“The Microbiome in the Environment and You”

Joint Presentation by Larry Smarr and Rob Knight, UC San Diego

From ‘Omics to Action

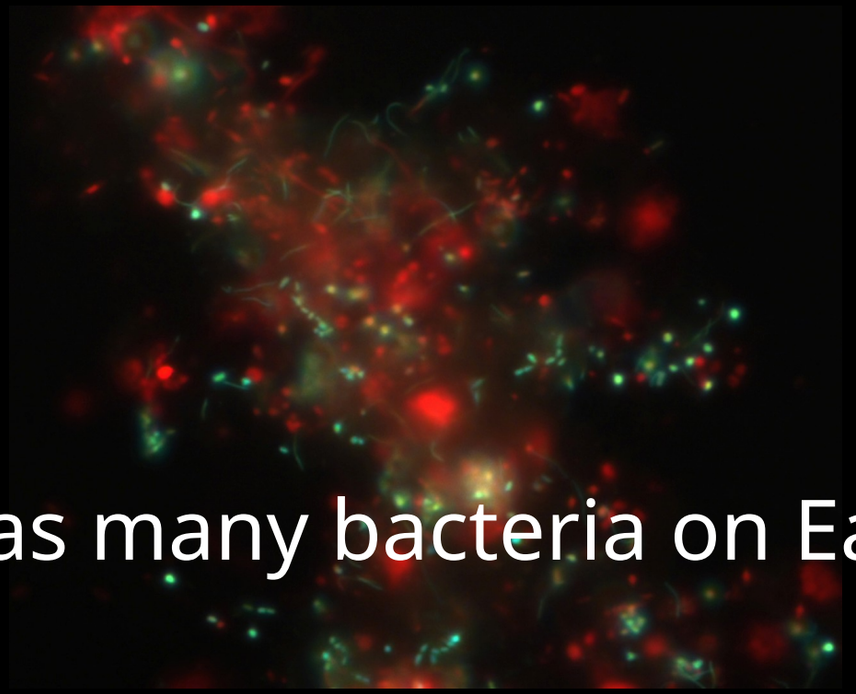
Exponential Medicine 2017

San Diego, CA

November 7, 2017

Earth is a microbial planet...



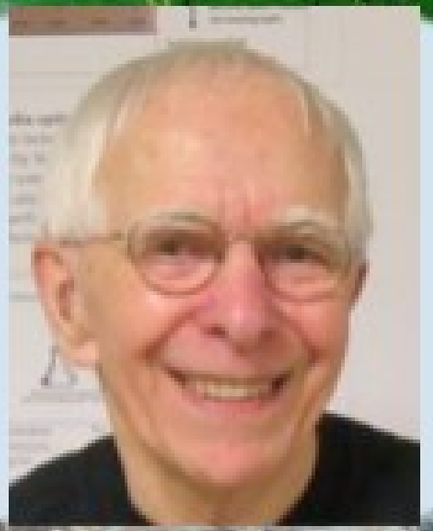


...there are 100 million times as many bacteria on Ea
as stars in the universe.

Microbiology is the ultimate Big Data science!

Once the diversity of the microbial world is catalogued, it will make astronomy look like a pitiful science.

- Julian Davies, Professor Emeritus, Microbiology and Immunology, UBC





>27,000 samples, crowdsourced

Initiated by Dept. of Energy at Argonne National Lab, but…



illumina® eppendorf

IDT INTEGRATED DNA TECHNOLOGIES

MO BIO Laboratories, Inc.

John Templeton Foundation

W. M. KECK FOUNDATION

earth microbiome project

Temperature





0-100°C

pH



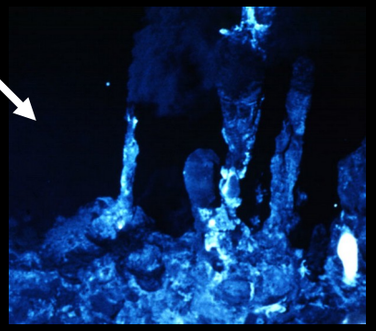
1-12



2007:
202 samples
21,752
sequences

Pressure





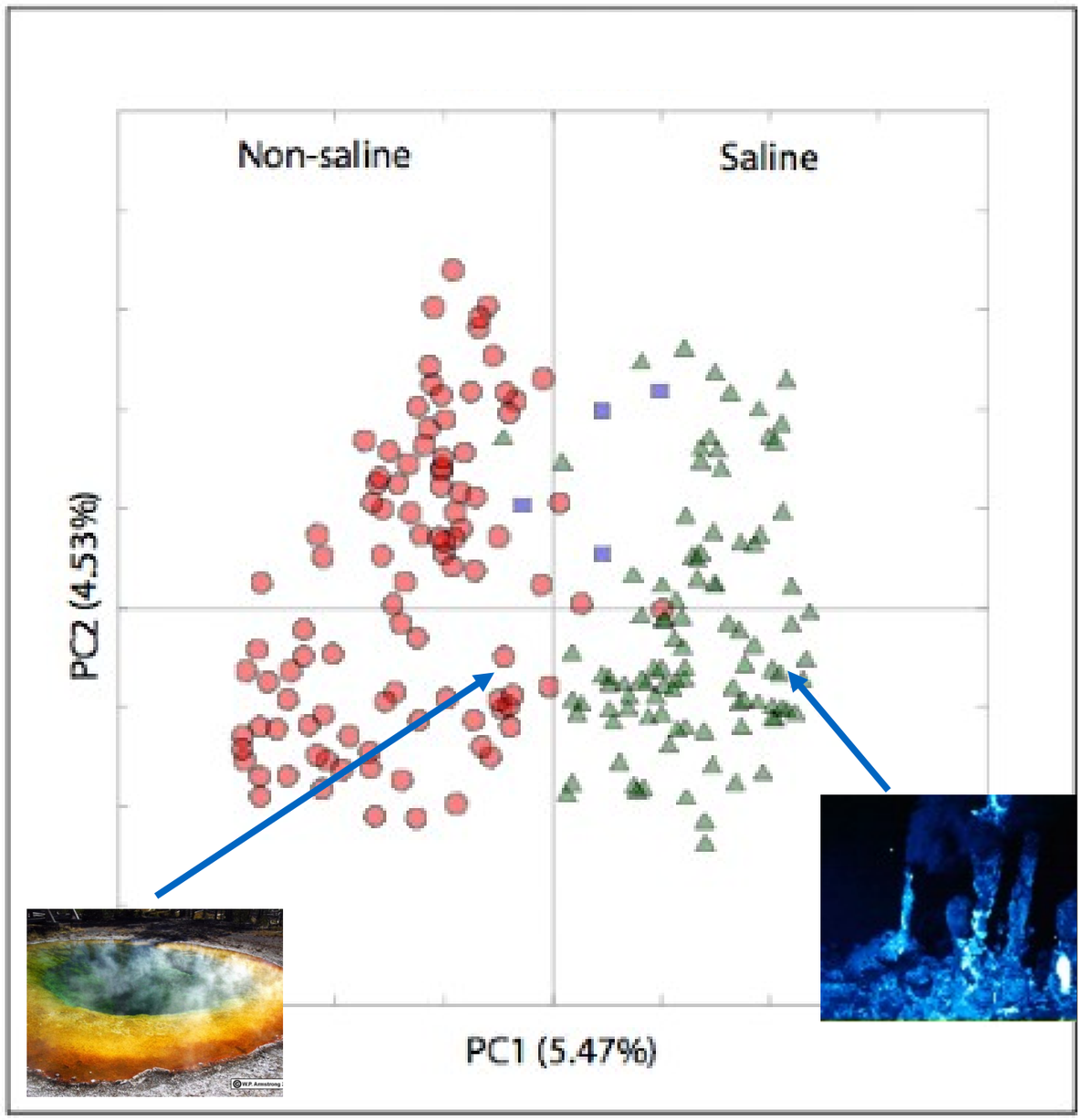
1-200 atm

Nutrient Availability

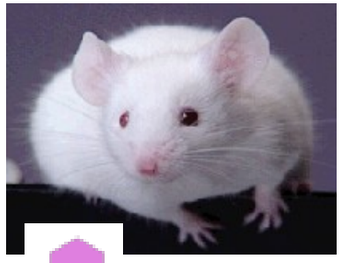


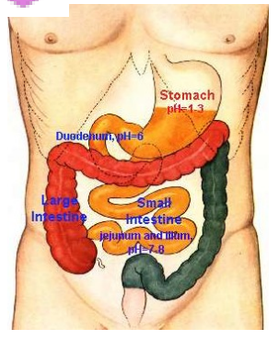


Oligotrophic
Eutrophic


Non-saline
Saline
PC2 (4.53%)
PC1 (5.47%)


Non-saline
Saline
Mixed




Stomach
pH=1.3
Duodenum,pH=6
Large Intestine
Small intestine
jejunum and ilium,
pH=7.8



