Towards Digitally Enabled Genomic Medicine: the Patient of Tomorrow

Banquet Keynote Speaker
The 3rd International Symposium on LifeChips
Calit2@UC Irvine
February 9, 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. The LifeChips program is one of Calit2's leading examples of this transformation. 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

- **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

www.bodymedia.com



- **Post-Genomic Individualized Medicine**
  - Combine
    - Genetic Code
    - Body Data Flow
  - Use Powerful AI Data Mining Techniques

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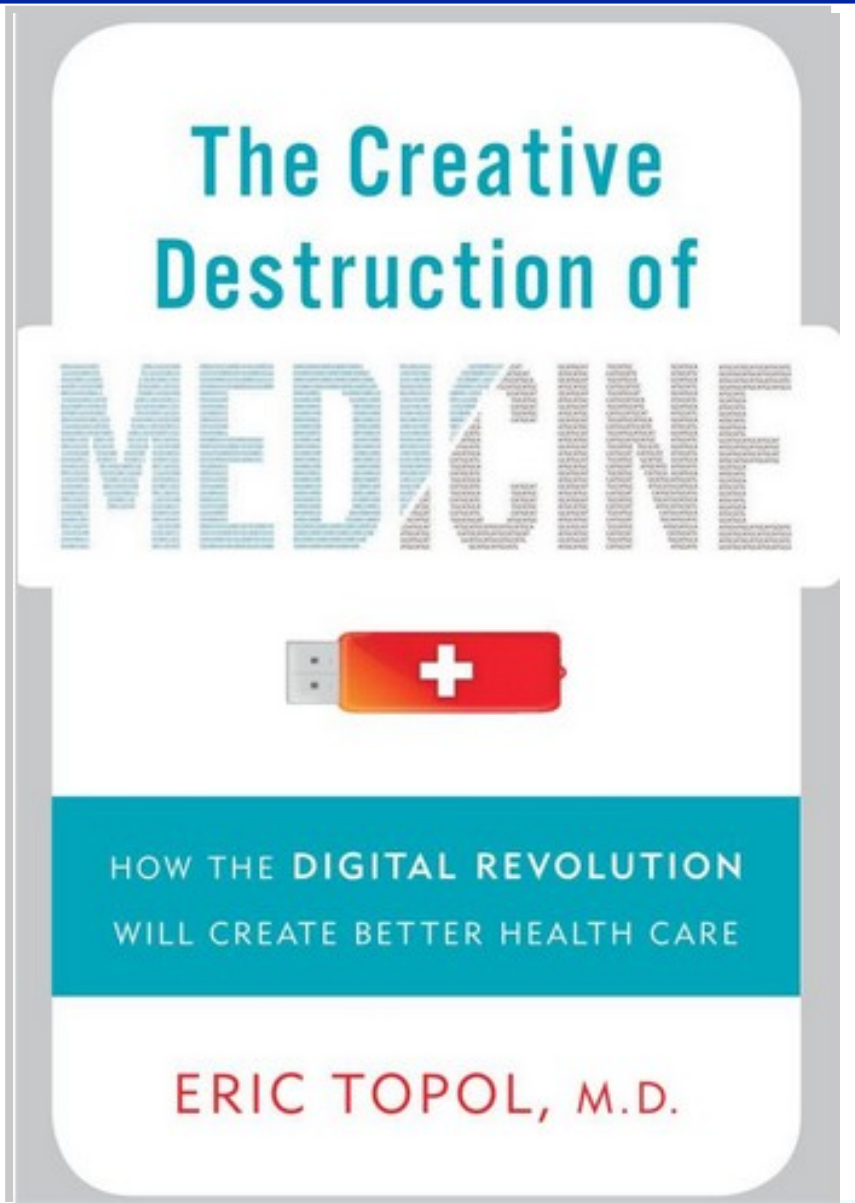
The Content of This Slide from 2001 Larry Smarr
Calit2 Talk on Digitally Enabled Genomic Medicine

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



July/August 2011

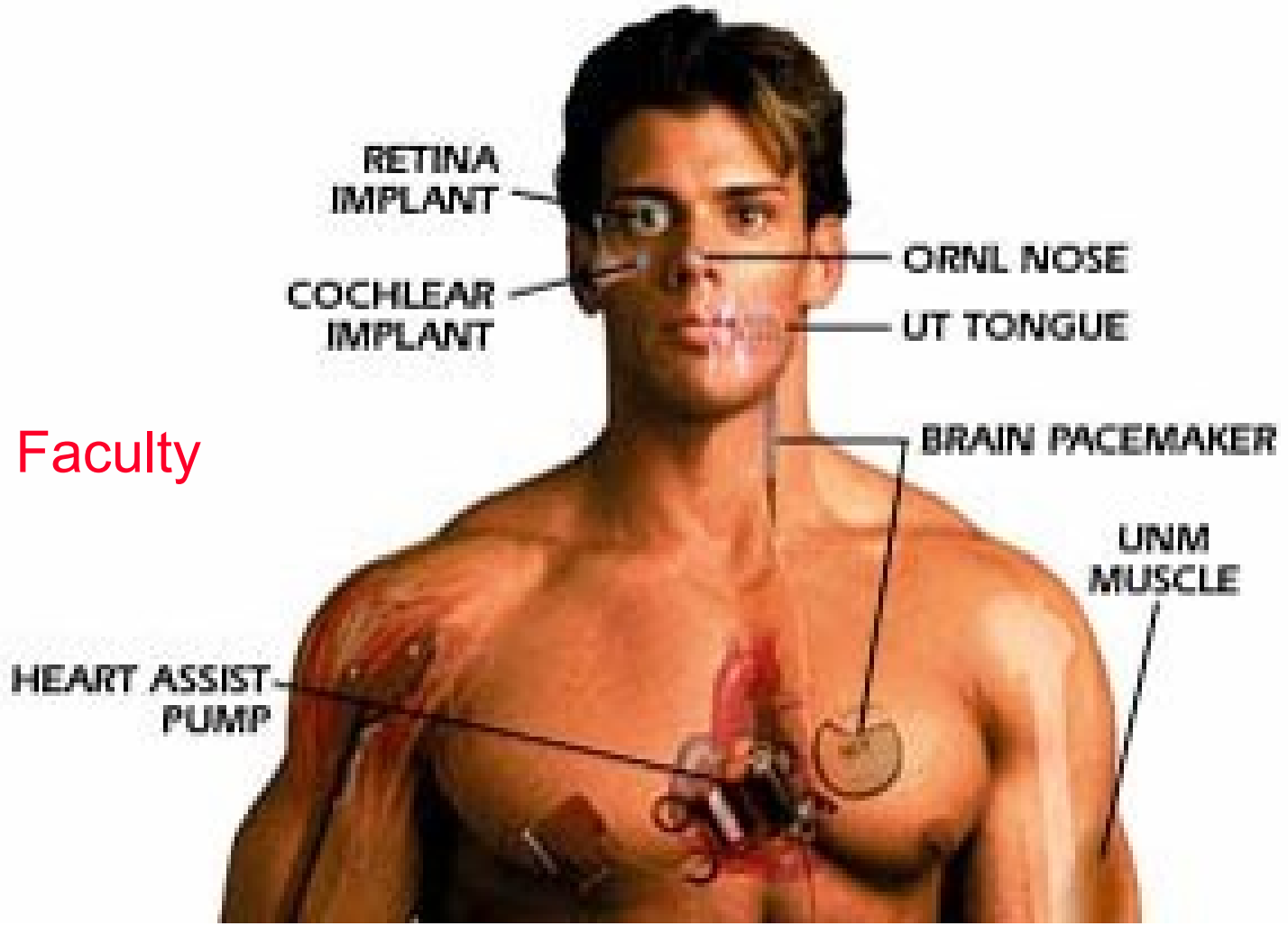


February 2012

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

65 UCI Faculty



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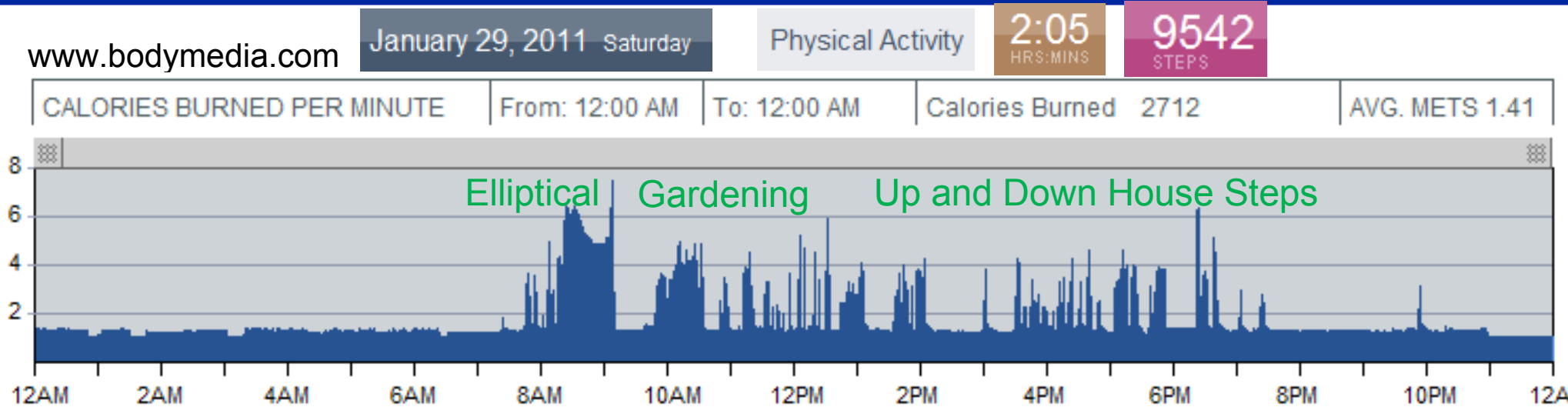
lifechips
university of california, irvine
www.lifechips.org

