"Leveraging Biomedical Big Data: Quantified Self & Beyond"

Invited Talk

FutureMed

Singularity University

NASA Ames Campus

February 5, 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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Where I Believe We are Headed: Predictive, Personalized, Preventive, & Participatory Medicine

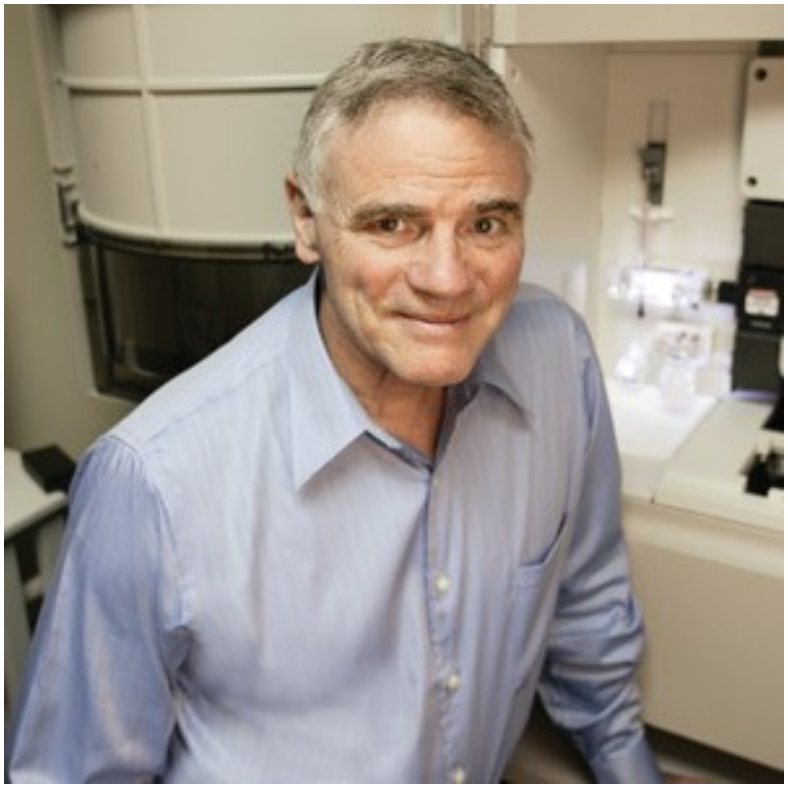
Newsweek

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

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

it²

From Measuring Macro-Variables to Measuring Your Internal Variables



The Patient of the Future

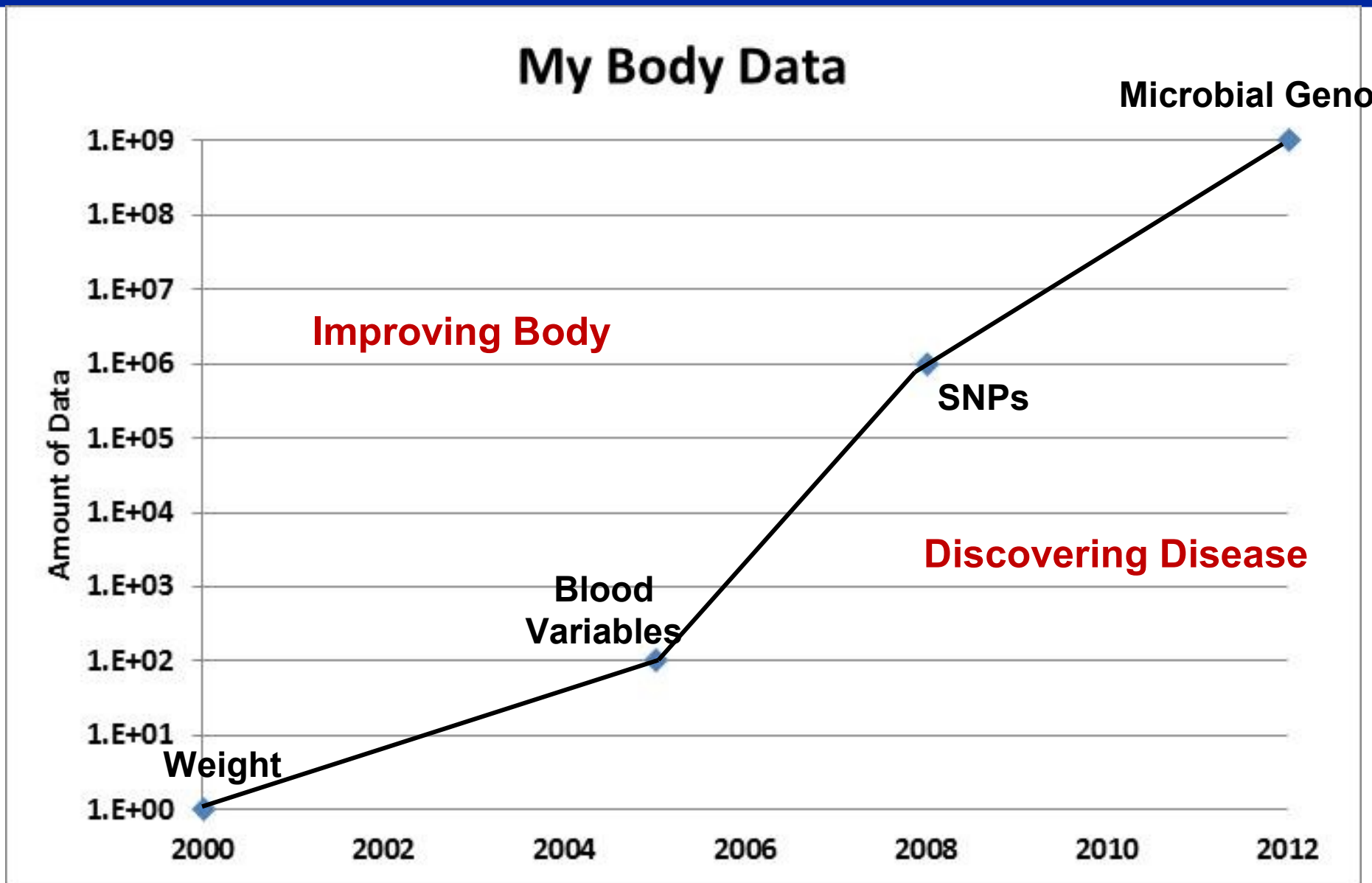
Internet pioneer Larry Smarr's quest to quantify everything about his health led him to a startling discovery, an unusual partnership with his doctor, and more control over his life.

www.technologyreview.com/biomedicine/39636

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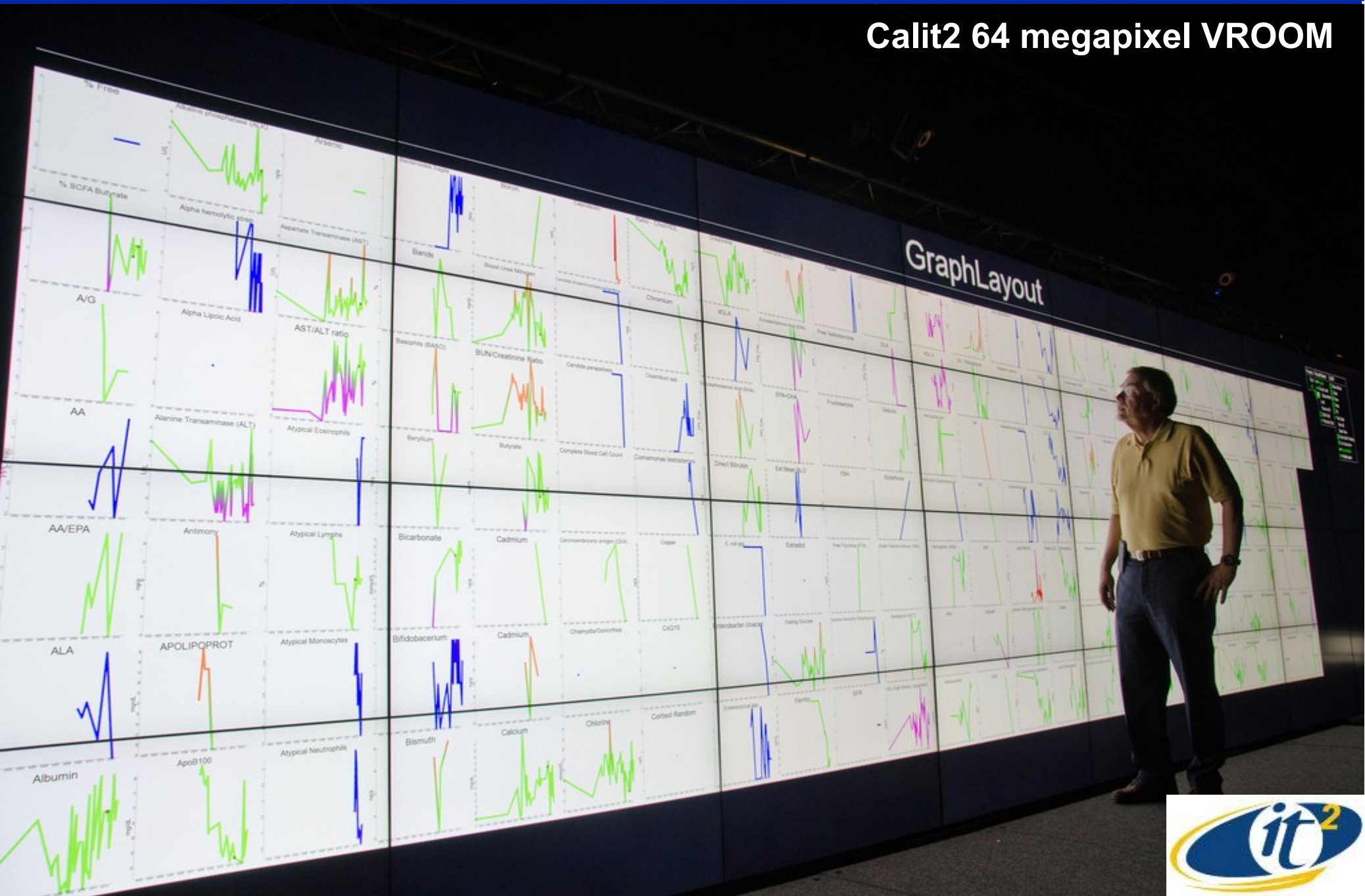
it²