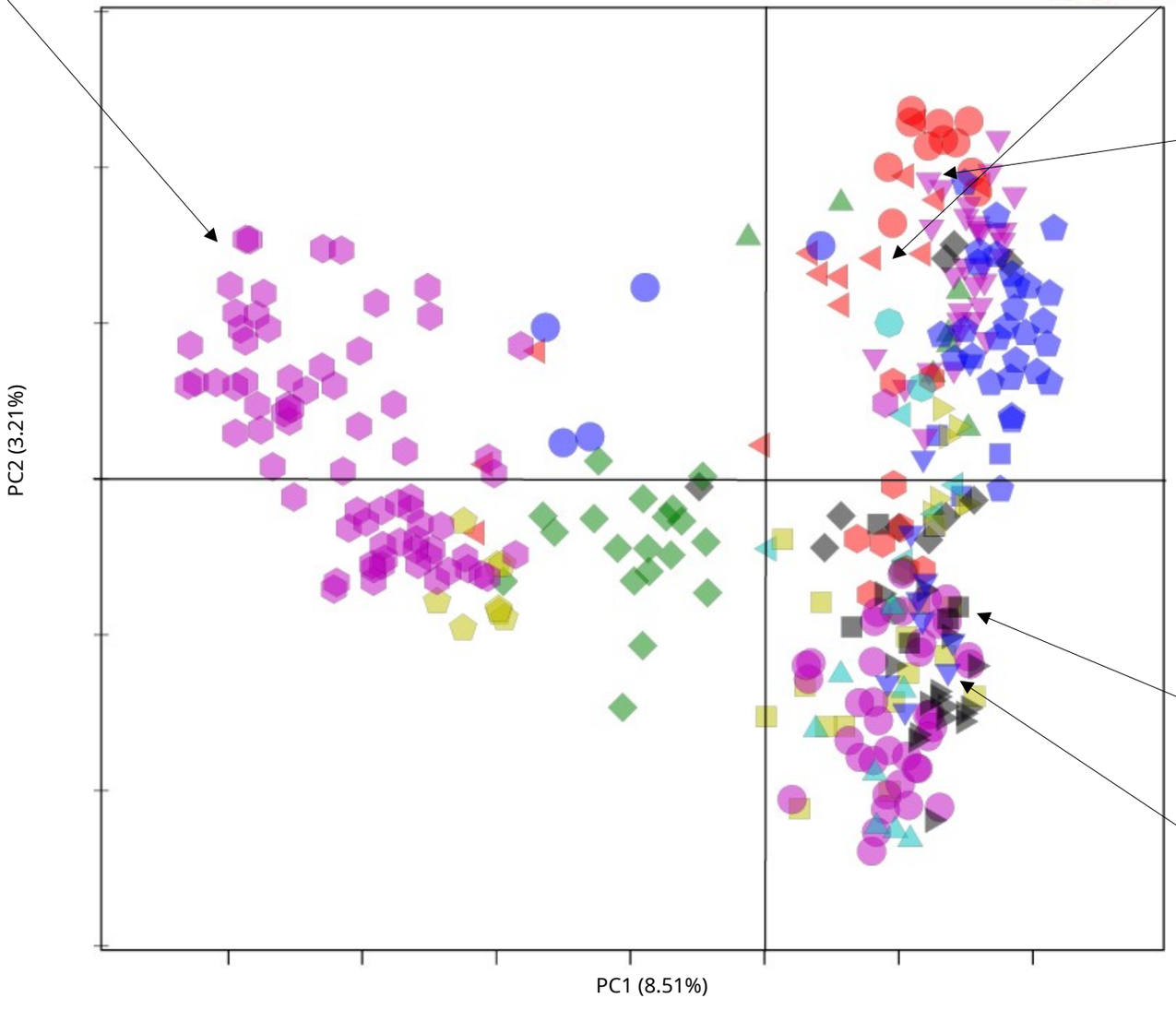


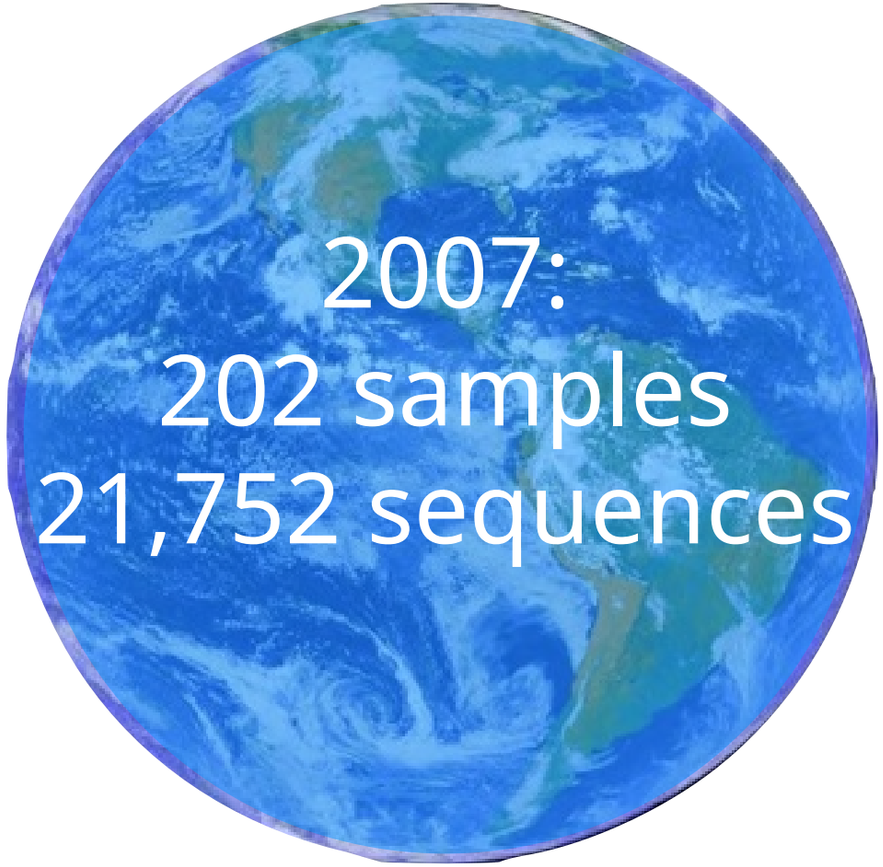


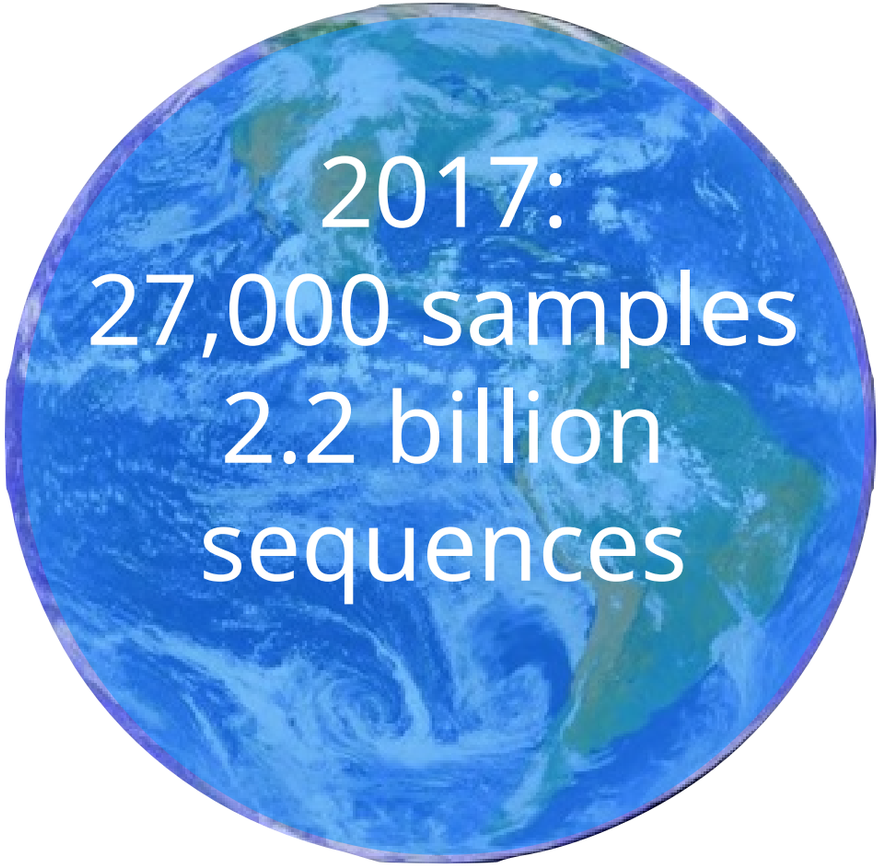







PC2 (3.21%)
PC1 (8.51%)


2007:
202 samples
21,752 sequences

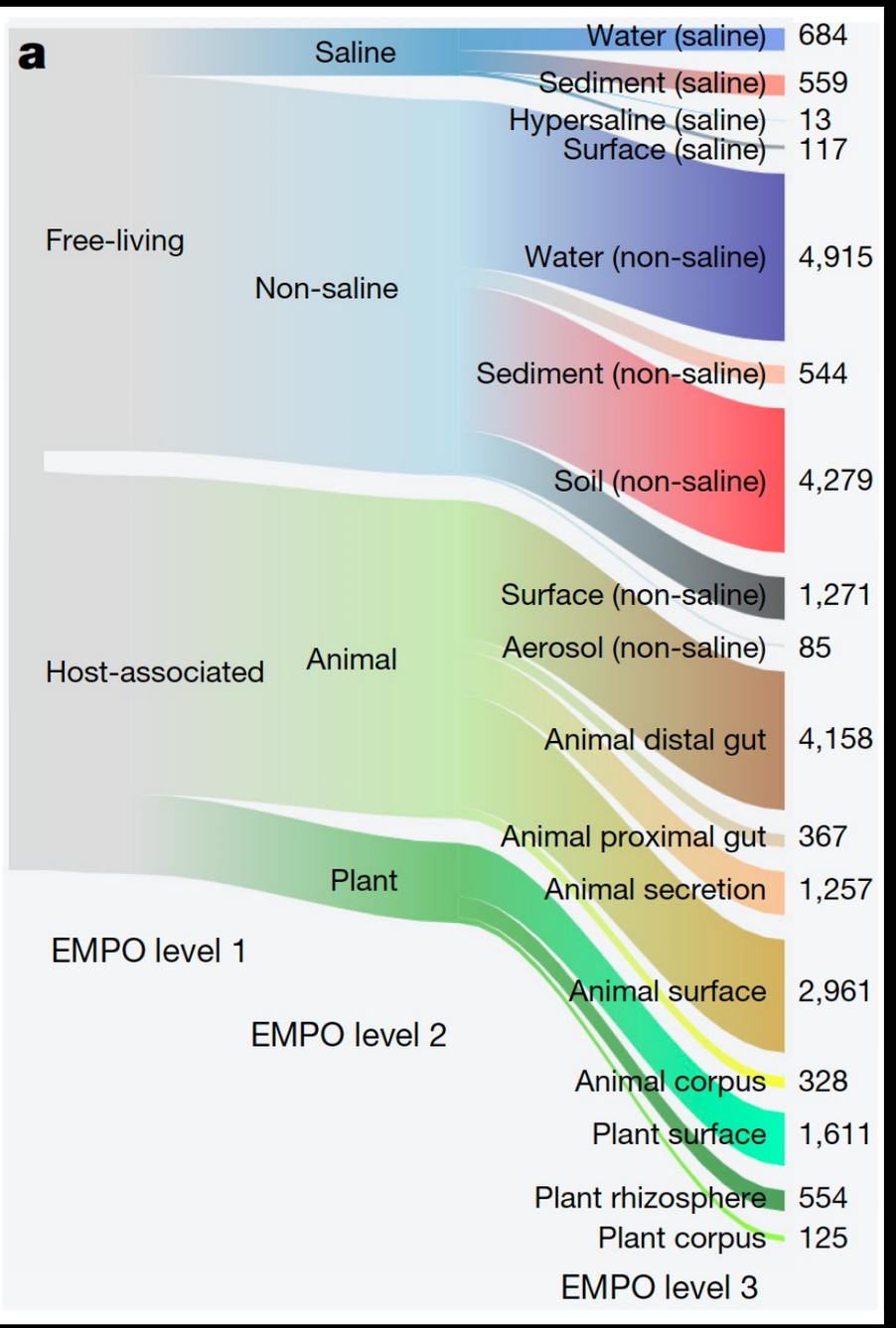

2017:
27,000 samples
2.2 billion
sequences

A communal catalogue reveals Earth's multiscale microbial diversity

Luke R. Thompson[1,2,3], Jon G. Sanders[1], Daniel McDonald[1], Amnon Amir[1], Joshua Ladau[4], Kenneth J. Locey[5], Robert J. Prill[6], Anupriya Tripathi[1,7,8], Sean M. Gibbons[9,10], Gail Ackermann[1], Jose A. Navas-Molina[1,11], Stefan Janssen[1], Evguenia Kopylova[1], Yoshiki Vázquez-Baeza[1,11], Antonio González[1], James T. Morton[1,11], Siavash Mirarab[12], Zhenjiang Zech Xu[1], Lingjing Jiang[1,13], Mohamed F. Haroon[14], Jad Kanbar[1], Qiyun Zhu[1], Se Jin Song[1], Tomasz Kosciolek[1], Nicholas A. Bokulich[15], Joshua Lefler[1], Colin J. Brislawn[16], Gregory Humphrey[1], Sarah M. Owens[17], Jarrad Hampton-Marcell[17,18], Donna Berg-Lyons[19], Valerie McKenzie[20], Noah Fierer[20,21], Jed A. Fuhrman[22], Aaron Clauset[19,23], Rick L. Stevens[24,25], Ashley Shade[26,27,28], Katherine S. Pollard[4], Kelly D. Goodwin[3], Janet K. Jansson[16], Jack A. Gilbert[17,29], Rob Knight[1,11,30] & The Earth Microbiome Project Consortium*

