"Observing the Dynamics of the Human Immune System Coupled to the Microbiome in Health and Disease"

CASIS Workshop on Biomedical Research Aboard the ISS

Columbia University

New York City, NY

May 28, 2014

Dr. Larry Smarr

Director, California Institute for Telecommunications and Information Technology

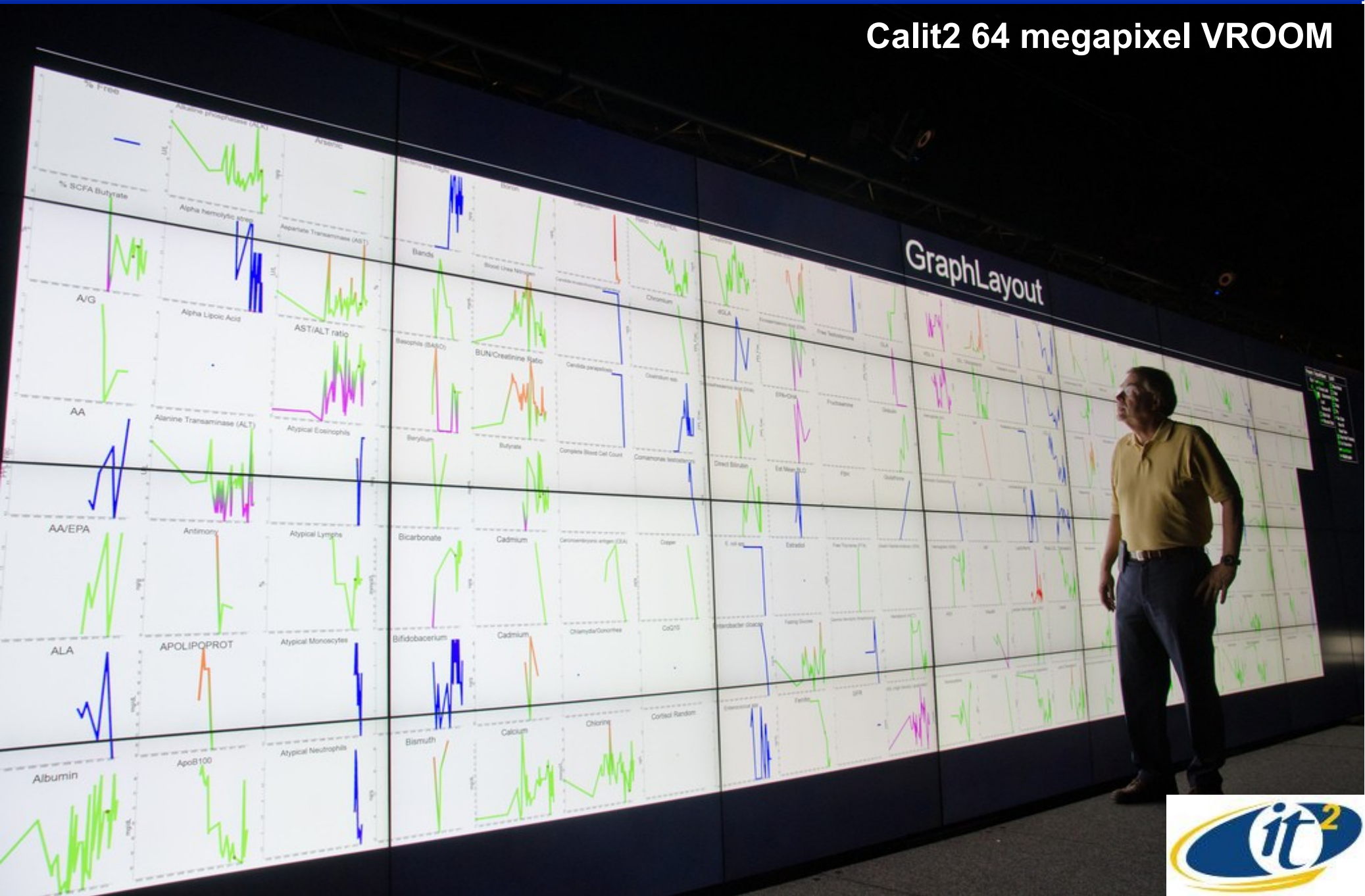
Harry E. Gruber Professor,

