From Digitally Enabled Genomic Medicine to Personalized Healthcare

Invited Colloquium
Philips Eindhoven
Eindhoven, Netherlands
December 8, 2011

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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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

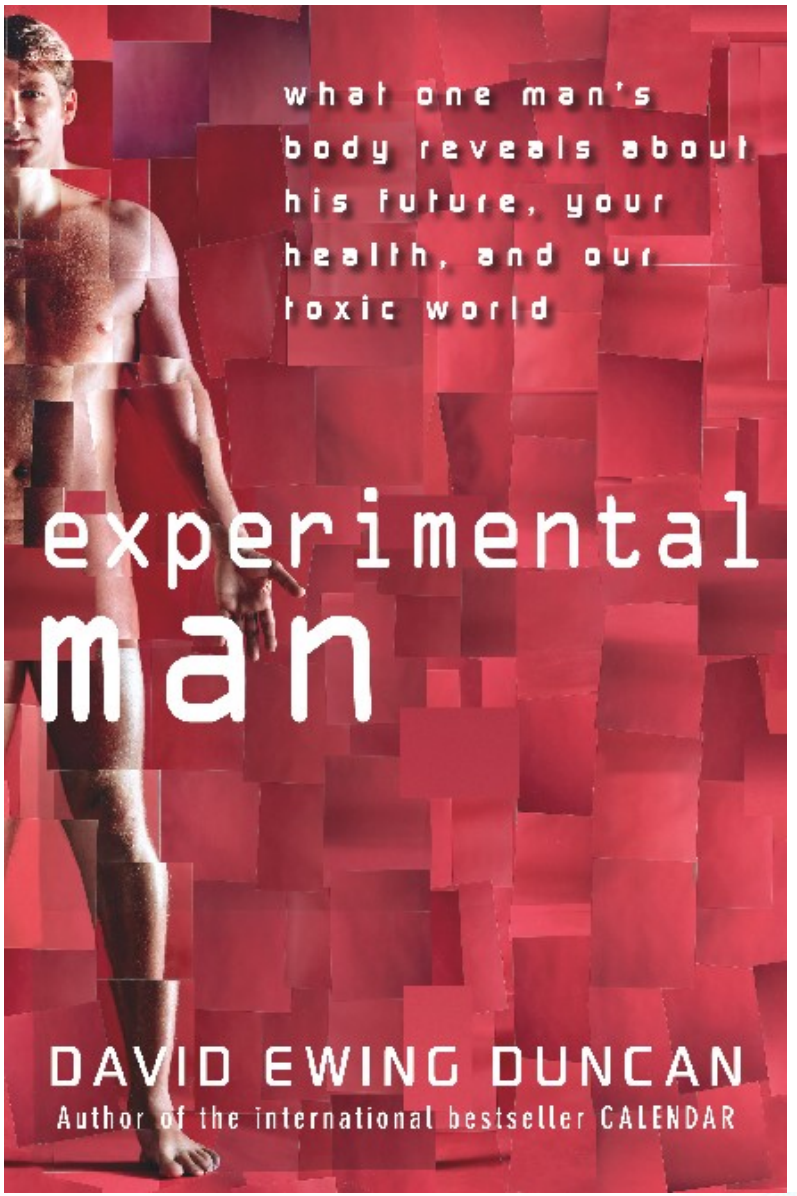
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The Content of This Slide from 2001 Larry Smarr
Calit2 Talk on Digitally Enabled Genomic Medicine

it²

Personal Time Series Tracking is an Emerging Trend





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it²

San Diego Has Become the National Center for Wireless Health



QUALCOMM Wireless Health

Gary & Mary West Wireless Health Institute™

CW PHS
Center For Wireless & Population Health Systems

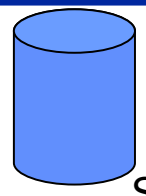
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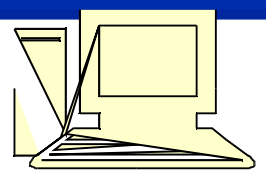
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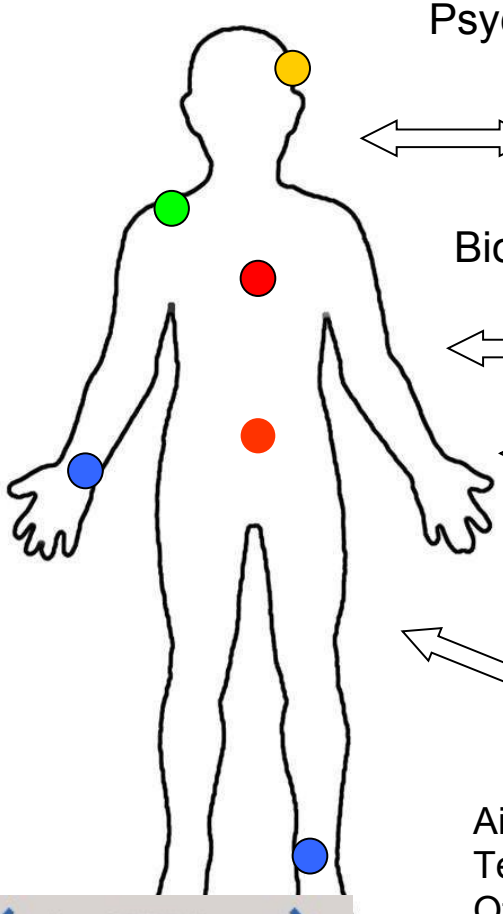
Over the Next Decade an Explosion of Health Sensing: Center for Wireless &Population Health Systems

Geocoded data on safety, location of recreation, food, hazards, etc









Psychological & Social sensors
Mood, Social network (peers/family)
Attention, voice analysis

Biological sensors
BP, Resp, HR, Blood (e.g. glucose, electrolytes, pharmacological, hormone), Transdermal, Implants

Diet & Physical Activity sensors
Physical activity (PAEE, type), sedentary
Posture/orientation, diet intake (photo/bar code)

Wearable Environmental sensors
Air quality (particulate, ozone, etc)
Temperature, GPS, Sound, Video,
Other devices & embedded sensors

Sensor data
+
Clinical & Personal Health Record Data
+
Ecological data on determinants of health
+
Analysis & comparison of parameters in near-real time (normative and ipsative)
+
Sufficient population-level data to comprehend trends, model them and predict health outcomes
+
Feedback in near real-time via SMS, audio, haptic or other cues for behavior or change in Rx device

= True Preventive Medicine!

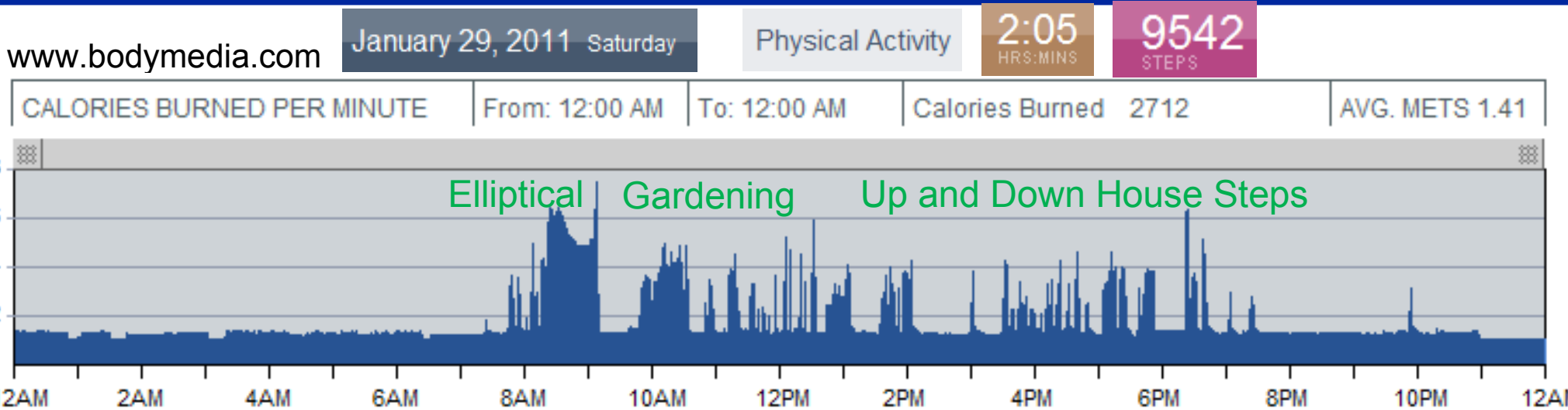
CW PHS
Center For Wireless & Population Health Systems

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Wireless Monitoring Helps Drive Exercise Goals

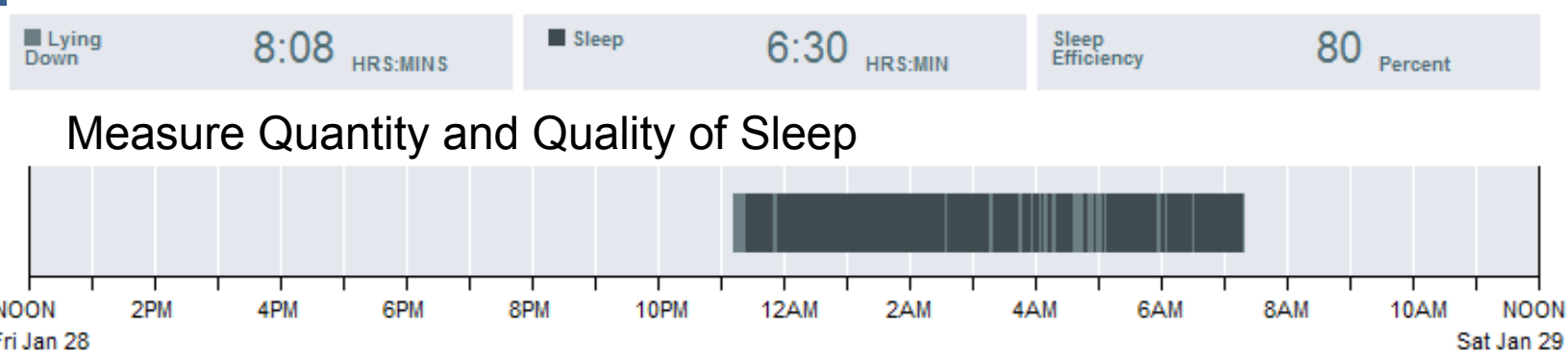
BODYMEDIA®
Know your Body. Change your life