it²

"LifeChip" Wireless Monitoring Helps Drive Exercise Goals

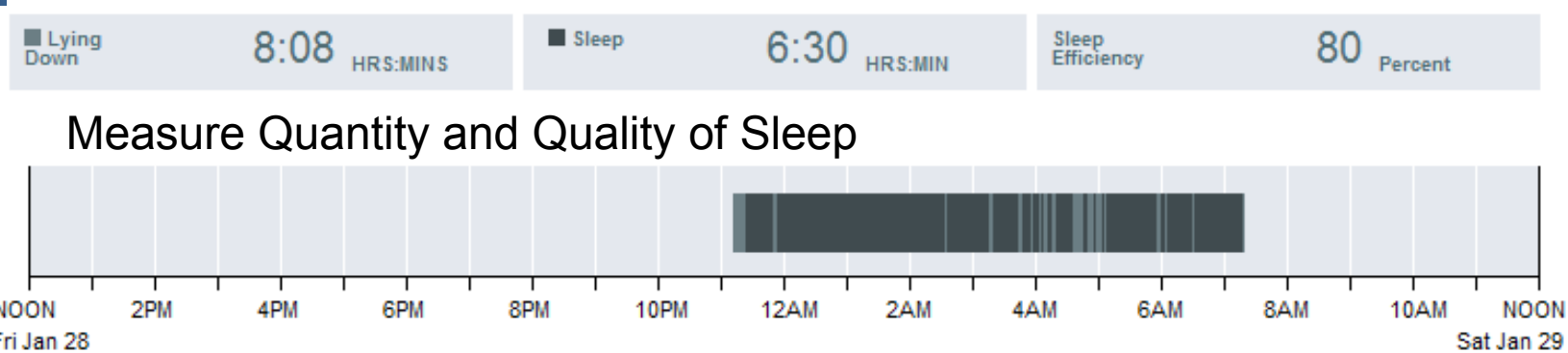
BODYMEDIA® Know your Body. Change your life

www.bodymedia.com





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

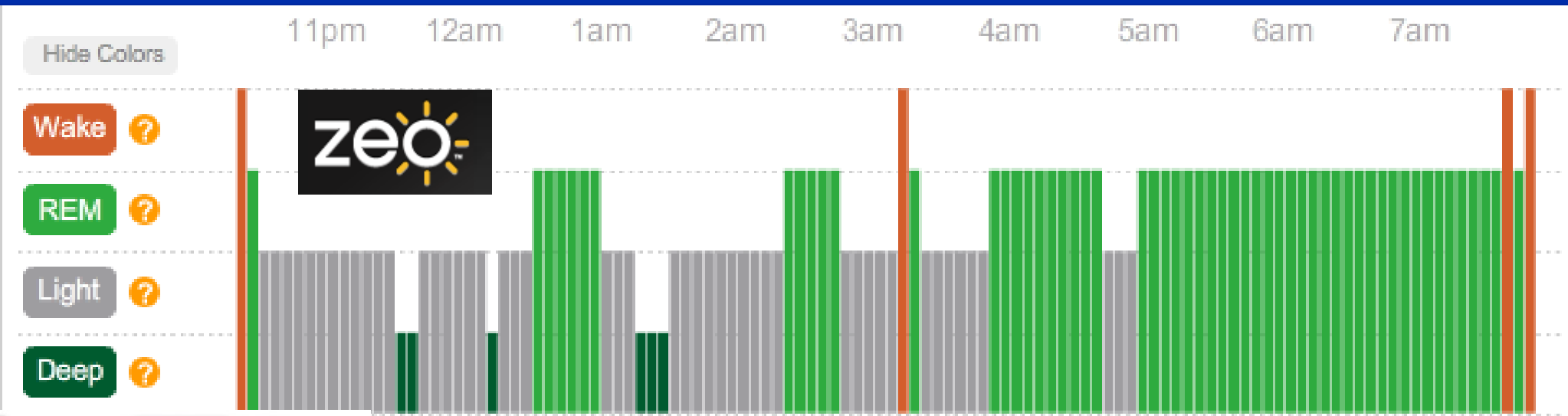


25 Week Ave: 6:51 hrs with 81% Efficiency

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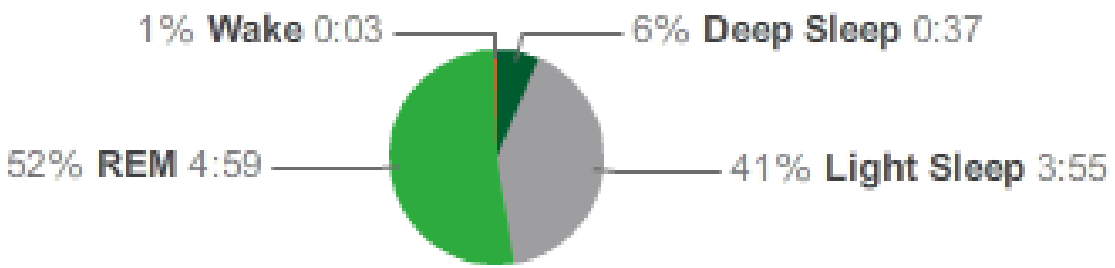
Quantifying My Sleep Pattern Using a Zeo "LifeChip" - Surprisingly About Half My Sleep is REM!





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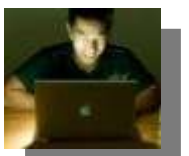
REM is Normally 20% of Sleep
Mine is Between 45-65% of Sleep

An Infant Typically
Has 50% REM

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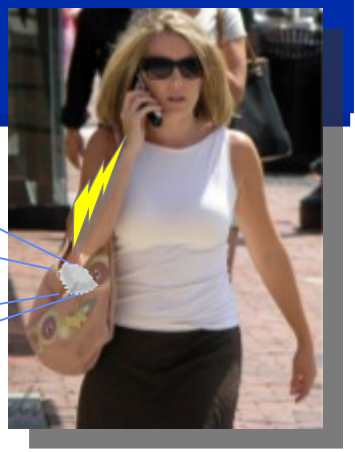
CitiSense –New NSF Grant for Fine-Grained Environmental Sensing Using Cell Phones





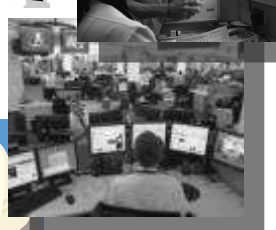
4oz
30 compounds













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

Integrate Into a "LifeChip"

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

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

Age 51





Age 61

HEALTH IT, PEOPLE, WIRELESS

How Internet Pioneer Larry Smarr Lost 20 Pounds by Becoming a "Quantified Self"

Luke Timmerman 5/12/10

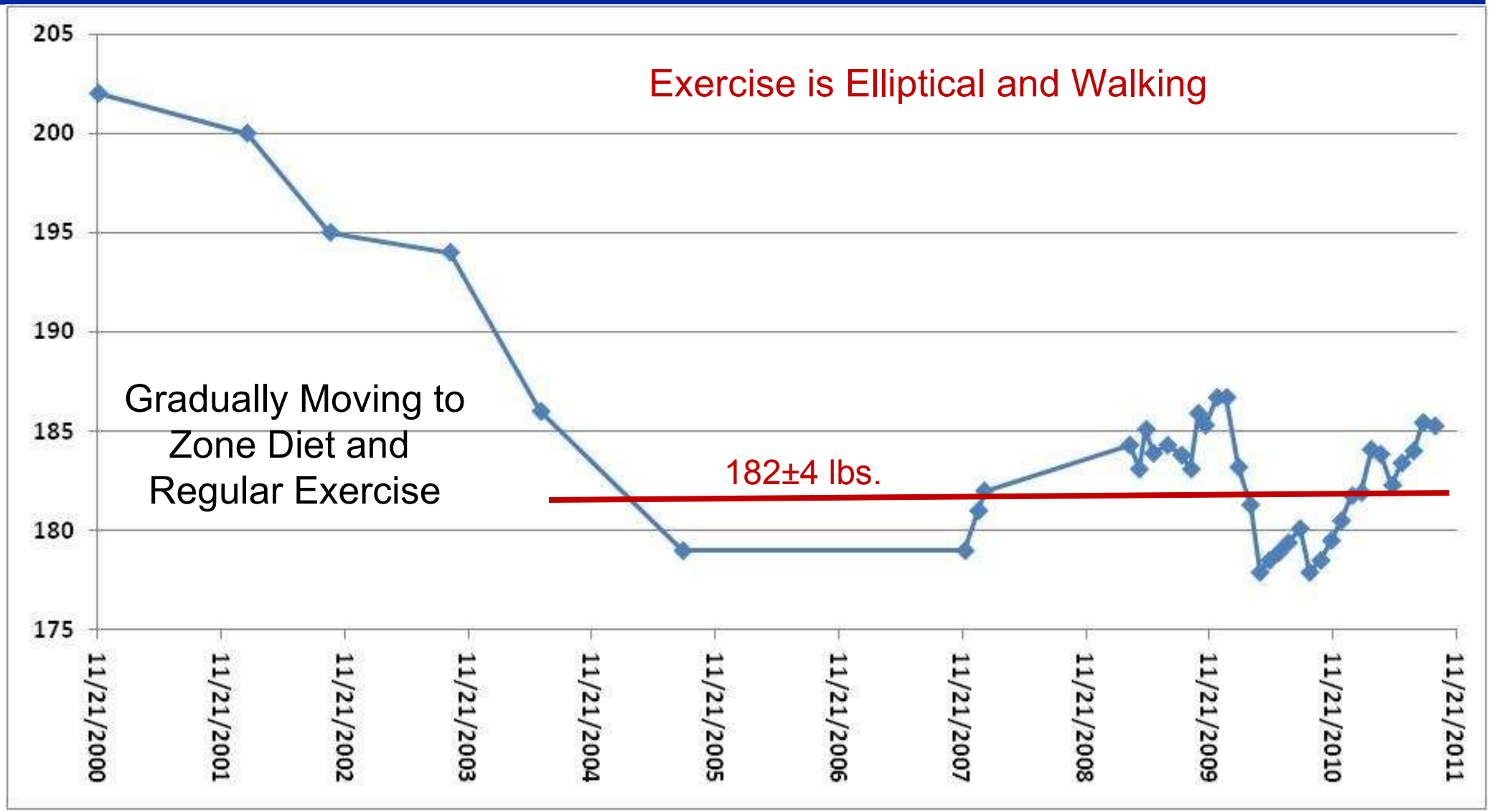
Now the Top Listed Article By Google for "Larry Smarr"

