# Towards Digitally Enabled Genomic Medicine: the Patient of The Future

**Invited Speaker**

**Hacking Life**

**TTI/Vanguard Conference**

**San Jose, CA**

**February 22, 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

http://lsmarr.calit2.net

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# Abstract

Calit2 has, for over a decade, had a driving vision that healthcare is being transformed into digitally enabled genomic medicine. To put a more personal face on the "patient of the future," I have been increasingly quantifying my own body over the last ten years. This involves not only non-invasive macro-variables such as weight, pulse, blood pressure, caloric intake and burn, but also invasive blood, saliva, and stool measurements. I currently track over 100 molecular and blood cell types in my blood and dozens of molecular and microbial variables in my stool. Through saliva I have 1 million single nucleotide polymorphisms (SNPs) in my human DNA. My gut microbiome is currently being genetically sequenced. I will show how one can discover emerging disease states before they develop serious symptoms by graphing time series of these key variables. Also I will illustrate the power of multi-variant analysis across all these internal variables. My hope is that by "living in the future" I can be a model for understanding more clearly the new approaches that will arise in wellness and health care.

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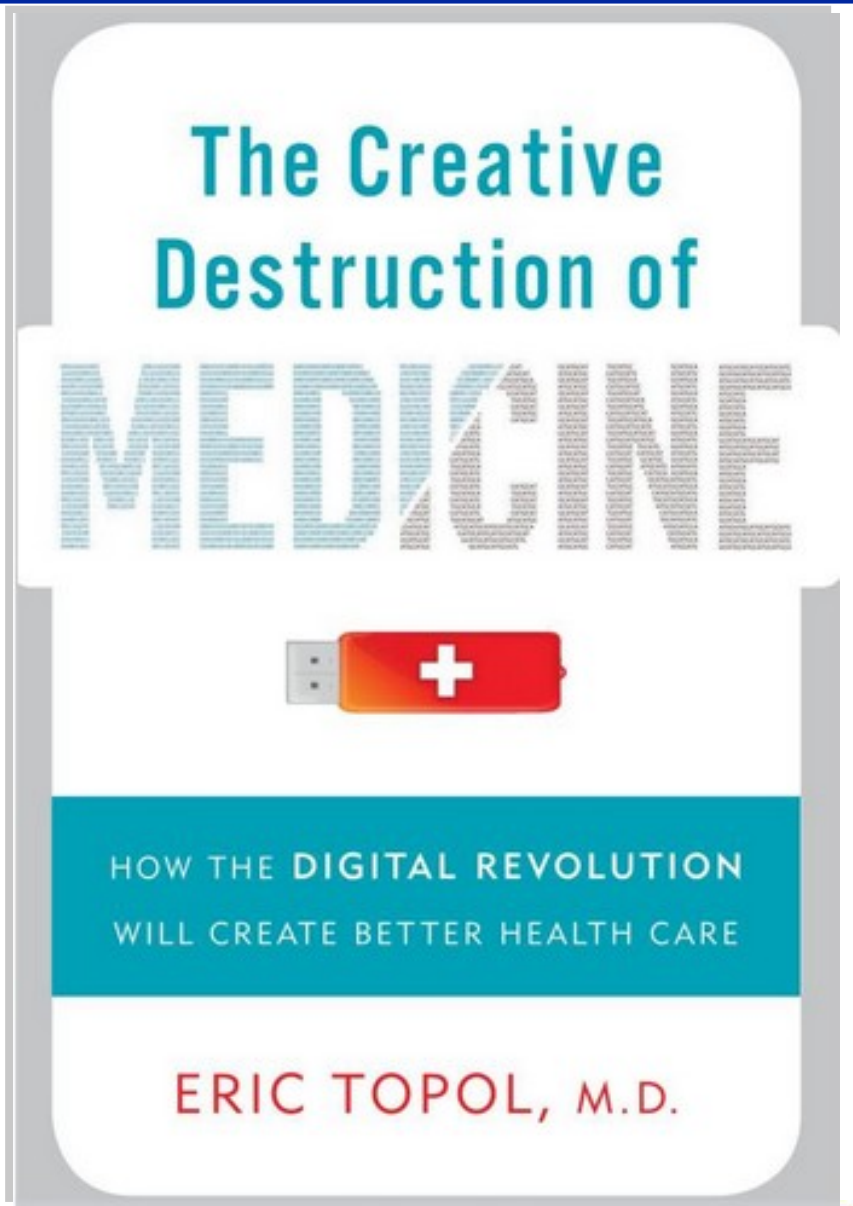
The Content of This Slide from 2001 Larry Smarr
Calit2 Talk on Digitally Enabled Genomic Medicine

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




July/August 2011



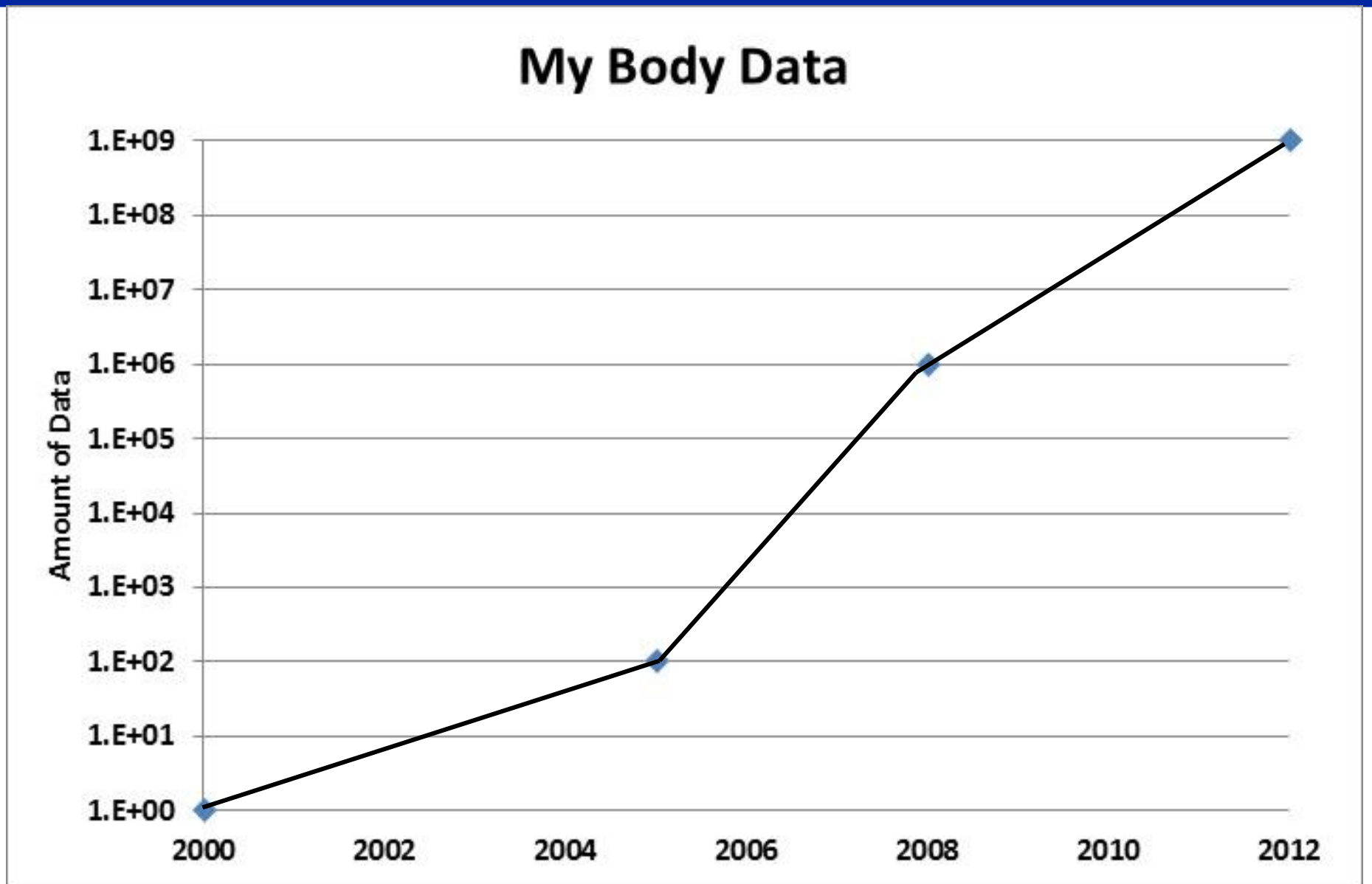

February 2012



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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





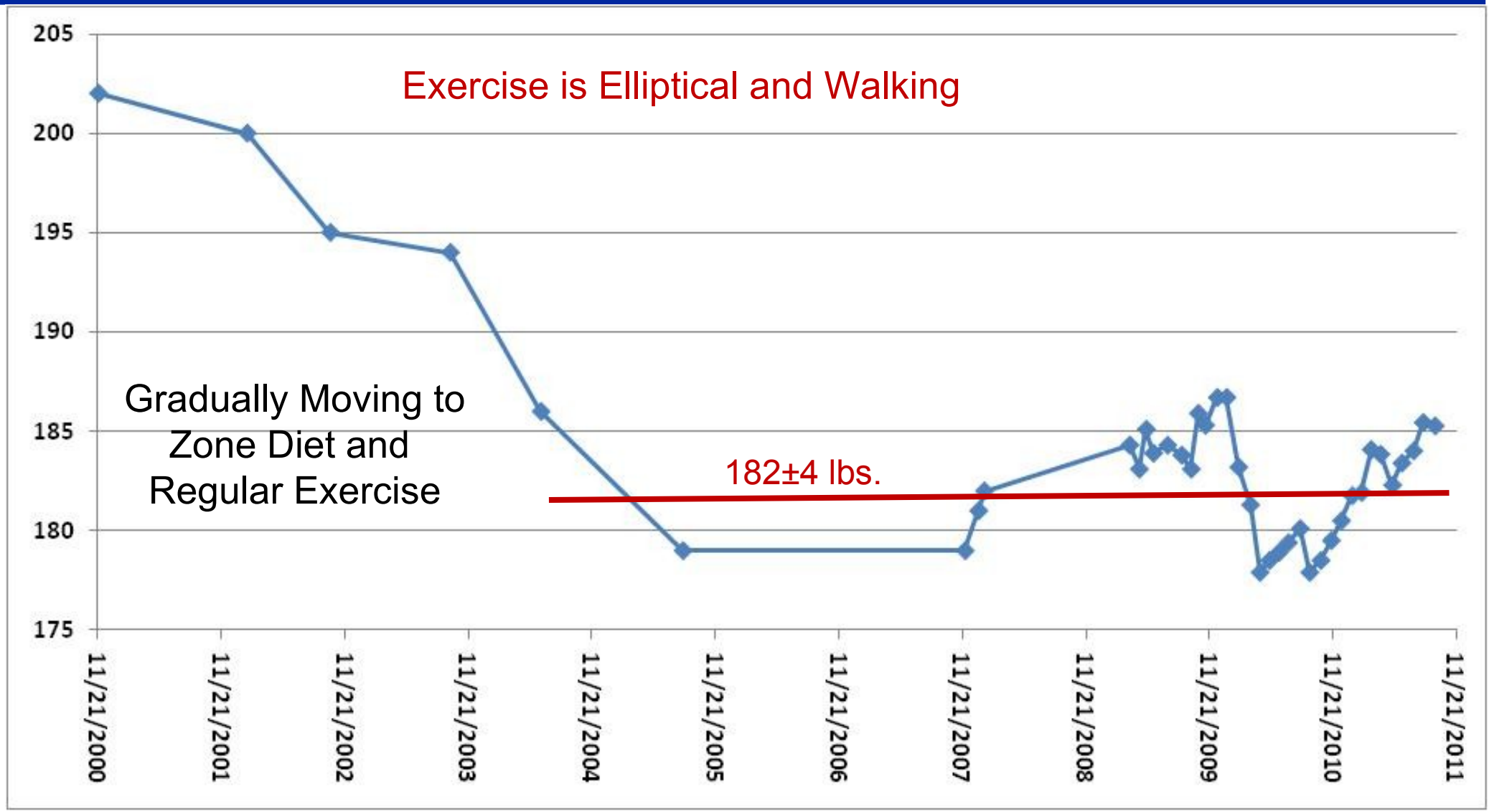


Age 61

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

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# Goal: Lose Weight by Changing What & How Much I Eat, While Increasing Aerobic and Weight Bearing Exercise




