“Toward Novel Human Microbiome Surveillance Diagnostics to Support Public Health”

Invited Talk

Institute for Public Health

University of California San Diego

April 21, 2015

Dr. Larry Smarr

Director, California Institute for Telecommunications and Information Technology

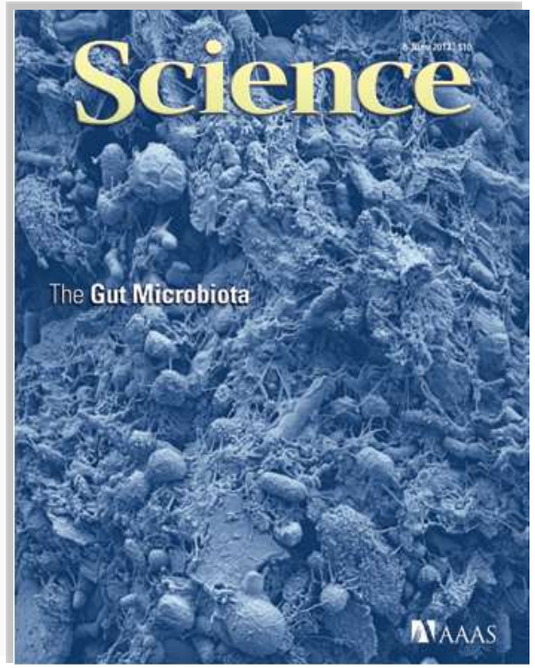
Harry E. Gruber Professor,

Dept. of Computer Science and Engineering

Jacobs School of Engineering, UCSD

http://lsmarr.calit2.net

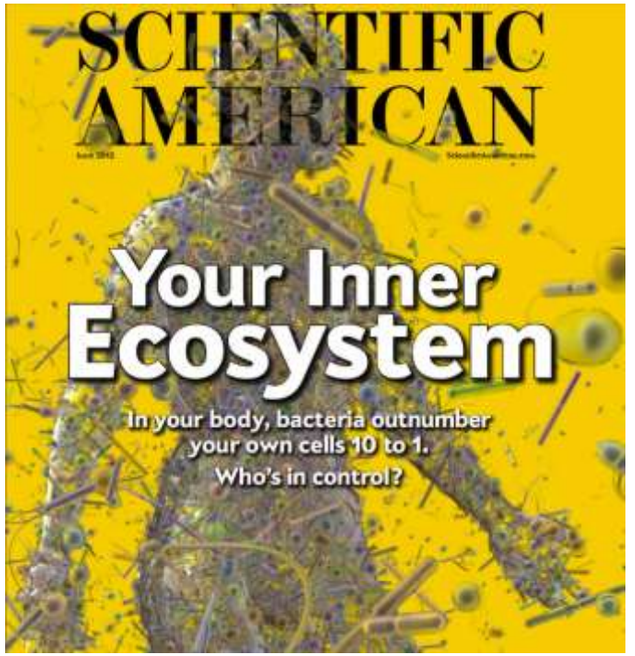
Intense Scientific Research is Underway on Understanding the Human Microbiome in Health and Disease



June 8, 2012



June 14, 2012



June, 2012



August 18, 2012

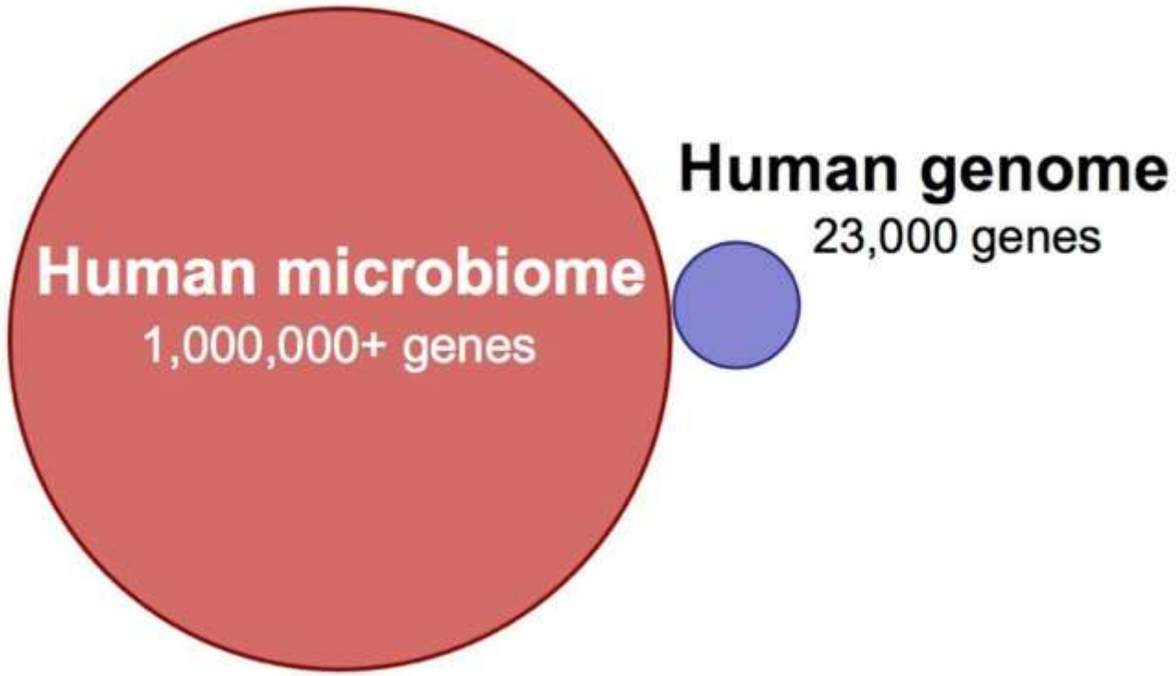
HMP

NIH National Institutes of Health
Office of Strategic Coordination - The Common Fund

Human Microbiome Project

The Vast Majority of Your Cells and Genes Are Not Human And Currently Outside of Mainstream Medicine