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www.xconomy.com/san-diego/2010/05/12/how-internet-pioneer-larry-smarr-lost-20-pounds-by-becoming-a-quantified-self/

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



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Blood Pressure 134/73 Pulse 55
Resting Pulse Lowered to 45

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Goal: Quantify Your Food Intake So You Can "Tune" Your Glucose/Insulin System and Lower Inflammation

Computed Average Over 12 Days When at Home for Maximum Accuracy
Measure All Food and Drink Components,
Then Use USDA Lookup to Compute Each Item

calories	fat	carb	protein		fiber	sugar	sodium
kcal	g	g	g		g	g	mg
1441	46	122	80	0	26	53	1358

Measuring Daily Food Intake
Needs More "LifeChips"!

- **Quality of Food**
  - **All Organic and Mostly Locally Grown**
  - **Carbs are Low Glycemic Index**
    - **No Added Sugar or Refined Flour – Mostly Fruits and Vegetables**
  - **Proteins are Lean**
    - **Meat is Grass Fed – No Corn or Antibiotics**
    - **Fish is Wild, Often Locally Caught**
  - **Fats are Omega-3 Rich**
    - **Supplemented by 7g Daily Pharmaceutically Purified Fish Oil Pills**

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

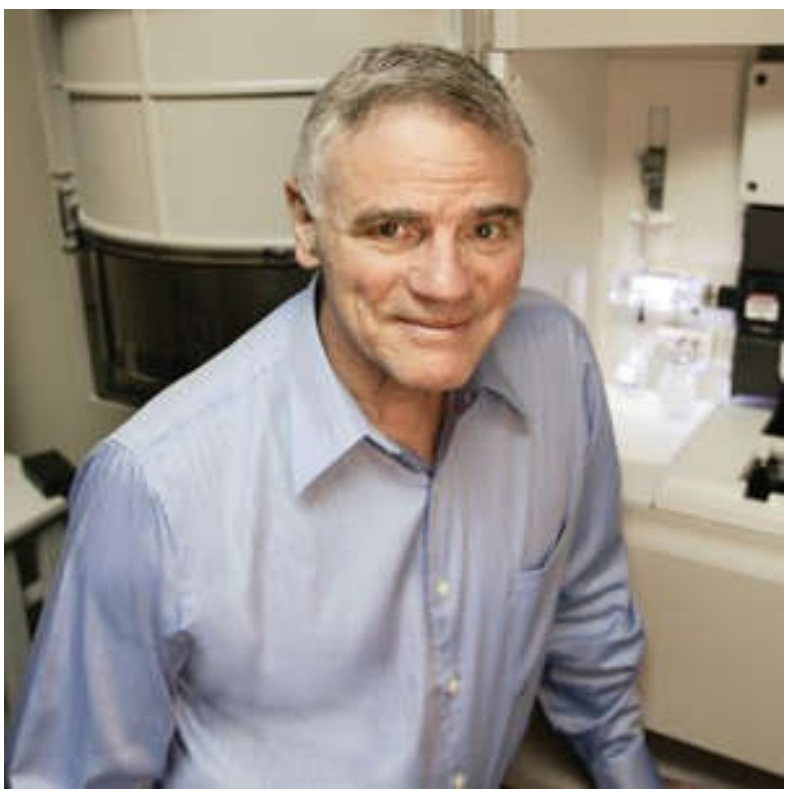
Newsweek

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



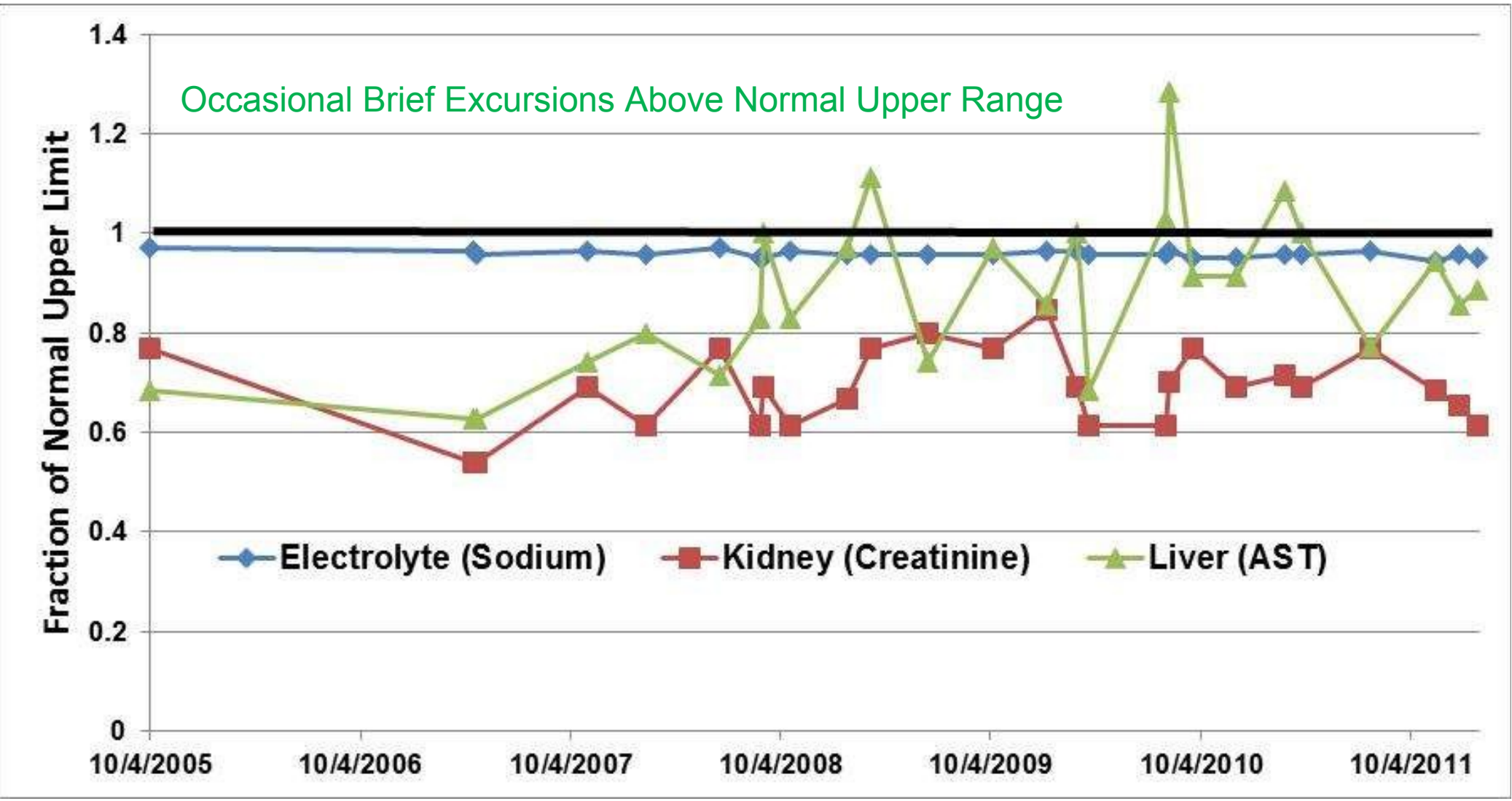
Using a "LifeChip"
Quantify ~2500 Blood Proteins,
50 Each from 50 Organs or Cell Types
from a Single Drop of Blood
To Create a Time Series

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

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Most Blood Variables Stay Within Normal Range: Fraction of Normal Upper Range For Three Variables