Current Weight 178.6

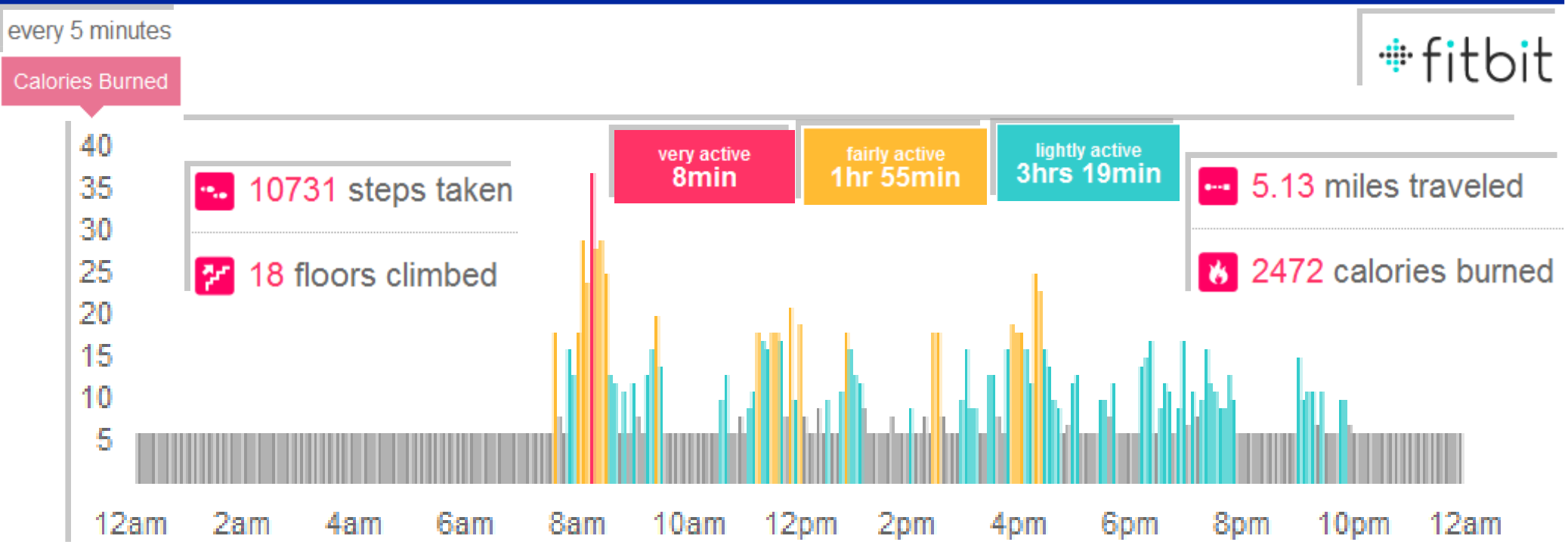
Blood Pressure 134/73 Pulse 55

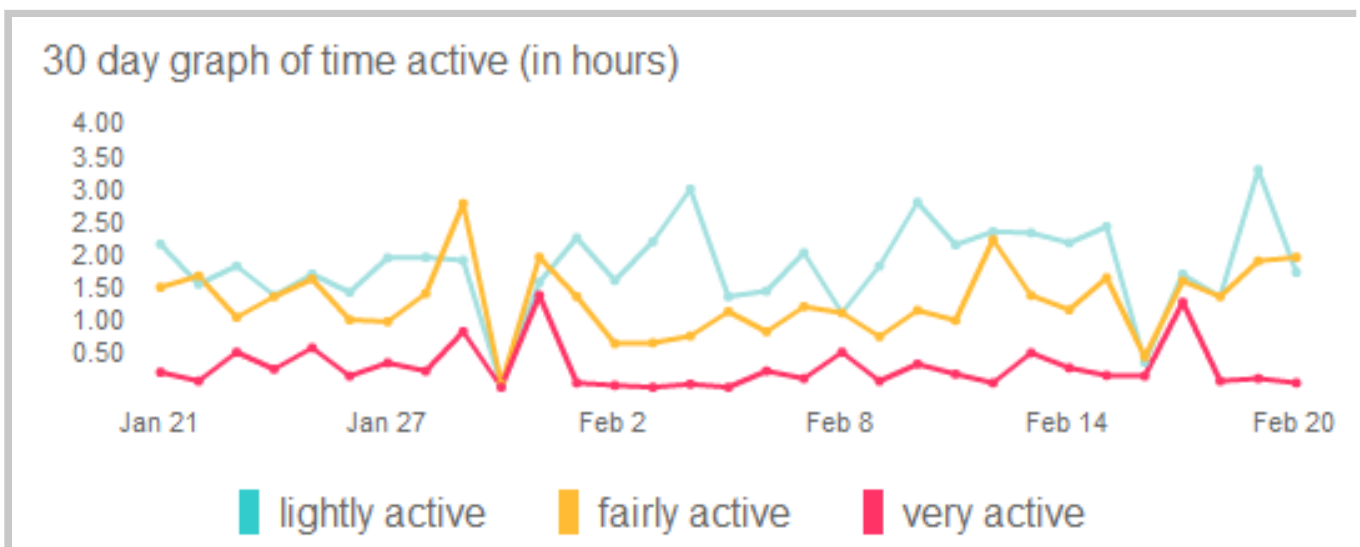
Resting Pulse Lowered to 45

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# Wireless Monitoring Helps Drive Exercise Goals



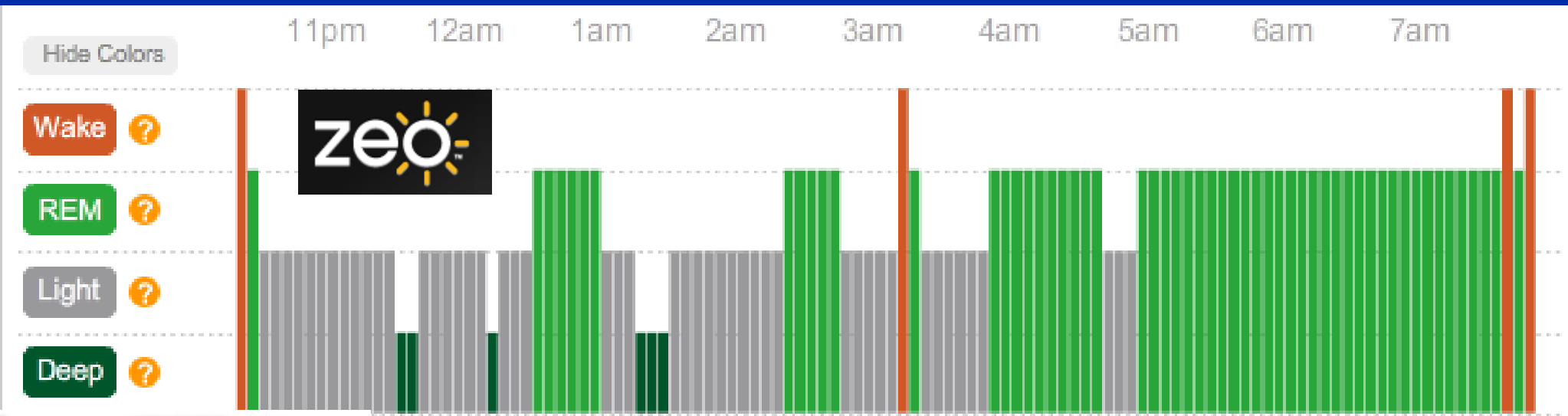






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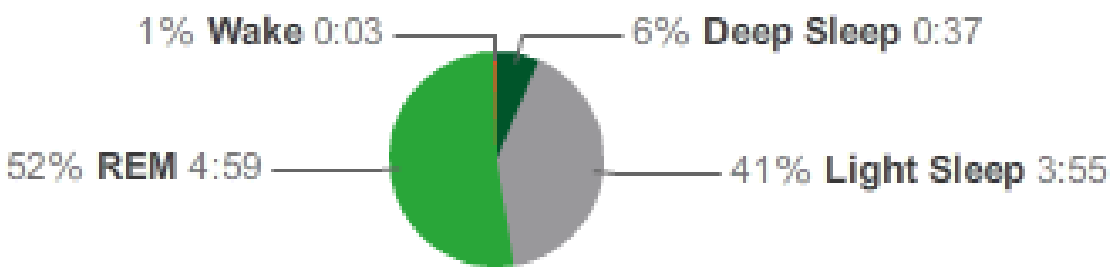
# Quantifying My Sleep Pattern Using a Zeo - Surprisingly About Half My Sleep is REM!






**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

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

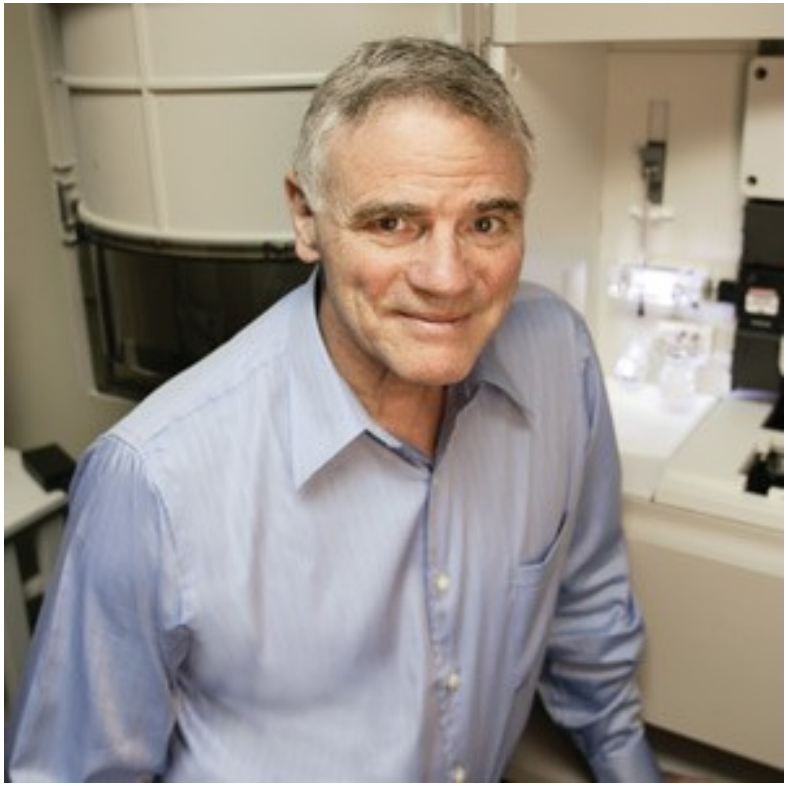
Newsweek

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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# On-Line Blood, Stool, Urine, & Saliva Tests Are Becoming Routine