www.bodymedia.com





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

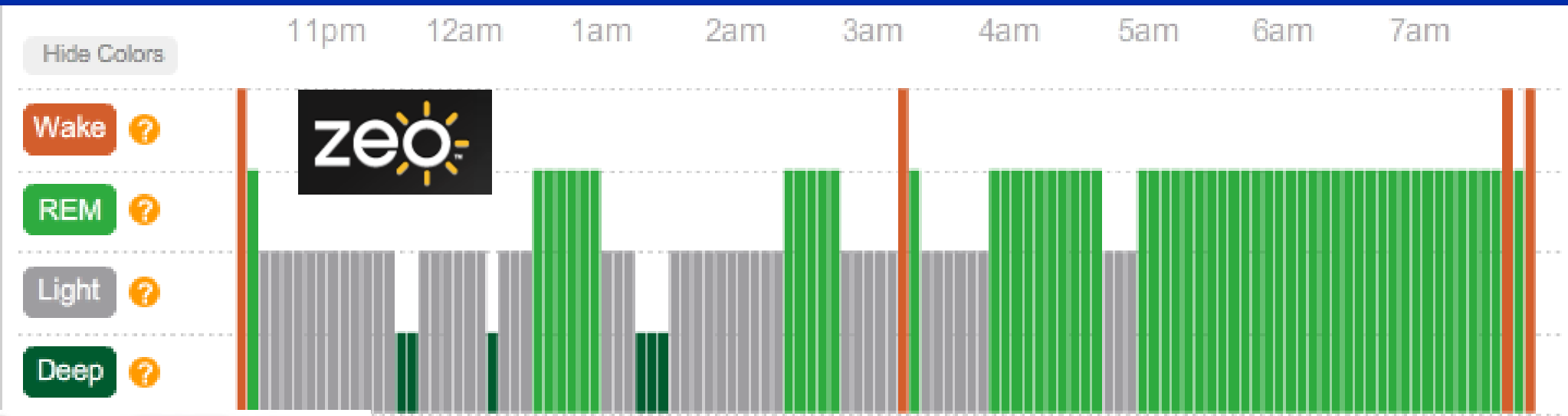


25 Week Ave: 6:51 hrs with 81% Efficiency

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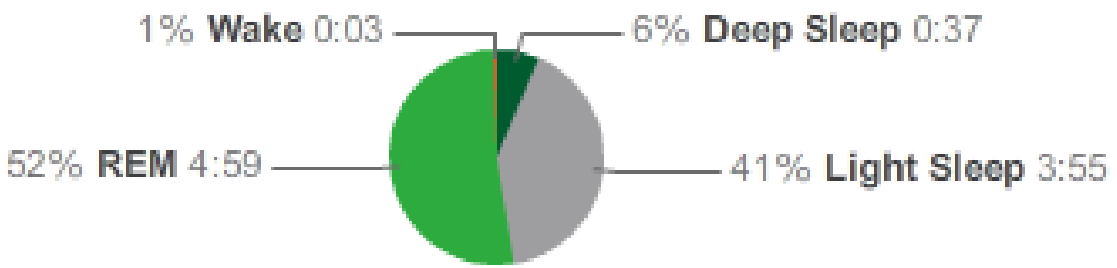
Quantifying My Sleep Pattern Using Zeo - Surprisingly About Half My Sleep is REM!





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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Physical Activity Location Measurement System (PALMS)

- **Integrated Suite of Sensors & Software Enabling Continuous Capture & Analysis of Temporal / Spatial Data**
  - **Characteristics of Physical Activity & Other Data Important to Exposure Biology Research**

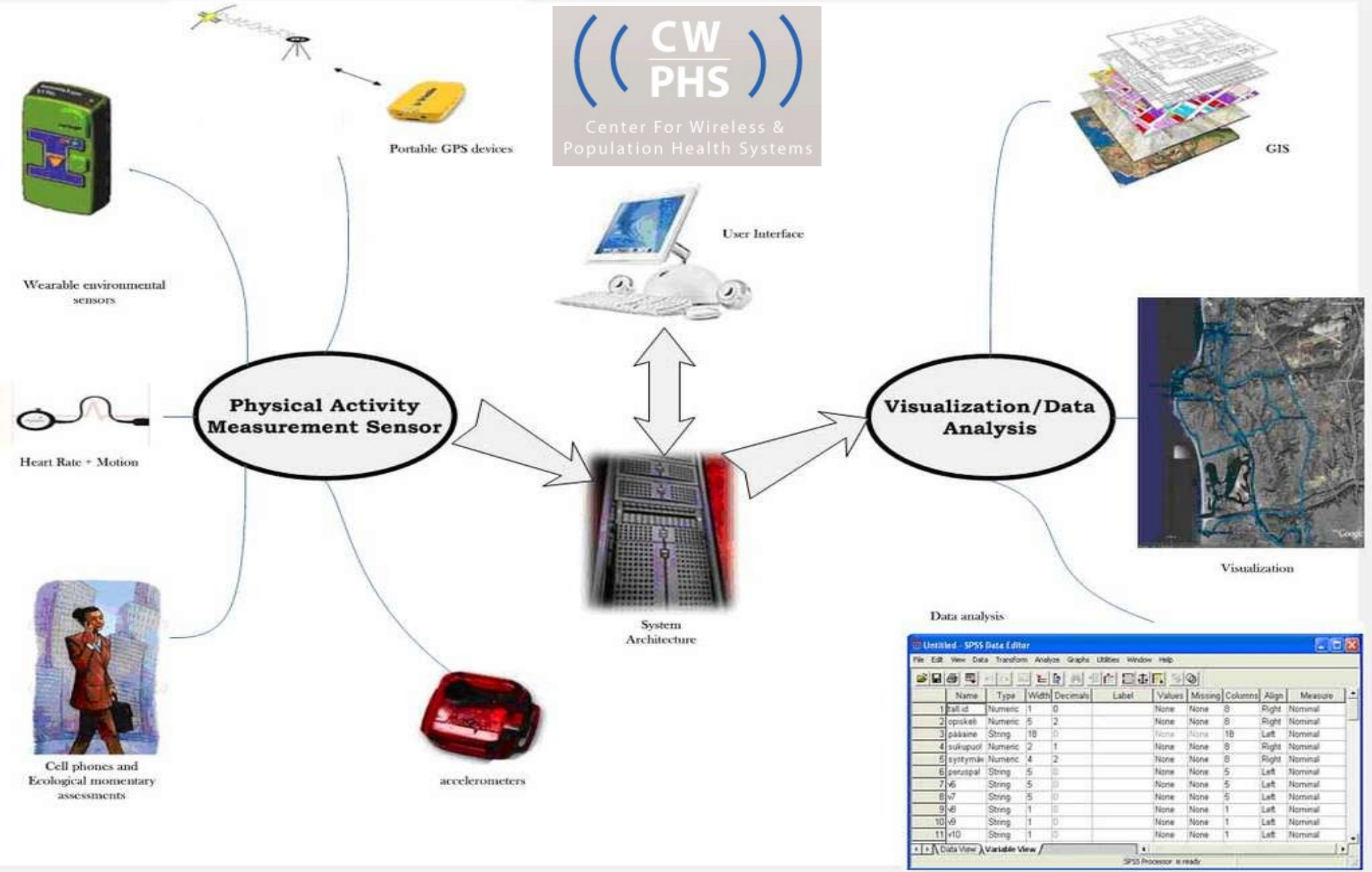
- **PALMS Supports Gathering Data from Multiple Participants Within Studies & Aggregating / Comparing Data Between & Among Multiple Researchers Across Studies**

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Funded through the NIH Gene, Environment and Health Initiative
Exposure Biology Program
NIH/NCI Grant 1 U01 CA130771



PALMS Overview
Measuring Your Personal Exposome

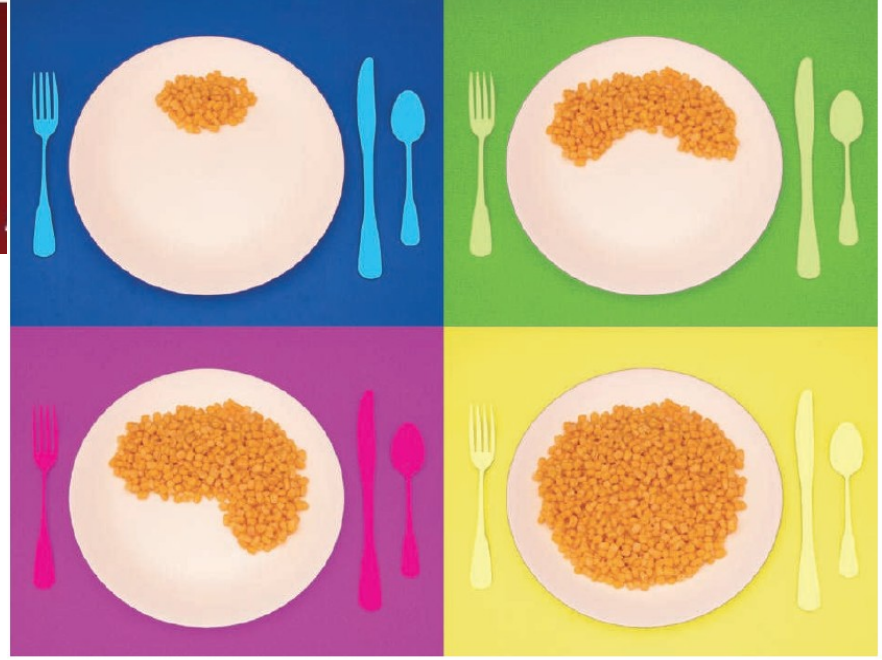


nature International weekly journal of science

Home | News & Comment | Research | Careers & Jobs | Current Issue | Archive |



PALMS was Recently Featured in Nature on Measuring the Exposome



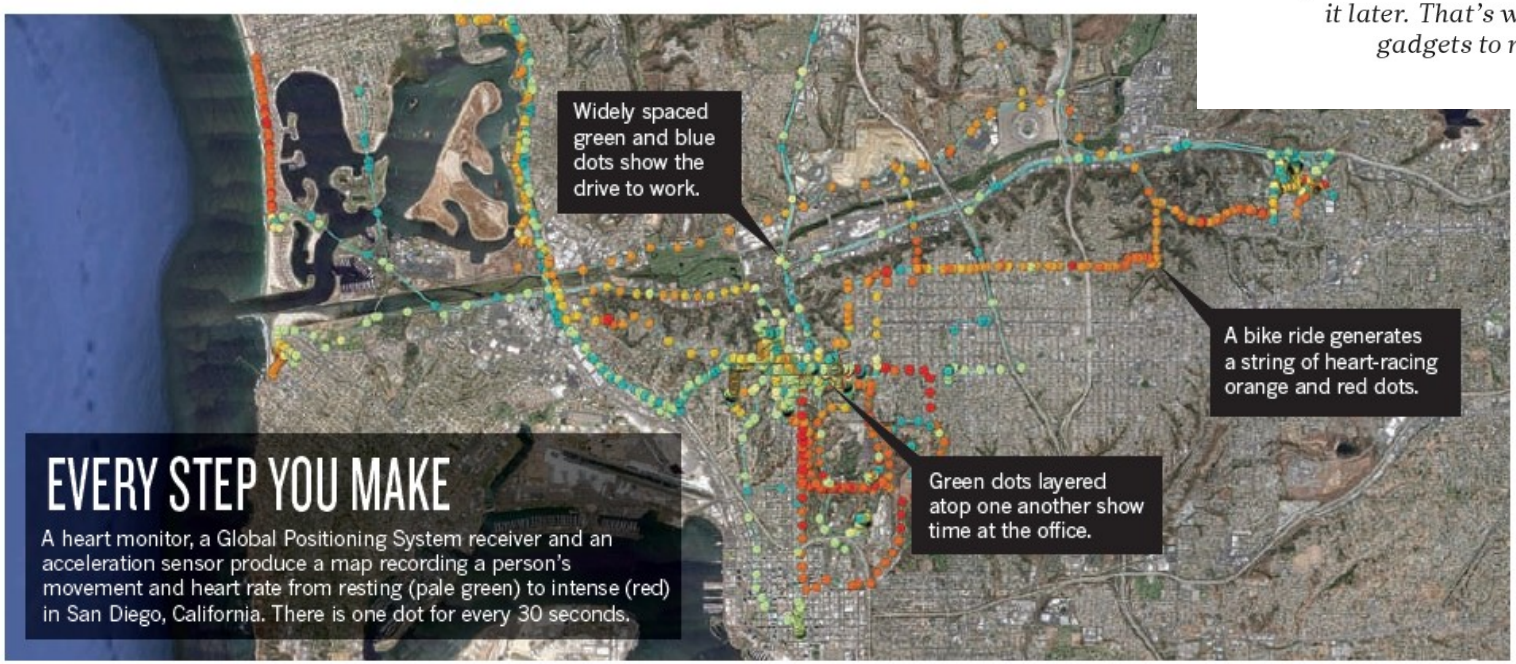
Feb 16, 2011

NEWS FEATURE

EVERY BITE YOU TAKE

If a camera snaps everything you eat, you can't lie about it later. That's why scientists are building high-tech gadgets to measure the human 'exposome'.

