“Toward Personalized Wellness: An Ounce of Prevention is Worth a Pound of Care”

Invited Talk
American Philosophical Society
Philadelphia, PA
November 10, 2018

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
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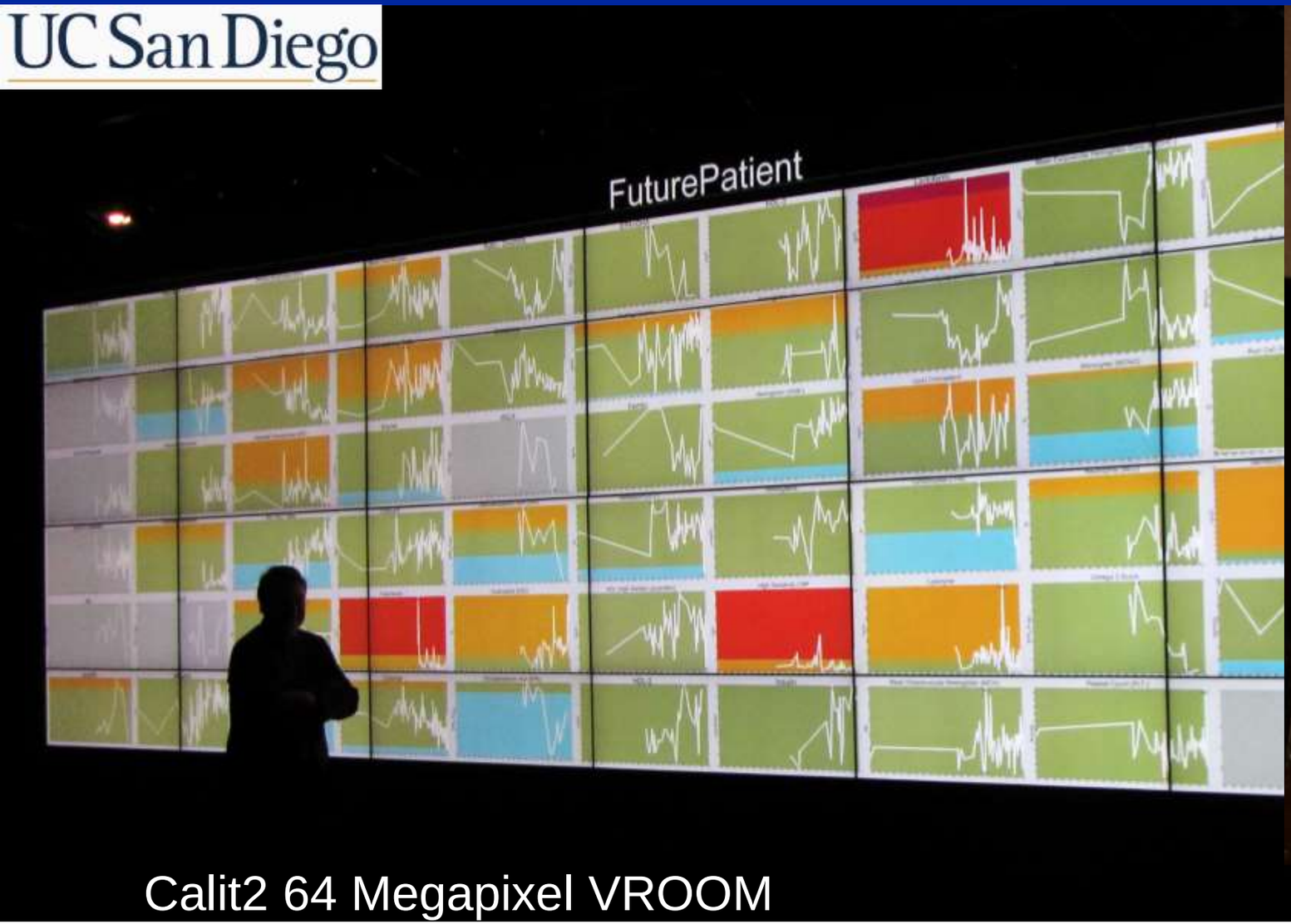
“Know Thyself”
From the Temple of Apollo to the Quantified Self



From the Reichert-Haus in Ludwigshafen, Germany

To Know Myself, I Began Tracking My Internal Biomarkers To Better Understand My Body's System Dynamics

UC San Diego



Calit2 64 Megapixel VROOM

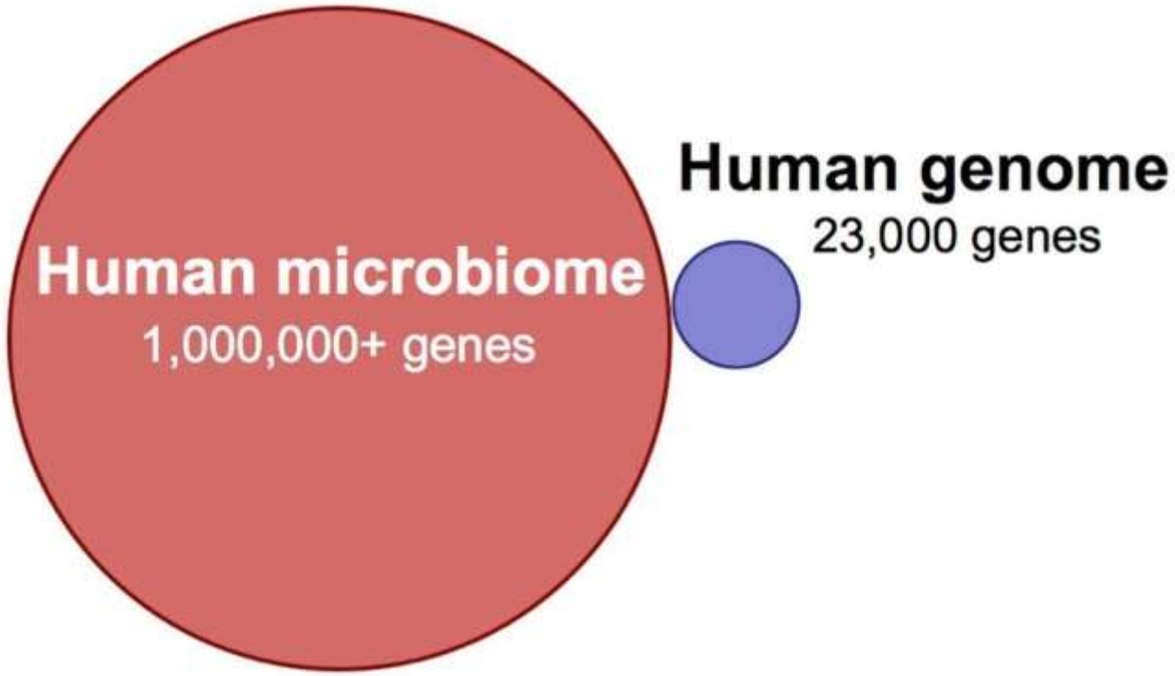


My Quarterly Blood Draw

For a Detailed 45-Minute Video of Me Exploring My Biomarkers and Microbiome on the Wall, Google "Larry Smarr Future Patient"

I Quickly Realized That To Personalize My Wellness, I First Had to Expand My Concept of "Person"

Your Body Has 40 Trillion Microbe Cells: 10 Times The Number of DNA-Bearing Human Cells