25% of All Medical Tests
are Conducted
Outside the Hospital Laboratory



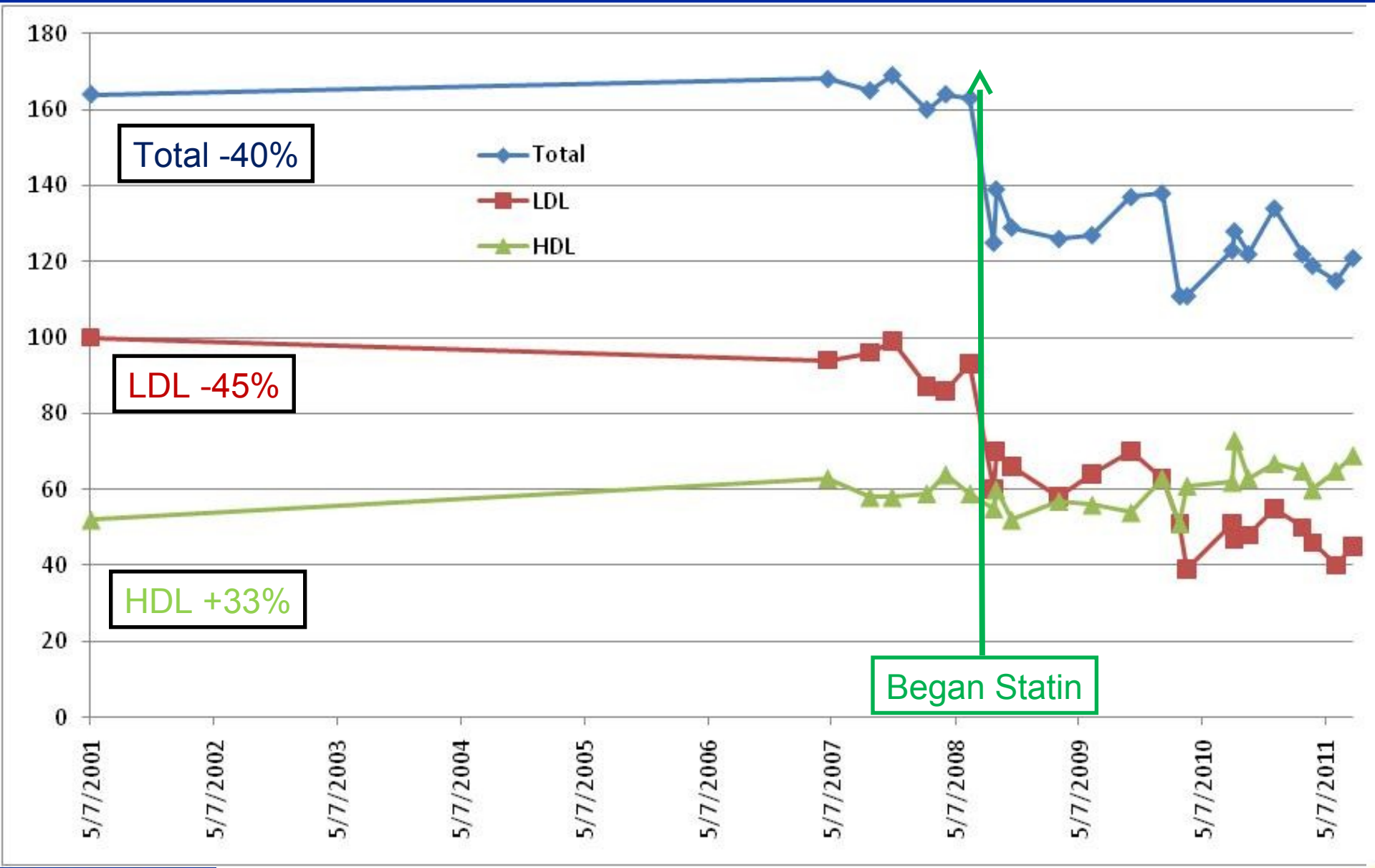

*State law prohibits direct access laboratory testing in Massachusetts, New York, New Jersey and Rhode Island.*

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I Track Over 100 Blood Molecules
Every Quarter

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# Goal: Change Your Cholesterol Levels to Lower LDL, Raise HDL, While Lowering Total

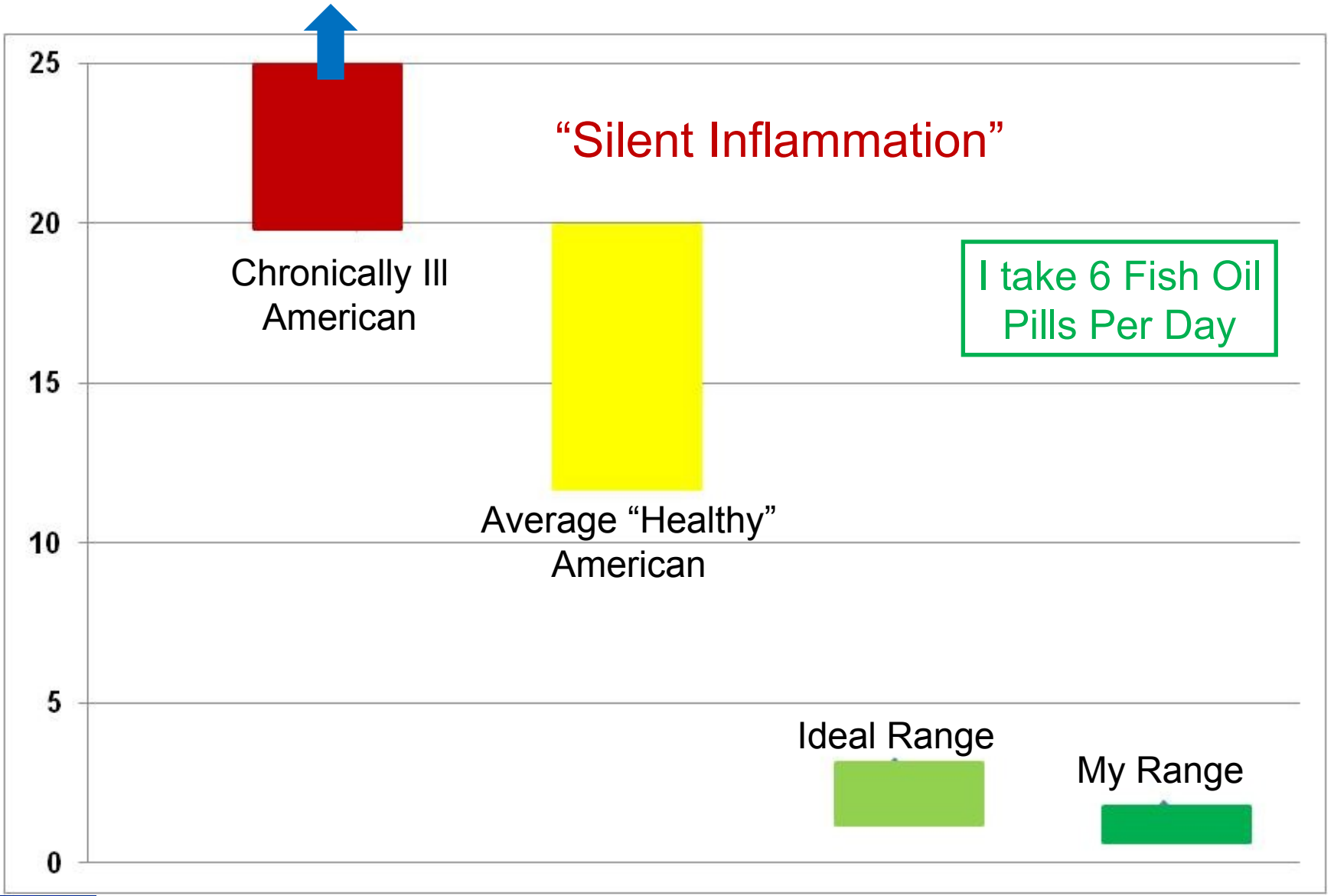



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Raising “Good” HDL Seems Most Difficult

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# Goal: Lower Ratio of Arachidonic Acid to EPA to Reduce Pro-Inflammatory Potential of Your Cells




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

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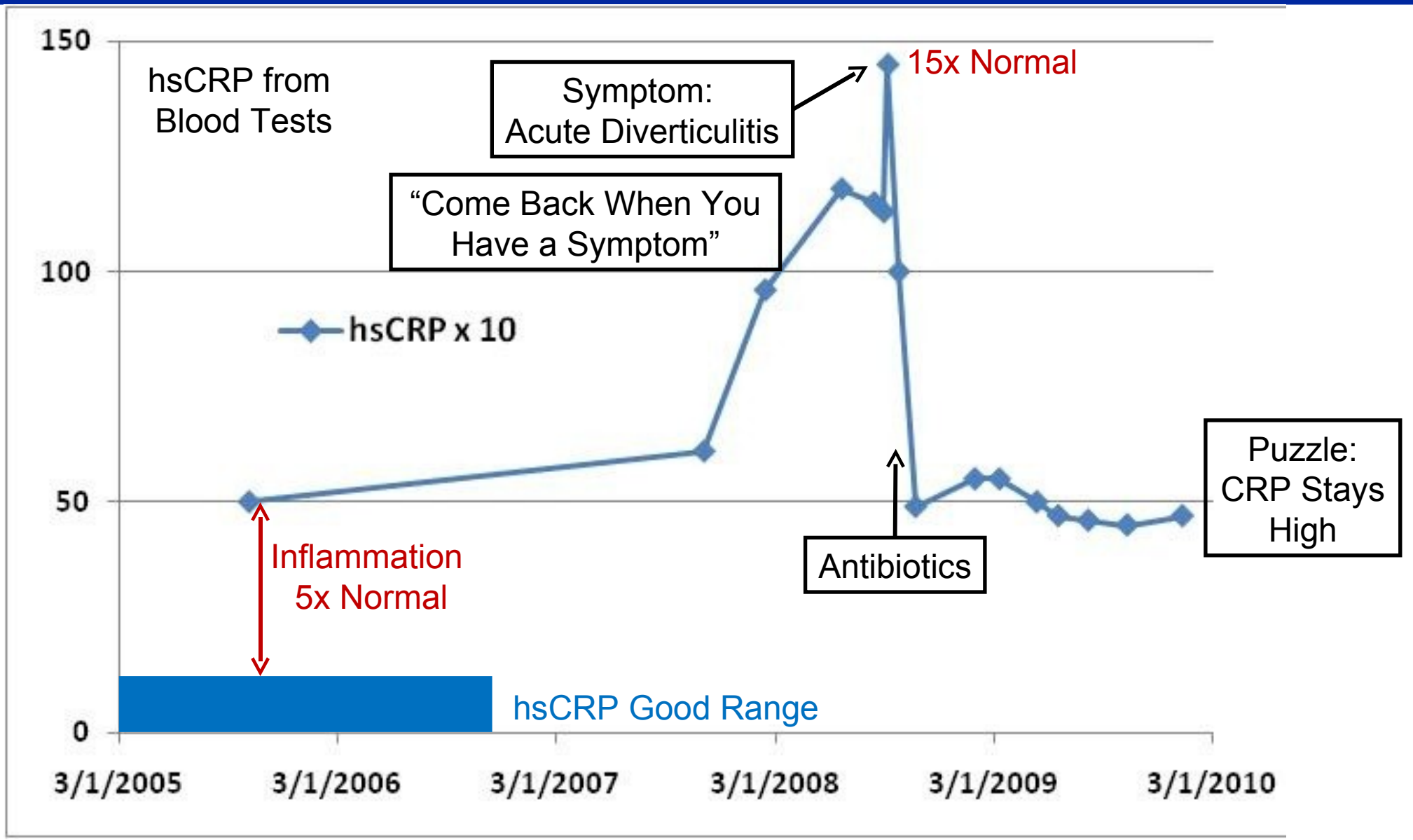
# Blood Tests I Do Quarterly to Annually In Addition to Lipids & Omegas

