“N-of-1 Experience in Personalized Lifestyle Medicine”

Invited Talk

2018 Thought Leaders Consortium

The Science of Precision:

What’s Next for Personalized Lifestyle Health Care

Tucson, Arizona

October 13, 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

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



From the Reichert-Haus in Ludwigshafen, Germany

“Knowing Me” Led Me to Become a Digitally-Enabled “Patient of the Future”: Measuring the State of My Body and “Tuning” It

I Arrived in La Jolla in 2000 After 20 Years in the Midwest and Decided to Move Against the Obesity Trend

Age 51





Age 61

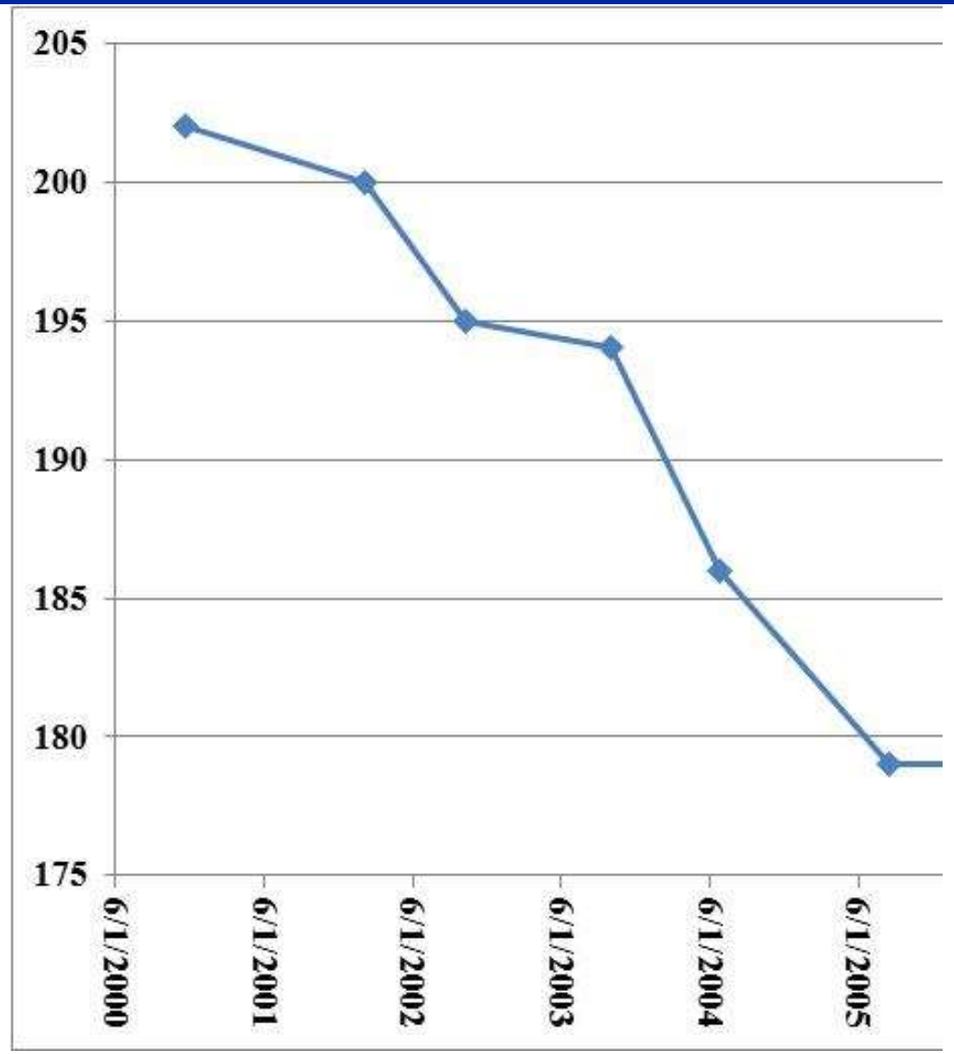
HEALTH IT, PEOPLE, WIRELESS

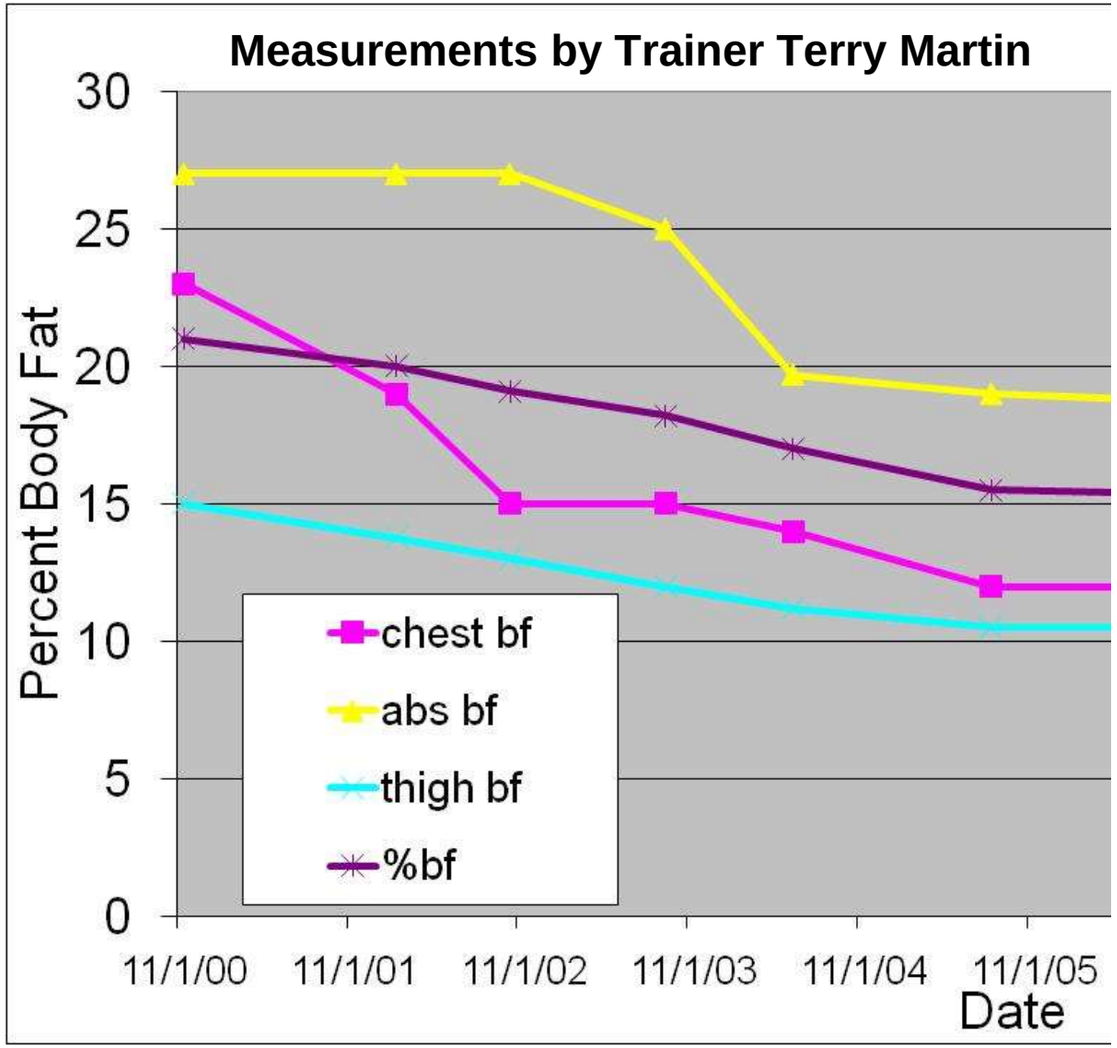
How Internet Pioneer Larry Smarr Lost 20 Pounds by Becoming a “Quantified Self”

Luke Timmerman 5/12/10

www.xconomy.com/san-diego/2010/05/12/how-internet-pioneer-larry-smarr-lost-20-pounds-by-becoming-a-quantified-self/

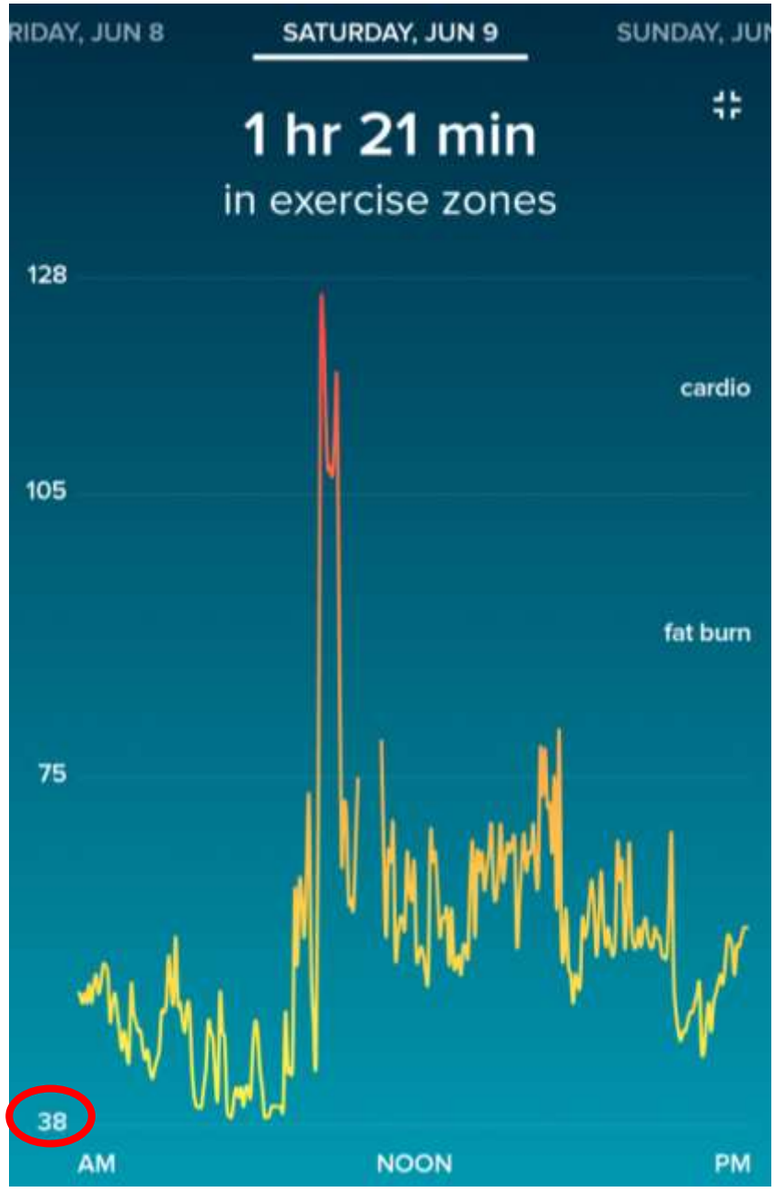
I Started By Reducing My Weight and Body Fat Through Nutrition and Exercise