nature

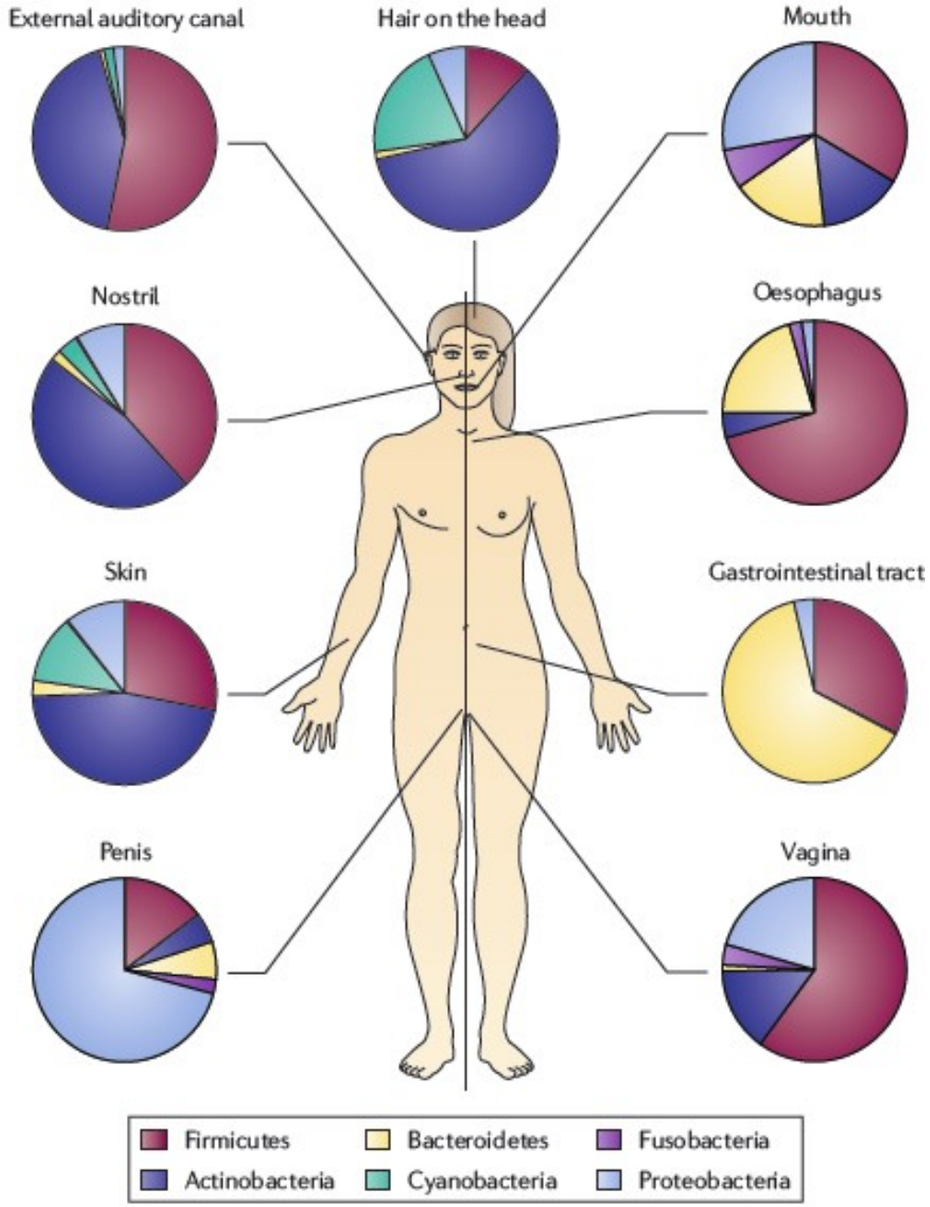
November 1, 2017


a
Saline
Free-living
Non-saline
Host-associated
Animal
Plant
EMPO level 1
EMPO level 2
Water (saline) 684
Sediment (saline) 559
Hypersaline (saline) 13
Surface (saline) 117
Water (non-saline) 4,915
Sediment (non-saline) 544
Soil (non-saline) 4,279
Surface (non-saline) 1,271
Aerosol (non-saline) 85
Animal distal gut 4,158
Animal proximal gut 367
Animal secretion 1,257
Animal surface 2,961
Animal corpus 328
Plant surface 1,611
Plant rhizosphere 554
Plant corpus 125
EMPO level 3

Treating the Human Superorganism: Your Body is an Ecology!

Human Microbiome Project

The NIH Common Fund
WE ACCELERATE DISCOVERY.

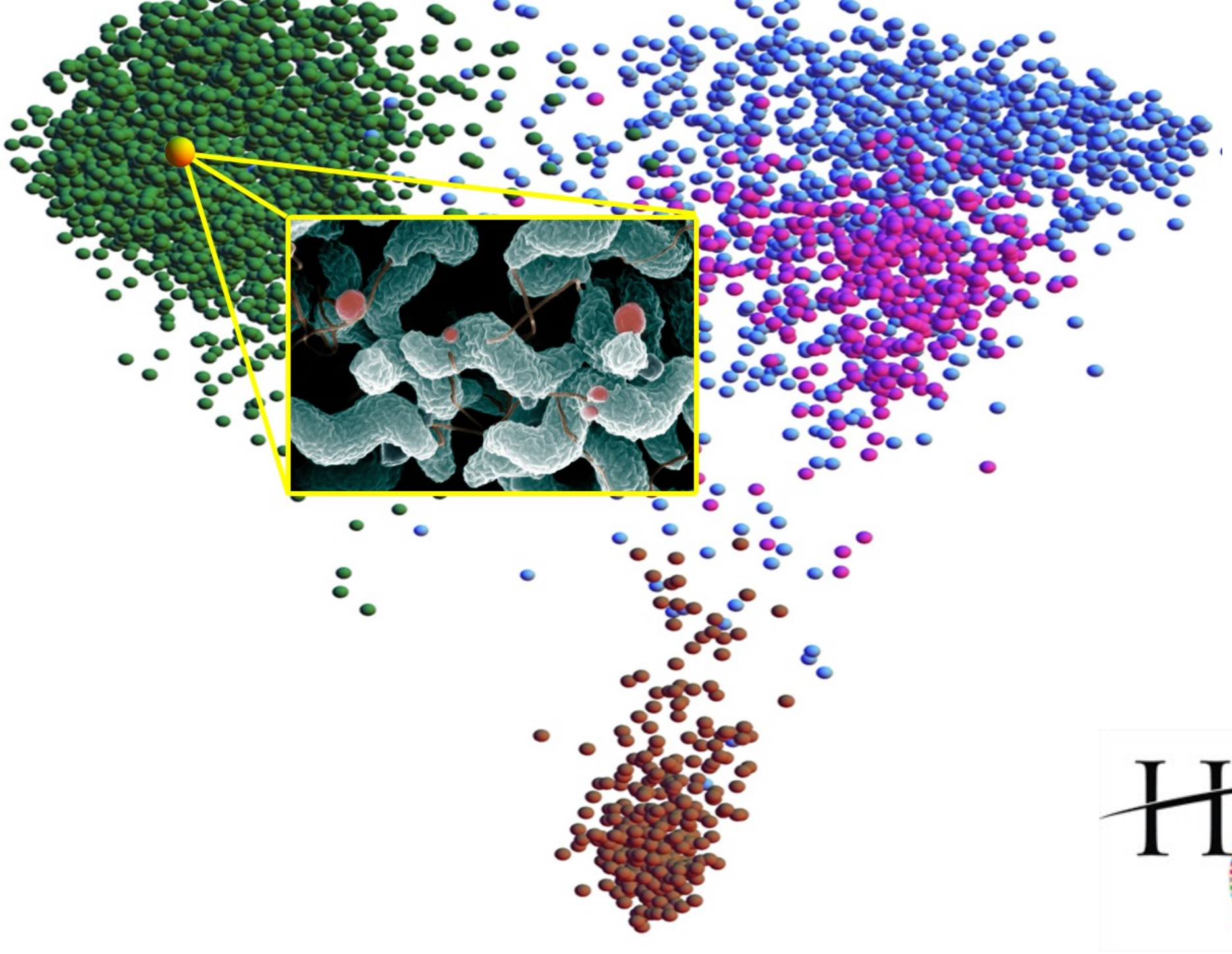


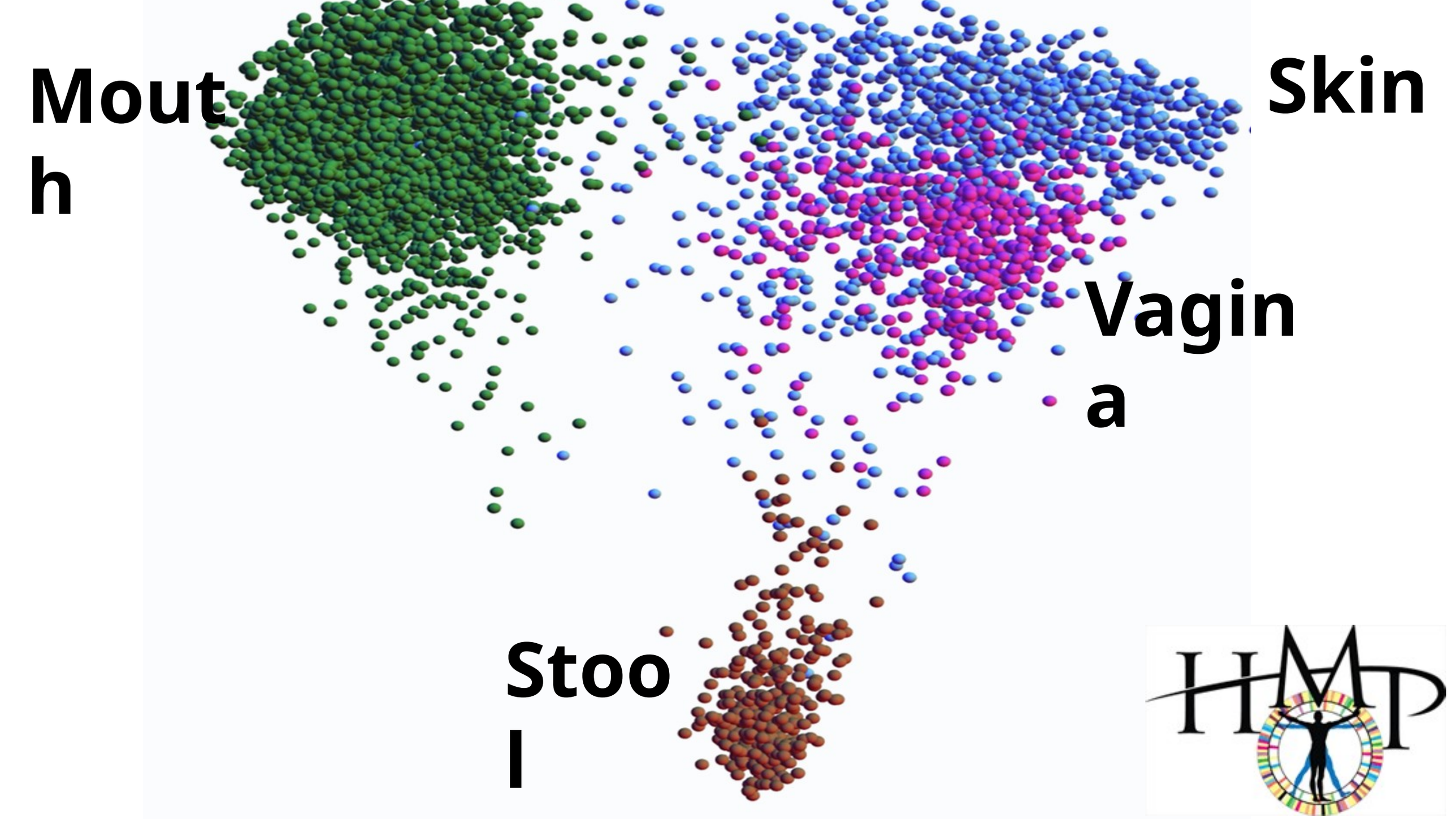
Nature Reviews Microbiology
v.9, p. 279 (2011)