99.9% of Your DNA Genes Are in Microbe Cells Not Human Cells

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

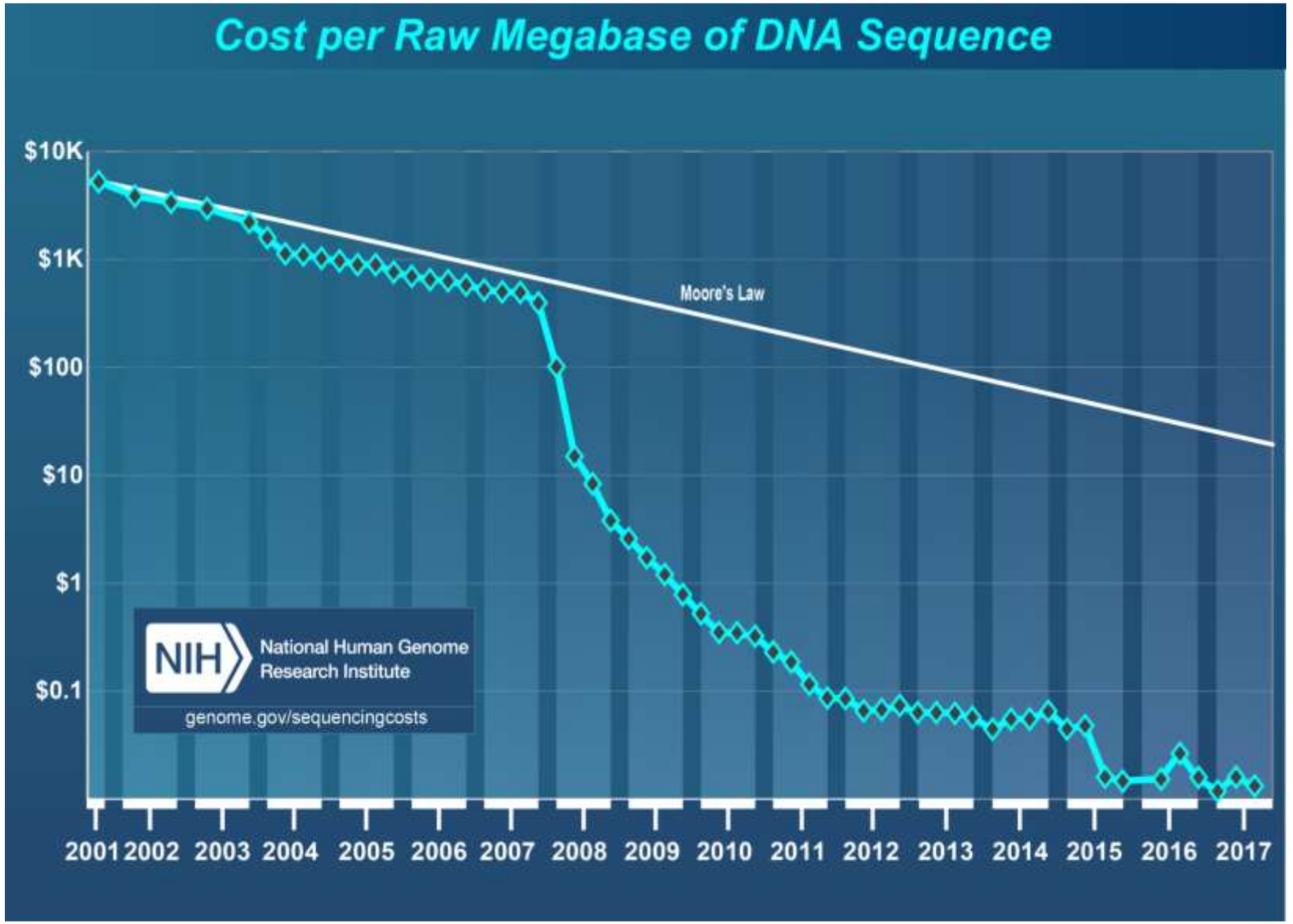
Your Gut Microbiome is Enormously Data Rich: Genome Sequencing Lets Us Read This Stored Data

100 Billion Bacteria Per Milliliter of Stool,

Bacteria Have Several Million DNA Bases,

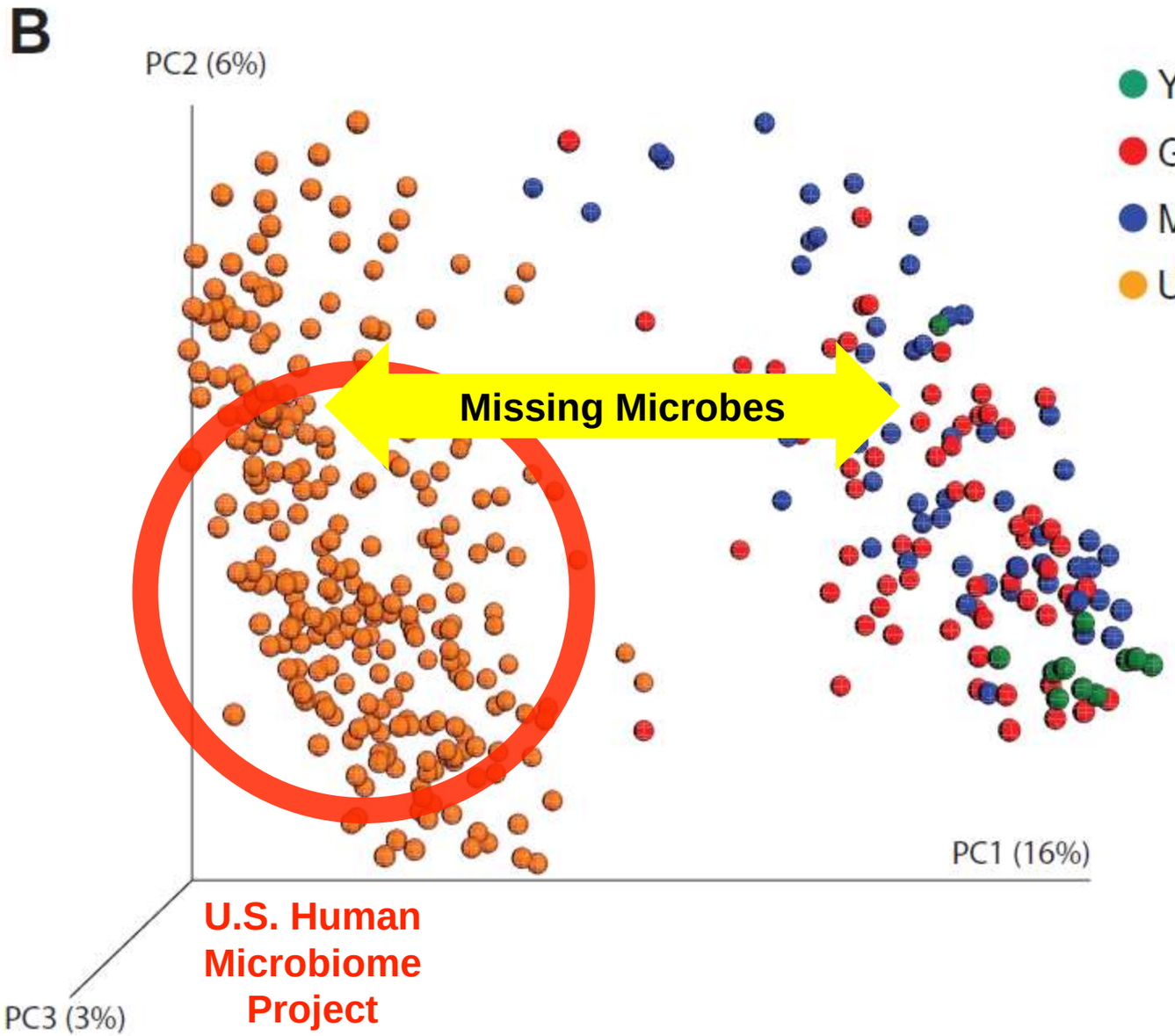
~ a 100 Million GB/ml of Stool

Analysis of the Microbiome Is Becoming Possible Because The Cost of Sequencing DNA Has Fallen Over 100,000x in the Last Ten Years



This Has Enabled a "Golden Age" of Discovery in Both Human and Microbiome Genetics

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



U.S. Human Microbiome Project

[Amerindians in Venezuela/Columbia]

[Africa]