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

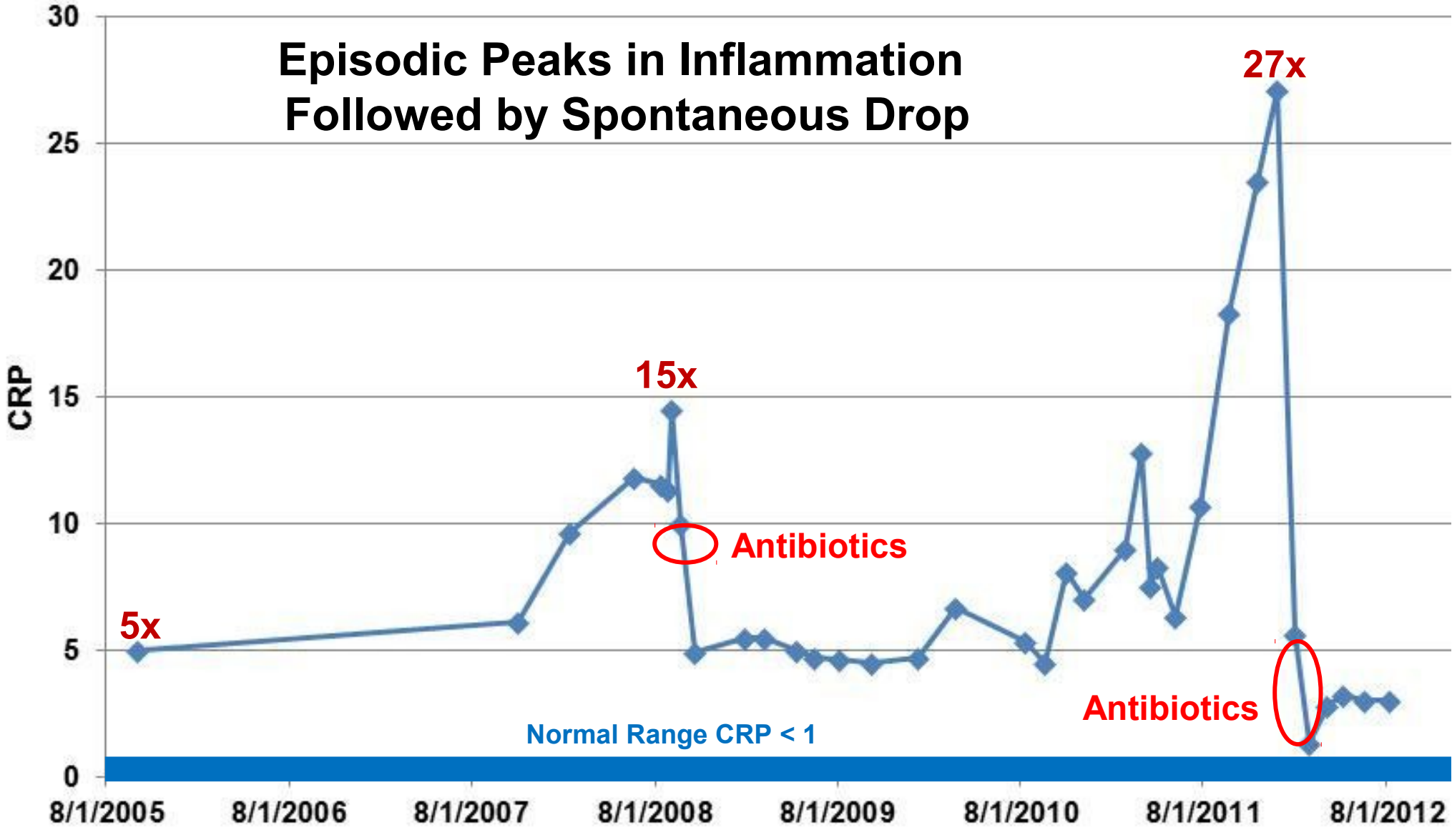


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Visualizing Time Series of 150 LS Blood and Stool Variables, Each Over 5 Years



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

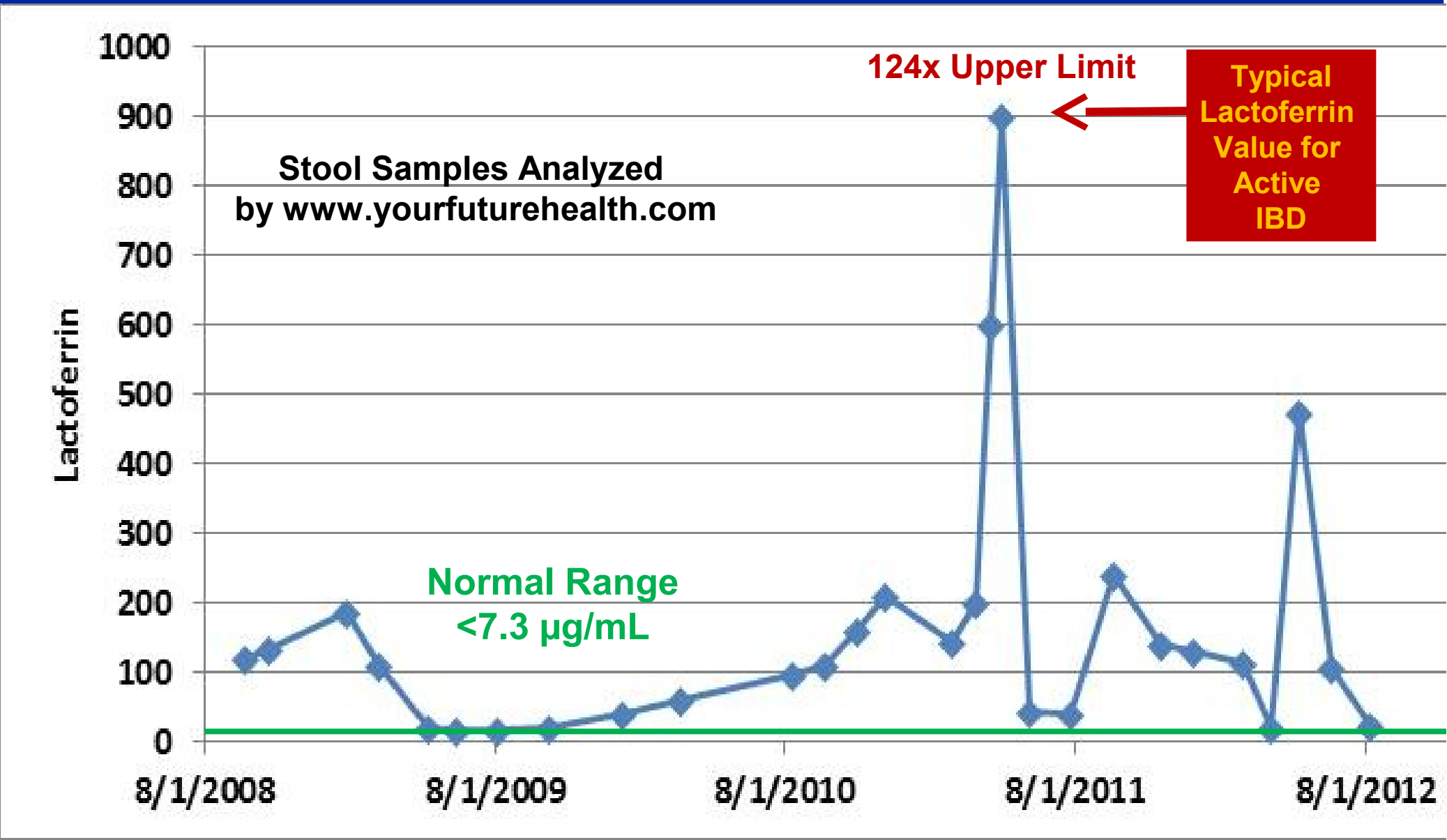


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Complex Reactive Protein (CRP) is a Blood Biomarker for Detecting Presence of Inflammation

