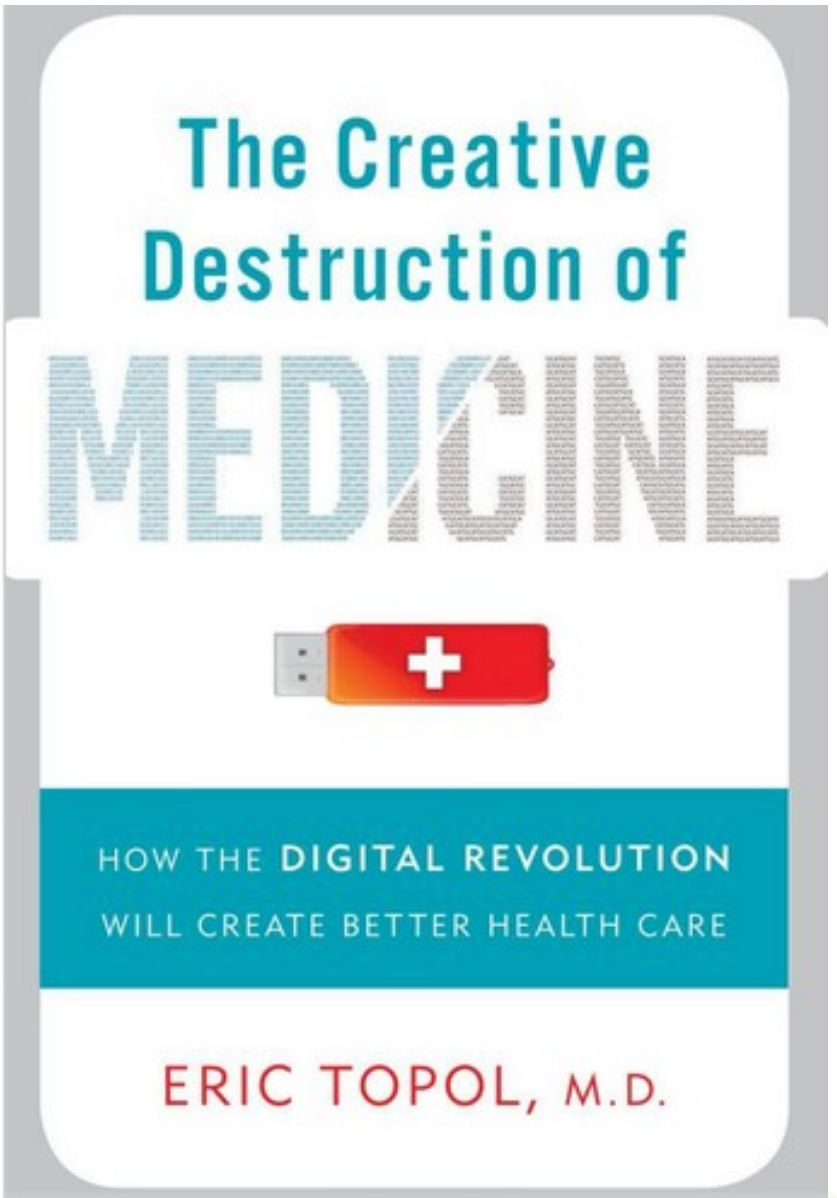
The Content of This Slide from 2001 Larry Smarr Calit2 Talk on Digitally Enabled Genomic Medicine

it²

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



July/August 2011

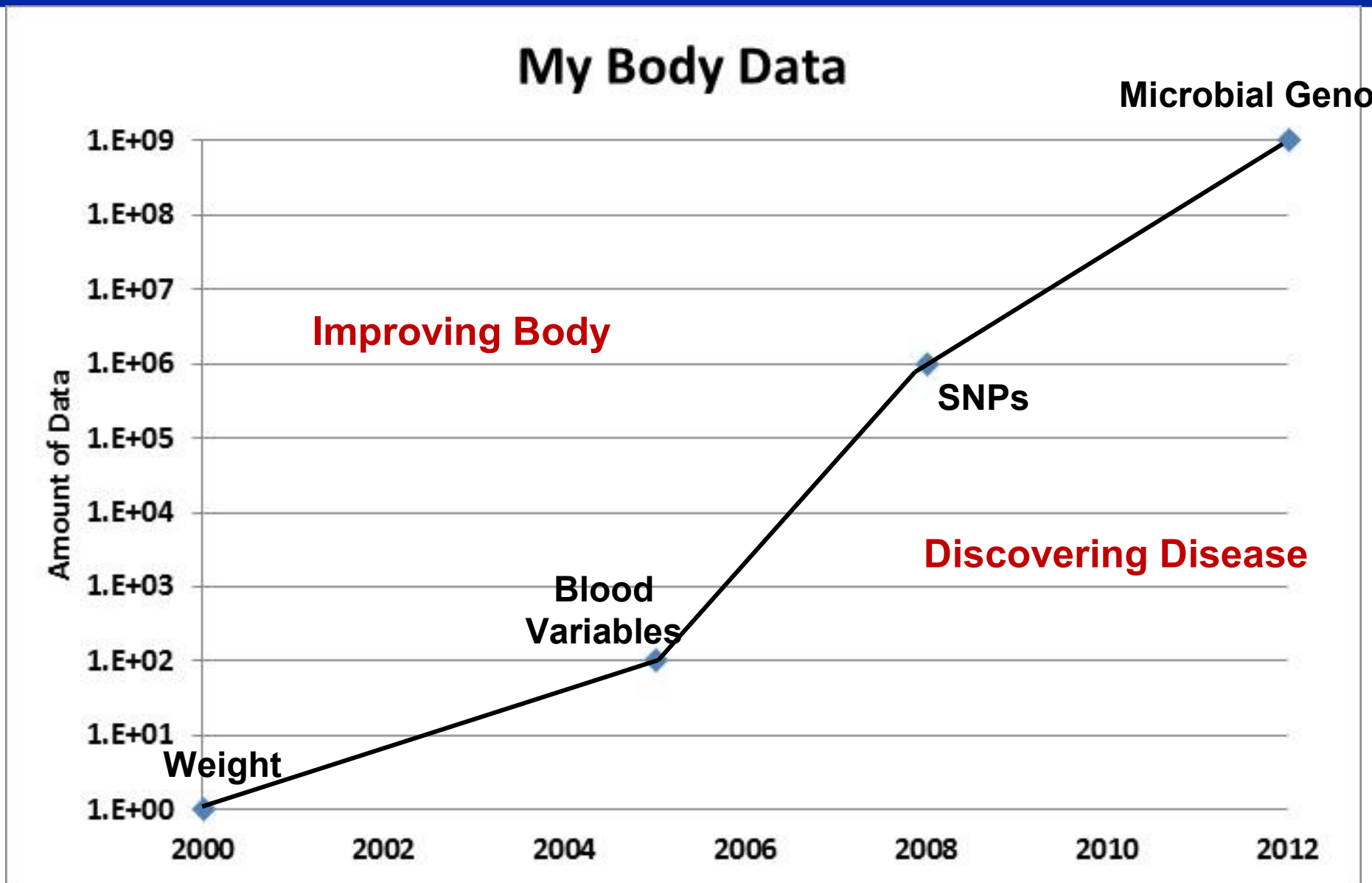


February 2012

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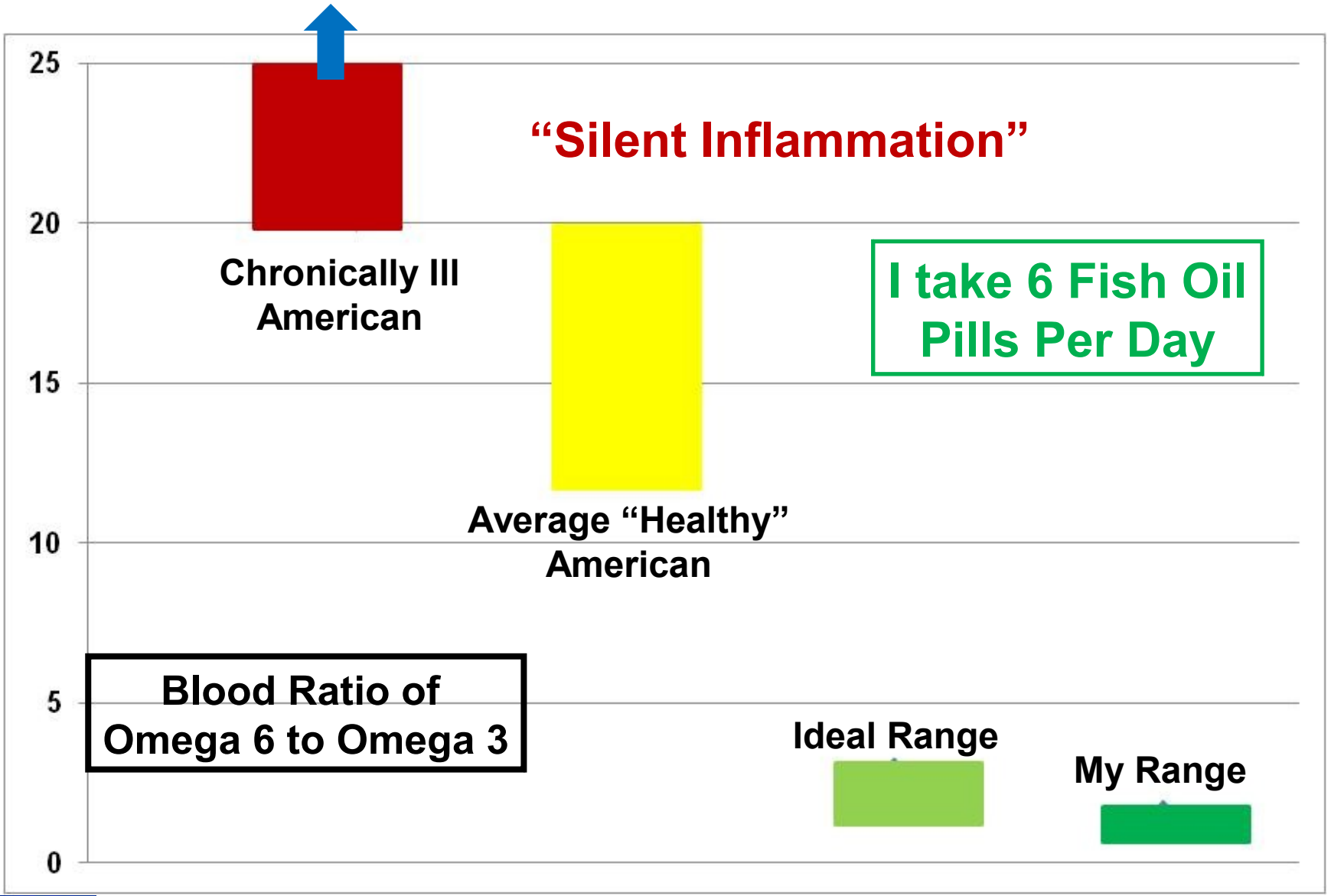
it²