- **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

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




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# CRP and LDL Cholesterol Co-Create Arterial Plaque

High CRP



Arterial Plaque Formation

CRP > 4.2, 5x Risk of Future Heart Disease

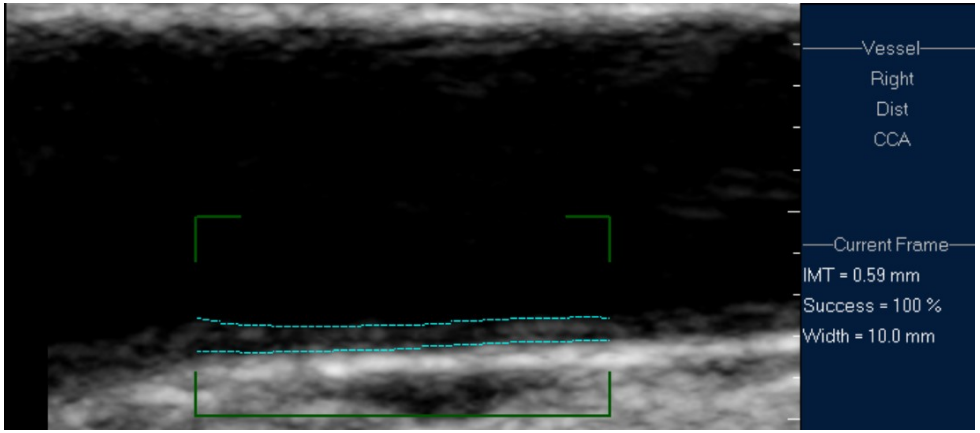
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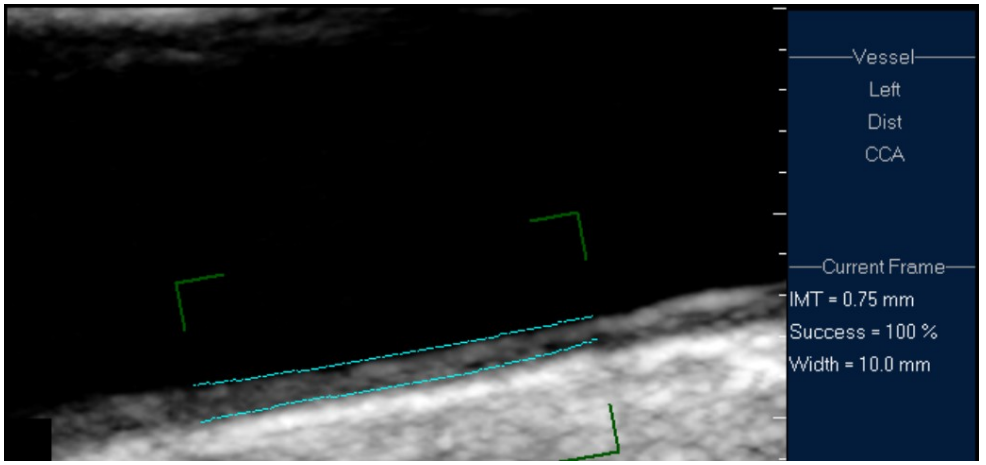
http://sjog.org.au/pathology/pathology_wa/doctor_resources/clinical_articles/high_sensitivity_crp.aspx

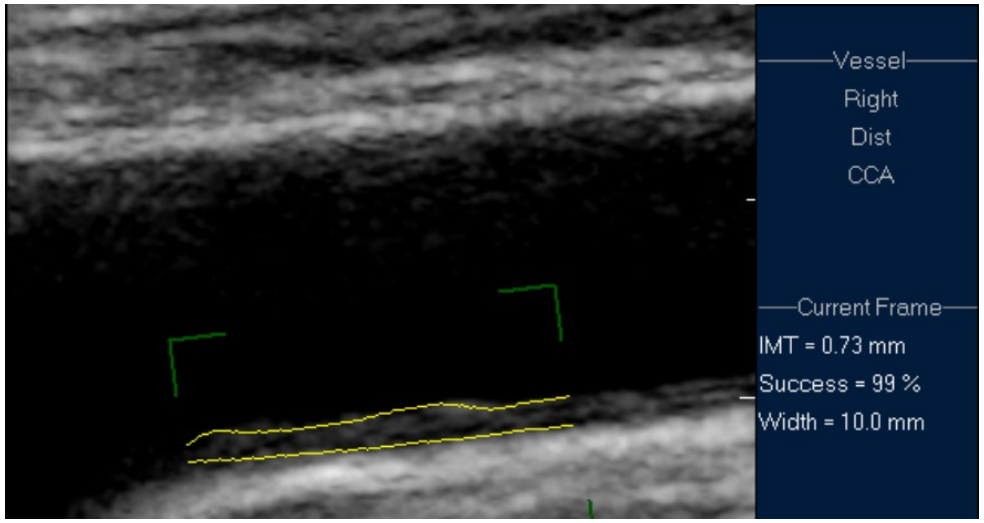
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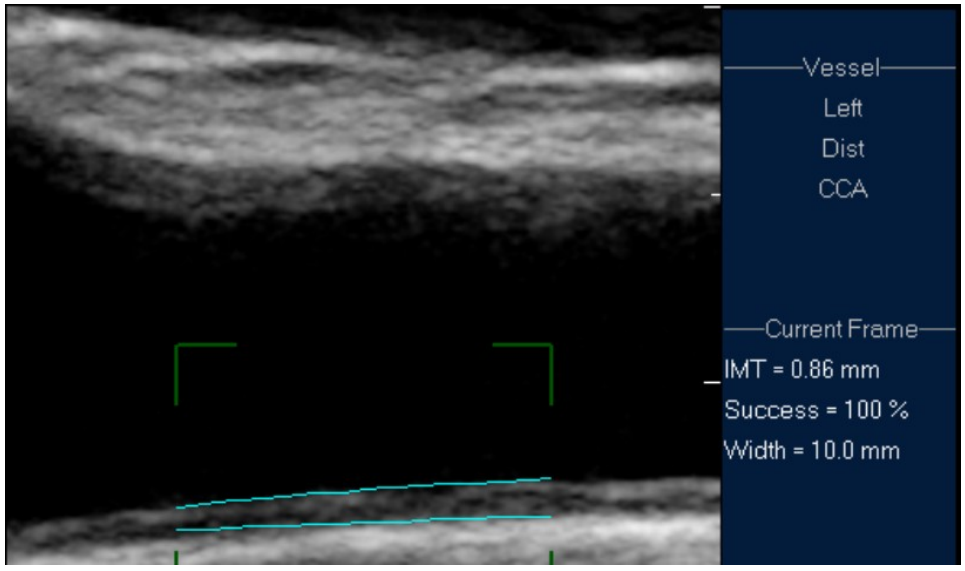
# Carotid Artery Ultrasound Reveals Artery Wall Thickness Significantly Increasing In Just Two Years

Oct 31 2008




October 14, 2010



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IMT Right 0.59 to 0.73mm
24% Thicker

IMT Left 0.75 to 0.84 mm
12% Thicker

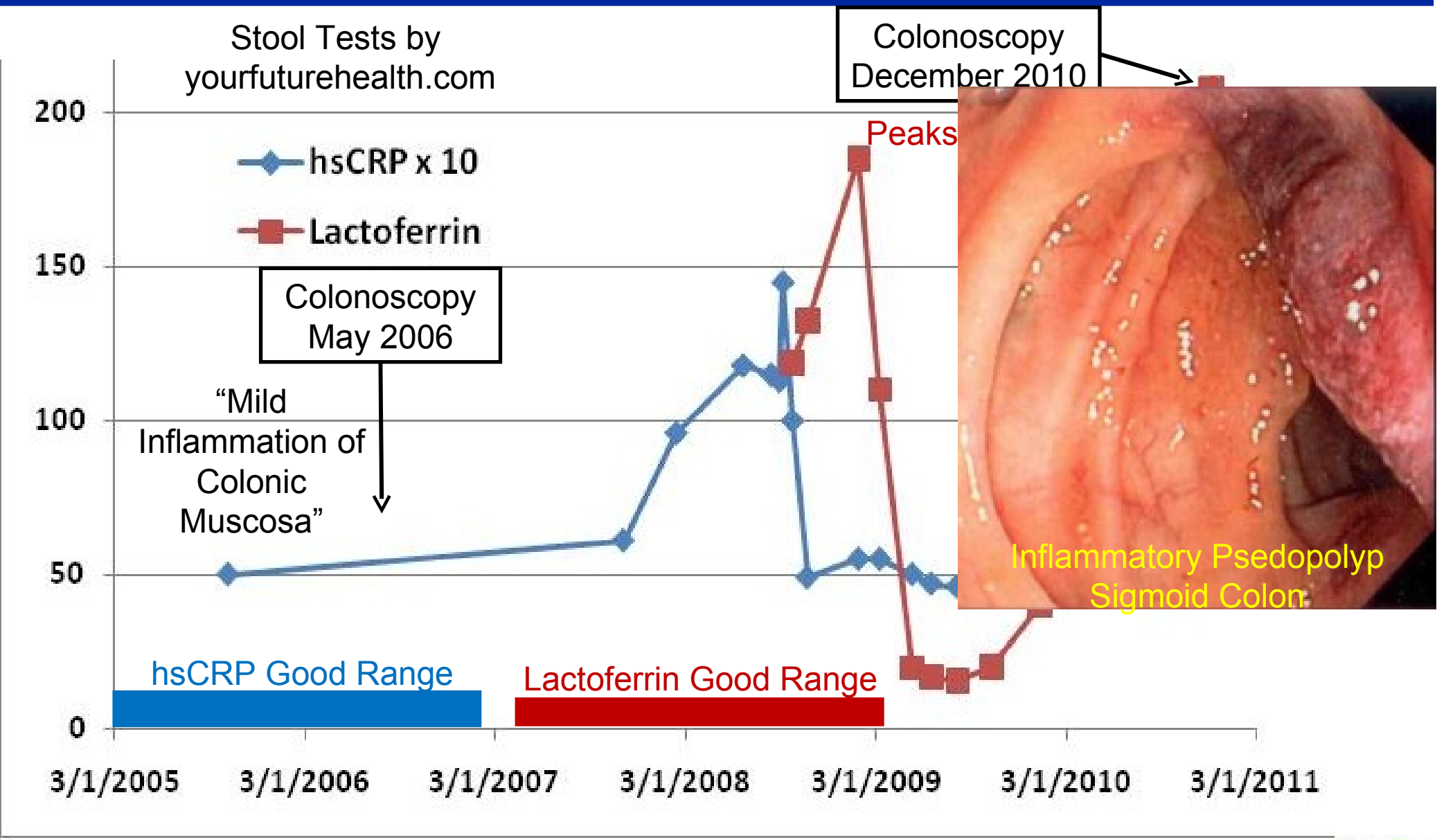
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# Paradox: Anti-Inflammatory Diet, Plus Low LDL, Yet Chronic Inflammation & Plaque Increases

- **What Could be the Source of the Chronic Inflammation?**
- **Started Taking Stool Samples as Well as Blood Samples**

Do Not Assume, Always Measure!