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

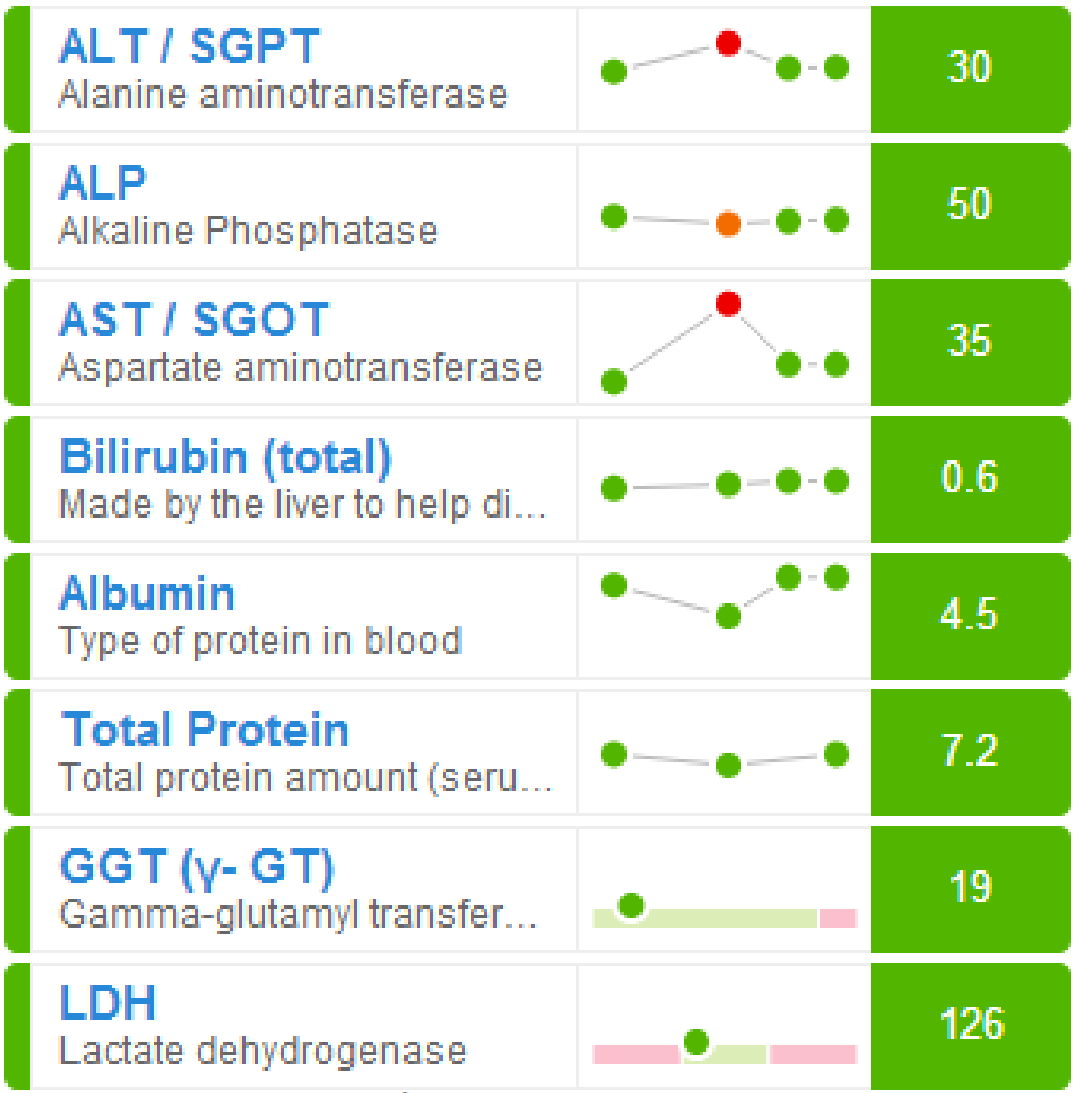


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Lactoferrin is a Sensitive and Specific Biomarker for Detecting Presence of Inflammatory Bowel Disease (IBD)

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Startup WellnessFX Enables You to Track Your Own Blood Variables



Liver Enzymes and Function Tests

WellnessFX Baseline includes:

- A blood draw at a partner lab
- A 20-minute health consultation with a practitioner you choose from our network*
- Your lab results loaded into your private WellnessFX dashboard
- Your satisfaction guaranteed

Get Started Today

Only $199*

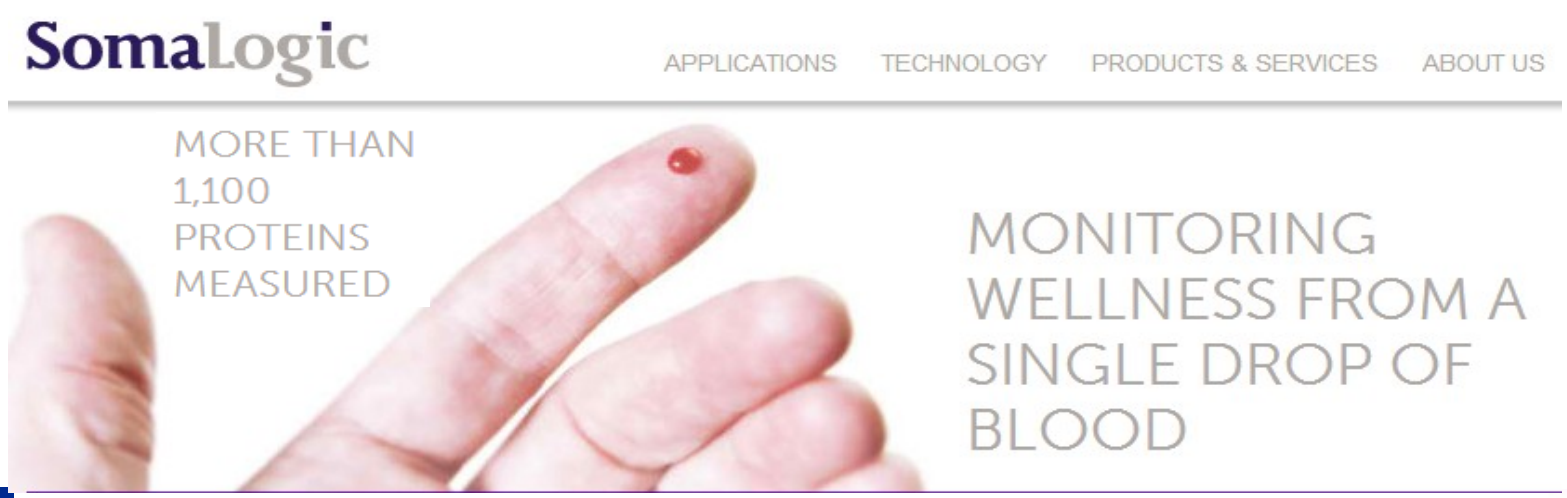
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LS Values from WellnessFX.com

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From Vials of Blood for a Few Variables to Thousands of Proteins from a Single Drop





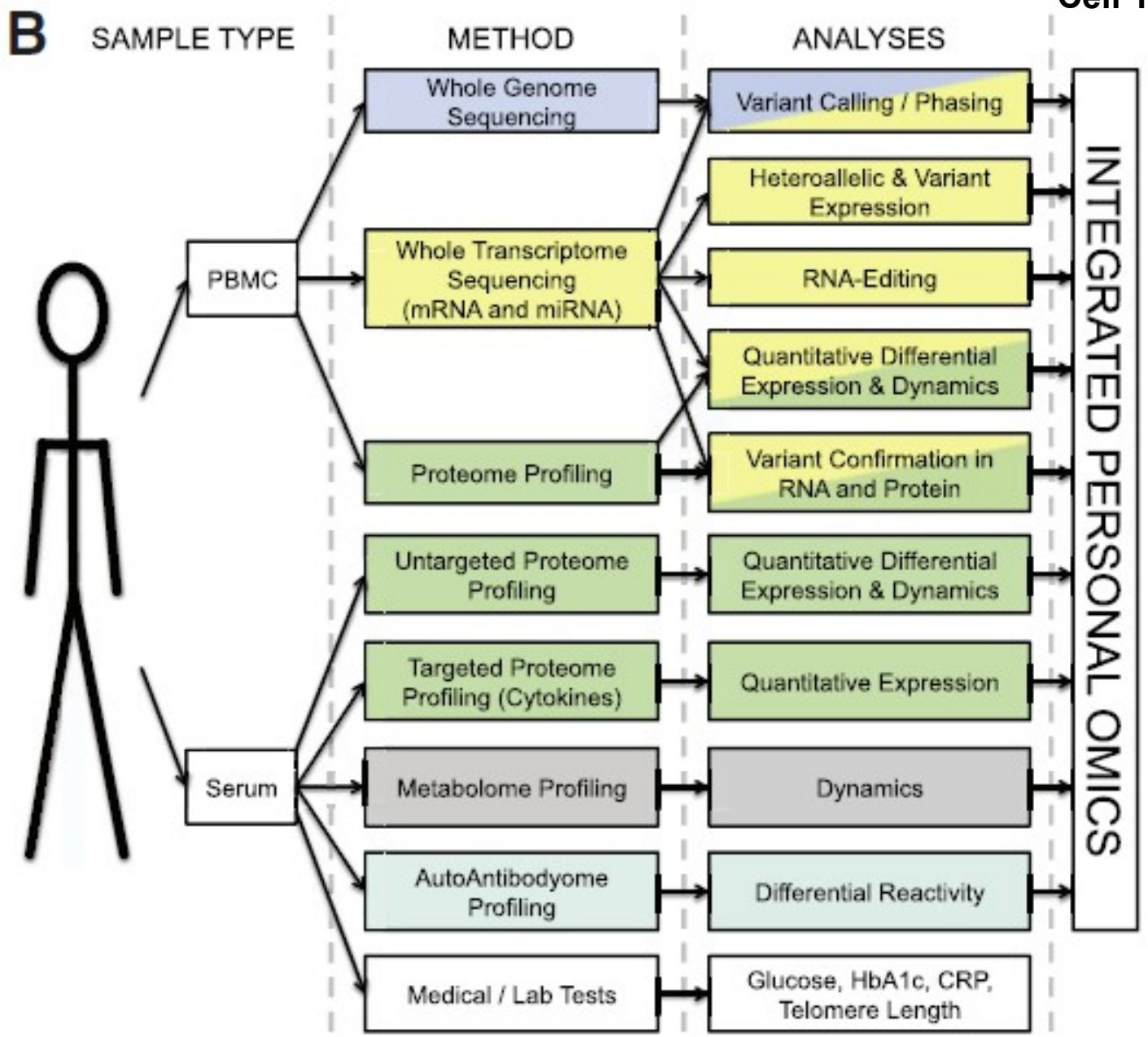
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www.somalogic.com/