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

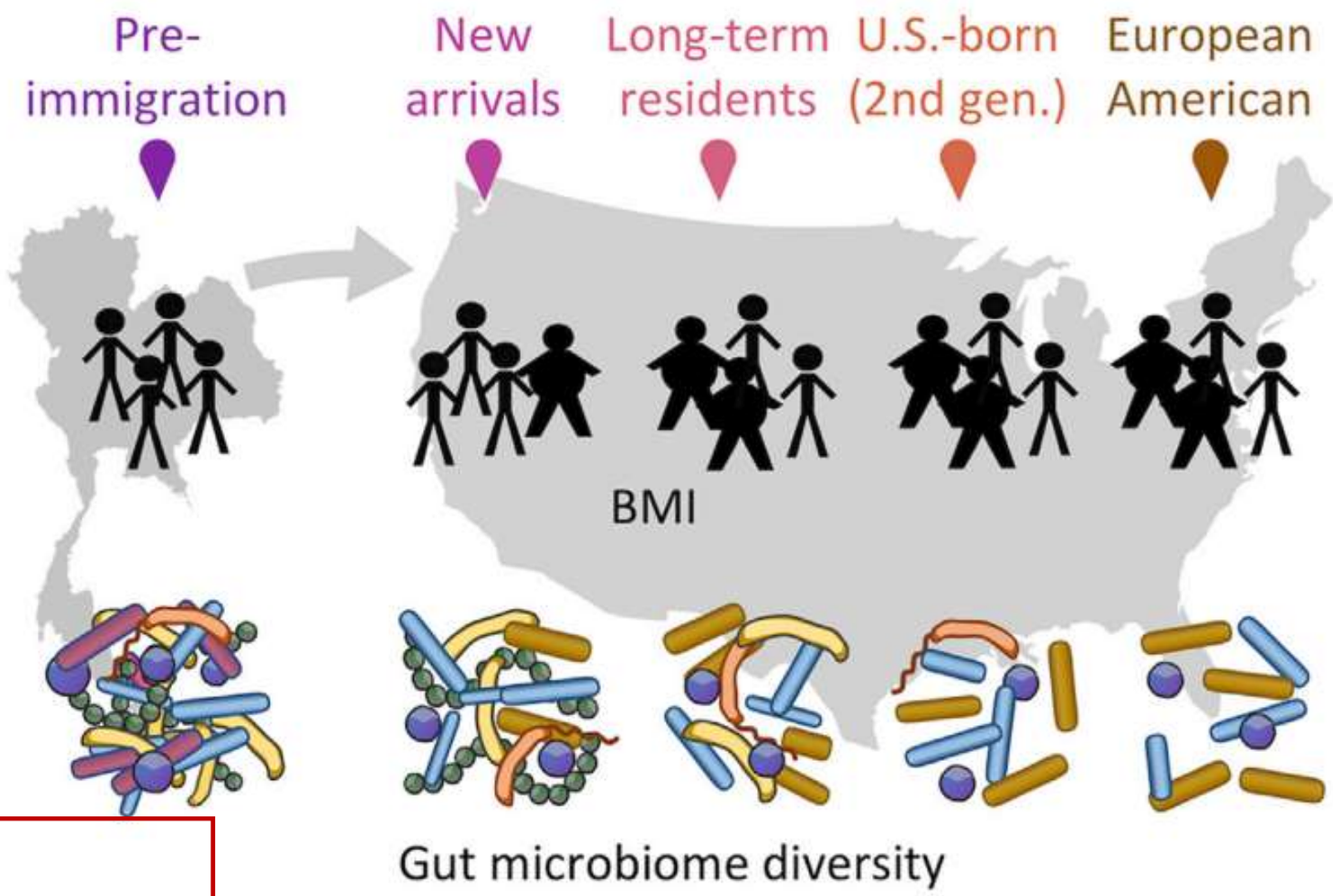
The “Western Diet” Seems to Increase Obesity and Reduce the Gut Microbiome Ecological Diversity

Cell

US Immigration Westernizes the Human Gut Microbiome

Pajau Vangay, …, Dan Knights

Cell *175*, 962–972, November 1, 2018



Highlights:

- **Loss of diversity increases with obesity**
- **US immigrants lose microbial plant fiber degradation**

Growing Evidence That Widely Used Artificial Food Additives Can Contribute to Obesity and Glucose Intolerance

nature
International journal of science

9 OCTOBER 2014 | VOL 514 | NATURE | 181

Artificial sweeteners induce glucose intolerance by altering the gut microbiota

Jotham Suez[1], Tal Korem[2]*, David Zeevi[2]*, Gili Zilberman-Schapira[1]*, Christoph A. Thaiss[1], Ori Maza[1], David Israeli[3], Niv Zmora[4,5,6], Shlomit Gilad[7], Adina Weinberger[2], Yael Kuperman[8], Alon Harmelin[8], Ilana Kolodkin-Gal[9], Hagit Shapiro[1], Zamir Halpern[5,6], Eran Segal[2] & Eran Elinav[1]

NATURE | NEWS

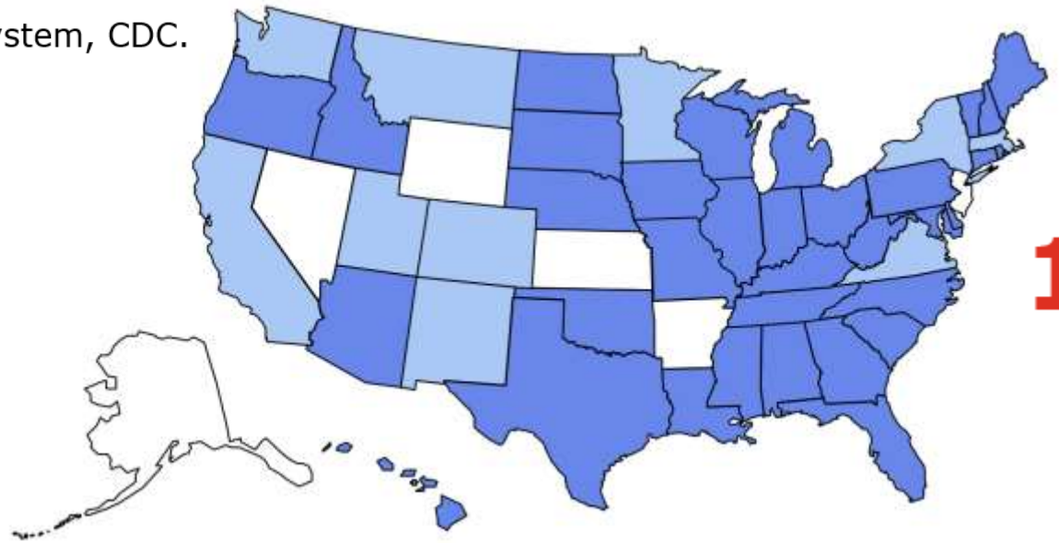
nature
International journal of science

Food preservatives linked to obesity and gut disease

Sara Reardon **February 25, 2015**

Could the Gut Microbiome Ecology Changes Shed New Light On The Obesity/Metabolic Syndrome Public Health Emergency?

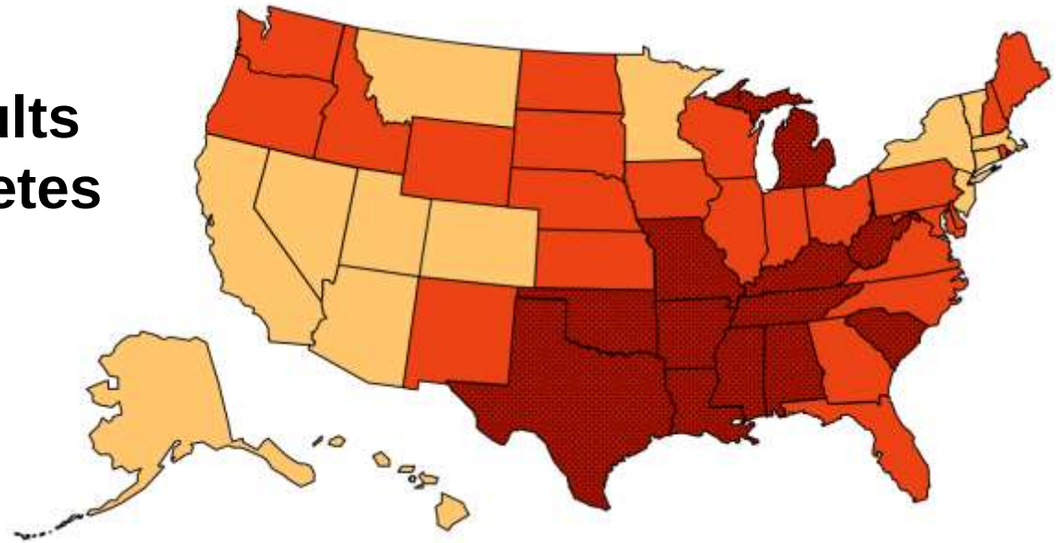
Source: Behavioral Risk Factor Surveillance System, CDC.