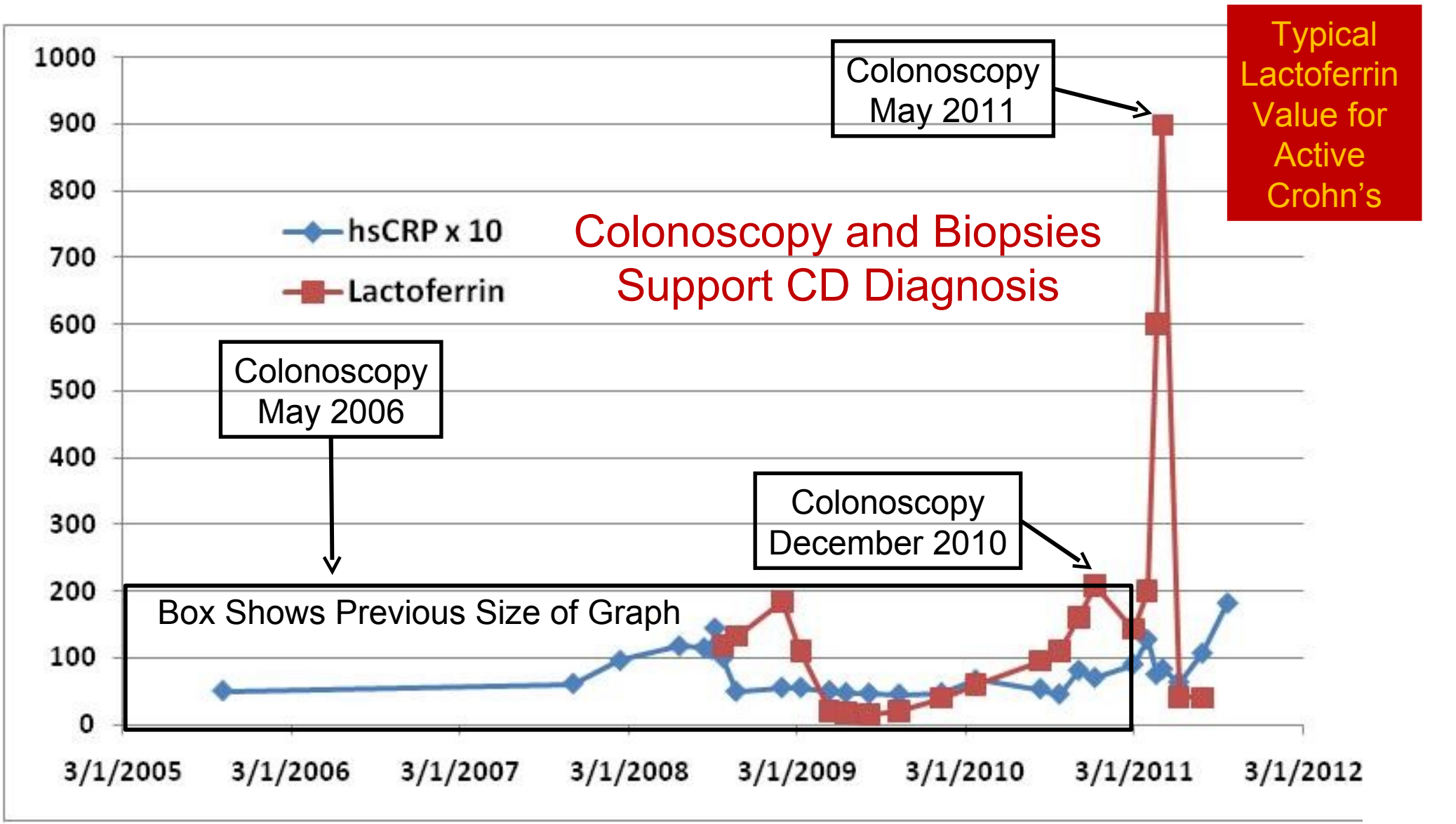
# Measuring Stool and Blood Markers Revealed Episodic Inflammation Peaks of CRP and Lactoferrin




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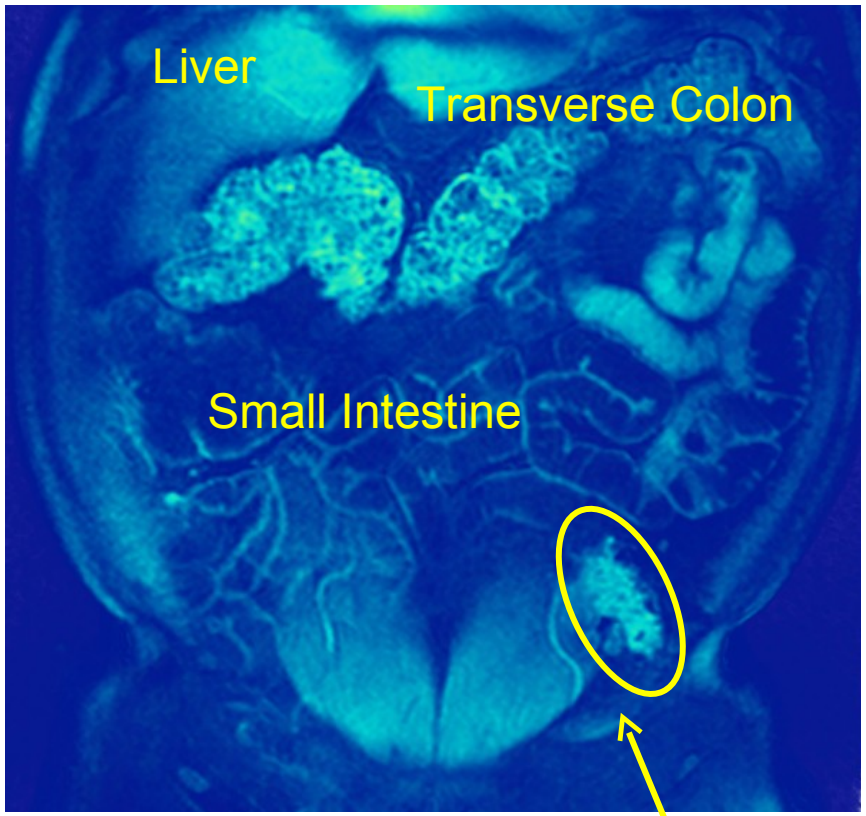
# Latest Data Point Reveals Lactoferrin Spike to Active Crohn's Disease (CD) Level



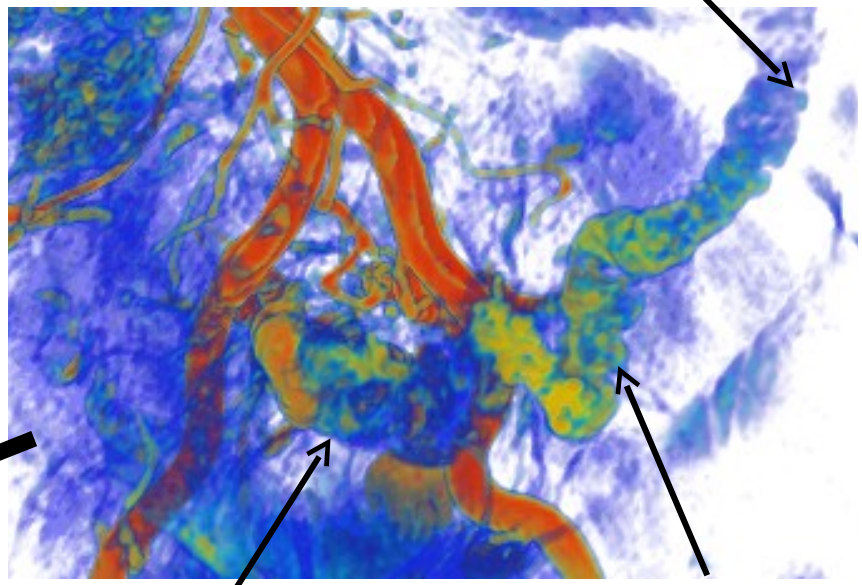

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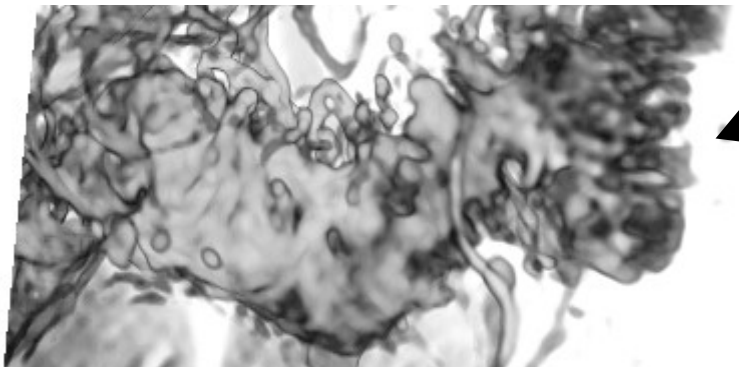
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# Confirming the Crohn's Hypothesis: Finding the "Smoking Gun" with MRI Imaging