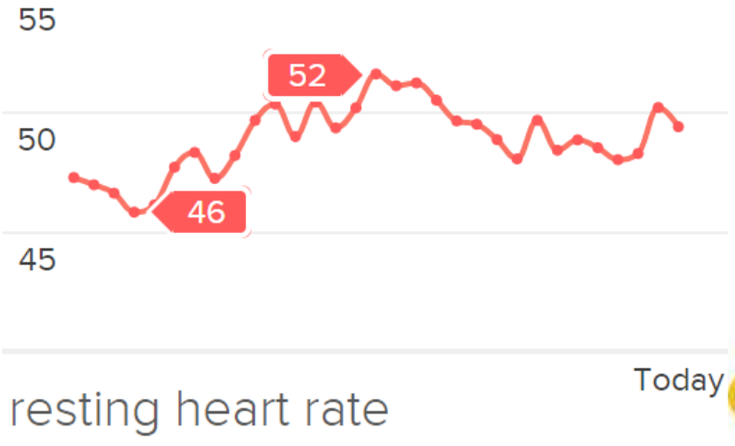
I Lost 23 lbs and More Than 1/3 of My Original Body Fat

Walking 3 Miles/Day and 2 Elliptical Sessions Per Week Has Lowered My Resting Heartrate







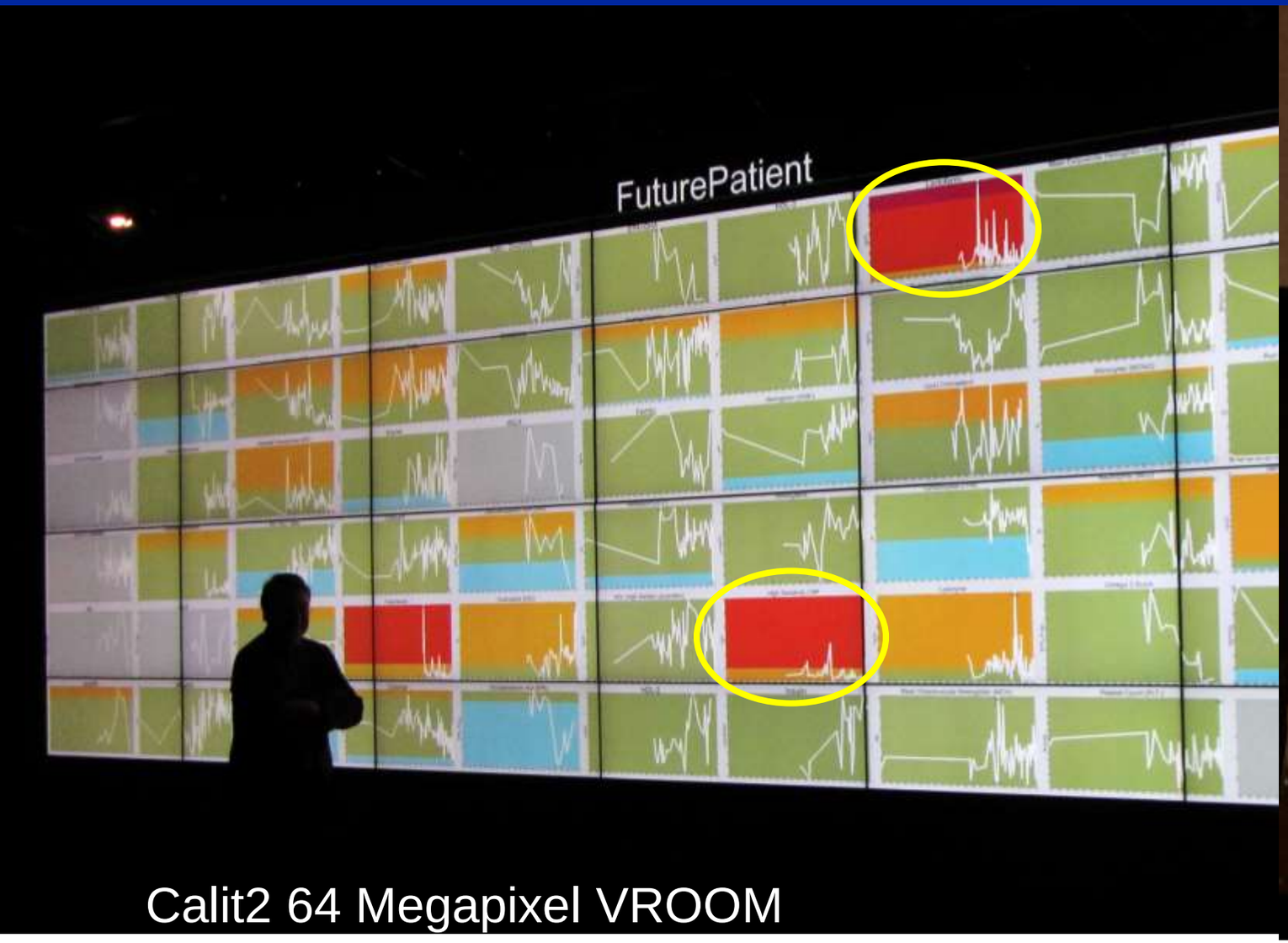