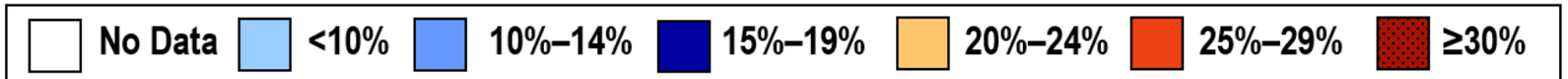
1990

% Obese
BMI ≥30

100 Million American Adults Have Diabetes or Prediabetes - CDC 2017



2010



Evidence is Mounting That There Is a Lean and an Obese Gut Microbiome

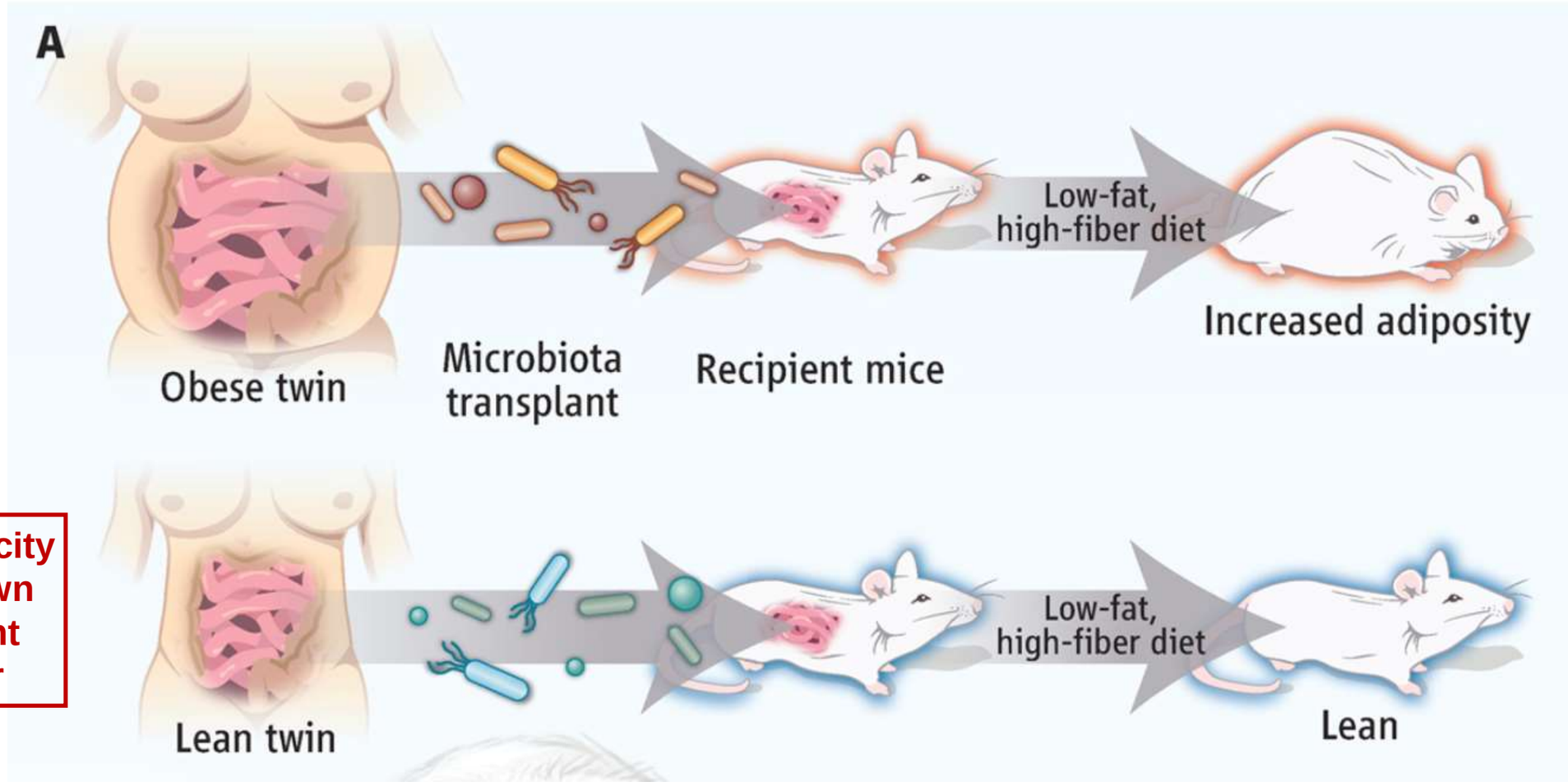
Science

PERSPECTIVE MICROBIOLOGY

Fighting Obesity with Bacteria

Alan W. Walker & Julian Parkhill

September 6, 2013



greater capacity to breakdown and ferment plant fiber

Are Changes in Our Microbiome Ecology Driving The Multi-Decadal Increase In Autoimmune and Other Non-Communicable Diseases?

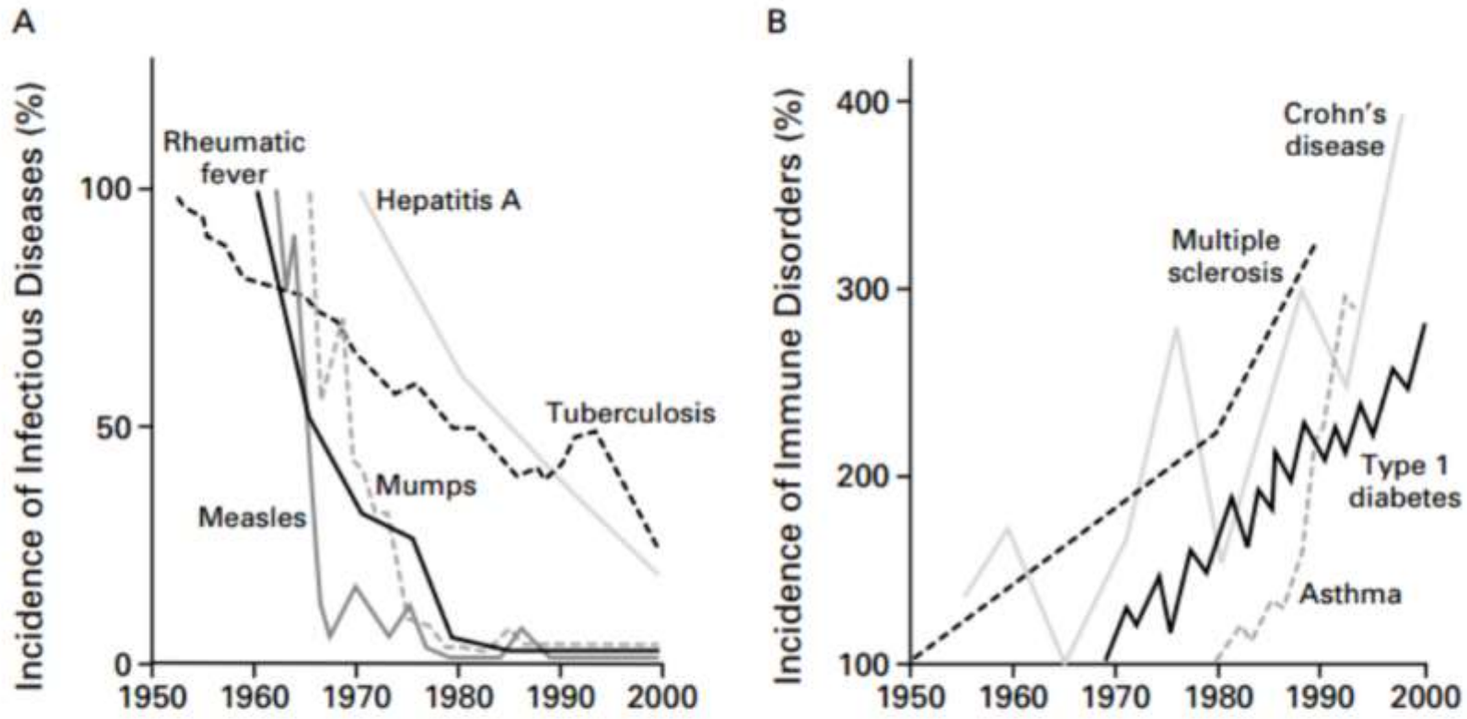
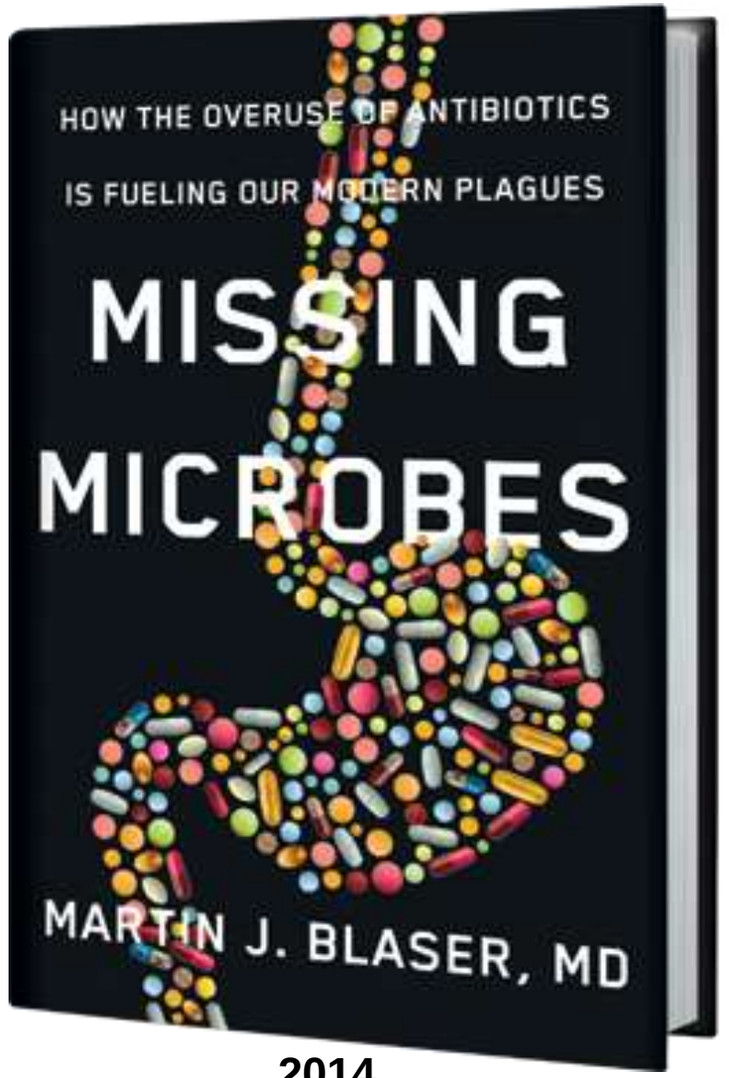


Figure 1. Inverse Relation between the Incidence of Prototypical Infectious Diseases (Panel A) and the Incidence of Immune Disorders (Panel B) from 1950 to 2000.

