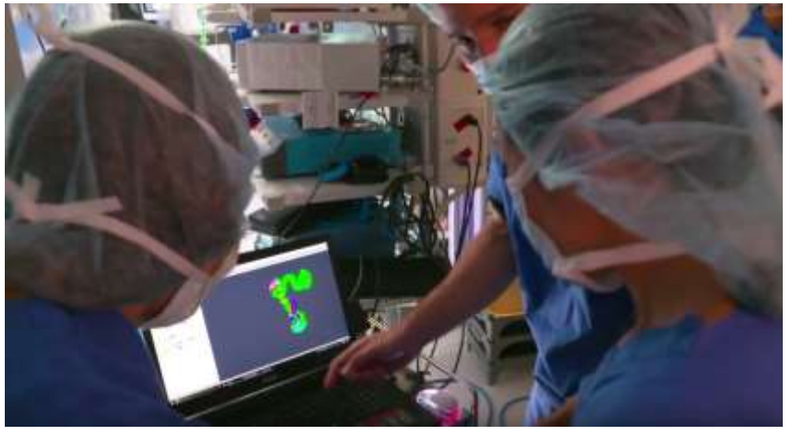
“Dynamics of the Microbiome-Driven by Medical Interventions and Dietary Change ”

Breakout Session
Exponential Medicine 2018
November 6, 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
http://lsmarr.calit2.net

Using Calit2 Organ Segmentation
During My Sigmoid Colon Resection Surgery on November 29, 2016

Dr. Schulze Rotating 3D Organs To Match Up With da Vinci Arms and Internal Camera





Patient Smarr With da Vinci Robot Arms Inside Him



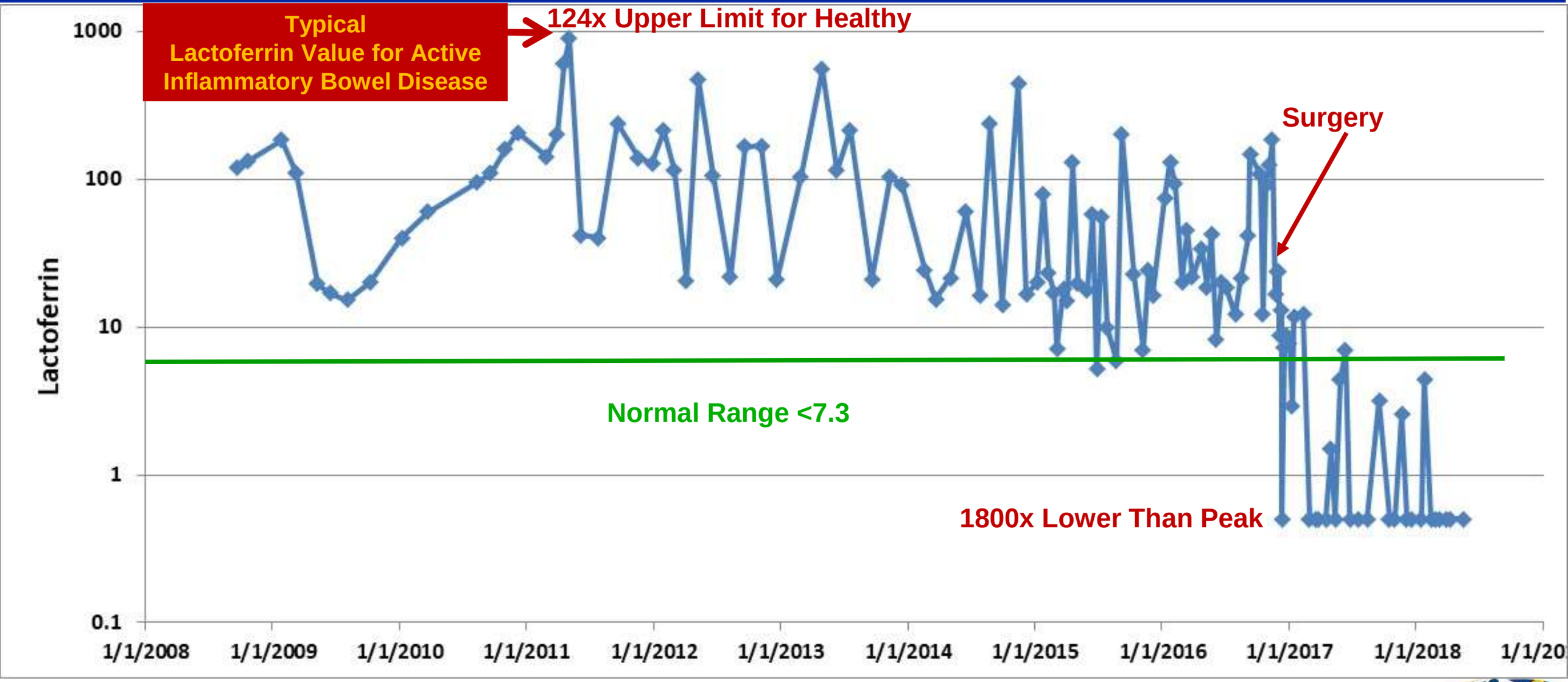


Dr. Ramamoorthy Operating Da Vinci Xi Robot During Surgery



OR Team Using Large Screens To Watch Dr. Schulze's da Vinci Images

Colonic Inflammation:
Abrupt Shift to Healthy Following Surgical Resection



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

Your Body Has 10 Times
As Many Microbe Cells As DNA-Bearing Human Cells

Your Body Hosts 40 Trillion Microbes

Your Microbiome is
Your "Near-Body" Environment
and its Cells
Contain ~100x as Many DNA Genes
As Your Human DNA-Bearing Cells

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

I Have Been Collaborating with the UCSD Knight Lab To Analyze My Gut Microbiome Dynamics

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





Larry's 40 Stool Samples Over 3.5 Years
to Rob's lab on April 30, 2015

AMERICAN SOCIETY FOR MICROBIOLOGY | mSystems
AN OPEN ACCESS JOURNAL PUBLISHED BY THE AMERICAN SOCIETY FOR MICROBIOLOGY

2018 May 15

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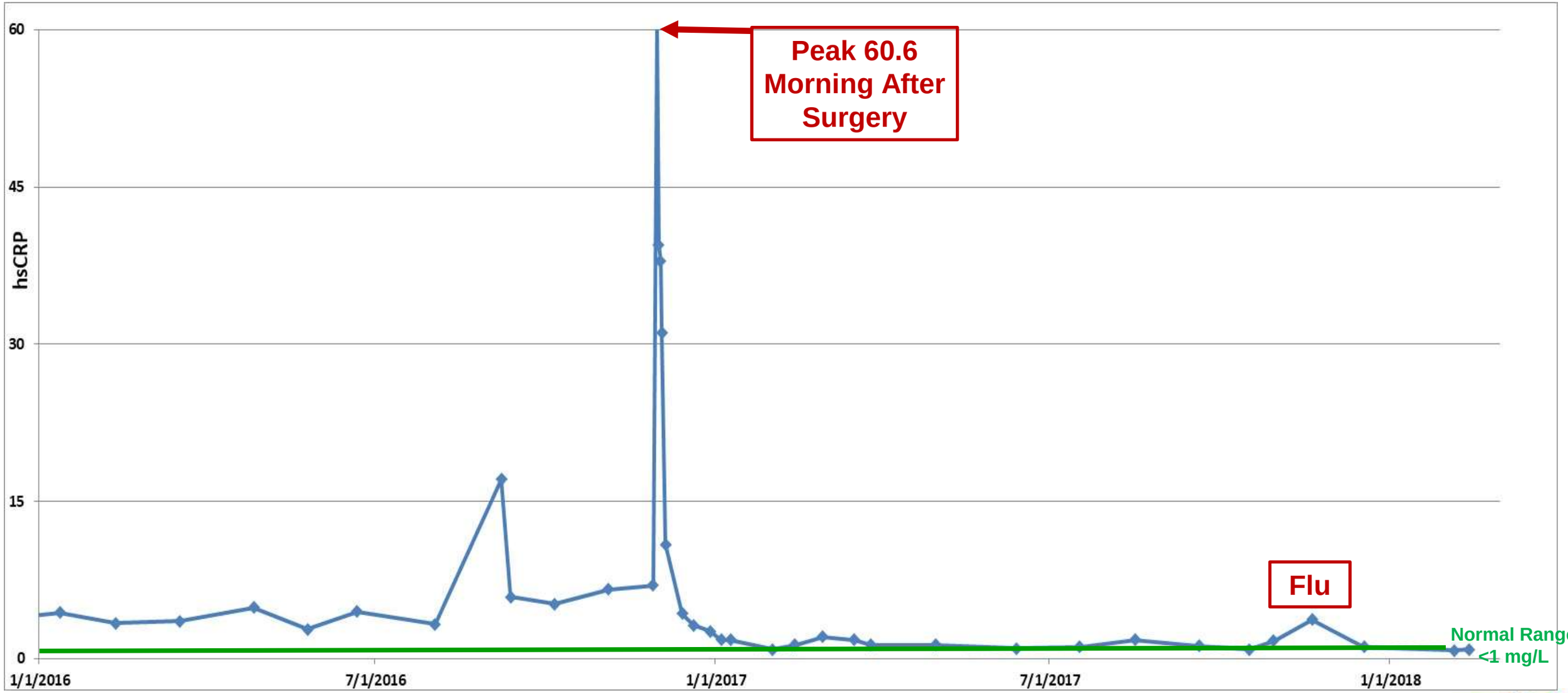
Research Article | Host-Microbe Biology