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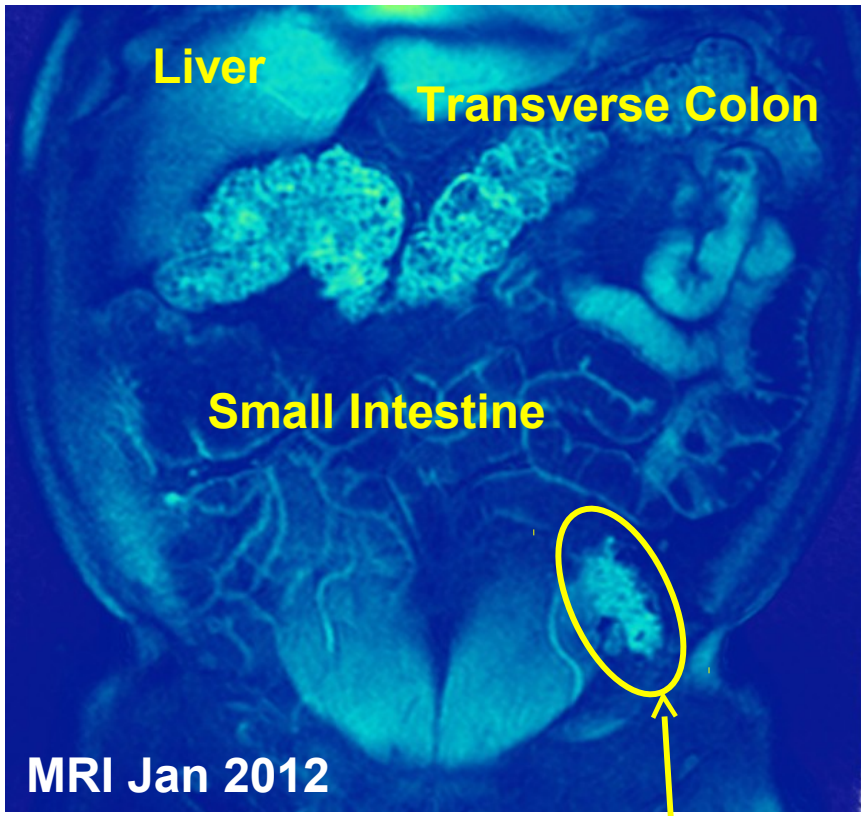
Integrative Personal Omics Profiling Reveals Details of Clinical Onset of Viruses and Diabetes

Cell 148, 1293–1307, March 16, 2012



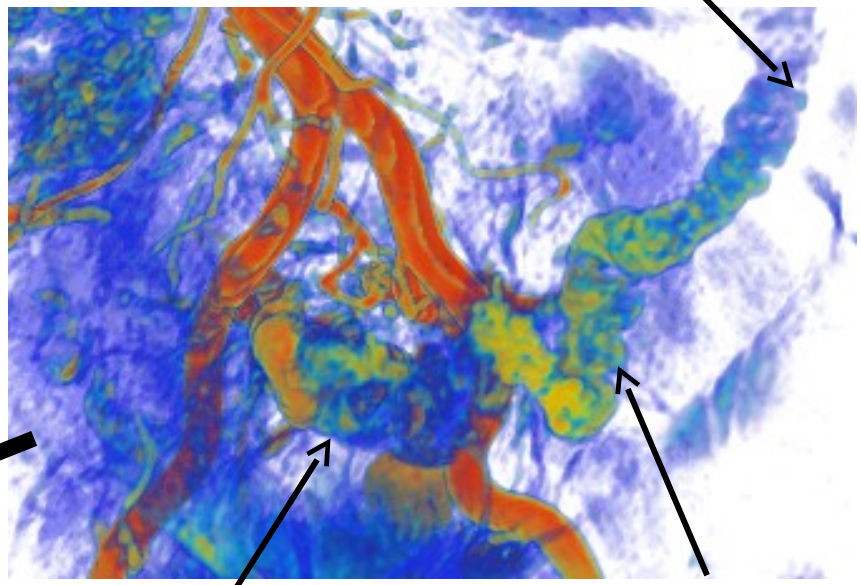
- **Michael Snyder, Chair of Genomics Stanford Univ.**
- **Genome 140x Coverage**
- **Blood Tests 20 Times in 14 Months**
  - **tracked nearly 20,000 distinct transcripts coding for 12,000 genes**
  - **measured the relative levels of more than 6,000 proteins and 1,000 metabolites in Snyder's blood**

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

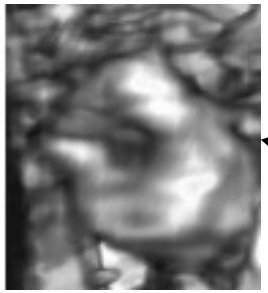
Descending Colon



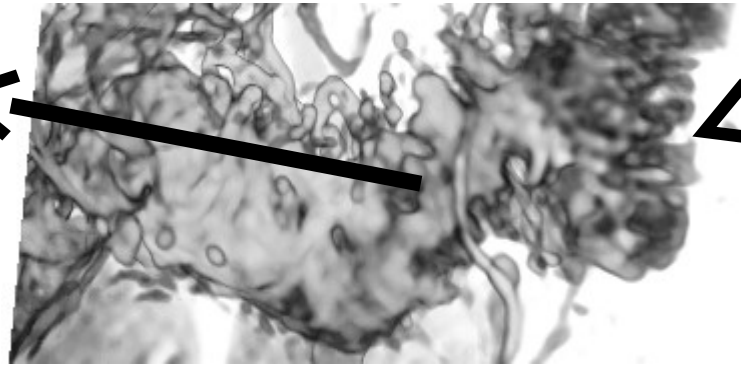
Major Kink

Sigmoid Colon
Threading Iliac Arteries

Cross Section



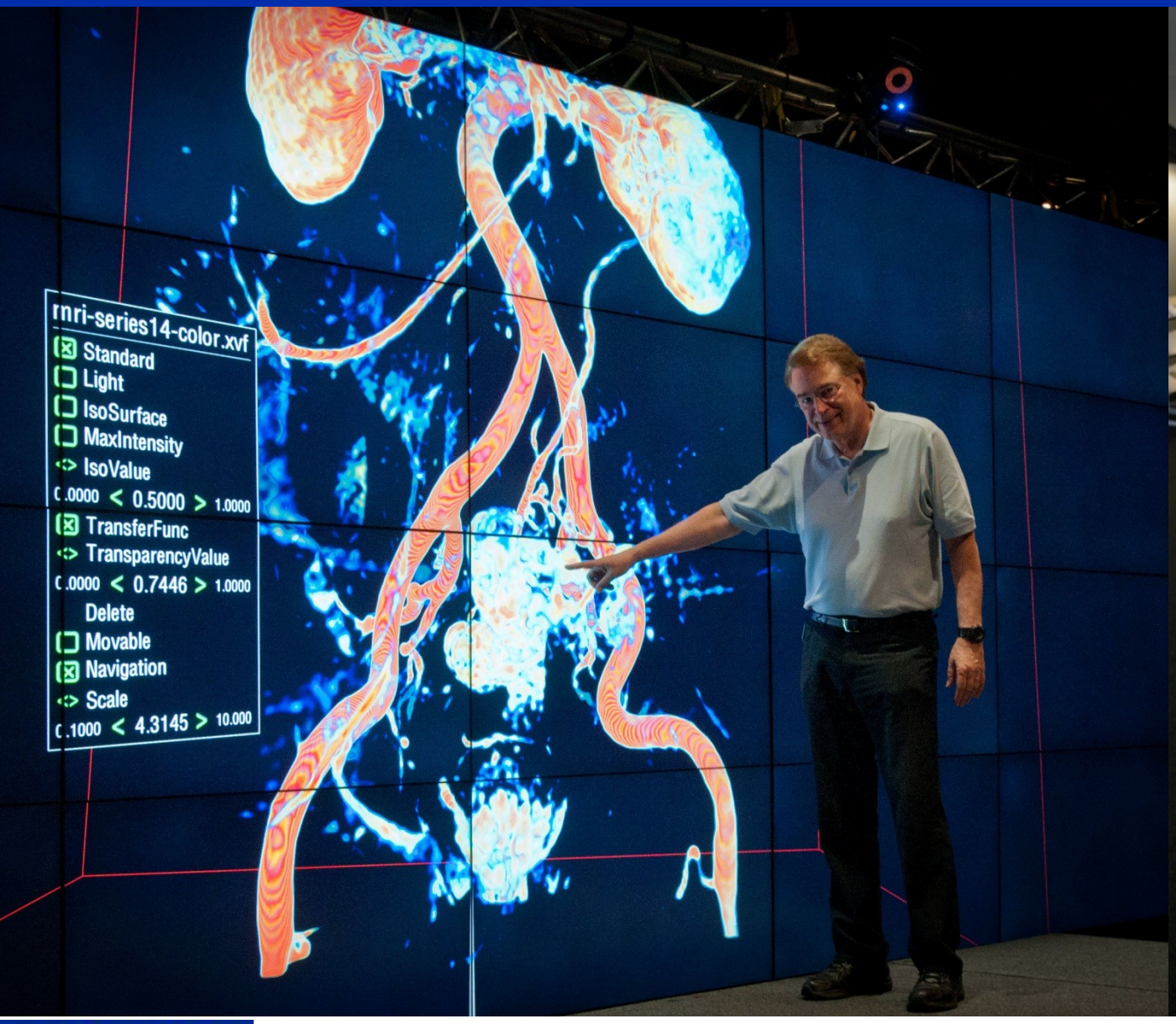
Diseased Sigmoid Colon



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Interactive Visualization and 3D Printed Hard Copy from LS MRI Data





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Research: Calit2 FutureHealth Team

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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!