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



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I Lowered My Body's Inflammation From Food By Increasing Omega-3s and Reducing Omega-6s



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

it²

I Track 100 Variables in Blood Tests Done Quarterly to Annually

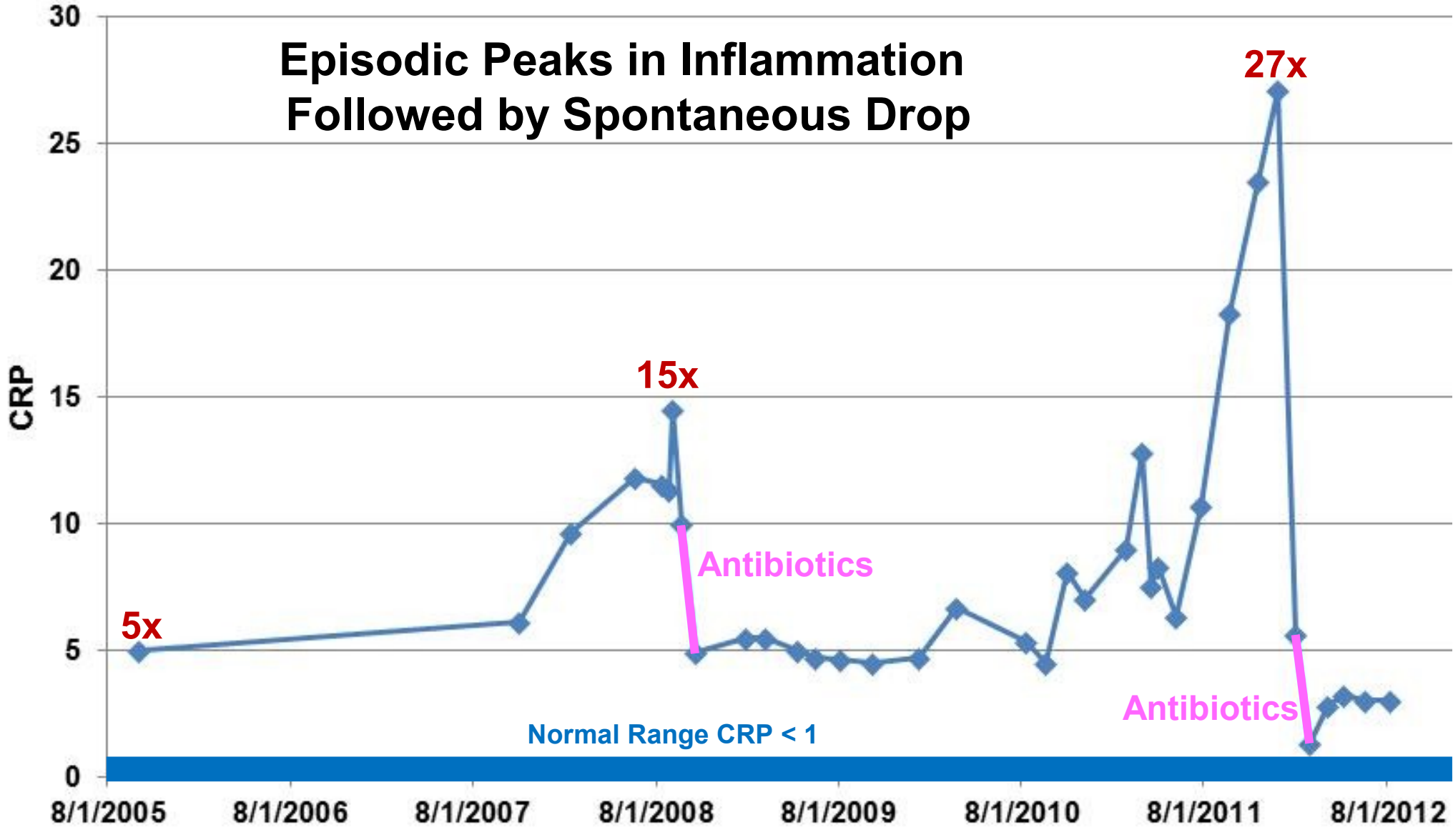
- **Electrolytes**
  - Sodium, Potassium, Calcium, Magnesium, Phosphorus, Boron, Chlorine, CO_2
- **Micronutrients**
  - Arsenic, Chromium, Cobalt, Copper, Iron, Manganese, Molybdenum, Selenium, Zinc
- **Blood Sugar Cycle**
  - Glucose, Insulin, A1C Hemoglobin
- **Cardio Risk**
  - Complex Reactive Protein
  - 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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Only One of These Was Far Out of Normal Range

it²

But, In Spite of My High Levels of Omega-3s, My Blood Measurements Revealed Chronic Inflammation

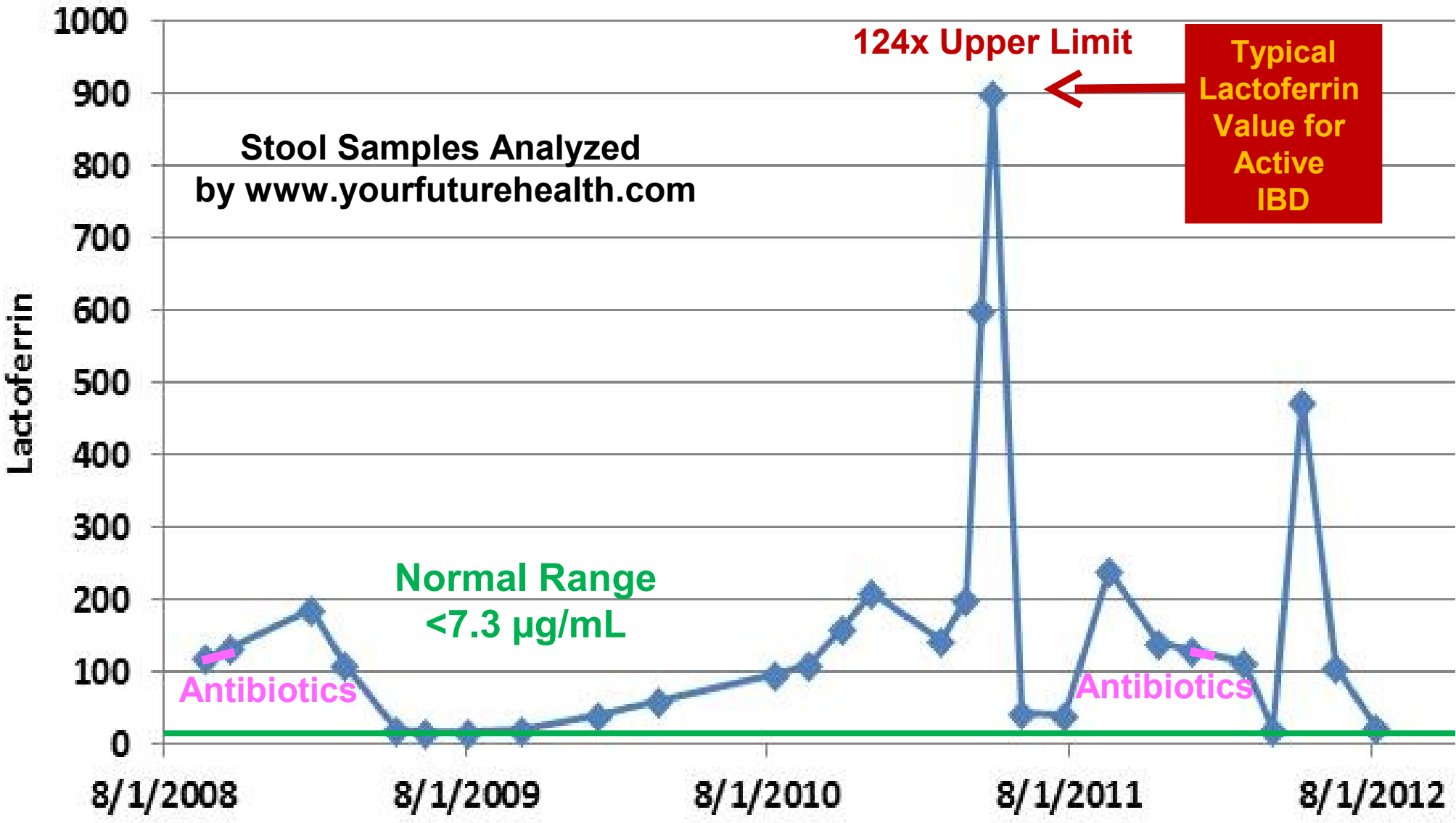


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Complex Reactive Protein (CRP) is a Blood Biomarker for Detecting Presence of Inflammation

it²

By Quantifying Stool Measurements Over Time I Discovered Source of Inflammation Was Likely in Colon