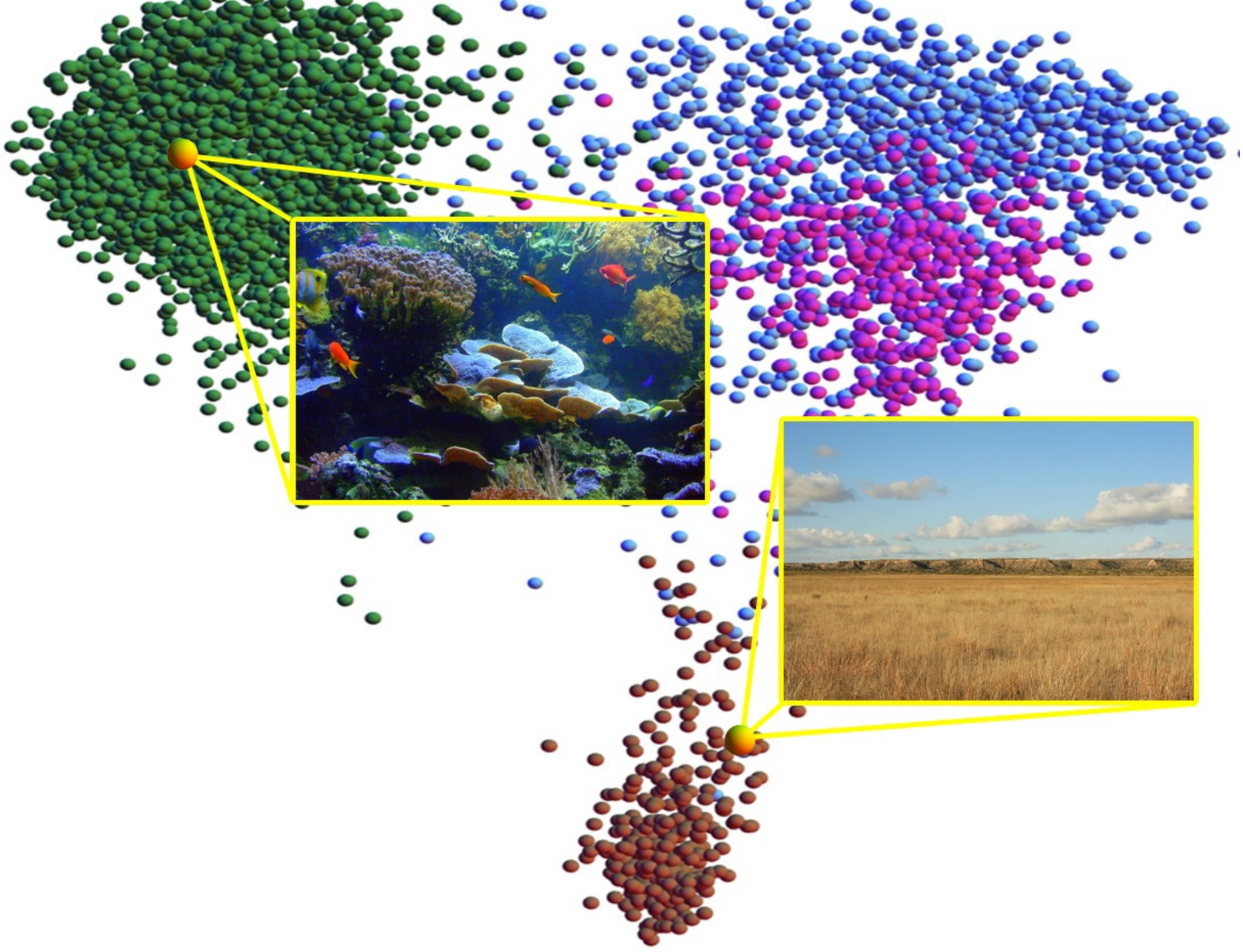
- >$2M raised
- >12000 kits
- >10000 samples sequenced and data in EBI incl 400 PGP samples...

...but we still need more!



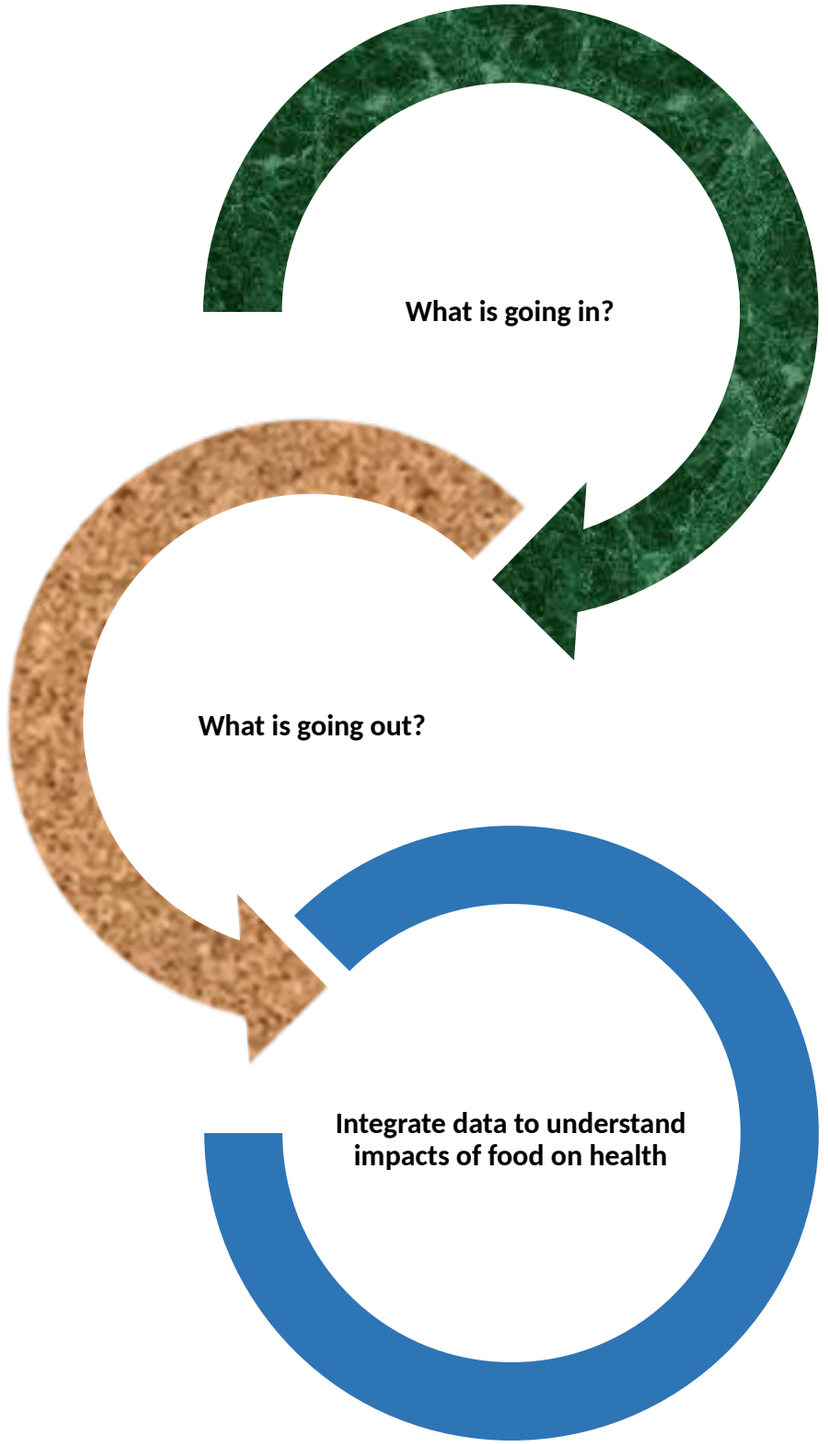

Mouth
Skin
Vagina
Stool





What is the impact on our internal microbiome from environmental influences such as the food we eat?

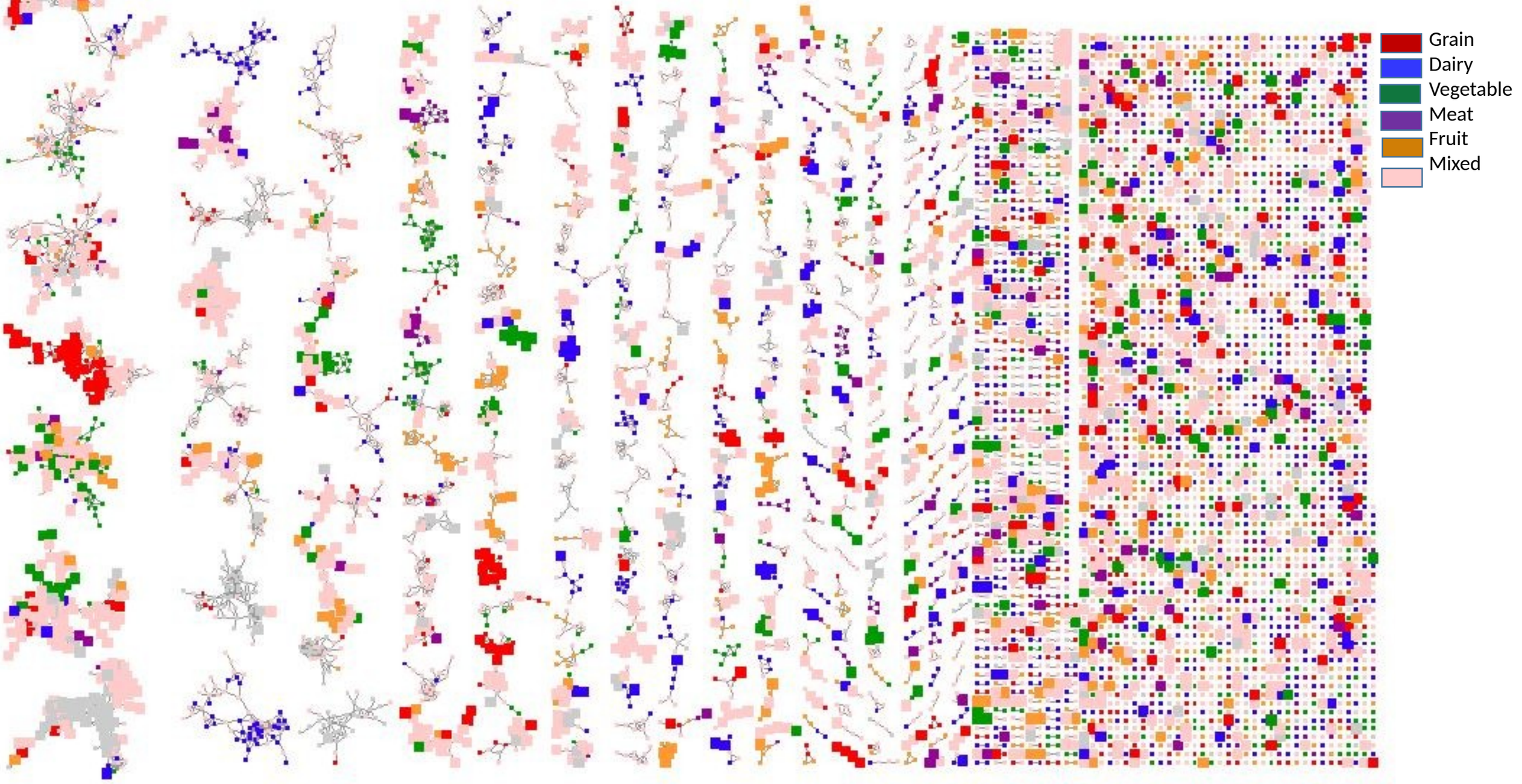
American Gut Project
www.americangut.org



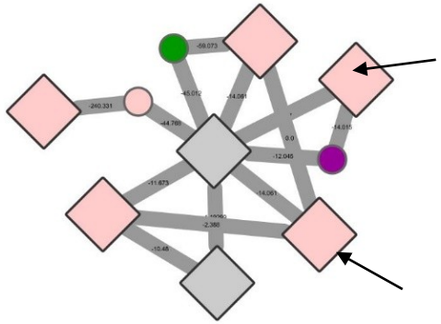
Global FoodOmics Project

Meta-analyses

Food Molecular Network



Expected molecules



piperine

piperyline

Unexpected molecules

Pesticide detection

5-hydroxy thiabendazole

thiabendazole

imazalil





nile/Pixabay

Fish fraud in Los Angeles sushi restaurants

Jan. 13, 2017

The fish in Los Angeles, California's sushi might actually be full of red herrings; that is, if you count the flounder passing for yellowfin in that spicy tuna roll. A new study has found that **almost half the fish served at top sushi restaurants across Los Angeles was mislabeled**, Yahoo! News reports. The study, published this week in *Conservation Biology*, ran DNA tests on 364 samples of 10 different fish from 26 restaurants over the course of 4 years. Of their sample, **47% was "fake,"** meaning it was being labeled as something it wasn't. For example, halibut, red snapper, and yellowfin tuna were almost always swapped out for an overexploited alternative like flounder. The researchers' recommendation to avoid getting hoodwinked? Order salmon.



