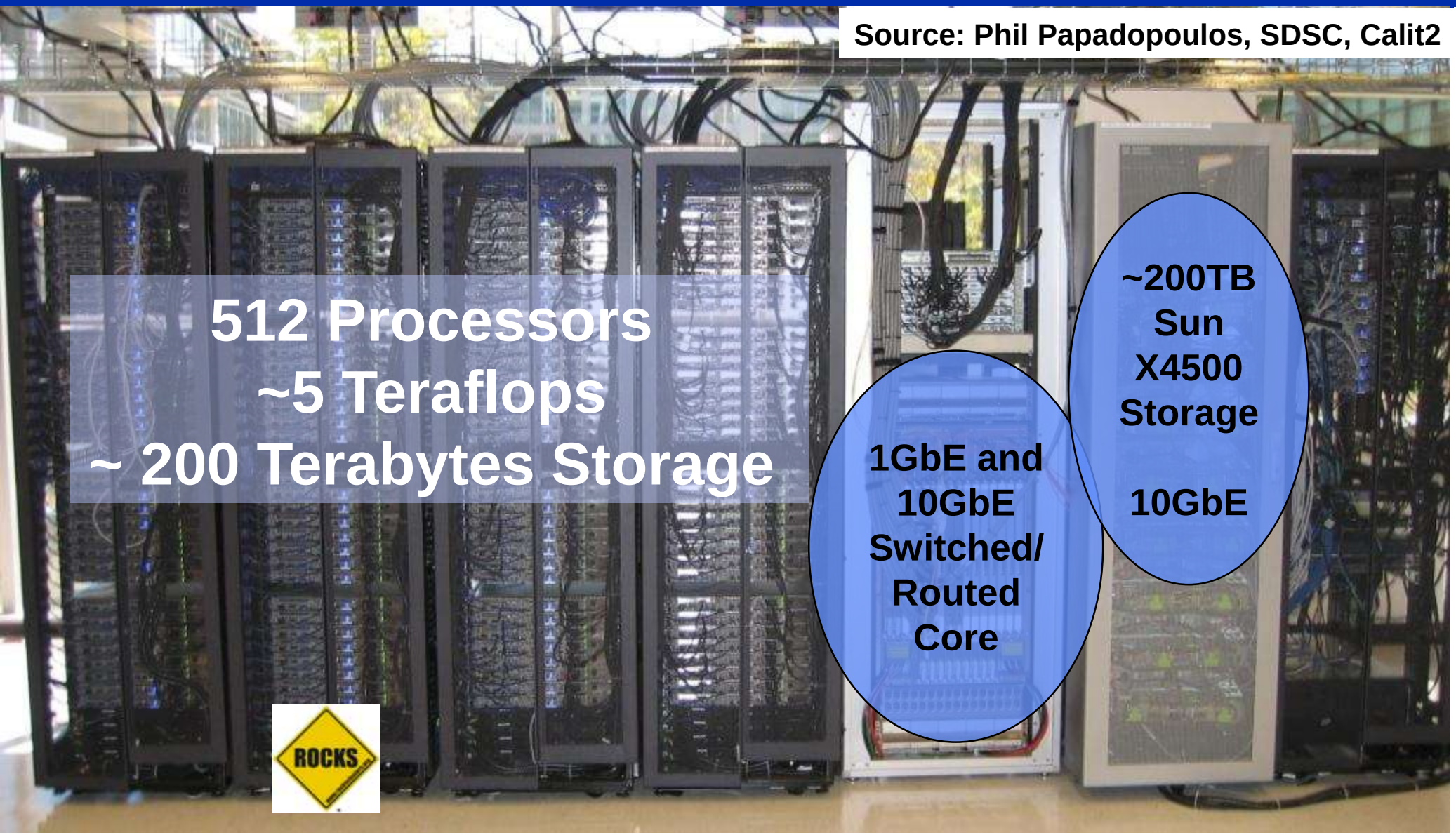
# "Quantified Self-
# On Being a Personal Genomic Observatory"

**Keynote in the**
**"Humans as Genomic Observatories" Meeting**
**Session in the Genomics Standards Consortium GSC 15**
**April 24, 2013**

**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**

# Calit2 Community Cyberinfrastructure for Advanced Microbial Ecology Research and Analysis (CAMERA)

Source: Phil Papadopoulos, SDSC, Calit2




5000 Users
90 Countries

Gordon and Betty MOORE FOUNDATION

SDSC

J. Craig Venter INSTITUTE

it²

# Access to Computing Resources Tailored by User's Requirements and Resources










UCSD Triton



NSF/SDSC
Gordon



NSF/SDSC
Trestles



NSF/TACC
Lonestar



NSF/TACC
Ranger




NSF/RCAC
Steele

**Infrastructure Services Extend CAMERA Computations to 3rd Party Compute Resources**

Windows Azure

amazon web services

Gordon and Betty MOORE FOUNDATION

Source:
Jeff Grethe,
CRBS, UCSD

EAGER: Multi-Domain, Workflow-Driven Computation System for Microbial Ecology Research and Analysis

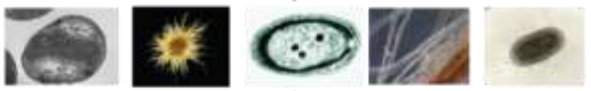
# CAMERA

## *A Community Gateway to Data & Analysis Functions*



Environmental Sample

[ Geochemistry / Hydrology / Minerology / Temperature / Pressure / Location / Time ]

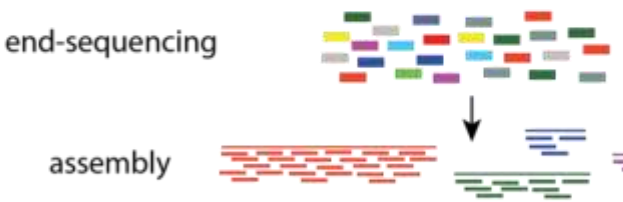




whole genome shotgun sequencing

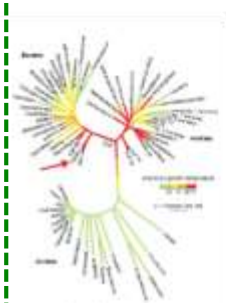



***Data***

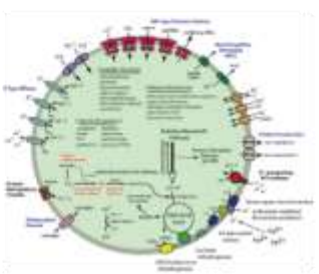



***Data Analysis***

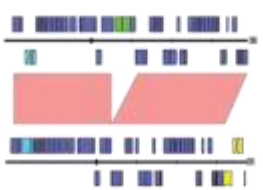
Analyze Sequence Data



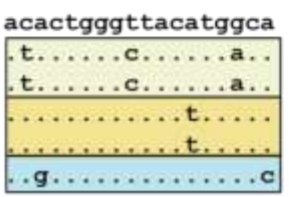
phylogeny



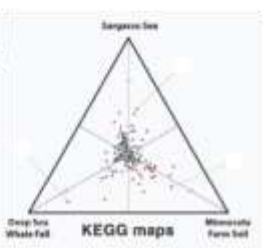
metabolic reconstruction



comparative genomics




population genetics




compare environments

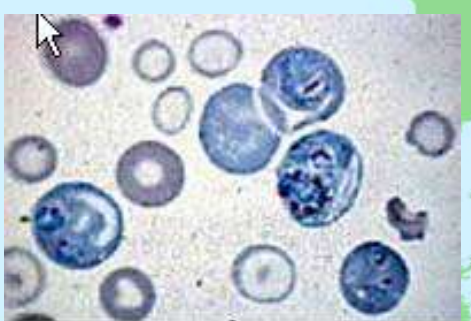
# Marine Genome Sequencing Project – CAMERA Anchor Dataset Launched March 13, 2007