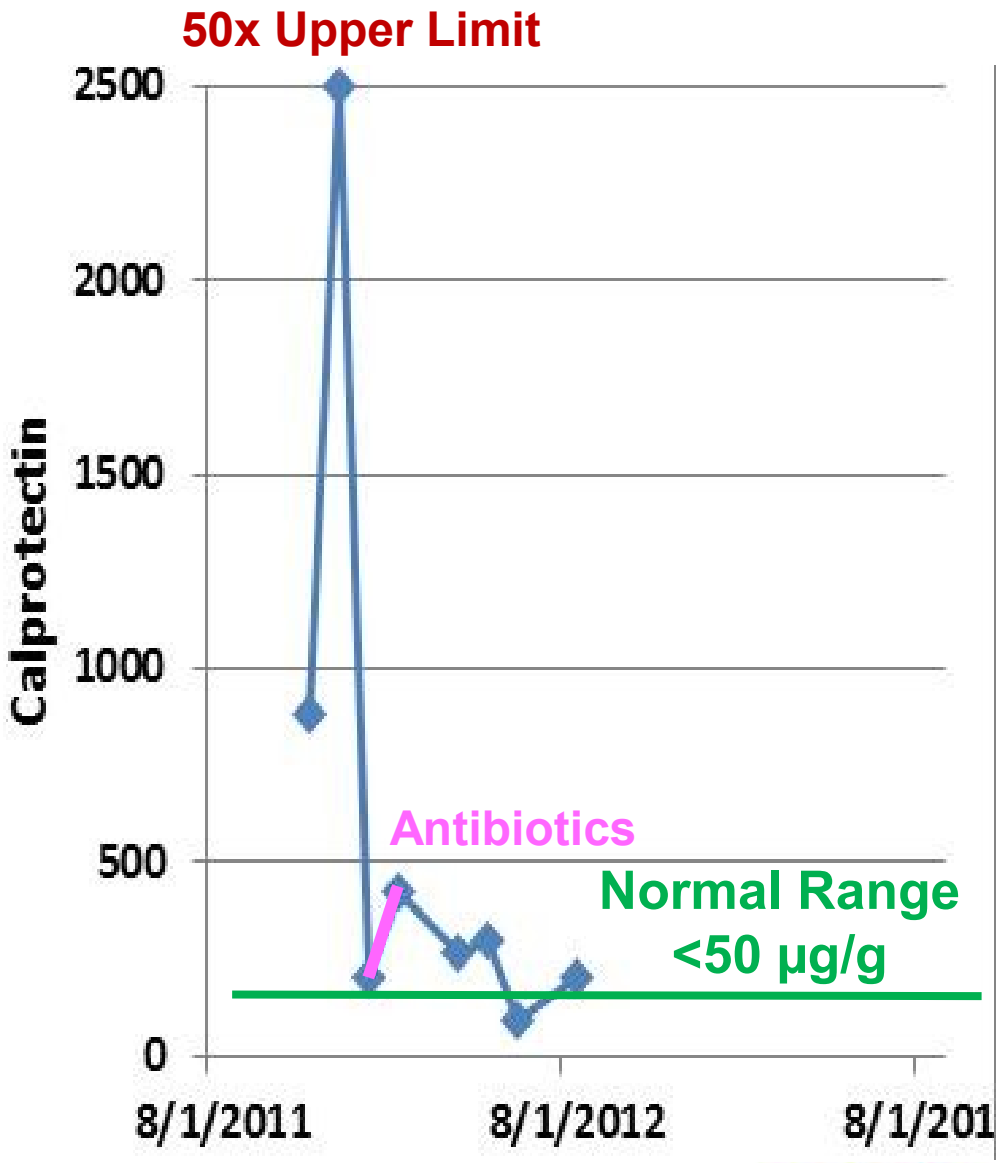
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Lactoferrin is a Sensitive and Specific Biomarker for Detecting Presence of Inflammatory Bowel Disease (IBD)

it²

Confirmation of IBD Using Calprotectin Biomarker From Stool Sample

"It is worth noting that calprotectin concentrations correlate more closely with histological than macroscopic (endoscopic) findings, suggesting that this biological marker is more sensitive than endoscopy in evaluating IBD's activity."
--Fecal Calprotectin and Lactoferrin for the Prediction of Inflammatory Bowel Disease Relapse, Gisbert, et al., Inflamm. Bowel Dis. 15, 1190-1198 (2009)

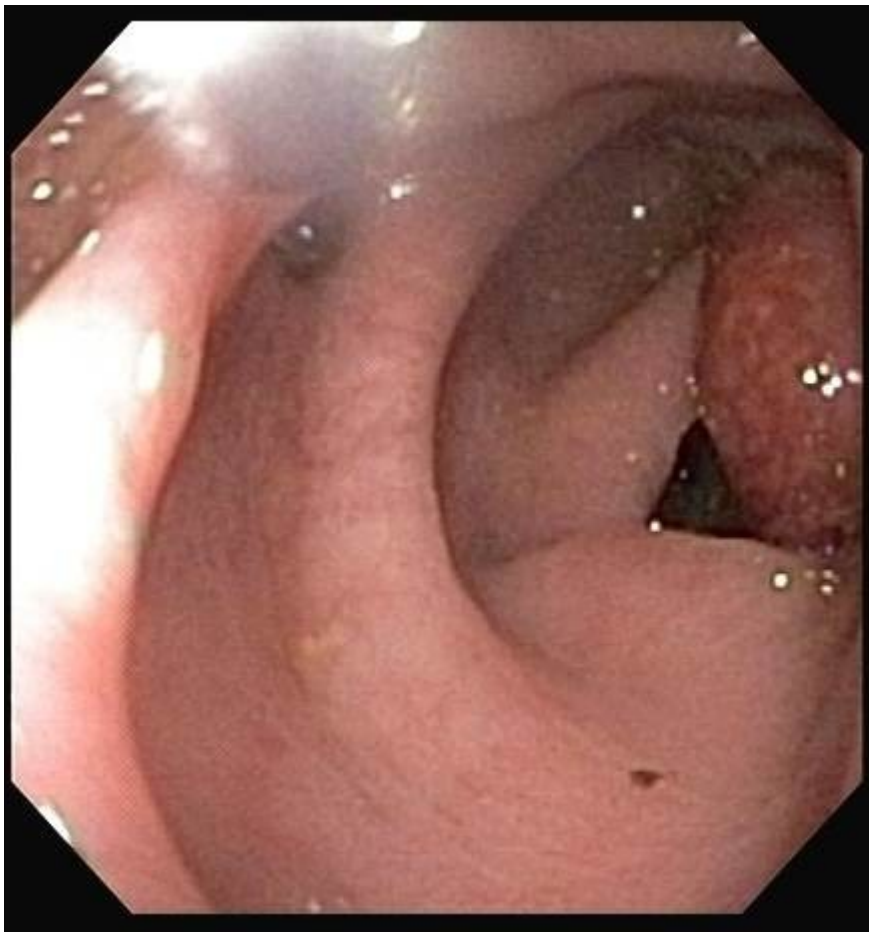


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Colonoscopy Images Show 6 Inches of Sigmoid Colon Inflammation