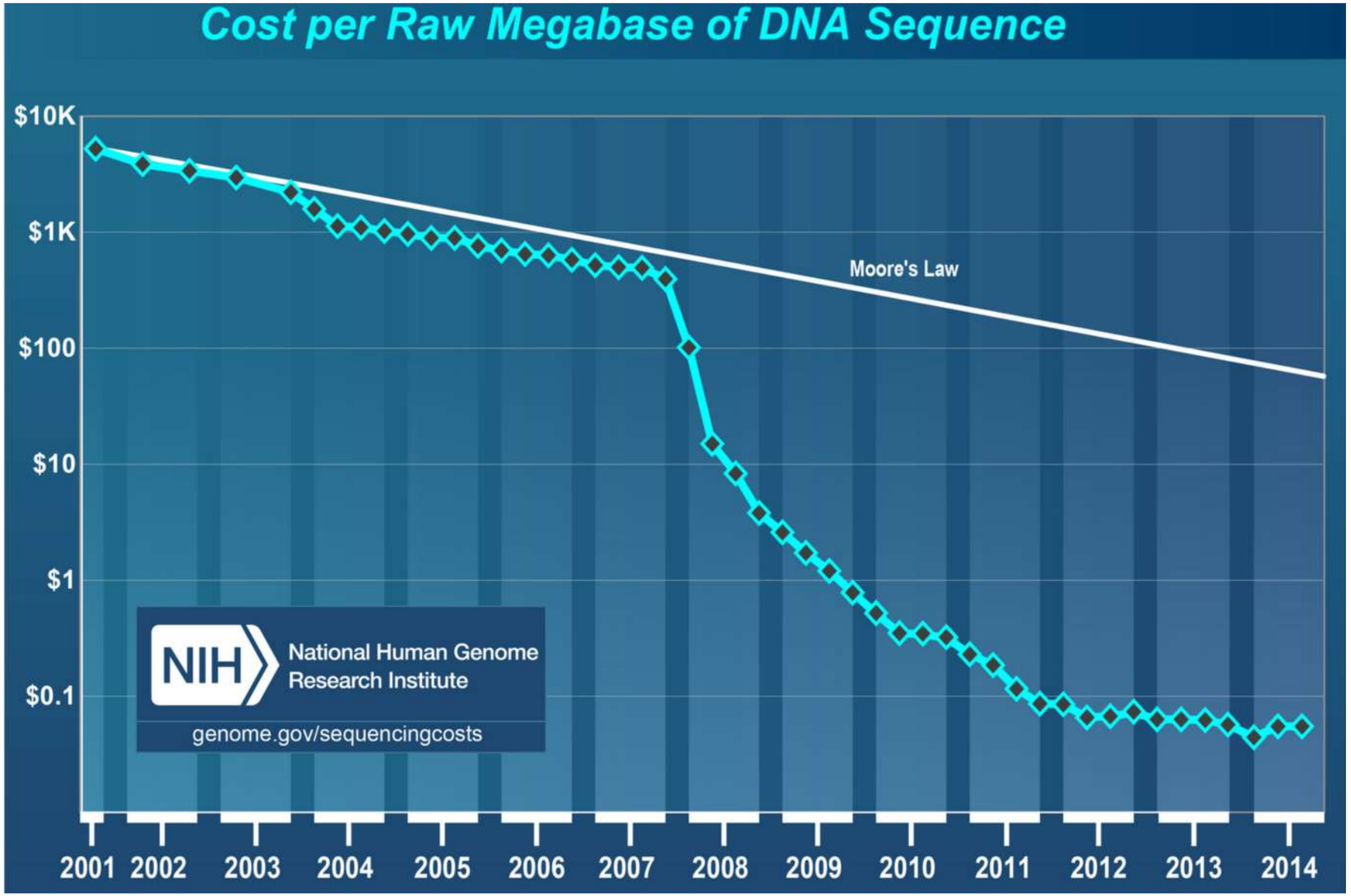
Your Body Has 10 Times As Many Microbe Cells As Human Cells



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

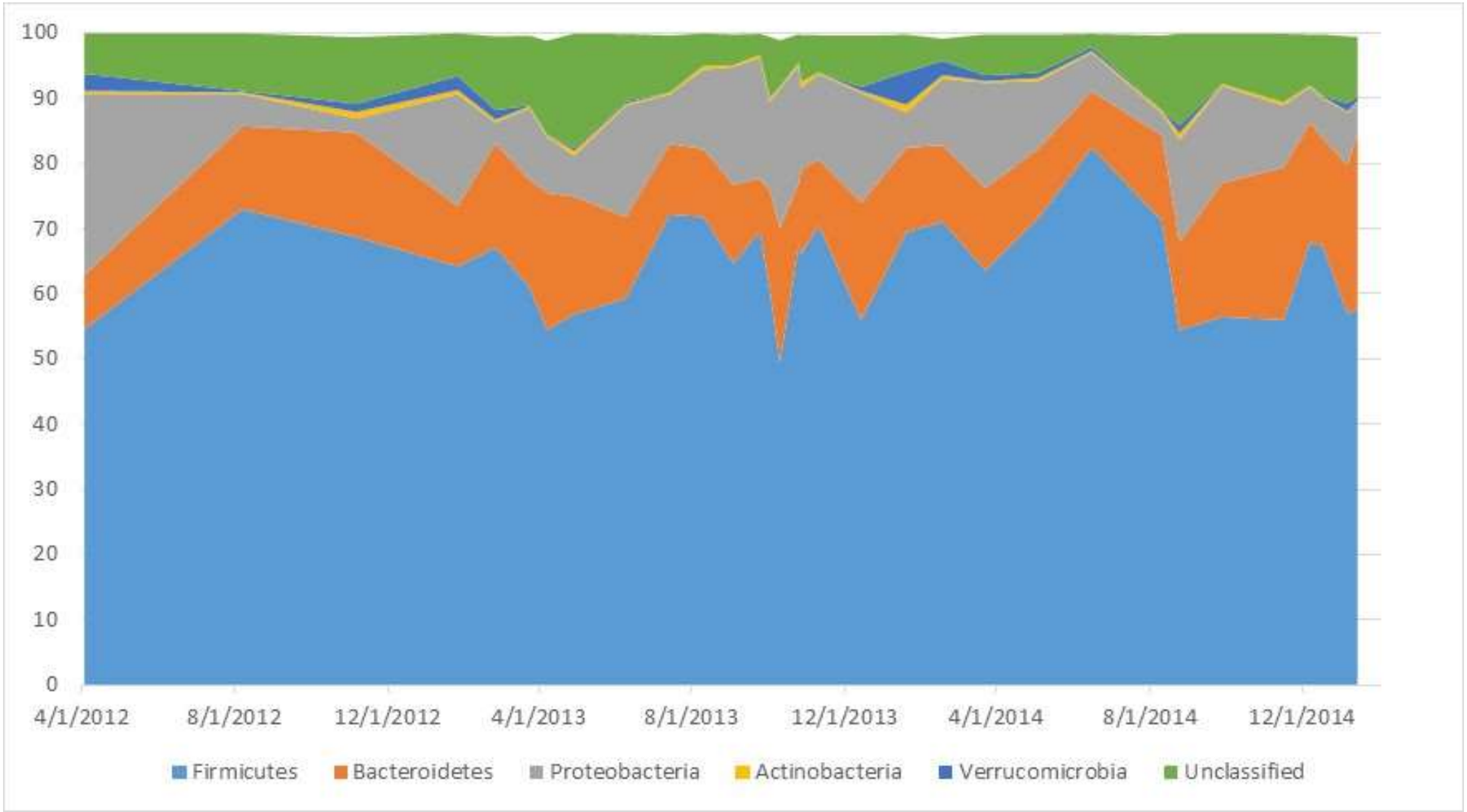
Inclusion of the "Dark Matter" of the Body Will Radically Alter Medicine