Dept. of Computer Science and Engineering

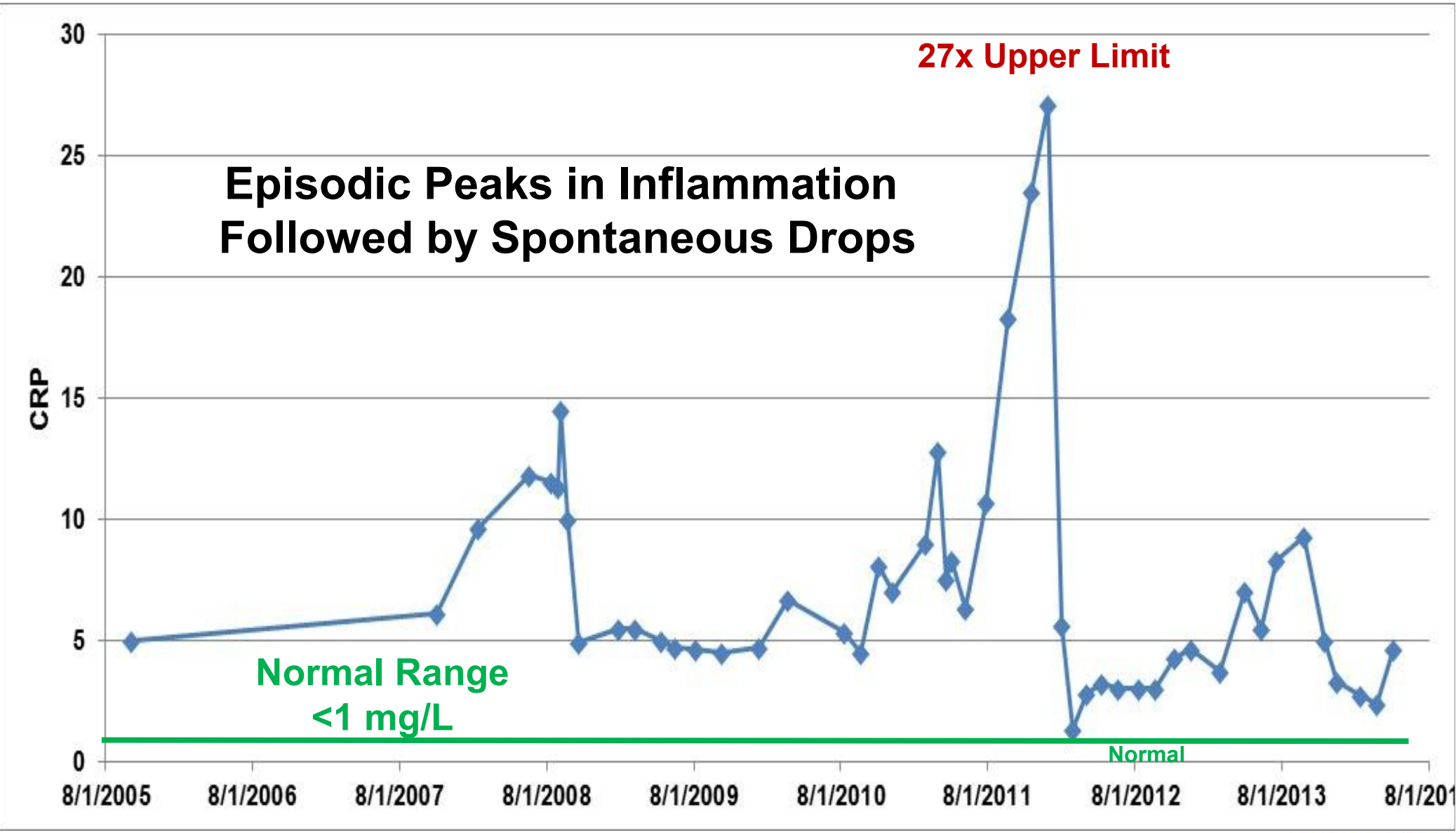
Jacobs School of Engineering, UCSD

http://lsmarr.calit2.net

Visualizing 5-10 Year Time Series of 150 Blood & Stool Variables Led Me to Discover a Chronic Disease

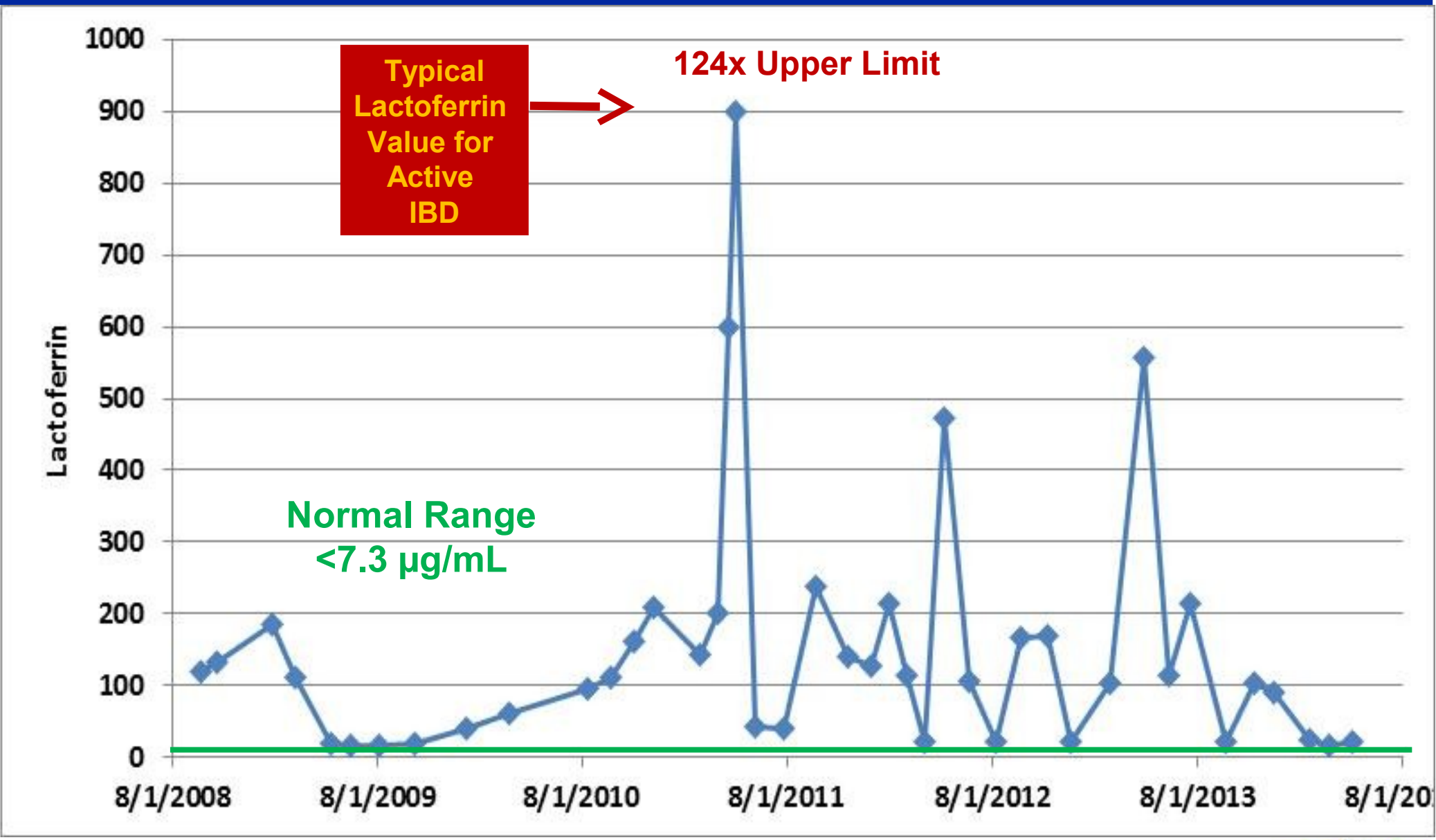


Only One of My Blood Measurements Was Far Out of Range--Indicating Chronic Inflammation