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

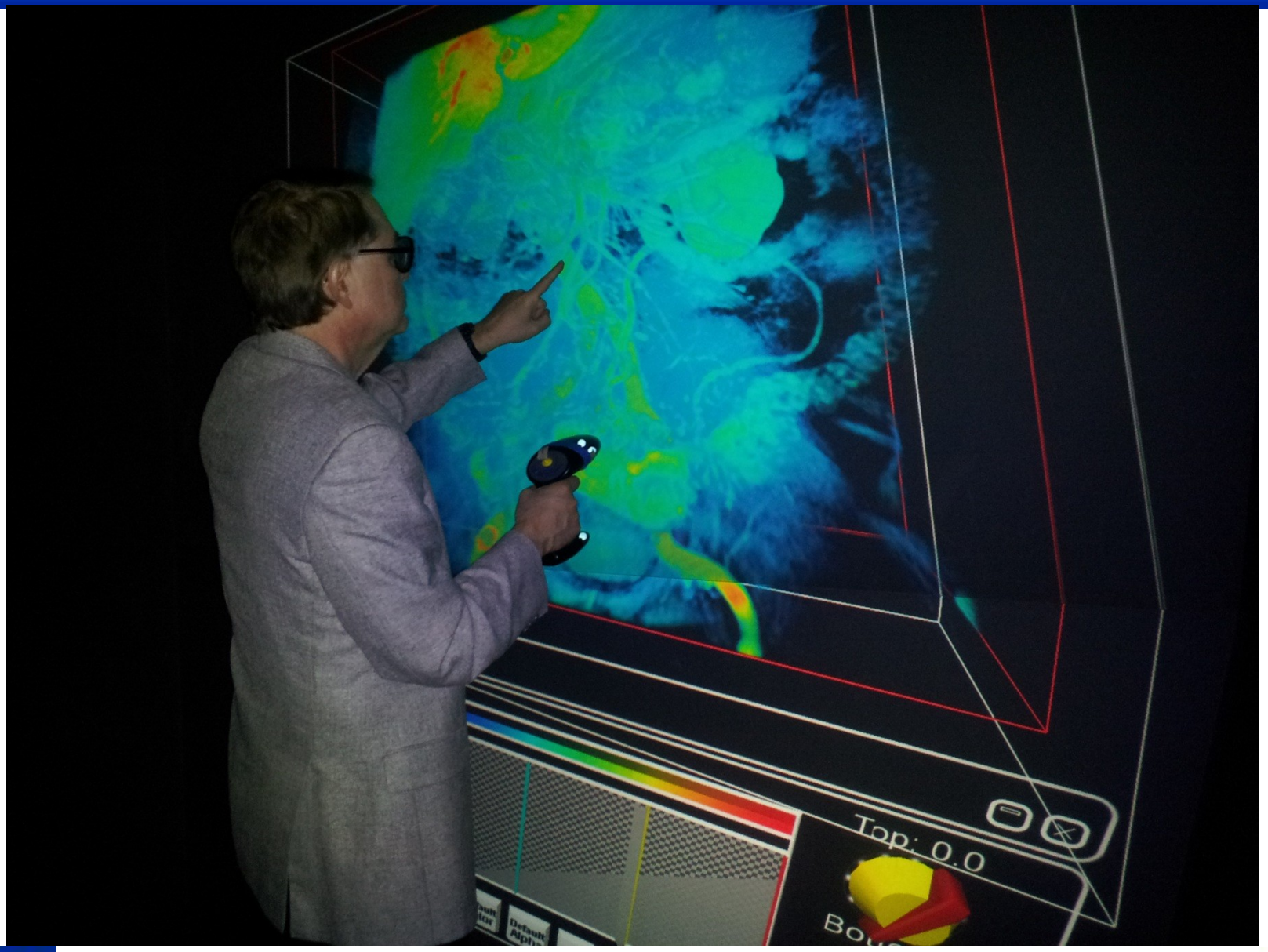


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# Exploring My Internal Organs in the Calit2 Virtual Reality CAVE Using DeskVOX Software




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Photo & DeskVOX Software Courtesy of Jurgen Schulze, Calit2

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# Autoimmune Diseases
# Effect 5-8% of Americans

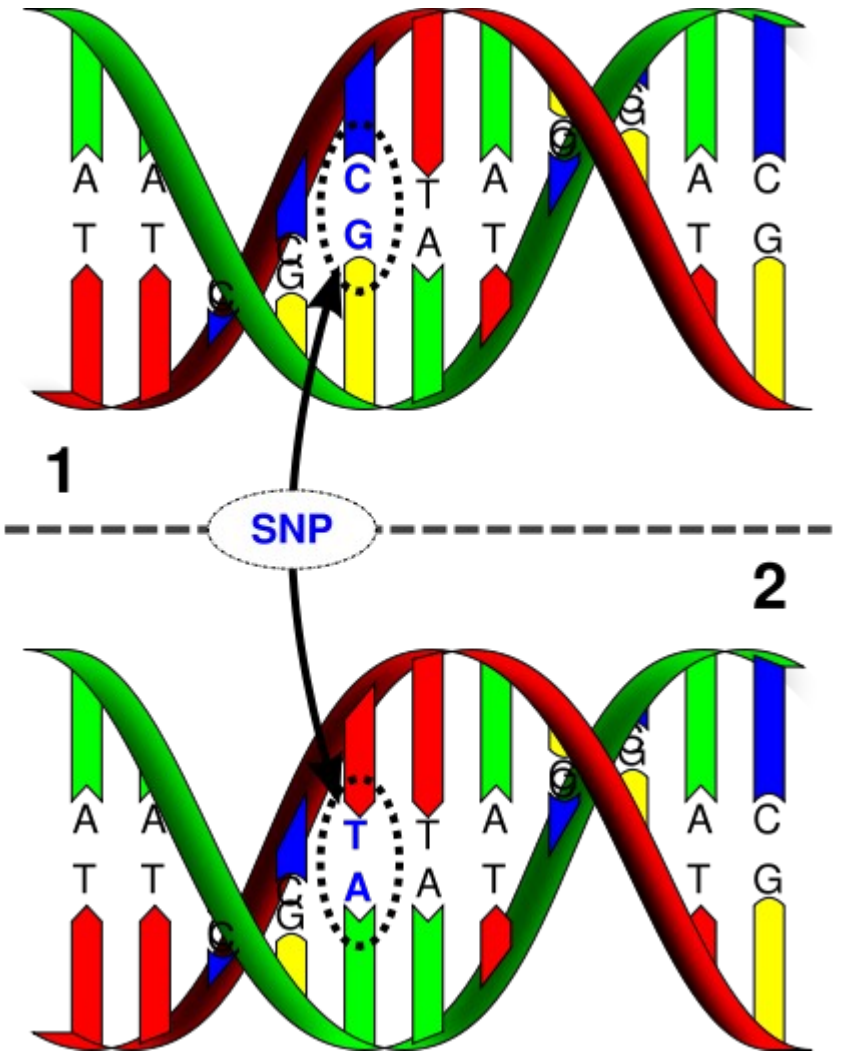
- **Crohn's Disease**
- **Ulcerative Colitis**
- **Rheumatoid Arthritis**
- **Multiple Sclerosis**
- **Psoriasis**
- **Type 1 Diabetes,**
- **Ankylosing Spondylitis**
- **Lupus Erythematosus**
- **Plus Over 70 Others**

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)

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

Person A



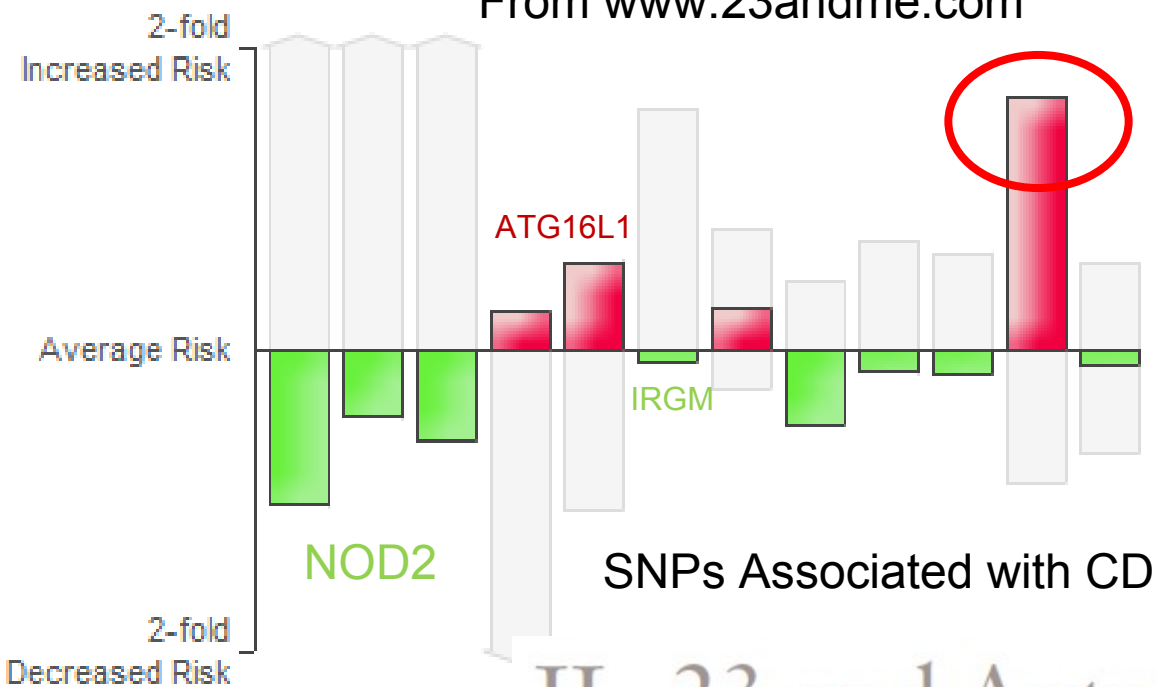

Person B

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




SNPs Associated with CD

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]

IL-23 and Autoimmunity: New Insights into the Pathogenesis of Inflammatory Bowel Disease

Clara Abraham[1] and Judy H. Cho[1,2]

Section of Digestive Diseases, Departments of [1]Medicine and [2]Genetics, Yale University,

2009

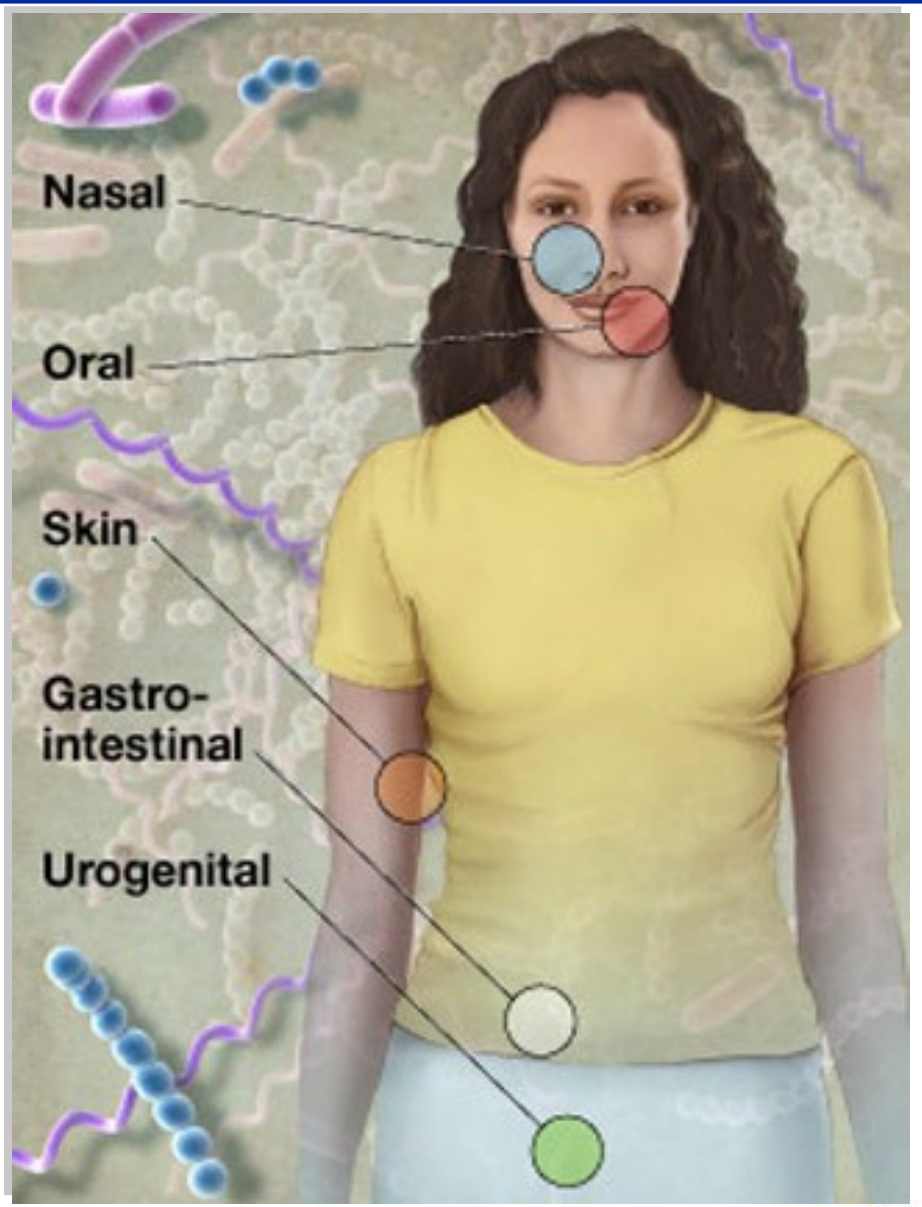
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# You Are a SuperOrganism:
# The Human Genome Contains <1% of the Bodies Genes