PHOTOGRAPH BY SHEI

JUNE 6, 2014

Shrimp Receive Antibiotics in Factory Farms of the Sea

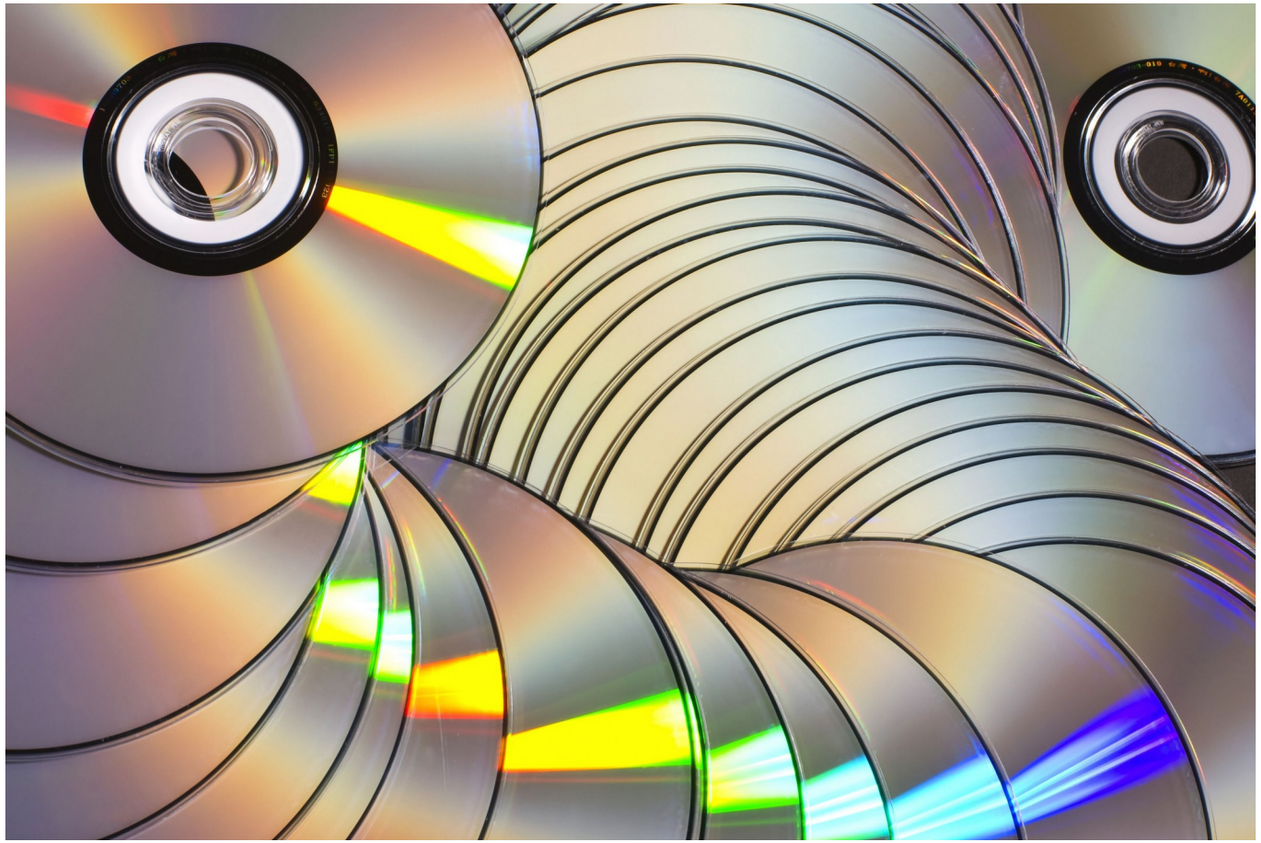
by **Maryn McKenna**

We are discovering the impact on the microbiome from common medical interventions


Larry’s stool to Rob’s lab

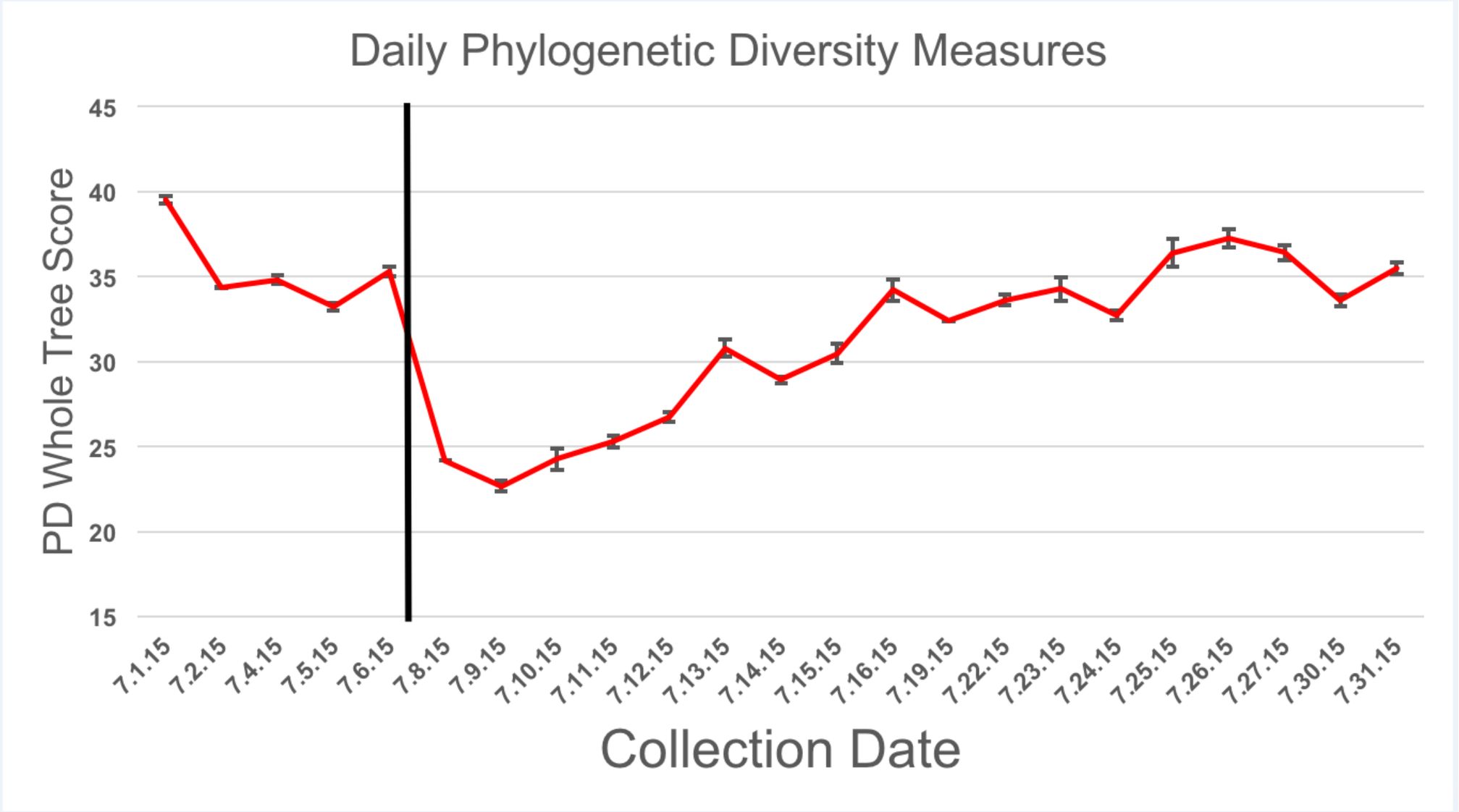
Human Stool Contains a Vast Amount of Information: 1 Gram Contains ~1 Billion Microbes, Each With >1 Million DNA Bases





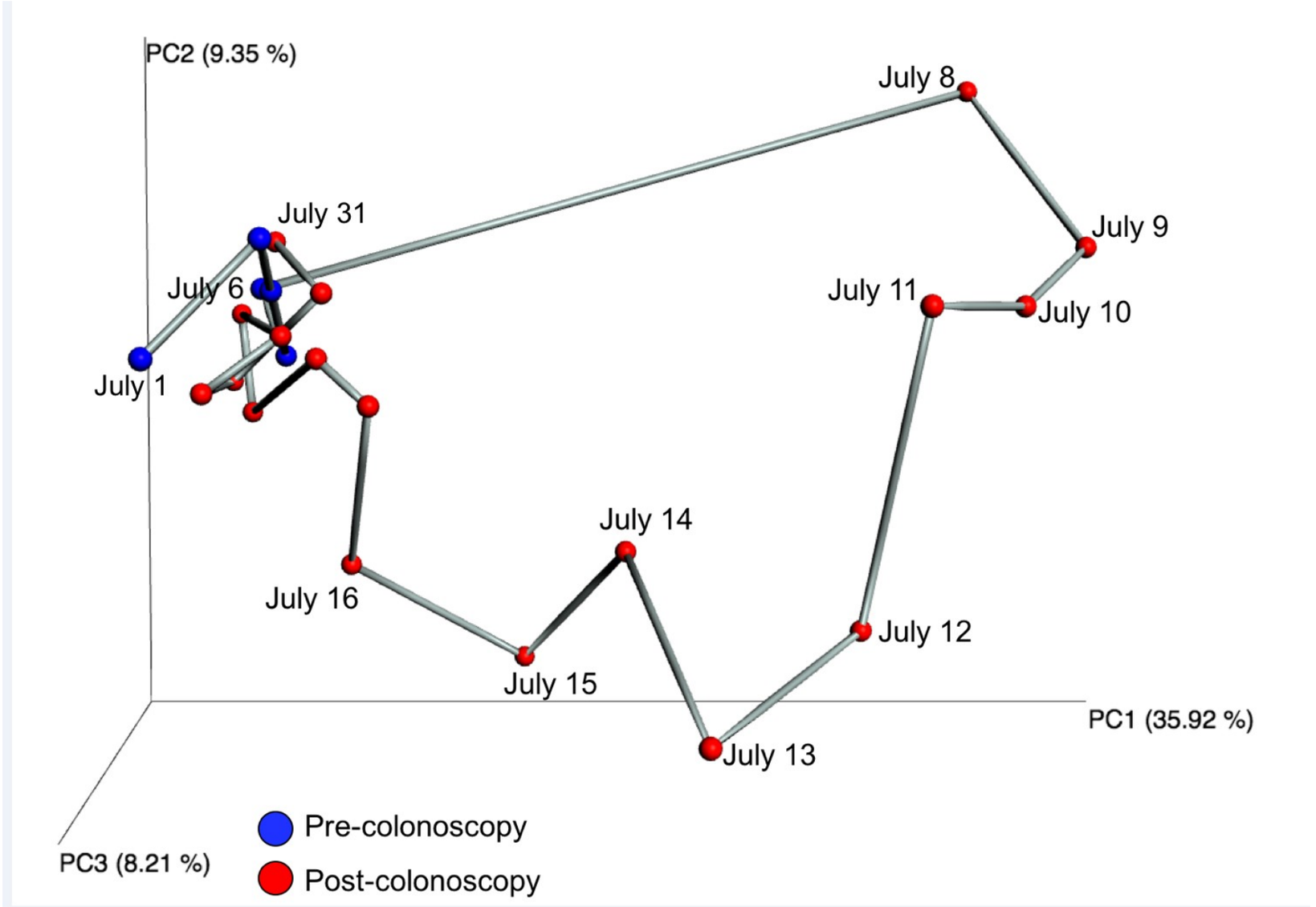
1 Teaspoon Stool Has the Information Content of 1 ton of DVDs

Microbiome Ecology Diversity Immediately Drops After Colon Cleanse — Followed By Slow Recovery



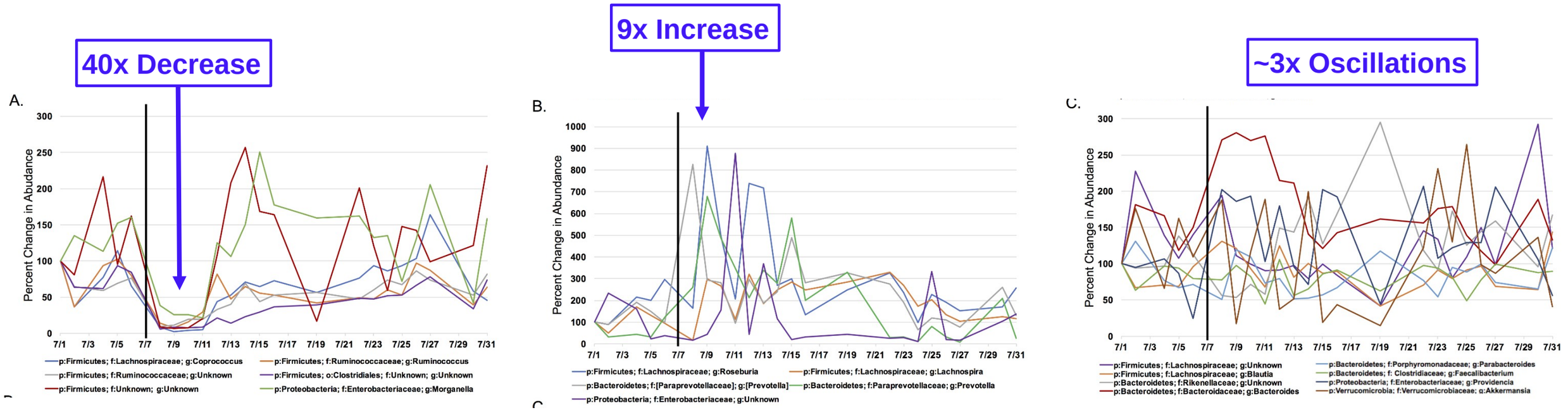
Source: Smarr, Hyde, McDonald, Sandborn, Knight