From Measuring Macro-Variables to Measuring Your Internal Variables

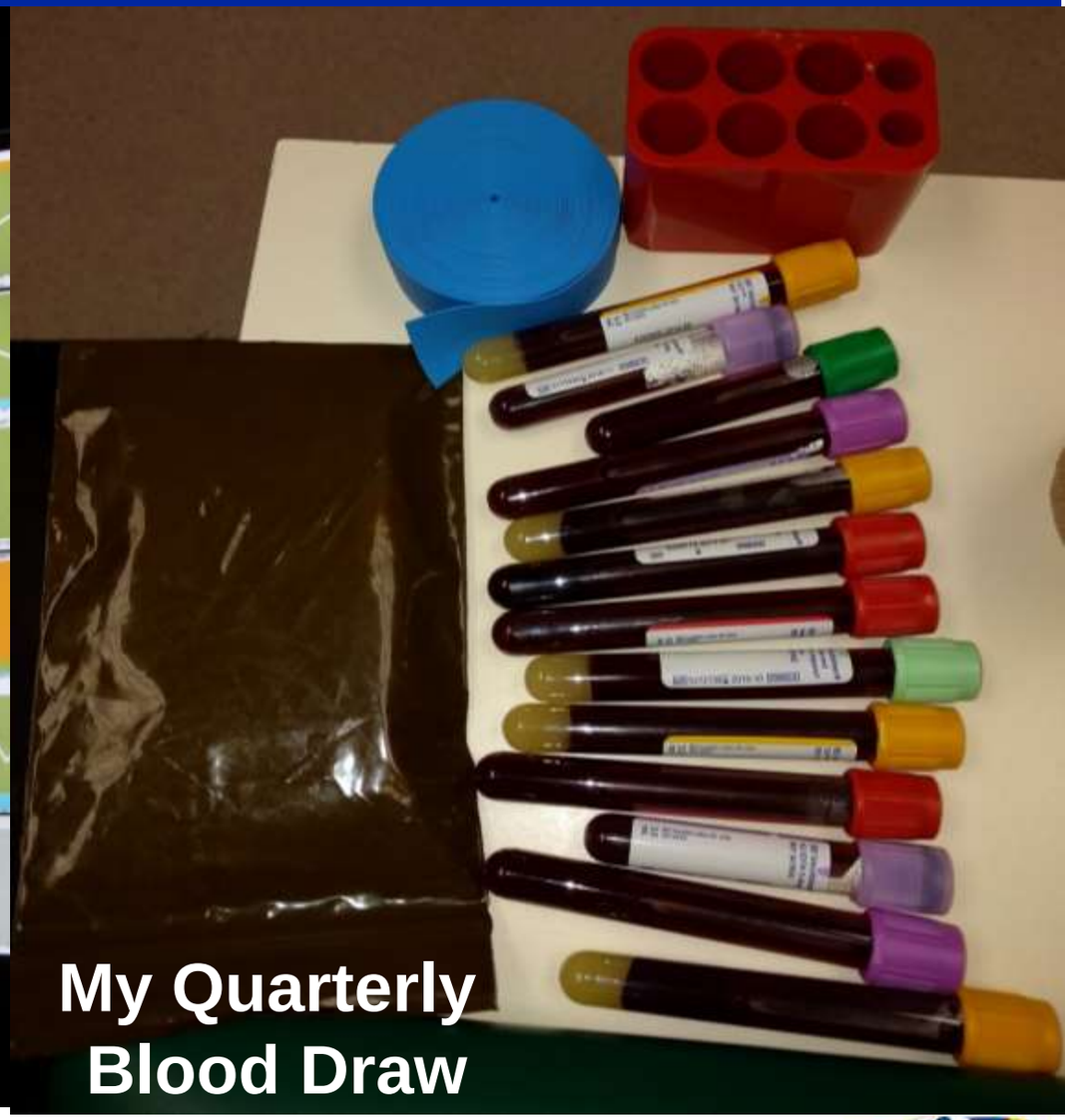


www.technologyreview.com/biomedicine/39636

I Started Tracking Biomarkers for Health, But Unexpectedly Discovered Disease