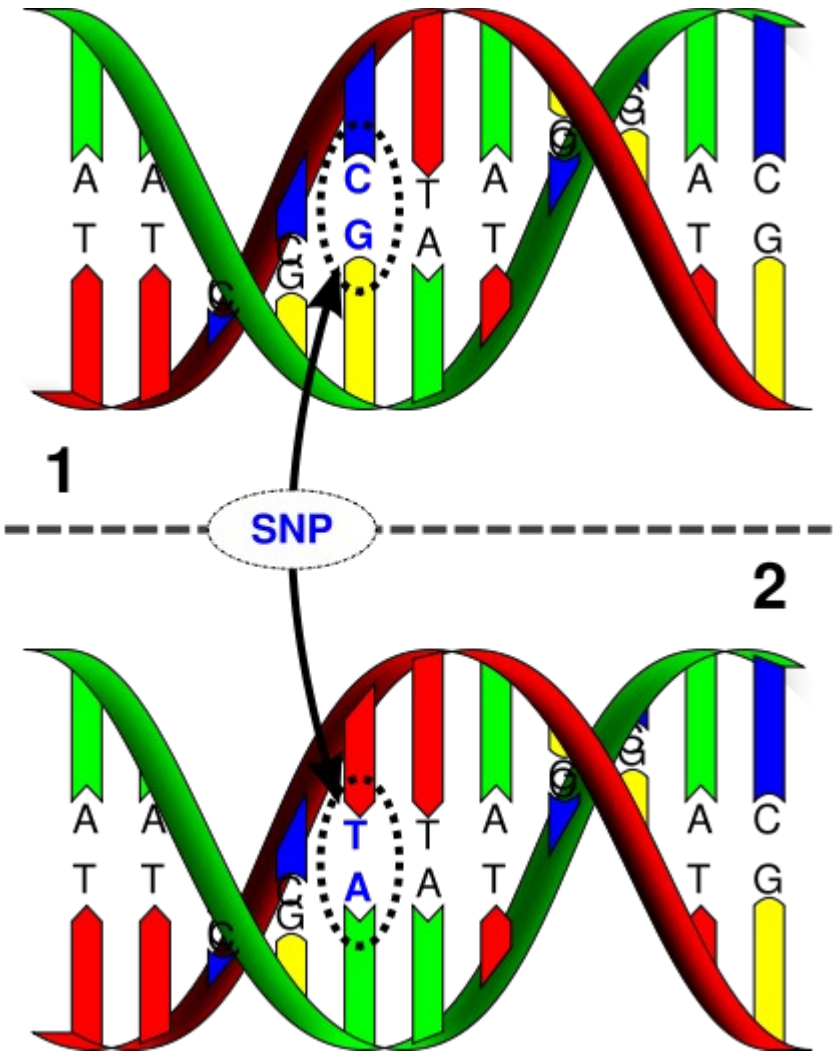
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Paul B. Eckburg & David A. Relman
Clin Infect Dis. 44:256-262 (2007)

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

Person A



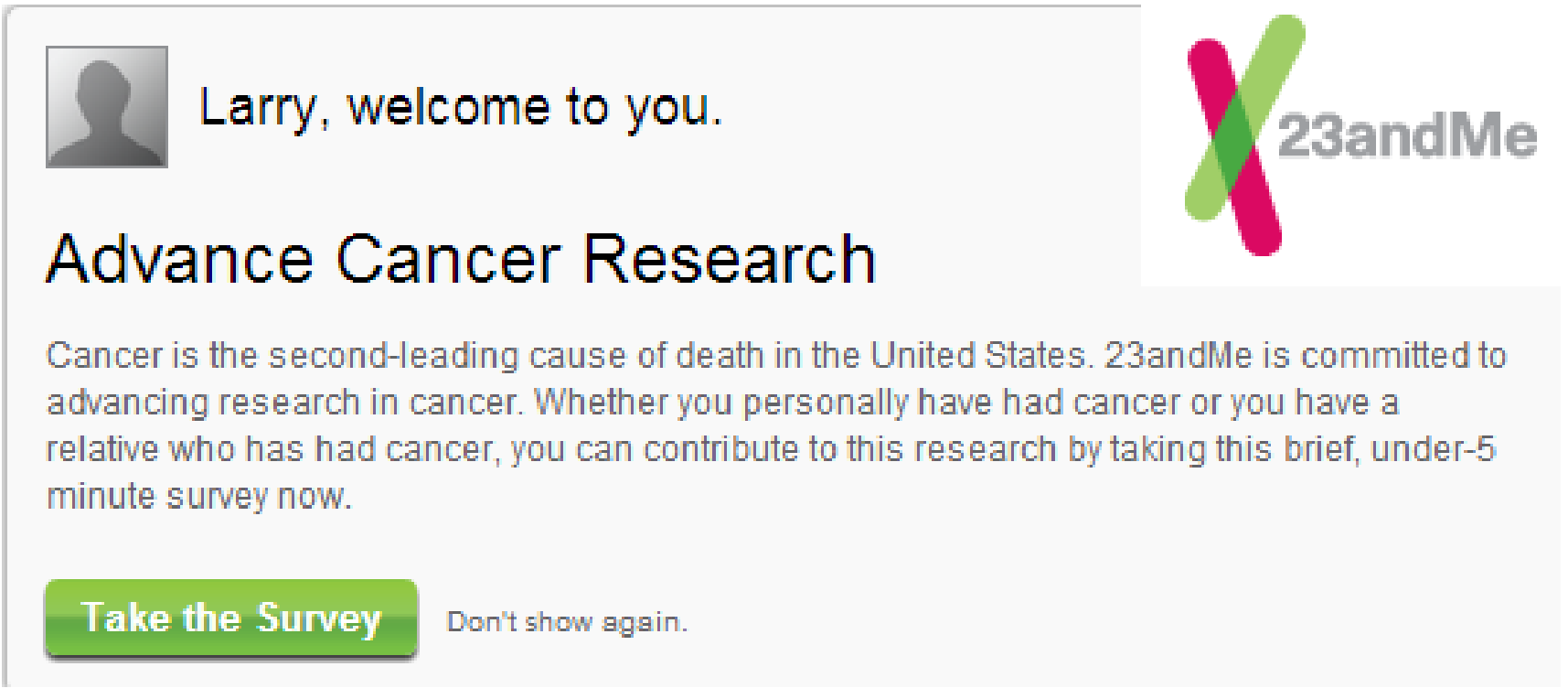
Person B

SNPs Occur Every 100 to 300 Bases Along Human DNA

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www.23andme.com Tracks One Million SNPs

Soon a Trillion SNPs in a Startup!
Incredible Opportunities for Crowdsourcing

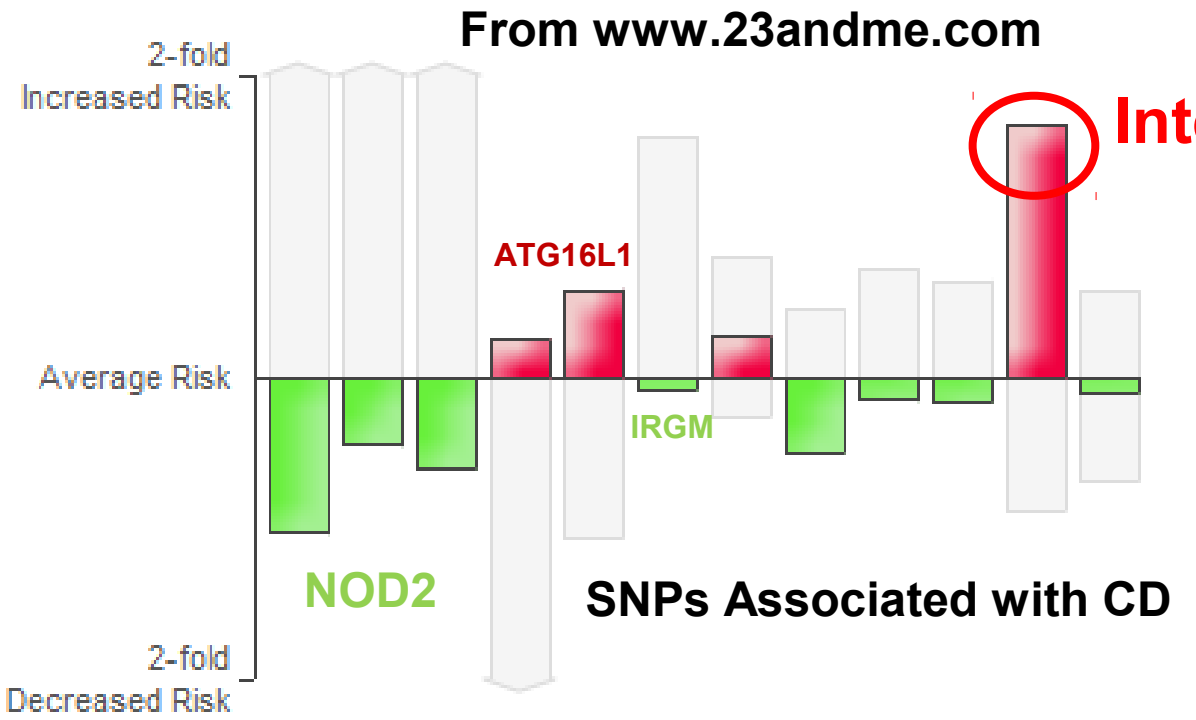


23andMe looks at 1,000,000 SNPs scattered across the 23 pairs of chromosomes

Company Sets Growth Goal Of One Million Customers, Reduces Price to $99 from $299