The Cost of Sequencing DNA Has Fallen Over 10,000x in the Last Ten Years



This Has Enabled Sequencing of Both Human and Microbial Genomes

Inexpensive 16S Time Series of Human Microbiome Now Possible Through Ubiome



Full Disclosure: I am a Scientific Advisor to Ubiome

Gut Kit **$89**

µBiome

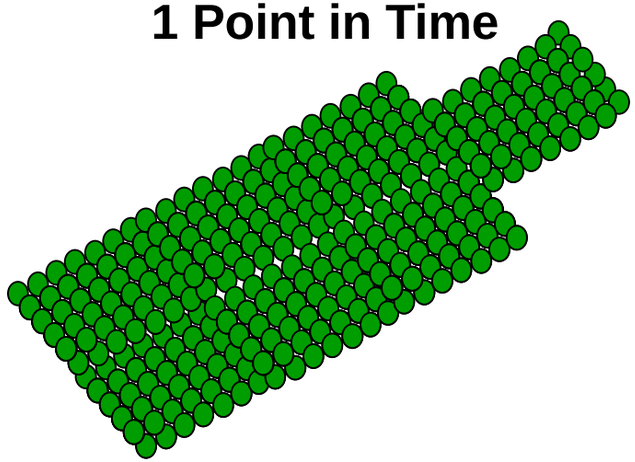
Larry Smarr Gut Microbiome Over Nearly Three Years: Ubiome 32 Time Samples by Phyla

For Deep Analysis of Changes in the Gut Microbiome Ecology Our Team Compared a Healthy Population with 3 Types of IBD

Each Sample Has 100-200 Million Illumina Short Reads (100 bases)

"Healthy" Individuals

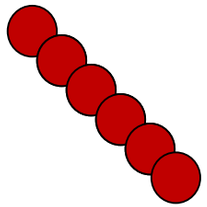
250 Subjects
1 Point in Time



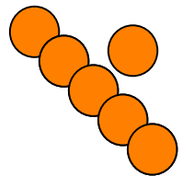
Inflammatory Bowel Disease (IBD) Patients

Larry Smarr
(Colonic Crohn's)

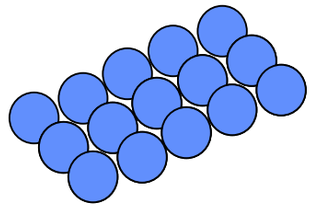
7 Points in Time



2 Ulcerative Colitis Patients,
6 Points in Time



5 Ileal Crohn's Patients,
3 Points in Time

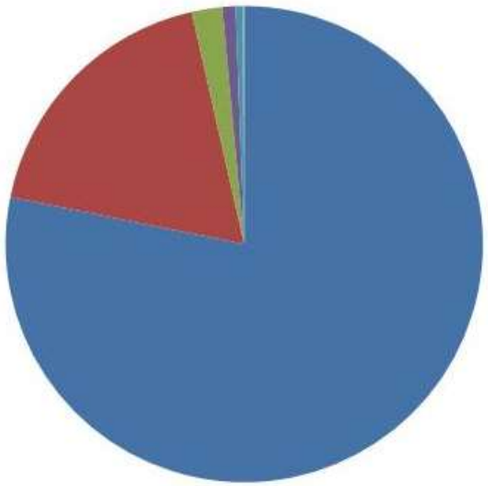


Total of 27 Billion Reads
Or 2.7 Trillion Bases

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

We Found Major State Shifts in Microbial Ecology Phyla Between Healthy and Three Forms of IBD

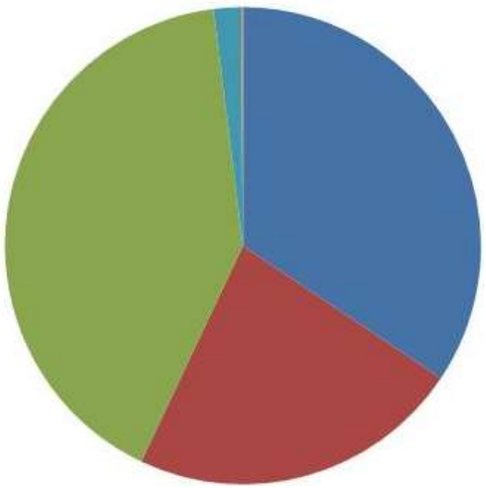
Average HE



Most Common Microbial Phyla

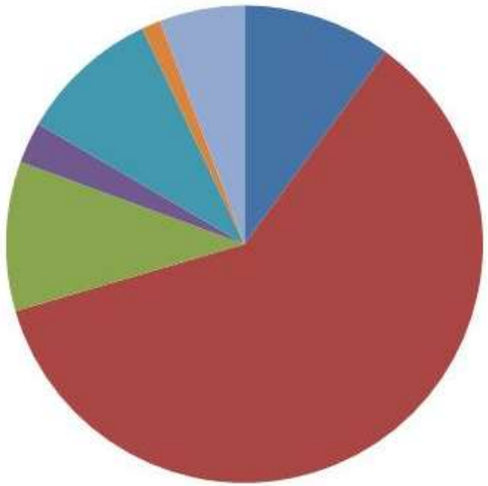
- Bacteroidetes
- Firmicutes
- Proteobacteria
- Verrucomicrobia
- Actinobacteria
- Fusobacteria
- Euryarchaeota