Dec 2010



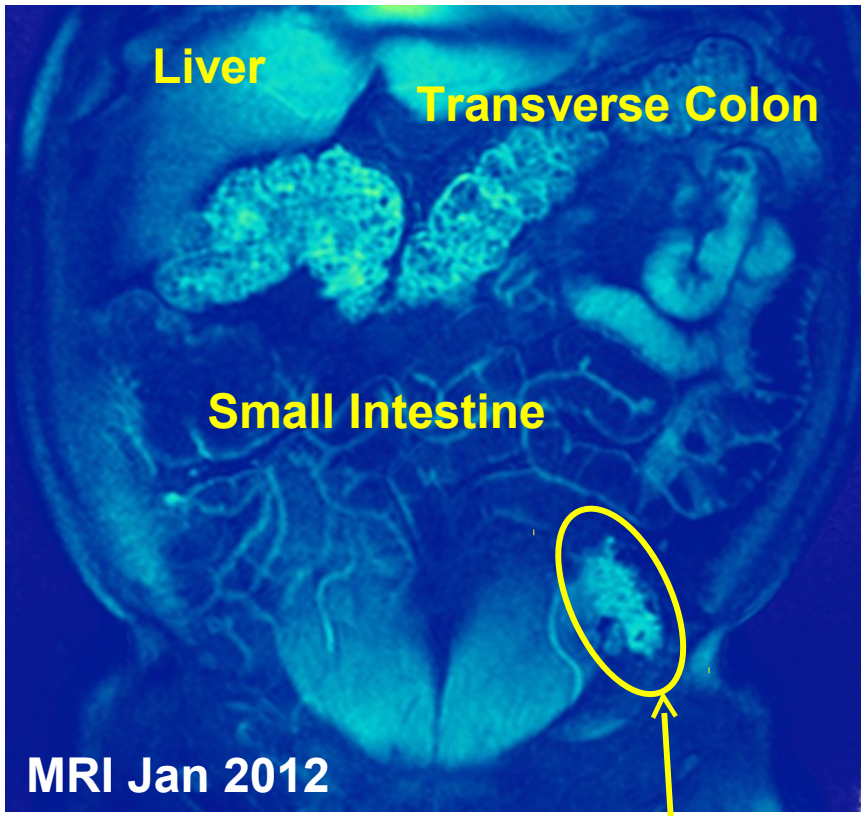
May 2011

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2010 Image from Scripps Health
2011 Image from UCSD Health Services

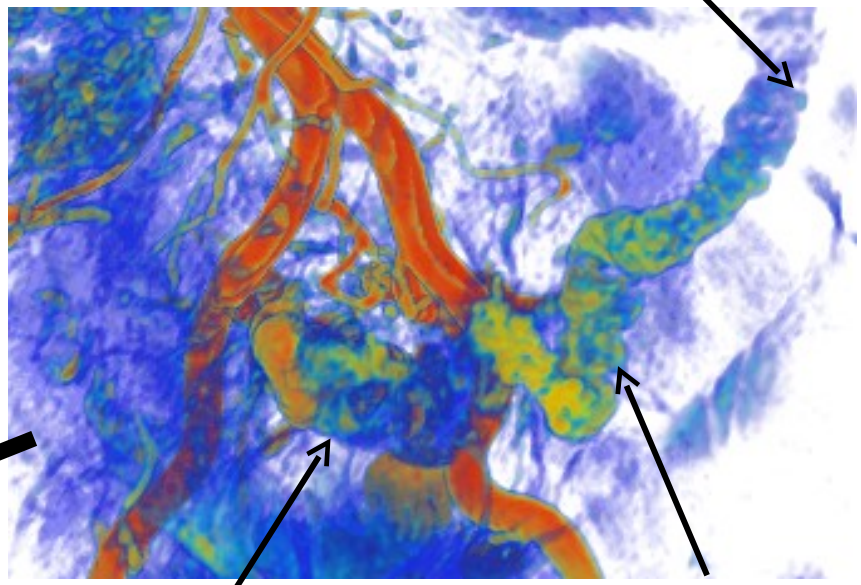
it²

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

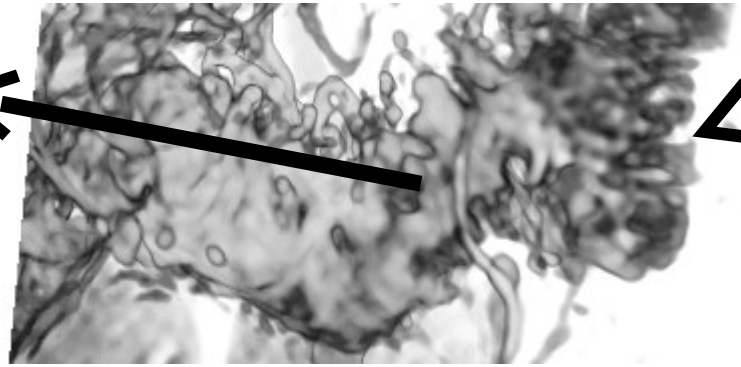
Descending Colon



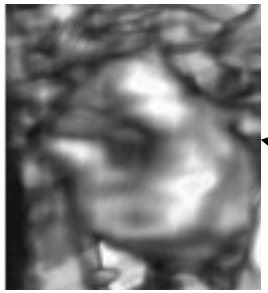
Major Kink

Sigmoid Colon Threading Iliac Arteries

Diseased Sigmoid Colon



Cross Section

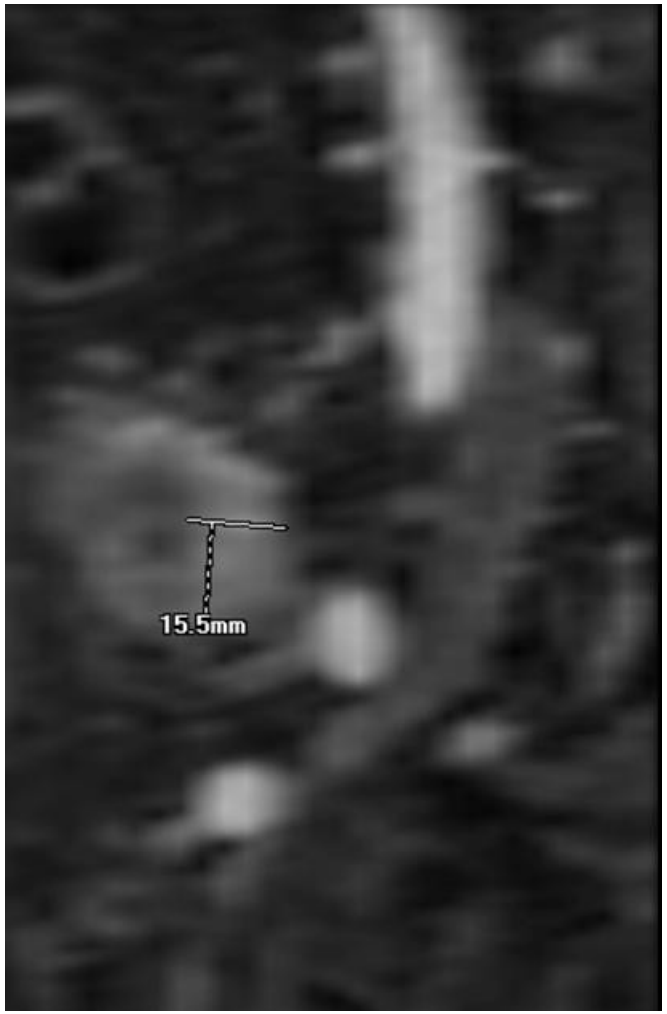


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Comparison of DeskVOX with Clinical MRI Slice Program Confirms Inflammation