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



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

News and Views

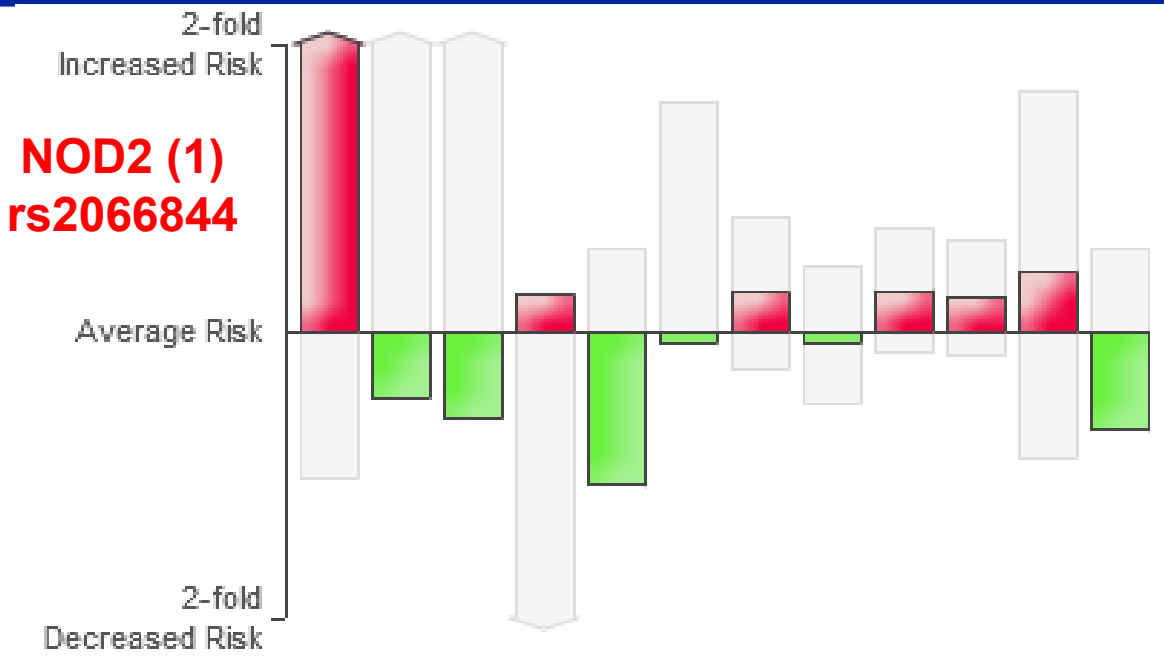
Nature Medicine **13**, 26 - 28 (2007)
doi:10.1038/nm0107-26

IL-23: a master regulator in Crohn disease

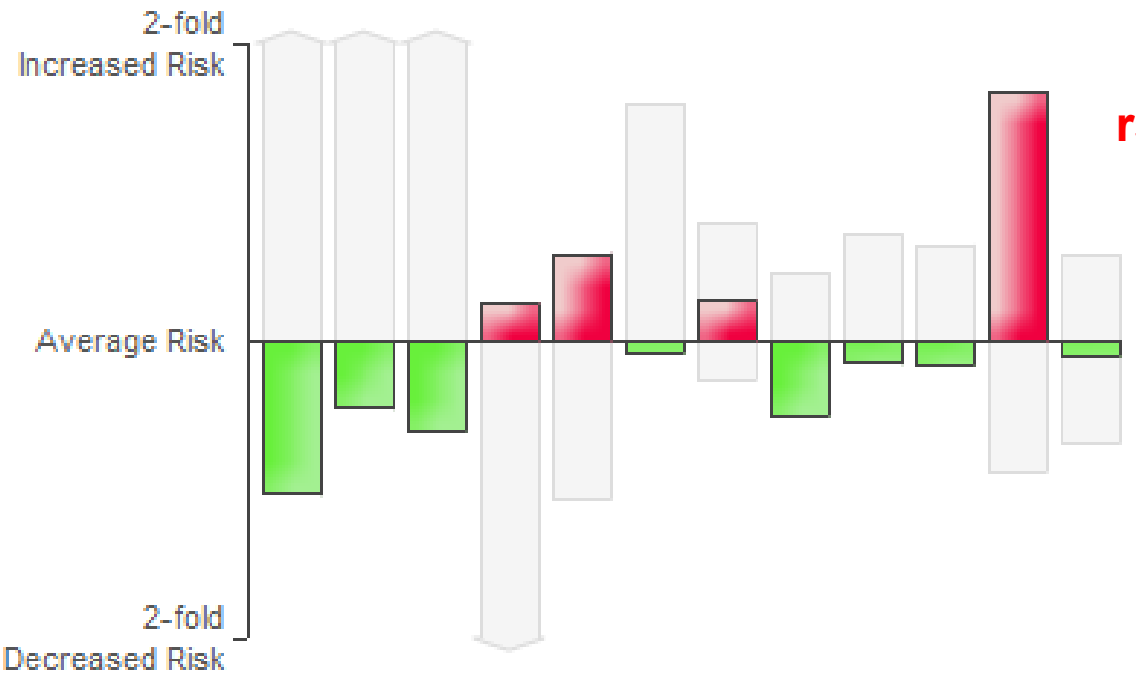
Markus F Neurath[1]

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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!



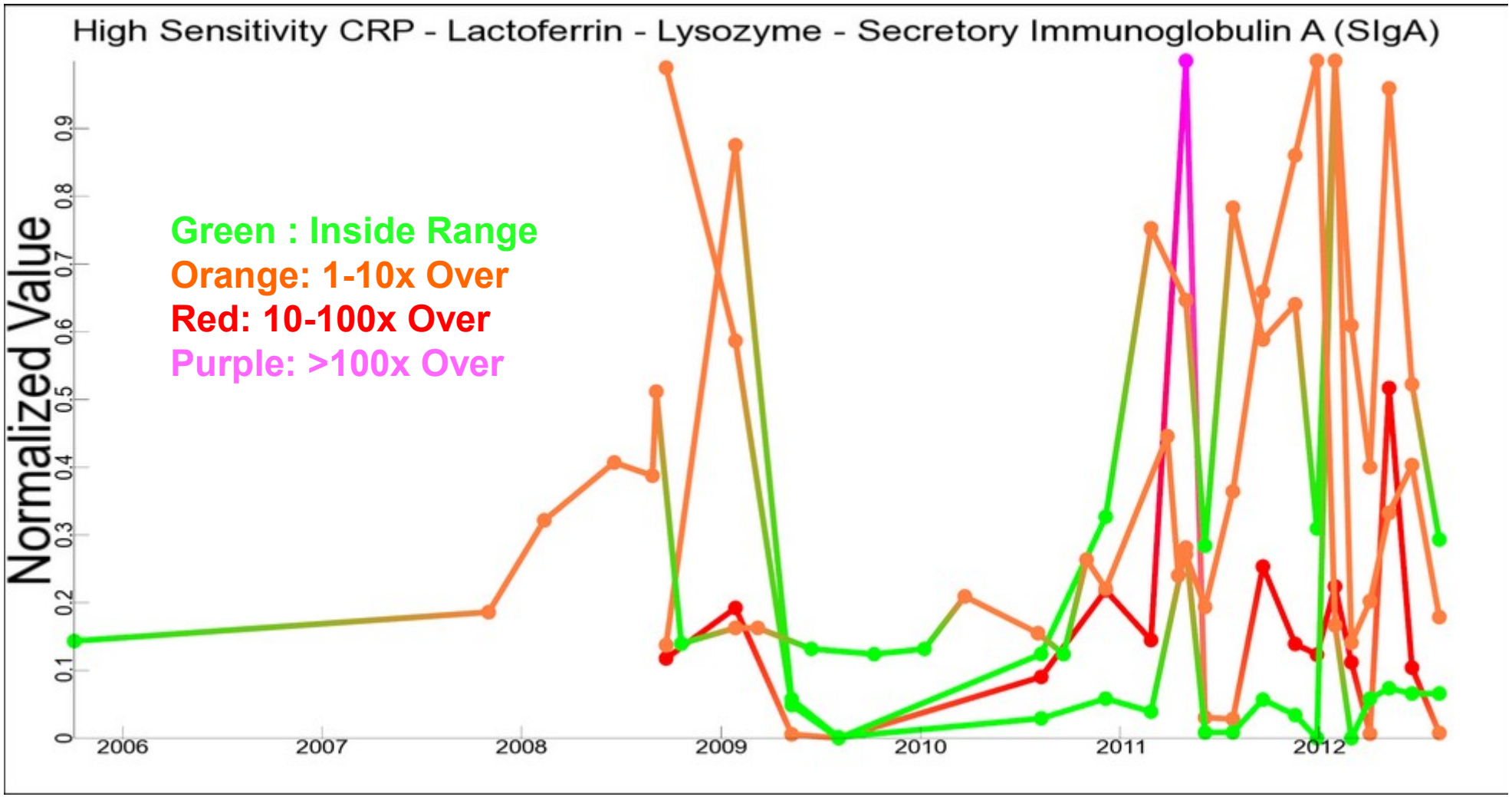
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Hear Crohnology Founder Sean Ahrens Friday

www.crohnology.com

it2

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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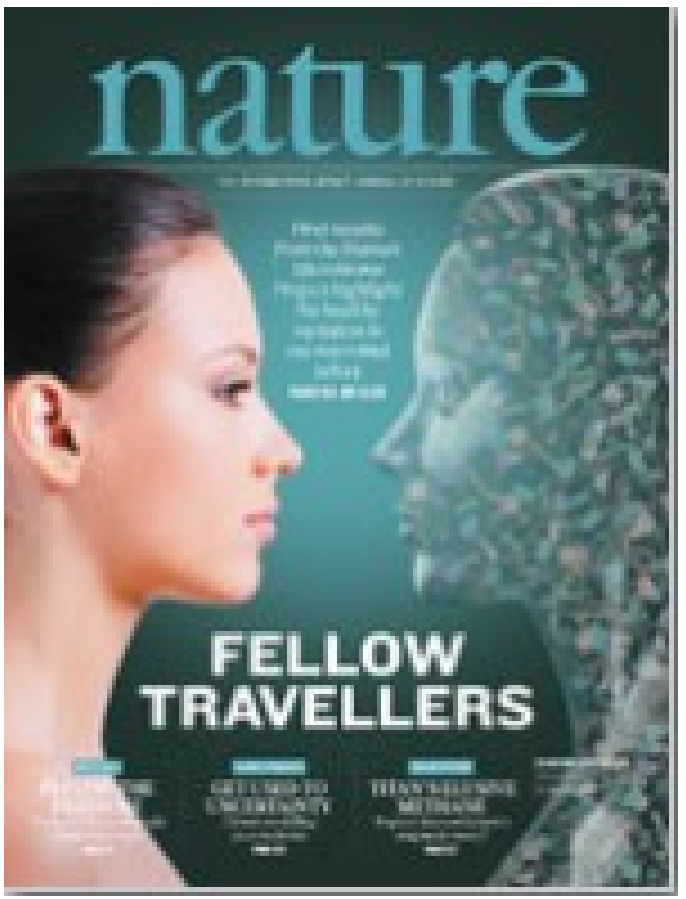
Source: Photo of Calit2 64-megapixel VROOM