Average Ulcerative Colitis



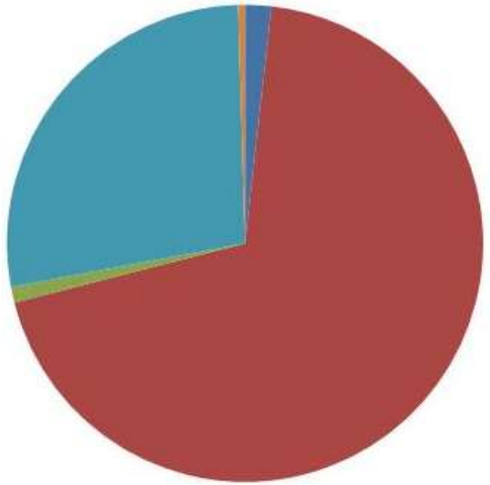
Explosion of Proteobacteria

Average LS Colonic Crohn's Disease



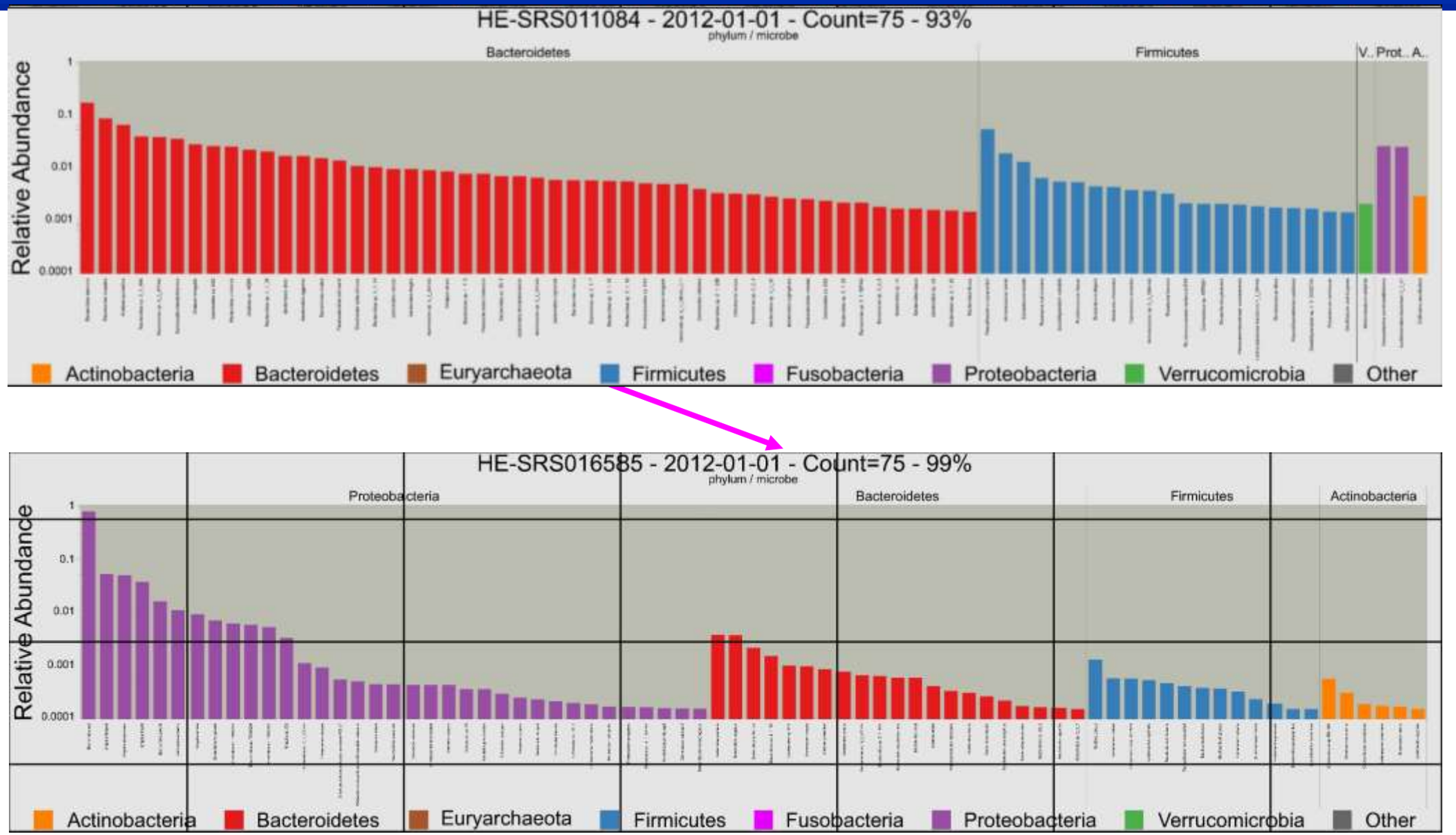
Hybrid of UC and CD
High Level of Archaea