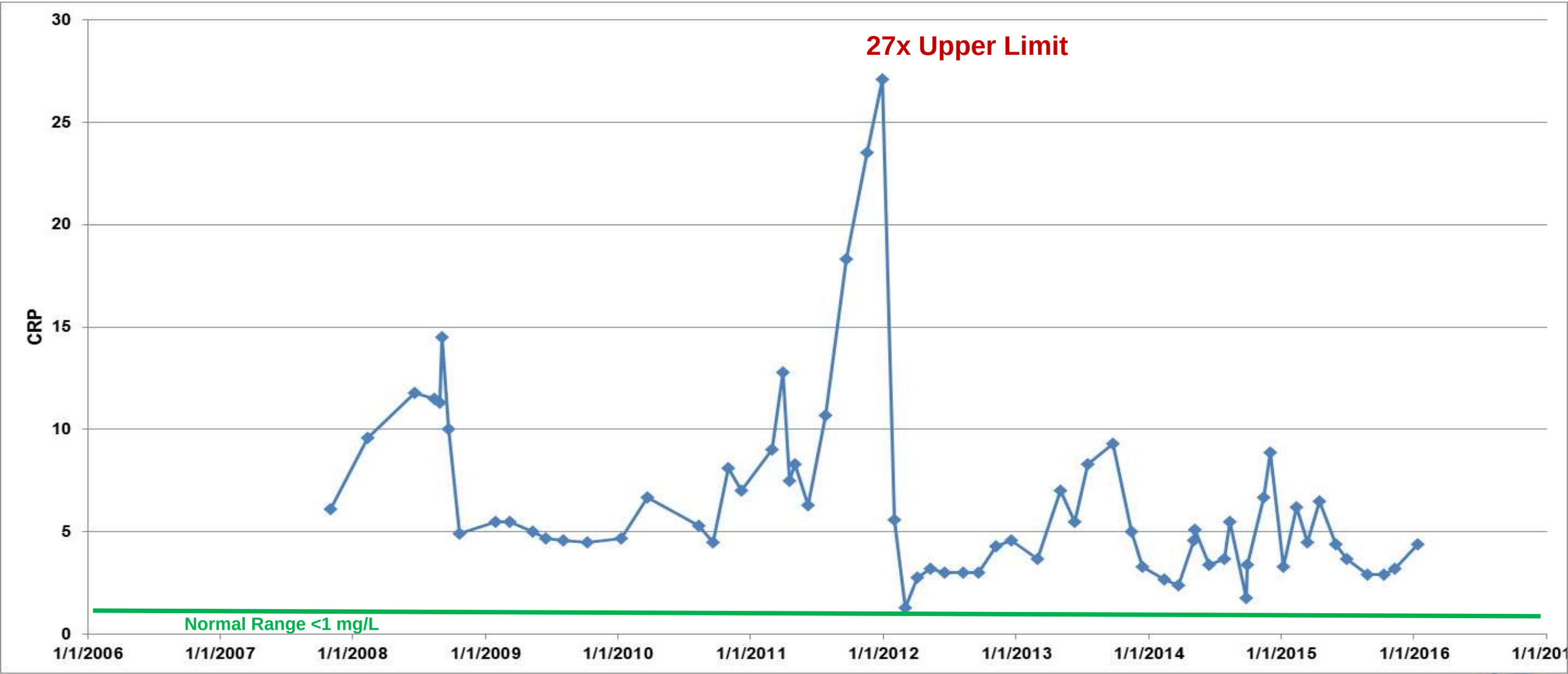
Calit2 64 Megapixel VROOM



My Quarterly Blood Draw

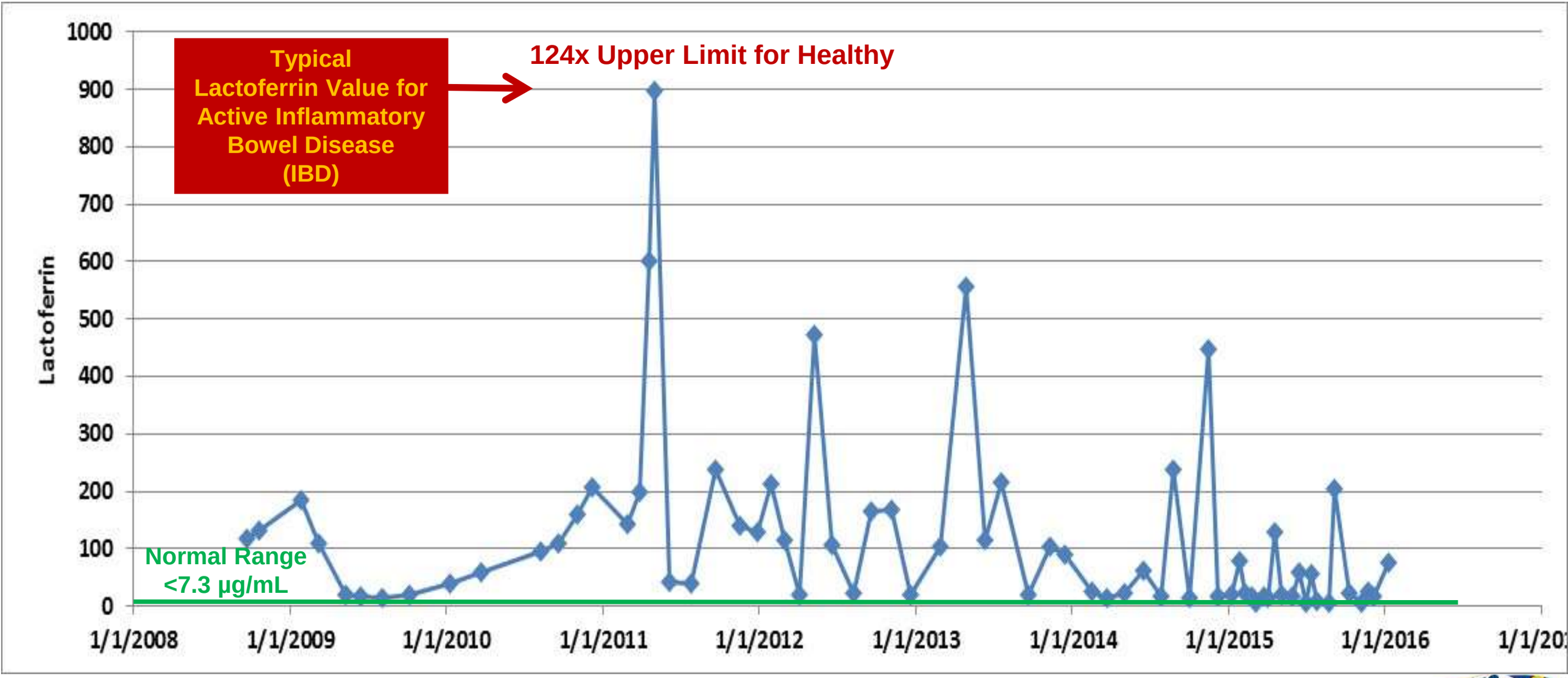
For a Detailed 45-Minute Video of Me Exploring My Biomarkers and Microbiome on the Wall, See www.youtube.com/watch?v=9FhlA_3pLHY