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

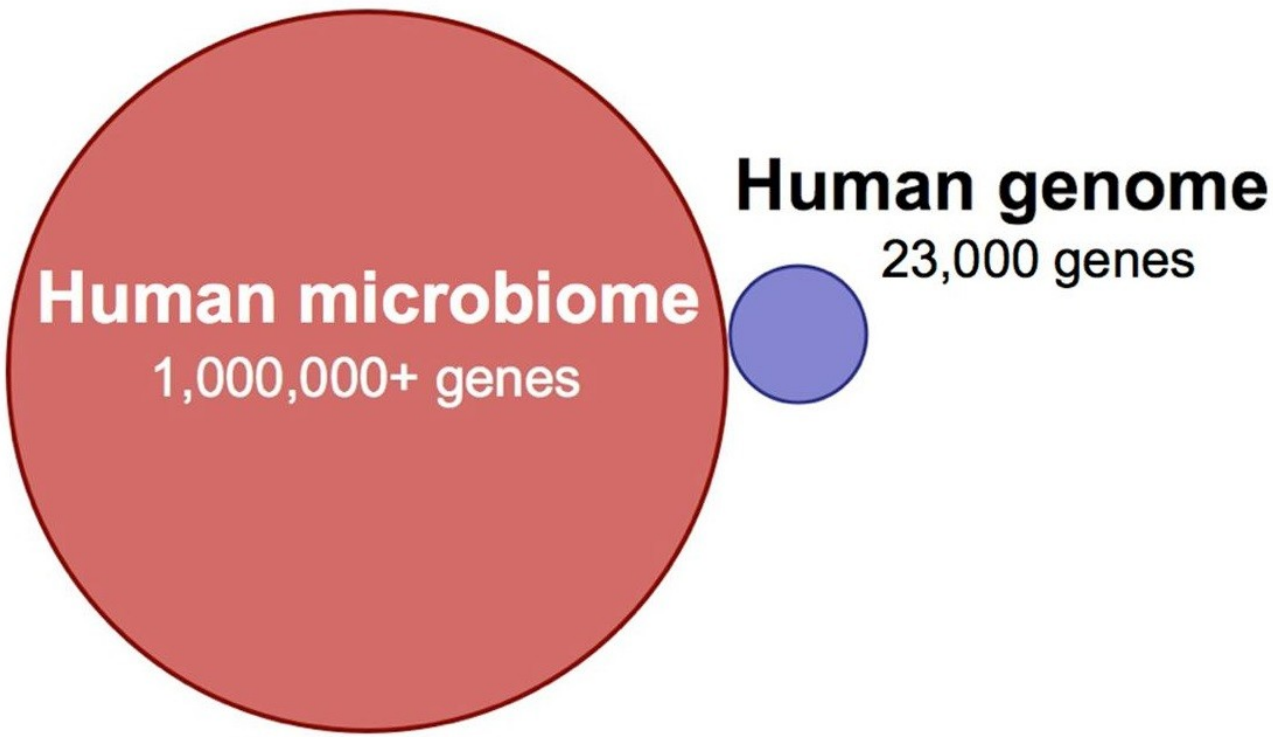
But by Using Stool Analysis Time Series, I Discovered I Had Oscillating Immune Variables Far Above Normal



Lactoferrin is a Protein Shed from Neutrophils -
An Immune System Antibacterial that Sequesters Iron

The Natural Partner in the Oscillating Immune System Would Be The Gut Microbiome Ecology

Your Body Has 10 Times As Many Microbe Cells As Human Cells



99% of Your DNA Genes Are in Microbe Cells Not Human Cells

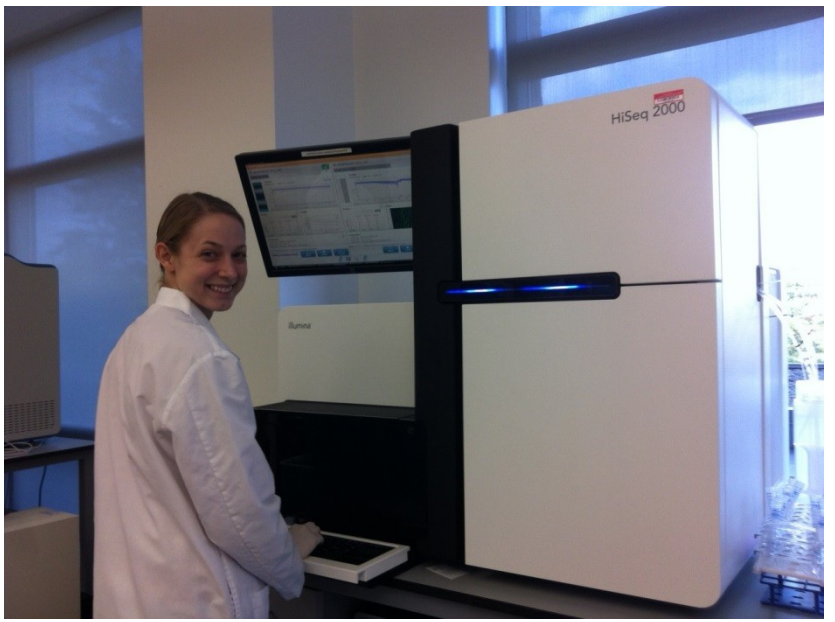
Inclusion of the Microbiome Will Radically Change Medicine