Large Jump In Microbiome Ecology After Cleanse — Then "Wanders" for Two Weeks Back to Normal



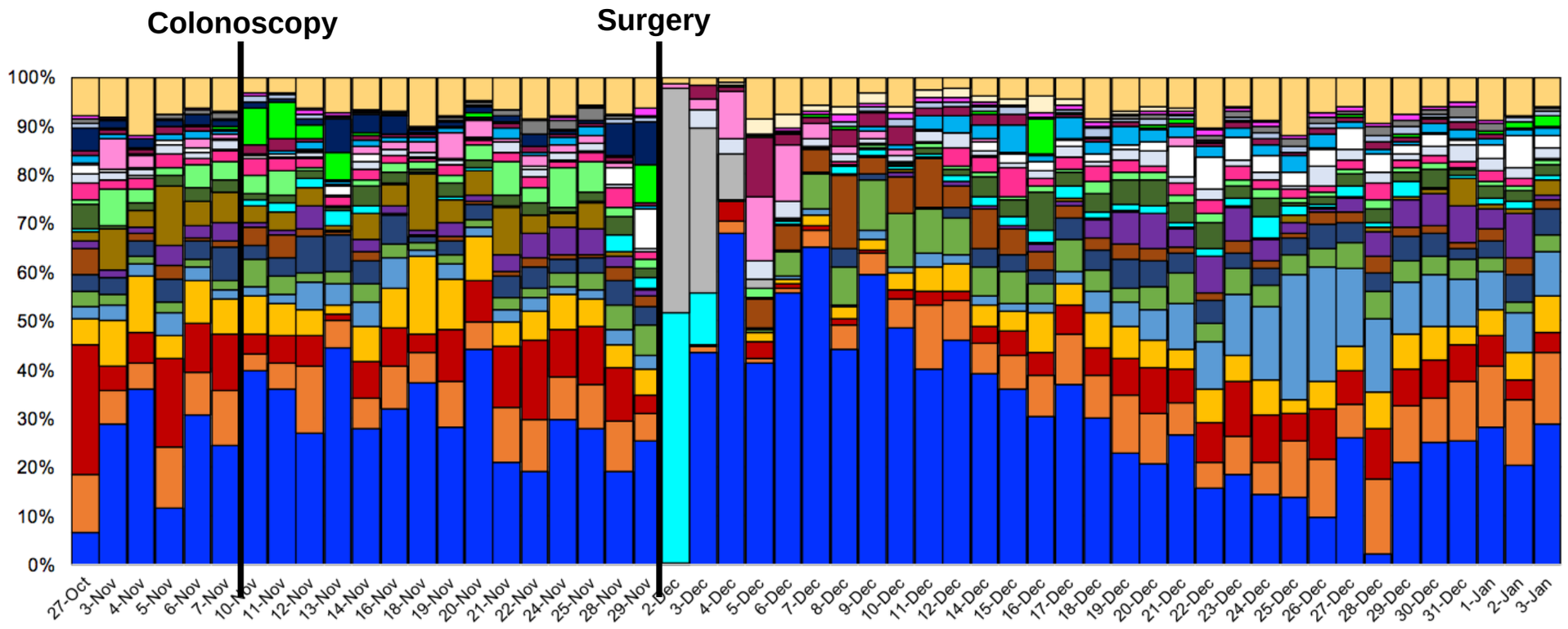
Source: Smarr, Hyde, McDonald, Sandborn, Knight

Colonoscopy Cleanse Differentially Impacts Gut Microbiome Genus Relative Abundance



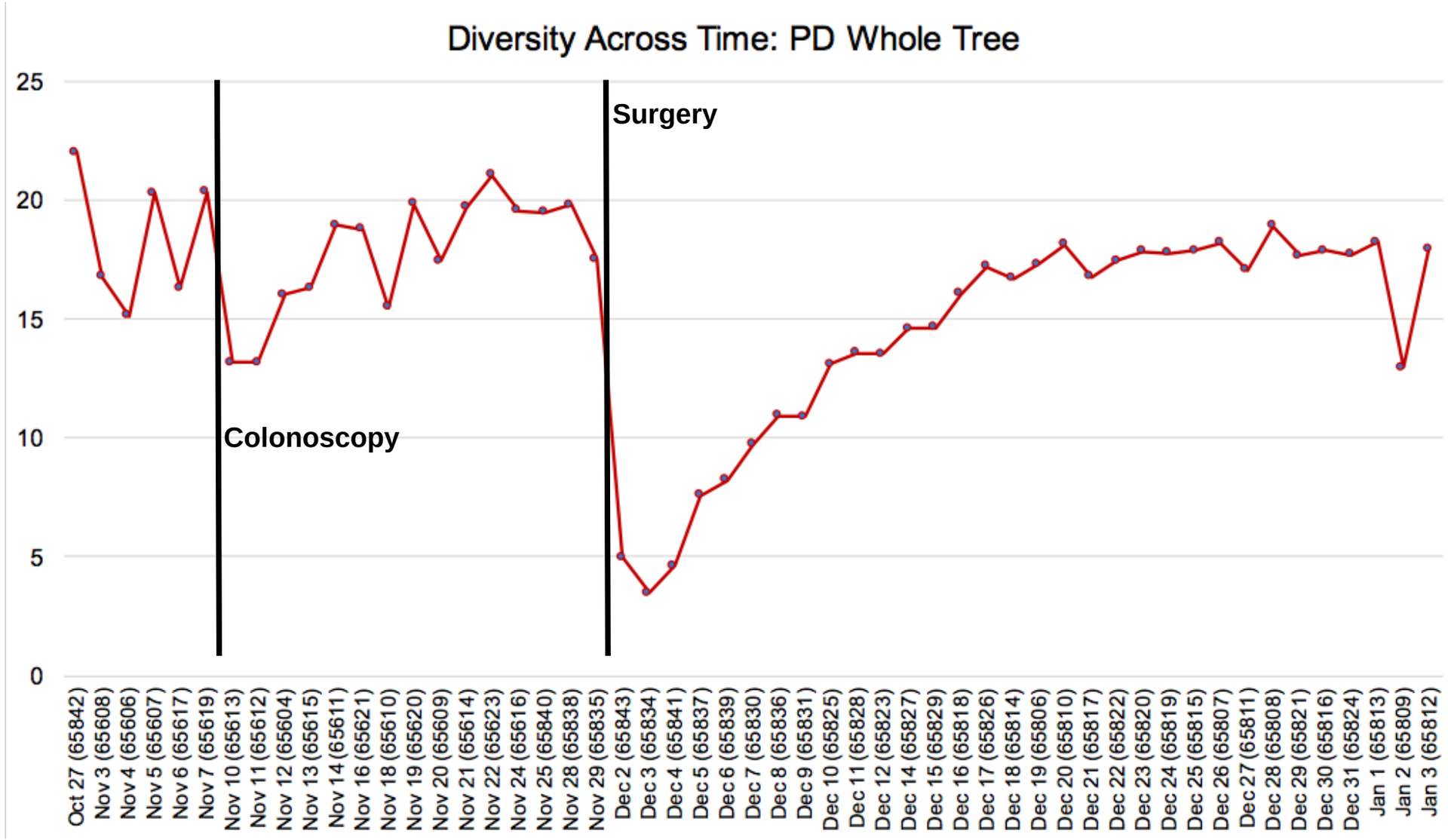
Source: Smarr, Hyde, McDonald, Sandborn, Knight

Gut Microbiome Genus-Level Profiles
Daily Samples Before and After Abdominal Surgery



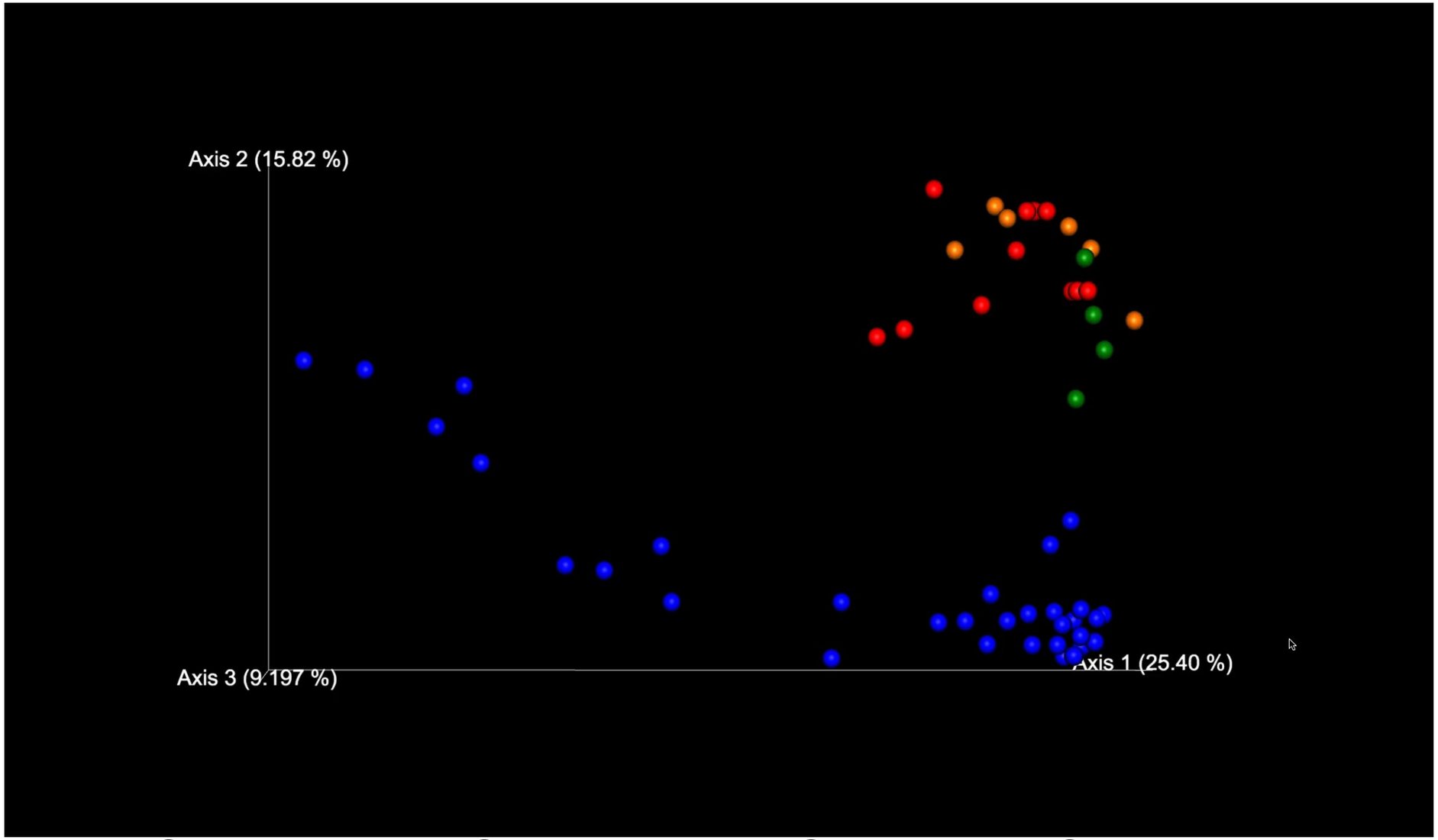
Source: Embriette Hyde, UCSD

Much Larger Drop in Microbiome Ecology Diversity Following Surgery Than Following Colonoscopy