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

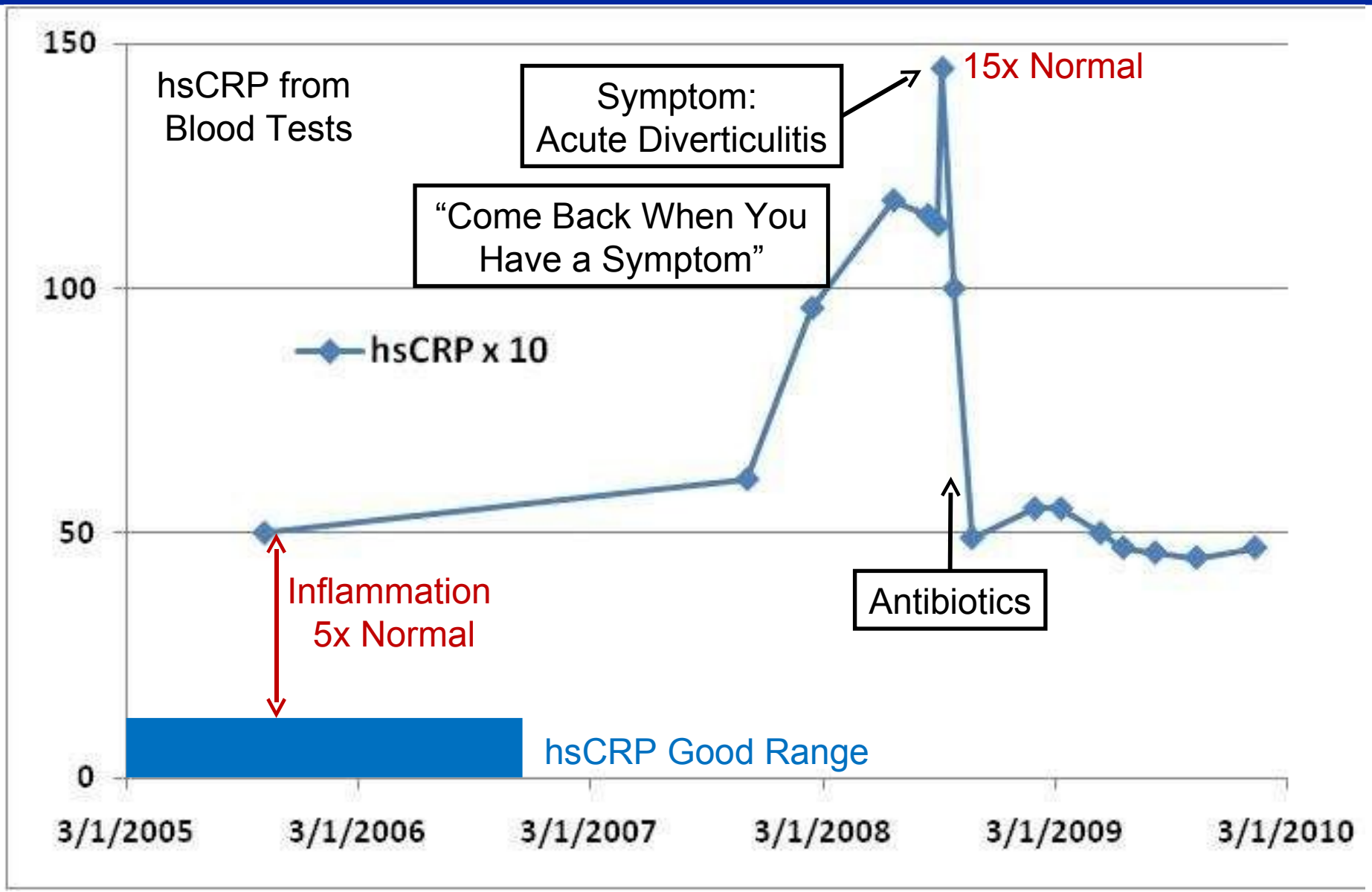
- **Electrolytes**
  - Sodium, Potassium, Calcium, Magnesium, Phosphorus, Boron, Chlorine, CO_2
- **Micronutrients**
  - Arsenic, Chromium, Cobalt, Copper, Iron, Manganese, Molybdenum, Selenium, Zinc
- **Blood Sugar Cycle**
  - Glucose, Insulin, A1C Hemoglobin
- **Cardio Risk**
  - ~~Complex Reactive 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

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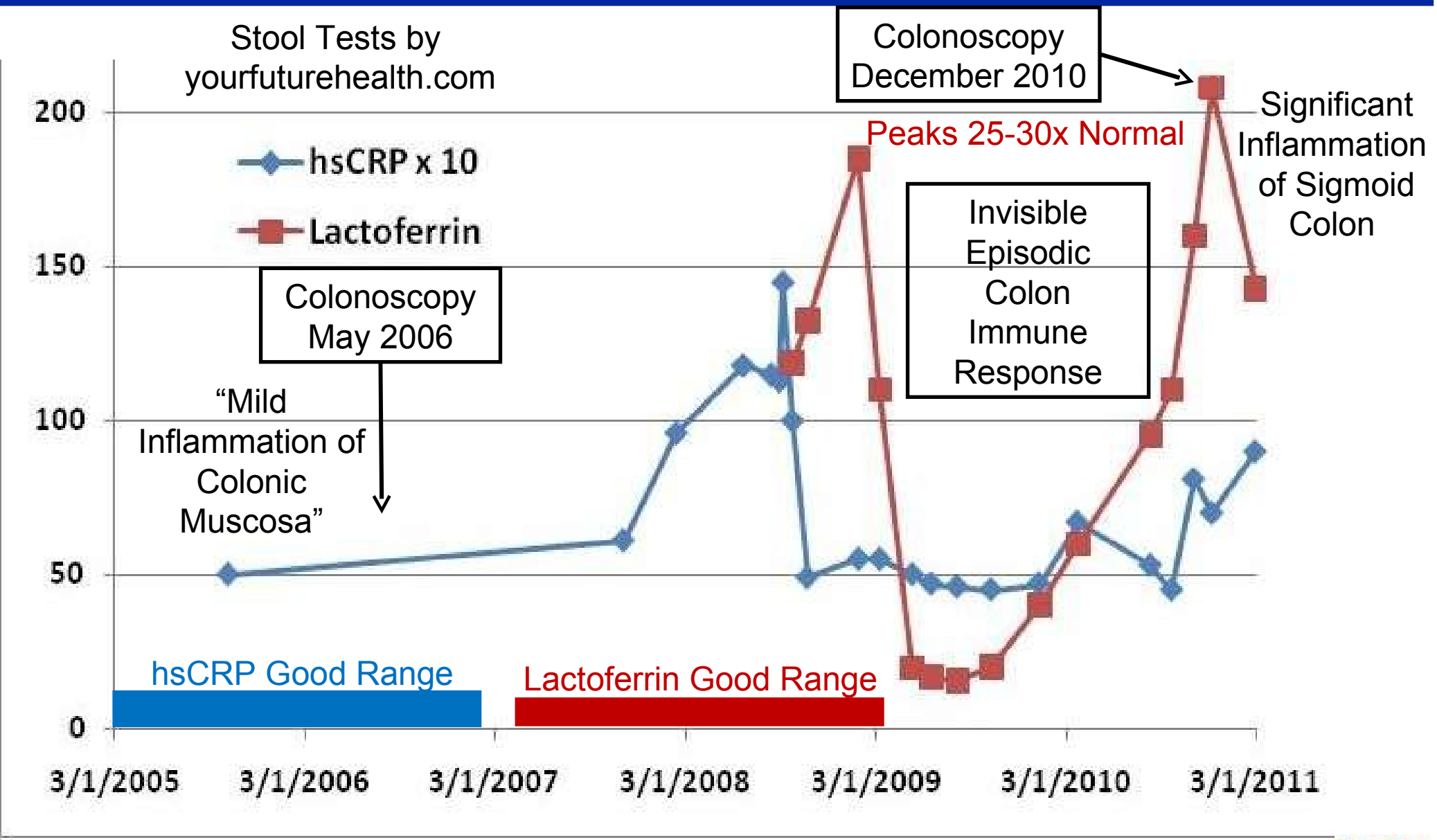
But, In Spite of My High Levels of Omega-3s, Blood Measurements Show Chronic Inflammation