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

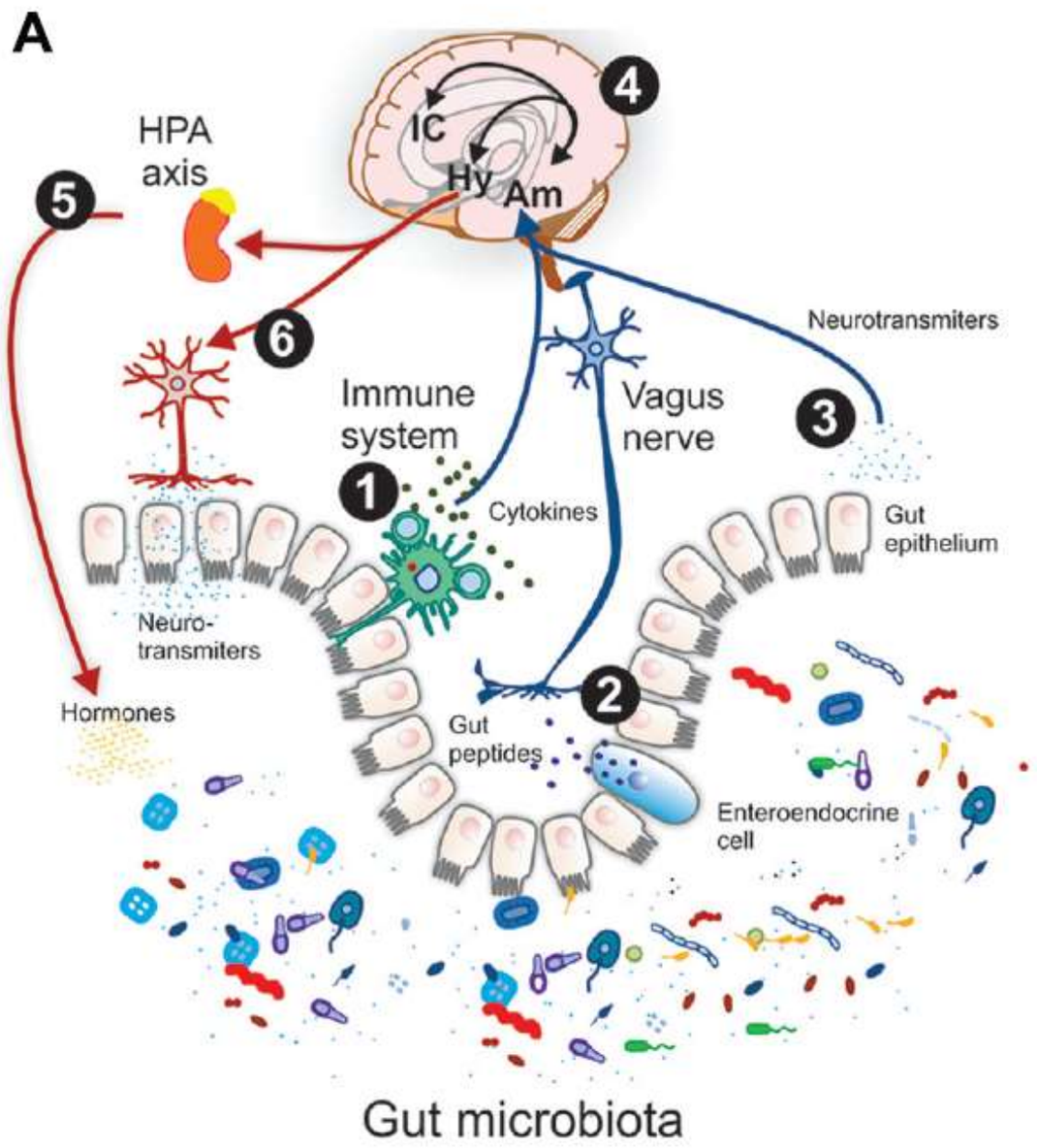


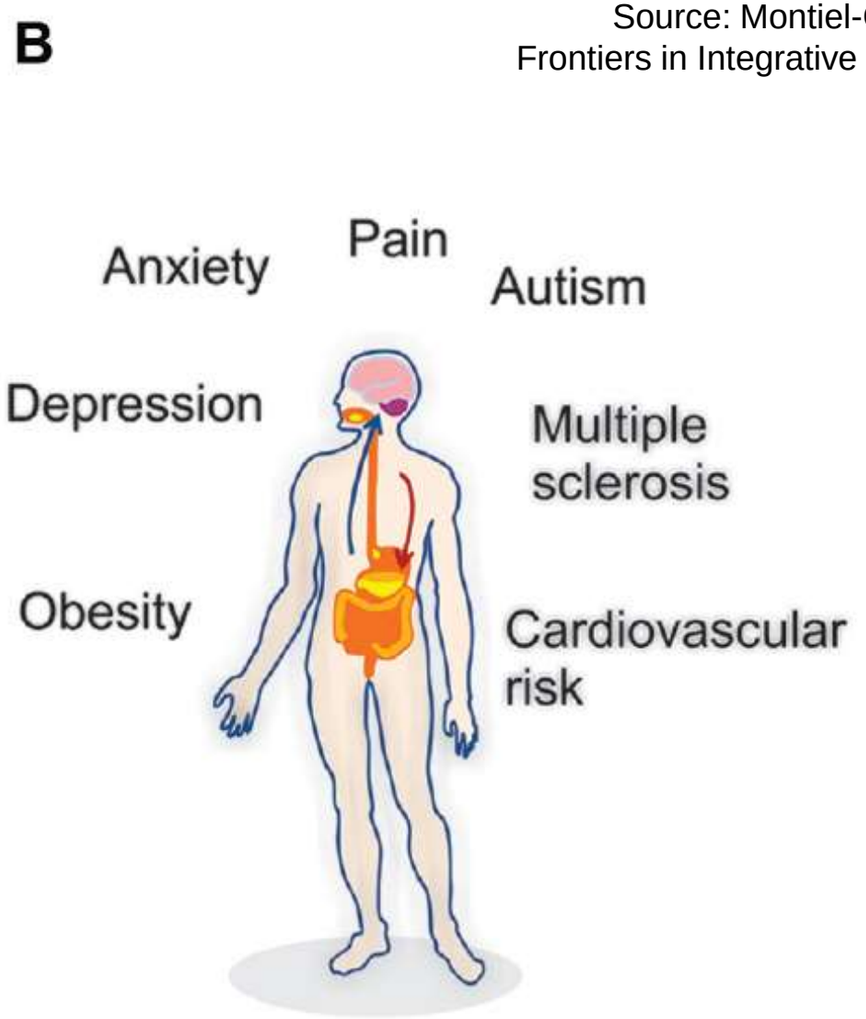
2014

Blaser Served as President of the Infectious Diseases Society of America and is a Member of the National Academy of Medicine

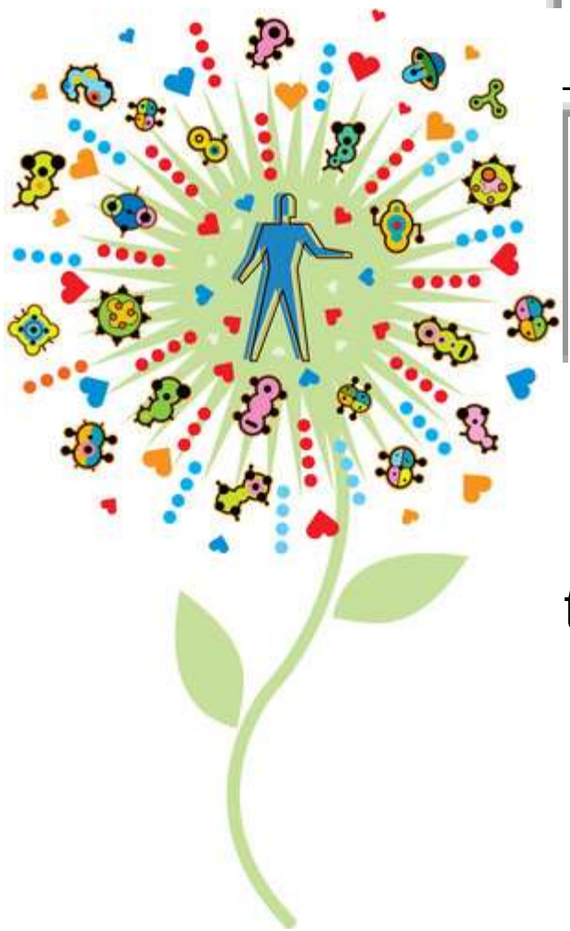
The Microbiome–Gut–Brain Axis Connects Altered Microbiome Ecology To Shifts in Behavior and Disease Throughout the Body

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





Can We “Garden” Our Way Back to Health?
New Tools for Managing the Microbiome



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.”