Human Microbiome Project

HMP

There are 10 Times More
Bacterial Cells Than
of Human Cells in Your Body



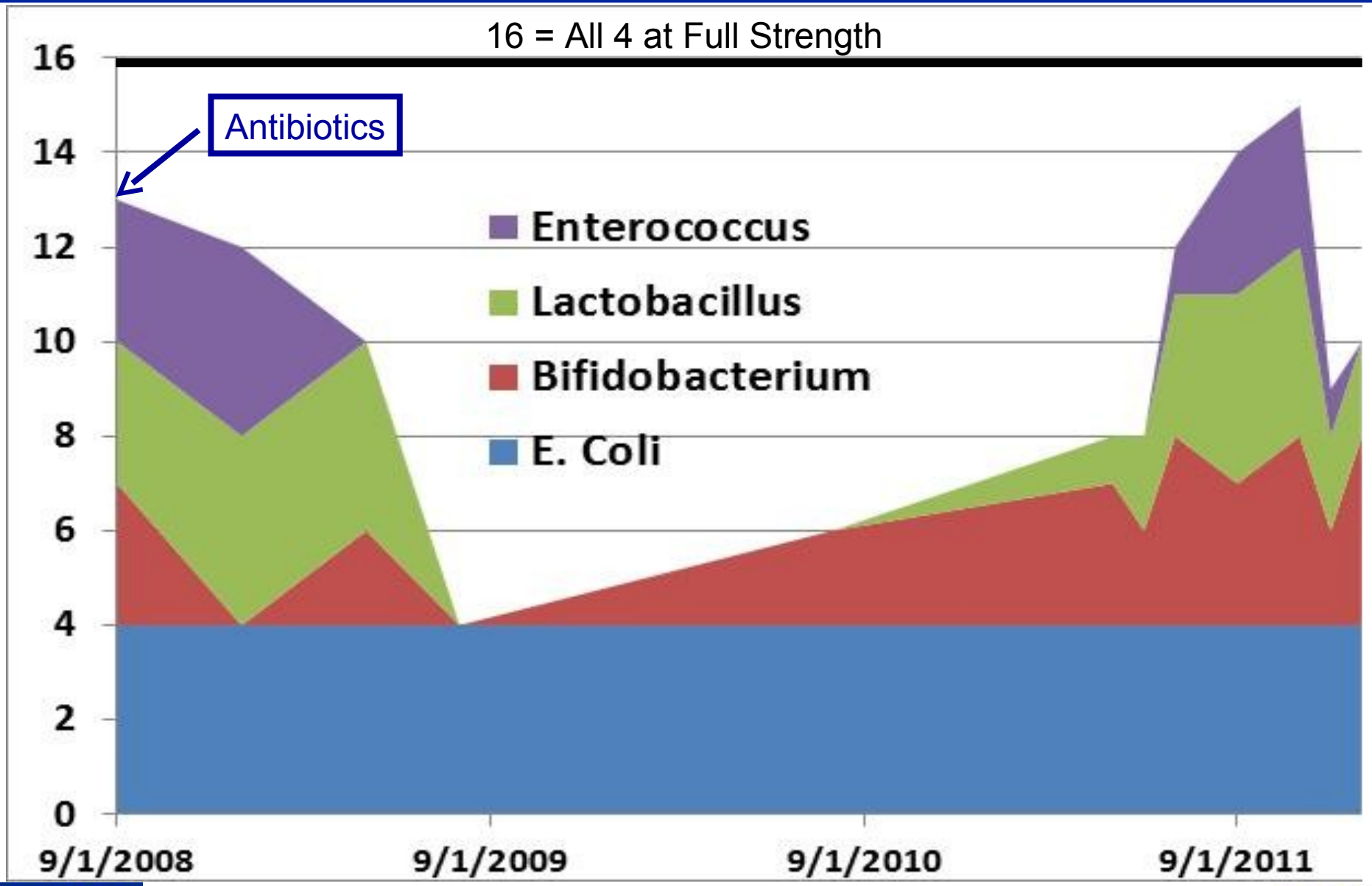

The NIH Common Fund
WE ACCELERATE DISCOVERY.

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http://commonfund.nih.gov/hmp/

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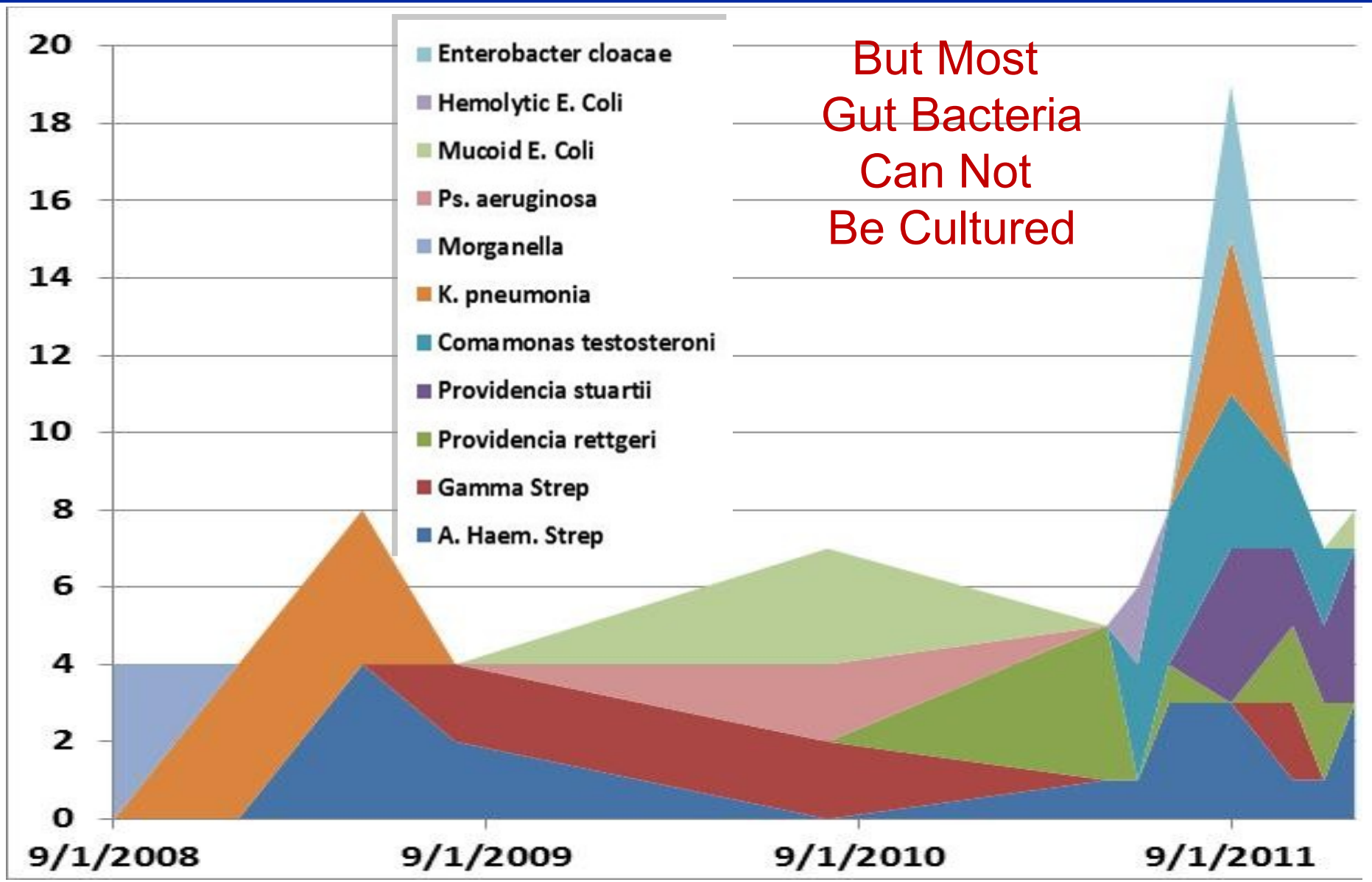
# Except for E. Coli, My "Good" Cultured Gut Bacteria Collapsed After Antibiotics




Antibiotics: Levaquin & Metronidaloze

Values From yourfuturehealth.com stool test

# My Cultured Dysbiotic Bacteria Have Been Flourishing

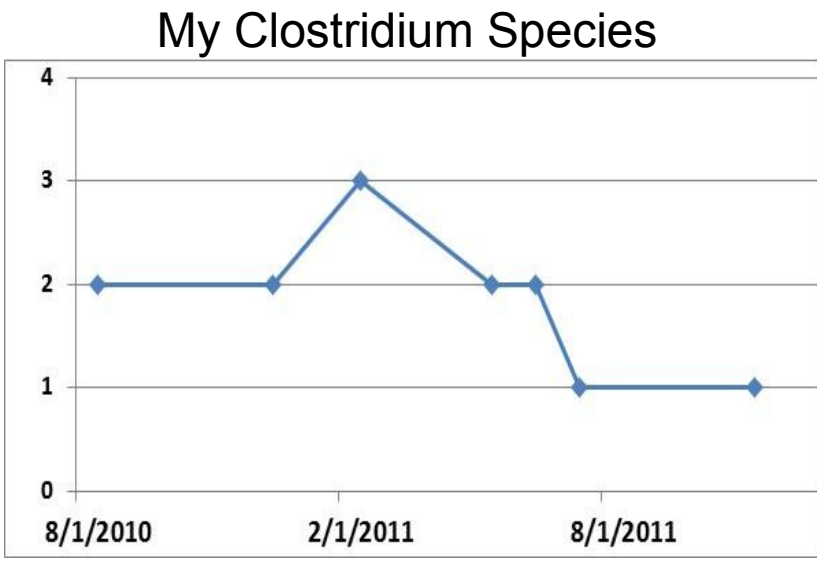



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# Crohn's Disease Patients Have Number of Clostridium Gut Microbe Species Reduced by Over 2/3!

- **My Clostridia Species Were Dropping to Low Values**
  - **Clostridia are are primarily responsible for butyrate production, the main energy source for colonic epithelial wall**
  - **Clostridia provide proinflammatory cytokines *inhibition* in the colonic muscosa**
- **My Butyrate Values Were Very Low**
  - **"Loss of butyrate producers observed here could upset the dialogue between host epithelial cells and resident microorganisms, hence contributing to the development of CD associated ulcerations."**

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."