American Gut: an Open Platform for Citizen Science Microbiome Research

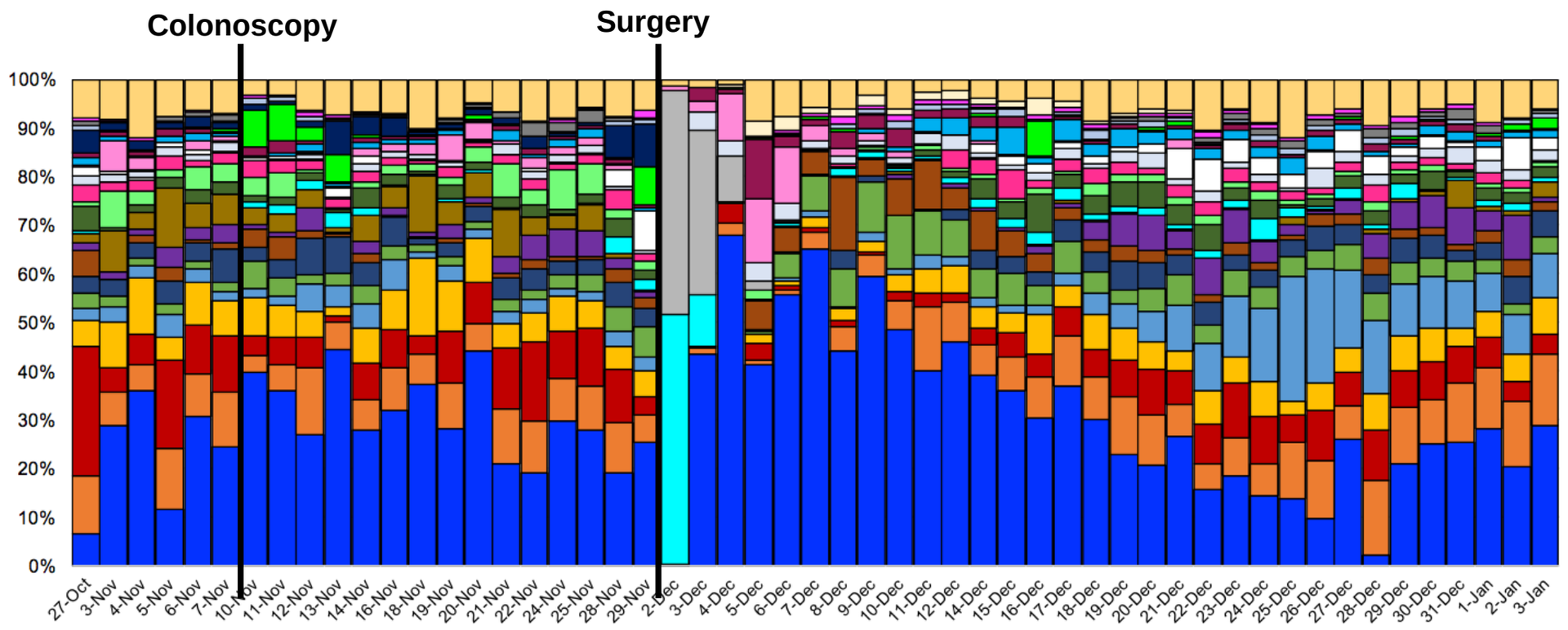
Daniel McDonald, Embriette Hyde, Justine W. Debelius, James T. Morton, Antonio Gonzalez, Gail Ackermann, Alexander A. Aksenov, Bahar Behsaz, Caitriona Brennan, Yingfeng Chen, Lindsay DeRight Goldasich, Pieter C. Dorrestein, Robert R. Dunn, Ashkaan K. Fahimipour, James Gaffney, Jack A. Gilbert, Grant Gogul, Jessica L. Green, Philip Hugenholtz, Greg Humphrey, Curtis Huttenhower, Matthew A. Jackson, Stefan Janssen, Dilip V. Jeste, Lingjing Jiang, Scott T. Kelley, Dan Knights, Tomasz Kosciolek, Joshua Ladau, Jeff Leach, Clarisse Marotz, Dmitry Meleshko, Alexey V. Melnik, Jessica L. Metcalf, Hosein Mohimani, Emmanuel Montassier, Jose Navas-Molina, Tanya T. Nguyen, Shyamal Peddada, Pavel Pevzner, Katherine S. Pollard, Gholamali Rahnavard, Adam Robbins-Pianka, Naseer Sangwan, Joshua Shorenstein, Larry Smarr, Se Jin Song, Timothy Spector, Austin D. Swafford, Varykina G. Thackray, Luke R. Thompson, Anupriya Tripathi, Yoshiki Vázquez-Baeza, Alison Vrbanac, Paul Wischmeyer, Elaine Wolfe, Qiyun Zhu, The American Gut Consortium, Rob Knight

Casey S. Greene, Editor

Using hsCRP to Track Inflammation Following Surgery to Detect Post-Surgical Complications

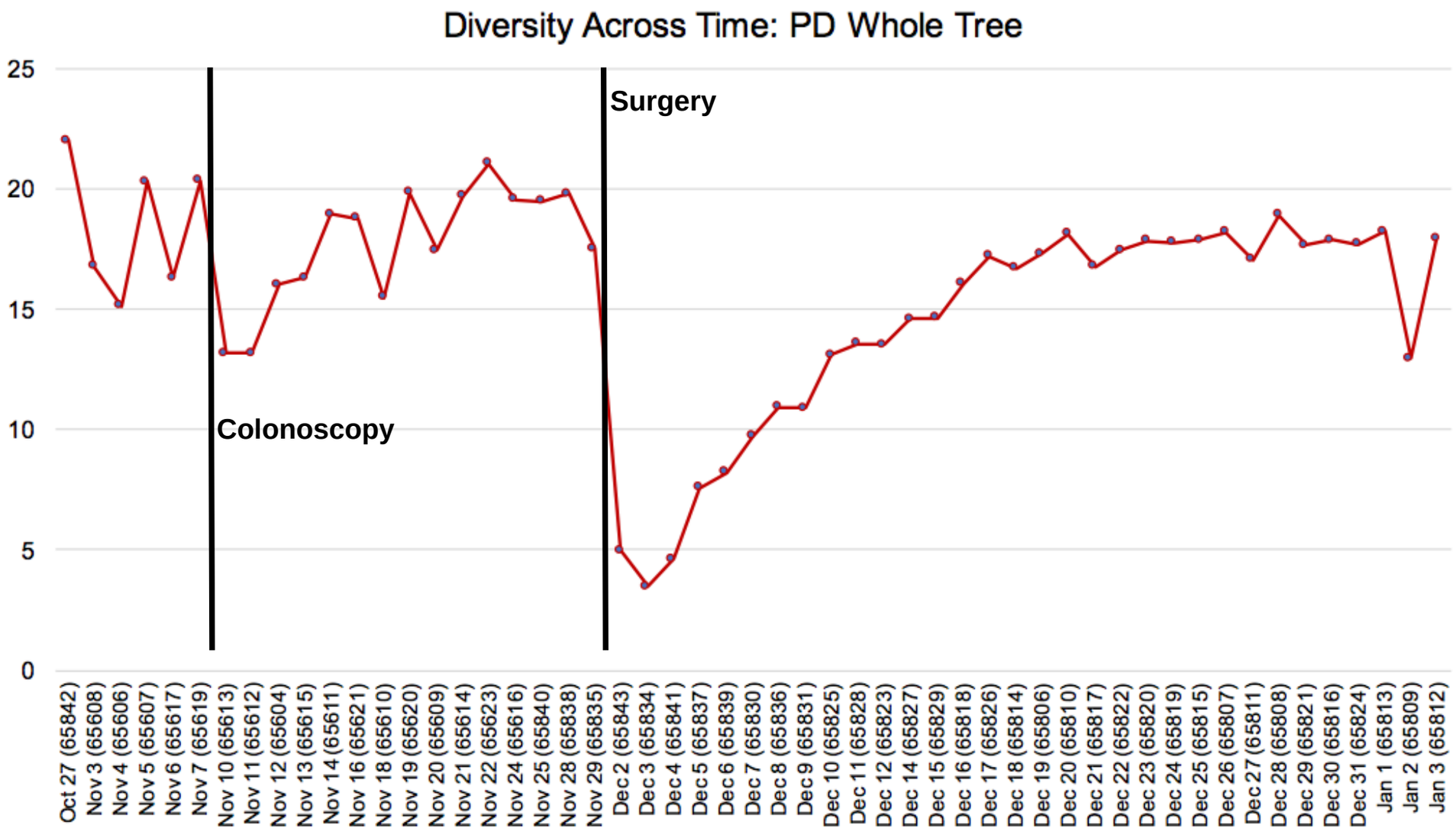


Gut Microbiome Genus-Level Profiles
Daily Samples Before and After Abdominal Surgery