Image from Cynthia Santillan, UCSD Health Services



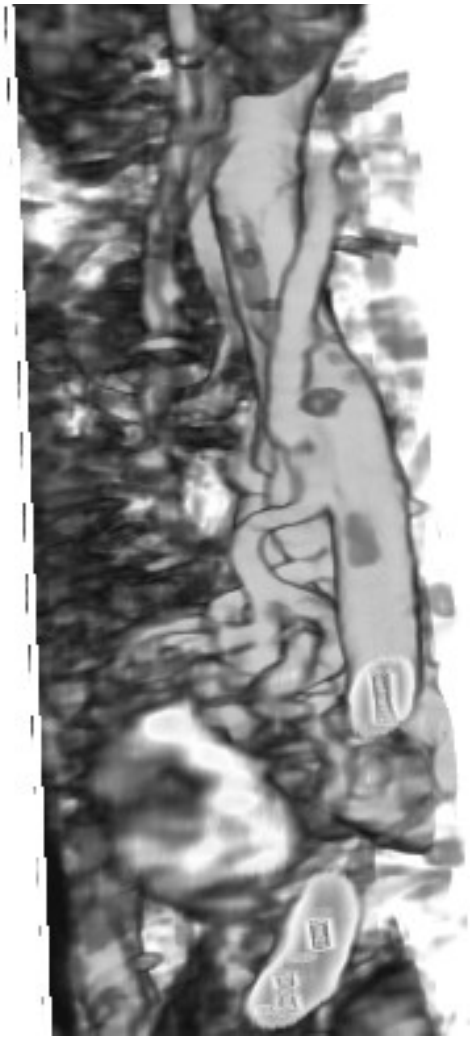
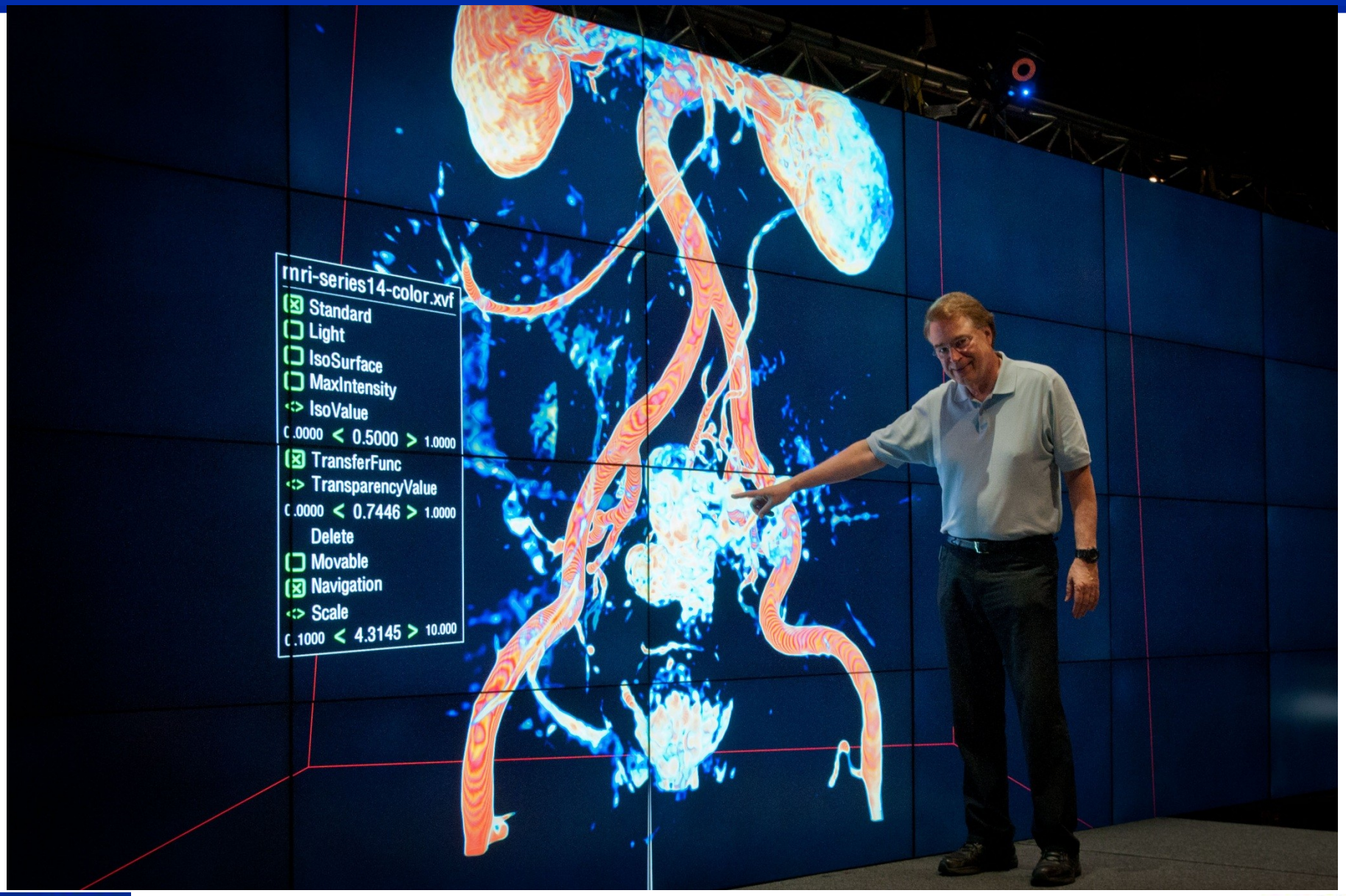


Image from Jurgen Schultz, Calit2

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Scalable Visualization for 3D Interactive Body Imaging



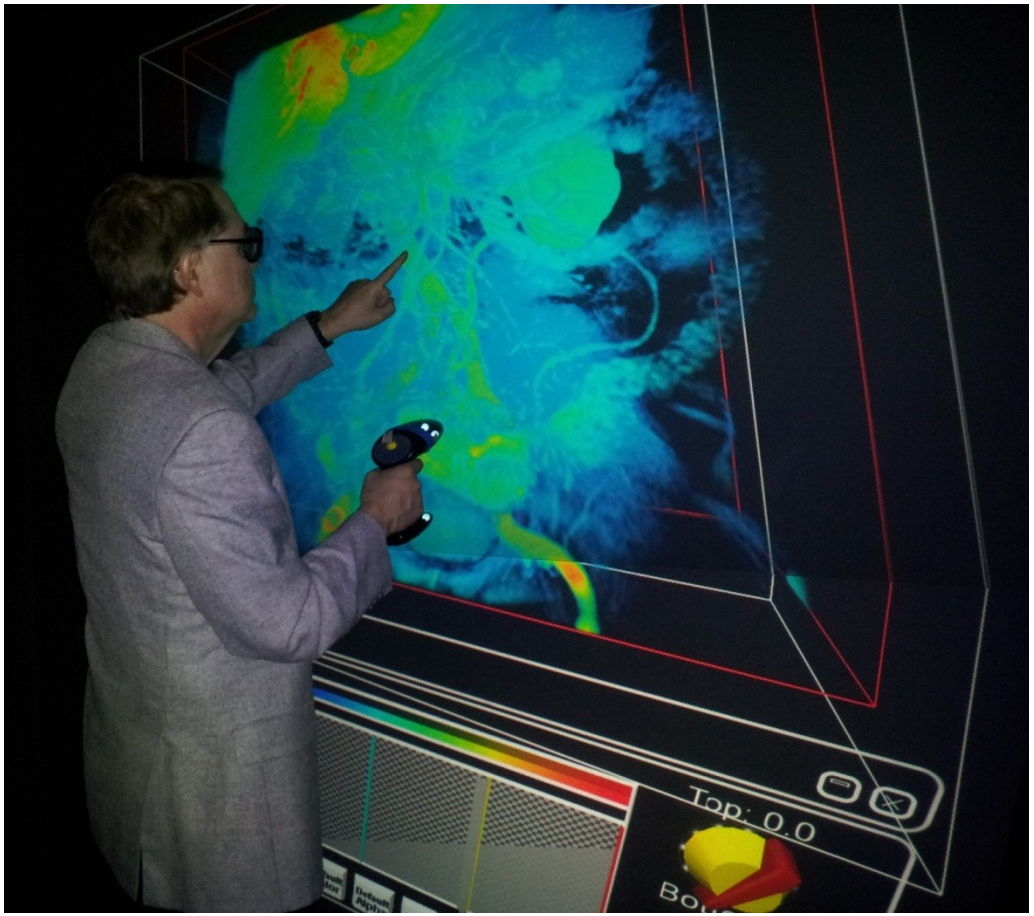
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DeskVOX Software Courtesy of Jurgen Schulze, Calit2

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3D Imaging of MR Enterography Data: Virtual Reality and Hard Copy

- **Videos of Me Giving Tours of My Organs:**
  - **http://www.youtube.com/watch?v=9c4DtJ_L_Ps**
  - **www.theatlantic.com/magazine/archive/2012/07/the-measured-man/309018/**





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Photo & DeskVOX Software Courtesy of Jurgen Schulze, Calit2

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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!

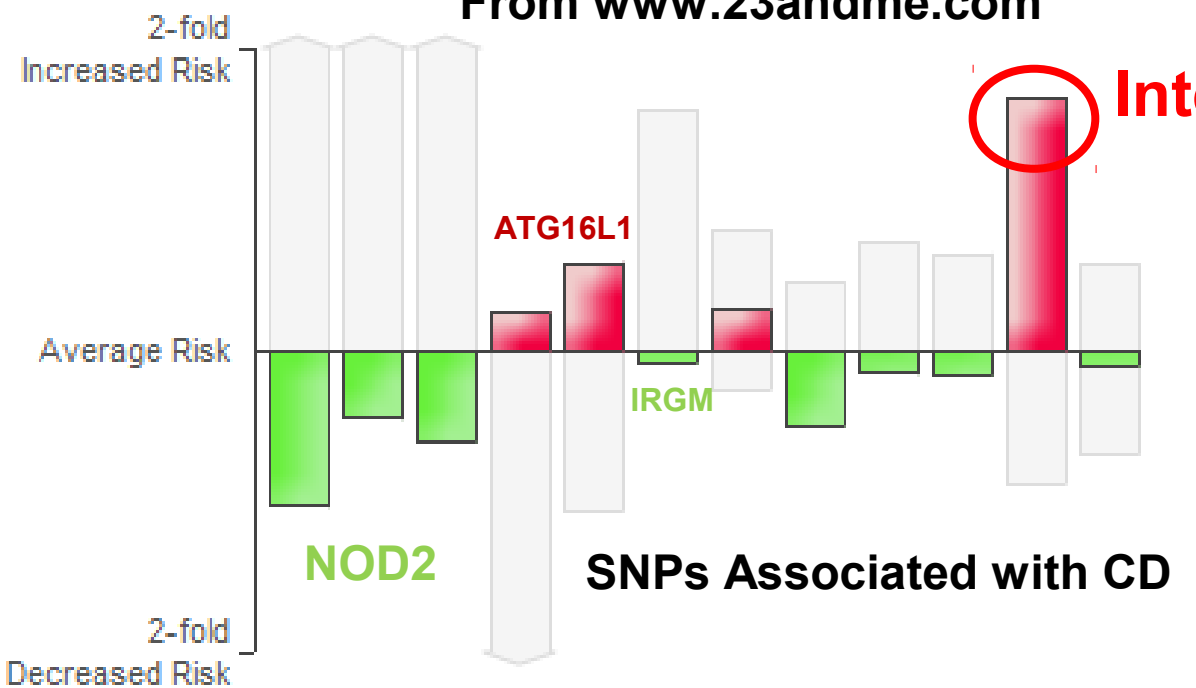
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Paul B. Eckburg & David A. Relman
Clin Infect Dis. 44:256-262 (2007)

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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