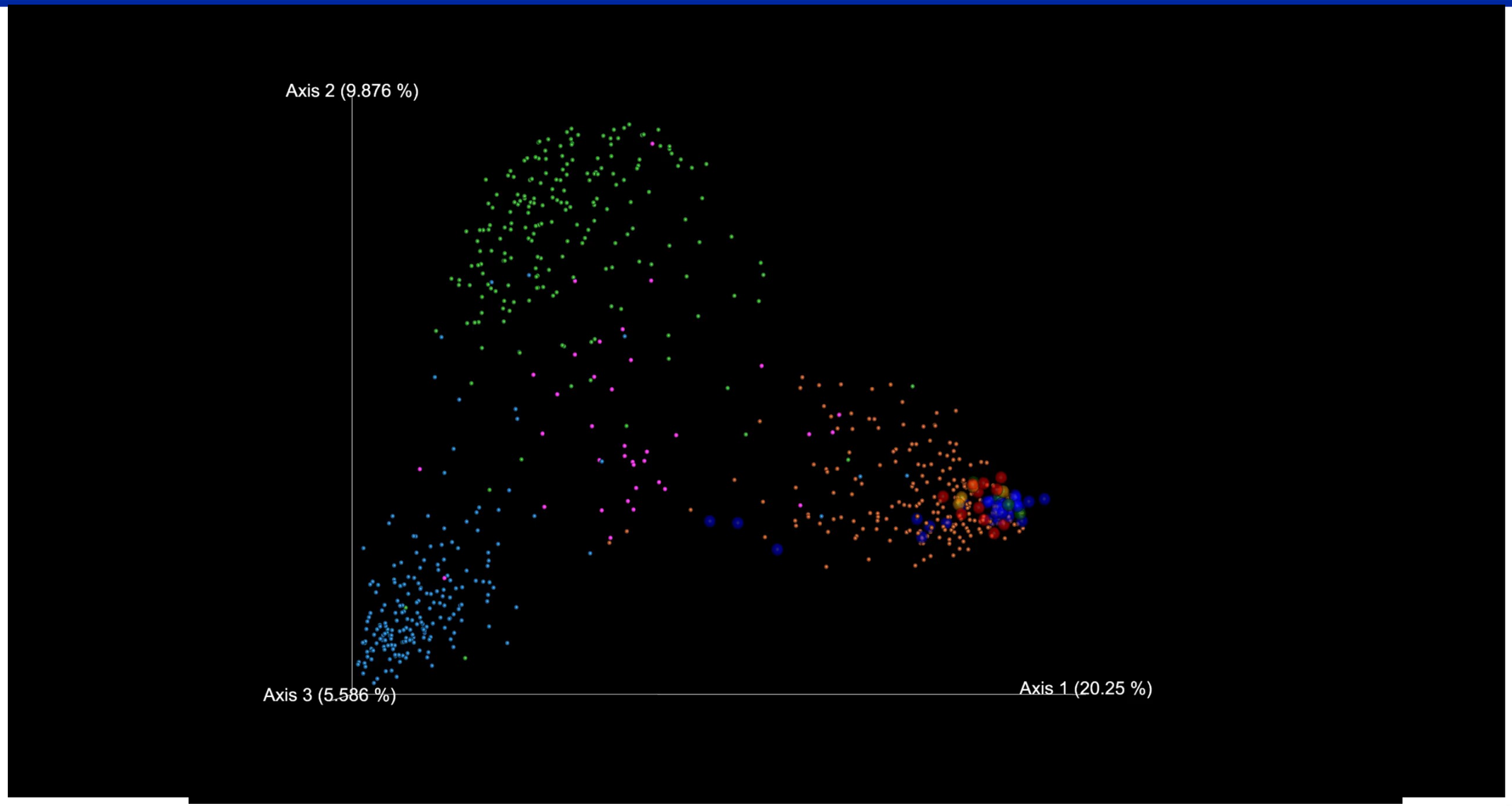
Source: Embriette Hyde, UCSD

Major Shift in Gut Microbiome Ecology Following Abdominal Surgery With Return to New Equilibrium State



Source: Embriette Hyde, UCSD

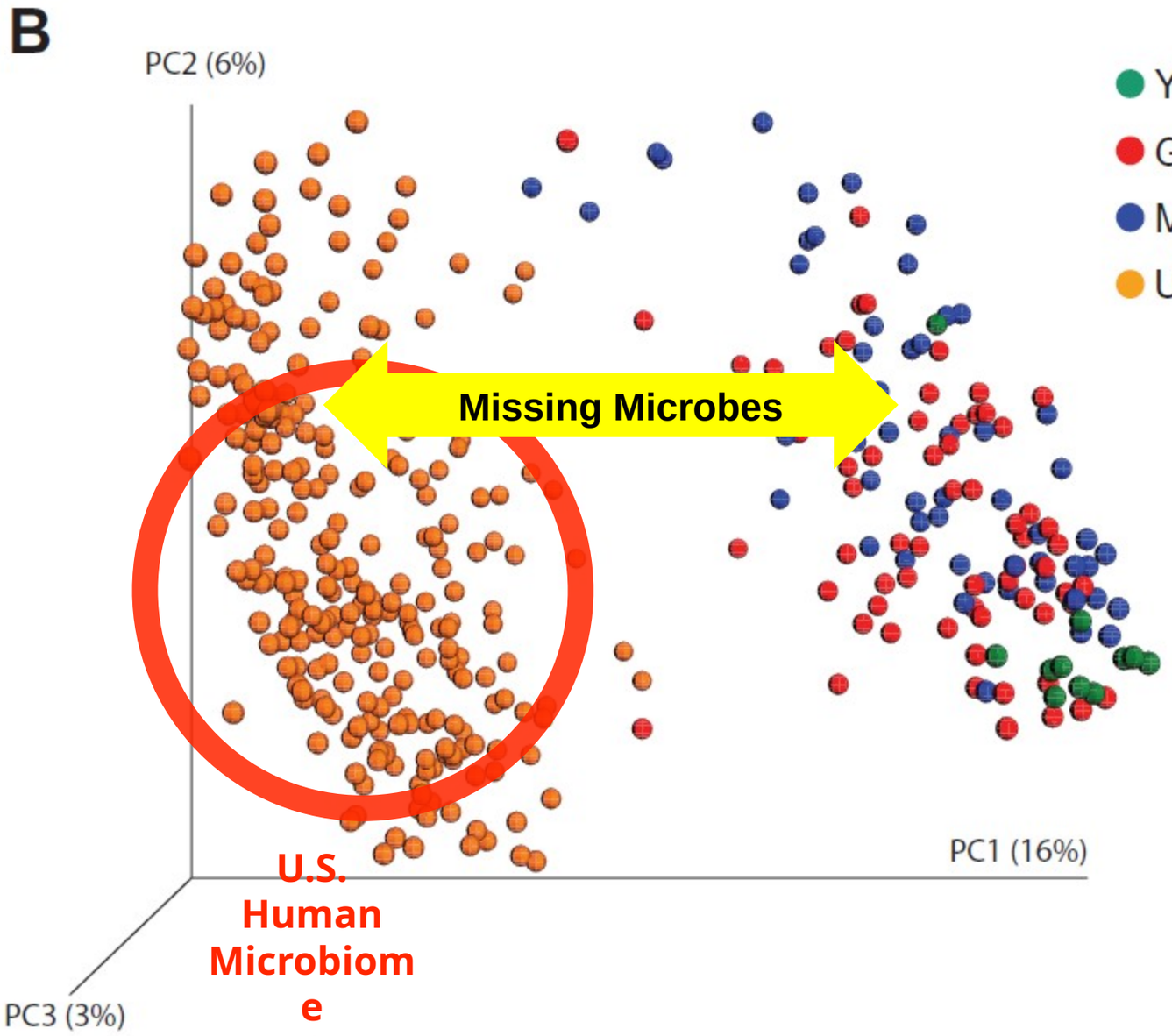
The Colonoscopy Didn’t Make Me Look Like a New Person — But the Surgery Did!



Pre-colonoscopy Post-colonoscopy Pre-surgery

Why do we care about modifications of the gut microbiome?

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



[Amerindians in Venezuela/Columbia]

[Africa]



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

We Must Move From Combating Single Microbe Diseases to Developing the Human/Microbiome System Approach to Public Health

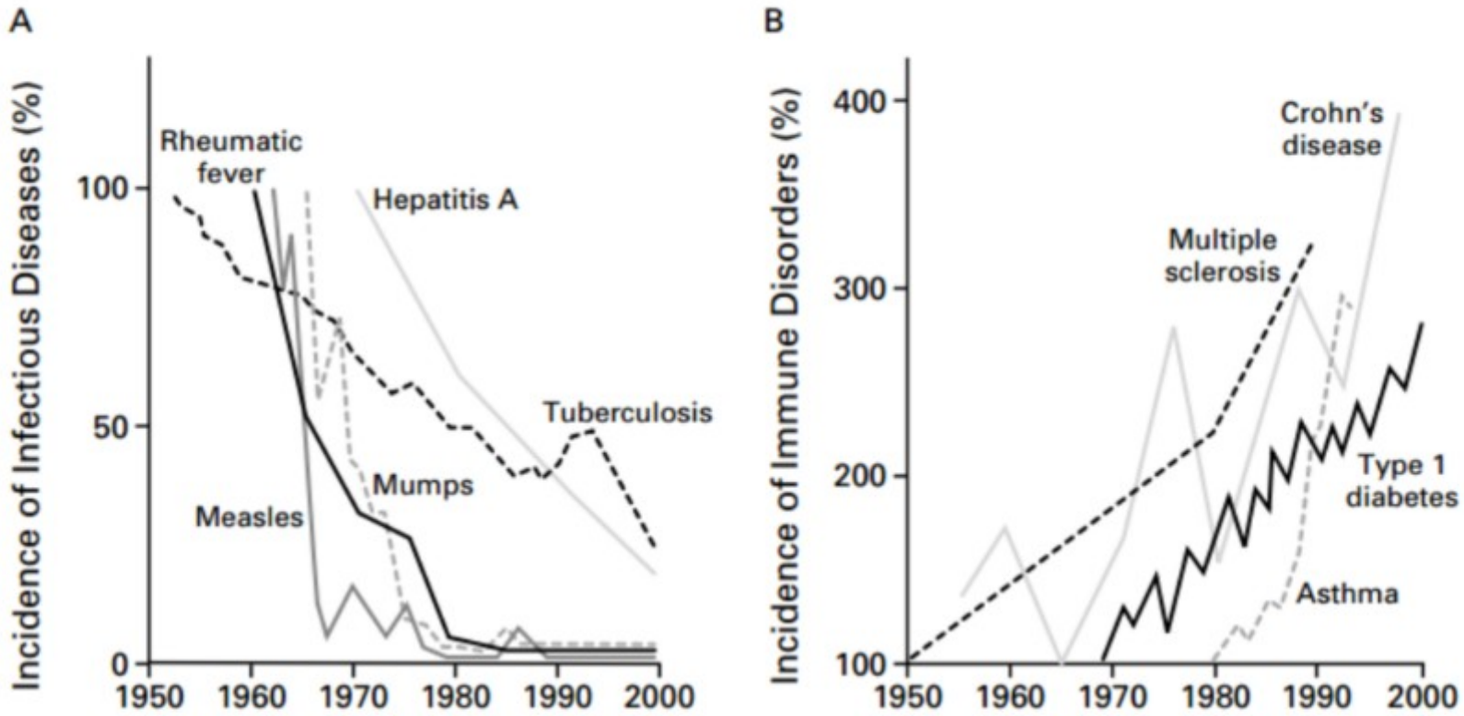
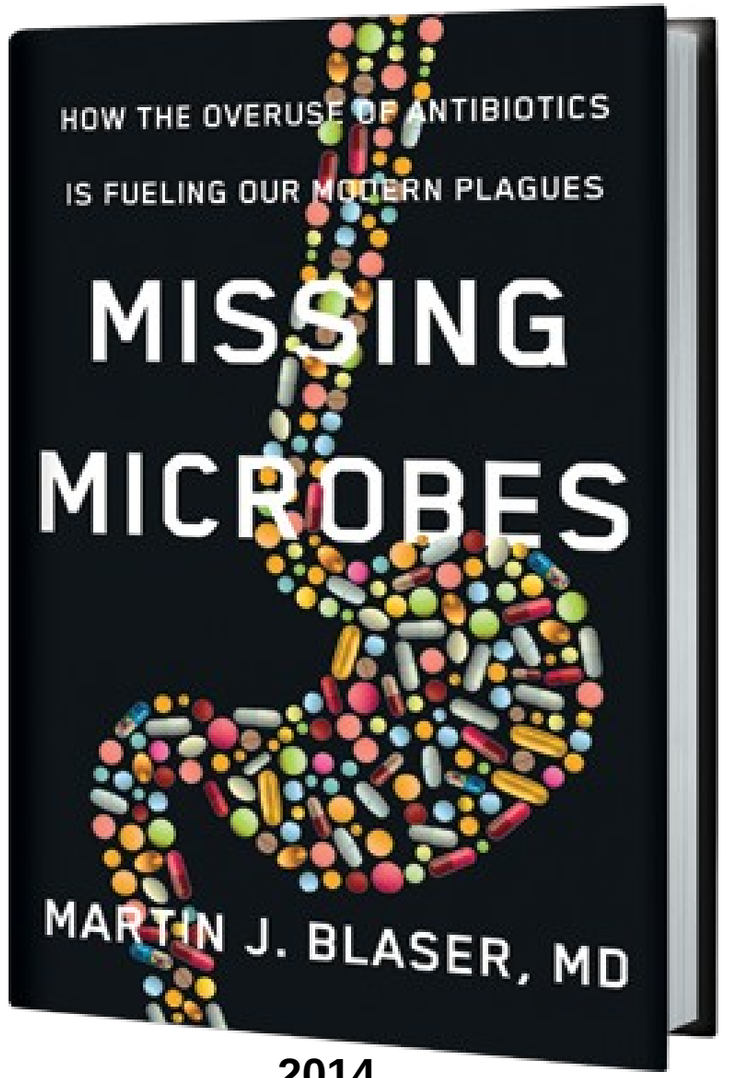