J. Craig Venter™ INSTITUTE

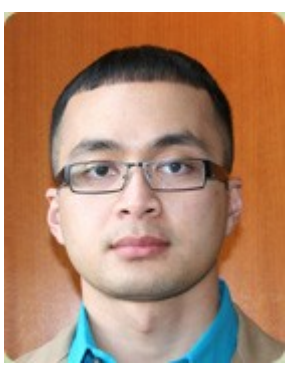
it²

To Map Out the Dynamics of My Microbiome Ecology I Partnered with the J. Craig Venter Institute

- JCVI Did Metagenomic Sequencing on Seven of My Stool Samples Over 1.5 Years
- Sequencing on Illumina HiSeq 2000
  - Generated 200 Million 100bp Reads
- JCVI Lab Manager, Genomic Medicine
  - Manolito Torralba
- IRB PI Karen Nelson
  - President JCVI



Illumina HiSeq 2000 at JCVI



Manolito Torralba, JCVI



Karen Nelson, JCVI

J. Craig Venter INSTITUTE

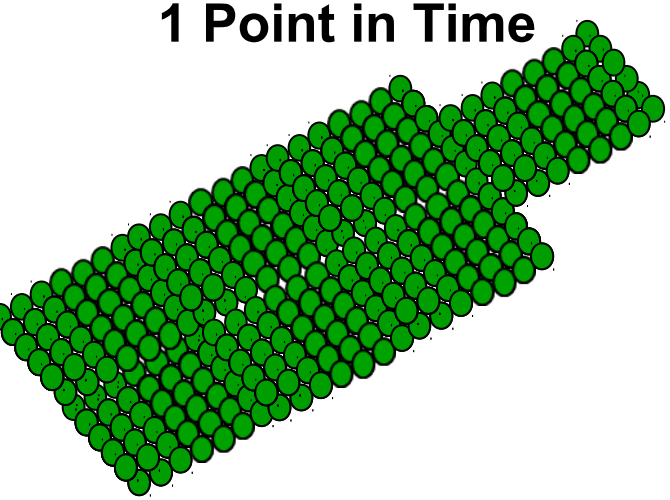
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We Downloaded Additional Gut Microbiomes from NIH HMP For Comparative Analysis

From Sequences to Bacterial Species Relative Abundance Required 25 CPU-Years at San Diego Supercomputer Center

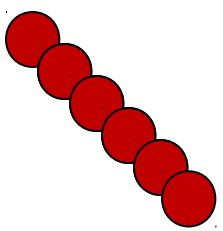
"Healthy" Individuals

250 Subjects
1 Point in Time



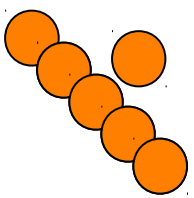
Larry Smarr

6 Points in Time

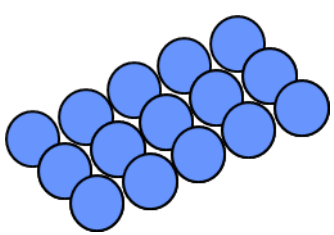


IBD Patients

2 Ulcerative Colitis Patients,
6 Points in Time



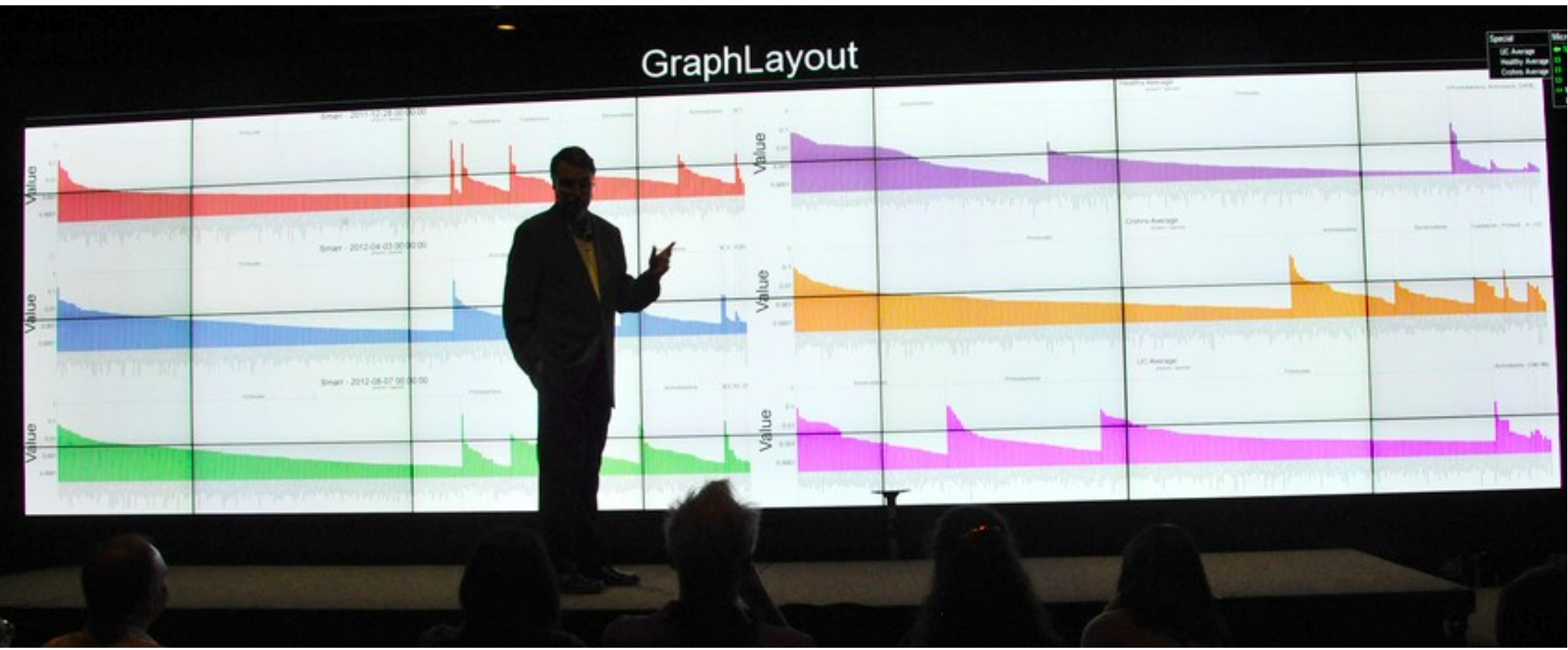
5 Ileal Crohn's Patients,
3 Points in Time