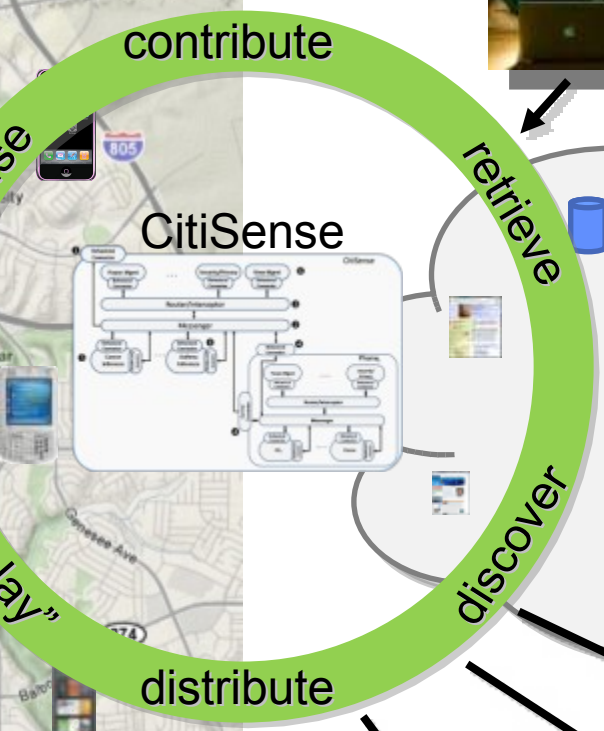
BY BRENDAN BORRELL



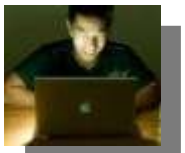
PALMS

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





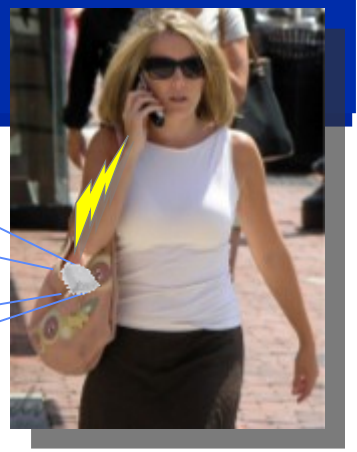
4oz
30 compounds

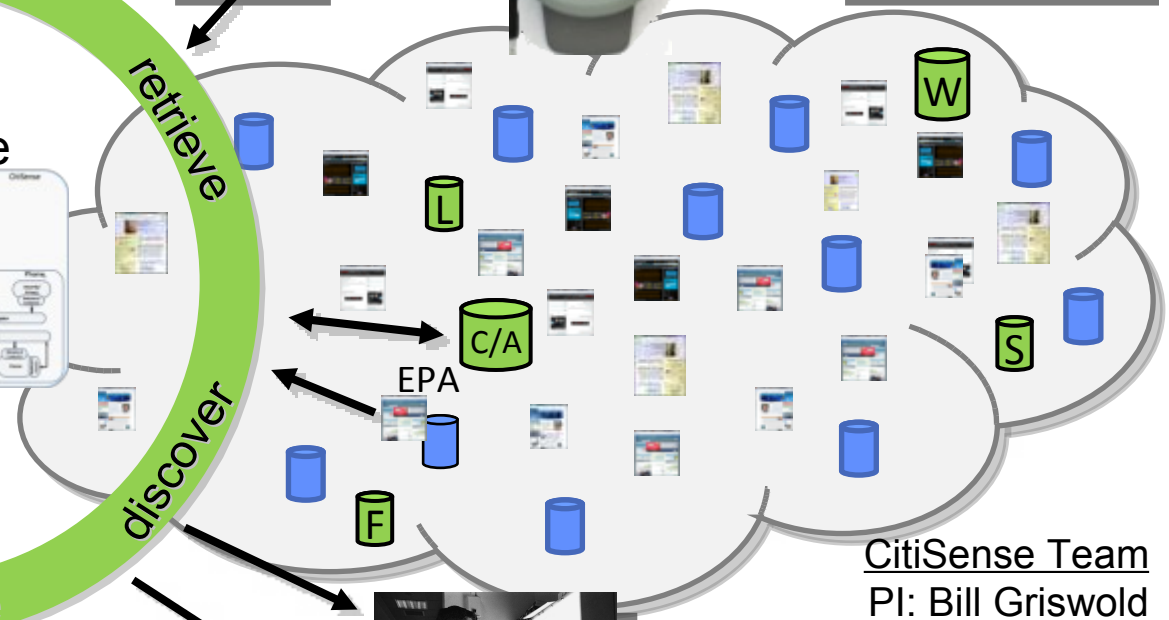


Seacoast Sci.

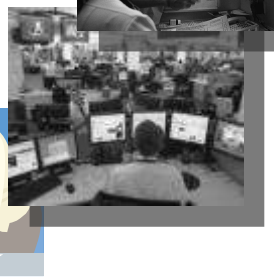


Intel MSP





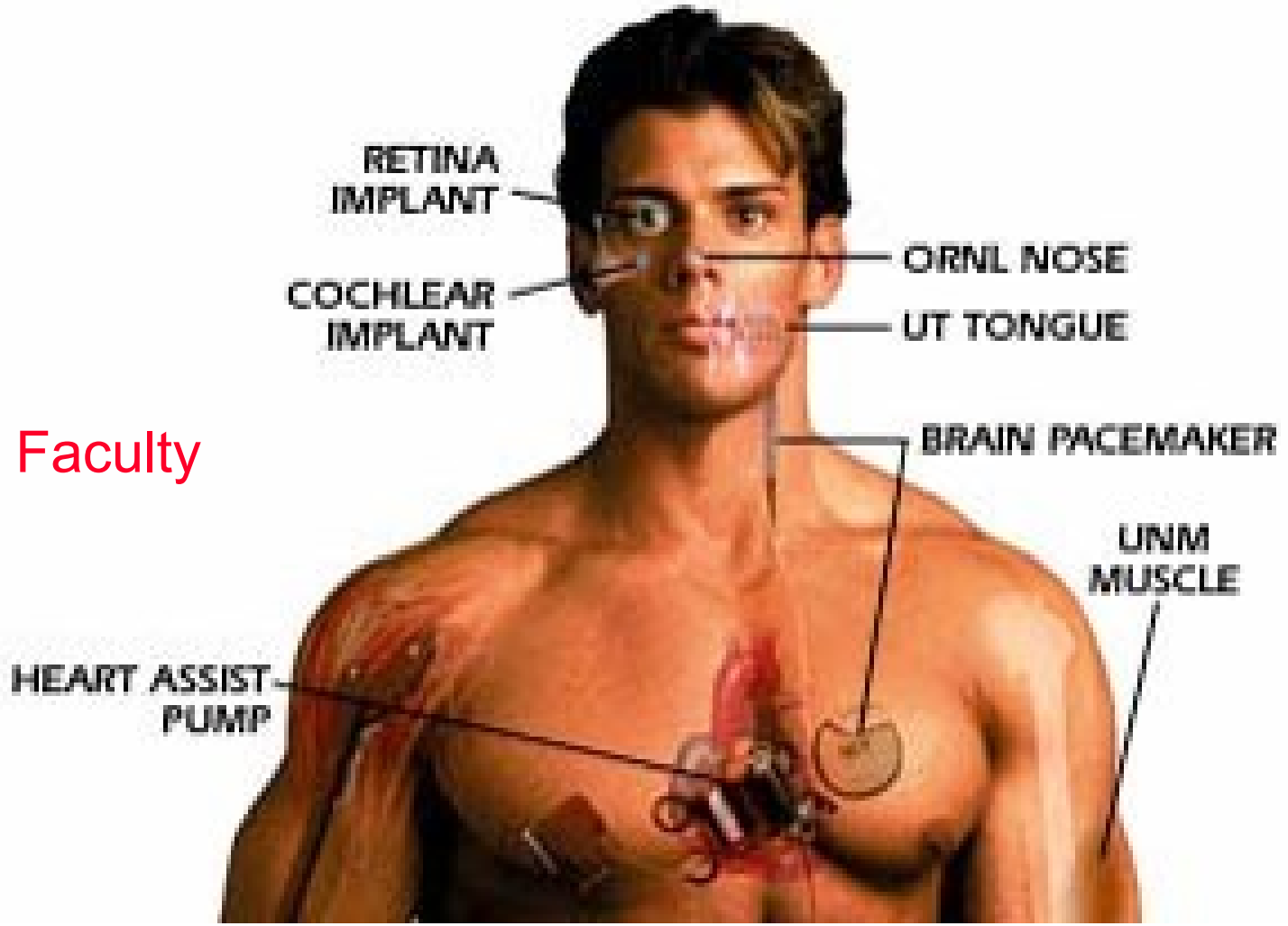




<u>CitiSense Team</u>
PI: Bill Griswold
Ingolf Krueger
Tajana Simunic Rosing
Sanjoy Dasgupta
Hovav Shacham
Kevin Patrick

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

65 UCI Faculty



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lifechips
university of california, irvine
www.lifechips.org

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I am the Future Digital Health Consumer: 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

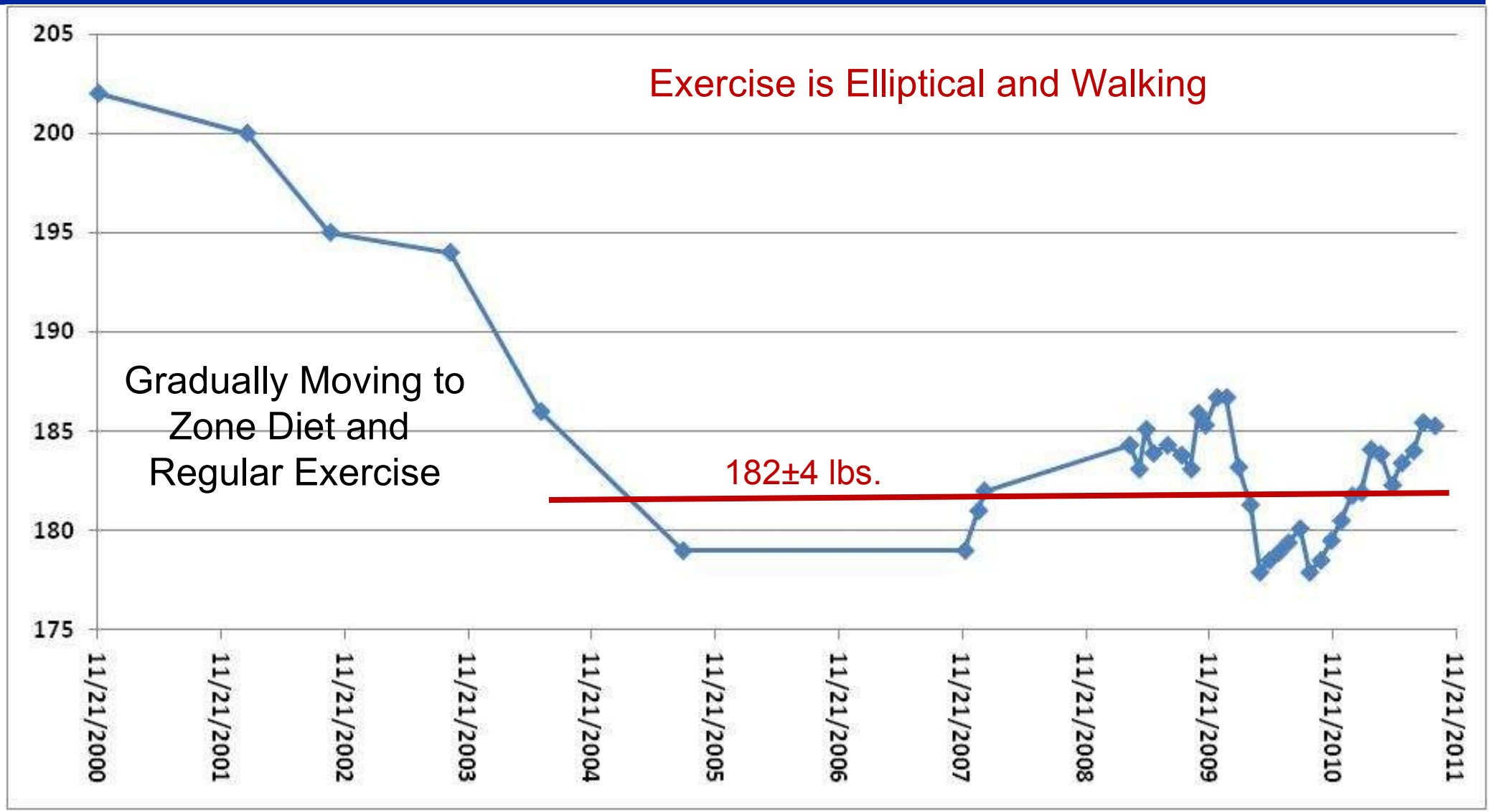
Now the Top Listed Article By Google for "Larry Smarr"