Figure 1. Inverse Relation between the Incidence of Prototypical Infectious Diseases (Panel A) and the Incidence of Immune Disorders (Panel B) from 1950 to 2000.

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

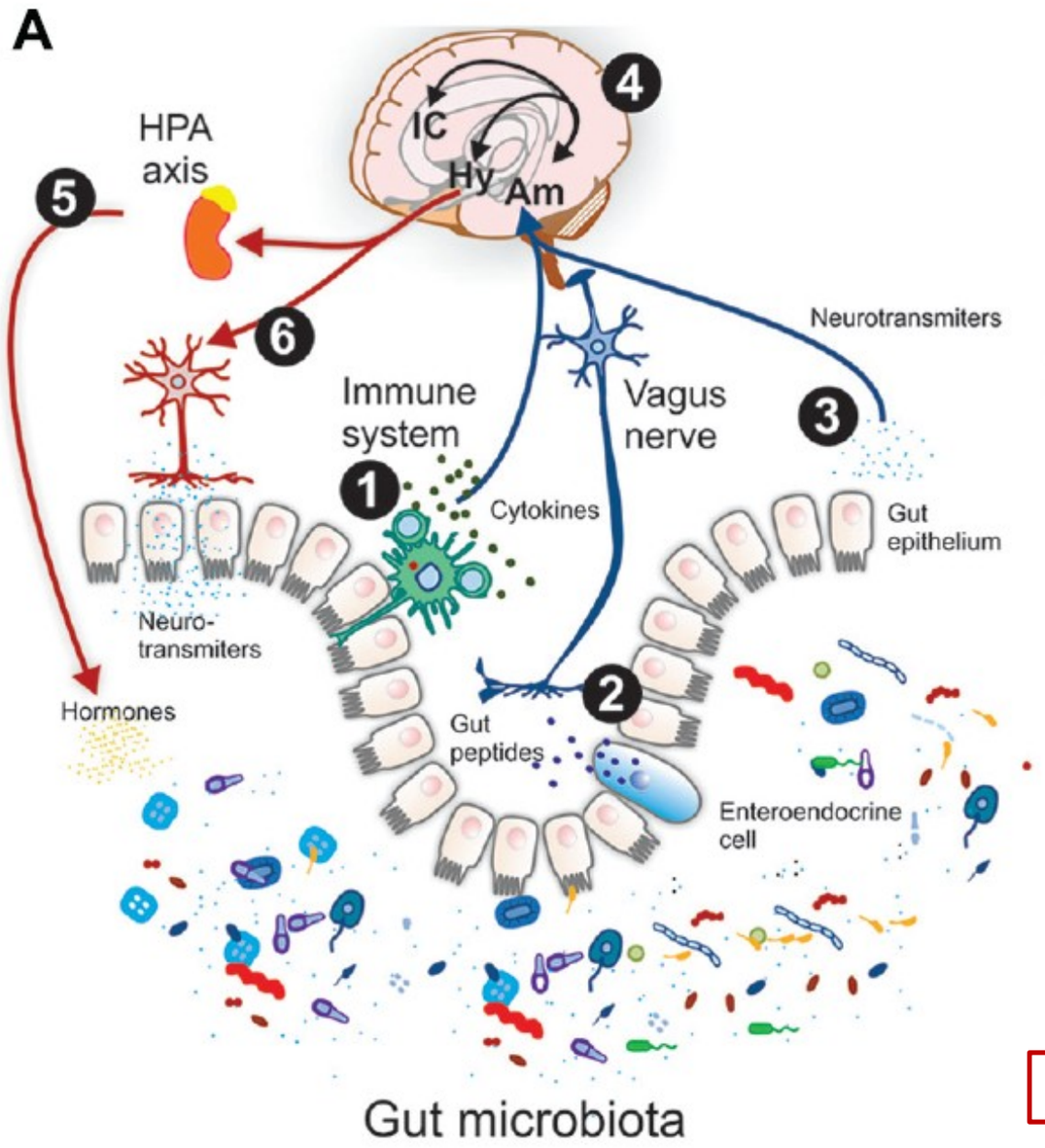


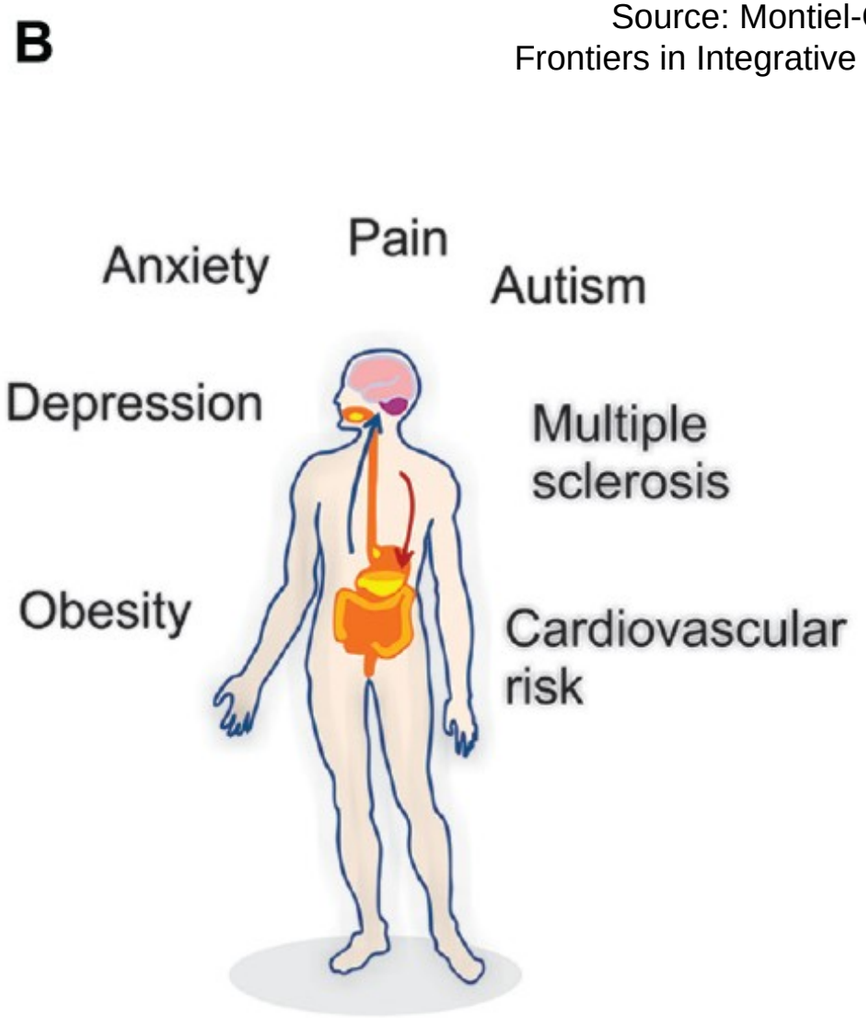
2014

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

The Microbiome–Gut–Brain Axis Provides New Systemic Insights into Shifts in Behavior and Disease

Source: Montiel-Castro, et al.
Frontiers in Integrative Neuroscience 2013





Particularly Important for Healthy Aging

Many New Research Studies are Demonstrating Deep Relationships Between the Gut Microbiome and Behavioral Disorders

Symposium

The Journal of Neuroscience 12 November 2014, 34(46): 15490-15496;

Gut Microbes and the Brain: Paradigm Shift in Neuroscience

Emeran A. Mayer[1], Rob Knight[2], Sarkis K. Mazmanian[3], John F. Cryan[4], and Kirsten Tillisch[1,5]

Review

Trends in Neurosciences Volume 36, Issue 5, p305–312, May 2013

Gut–brain axis: how the microbiome influences anxiety and depression

Jane A. Foster, Karen-Anne McVey Neufeld

frontiers in Cellular Neuroscience September 2013 | Volume 7 | Article 153

Alzheimer's disease and the microbiome

*Surjyadipta Bhattacharjee and Walter J. Lukiw**

January 2013, 15:337 Date: 10 Jan 2013 CURRENT PSYCHIATRY REPORTS

The Gut Microbiome: A New Frontier in Autism Research

Jennifer G. Mulle, William G. Sharp, Joseph F. Cubells

Article

Cell

Gut Microbiota Regulate Motor Deficits and Neuroinflammation in a Model of Parkinson's Disease

Timothy R. Sampson,[1,*] Justine W. Debelius,[2] Taren Thron,[1] Stefan Janssen,[2] Gauri G. Shastri,[1] Zehra Esra Ilhan,[3] Collin Challis,[1] Catherine E. Schretter,[1] Sandra Rocha,[4] Viviana Gradinaru,[1] Marie-Francoise Chesselet,[5] Ali Keshavarzian,[6] Kathleen M. Shannon,[7,9] Rosa Krajmalnik-Brown,[3] Pernilla Wittung-Stafshede,[4] Rob Knight,[2,8] and Sarkis K. Mazmanian[1,10,*]

Molecular Psychiatry (2014) 19, 1252–1257

PERSPECTIVE

Genomics of schizophrenia: time to consider the gut microbiome?

TG Dinan[1,2], YE Borre[1] and JF Cryan[1,3]

Gut Microbes Regulate Serotonin Production, 90% of Which is in the Large Intestine

AMERICAN PSYCHOLOGICAL ASSOCIATION

**“It's almost unthinkable
that the gut is not playing a critical role in mind states,"
says gastroenterologist Emeran Mayer, MD,
director of the Center for Neurobiology of Stress at UCLA**

By Dr. Siri Carpenter
September 2012, Vol 43,

"More and more studies are showing that mice or other model organisms with changes in their gut microbes exhibit altered behaviours," noted senior author Dr Elaine Hsiao of Caltech.

***Cell* 161 264-276 (2015)**

AMI American Microbiome Institute

April 13, 2015

Gut bacteria help regulate serotonin levels

Facebook of Life

TACGGAGGGTGCGAGCGTTAATCGGAATAACTGGGCGTAAAGGGCACGCAGGCGGACTTTTAAGTGAGATGTGAAATCCCCGAGCTTAAC

16S rRNA gene only a nickname—
complete genome is full name

we need the same cumulative
growth for **whole genome data**

Earth microbes

- ~ 10^{10} species
- ~ 10^{6} bp genomes
- ~ 10^{16} bytes storage*

Facebook

- processes ~10^{14} bytes/day
- stores ~ 10^{17} bytes**

* $30Bn sequencing costs, today

** as of 2014

Center for Microbiome Innovation

UC San Diego

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QIAGEN Pfizer illumina® XILTRIX iks INTERNATIONAL

...and over 120 UCSD Faculty