Total of 27 Billion Reads
Or 2.7 Trillion Bases

Source: Jerry Sheehan, Calit2
Weizhong Li, Sitao Wu, CRBS, UCSD

Using Scalable Visualization Allows Comparison of the Relative Abundance of 200 Gut Microbe Species

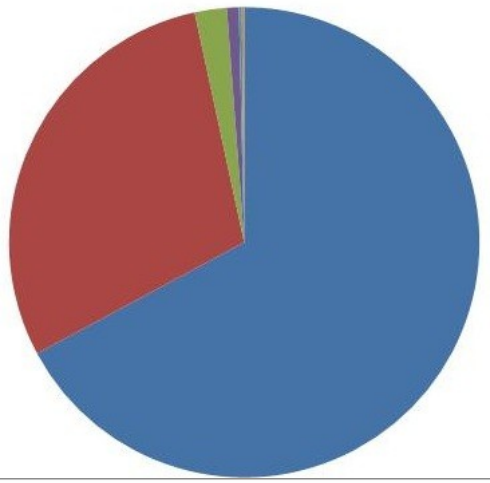


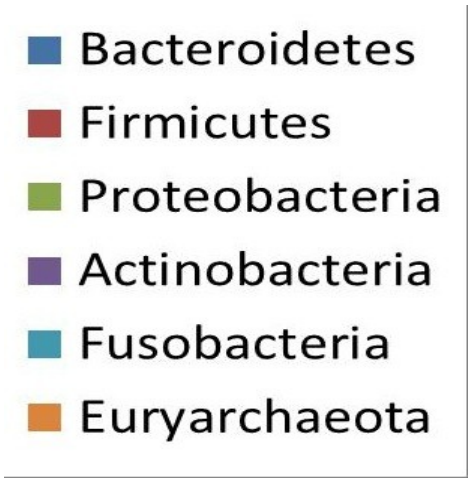
Comparing 3 LS Time Snapshots (Left)
with Healthy, Crohn's, UC (Right Top to Bottom)

Calit2 VROOM-FuturePatient Expedition

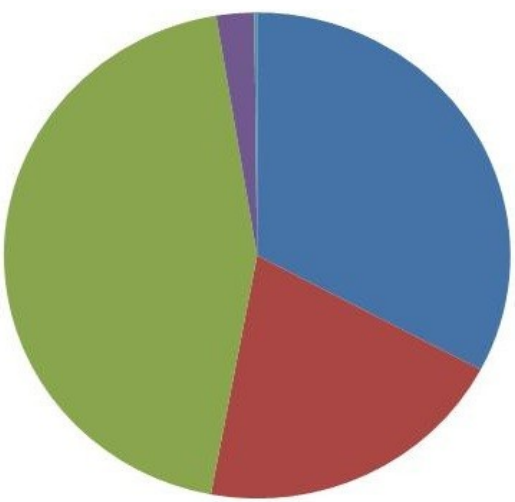
We Found Major Shifts in Microbial Ecology Between Healthy and Two Forms of IBD