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Intense Scientific Research is Underway on Understanding the Human Microbiome



June 8, 2012



June 14, 2012

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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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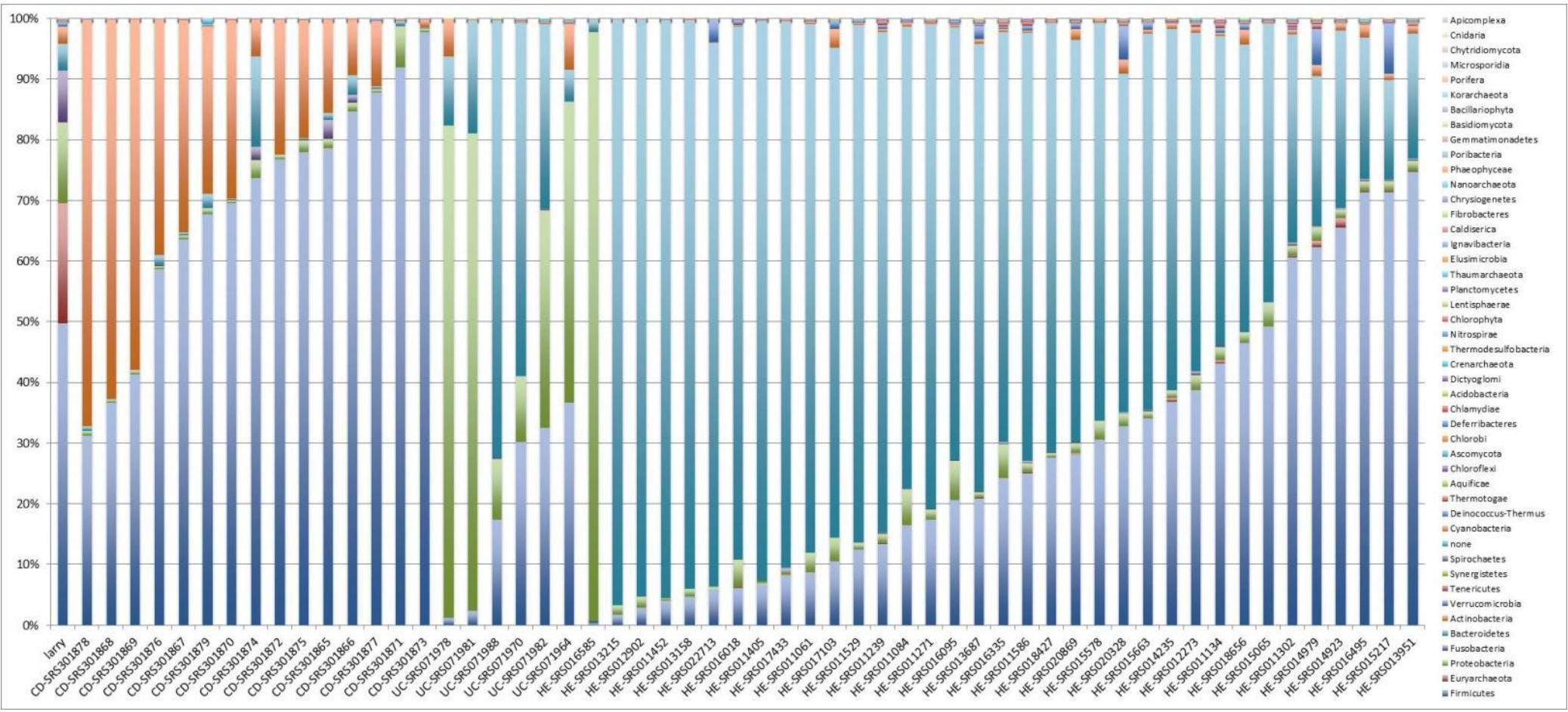
UC San Diego
HEALTH SCIENCES

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

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



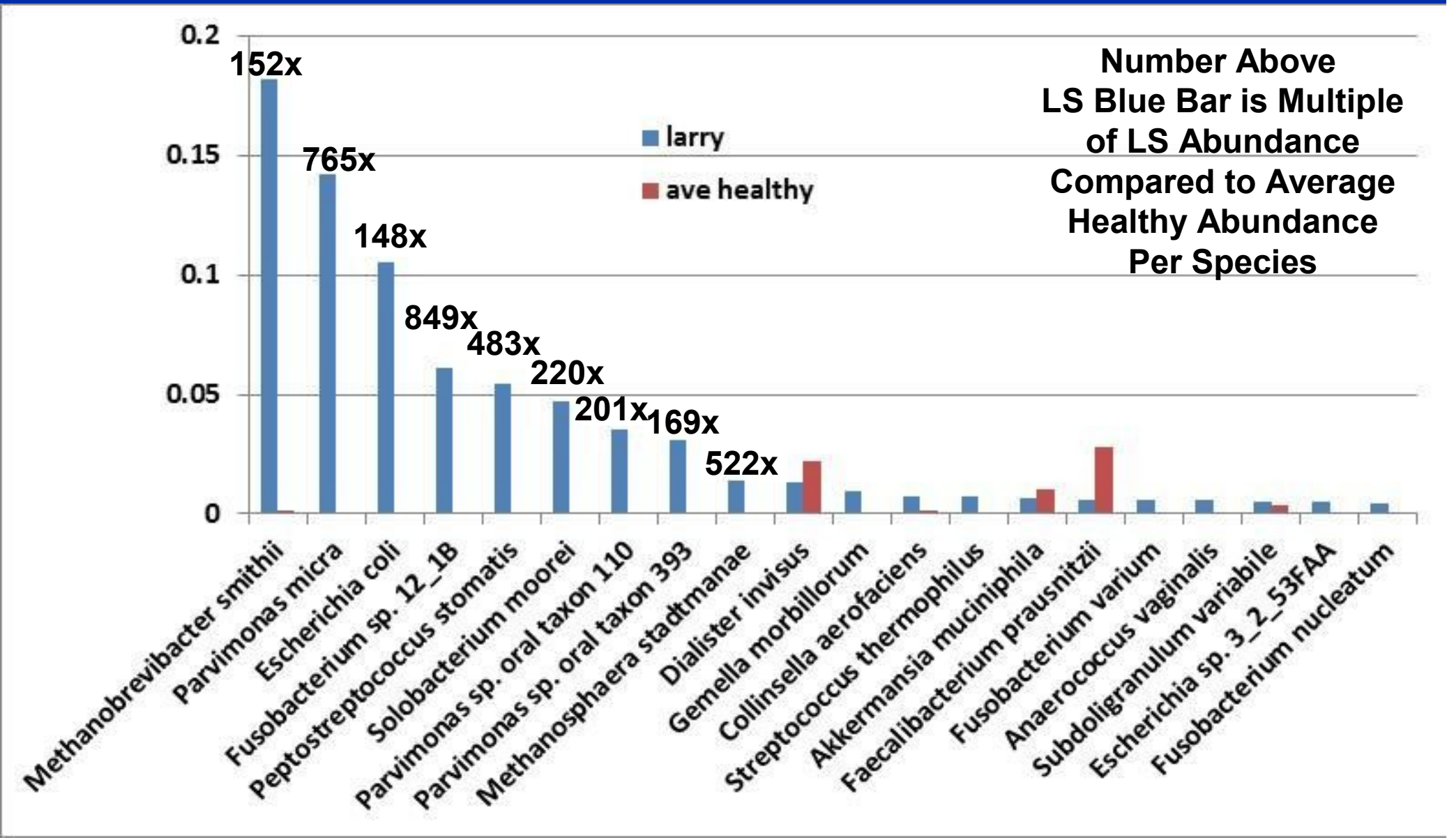
Derived from metagenomic sequencing of LS stool sample.
Each species is a bar,
height is logarithmic abundance,
species are divided into microbial phyla