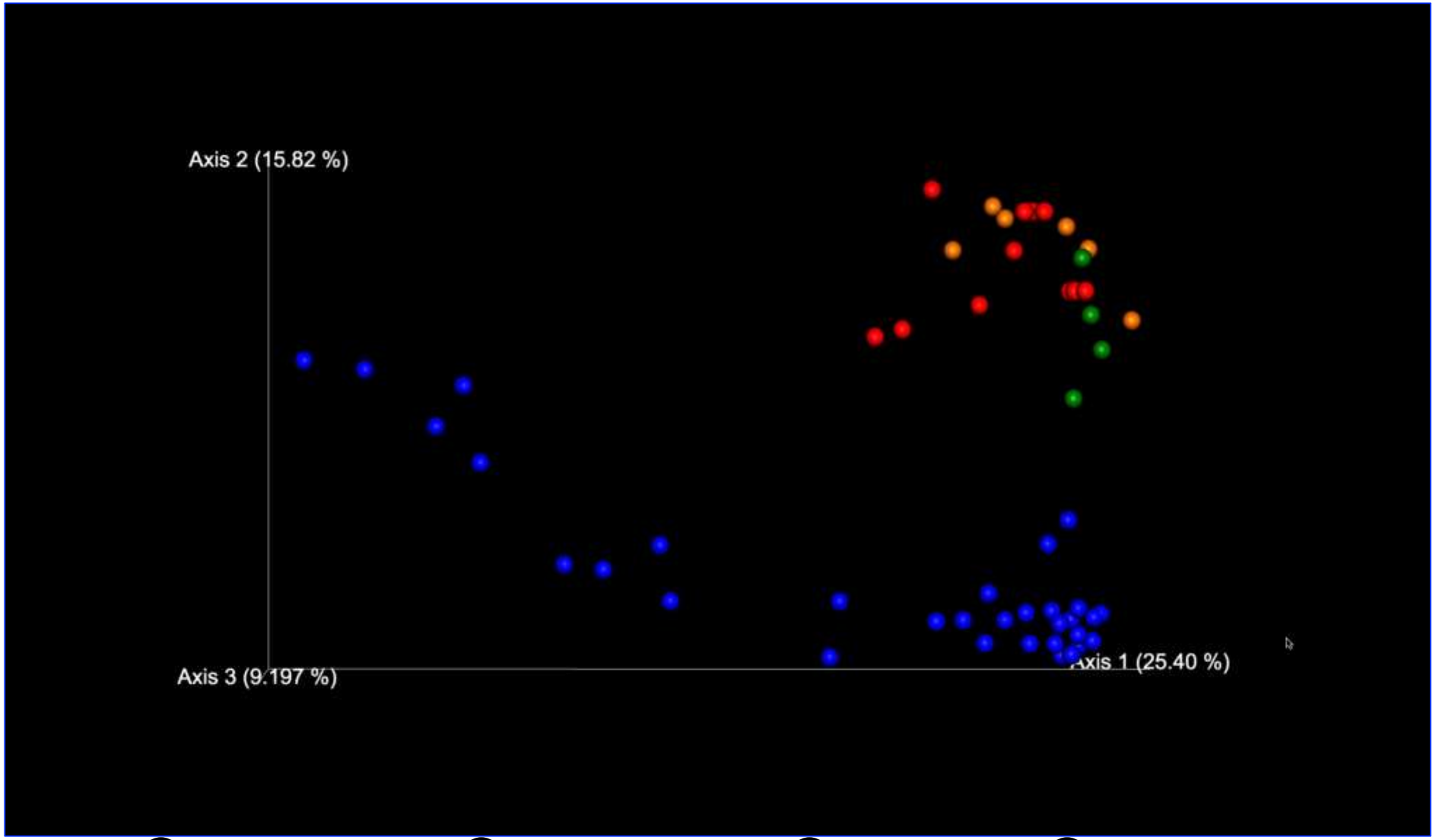
Source: Embriette Hyde, UCSD

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



Inflamed Disease State

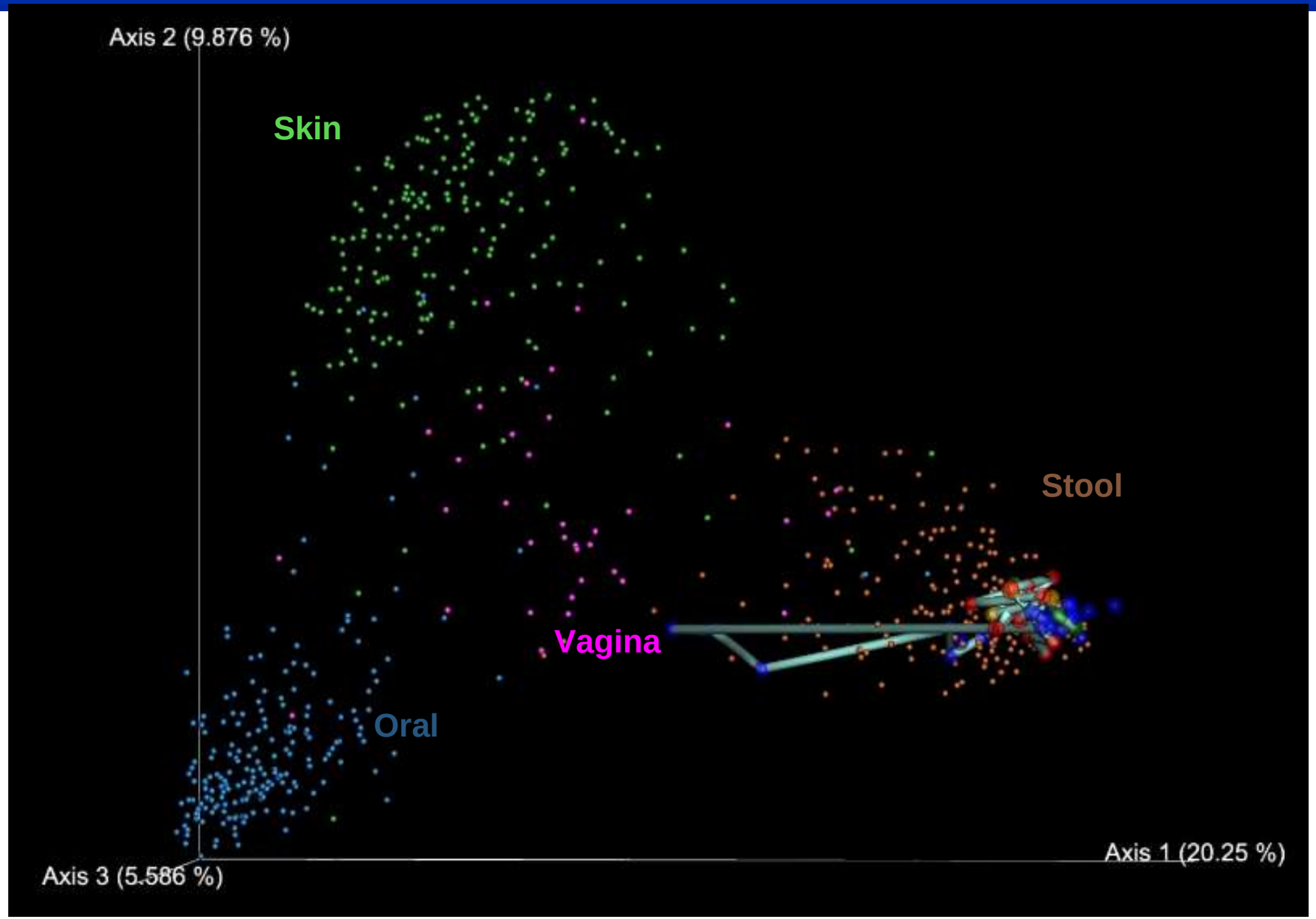
⇩

Healthy Post-Surgery State

Pre-colonoscopy Post-colonoscopy Pre-surgery Post-surgery

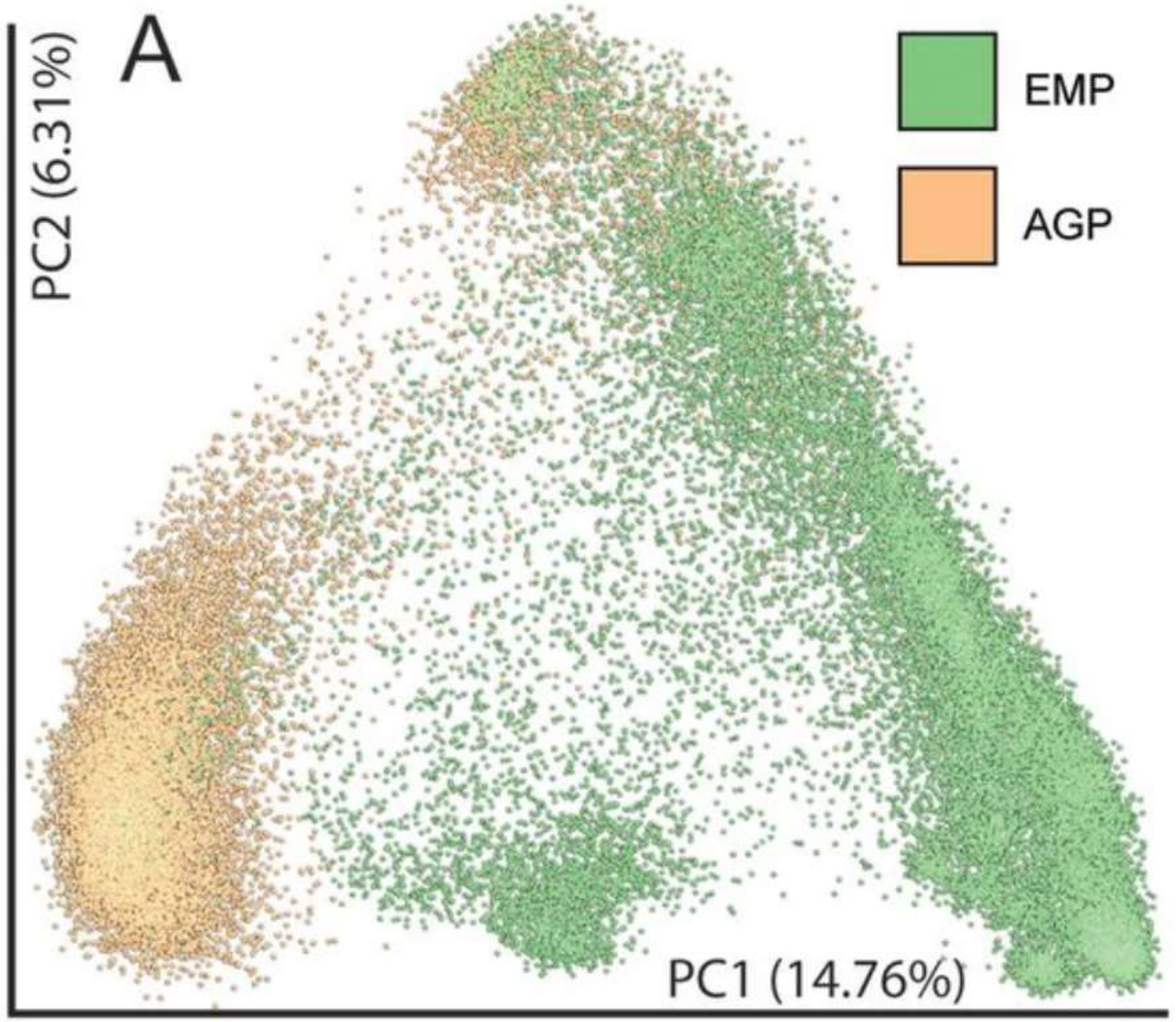
Source: Embriette Hyde, Yoshiki Vázquez Baeza, Knight Lab, UCSD