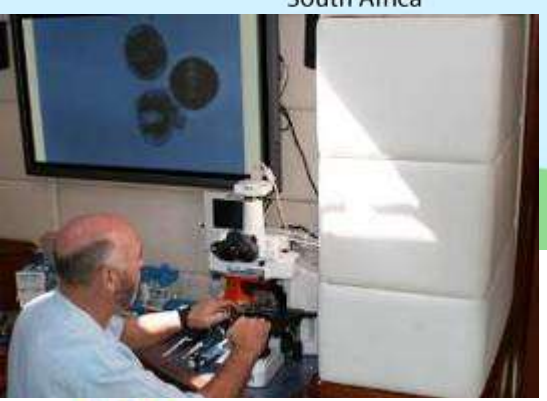


**Each Sample ~2000 Microbial Species**

Canada
United States
Mexico
Puerto Rico
Honduras
Costa Rica
Panama
Galapagos Islands
x 10 samples
French Polynesia
Cook Islands
Vanuatu
Fiji
Tonga
New Caledonia
x 17 samples
Australia
x 8 samples
Cocos-Keeling Is.
Tanzania/ Zanzibar
x 7 samples
Seychelles
Madagascar
South Africa

**Specify Ocean Data**





Analyzed  Sampled, but not Analyzed

MARINE MICROBIOLOGY INITIATIVE

camera
Marine Microbial Ecology

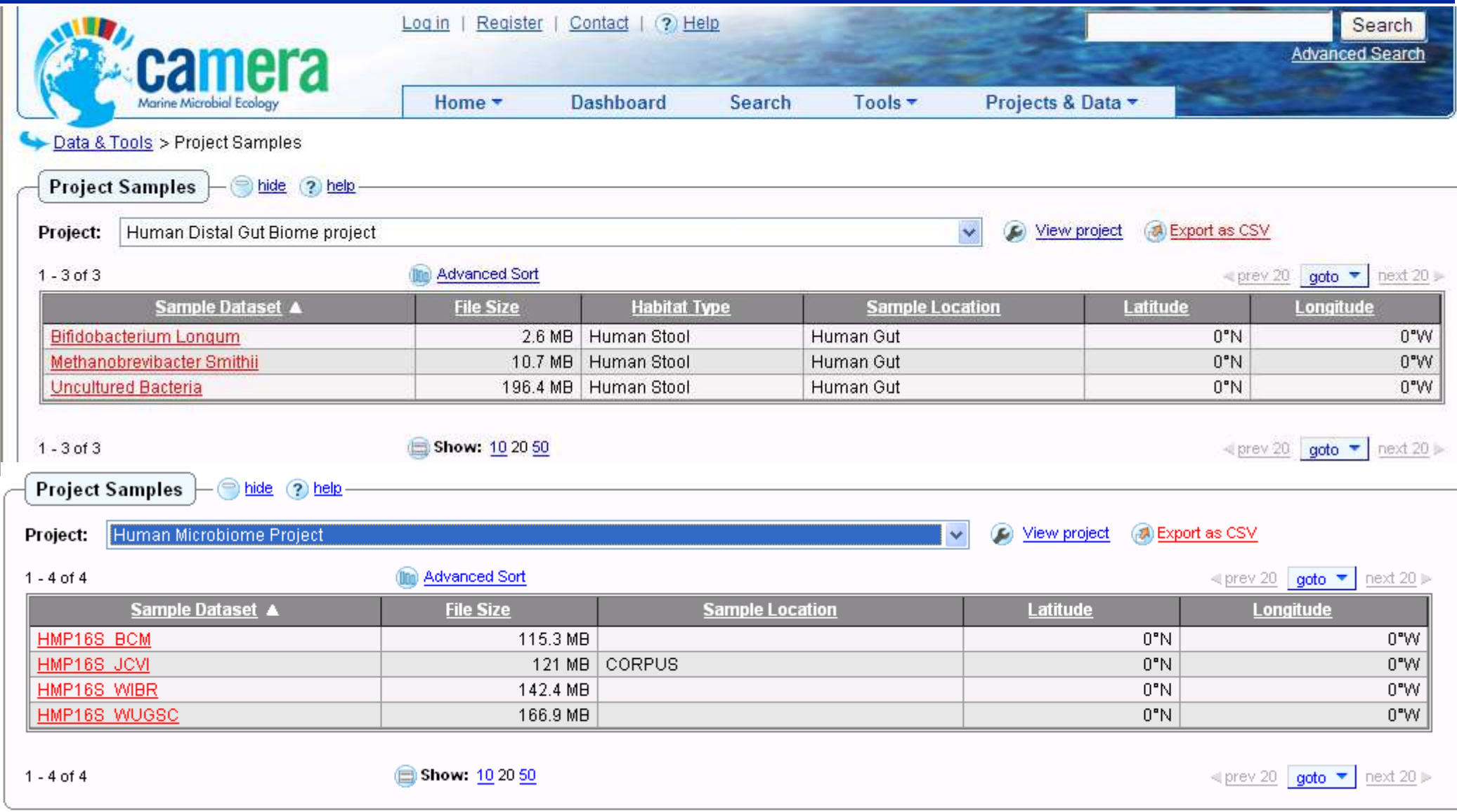
Gordon and Betty MOORE FOUNDATION

## Measuring the Genetic Diversity of Ocean Microbes

J. Craig Venter INSTITUTE

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# The Human Microbiome Is a Microbial Environment Being Metagenomically Sampled



camera
Marine Microbial Ecology

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Data & Tools > Project Samples

**Project Samples** hide help

**Project:** Human Distal Gut Biome project — View project — Export as CSV

1 - 3 of 3 — Advanced Sort — prev 20 goto next 20

| Sample Dataset ▲ | File Size | Habitat Type | Sample Location | Latitude | Longitude |
|---|---|---|---|---|---|
| Bifidobacterium Longum | 2.6 MB | Human Stool | Human Gut | 0°N | 0°W |
| Methanobrevibacter Smithii | 10.7 MB | Human Stool | Human Gut | 0°N | 0°W |
| Uncultured Bacteria | 196.4 MB | Human Stool | Human Gut | 0°N | 0°W |