News and Views

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

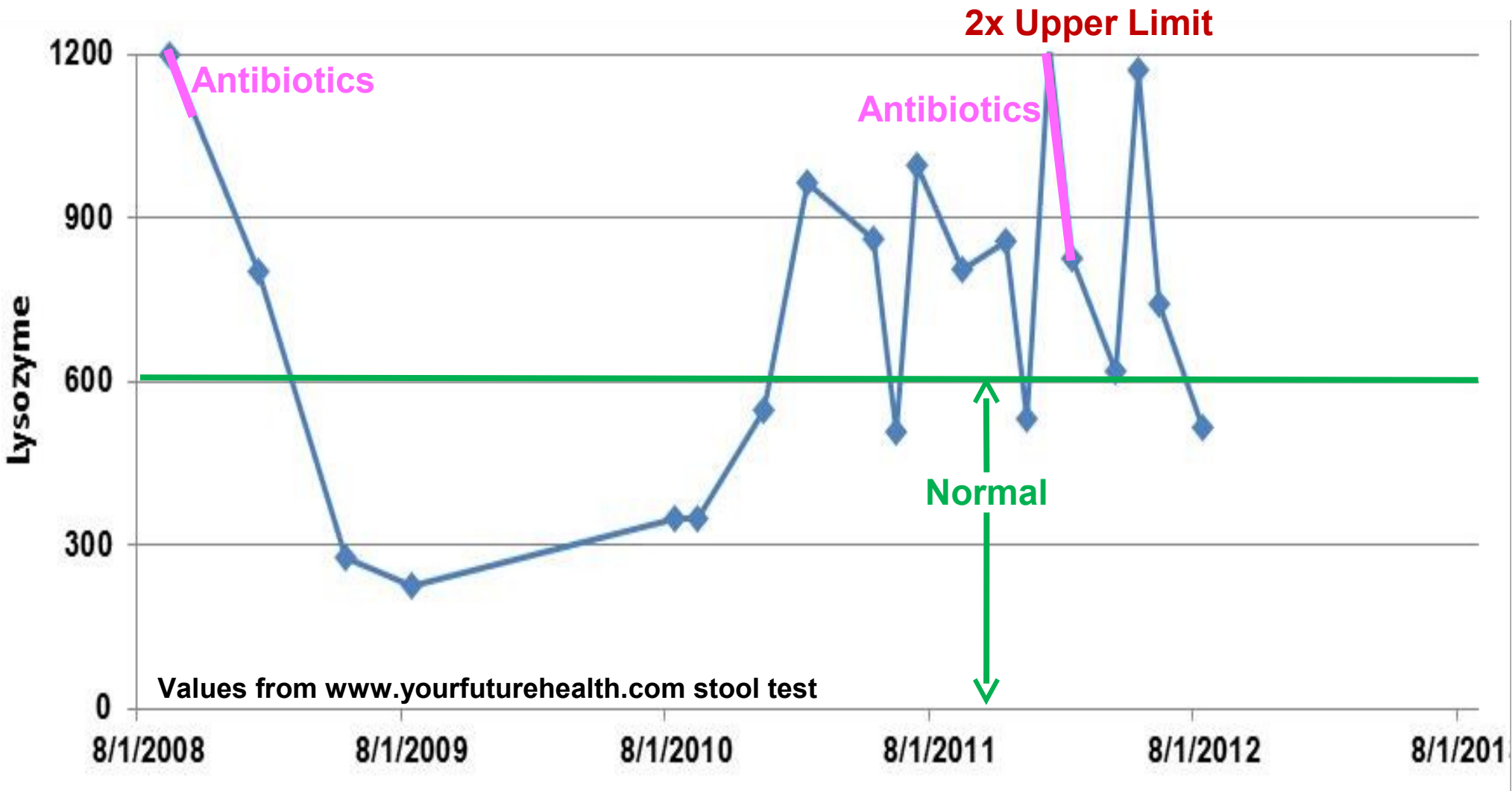
IL-23: a master regulator in Crohn disease

Markus F Neurath[1]

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I Tracked My Innate Immune System By Measuring Lysozyme From Stool Samples Over Time

My Immune System Seems to Be Fighting Bacteria Episodically

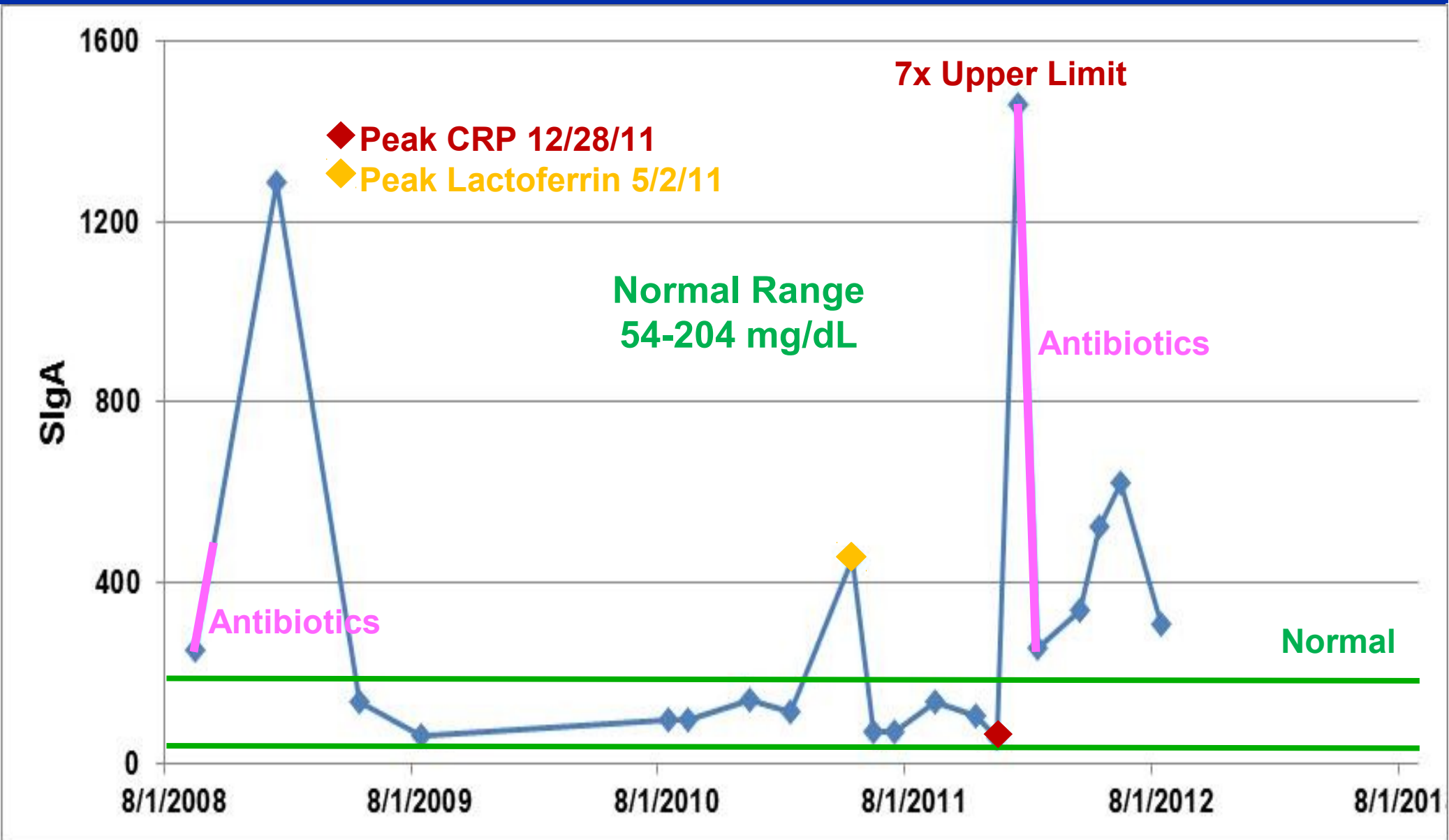


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Lysozyme is an Enzyme of the Innate Immune System that Attacks Bacterial Cell Walls