Monticello's Vegetable Garden Terrace: Jefferson Grew 330 Varieties of Over 70 Species of Vegetables



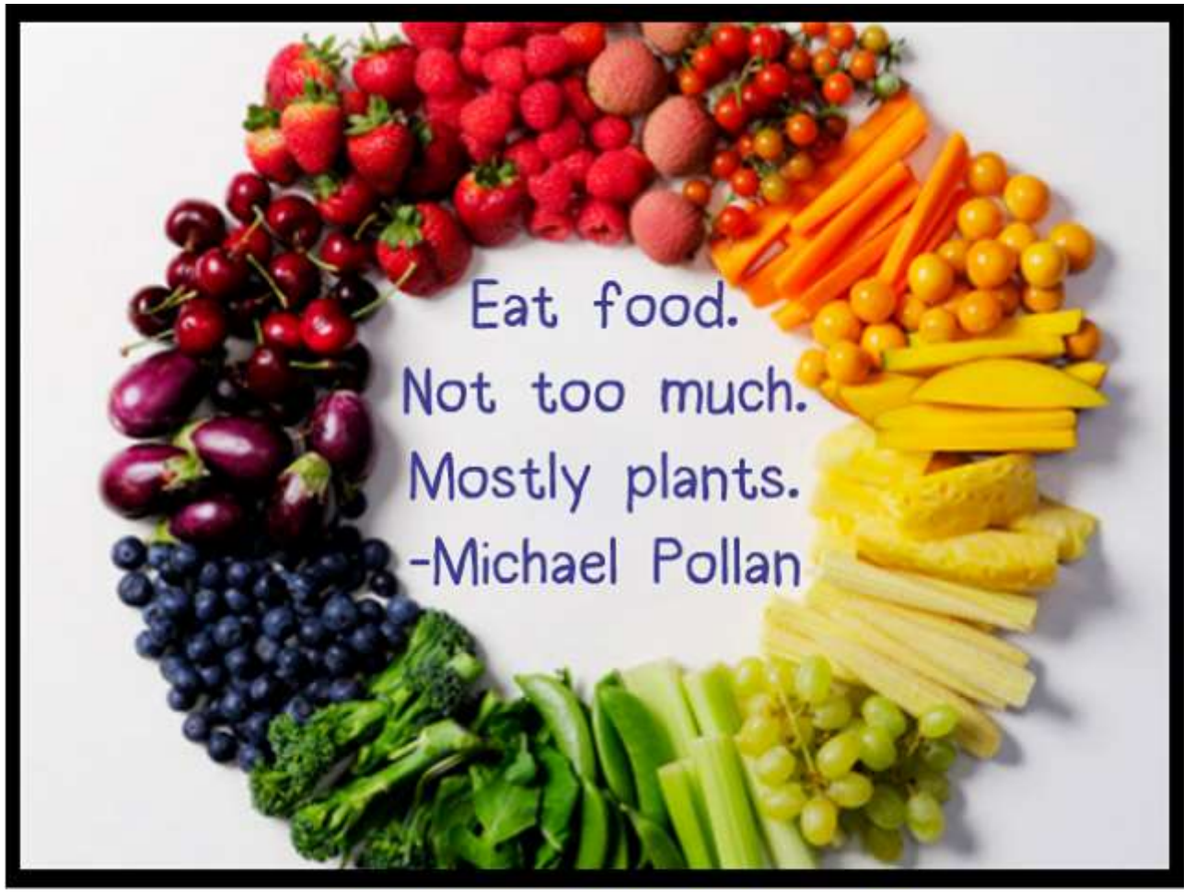
©Thomas Jefferson Foundation at Monticello. Photo by Robert Llewellyn

200 Years of Food Wisdom:
Eat Mostly Plants

**"I have lived temperately,
eating little animal food,
& that, not as an aliment
so much as a condiment
for the vegetables,
which constitute my principal diet."
-Thomas Jefferson, age 76**

Jefferson to Dr. Vine Utley, March 21, 1819,

AN ARTICLE COURTESY OF THE
THOMAS JEFFERSON
ENCYCLOPEDIA MORE »



Michael Pollan, In Defense of Food, 2009

www.pinterest.nz/pin/573575702526997325/

Adding Vegetable Fiber to the Diet Seems to Counter Obesity By Increasing Microbiome Diversity

Cell Host & Microbe 10 January 2018

Fiber-Mediated Nourishment of Gut Microbiota Protects against Diet-Induced Obesity by Restoring IL-22-Mediated Colonic Health

Jun Zou, Benoit Chassaing, Vishal Singh, Michael Pellizzon, Matthew Ricci, Michael D. Fythe, Matam Vijay Kumar, Andrew T. Gewirtz

american gut

The more different types of plants a person eats, the higher their gut microbiome diversity.

American Gut: an Open Platform for Citizen Science Microbiome Research

AMERICAN SOCIETY FOR MICROBIOLOGY | mSystems

May 15, 2018

Can I Increase My Microbiome Diversity By Consuming ~60 Plant Species Per Day?







Real Food, Mostly Plants

UC San Diego

Aligning Your Eating Pattern With Your Body's Circadian Rhythm Is As Important As What You Eat

Time-Restricted Feeding Is a Preventative and Therapeutic Intervention against Diverse Nutritional Challenges

Cell Metabolism
December 2, 2014

Amandine Chaix,[1] Amir Zarrinpar,[1,2] Phuong Miu,[1] and Satchidananda Panda[1,*]
[1]Salk Institute for Biological Studies, La Jolla, CA 92037, USA
[2]Division of Gastroenterology, University of California, San Diego, La Jolla, CA 92093, USA