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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

Still Need to Lower Sugar &
Increase Protein and Decrease Fat by 15%

- **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

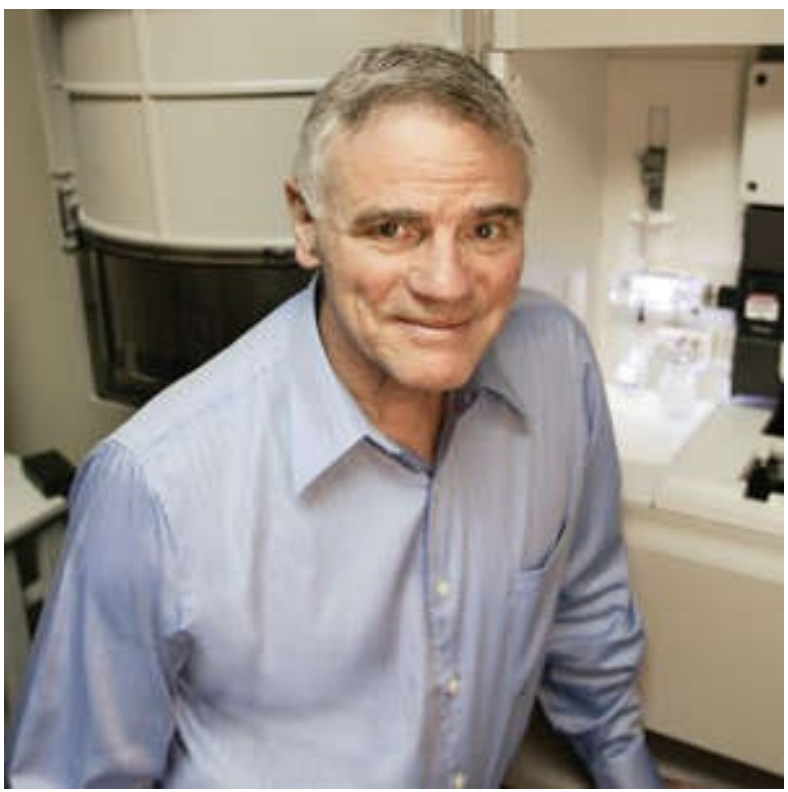
Newsweek

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



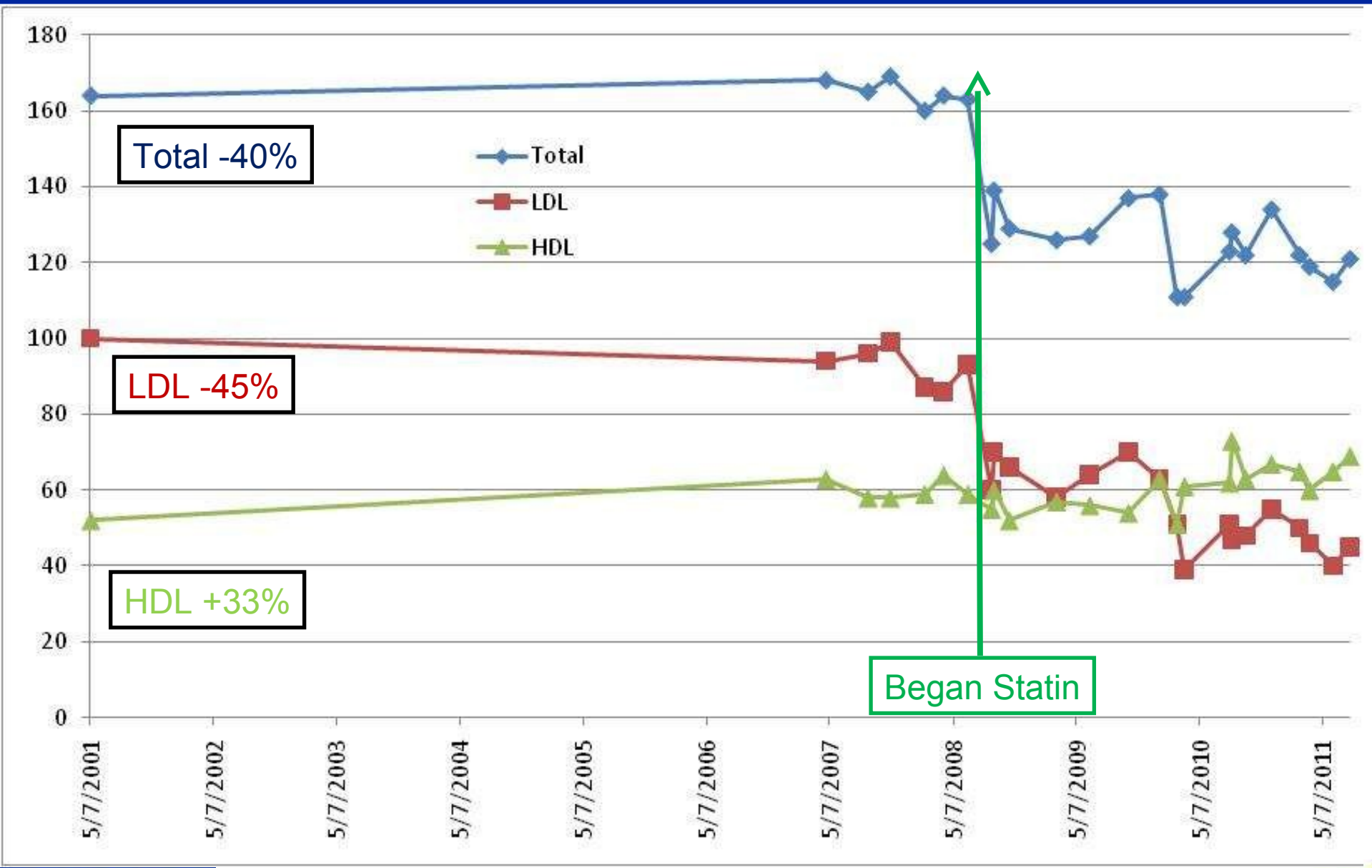
Quantify ~2500 Blood Proteins,
50 Each from 50 Organs or Cell Types
from a Single Drop of Blood
To Create a Time Series

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

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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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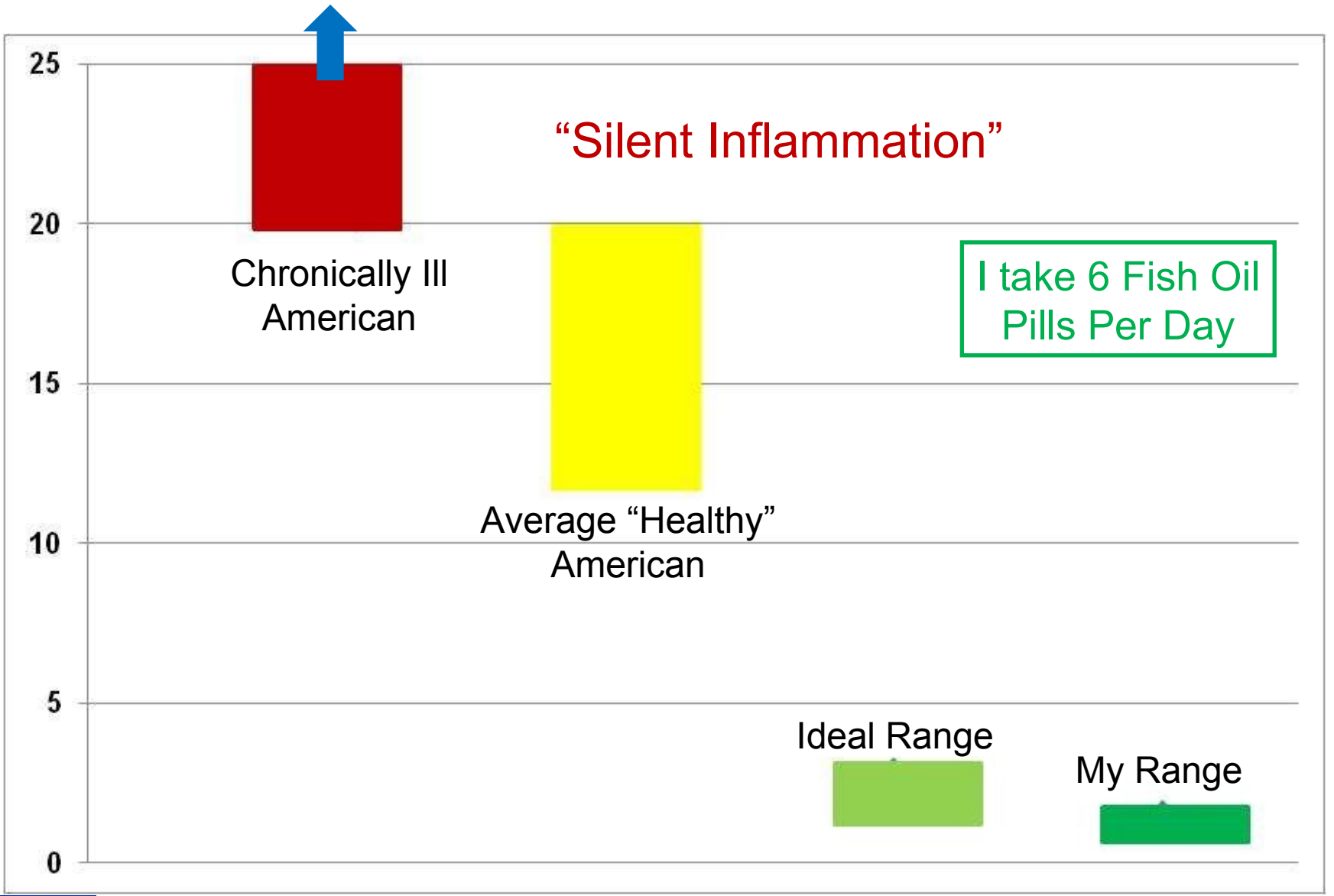
Goal: Lower Triglycerides and Cholesterol Ratios to Reduce Future Risk of Diabetes and Heart Disease

- **TG**
  - **High Risk 200-500**
  - **Best <150**
  - **My TG ~35**
- **TG/HDL**
  - **Ratio>4 Are Pre-Diabetic or Have Type 2 Diabetes**
  - **Average American Has a Ratio of ~3.3**
  - **My Ratio 0.5**

"The Ratio of Triglycerides to HDL Cholesterol (TG/HDL-C) is the Single Most Powerful Lipid Predictor of Extensive Coronary Disease."
[Clinics 2008; v.64: 427-432]