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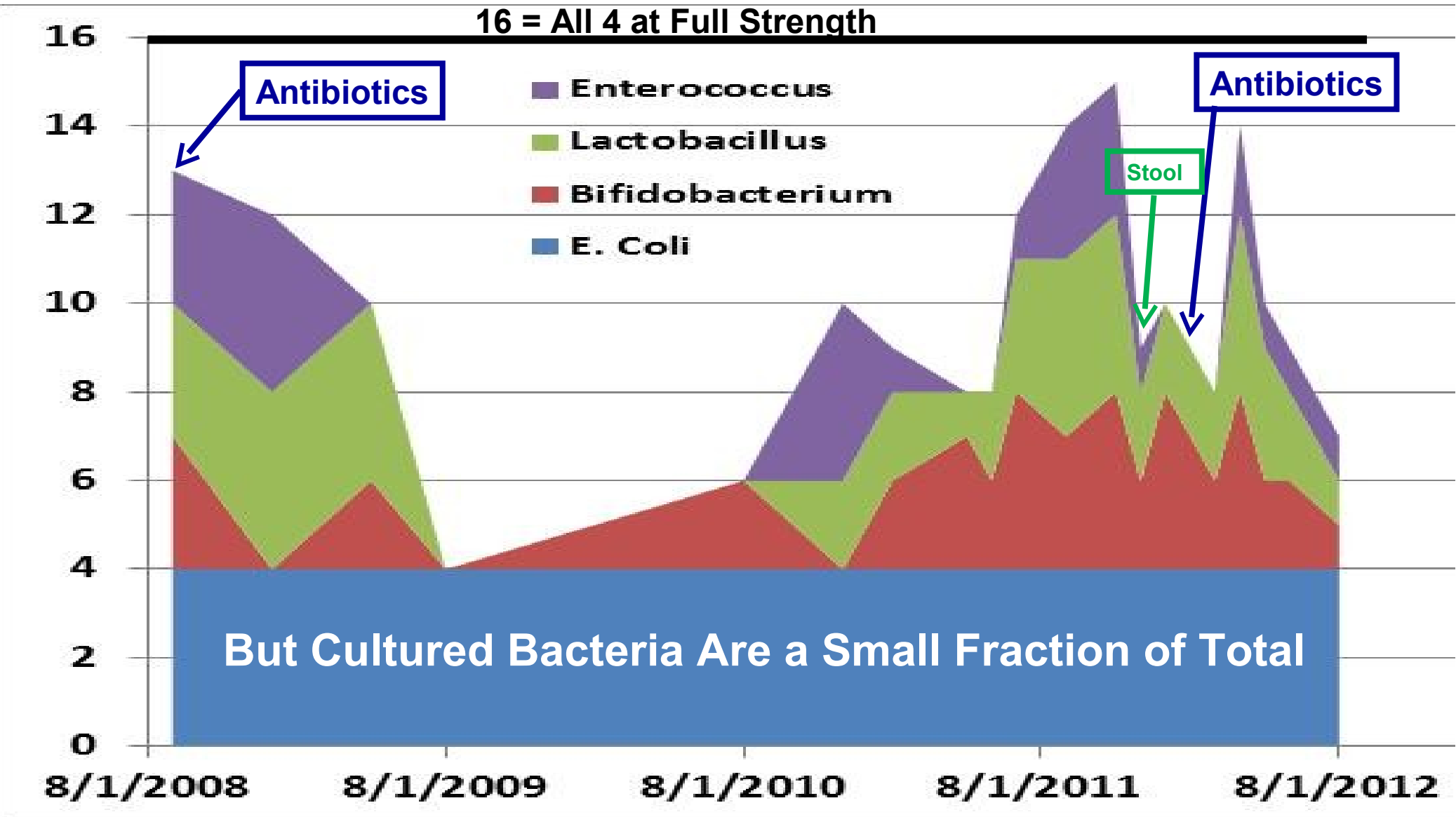
I Tracked My Adaptive Immune System By Measuring Secretory IgA From Stool Samples



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Your Human Cells are Only 10% of Your Superorganism: How Can We Track the 90% which are Microbes?



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Values From www.yourfuturehealth.com stool test

it²

Determining My Gut Microbes and 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
Per Person Analyzed!

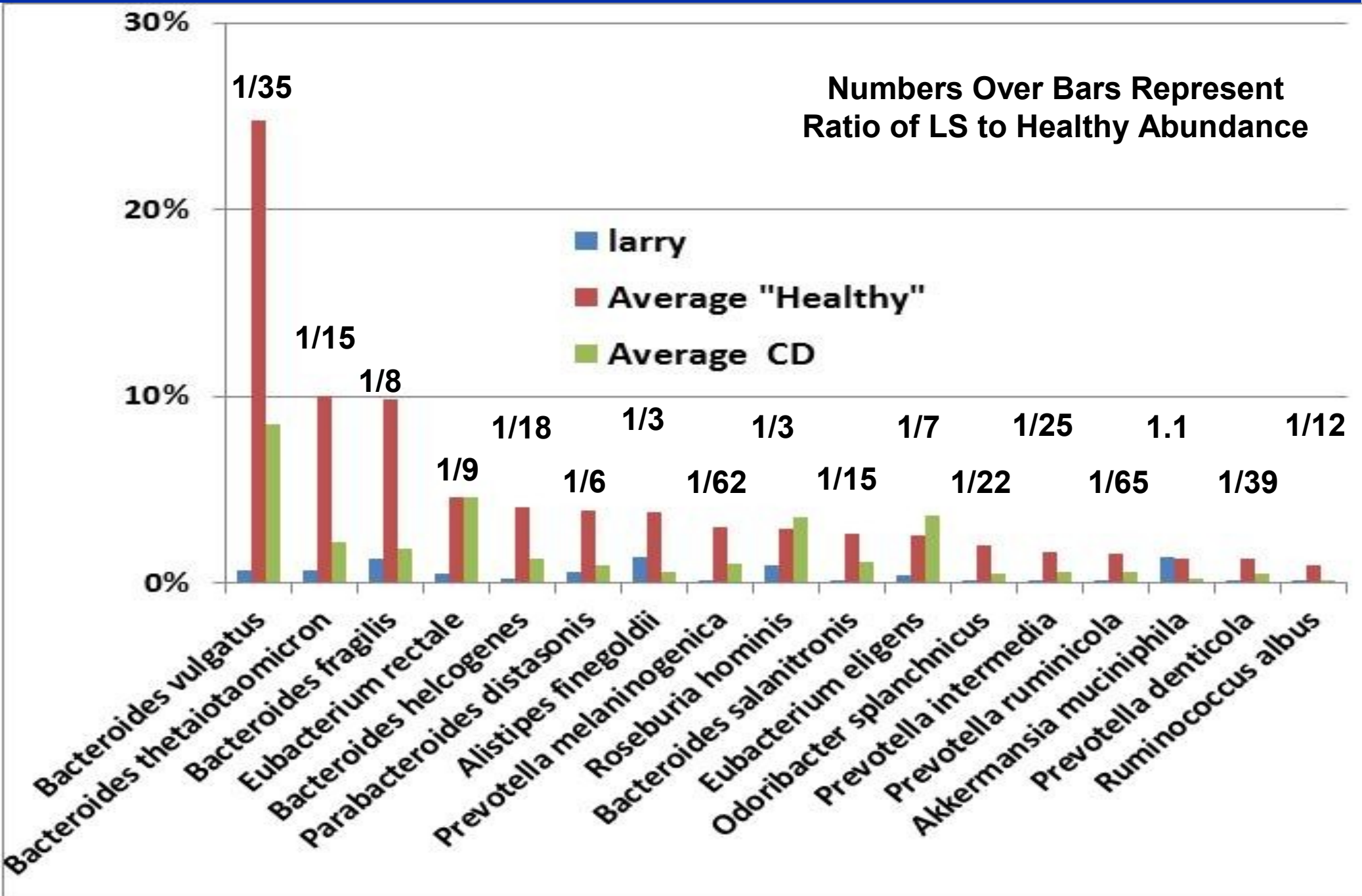
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UC San Diego
HEALTH SCIENCES