Only One of My Blood Measurements Was Far Out of Range--Indicating Chronic Inflammation



Complex Reactive Protein (CRP) is a Blood Biomarker for Detecting Presence of Inflammation

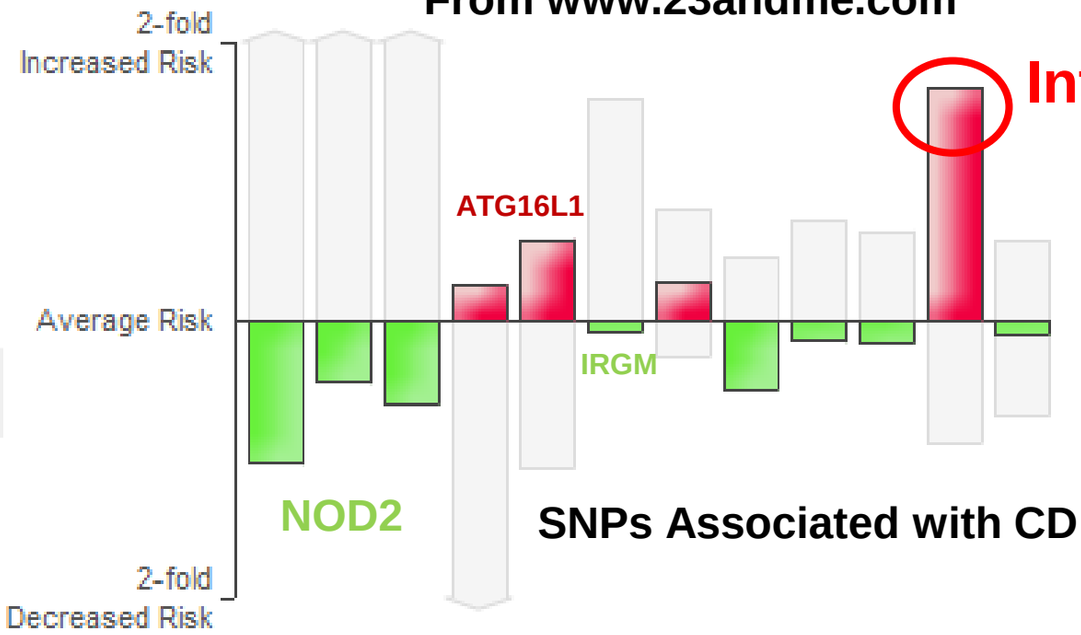
Longitudinal Stool Tests Revealed Large Excursions in My Immune System: Implying I Had Inflammatory Bowel Disease



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

I Found I Had One of the Earliest Known SNPs Associated with Crohn's Disease

From www.23andme.com



Polymorphism in Interleukin-23 Receptor Gene — 80% Higher Risk of Pro-inflammatory Immune Response

A Genome-Wide Association Study Identifies *IL23R* as an Inflammatory Bowel Disease Gene

Richard H. Düerr, *et al.*
Science **314**, 1461 (2006)