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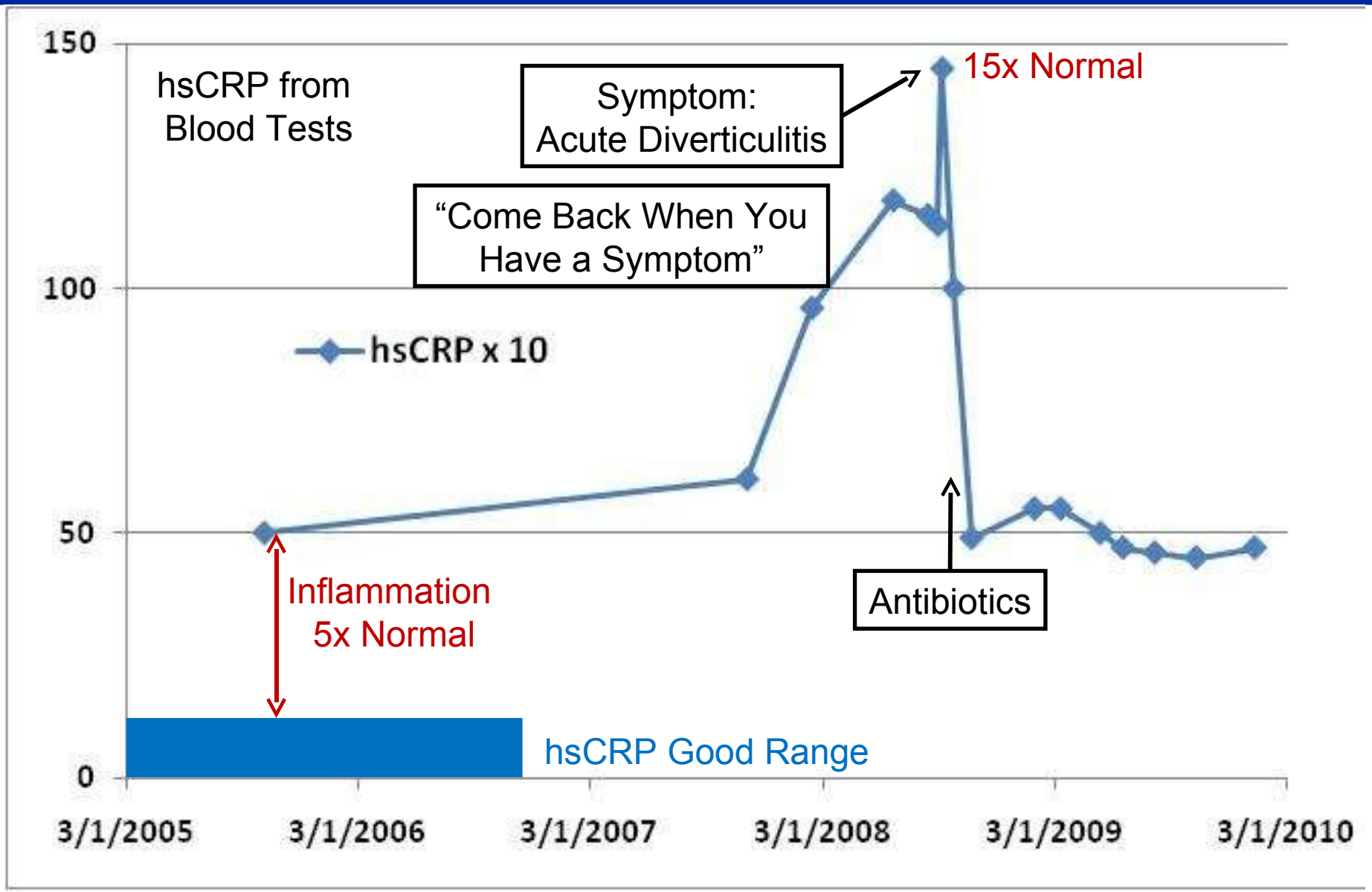
Blood Tests I Do Quarterly to Annually In Addition to Lipids & Omegas

- **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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it2

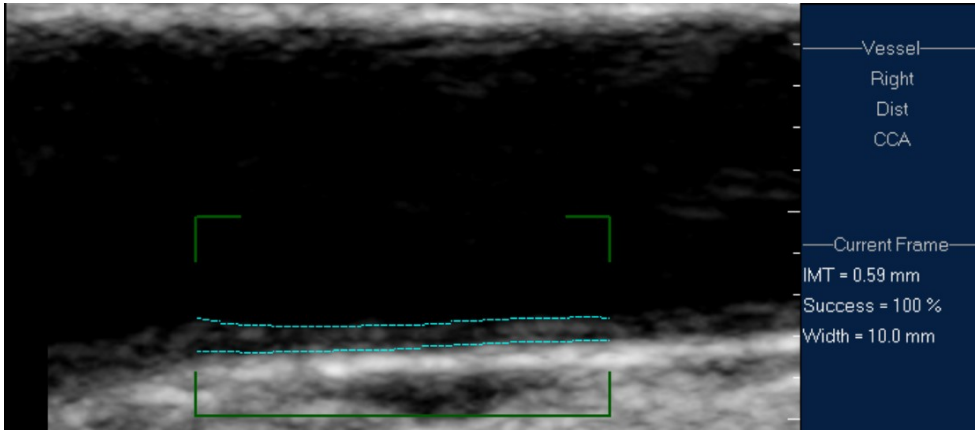
But, In Spite of My High Levels of Omega-3s, Blood Measurements Show Chronic Inflammation

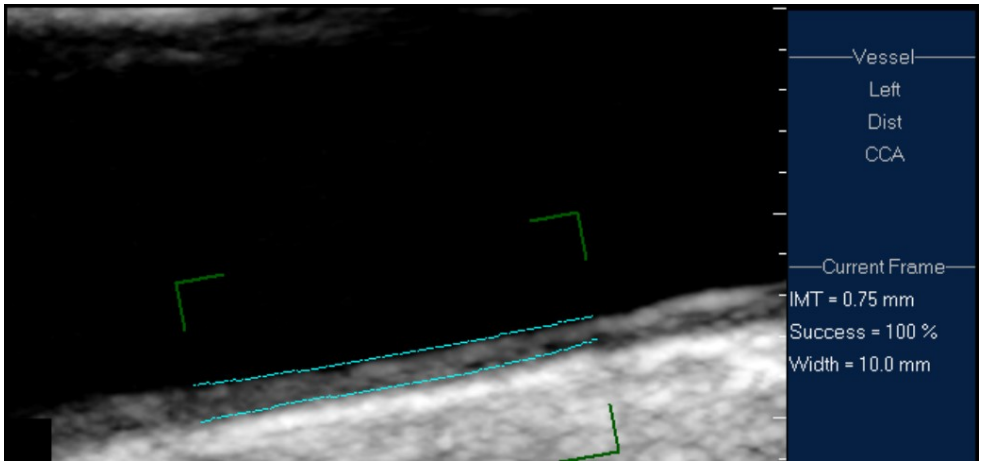


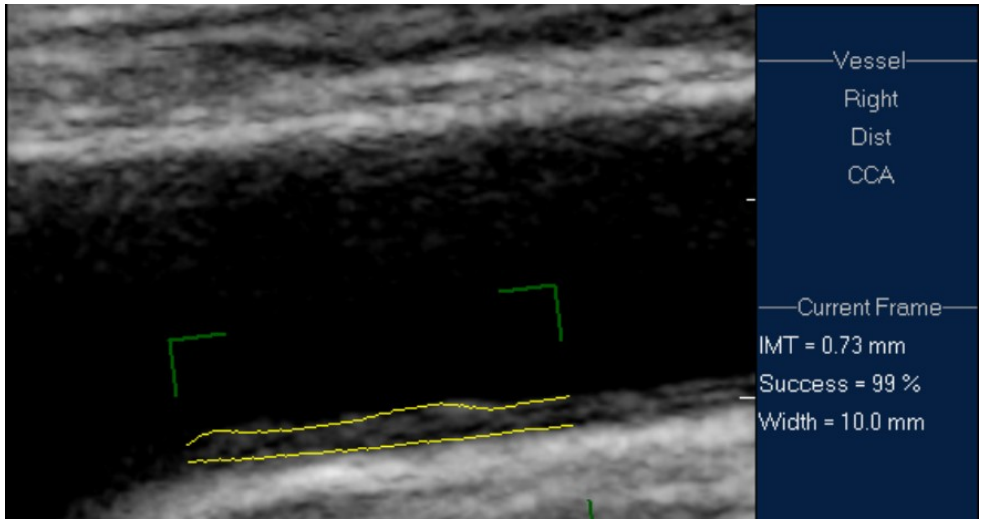
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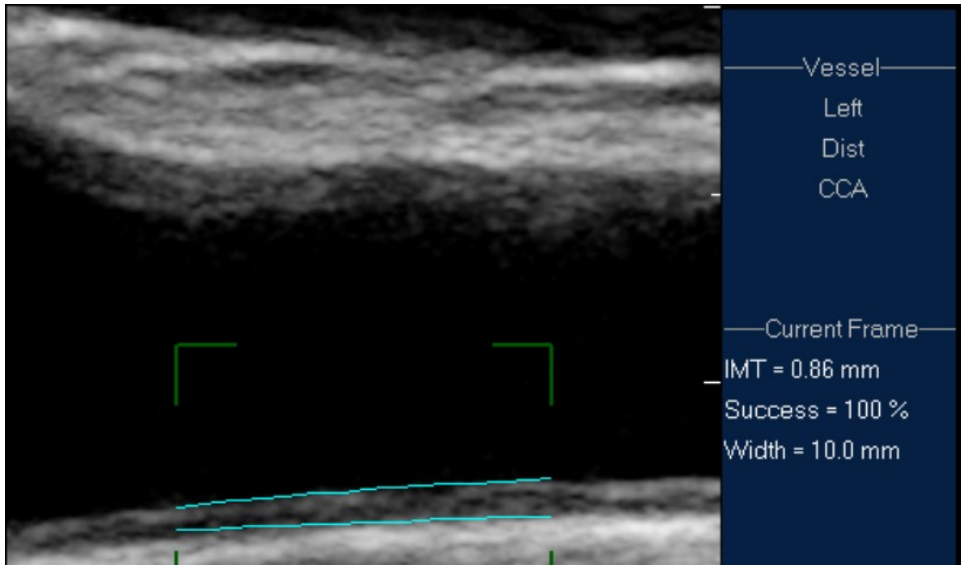
Carotid Artery Ultrasound Reveals Plaque Thickness Significantly Increasing In Just Two Years