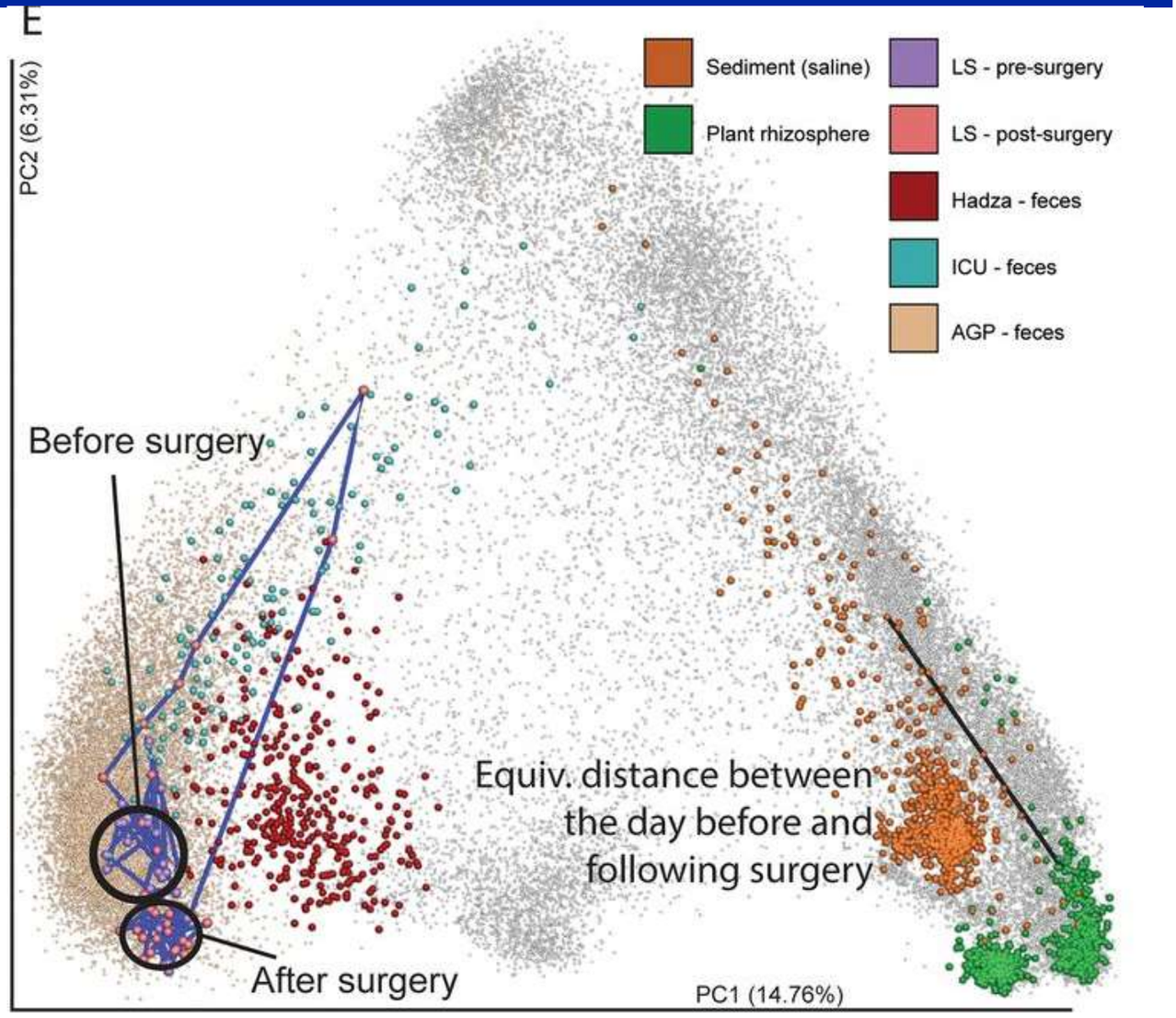
My Gut Microbiome Changed More After Surgery Than the Difference Between 10,000 Individuals!



Data From American Gut Project, UCSD. Rob Knight, Director

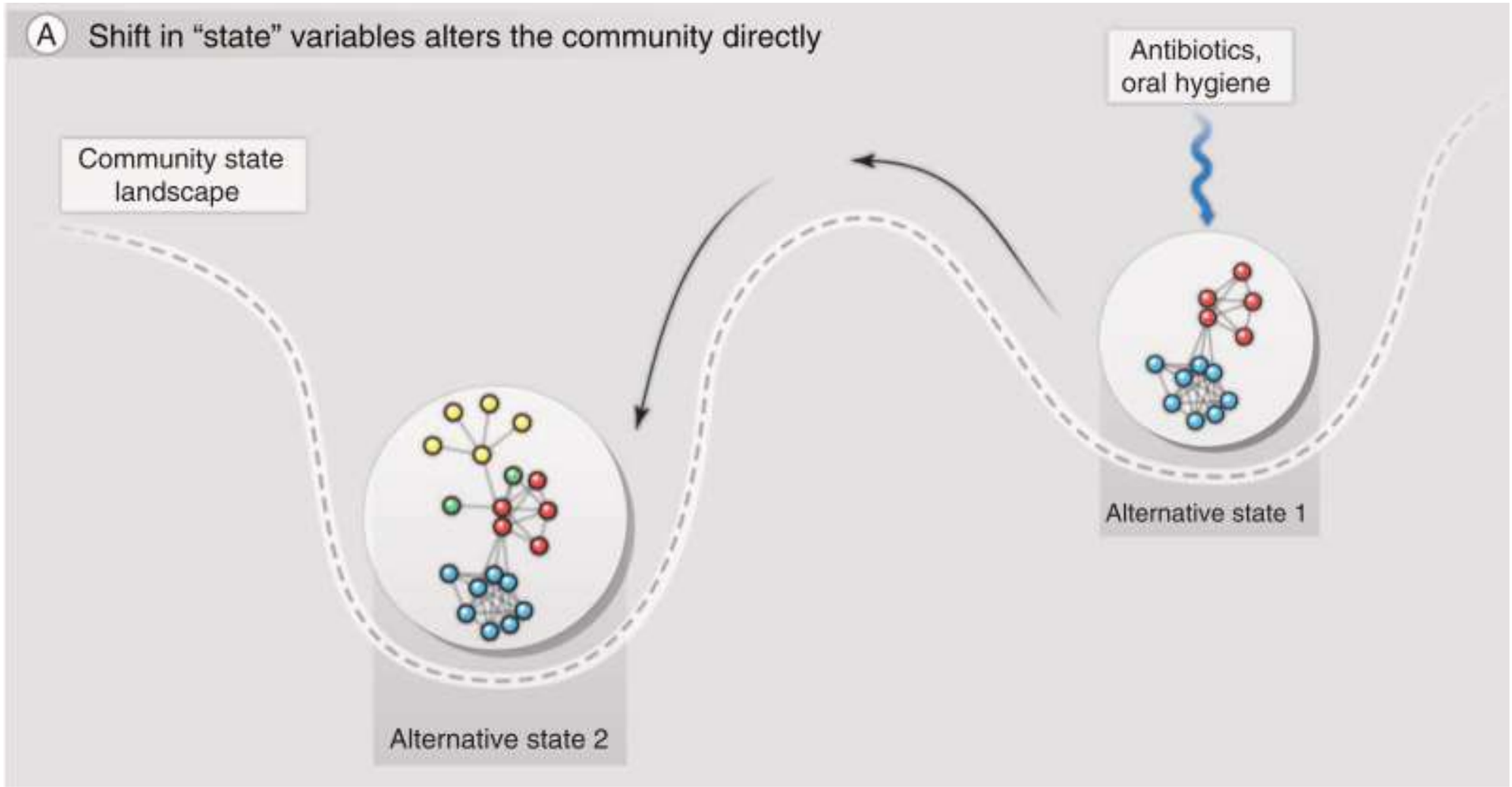
Extreme Gut Microbiome Ecology Changes Can Be Induced by Medical Procedures





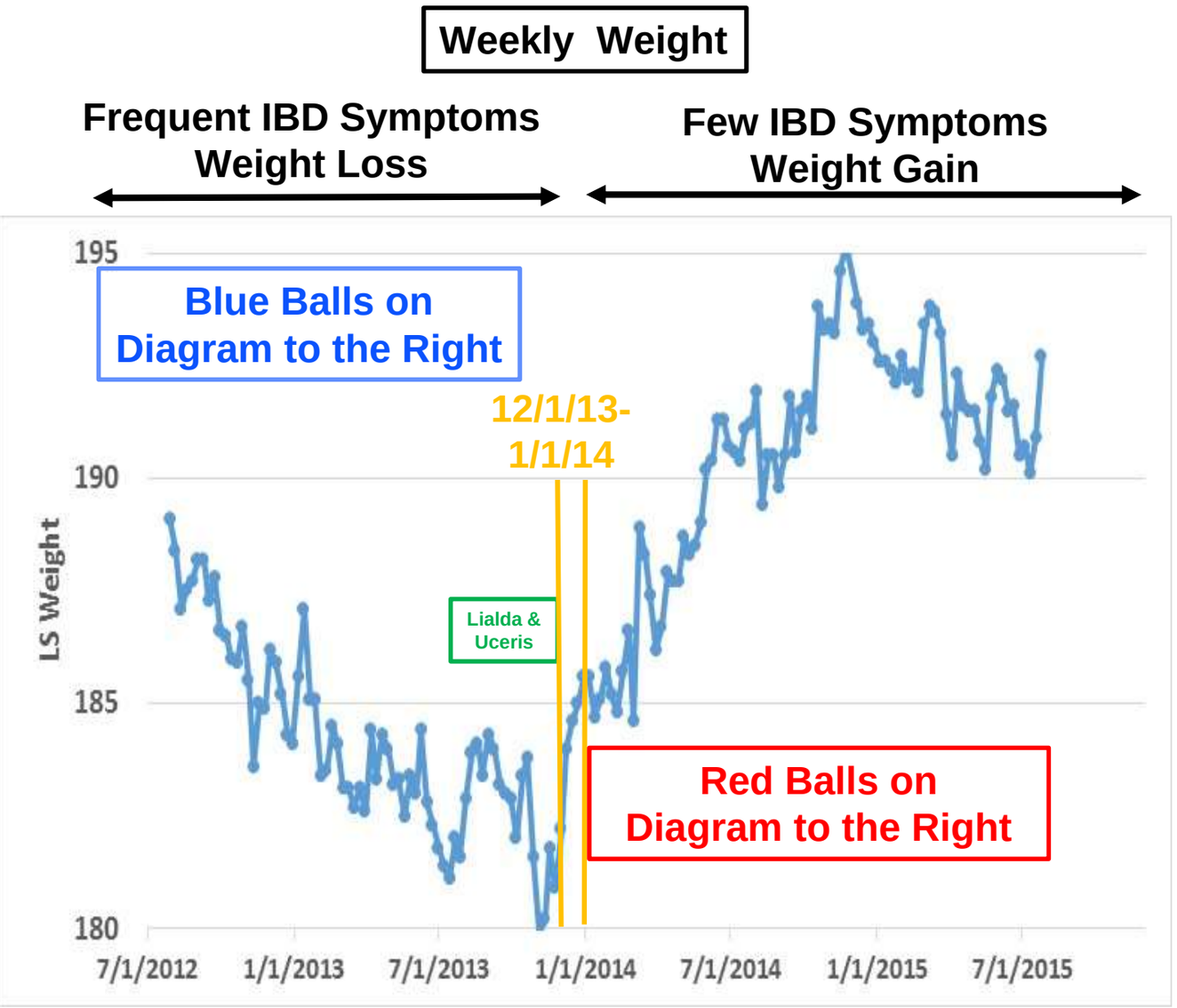
Daniel McDonald et al. mSystems 2018;
doi:10.1128/mSystems.00031-18