Average Ileal Crohn's Disease

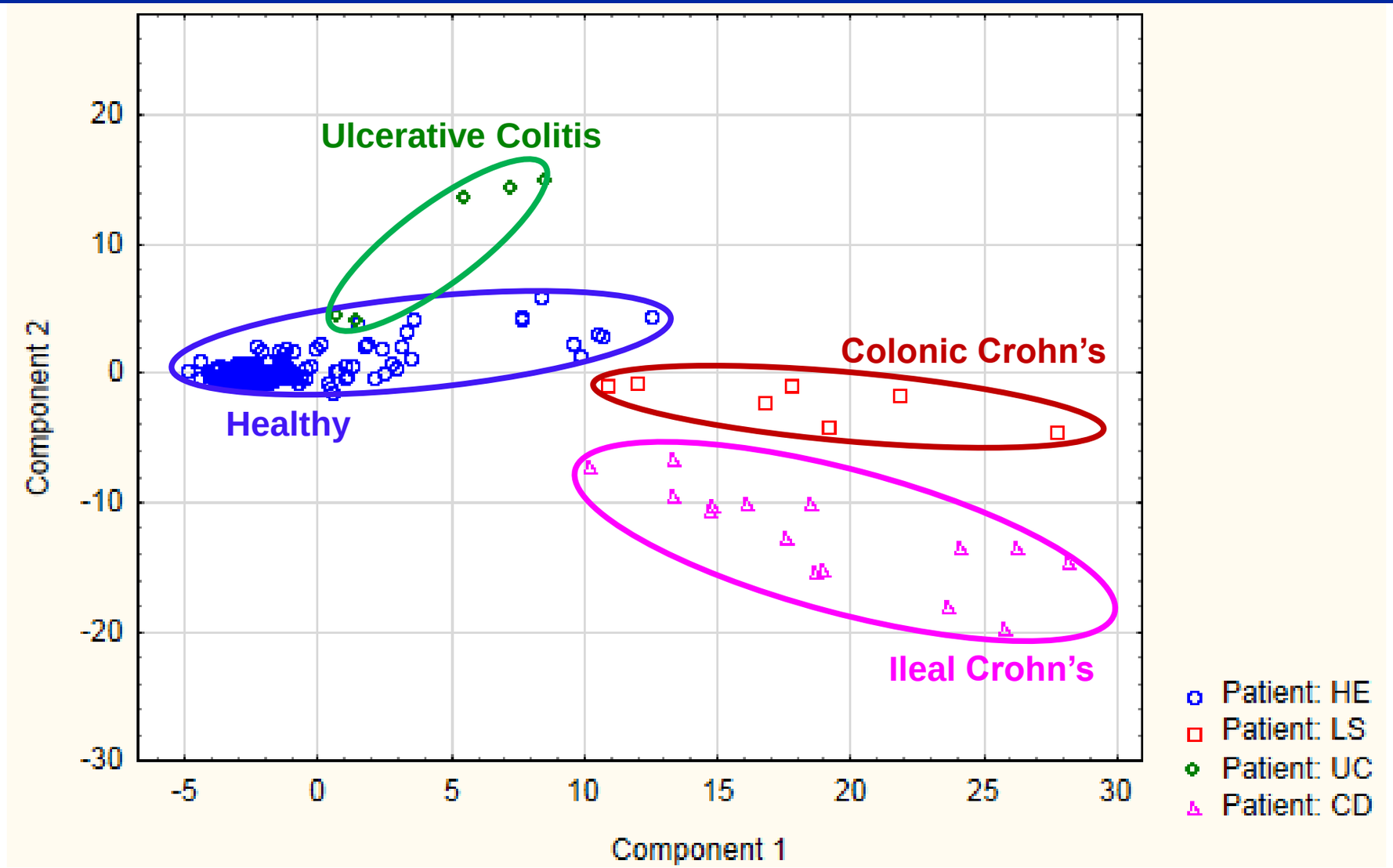


Collapse of Bacteroidetes
Explosion of Actinobacteria

Using Microbiome Profiles for Public Health Surveillance: Finding 1 Out of 155 “Healthy” Subjects For Further Medical Tests



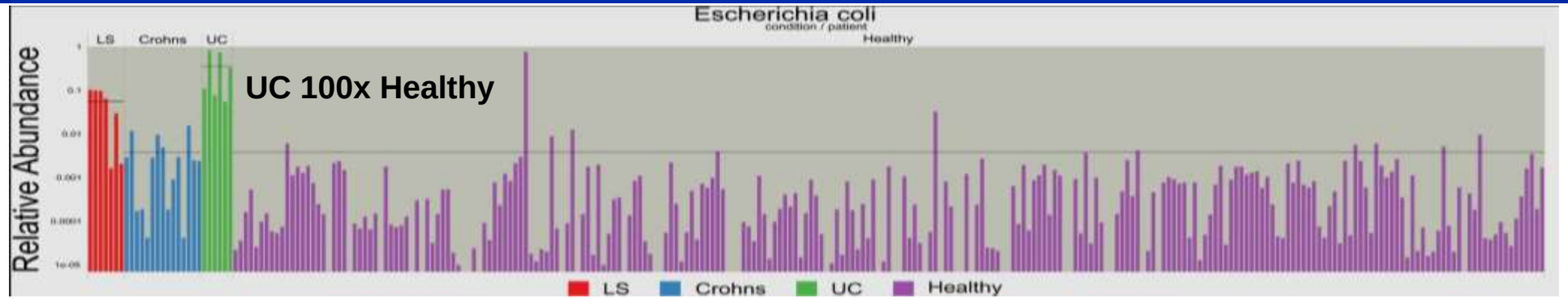
Dell Analytics Separates The 4 Patient Types in Our Data Using Our Microbiome Species Data