Oct 31 2008









October 14, 2010

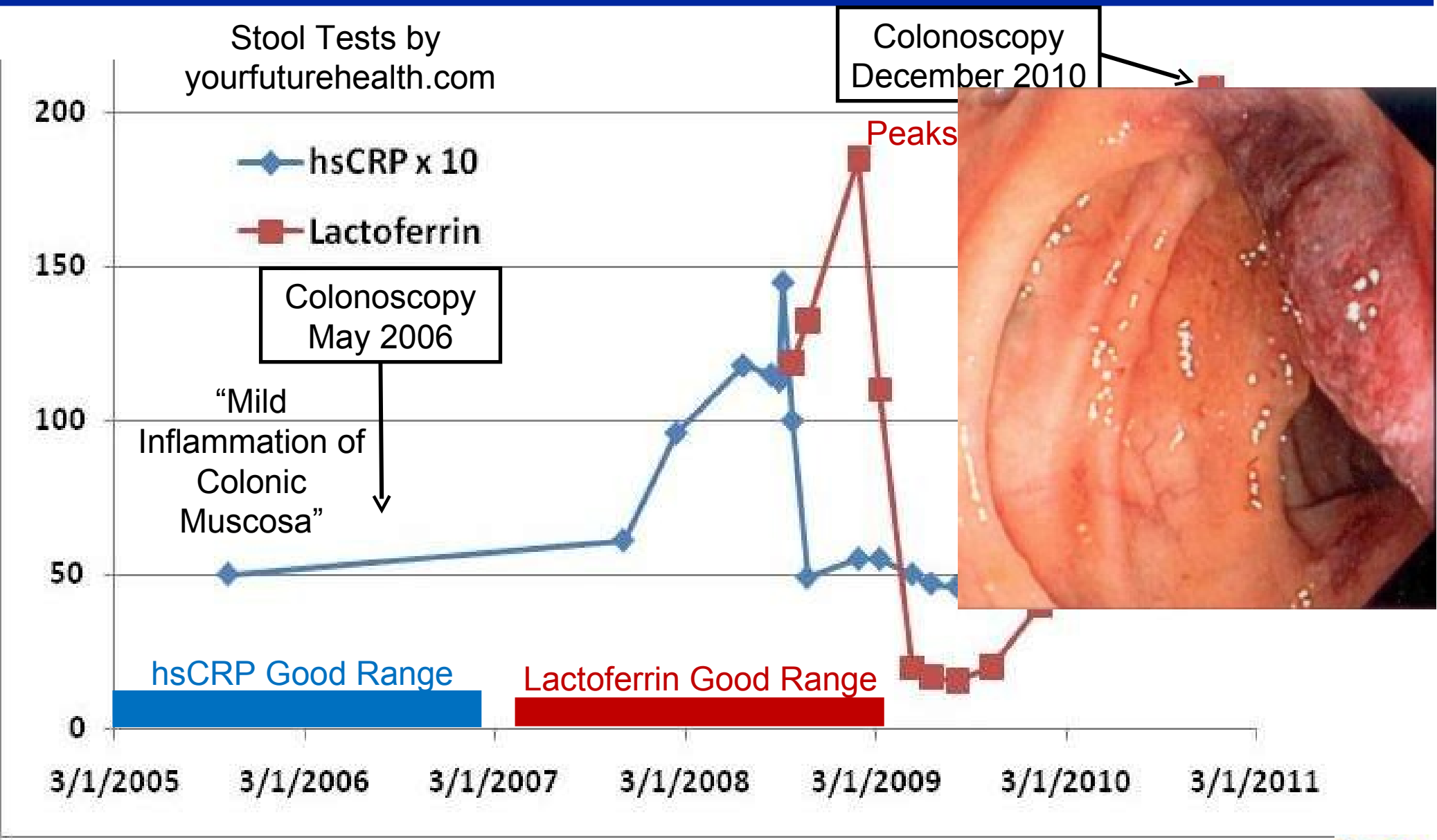
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Right 0.59 to 0.73mm
24% Thicker Plaque

Left 0.75 to 0.84 mm
12% Thicker Plaque

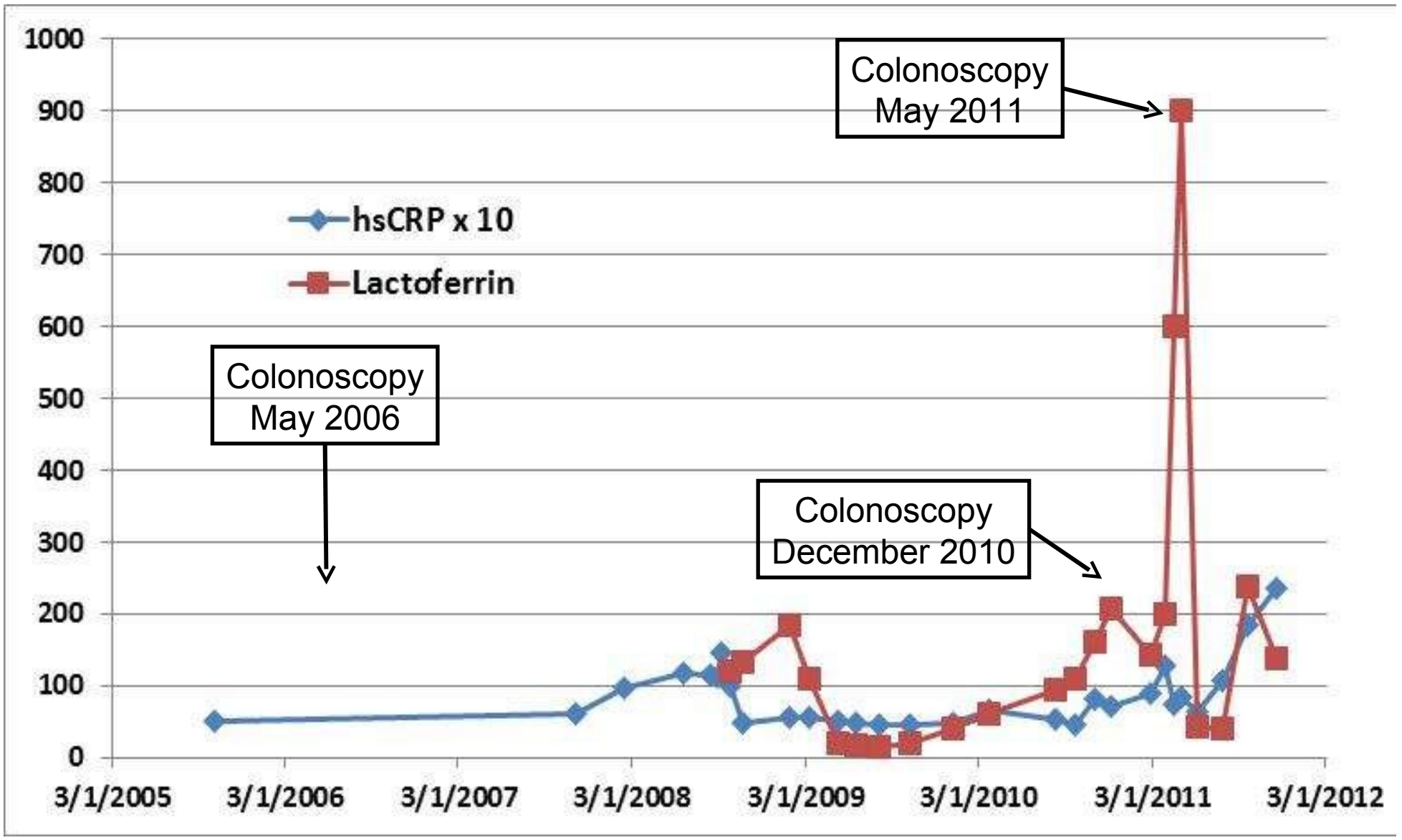
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Measuring Stool and Blood Markers Revealed Episodic Inflammation Peaks of CRP and Lactoferrin



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



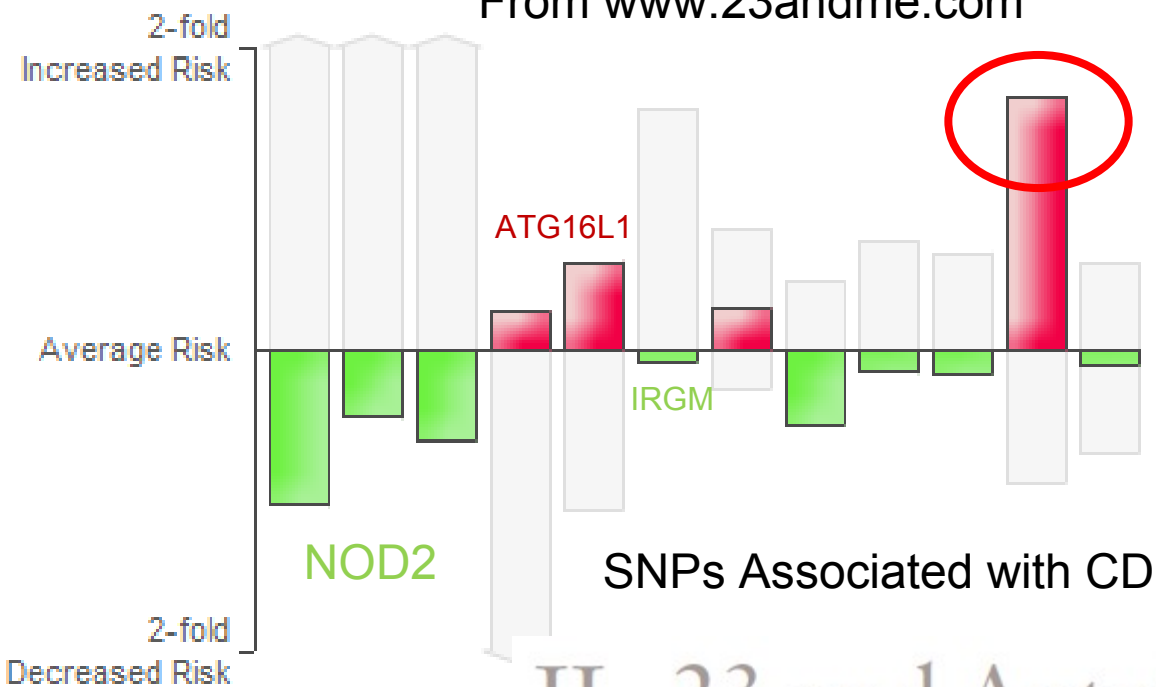
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Biopsies and Lactoferrin Values Confirm CD

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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]

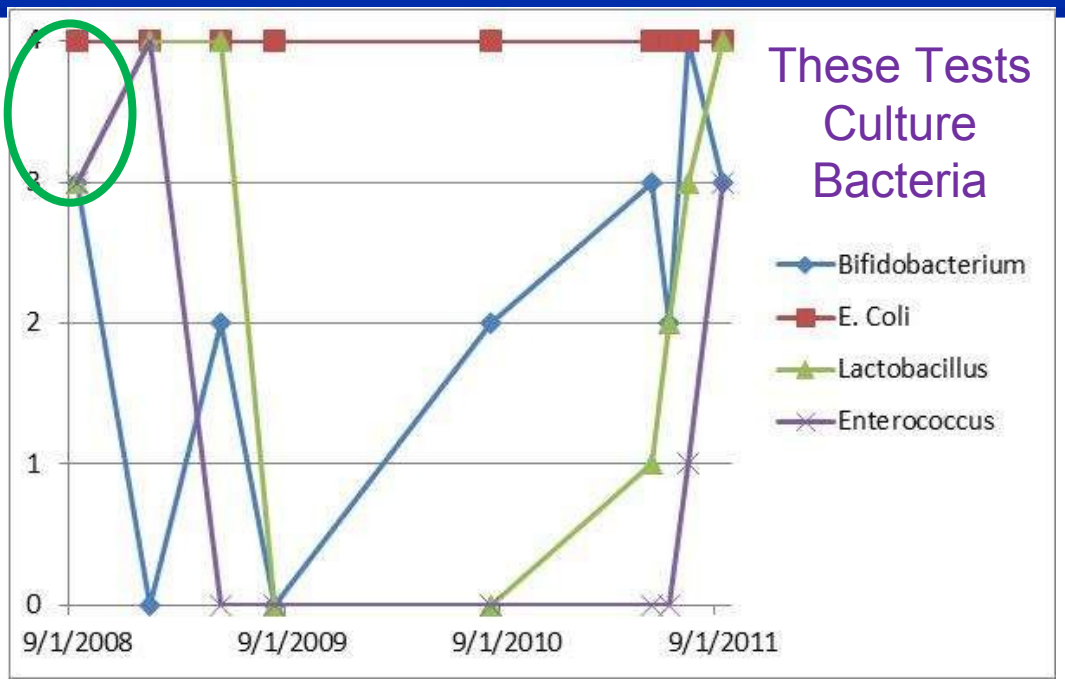
Section of Digestive Diseases, Departments of [1]Medicine and [2]Genetics, Yale University,