Lessons from Ecological Dynamics: Gut Microbiome Has Multiple Relatively Stable Equilibria

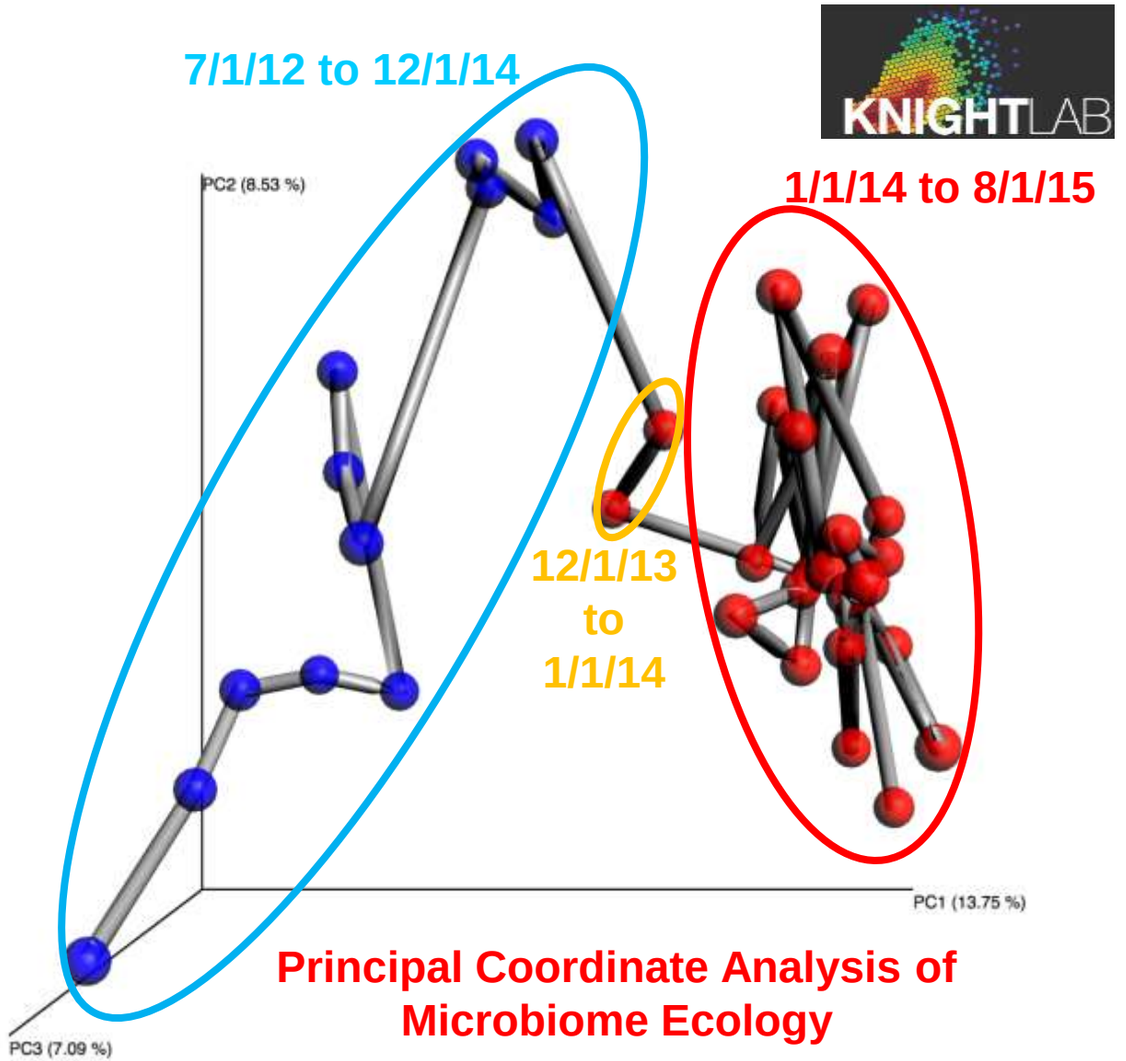


"The Application of Ecological Theory Toward an Understanding of the Human Microbiome," Elizabeth Costello, Keaton Stagaman, Les Dethlefsen, Brendan Bohannan, David Relman Science 336, 1255-62 (2012)

My Gut Microbiome Ecology Shifted After Drug Therapy Leading to Rapid Weight Gain, But Drop in IBD Symptoms



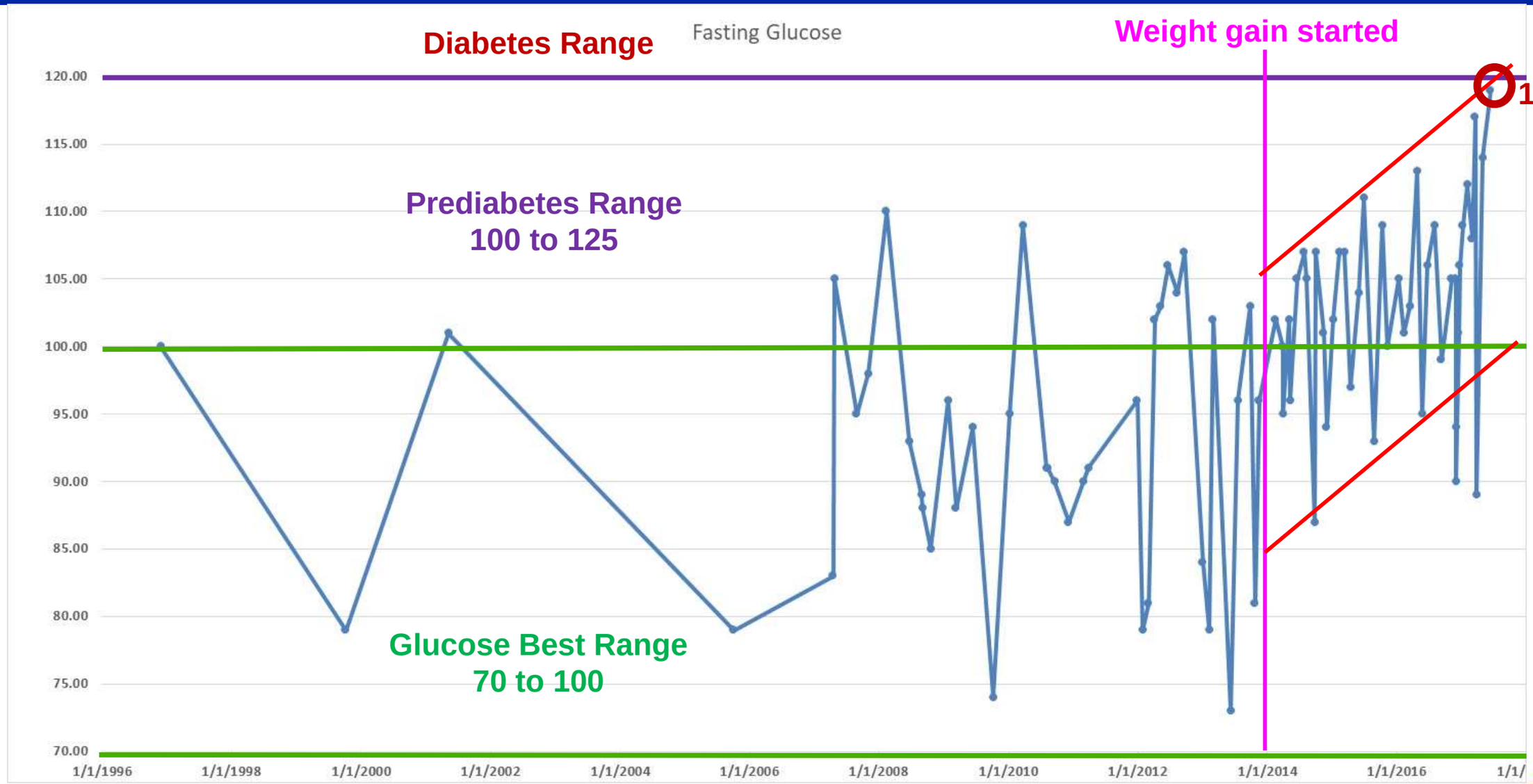
Weight Data from Larry Smarr, Calit2, UCSD