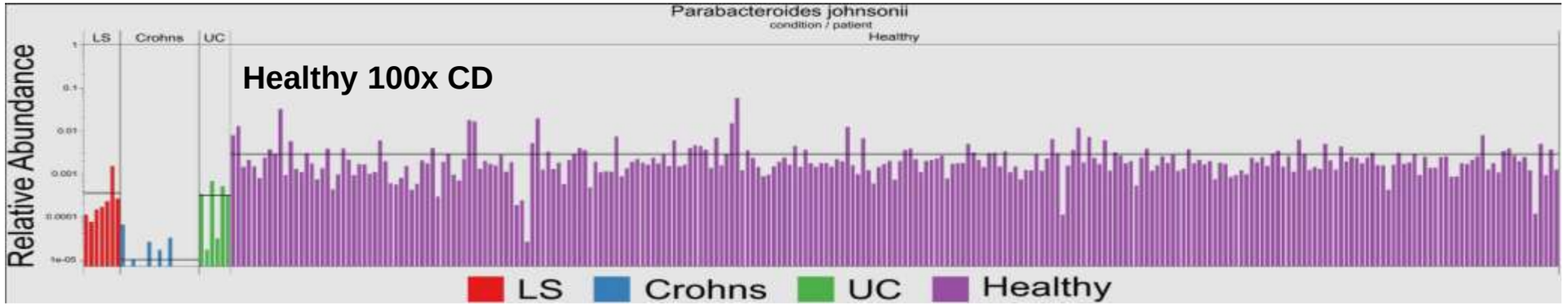


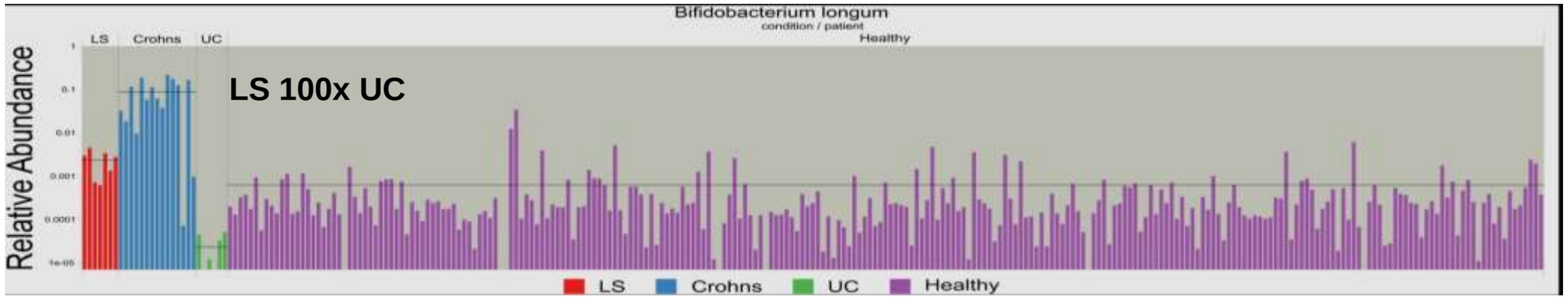
Source: Thomas Hill, Ph.D.
Executive Director Analytics
Dell | Information Management Group, Dell Software

Can We Find New Noninvasive Diagnostics In Microbiome Ecologies?

Our Relative Abundance Results Across ~300 People Provides Potential Microbial Ecological Diagnosis Tools



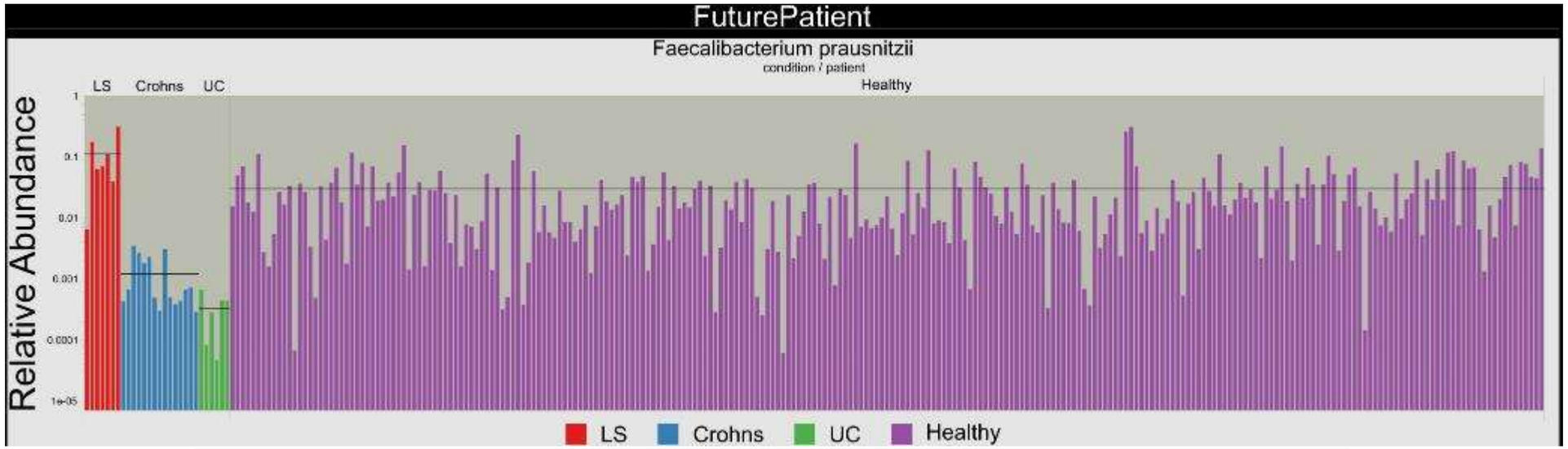




We Produced Similar Results for ~2500 Microbial Species

Relating Microbiome Shifts to Human Physiology: Microbial Fermenters Produce Butyrate, The Critical Energy Source for the Colonic Epithelial Cells

"Human colonic butyrate producers are Gram-positive Firmicutes, but are phylogenetically diverse, with the two most abundant groups related to Eubacterium rectale/Roseburia spp. and to Faecalibacterium prausnitzii."



Decreased abundance of *Faecalibacterium prausnitzii* in the gut microbiota of Crohn's disease

Takehide Fujimoto,* Hirotsugu Imaeda,† Kenichiro Takahashi,* Eiji Kasumi,* Shigeki Bamba,* Yoshihide Fujiyama† and Akira Andoh*

Diversity, metabolism and microbial ecology of butyrate-producing bacteria from the human large intestine

Petra Louis & Harry J. Flint

Trends in Microbiology 2012

UC San Diego Will Be Carrying Out a Major Clinical Study of IBD Using These Techniques

Announced November 7, 2014!