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

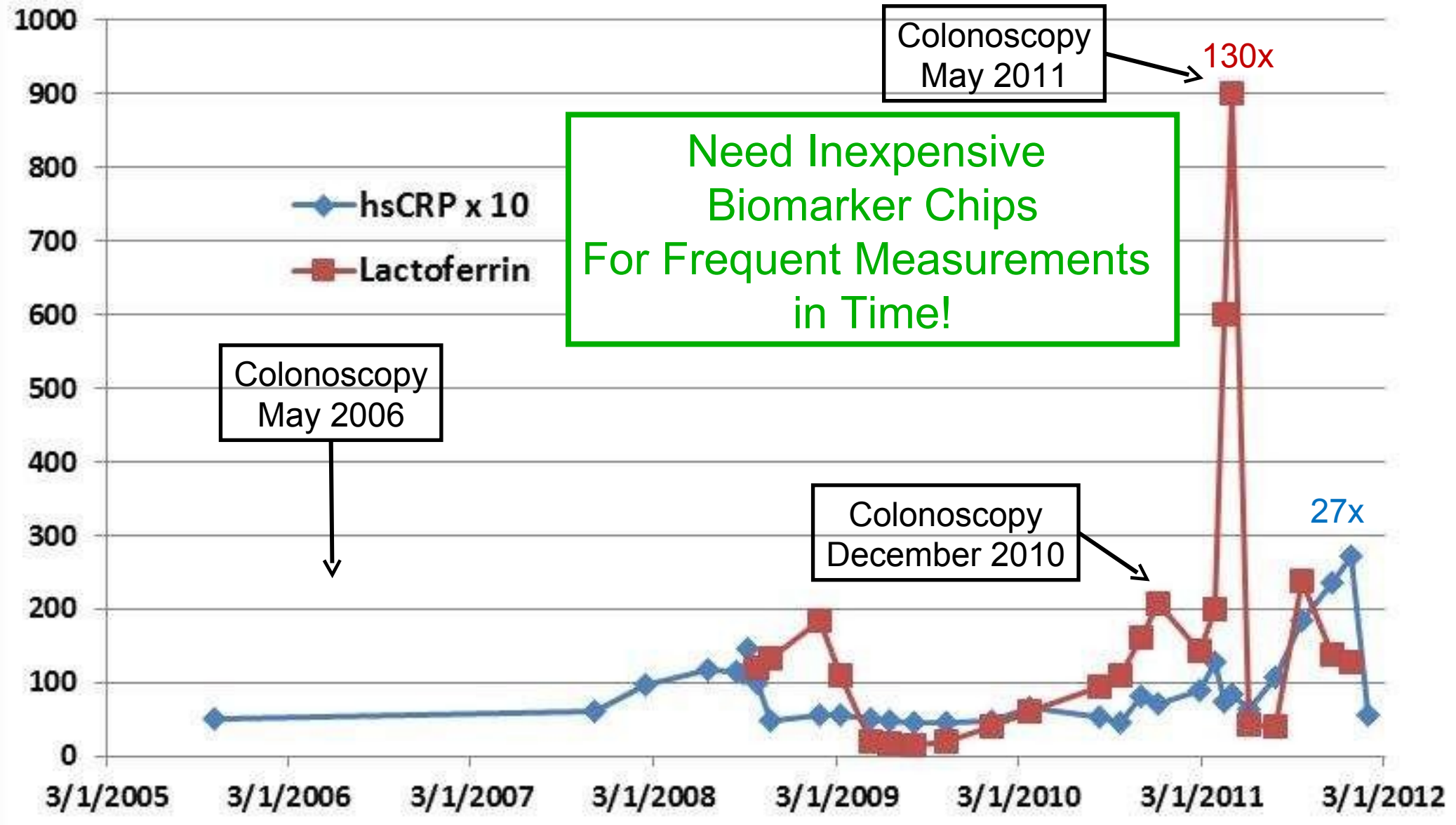


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Colonoscopy Biopsies, MRI, & Lactoferrin Biomarker Leads to Crohn's Disease Diagnosis

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High Level Crohn's Flares Are Quite Sudden: Will be Missed Without Frequent Measurements



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Autoimmune Diseases
Effect 5-8% of Americans

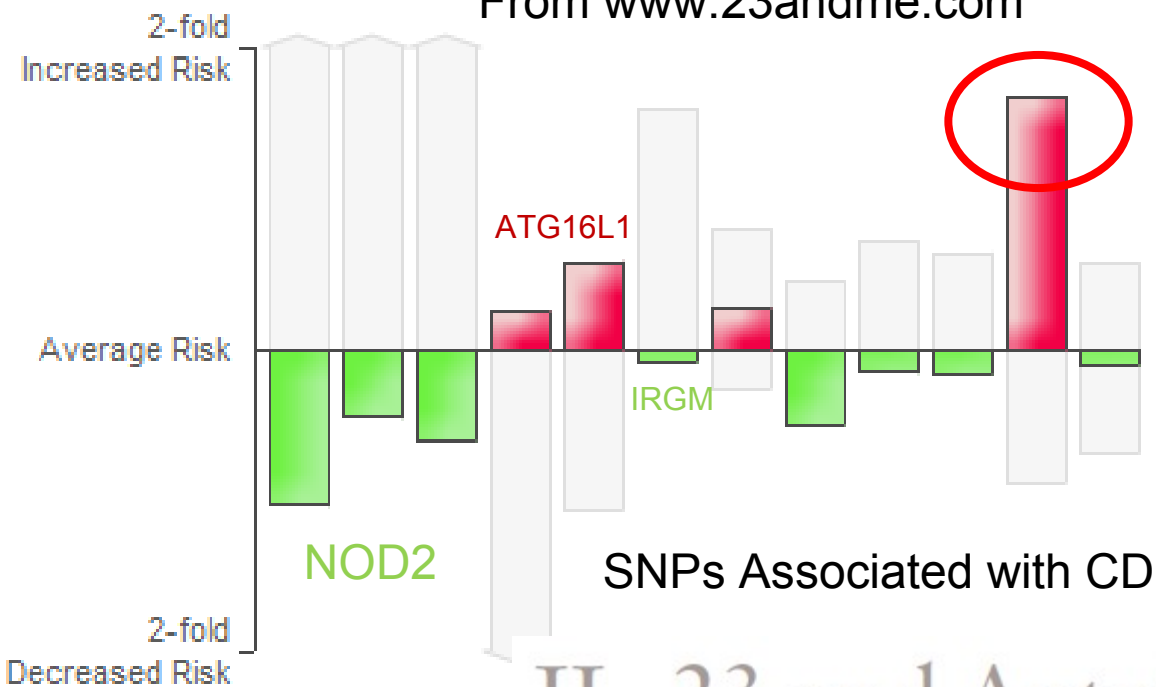
- **Crohn's Disease**
- **Ulcerative Colitis**
- **Rheumatoid Arthritis**
- **Multiple Sclerosis**
- **Psoriasis**
- **Type 1 Diabetes,**
- **Ankylosing Spondylitis**
- **Lupus Erythematosus**
- **Plus Over 70 Others**

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)

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,

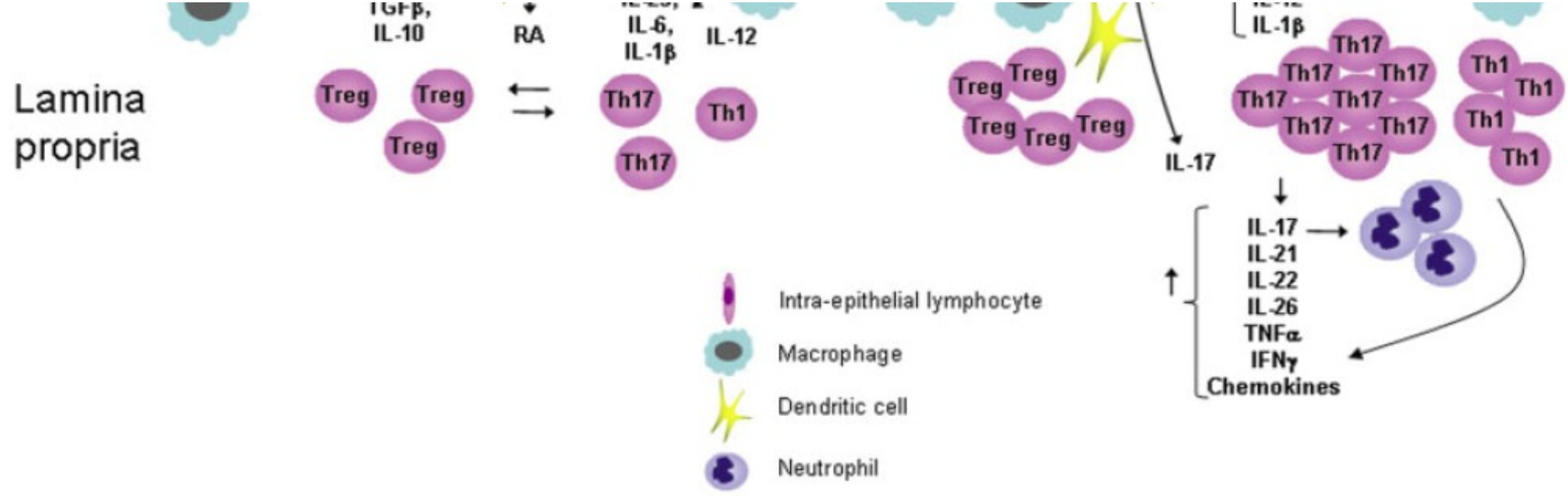
2009

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Genetic Mutation of IL-23 Leads to Pro-Inflammatory Excess

Anti-IL-12/23: The Next Big Thing in IBD?

Sandborn WJ, Feagan BG, Fedorak RN, et al. A randomized trial of Ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with moderate-to-severe Crohn's disease. Gastroenterology. 2008;135:1130–1141.



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Interleukin-23/Th17 Pathways and Inflammatory Bowel Disease

Clara Abraham, MD, and Judy Cho, MD

Inflamm Bowel Dis • Volume 15, Number 7, July 2009

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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



Complete genomics

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4 Million Newborns / Year in U.S.

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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

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.