Principal Coordinate Analysis of Microbiome Ecology

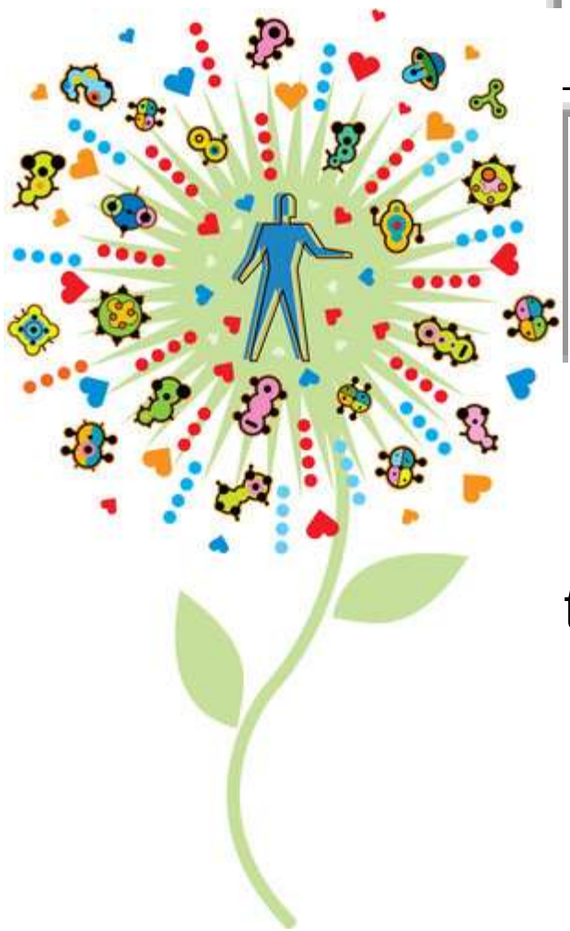
PCoA by Justine Debelius and Jose Navas, Knight Lab, UCSD

My Fasting Glucose Level Began to Rise After the Microbiome Shift – I Had Developed Metabolic Syndrome



20 Years of My Fasting Glucose Readings

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.”

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[5]

american gut

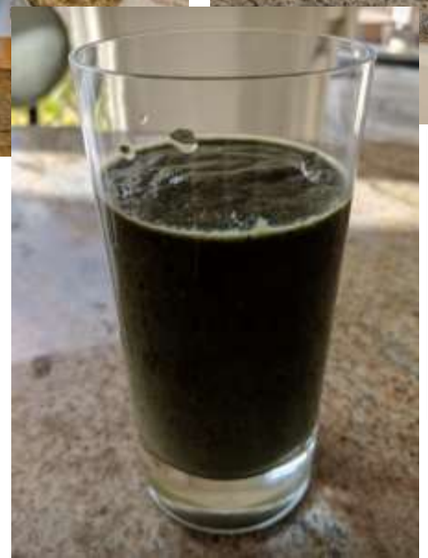
The more different types of plants a person eats, the higher their gut microbiome diversity.

mSystems. 2018 May 15;3(3)

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







UC San Diego's Rob Knight Lab is Currently Sequencing 100 Days of My Stool Samples

I Also Have Time-Stamped Annotated Photos of Everything I Consumed

UC San Diego

it²

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

Reverse Insulin Resistance with Intermittent Fasting



By: COURTNEY SPERLAZZA, MPH

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

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

- Hypothesis
  - In patients with metabolic syndrome who eat for ≥ 14 hours per day, limiting daily oral intake to 10 hours per day for 3 months while using a smartphone application will result in:
    - Weight loss
    - Improved glucose metabolism
    - Improved biomarkers associated with cardiovascular disease risk
- First study of TRE in metabolic syndrome
- First use of continuous glucose monitoring during TRE

UC San Diego

salk
Where cures begin.



Pam Taub, MD
Cardiology



Satchin Panda, PhD
Circadian Biology

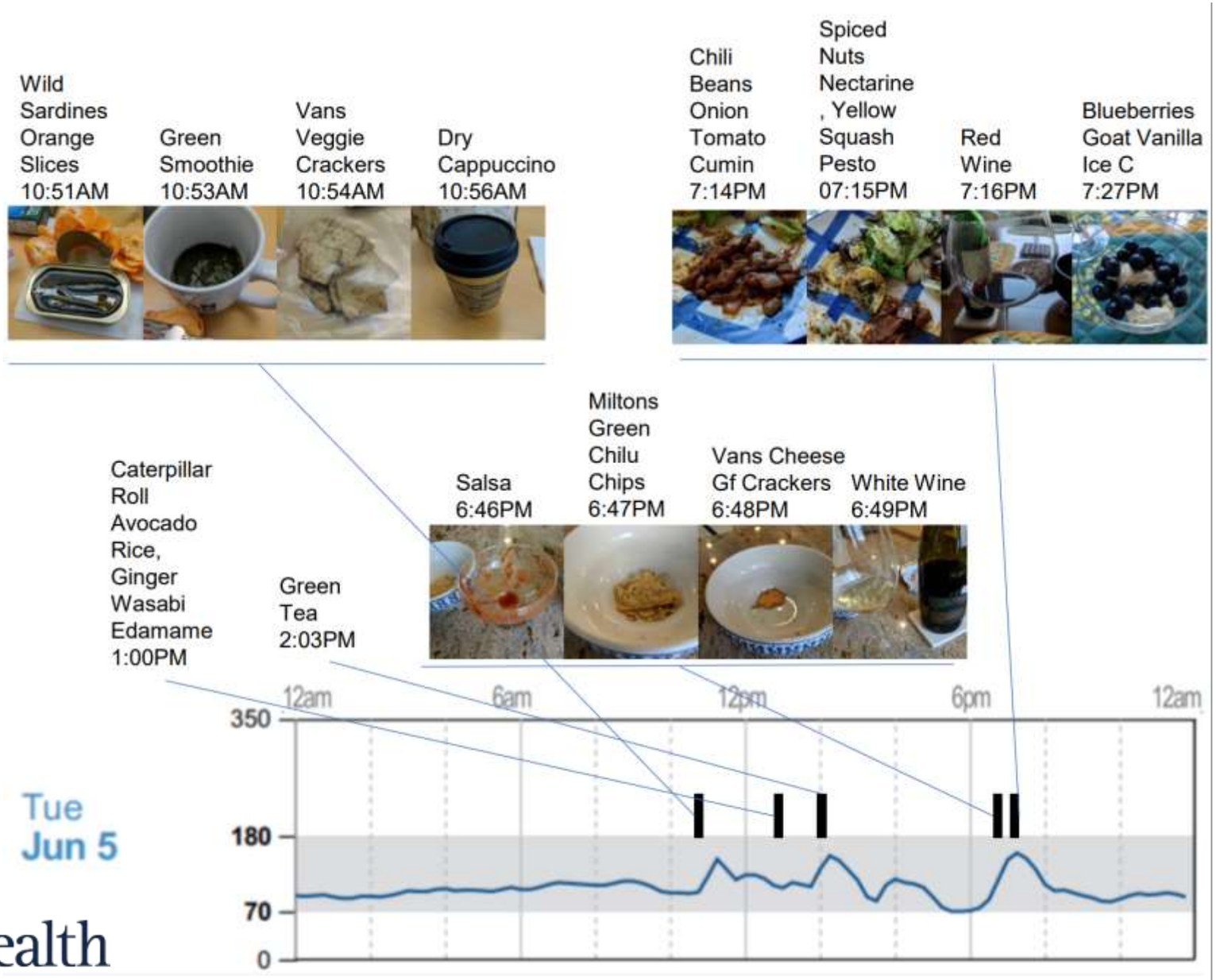
Correlating Time Stamped Annotated Food Intake Against Continuous Blood Glucose Readings

salk
Where cures begin.