1 - 3 of 3 — Show: 10 20 50 — prev 20 goto next 20

**Project Samples** hide help

**Project:** Human Microbiome Project — View project — Export as CSV

1 - 4 of 4 — Advanced Sort — prev 20 goto next 20

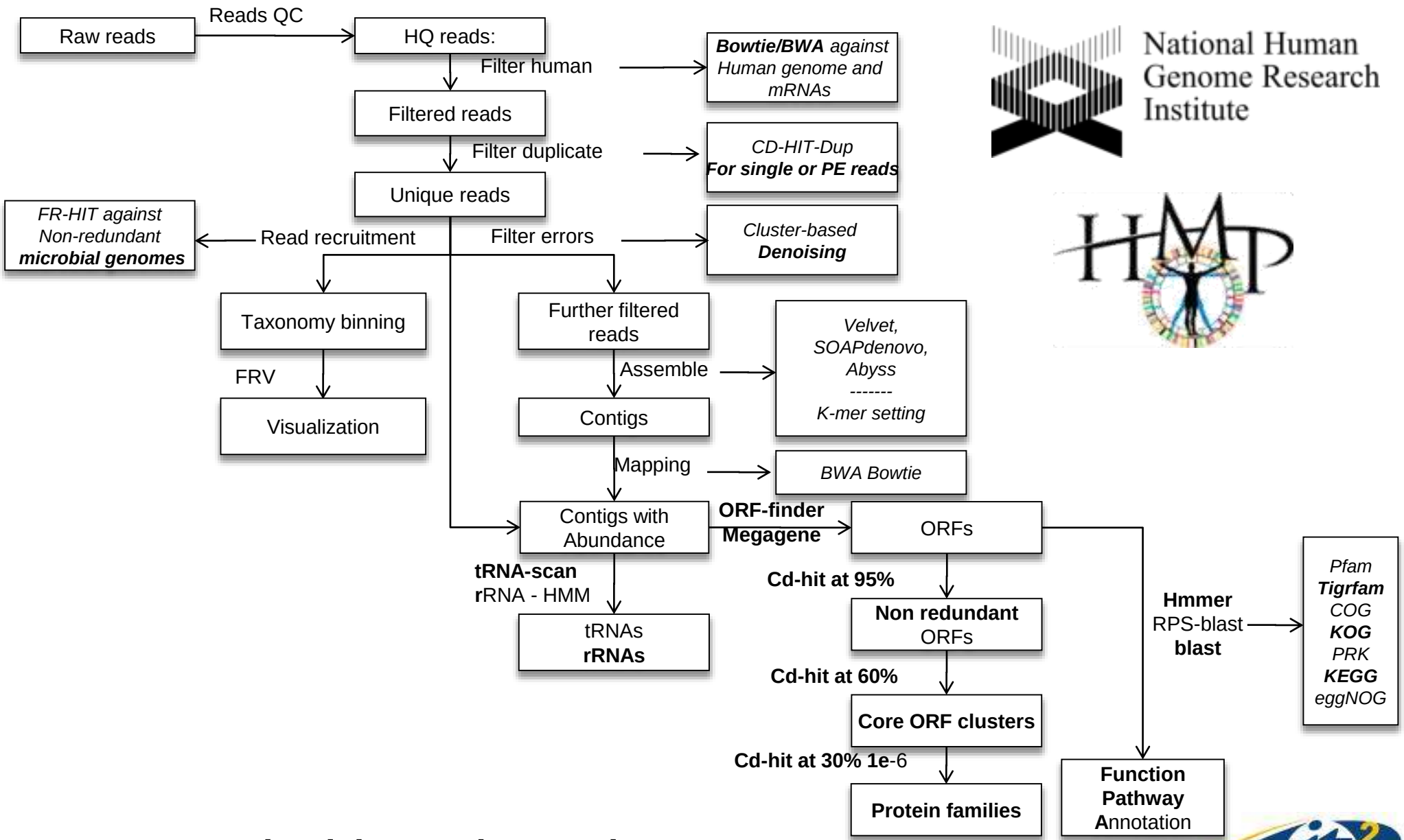
| Sample Dataset ▲ | File Size | Sample Location | Latitude | Longitude |
|---|---|---|---|---|
| HMP16S_BCM | 115.3 MB | | 0°N | 0°W |
| HMP16S_JCVI | 121 MB | CORPUS | 0°N | 0°W |
| HMP16S_WIBR | 142.4 MB | | 0°N | 0°W |
| HMP16S_WUGSC | 166.9 MB | | 0°N | 0°W |

1 - 4 of 4 — Show: 10 20 50 — prev 20 goto next 20

Gordon and Betty MOORE FOUNDATION

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# CAMERA and NIH Funded Weizhong Li Group's Metagenomic Computational NextGen Sequencing Pipeline