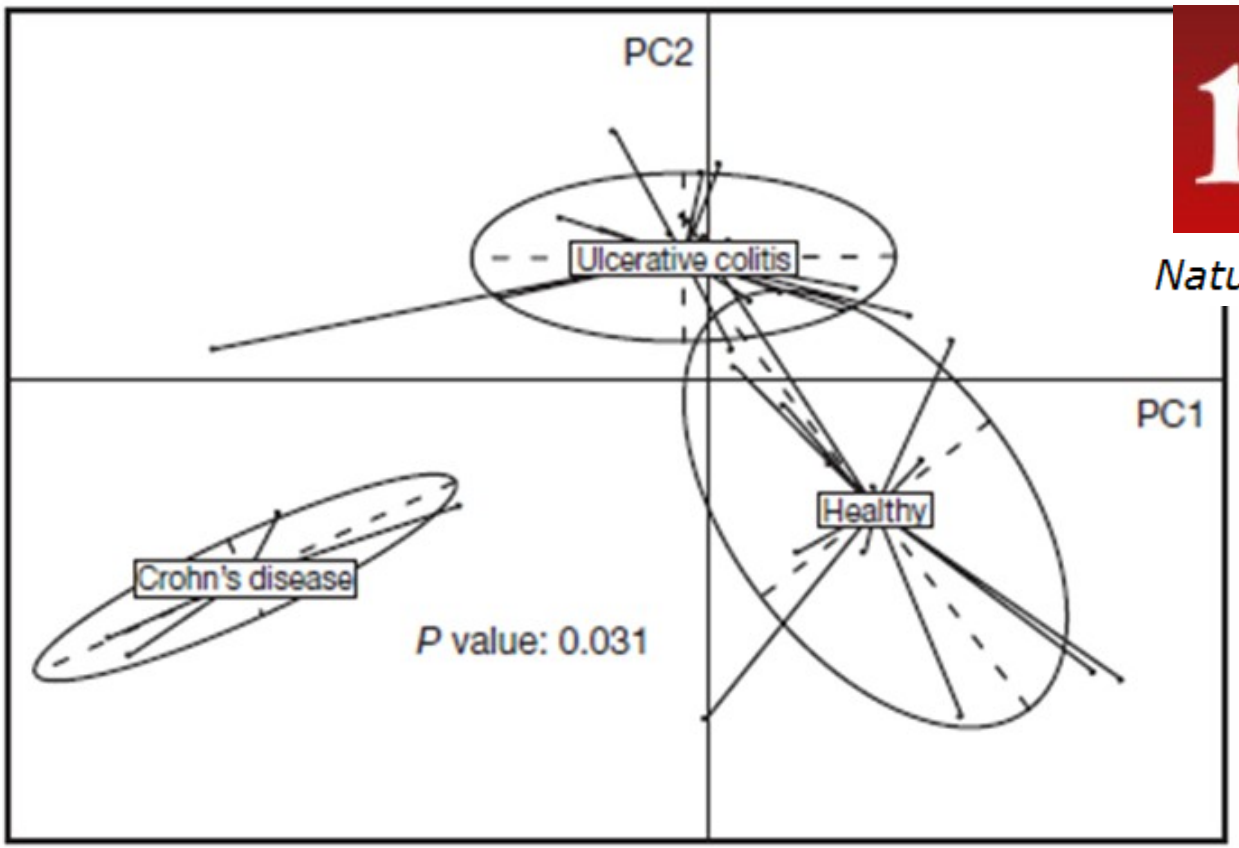
DNA microarray that can identify, within hours, over 50,000 different microbes




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# Microbial Metagenomics Can Diagnose Disease States




nature

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

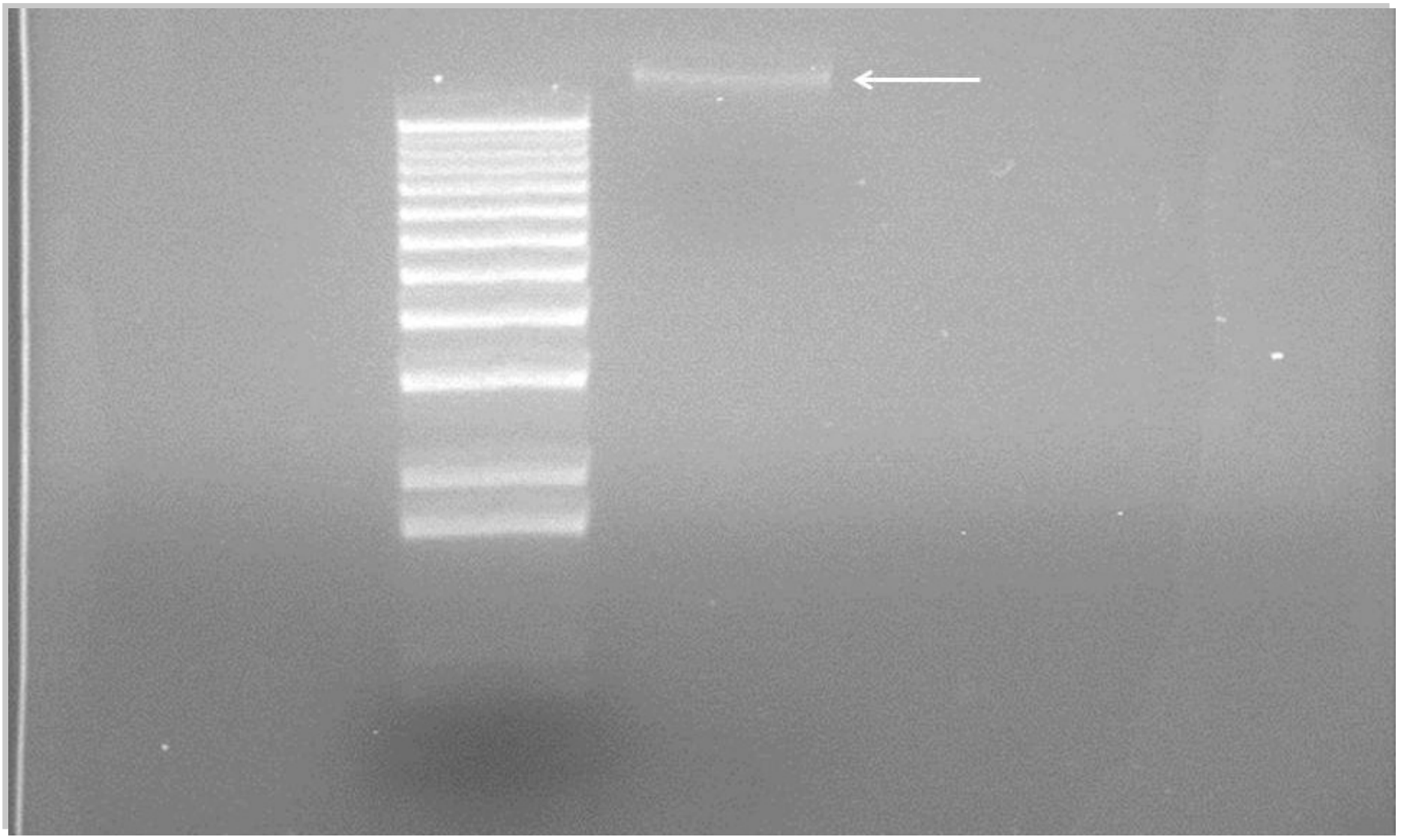
IBD Patients Harbored, on Average, *25% Fewer Microbial Genes* than the Individuals Not Suffering from IBD.

**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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# Publically Sharing Your Genome and Medical Records: Is it Crazy or the Future?

World DNA Day: April 25, 2012

GET Genomes Environments Traits CONFERENCE

I Have Been Accepted by PGP and Will Speak at GET 2012:
My Full Genome (6 Billion Bases) Will Be Sequenced This Year

## 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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# Crowd-Sourcing Health Studies Is Rapidly Growing With More Open Health Data




patientslikeme®







research surveys

23andWe begins with you. Learn about yourself while contributing to research.



**Genomera**

@genomera

*Open health studies on the web. Breaking open bottlenecks in health research and discovery with collective data sharing and analysis. The next wave in health.*

Mountain View, CA · http://genomera.com

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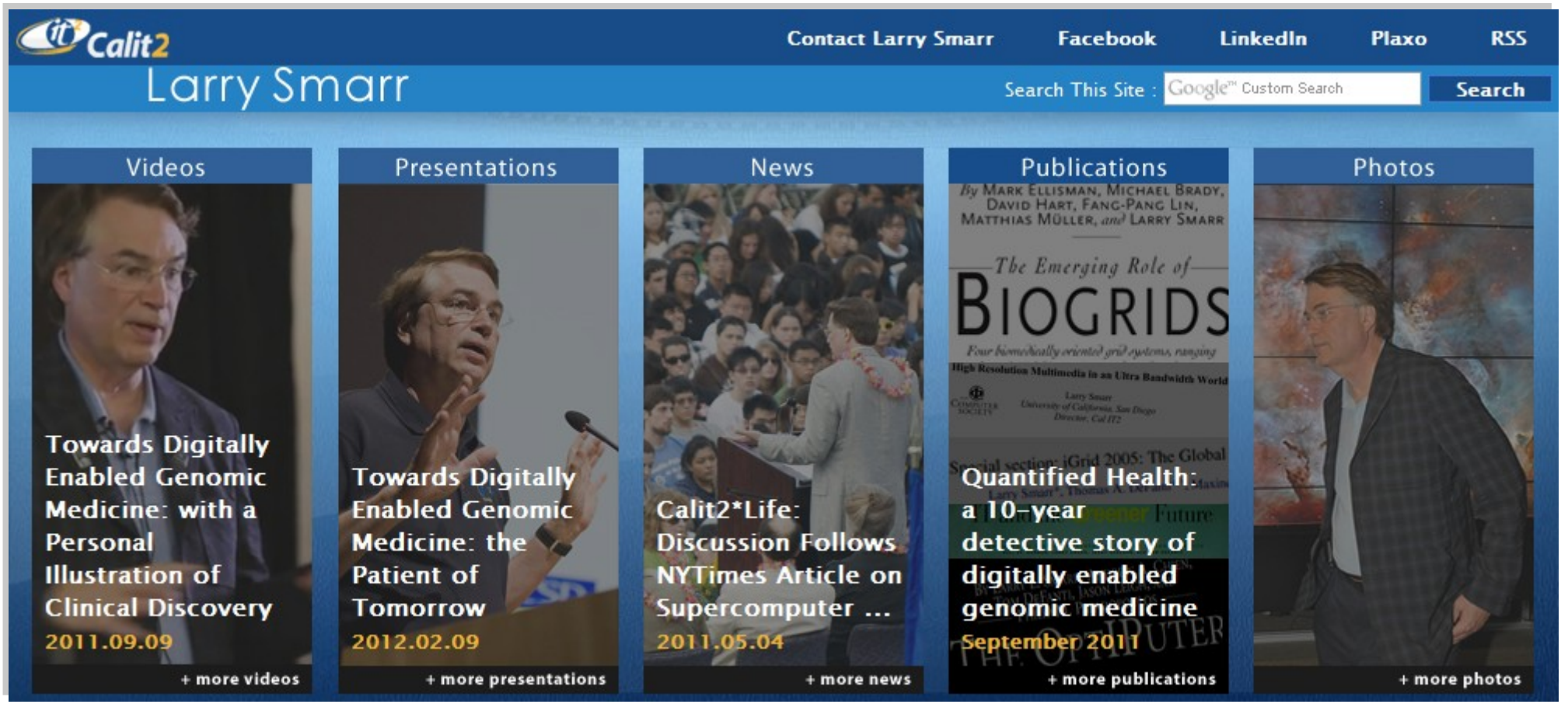
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# From “How Do You Feel?”, to “What Are Your Numbers?”

Where’s There’s Data
There’s Hope

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# For Further Information
# Visit My Portal




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http://lsmarr.calit2.net/