Inflammatory Bowel Disease Biobank For Healthy and Disease Patients

Already 185 Enrolled

Drs. William J. Sandborn, John Chang, & Brigid Boland
UCSD School of Medicine, Division of Gastroenterology

UCSD is Becoming a National Leader in the Human Microbiome

LOCAL TOPICS | SCIENCE & ENVIRONMENT | SCIENCE

UCSD hires star biologist Rob Knight

By Gary Robbins 1:30 P.M. JAN. 11, 2015 Updated 12:17 P.M. JAN. 12, 2015 PRINT COMMENTS 0



american gut

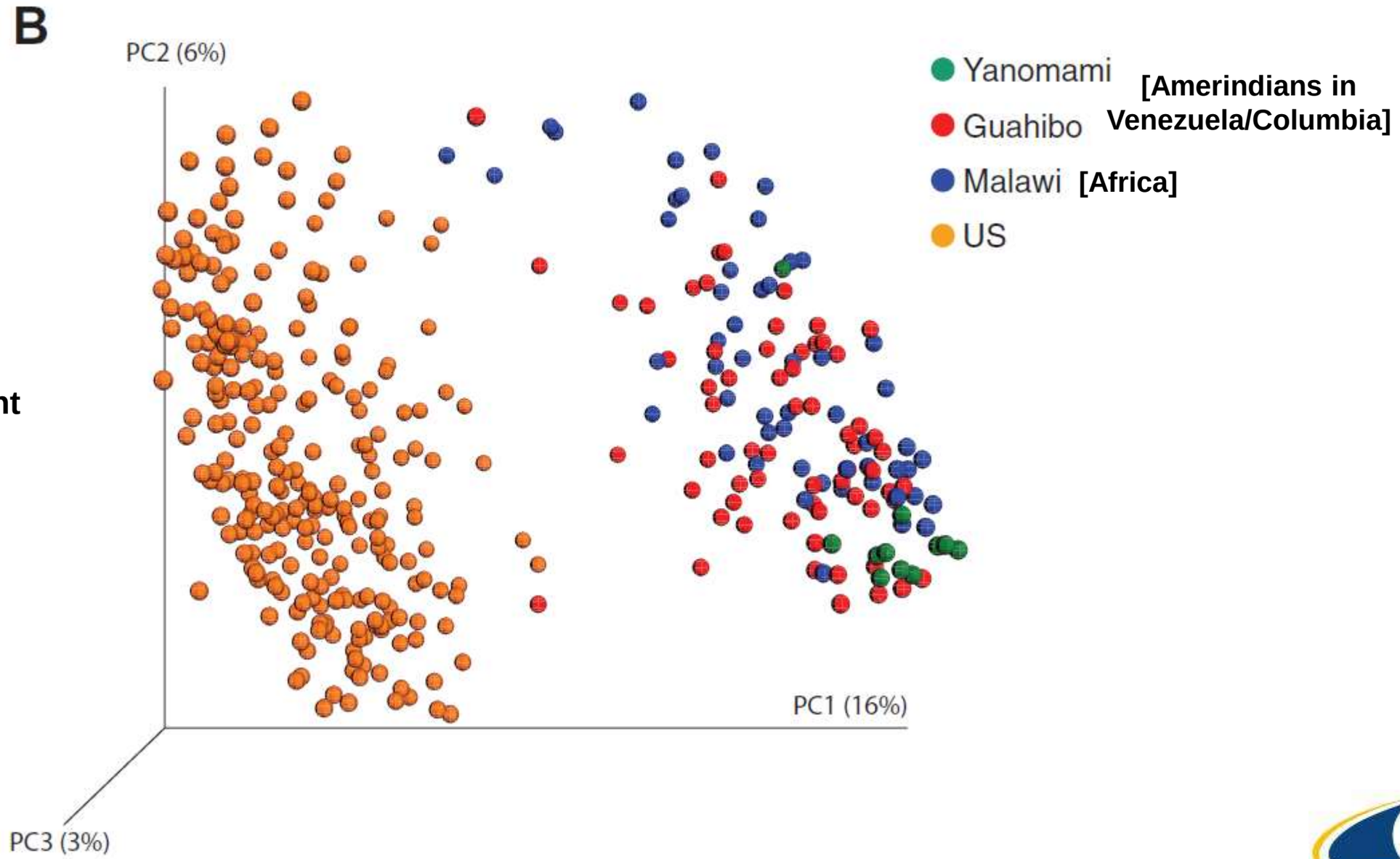
LATEST NEWS

THE KNIGHT LAB HAS MOVED TO UCSD!

BY JEFF LEACH ON MARCH 4, 2015

The United States Population's Human Gut Microbiome Has Diverged a Great Deal from Hunter-Gatherers

A New Paper Co-Authored With Rob Knight



[Amerindians in Venezuela/Columbia]

[Africa]

"The microbiome of uncontacted Amerindians," J. C. Clemente, et al. Science Advances 1, e1500183 (2015).

The UCSD Institute for Public Health Can Lead in Developing the Human/Microbiome System Approach to Public Health