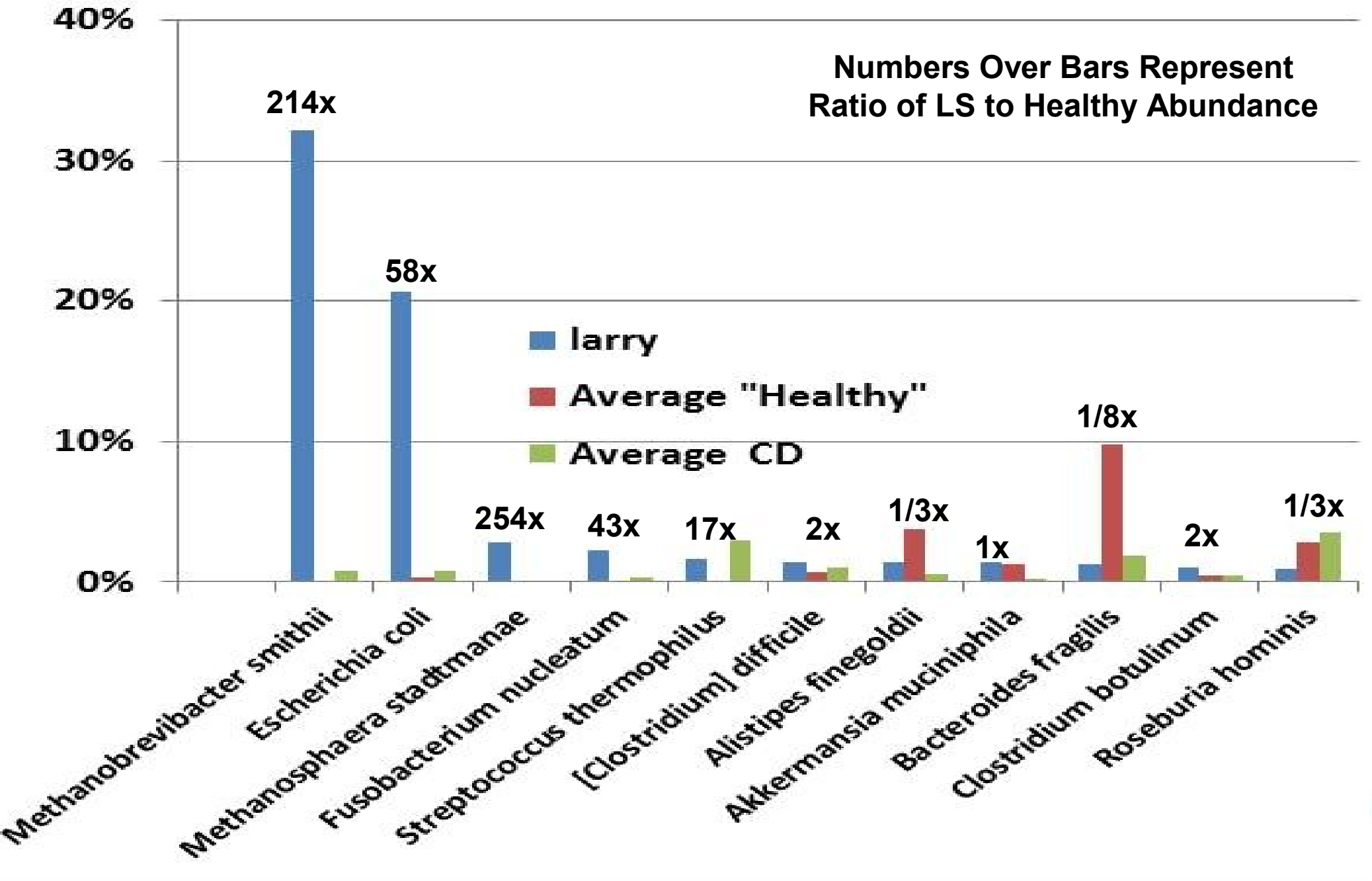
J. Craig Venter
INSTITUTE

it²

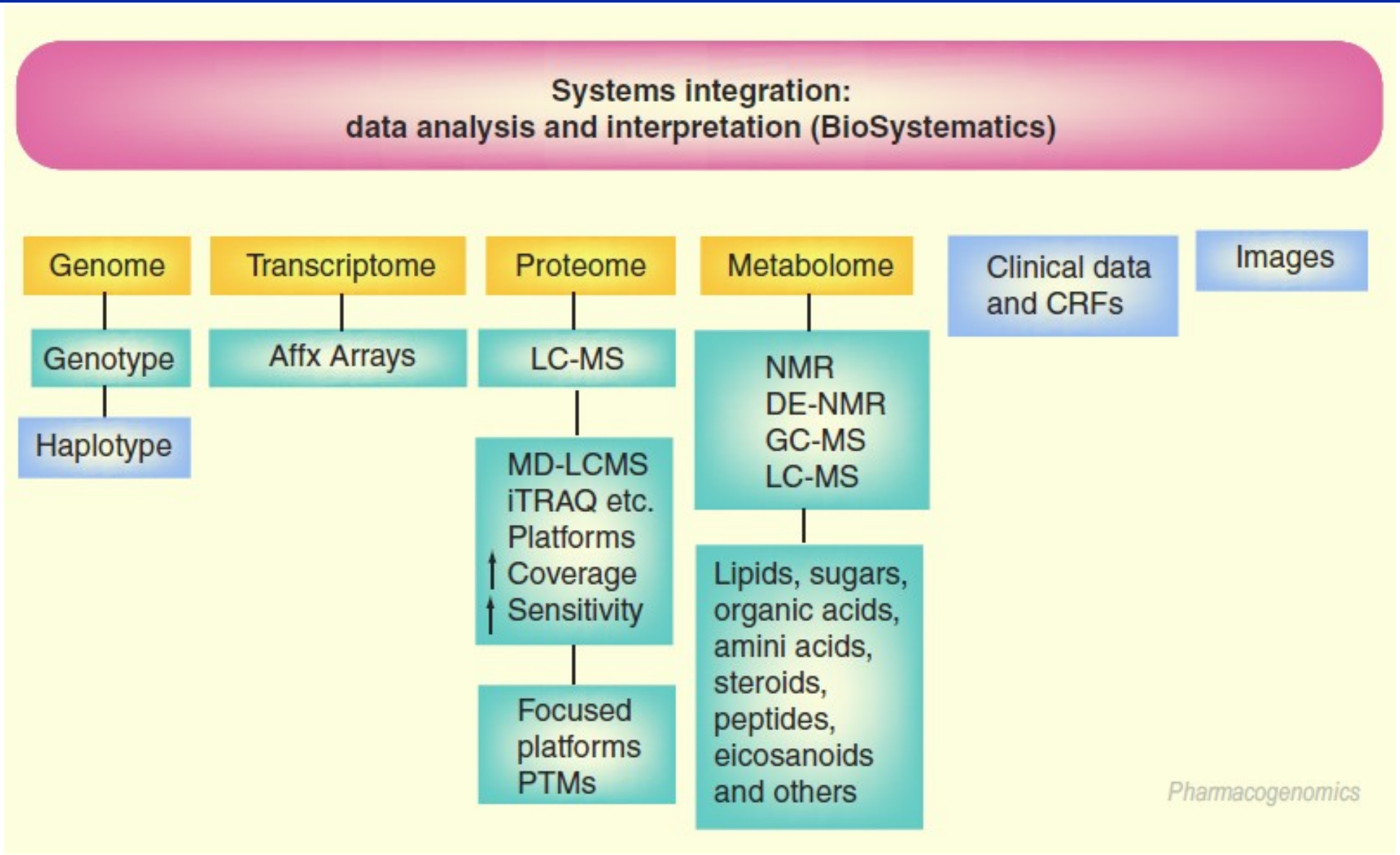
Almost All Abundant Species (≥1%) in Healthy Subjects Are *Severely Depleted* in LS Gut



LS Abundant Microbe Species (≥1%) Are *Dominated by Rare Species* in Healthy Subjects



Human Systems Biology
Needs Addition of Microbiome Systems Biology



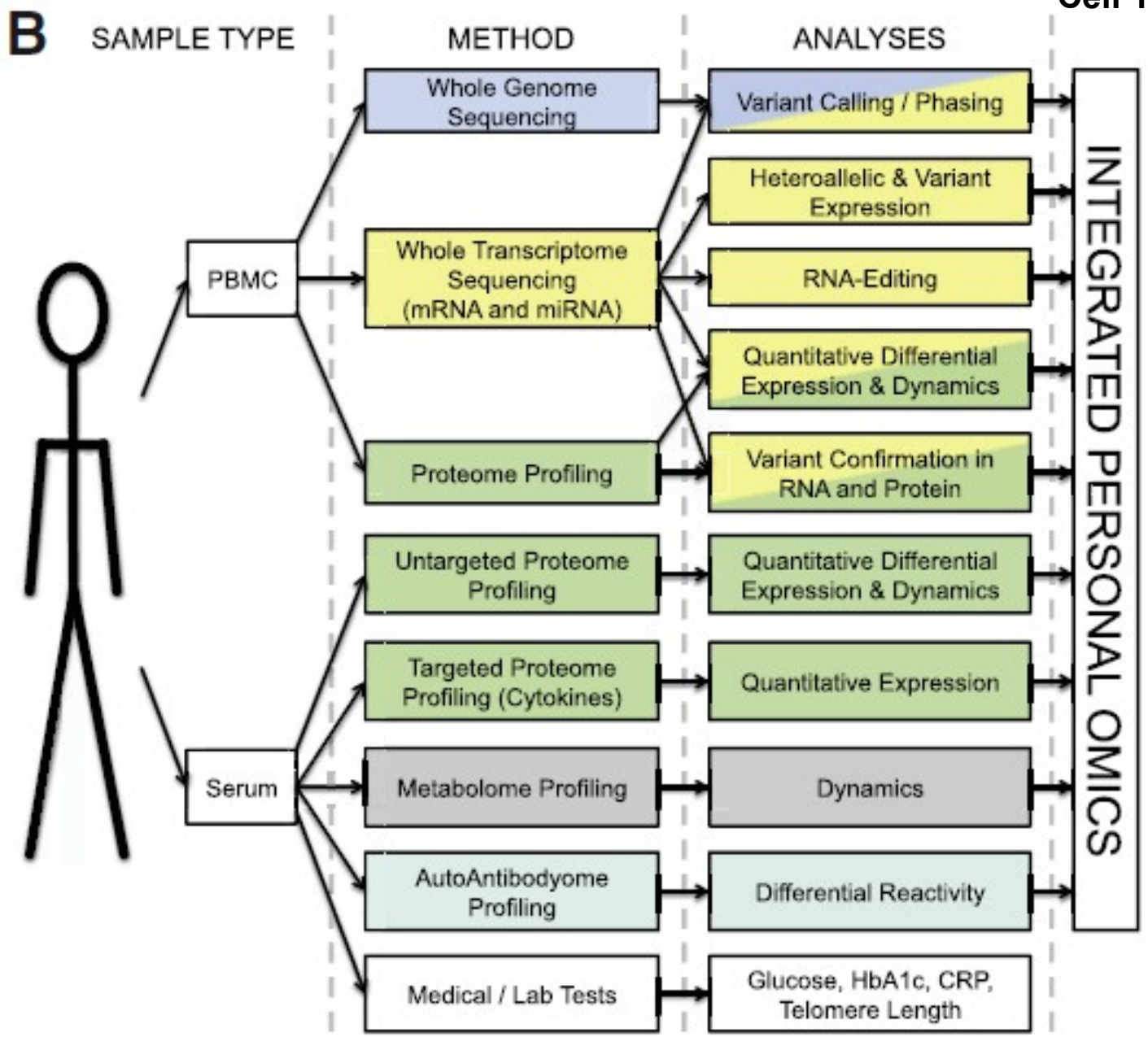
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Van der Greef, Pharmacogenomics, 7, 1087-94 (2006)

it²

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**