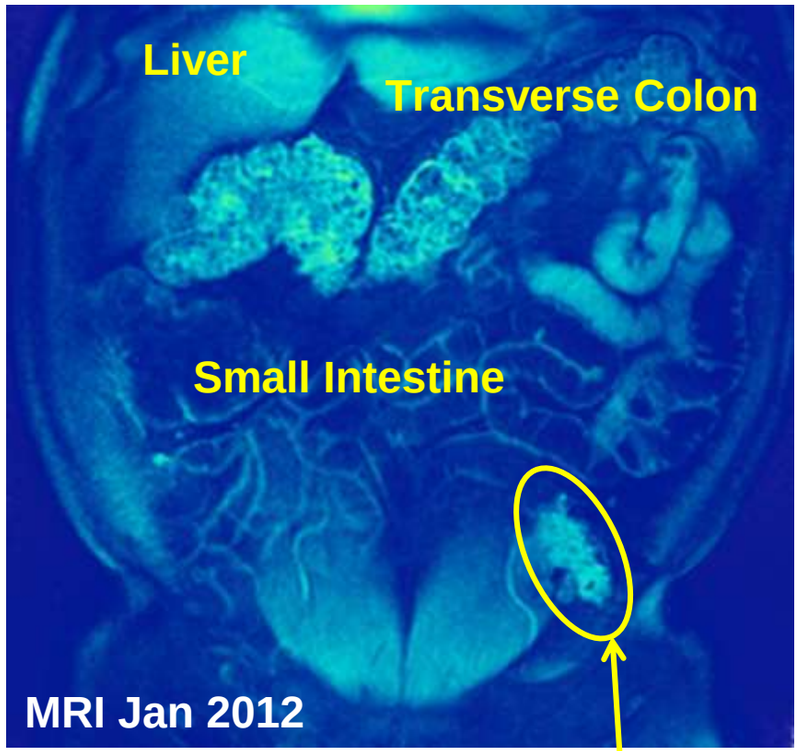
News and Views

Nature Medicine **13**, 26 - 28 (2007)
doi:10.1038/nm0107-26

IL-23: a master regulator in Crohn disease

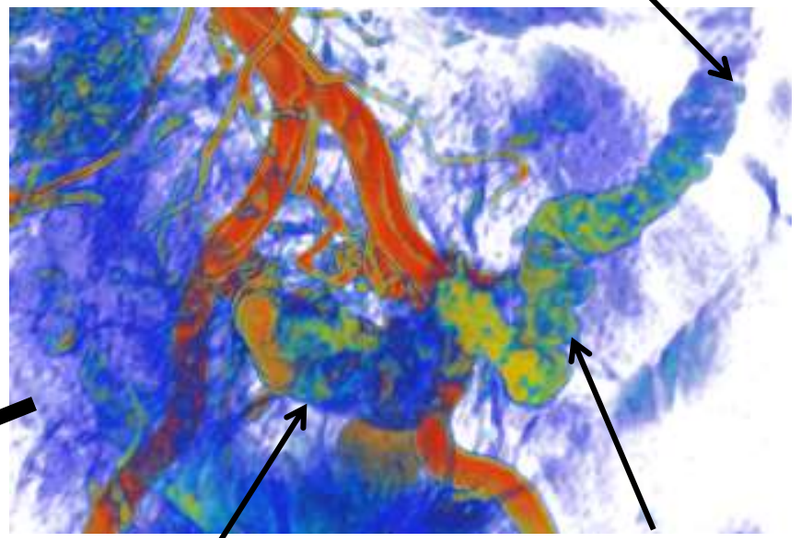
Markus F Neurath[1]

Confirming the IBD (Colonic Crohn's) Hypothesis in 2012: Finding the "Smoking Gun" with MRI Imaging



I Obtained the MRI Slices From UCSD Medical Services and Converted to Interactive 3D Working With Calit2 Staff