2009

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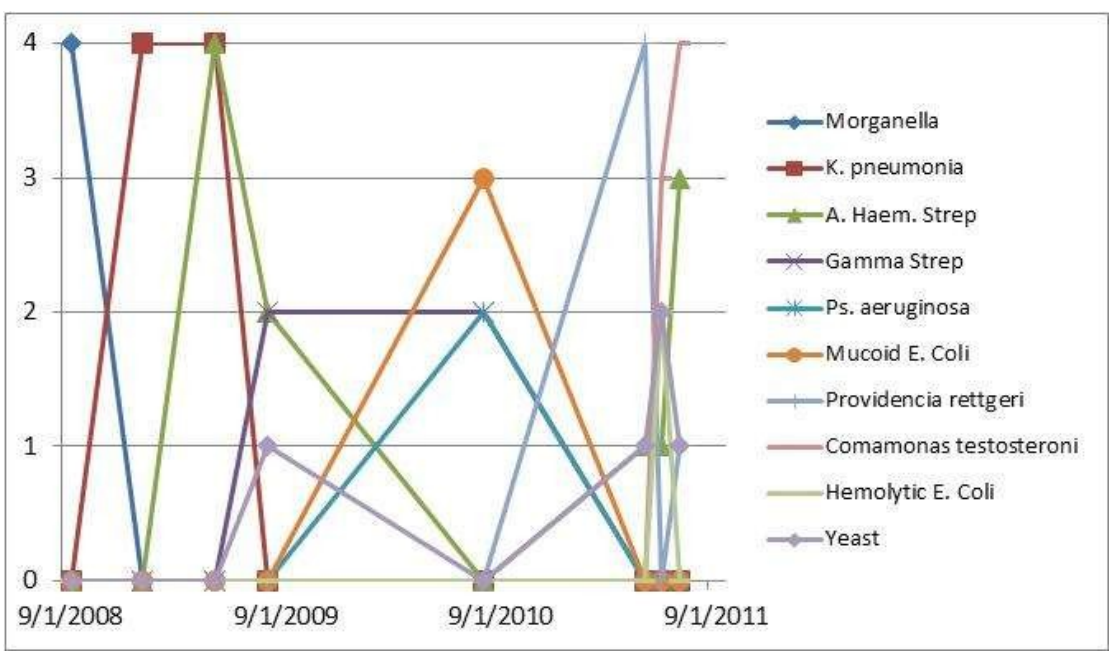
Antibiotics Are Highly Disruptive of Colon Microbiome--Takes 3-4 Years to Recover

All 3+ or 4+ Three Weeks Before Taking Antibiotics



"Good" Microbes

Three Years After 10 Days of Antibiotics Levaquin & Metronidaloze



Next Step Get DNA Microbe Metagenomics, Parasite, Yeast Test

"Bad" Microbes

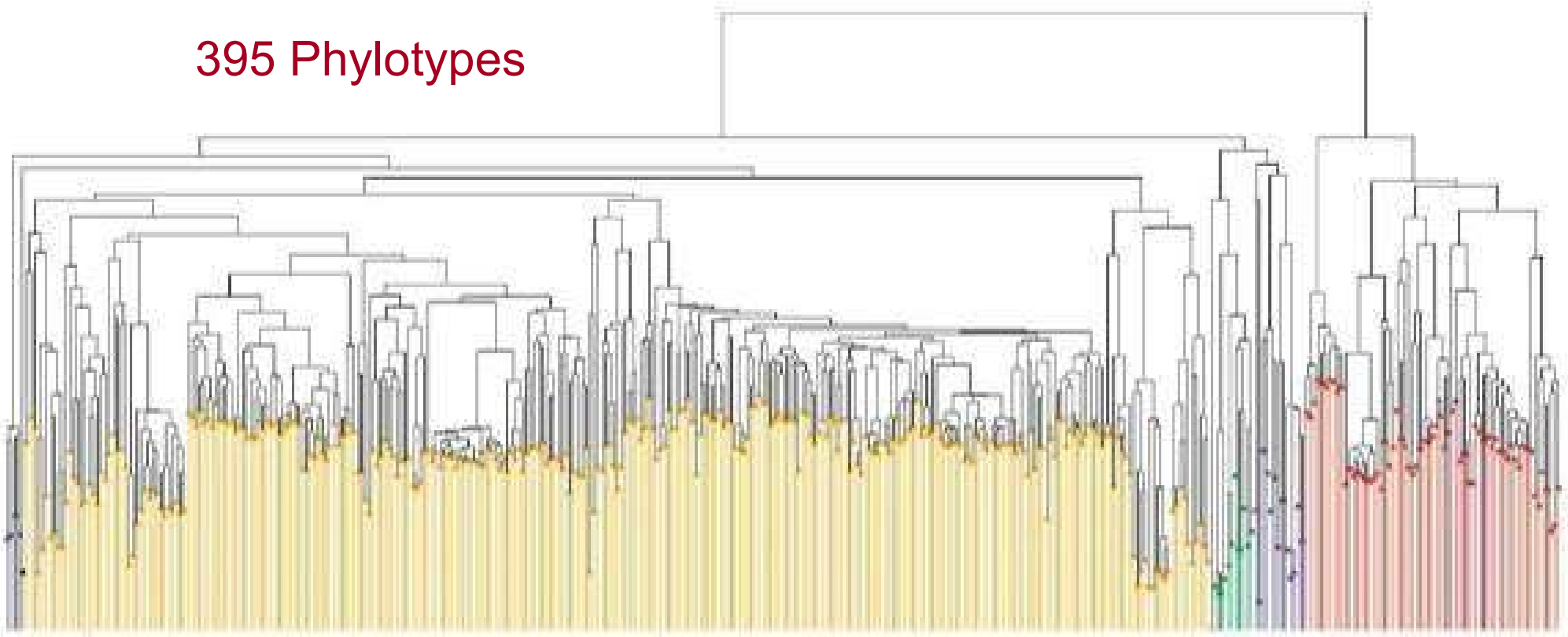
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The Human Microbiome is the Next Large NIH Drive to Understand Human Health and Disease

- **"A majority of the bacterial sequences corresponded to uncultivated species and novel microorganisms."**
- **"We discovered significant inter-subject variability."**
- **"Characterization of this immensely diverse ecosystem is the first step in elucidating its role in health and disease."**

395 Phylotypes

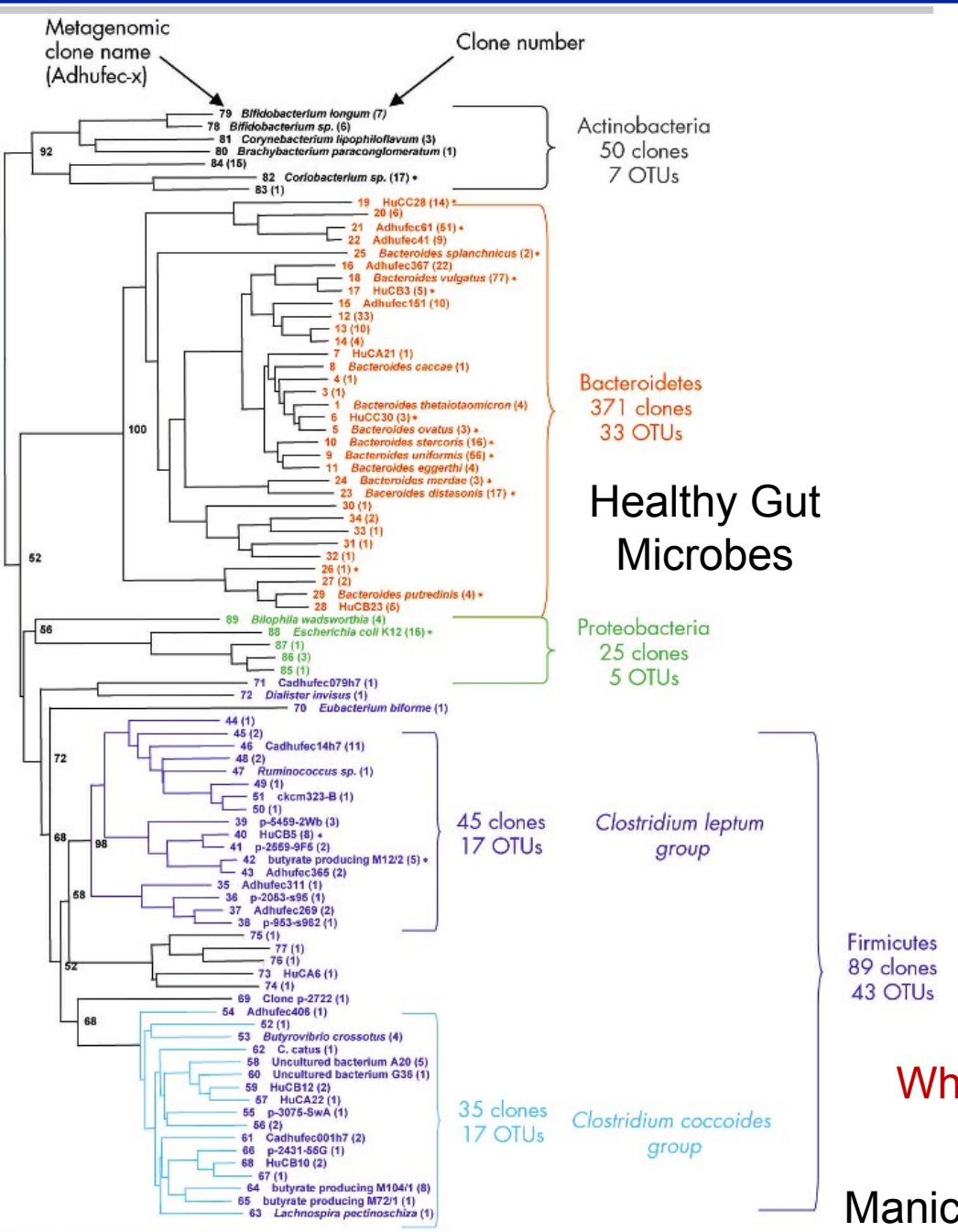


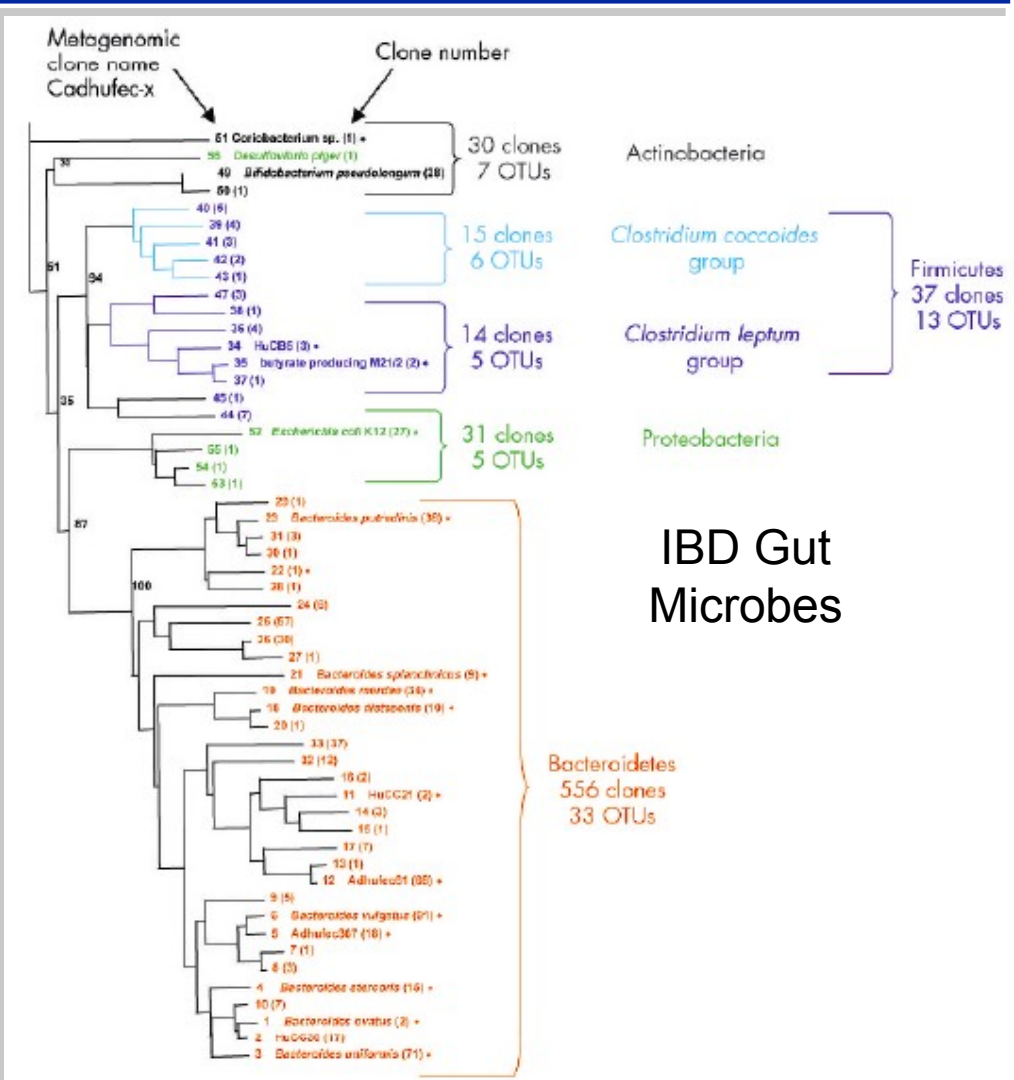
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"Diversity of the Human Intestinal Microbial Flora"
Paul B. Eckburg, et al *Science* (10 June 2005)