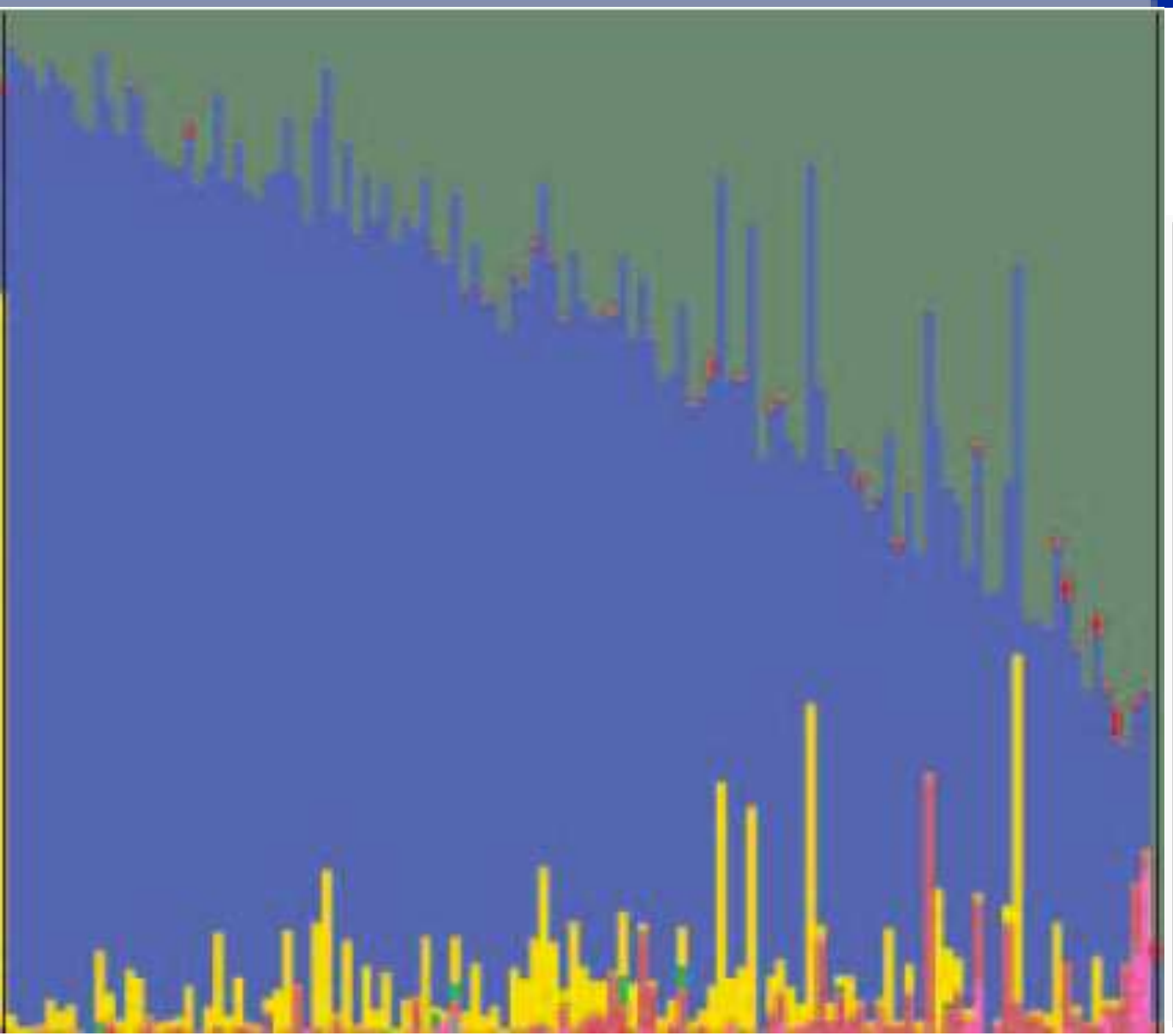



National Human Genome Research Institute

HMP

**PI: (Weizhong Li, UCSD):**
**NIH R01HG005978 (2010-2013, $1.1M)**

# What is a "Healthy" Gut Microbiome? Dominated by Bacteroidetes and Firmicute Phyla



- Firmicutes
- Actinobacteria
- Bacteroidetes
- Proteobacteria
- Fusobacteria
- Tenericutes
- Spirochaetes
- Cyanobacteria
- Verrucomicrobia
- TM7

**Source: "Structure, function and diversity of the healthy human microbiome," HMP Consortium, Nature, 486, 207-212 (2012)**

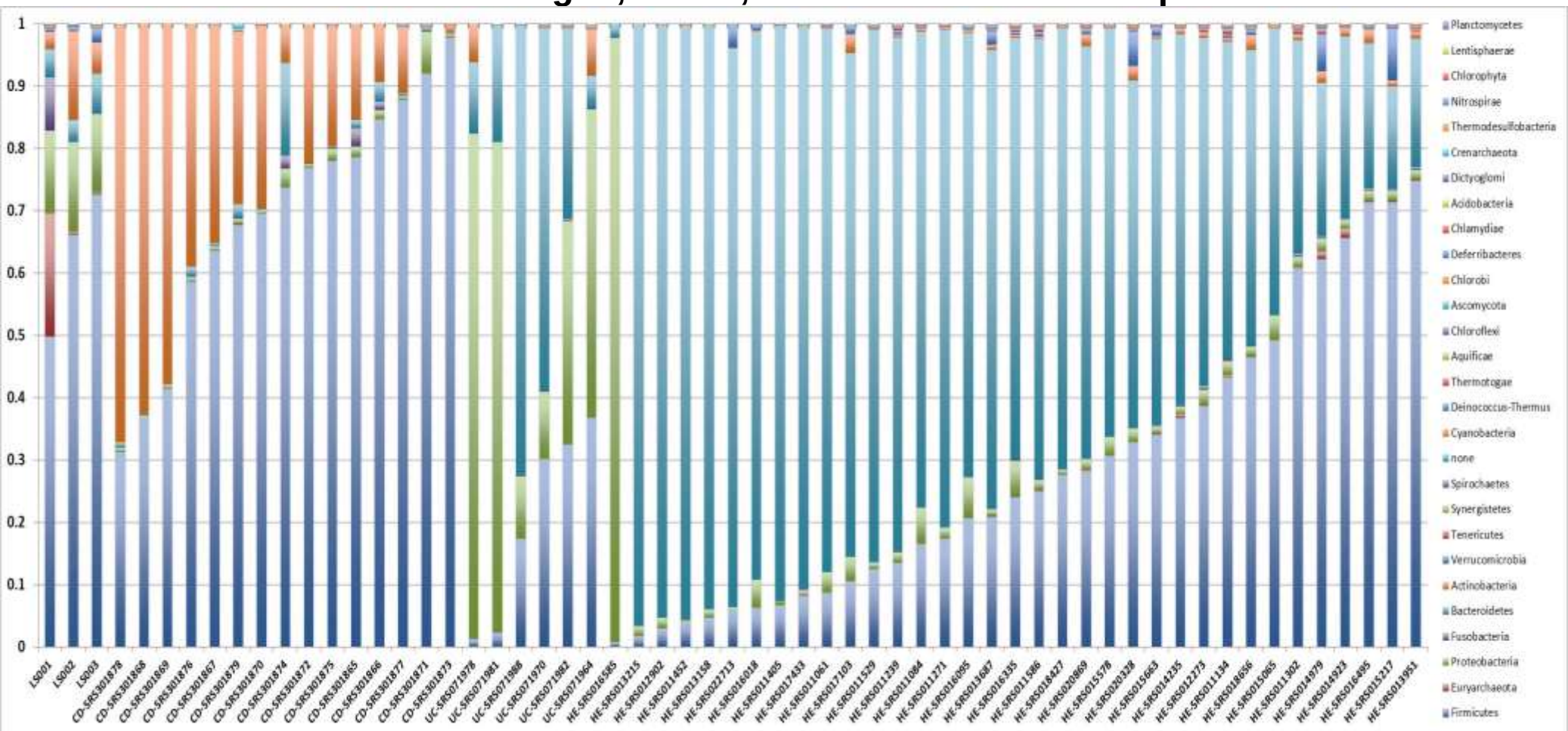
# To Map My Gut Microbes, I Sent a Stool Sample to the Venter Institute for Metagenomic Sequencing