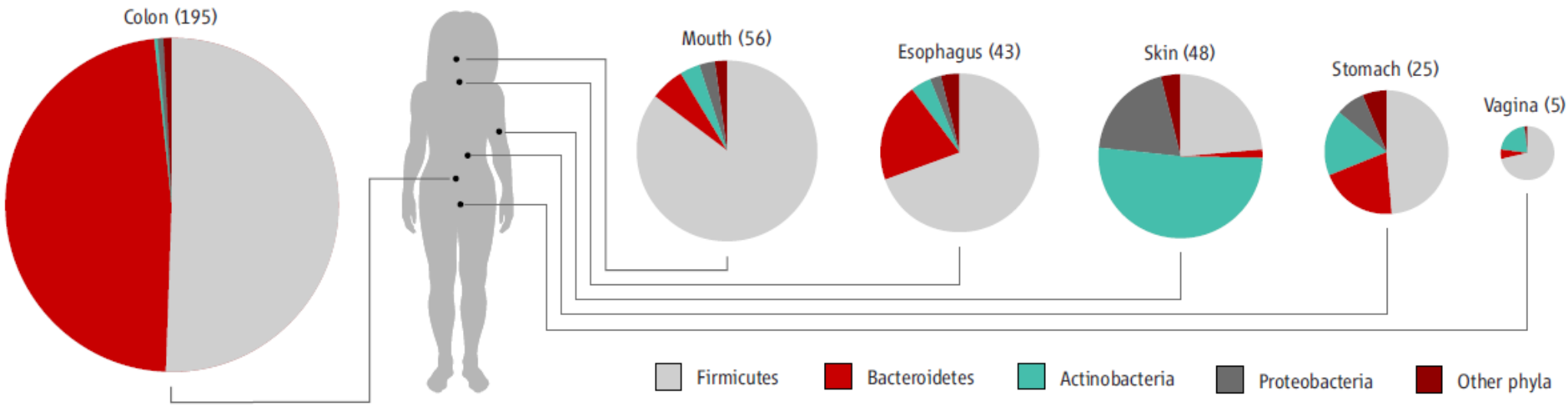
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You are a Superorganism: Microbes Are 90% of Your Cells!

Human Microbiome Project

The NIH Common Fund
WE ACCELERATE DISCOVERY.



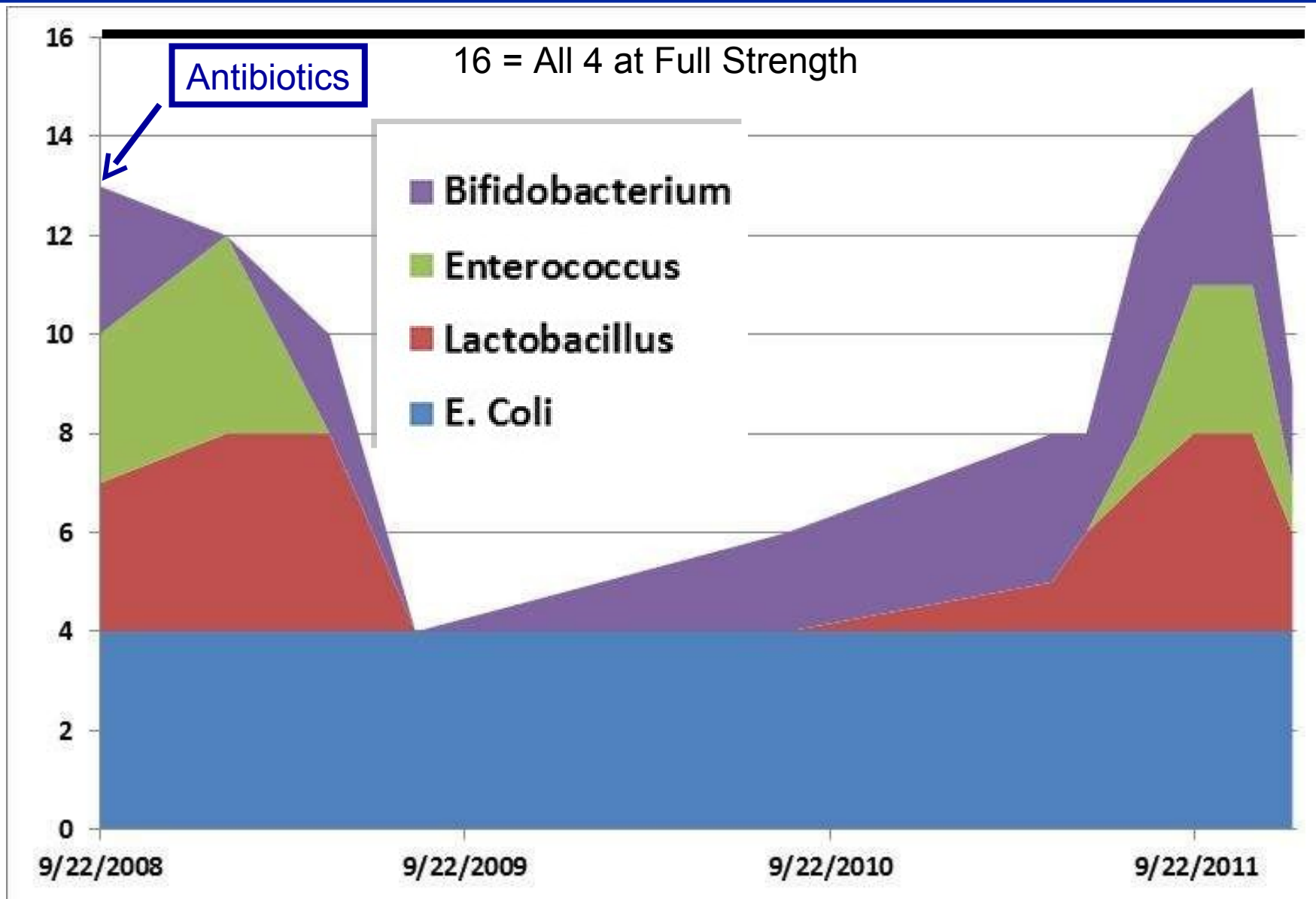
Firmicutes Are the Dominant Phyla in the Human Microbiome

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Science v.330, p. 1619 (2010)

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My "Good" Cultured Gut Bacteria Collapsed After Antibiotics