Reverse Insulin Resistance with Intermittent Fasting



By: COURTNEY SPERLAZZA, MPH
April 10, 2018

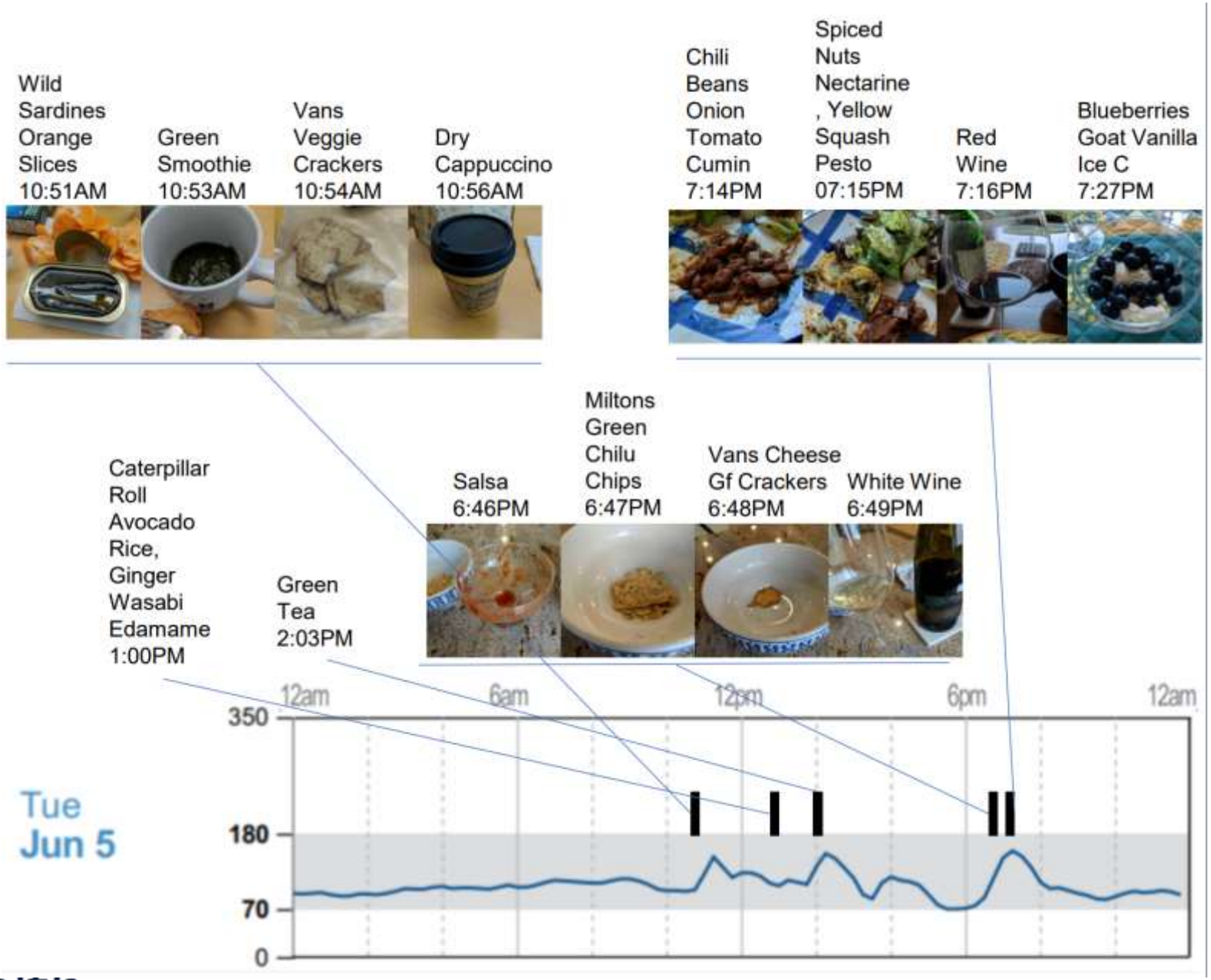
Not Too Much

I Volunteered to Become a Patient in the UCSD/Salk Pilot Study of Time-Restricted Eating (TRE) in Metabolic Syndrome

All Food/ Drink Photo/ Time-Stamped/ Annotated For 100-Days

Glucose Every 15 Minutes for Two Weeks Before and After 100-Day Trial





UC San Diego Health



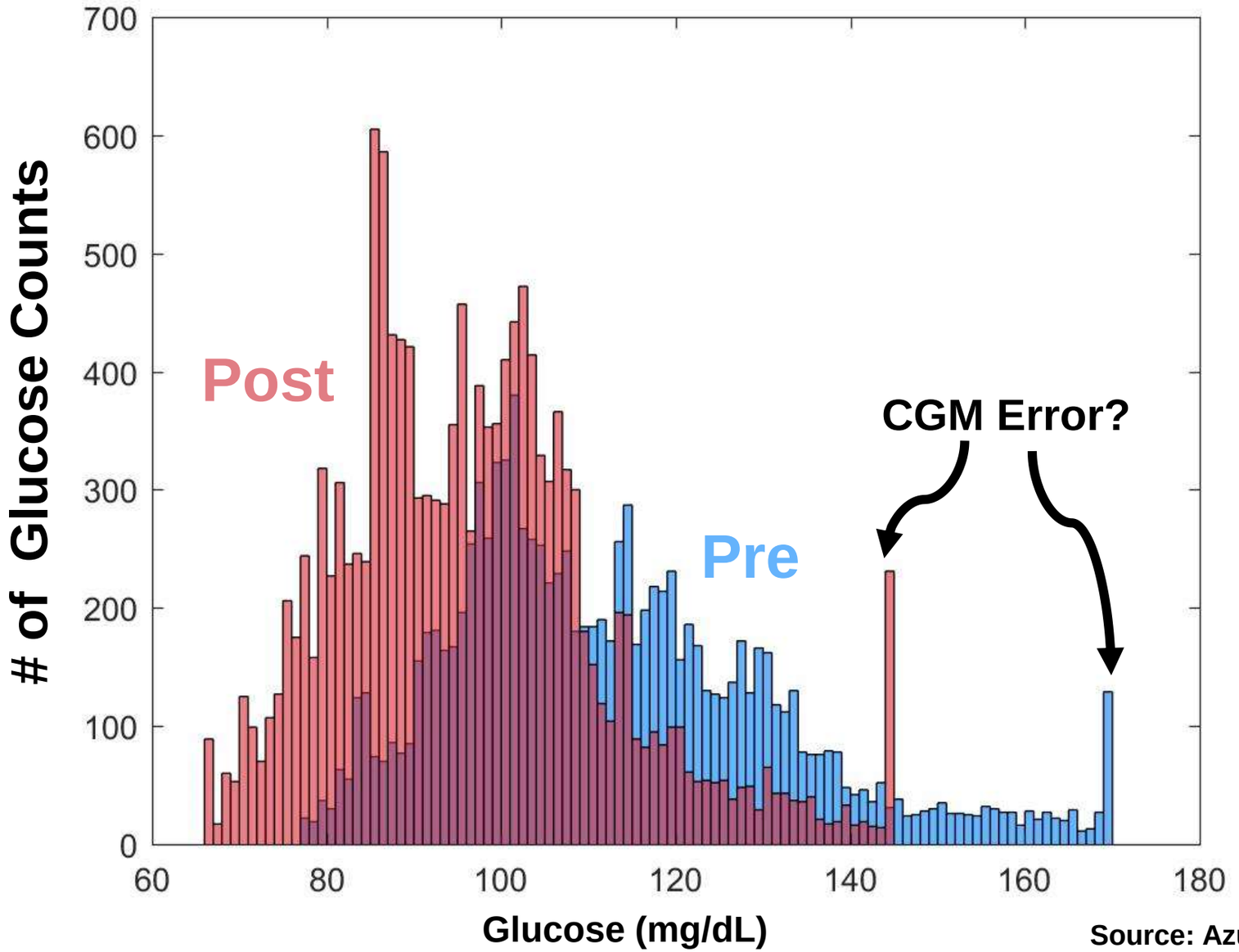
Pam Taub, MD
Cardiology



Satchin Panda, PhD
Circadian Biology

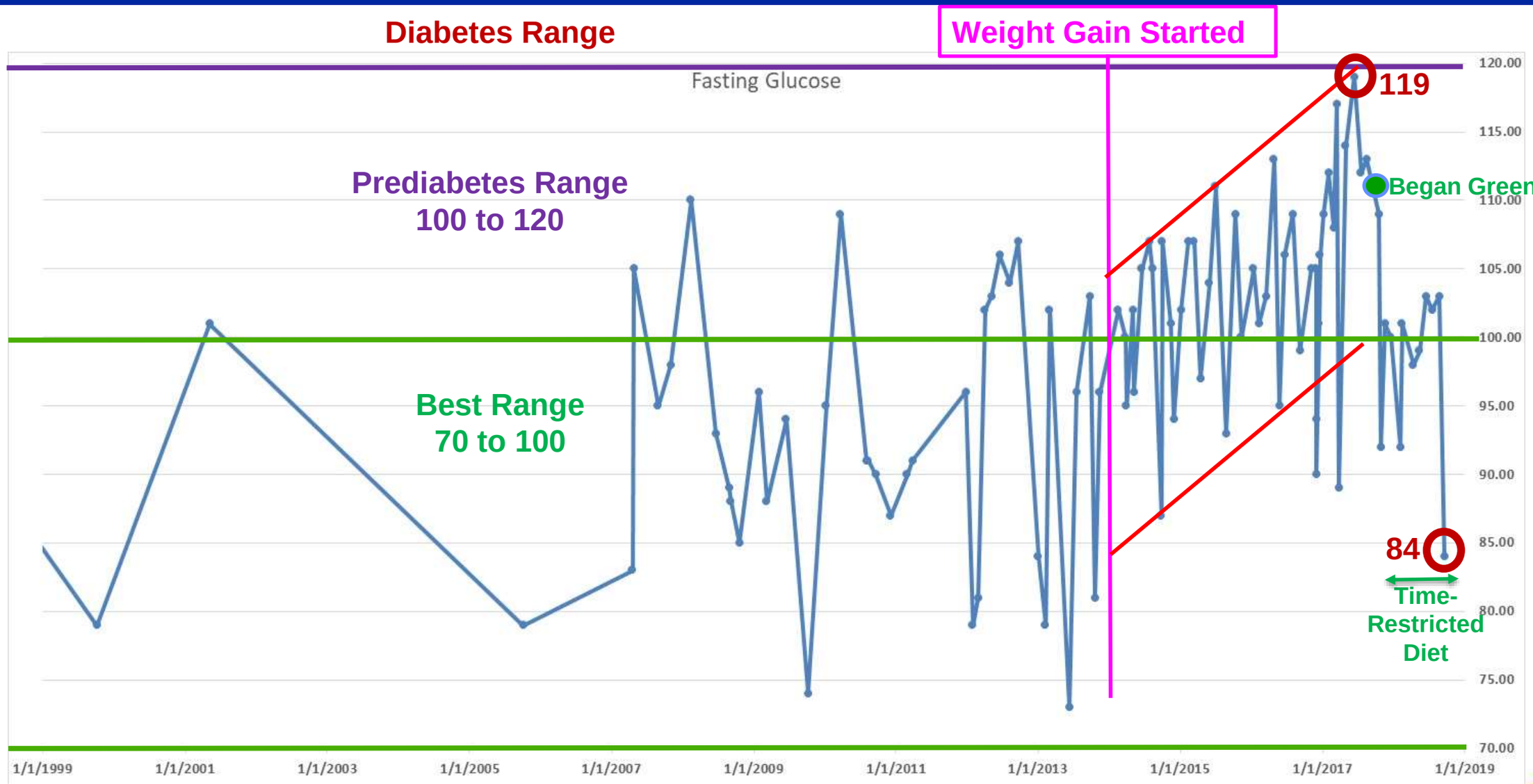
Emily Manoogian, Panda Lab, Salk Institute