**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**

# Phyla Gut Microbial Abundance Without Viruses: LS, Crohn's, UC, and Healthy Subjects

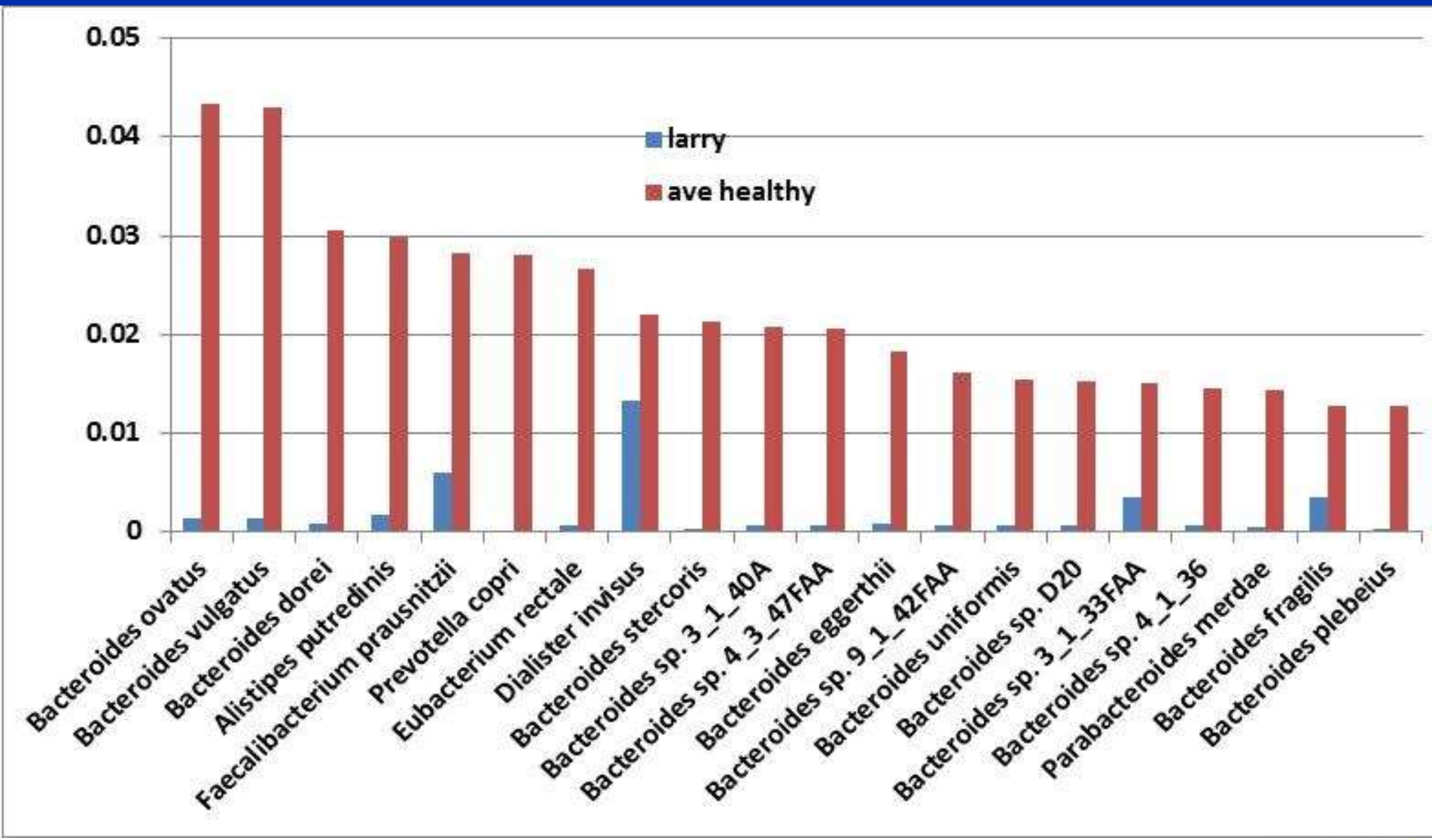
**Source: Weizhong Li, UCSD; Calit2 FuturePatient Expedition**




**LS** **Crohn's** **Ulcerative Colitis** **Healthy**

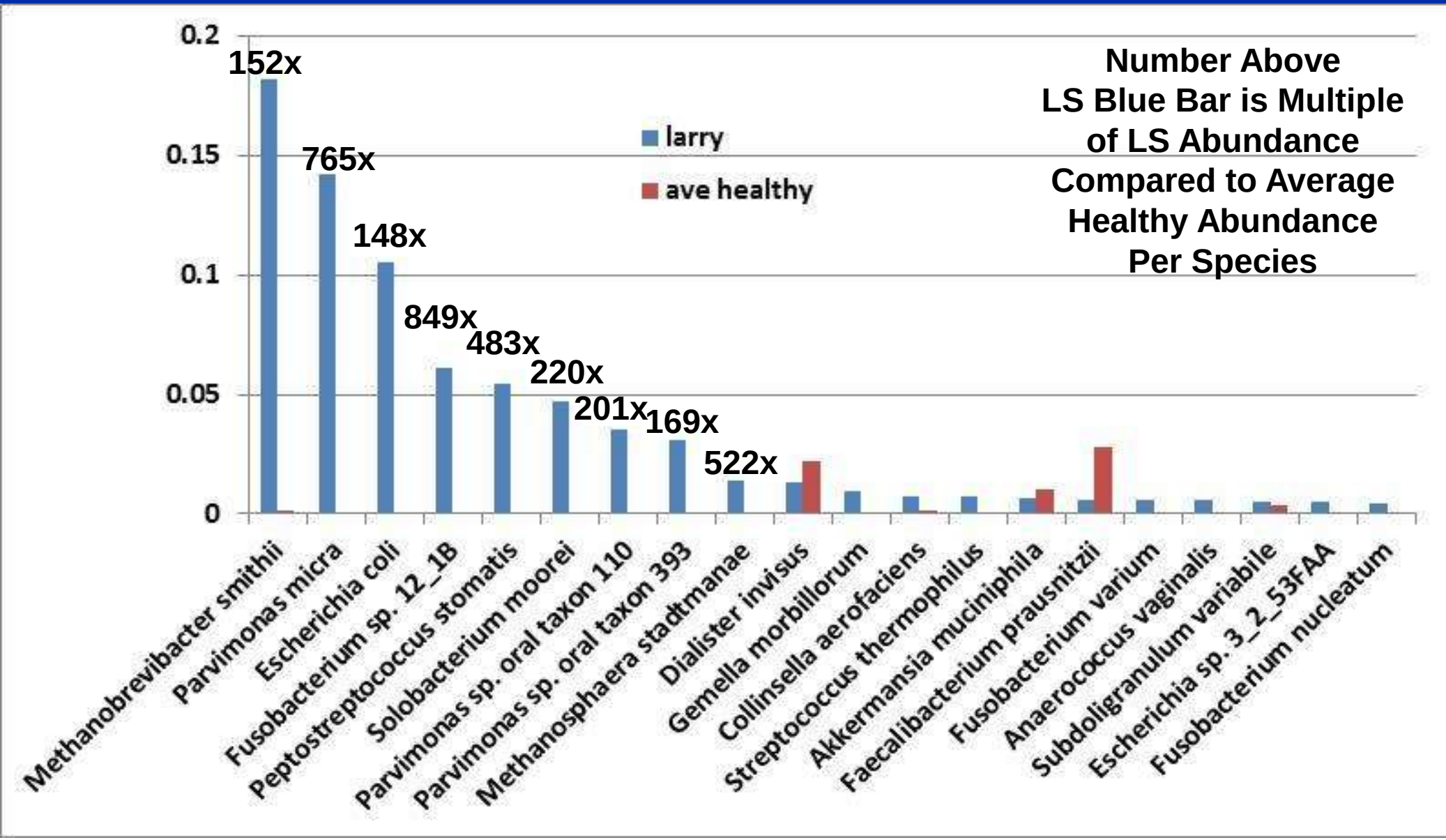
## Toward Noninvasive Microbial Ecology Diagnostics