Source: Photo of Calit2 64-megapixel VROOM

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

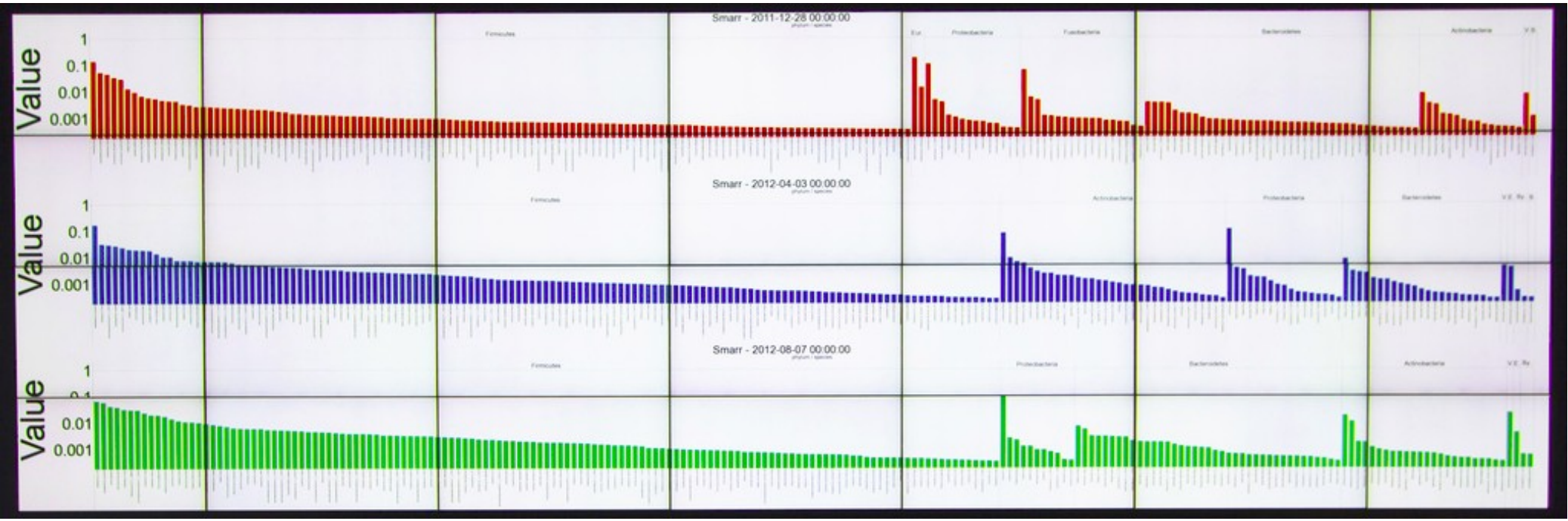


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Source: Sequencing JCVI; Analysis Weizhong Li, UCSD
LS December 28, 2012 Stool Sample

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200 LS Gut Microbe Species at 3 Times 12/28/11, 4/3/12, 8/7/12



Red is at Highest Value of CRP
Blue is the Day After End of Antibiotic/Prednisone Therapy
Green is Four Months Later

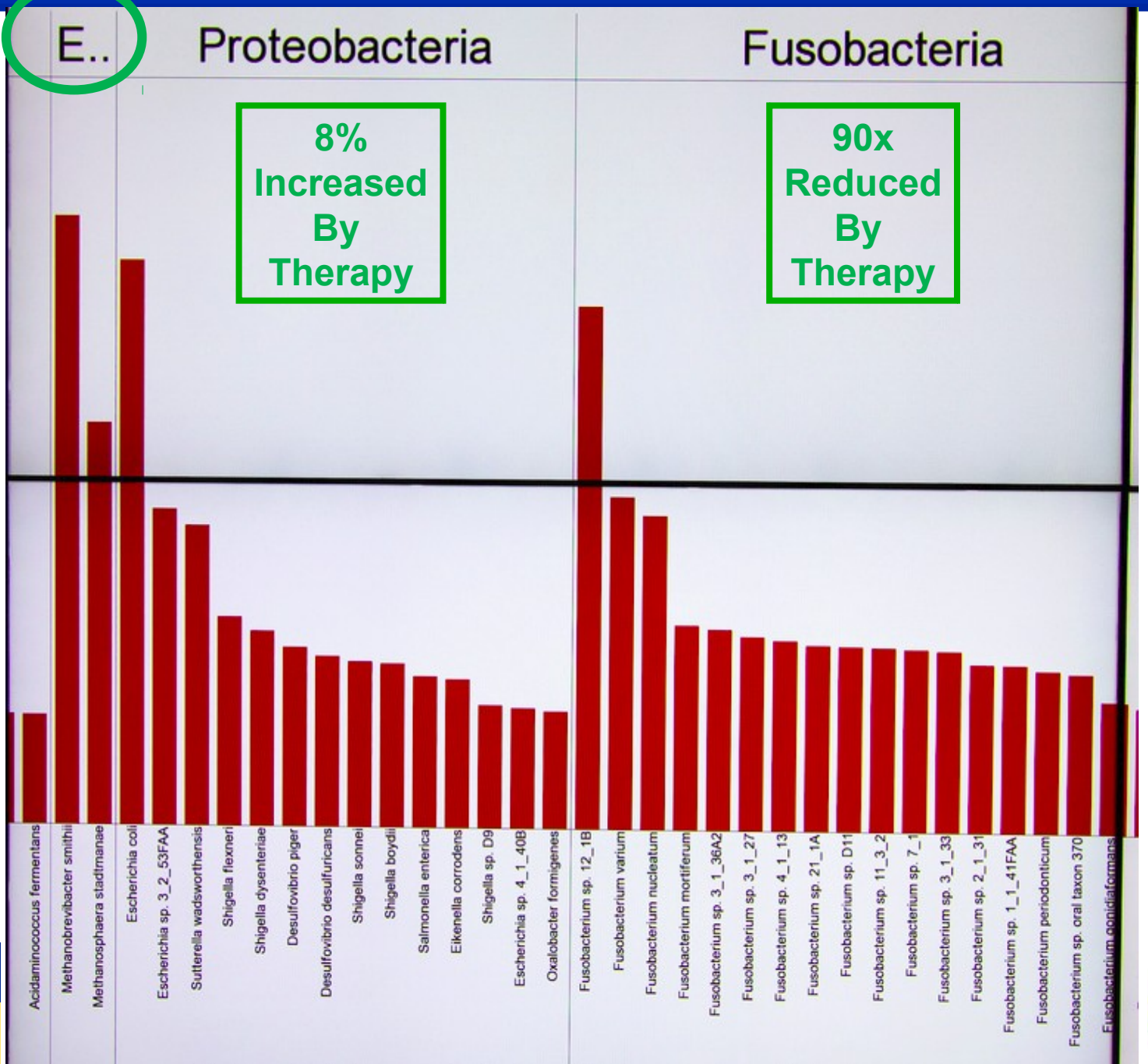
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Source: Photo of Calit2 64-megapixel VROOM

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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 Current IBD Therapies to Novel Systems Approaches

- **Current Therapies**
  - Diet
  - Probiotics
  - Drugs
  - Surgery
- **Emerging Directions**
  - Microbiome Transfer
  - Synthetic Microbiomes
  - Ecological Gardening
  - Targeted Bacteriophage

The Scientist » The Nutshell

Repoopulation Remedy

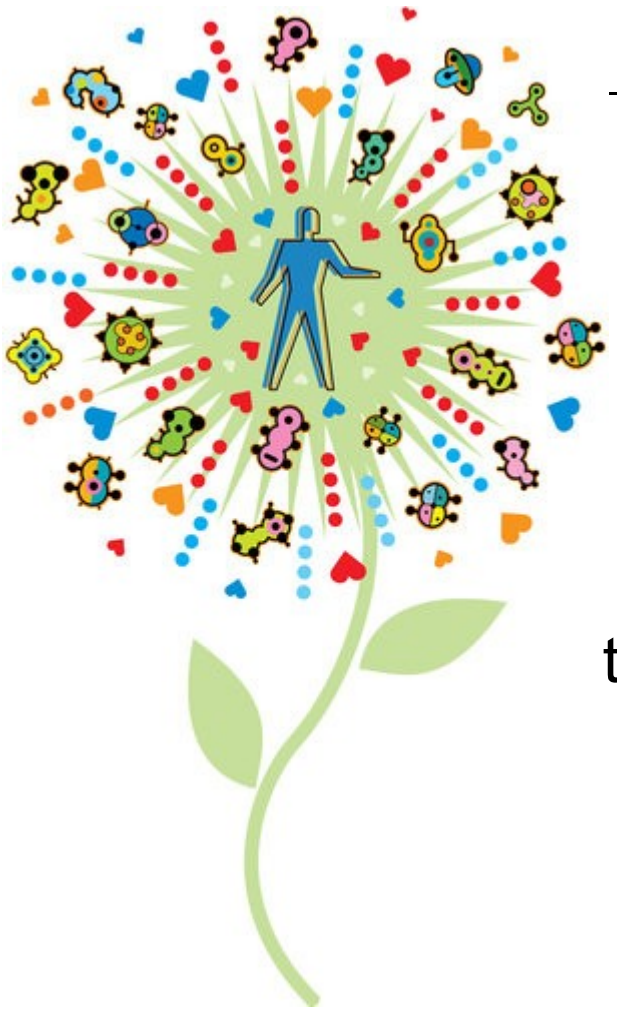
Transplanting synthetic stool made of beneficial microbes cures deadly diarrheal infections in two patients.

By Beth Marie Mole | January 9, 2013

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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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From the Single "Bad" Microbe Medical Target to the Microbiome Ecology Paradigm

REVIEW

Sci Transl Med 4, 137rv5 (2012);

MICROBIOLOGY

Microbiota-Targeted Therapies: An Ecological Perspective

Katherine P. Lemon,[1,2]* Gary C. Armitage,[3] David A. Relman,[4,5,6] Michael A. Fischbach[7,8]*

The Application of Ecological Theory Toward an Understanding of the Human Microbiome

Elizabeth K. Costello[1], Keaton Stagaman[2], Les Dethlefsen[1,3], Brendan J. M. Bohannan[2], David A. Relman[1,3,4,*]

Science 336, 1255 (2012)

Problem of Alternative Stable States In Ecological System Dynamics

Next Decade Will See New Microbiome "Gardening Tools"

Could Bacteria-Fighting Viruses Replace Overused Antibiotics? [Preview]

SCIENTIFIC AMERICAN™

August 7, 2012

Long ignored by mainstream researchers, the viruses that infect bacteria have a role to play in modern medicine, Vincent Fischetti says

By Brendan Borrell

Review Article

Immunocompatibility of Bacteriophages as Nanomedicines

Journal of Nanotechnology (2012)

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Startups Are Enabling Genomic Sequencing of Your Microbiome

uBiome -- Sequencing Your Microbiome

Be a citizen scientist and help us sequence the human microbiome. Learn about your health, advance science, and CHANGE THE WORLD!

Health – San Francisco, United States

http://ubiome.com/

SECOND GENOME
THE MICROBIOME COMPANY



$263,235

Raised of $100,000 Goal

14 *days left*

indiegogo

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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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