Glucose Profile Shifts Back to Healthy Range: Comparing Before and After 3 Months of 10-Hour Time-Restricted Eating



Source: Azure Grant, UCB

My Fasting Glucose Level Dropped Abruptly Into Normal Level During Time-Restricted Diet and Increased Plant Diversity



“An Ounce of Prevention is Worth a Pound of Care”: Diet Timing and Content Can Have a Major Impact on Metabolic Syndrome

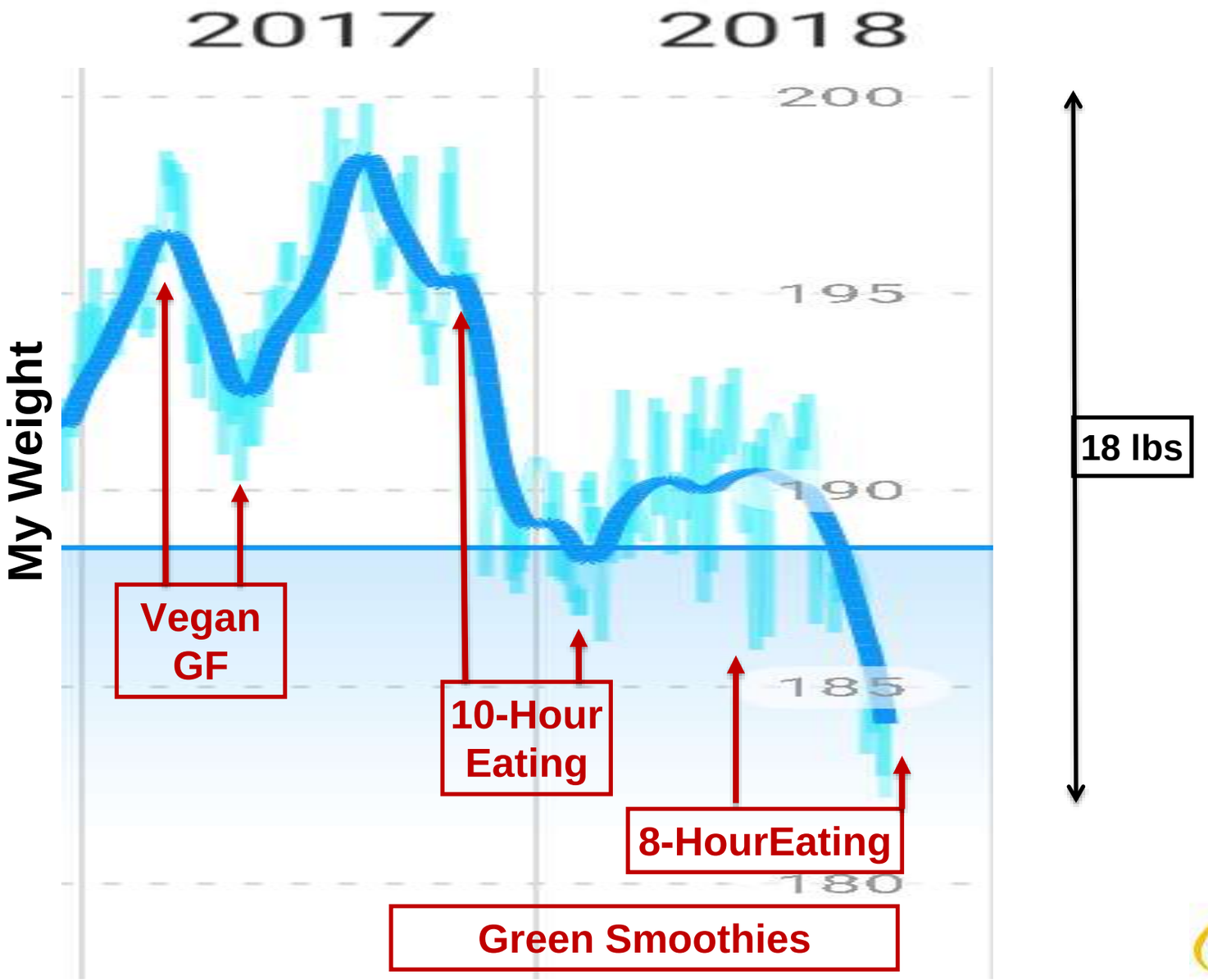
Next Step:
Analyze Microbiome Dynamics

135 Frozen Stool Samples 2012-2018

Plus

100 Daily Frozen Stool Samples During 10-Hour Restricted Eating Trial

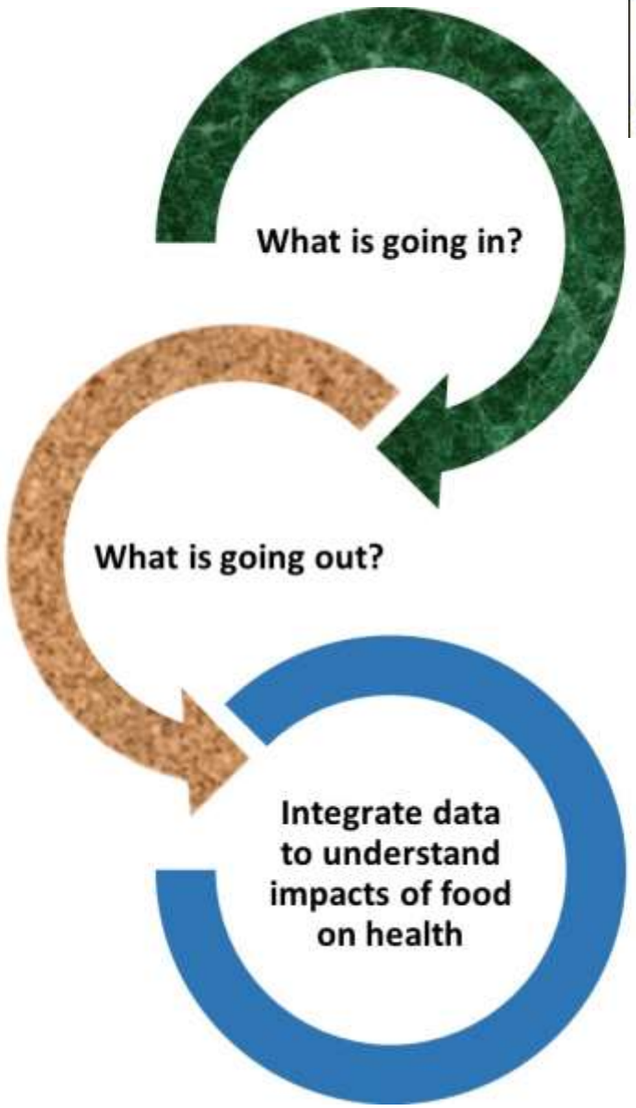
KNIGHTLAB



UC San Diego Is Carrying Out Detailed Input/Output Research Connecting Metagenomics and Metabolomics of Food and Gut Microbiome

KNIGHTLAB
UC San Diego

UCSD
the Dorrestein Lab.
The Skaggs School of Pharmacy and Pharmaceutical Sciences,
The Departments of Pharmacology, Chemistry and Biochemistry.
UNIVERSITY OF CALIFORNIA, SAN DIEGO



Global FoodOmics Project

American Gut Project

american gut

Meta-Analyses

CENTER FOR microbiome INNOVATION

THE DUTTON LAB @ UCSD

Projects Leaders: Julia Gauglitz, Rob Knight, Pieter Dorrestein, Rachael Dutton, UC San Diego

Thanks to Our Great Team!

Calit2@UCSD

Future Patient Team

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