# Almost All Abundant Species (≥1%) in Healthy Subjects Are *Severely Depleted* in LS Gut



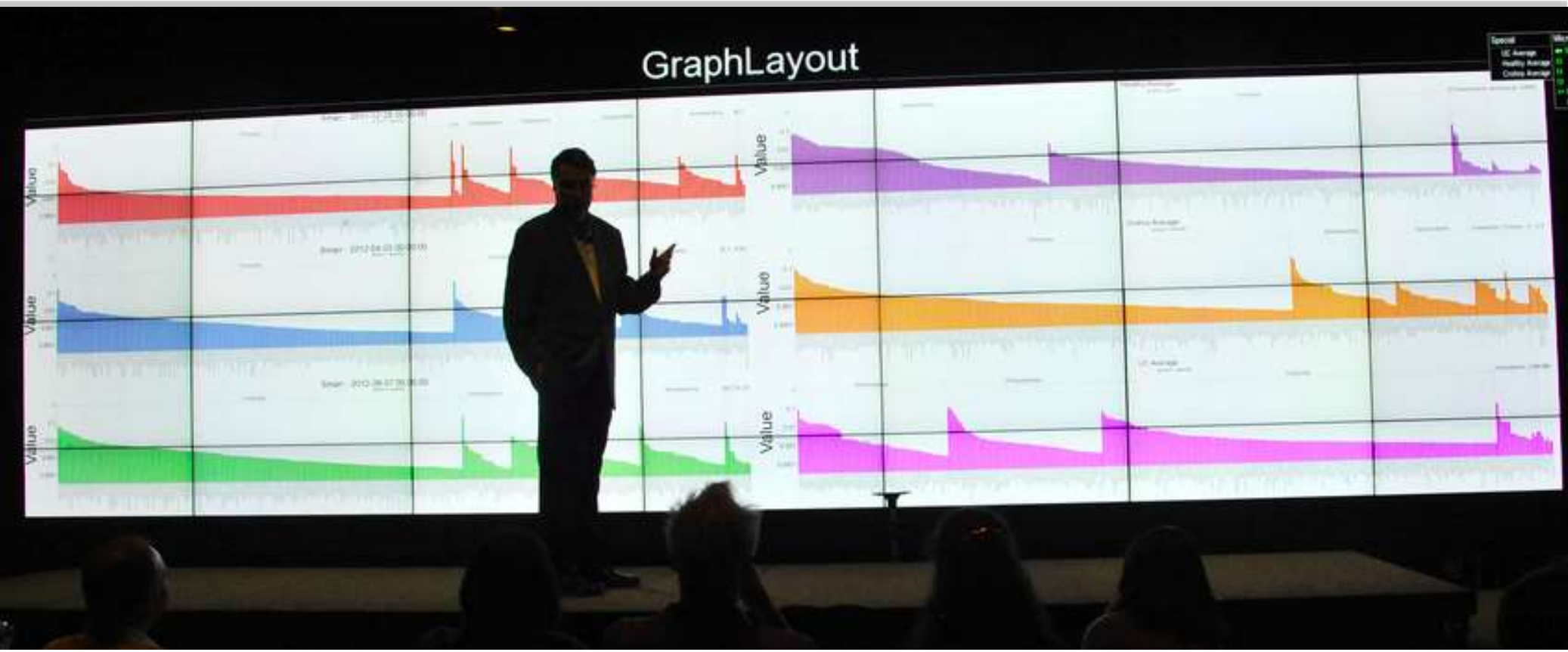

**Source: Sequencing JCVI; Analysis Weizhong Li, UCSD**
**LS December 28, 2011 Stool Sample**

# Top 20 Most Abundant Microbial Species In LS vs. Average Healthy Subject




Source: Sequencing JCVI; Analysis Weizhong Li, UCSD
LS December 28, 2011 Stool Sample

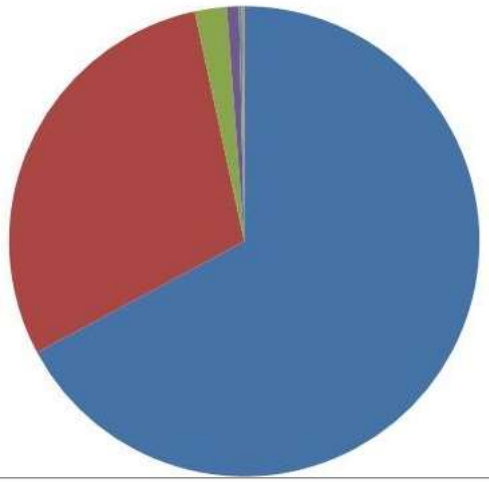
# Comparing 3 LS Time Snapshots (Left) with Healthy, Crohn's, UC (Right Top to Bottom)

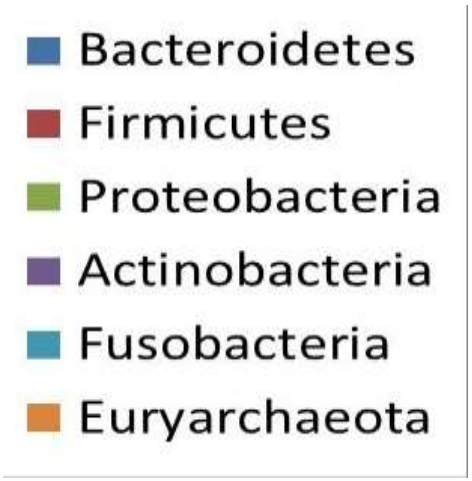


# We Find Major Shifts in Microbial Ecology Between Healthy and Two Forms of IBD

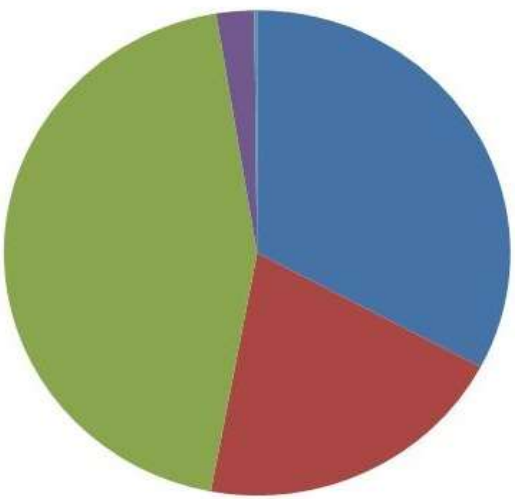
**Microbiome "Dysbiosis" or "Mass Extinction"?**