Ave. Healthy



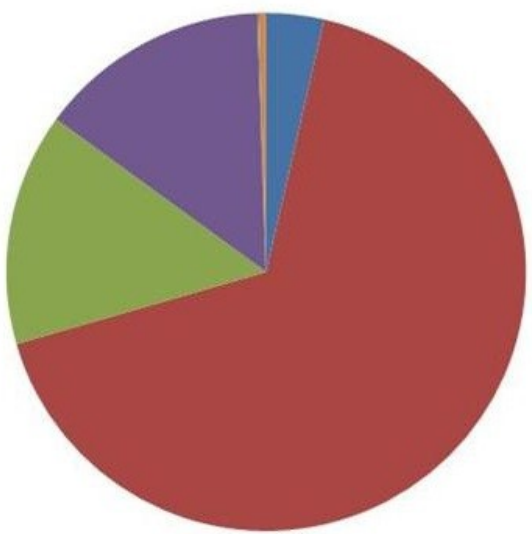


Ave. Ulcerative Colitis



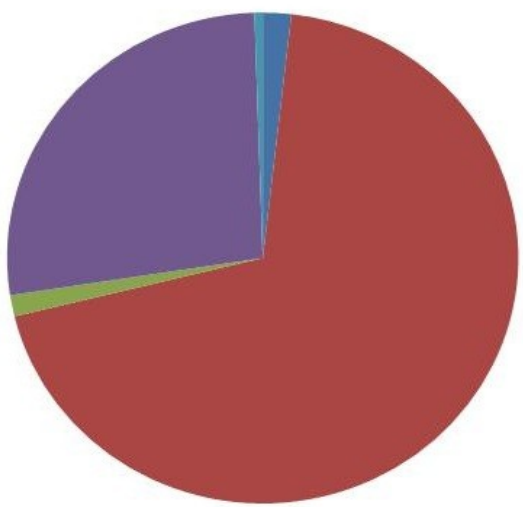
Explosion of Proteobacteria

LS Apr 2012



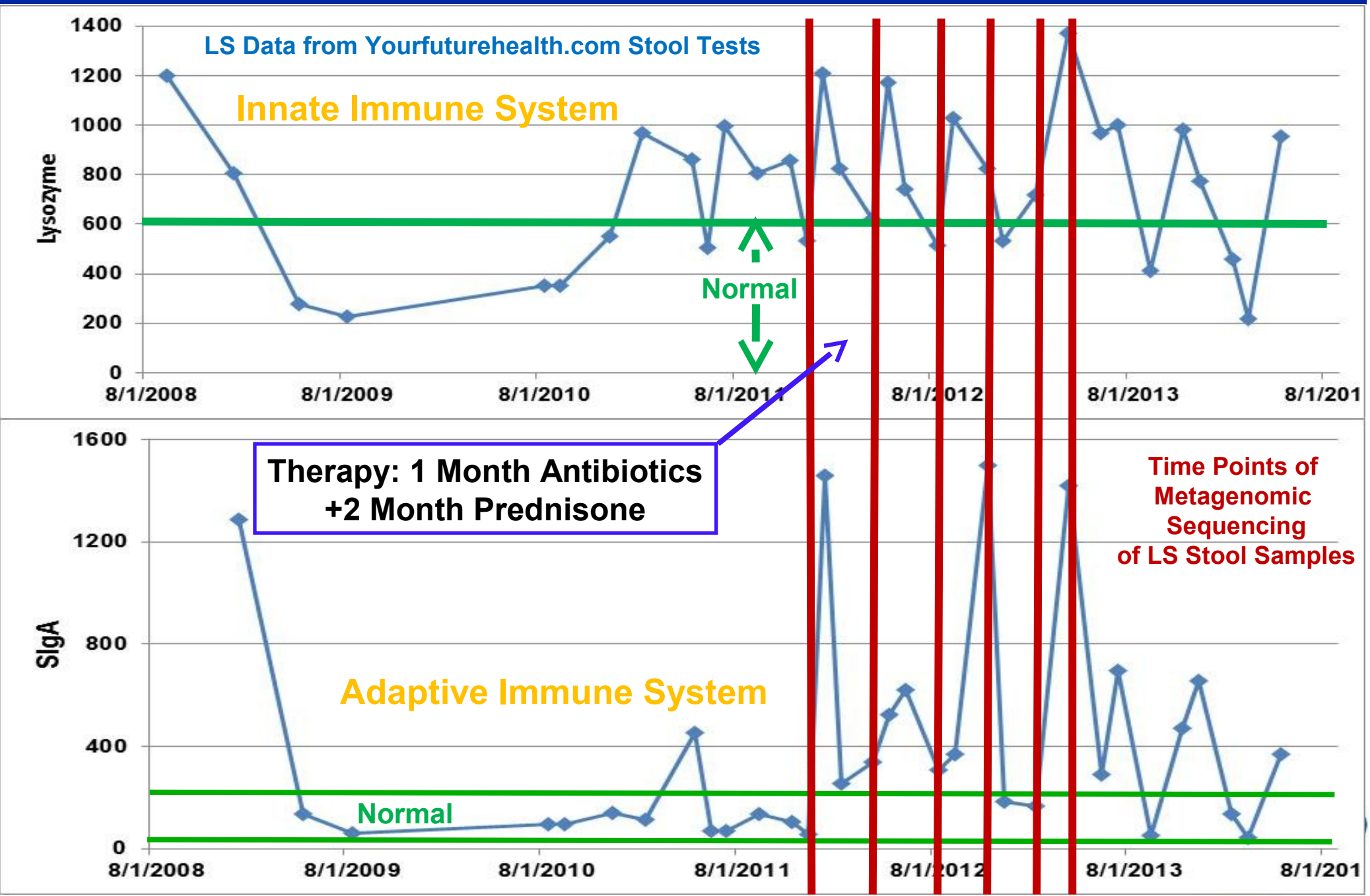
On the IBD Spectrum

Ave. Crohn's

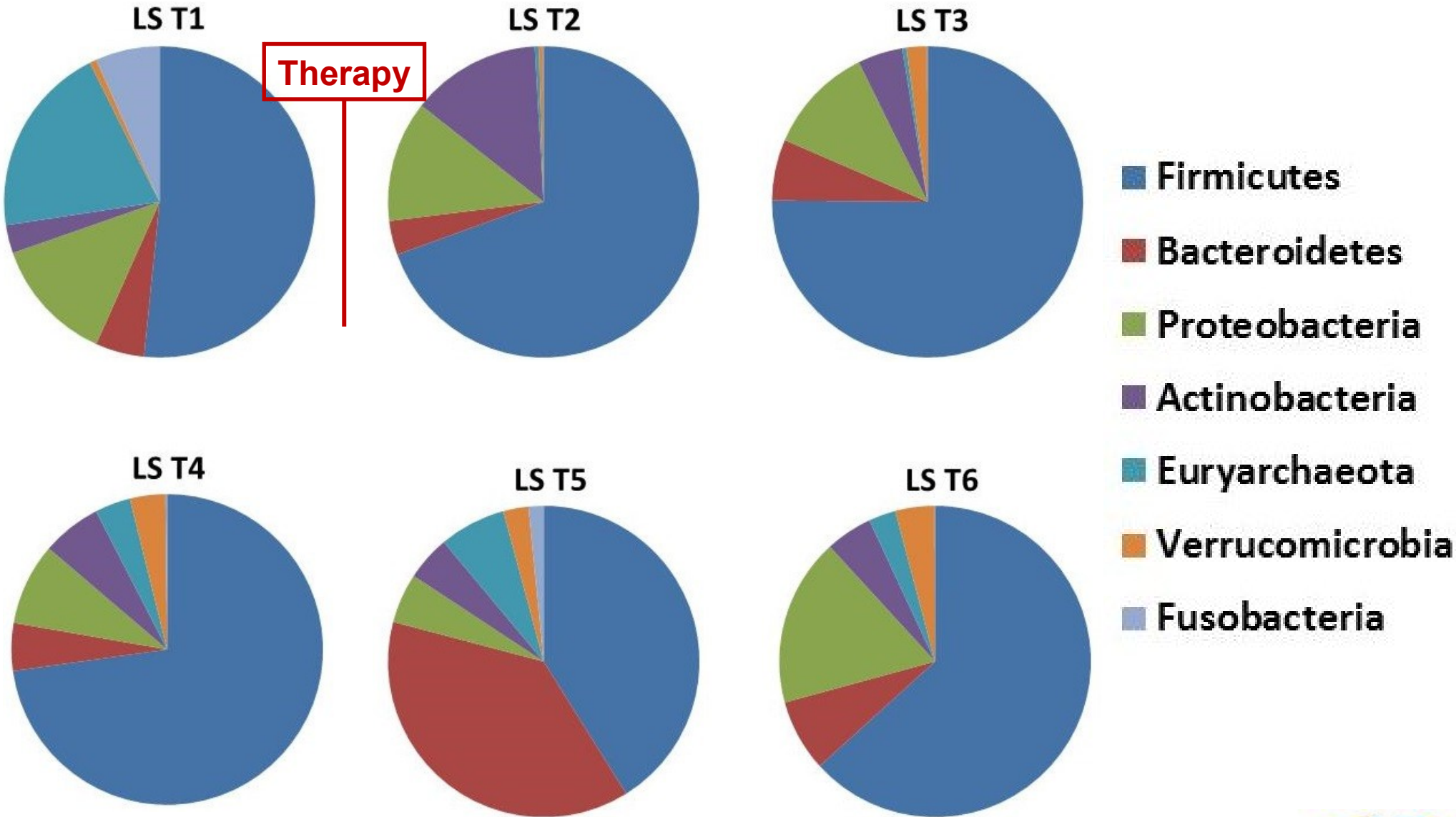