it²

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



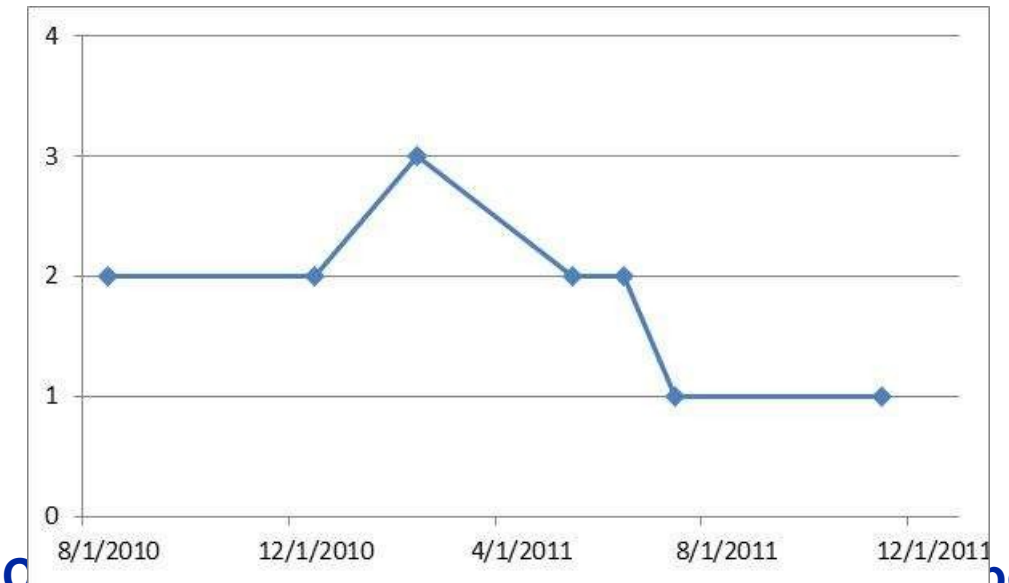


While Bacteroidetes Species Count is the Same

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

My Warning Signs From Cultured Microbes of IBD

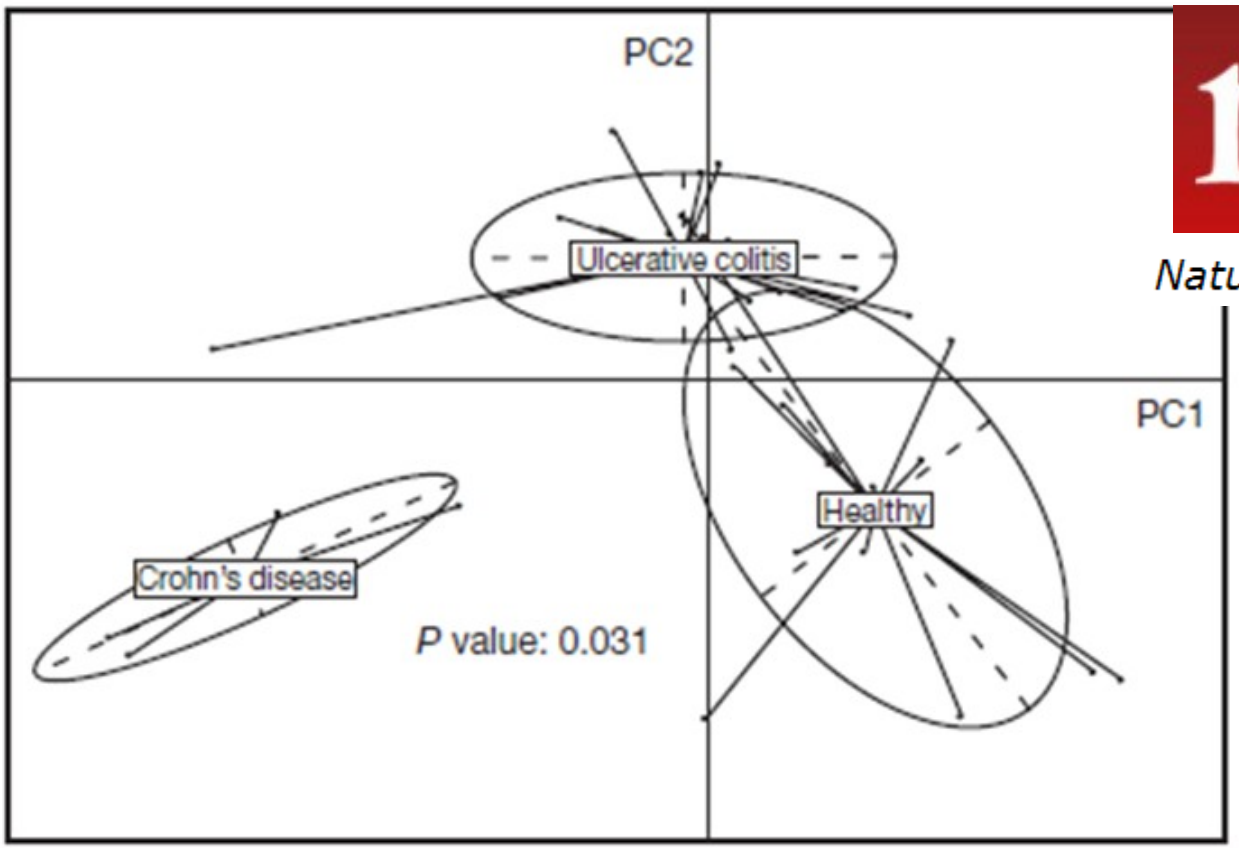
- **Clostridia Species Dropping to Low Values**



  - **Clostridia are the bacteria 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 Are 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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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],

To Understand Causes of IBD, One Needs to Look at Interplay of Genes and Colonic Microbes

Associations between IBD and genes that regulate microbial recognition and innate immune pathways indicate the important roles of host-microbe interactions in regulating intestinal immune homeostasis.

There is increasing evidence that intestinal microbes influence host immune development, immune responses, and susceptibility to human diseases such as IBD, diabetes mellitus, and obesity.

Interactions Between the Host Innate Immune System and Microbes in Inflammatory Bowel Disease

GASTROENTEROLOGY 2011;140:1729–1737



Clara Abraham*



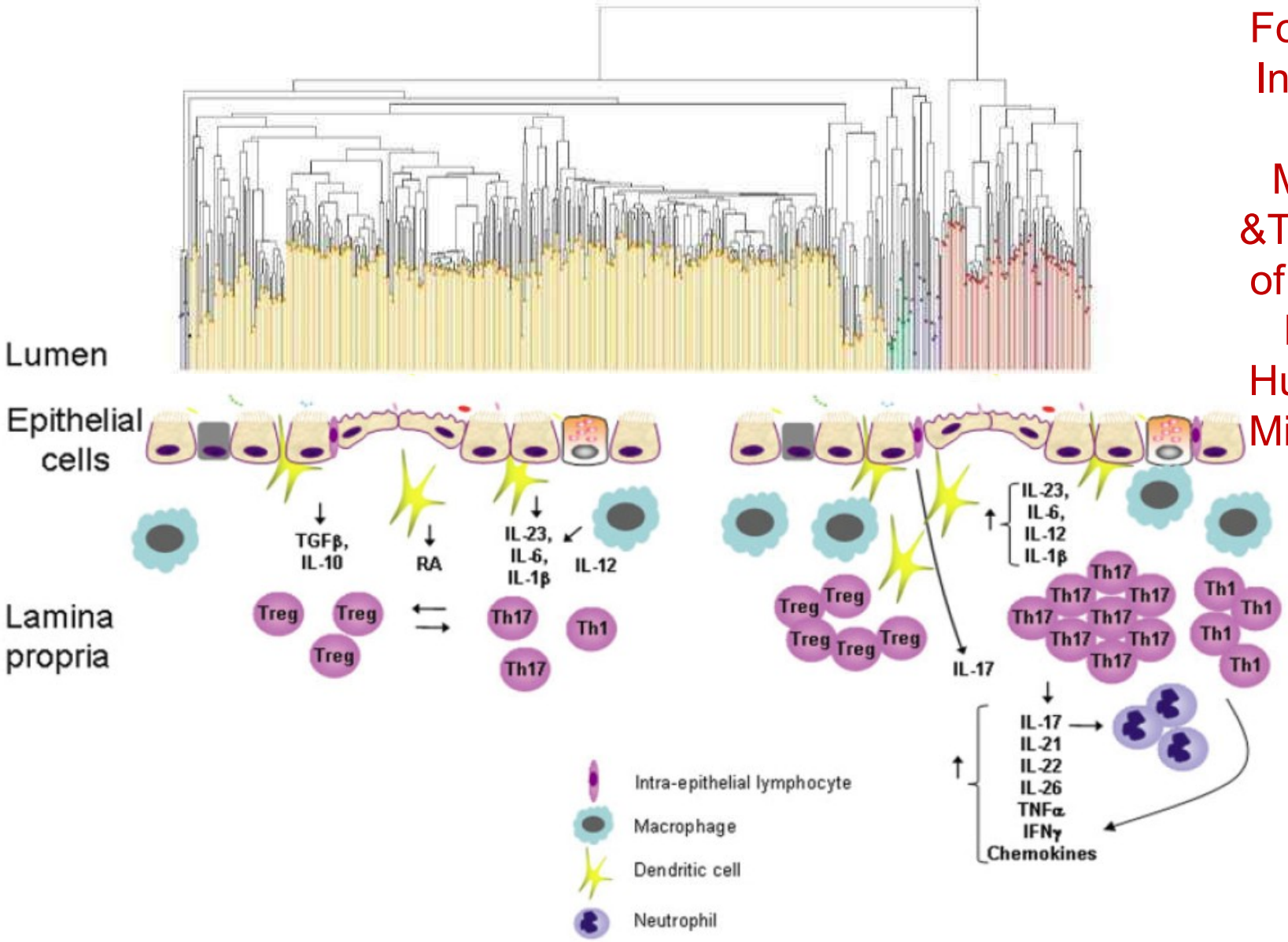
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Understanding Autoimmune Diseases Will Require Complete Genomes, Microbial Metagenomics Over Populations



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

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

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