Ave. Healthy



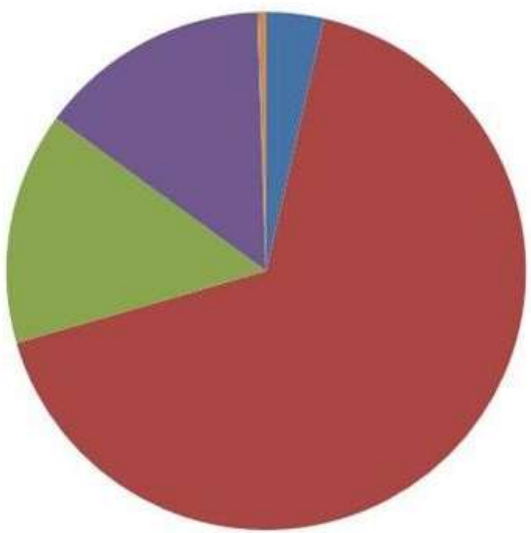



Ave. Ulcerative Colitis



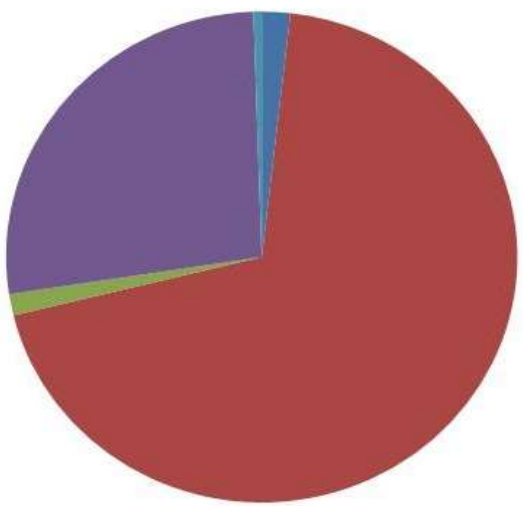
Explosion of Proteobacteria

LS Apr 2012



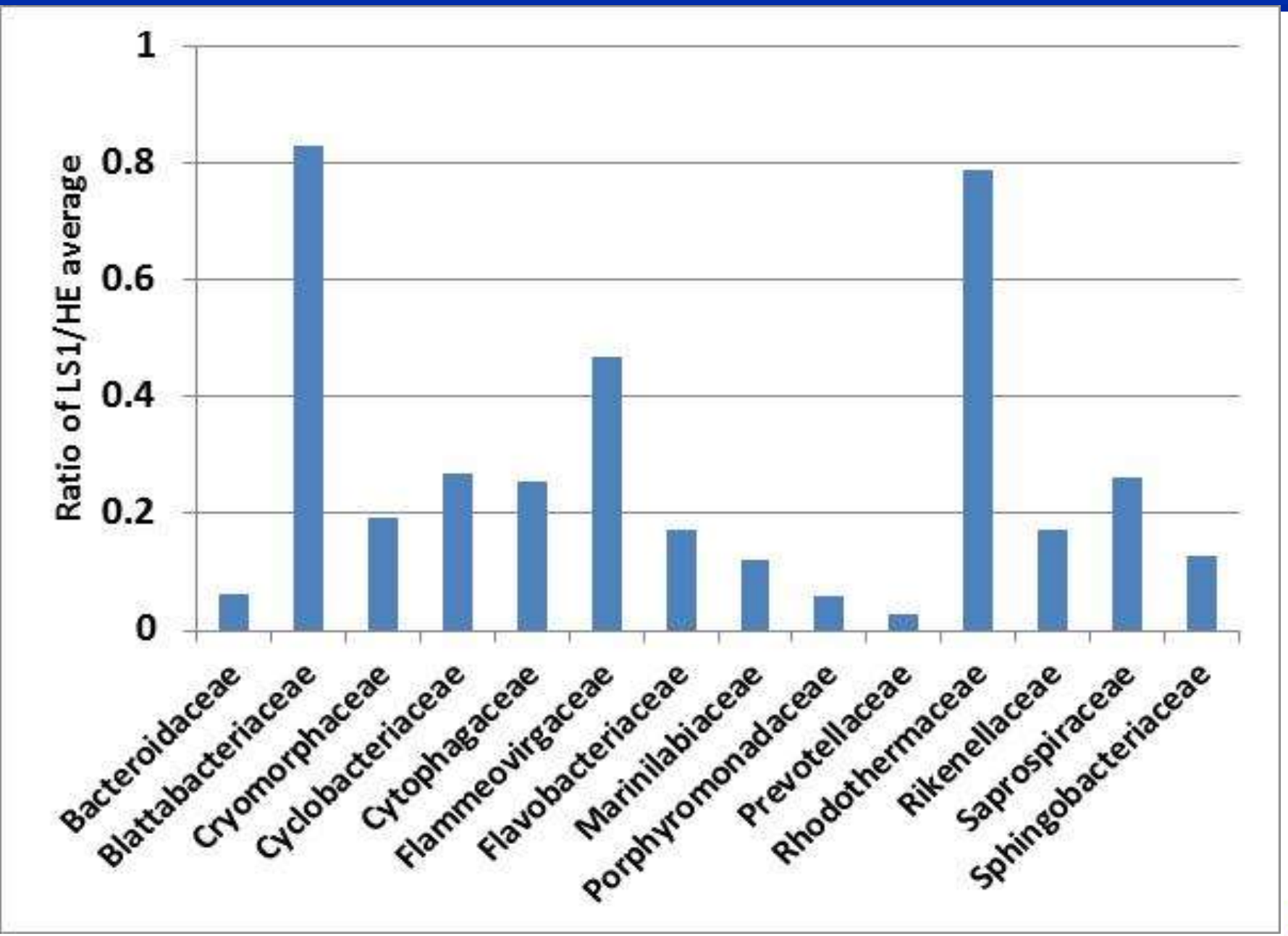
On the IBD Spectrum

Ave. Crohn's

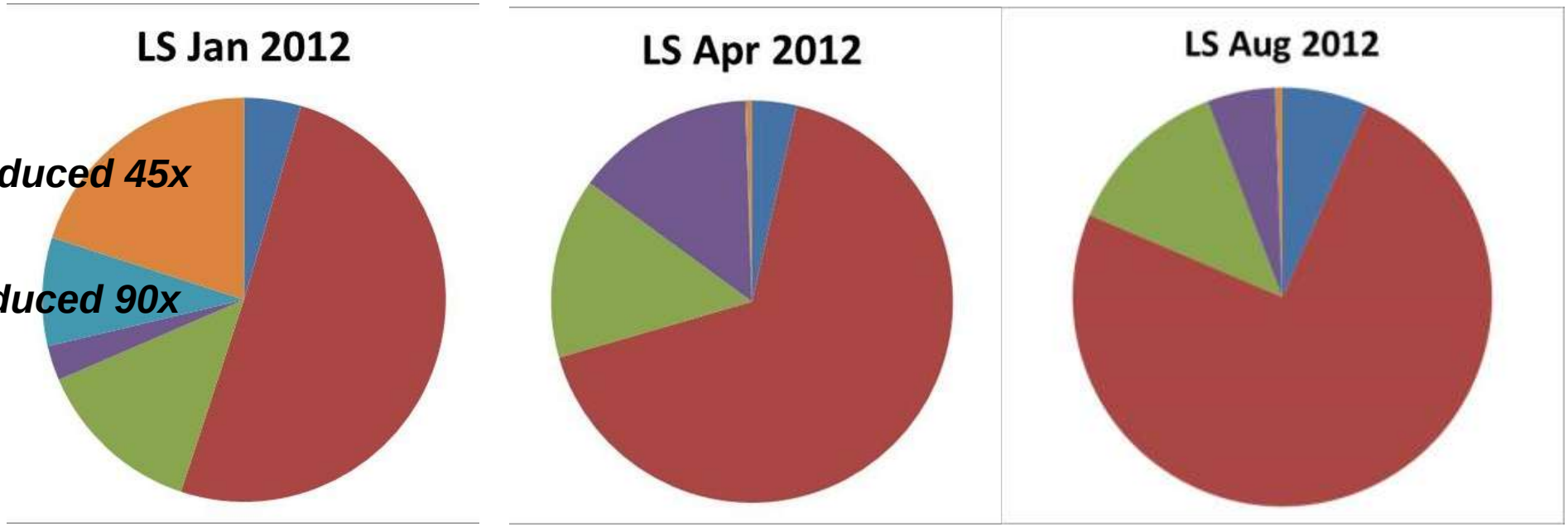


Collapse of Bacteroidetes

# I Have Massive Reduction in the Families of the Bacteroidetes Phylum in My Gut



# Major Changes in LS Microbiome Before and After 1 Month Antibiotic & 2 Month Prednisone Therapy



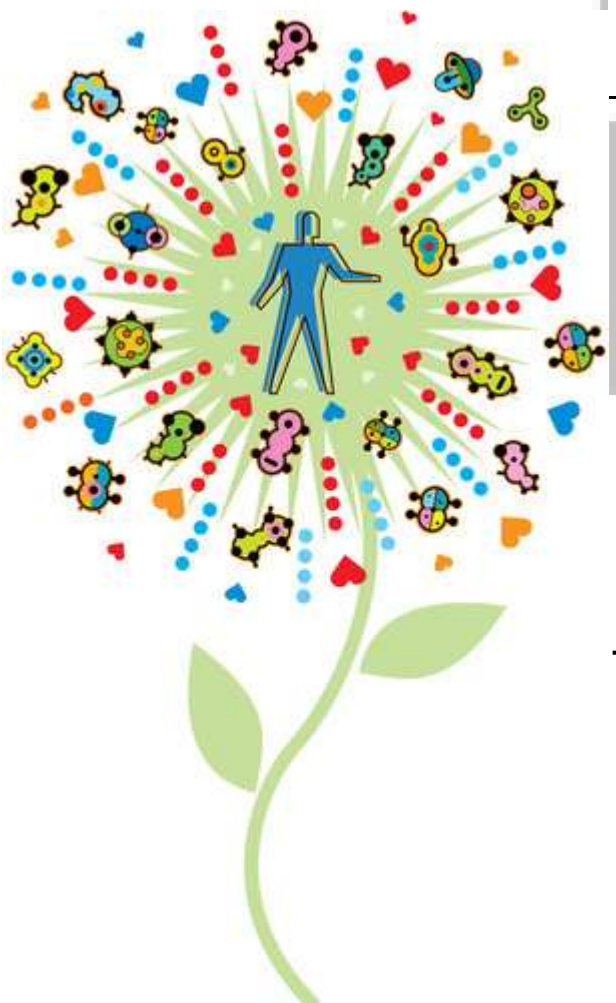

**Therapy Greatly Reduced Two Phyla, But Massive Reduction in Bacteroidetes And Large % Proteobacteria Remain**

**Small Changes With No Therapy**

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

**How Does One Get Back to a "Healthy" Gut Microbiome?**

# From War to Gardening



The New York Times

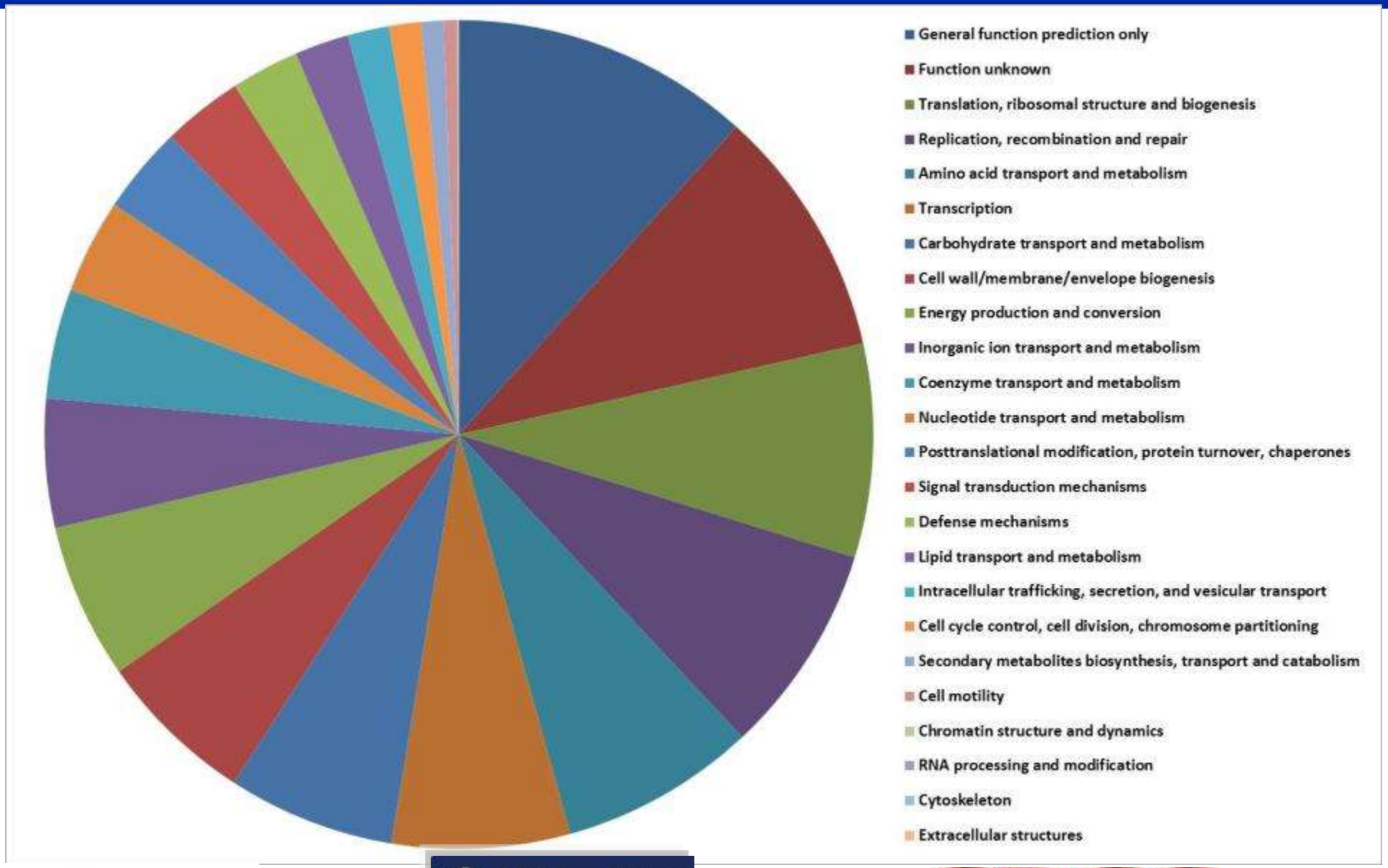
**Science**

## Tending the Body's Microbial Garden

By CARL ZIMMER
Published: June 18, 2012

"I would like to lose the language of warfare,"
said Julie Segre, a senior investigator at
the National Human Genome Research Institute.
"It does a disservice to all the bacteria
that have co-evolved with us
and are maintaining the health of our bodies."

# From Taxonomy to Function: Analysis of LS Clusters of Orthologous Groups (COGs)




J. Craig Venter INSTITUTE

UC San Diego Health Sciences

SDSC

it²

**Analysis: Weizhong Li & Sitao Wu, UCSD**

# What is Adequate Metadata to Define the Environment of the Human Microbiome?

- **Need the Variables that Determine Relative Abundances of Microbial Species**
  - **Genetics of Host**
  - **Immune System Variables**
  - **Other Environmental Variables (Food, Antibiotics, etc.)**
- **At What Scale Do We Need These Metadata Variables?**
  - **SNPs vs. Full Genome**
  - **Medical Tests vs. Proteomics, Metabolomics, Transcriptomics**
  - **Phenotyping of Signs and Symptoms**