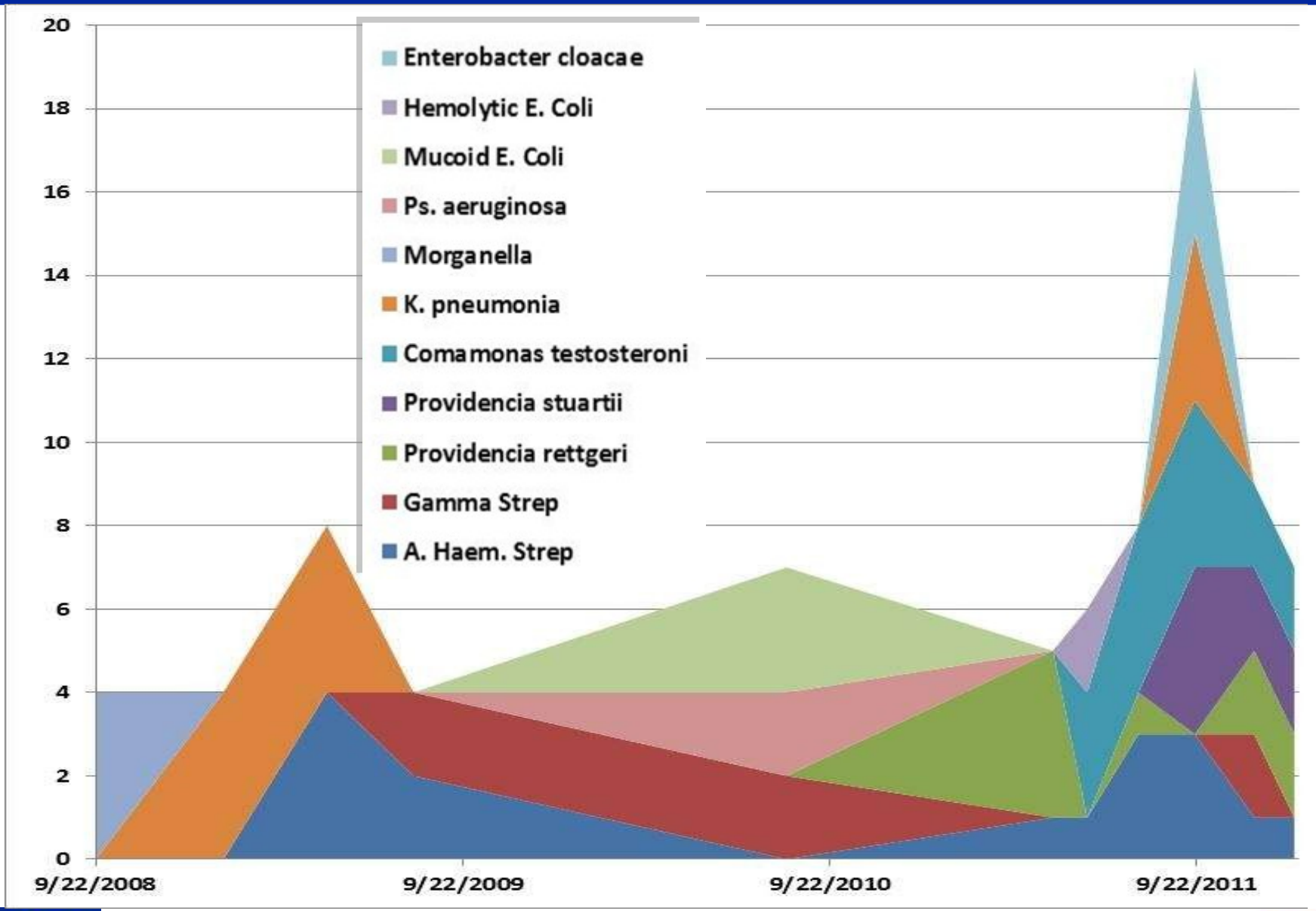
Antibiotics: Levaquin & Metronidaloze

Values From yourfuturehealth.com stool test

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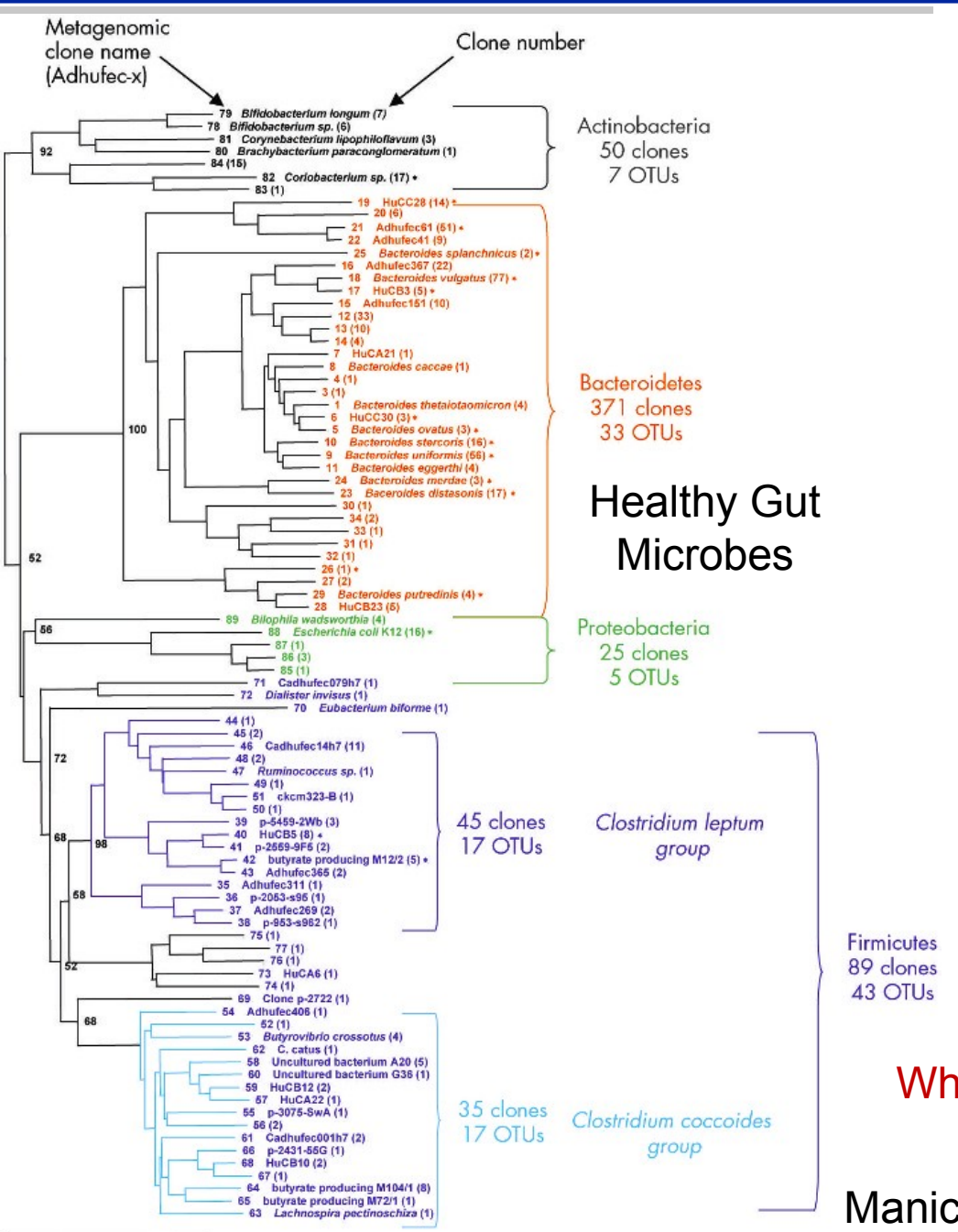
Dysbiotic Bacteria Have Been Flourishing

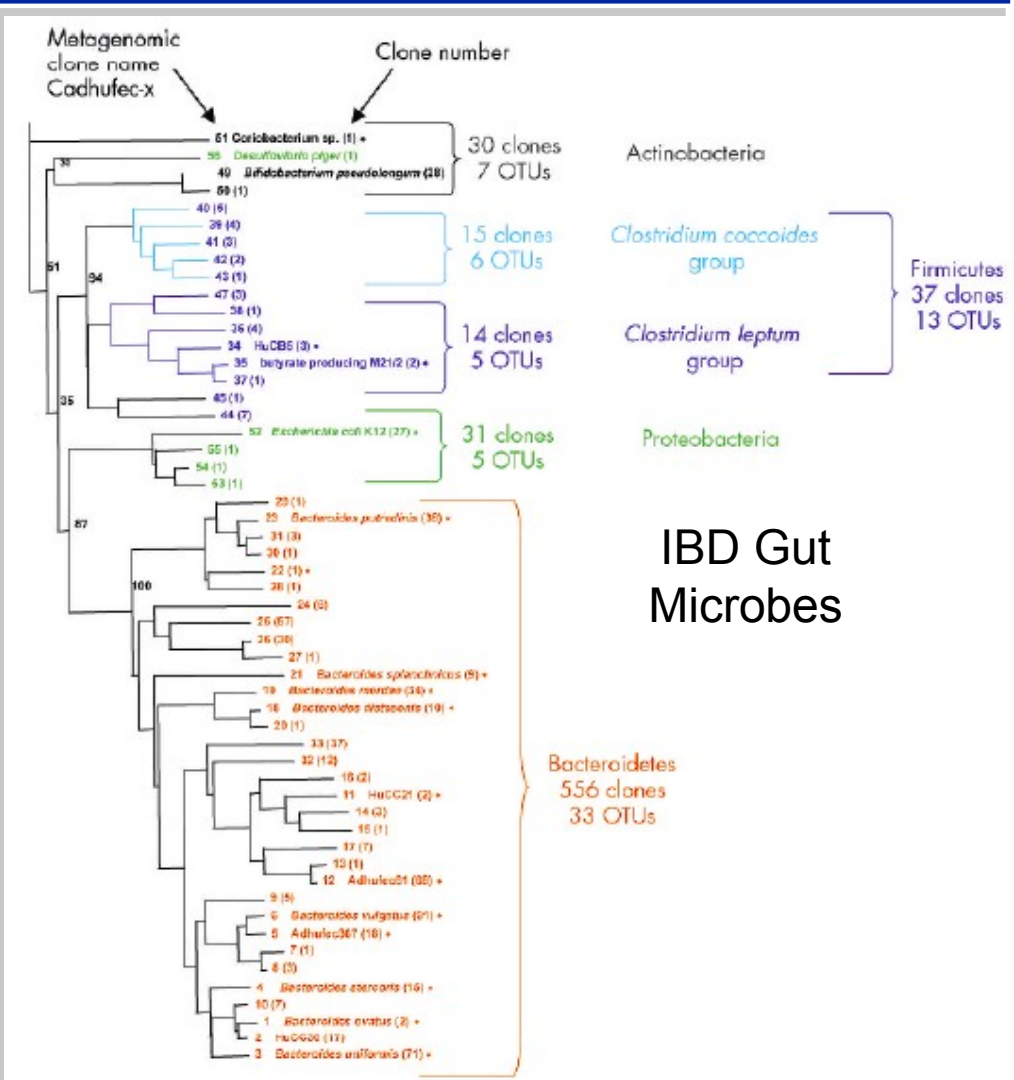


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Crohn's Disease Patients Have Number of Gut Microbe Species in Firmicutes Phyla Reduced by Over 2/3!





While Bacteroidetes Species Count is the Same

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

"LifeChips": From Research to Startups: 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."

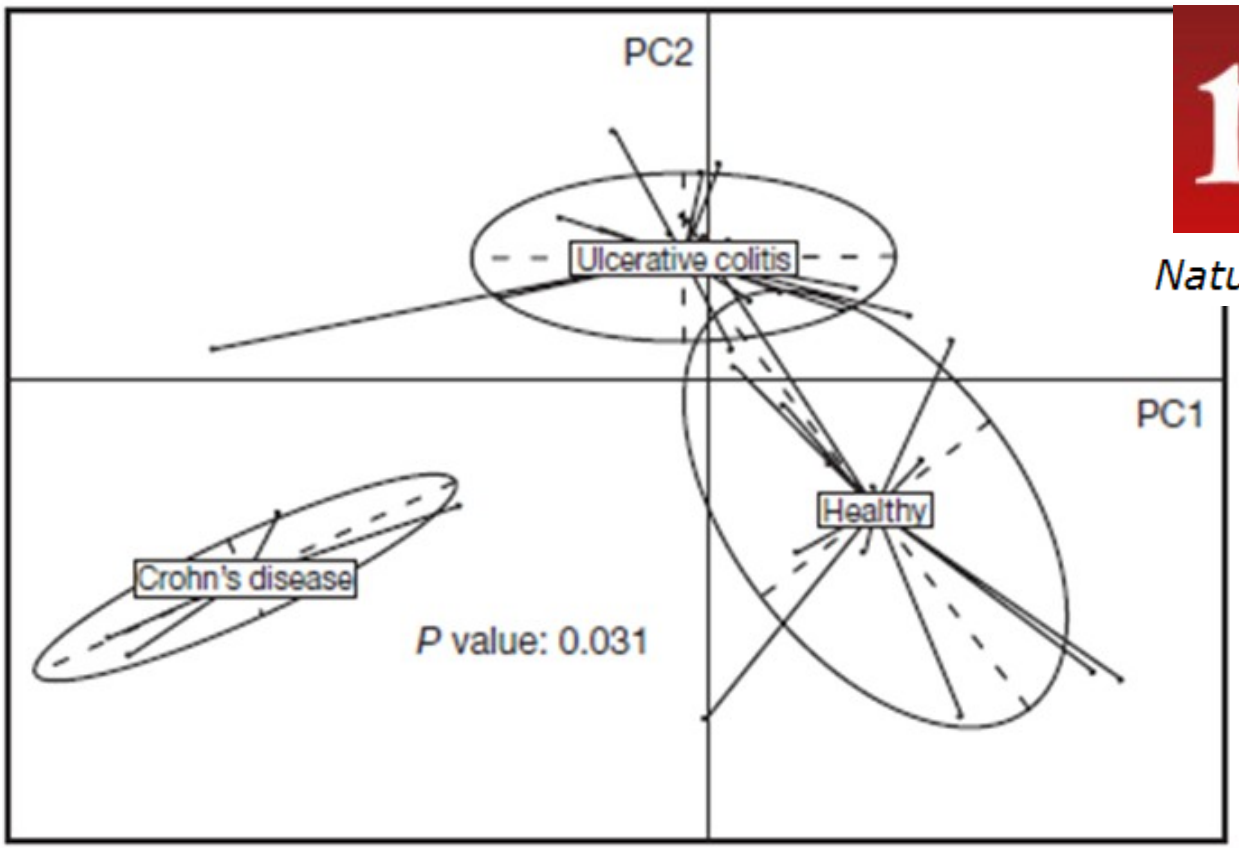
DNA microarray that can identify,
within hours,
over 50,000 different microbes