Collapse of Bacteroidetes

Comparing Changes in Gut Microbiome Ecology with Oscillations of the Innate and Adaptive Immune System

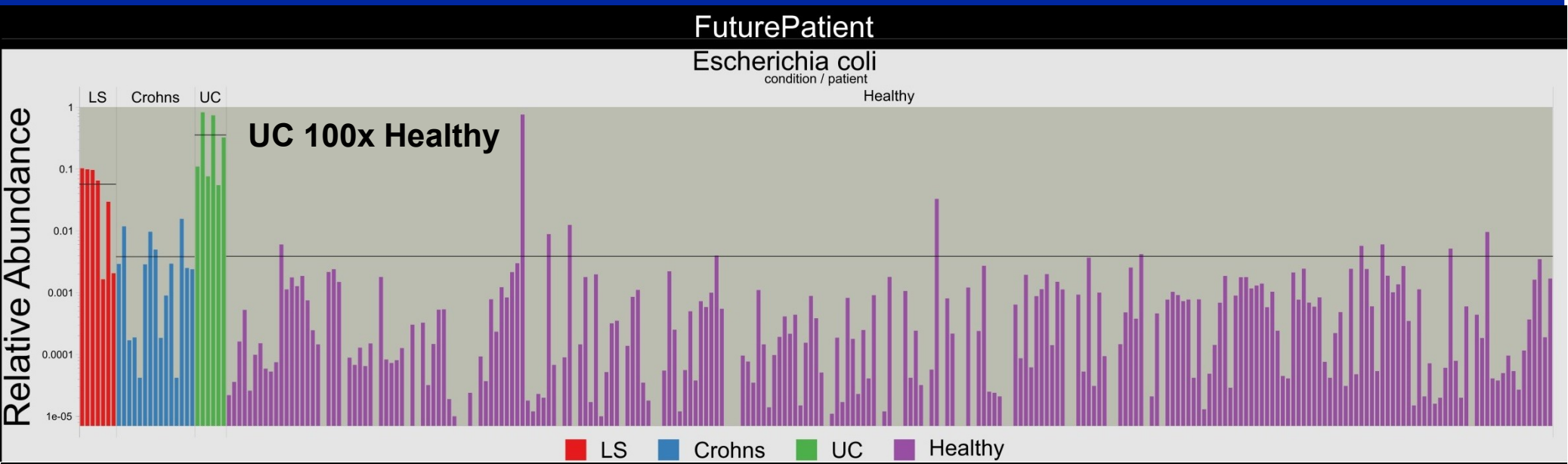


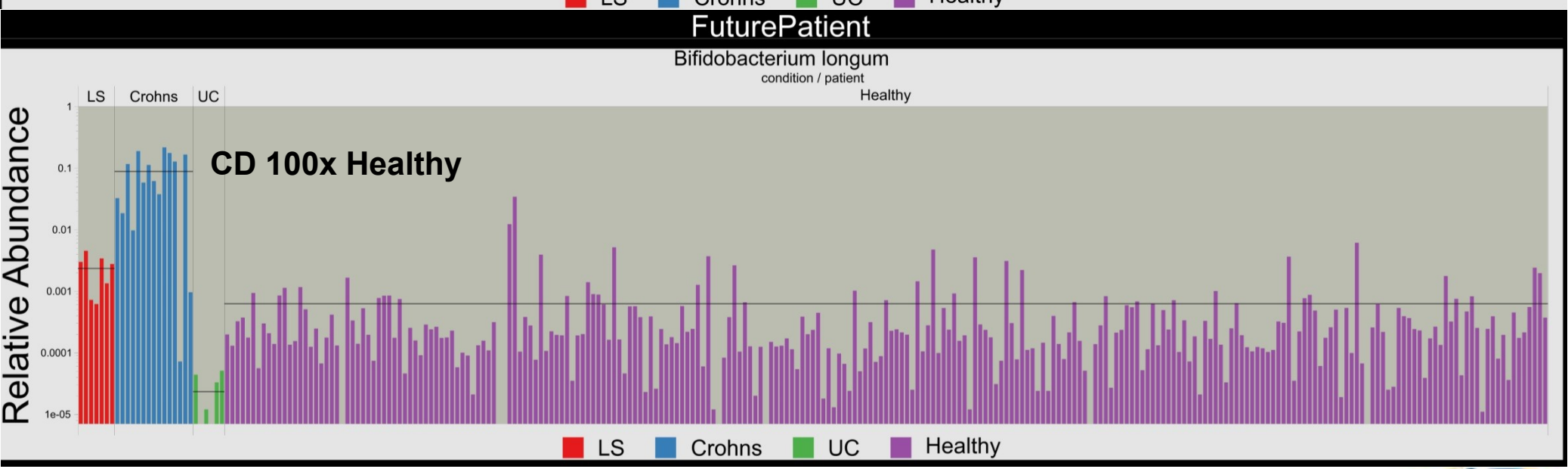
Time Series Reveals Autoimmune Dynamics of Gut Microbiome by Phyla