Graph Created by Emily Manoogian, Panda Lab, Salk Institute



UC San Diego Health



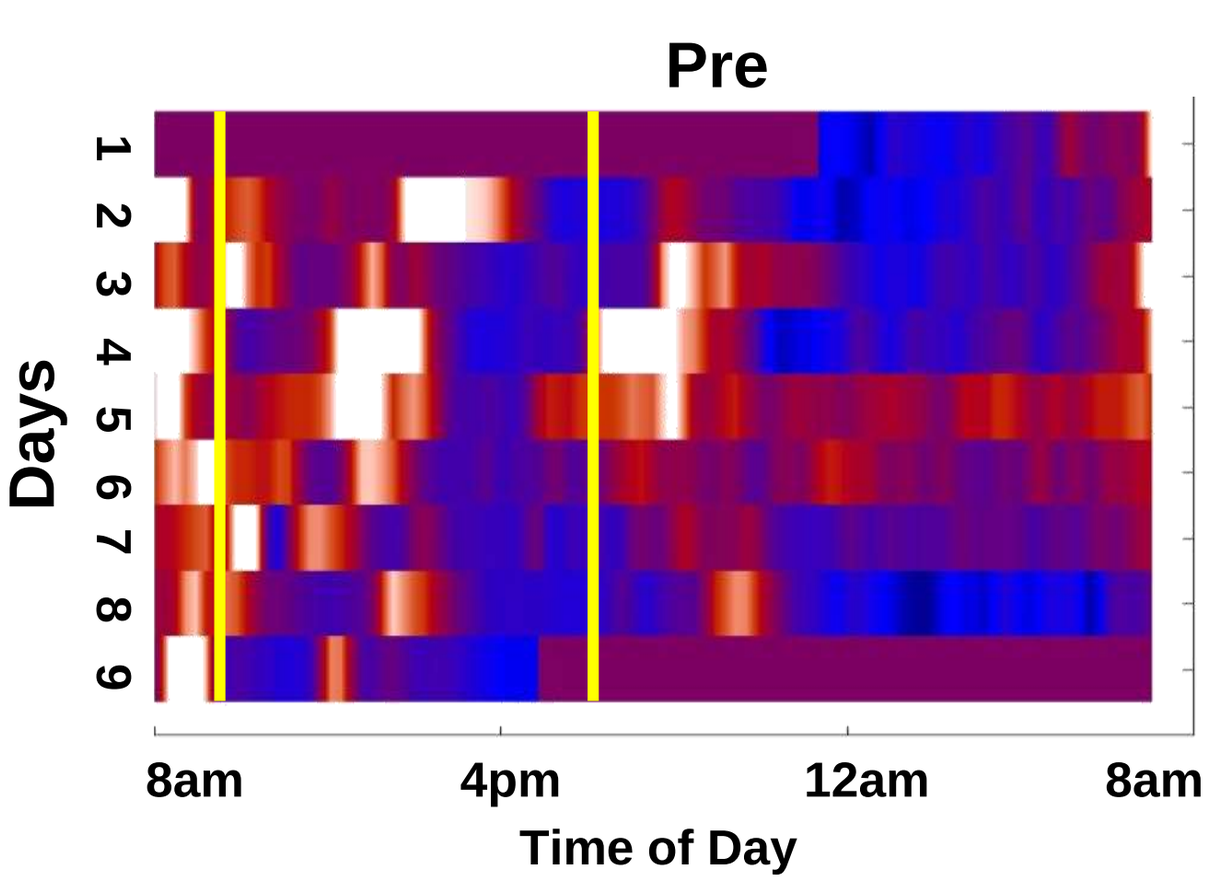
Panda/Taub Clinical Trial

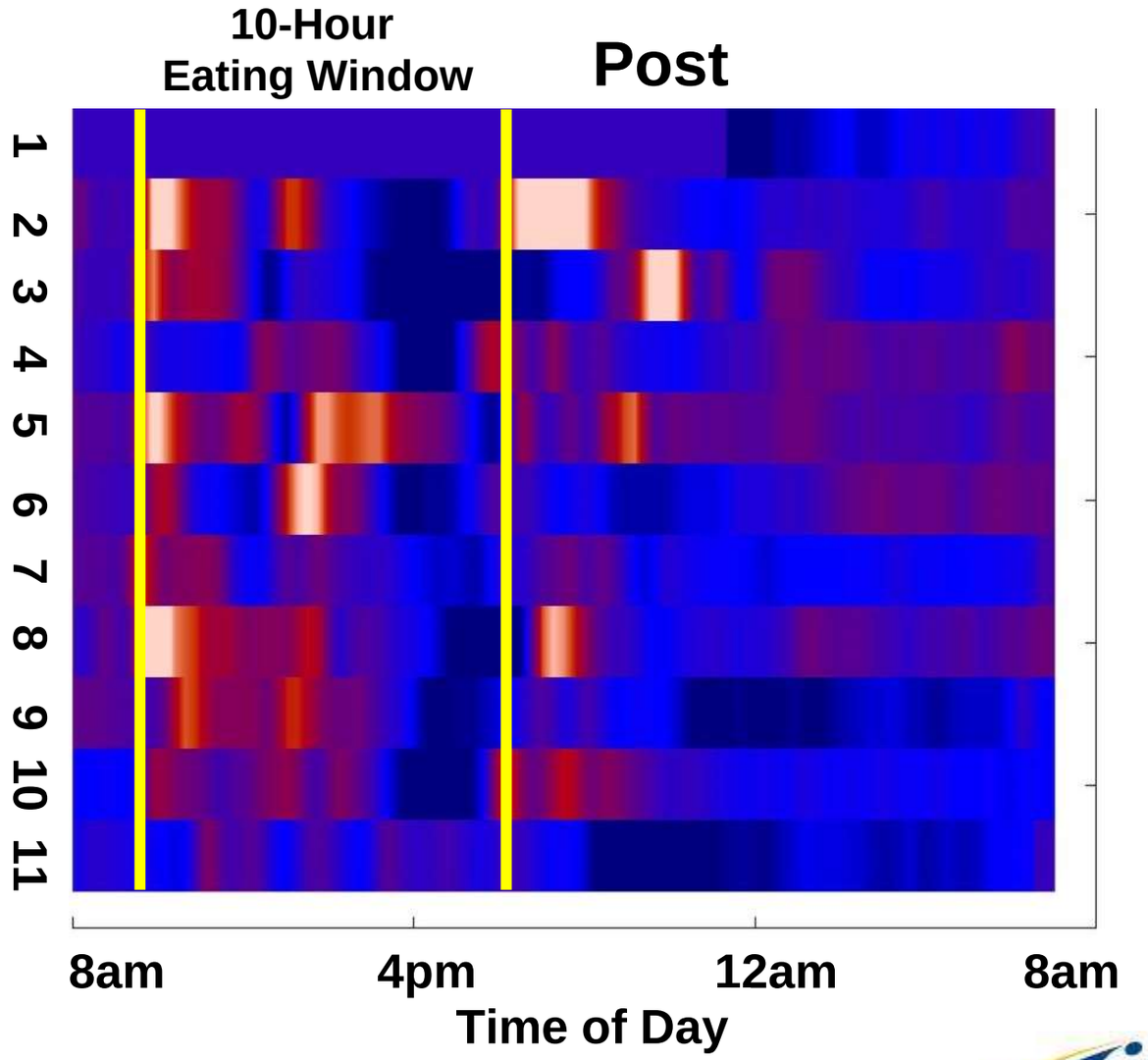
All Food/ Drink Photo/ Time-Stamped/ Annotated For 100-Days

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

it²

Heat Map of Continuous Glucose Monitor Every 15 Minutes Before and After 3 Months of Time-Restricted Eating

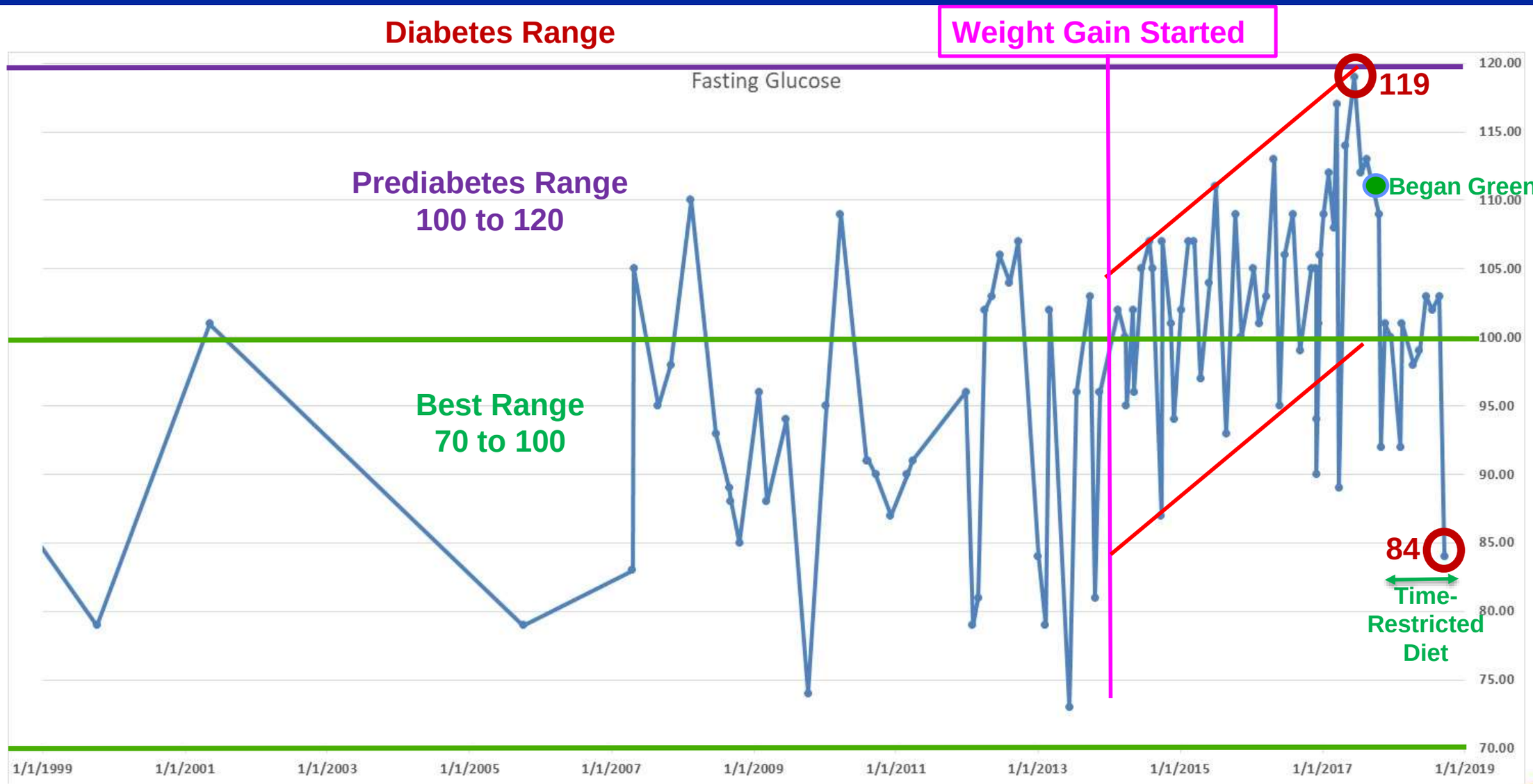




- **Other Improvements:**
  - **Waist 108cm to 102 cm**
  - **Weight 197 to 189**
  - **Blood Pressure 140/74 to 130/69**