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Microbial Metagenomics Can Diagnose Disease States



nature

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

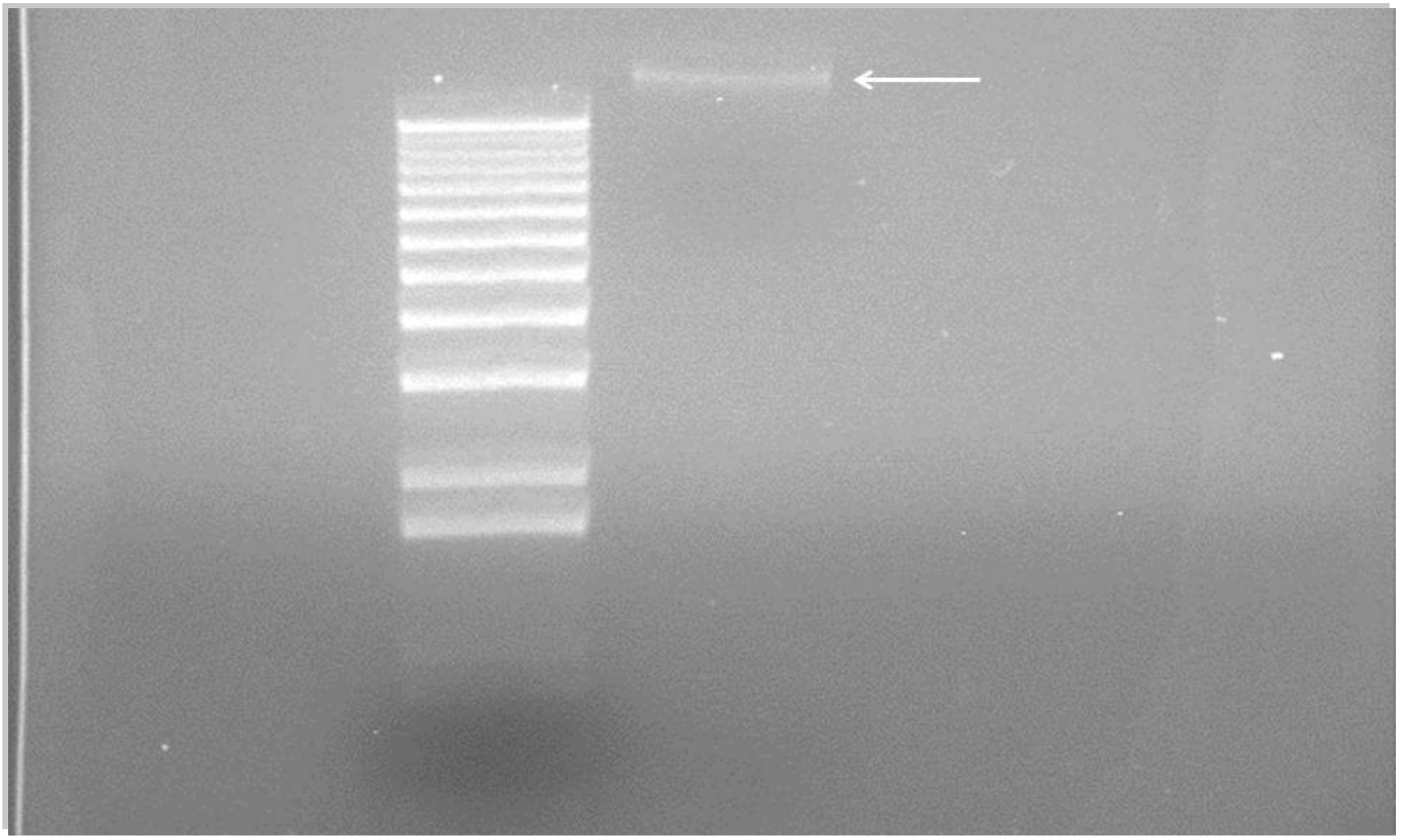
IBD Patients Harbored, on Average, *25% Fewer Microbial Genes* than the Individuals Not Suffering from IBD.

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



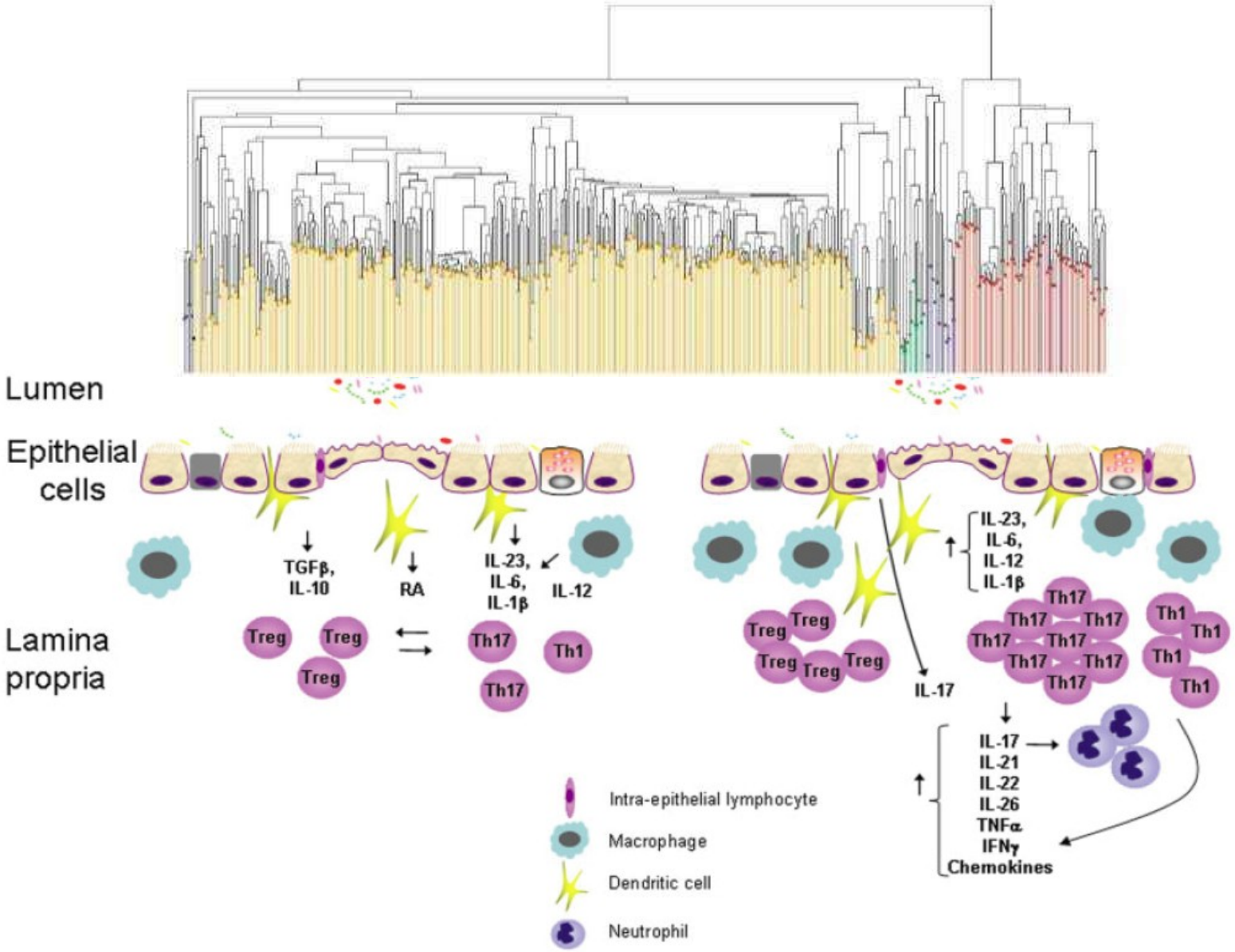
Gel Image of Extract from Smarr Sample-Next is Library Construction

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

January 25, 2012

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Understanding Autoimmune Diseases Will Require Complete Genomes, Microbial Metagenomics Over Populations



Follow Molecular Interactions with Proteomics, Metabolomics, &Transcriptomics of Joint Genomic Production of Human DNA and Microbiome DNA

****

More Jobs for LifeChips!

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~80% of Our Immune System is Based in our Gut

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