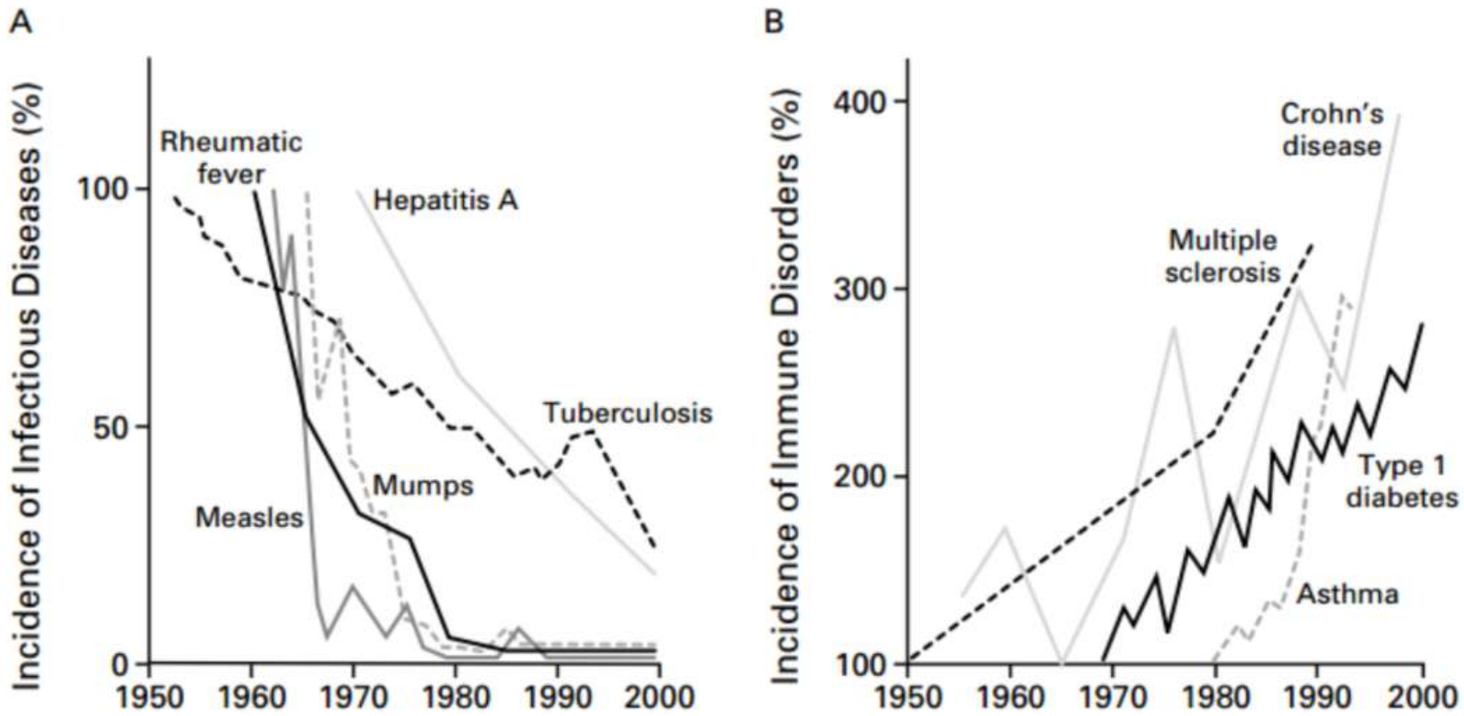
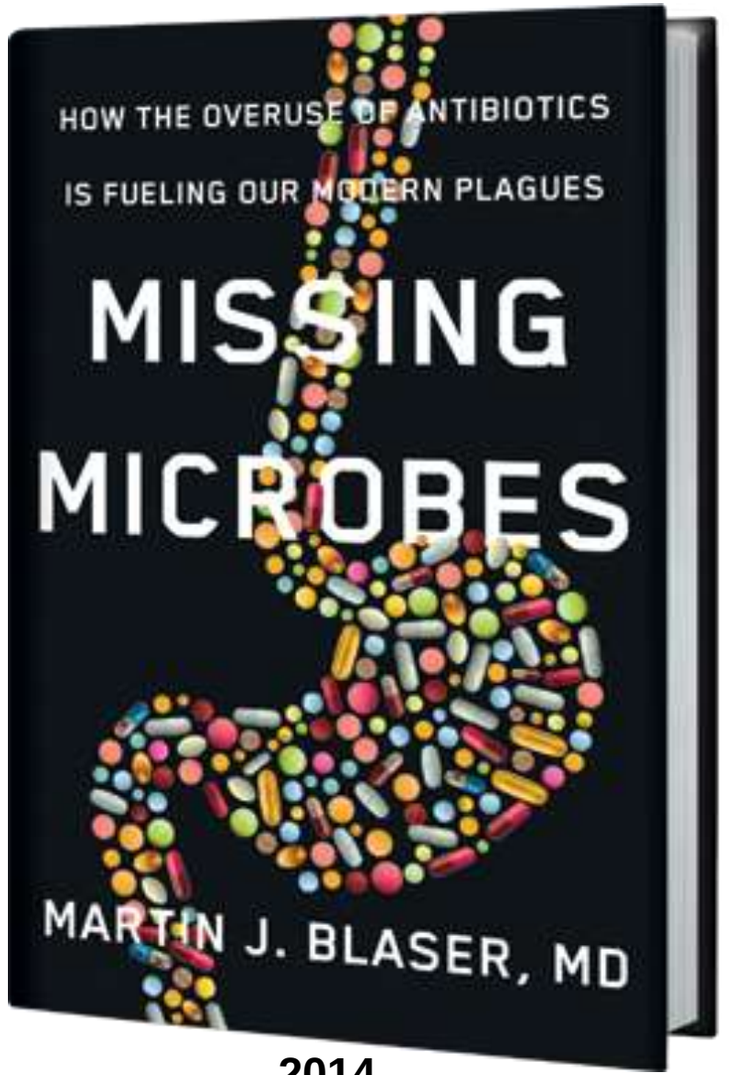


Figure 1. Inverse Relation between the Incidence of Prototypical Infectious Diseases (Panel A) and the Incidence of Immune Disorders (Panel B) from 1950 to 2000.

In Panel A, data concerning infectious diseases are derived from reports of the Centers for Disease Control and Prevention, except for the data on hepatitis A, which are derived from Joussemet et al.[12] In Panel B, data on immune disorders are derived from Swarbrick et al.,[10] Dubois et al.,[13] Tuomilehto et al.,[14] and Pugliatti et al.[15]

Bach (2002) N Engl J Med, Vol. 347, 911-920



2014

For Public Health It is Still About Microbes,
But from Single Species to Entire Ecologies

Thanks to Our Great Team!

UCSD Metagenomics Team
Weizhong Li
Sitao Wu

Calit2@UCSD Future Patient Team
Jerry Sheehan
Tom DeFanti
Kevin Patrick
Jurgen Schulze
Andrew Prudhomme
Philip Weber
Fred Raab
Joe Keefe
Ernesto Ramirez



JCVI Team
Karen Nelson
Shibu Yooseph
Manolito Torralba

SDSC Team
Michael Norman
Ilkay Altintas
Shweta Purawat
Mahidhar Tatineni
Robert Sinkovits

Dell/R Systems and Dell Analytics
Brian Kucic
John Thompson
Tom Hill

UCSD Health Sciences Team
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