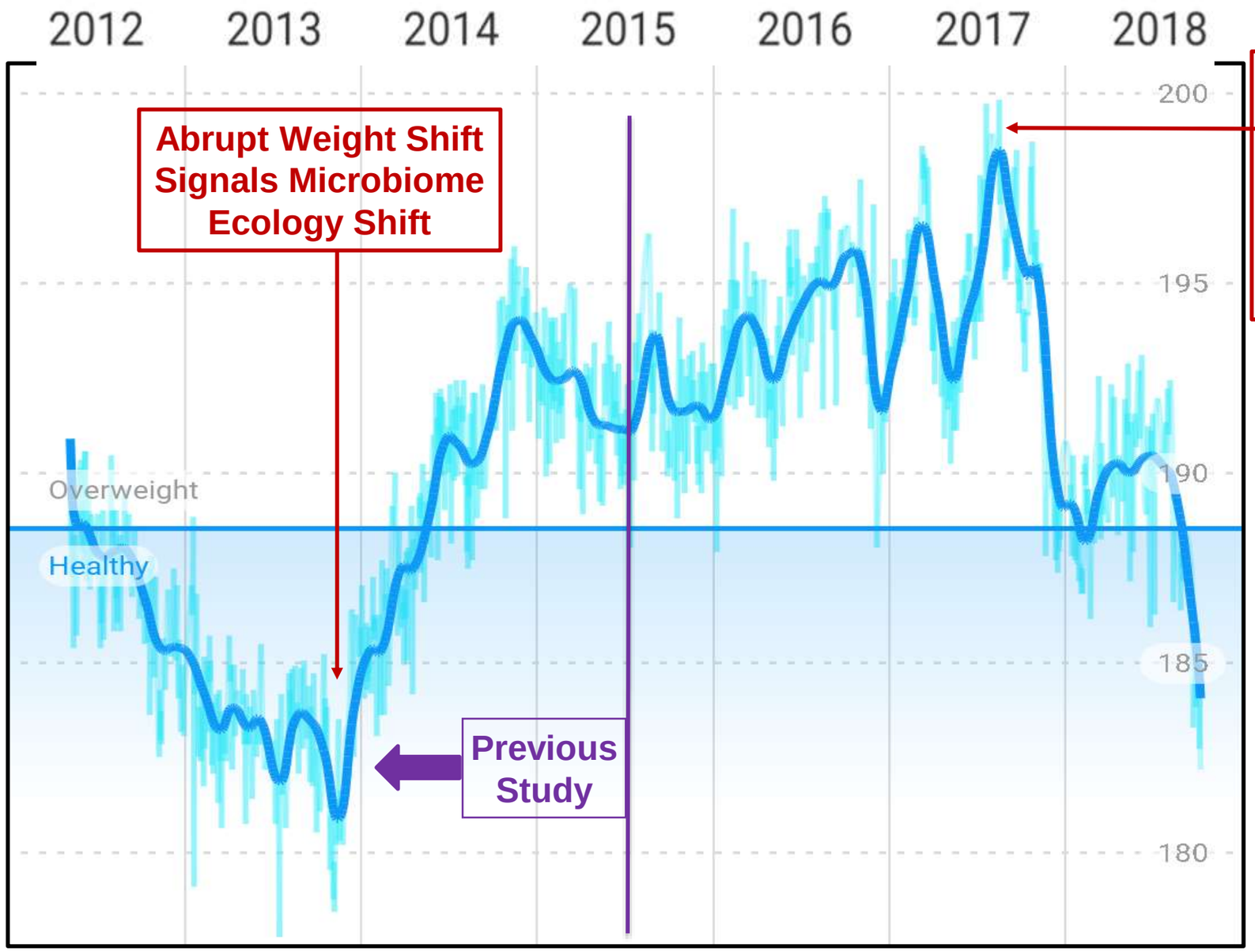
Data from Taub/Panda Clinical Trial
Graphics by Azure Grant, UC Berkeley

My Fasting Glucose Level Dropped Abruptly Into Normal Level after Green Smoothies and Time-Restricted Diet



How Can a Shifting Microbiome Ecology Alter Your Glucose Pathway?

Using My Daily Weight Time Series To Detect Internal Changes



Data From Withings WiFi Bathroom Scale

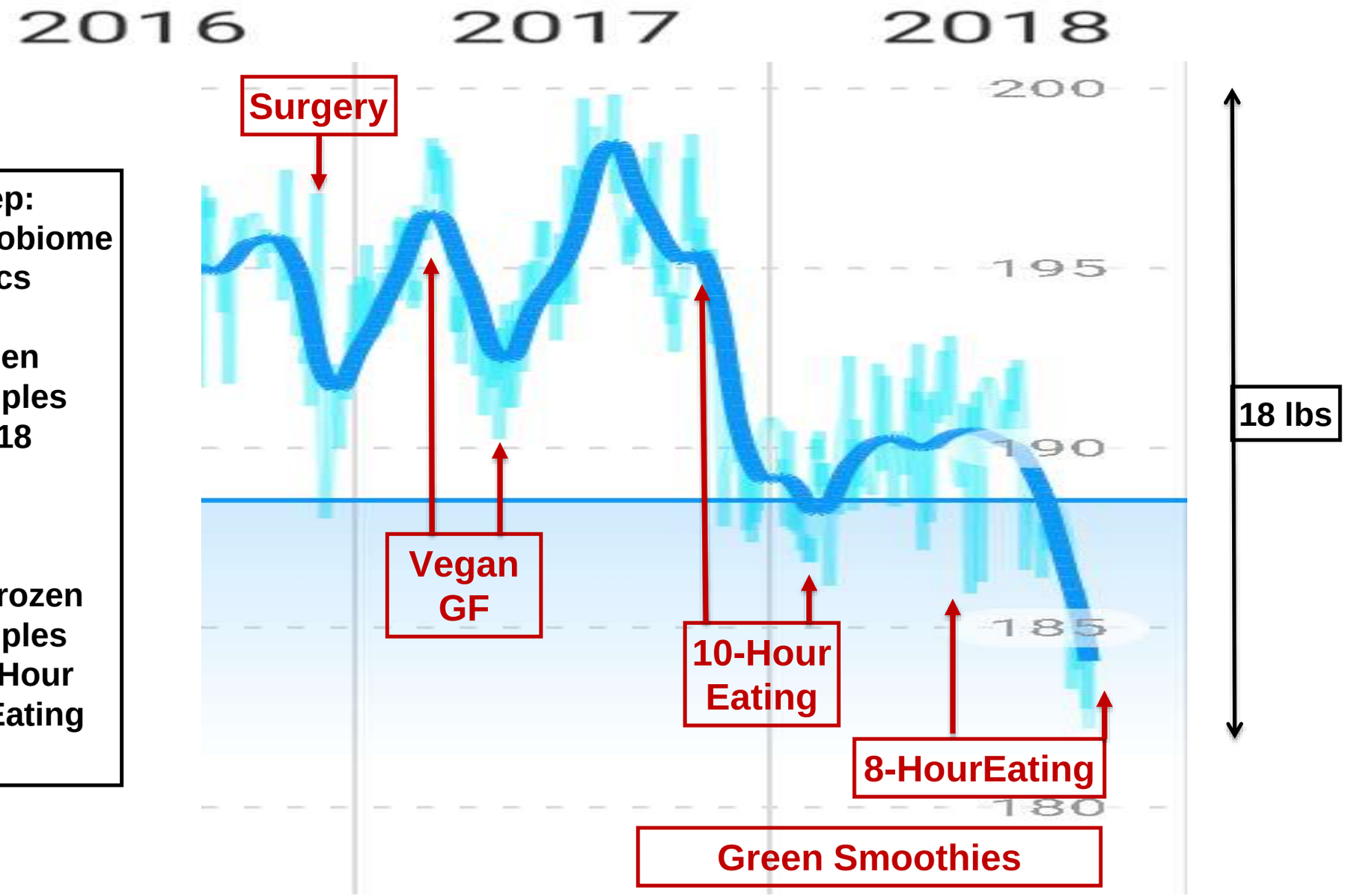
Diet Timing and Content
Can Have a Major Impact on Metabolic Syndrome

Next Step:
Analyze Microbiome Dynamics

135 Frozen Stool Samples 2012-2018

Plus

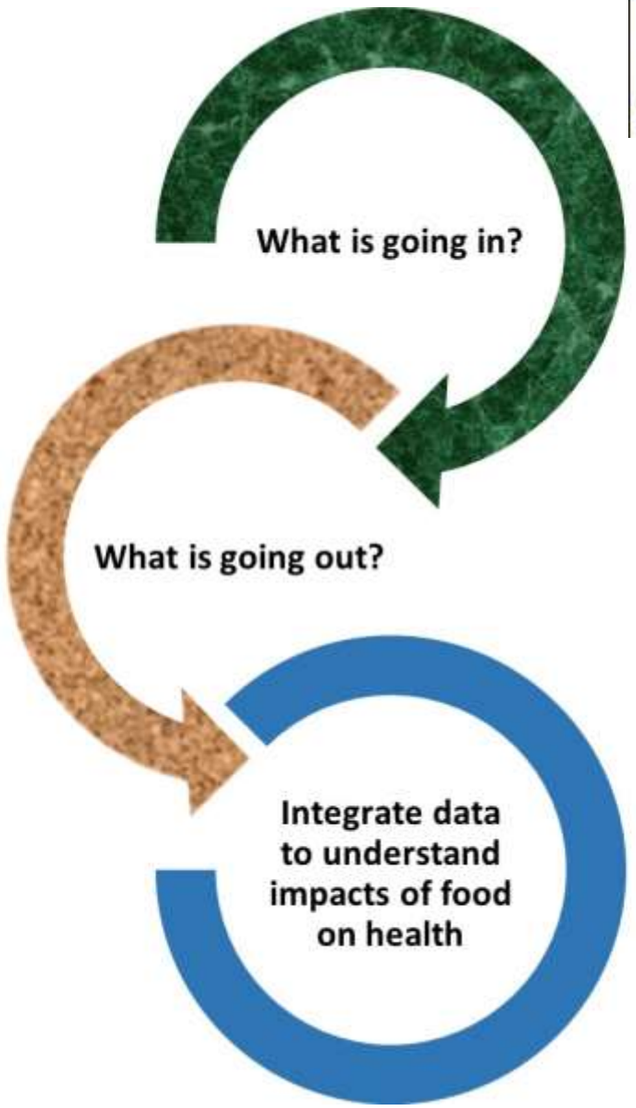
100 Daily Frozen Stool Samples During 10-Hour Restricted Eating Trial



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

Jerry Sheehan
Tom DeFanti
Joe Keefe
John Graham
Kevin Patrick
Mehrdad Yazdani
Jurgen Schulze
Andrew Prudhomme
Philip Weber
Fred Raab
Ernesto Ramirez



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UCSD Bioengineering

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Bernhard Palsson Lab