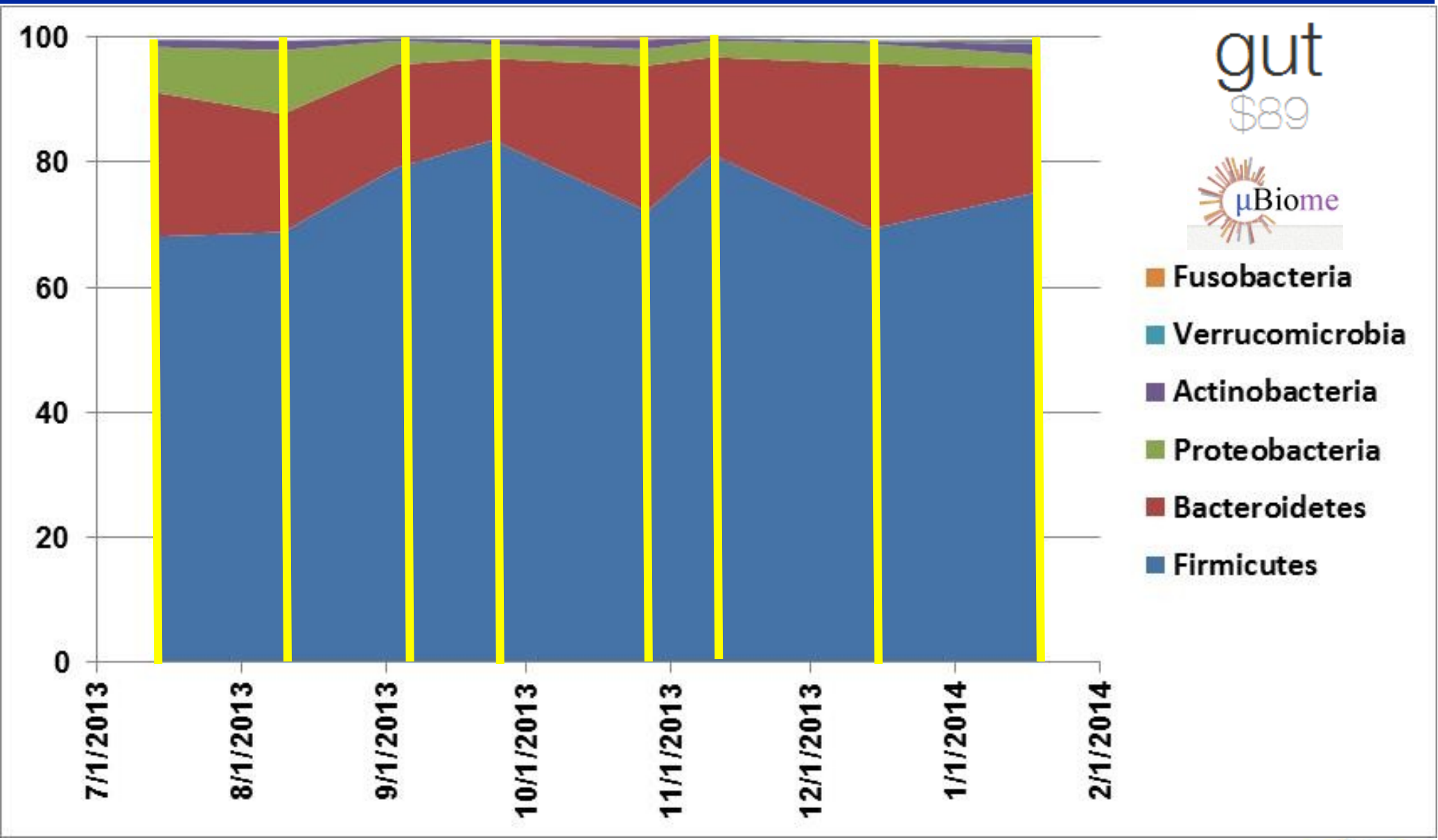
Six Metagenomic Time Samples Over 16 Months

Toward Microbiome Disease Diagnosis





Inexpensive 16S Time Series of Microbiome Now Possible Through Ubiome



Data source: LS (Yellow Lines Stool Samples); Sequencing and Analysis Ubiome

What Might We Learn?
Zero G as a Selection Pressure on Human Microbiome

Germs sent to space return 3 times as deadly

By Eric Berger | September 24, 2007 Houston Chronicle |

"Space flight alters cellular and physiological responses in astronauts including the immune response," said ASU's Cheryl Nickerson, who led a project aboard NASA's space shuttle. "However, relatively little was known about microbial changes to infectious disease risk in response to space flight."



Slide Presented by LS to NAC July 2013
From NAC Information Technology Infrastructure Committee