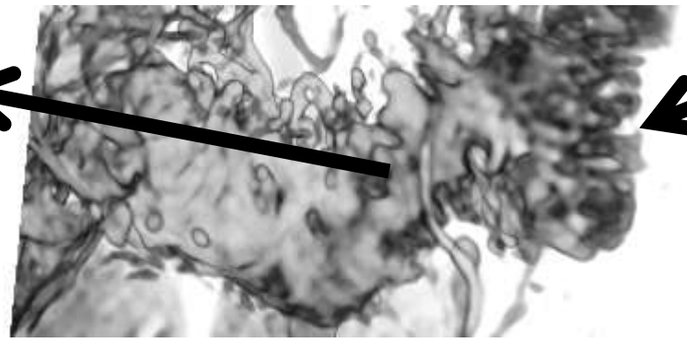
Descending Colon



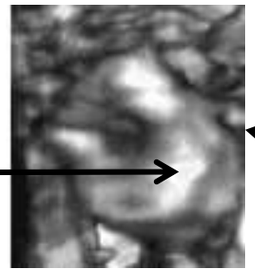
Major Kink

Sigmoid Colon
Threading Iliac Arteries

Diseased Sigmoid Colon

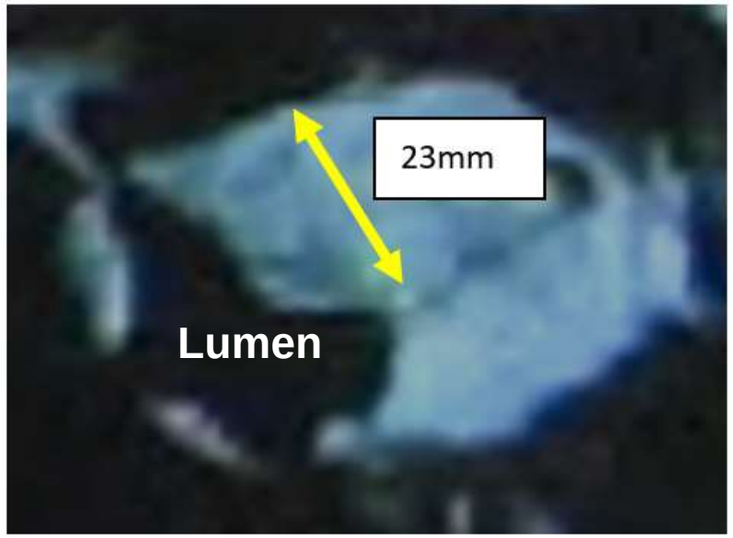


Cross Section

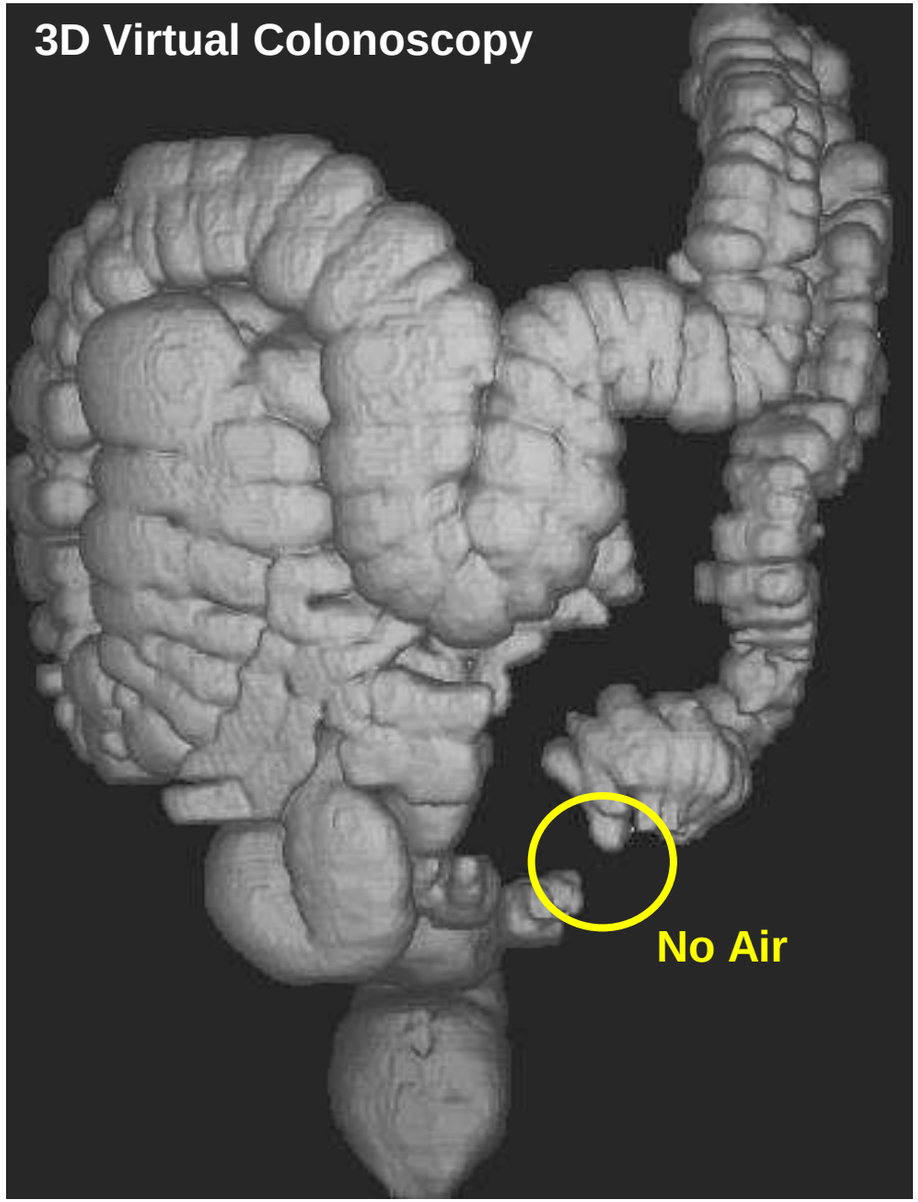


Severe Colon
Wall Swelling

Full Body CAT Scan at mm Resolution, Including Virtual Colonoscopy in June 2016 Convinced Me Time Had Come for Surgery



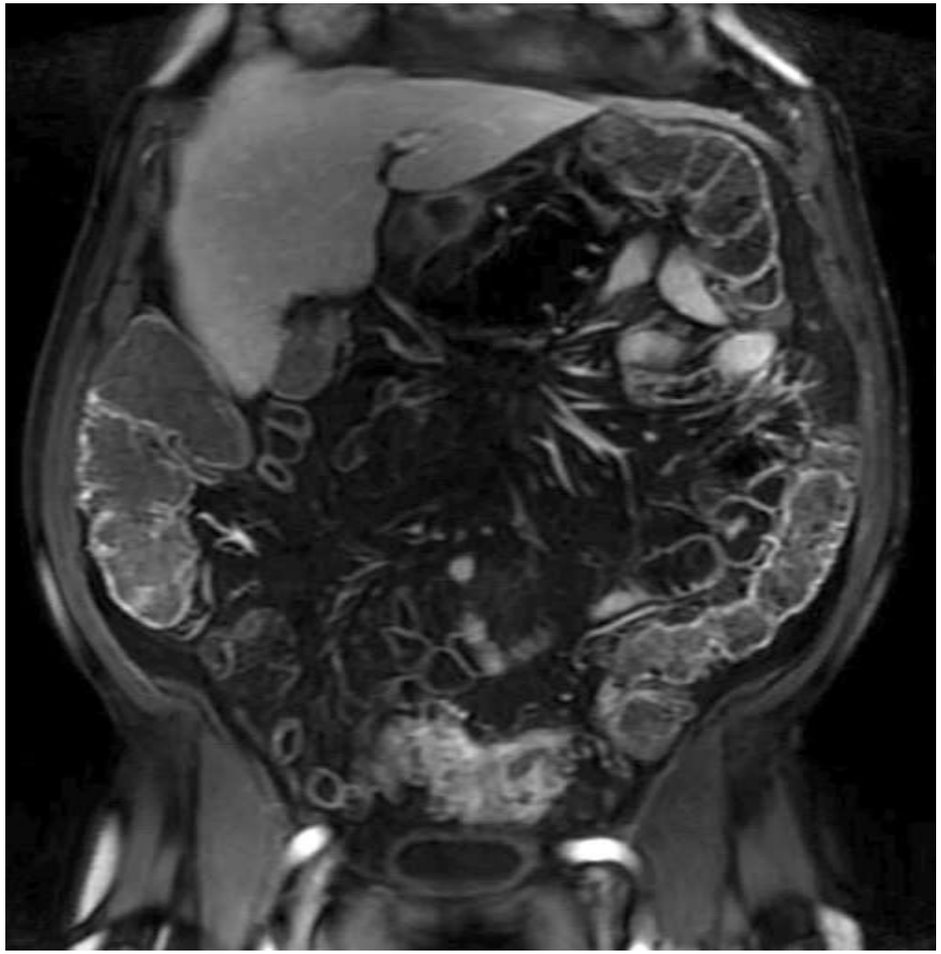
**“I would take it out.
All it can do is cause you trouble.”
-Harvey Eisenberg, MD
June 2016**



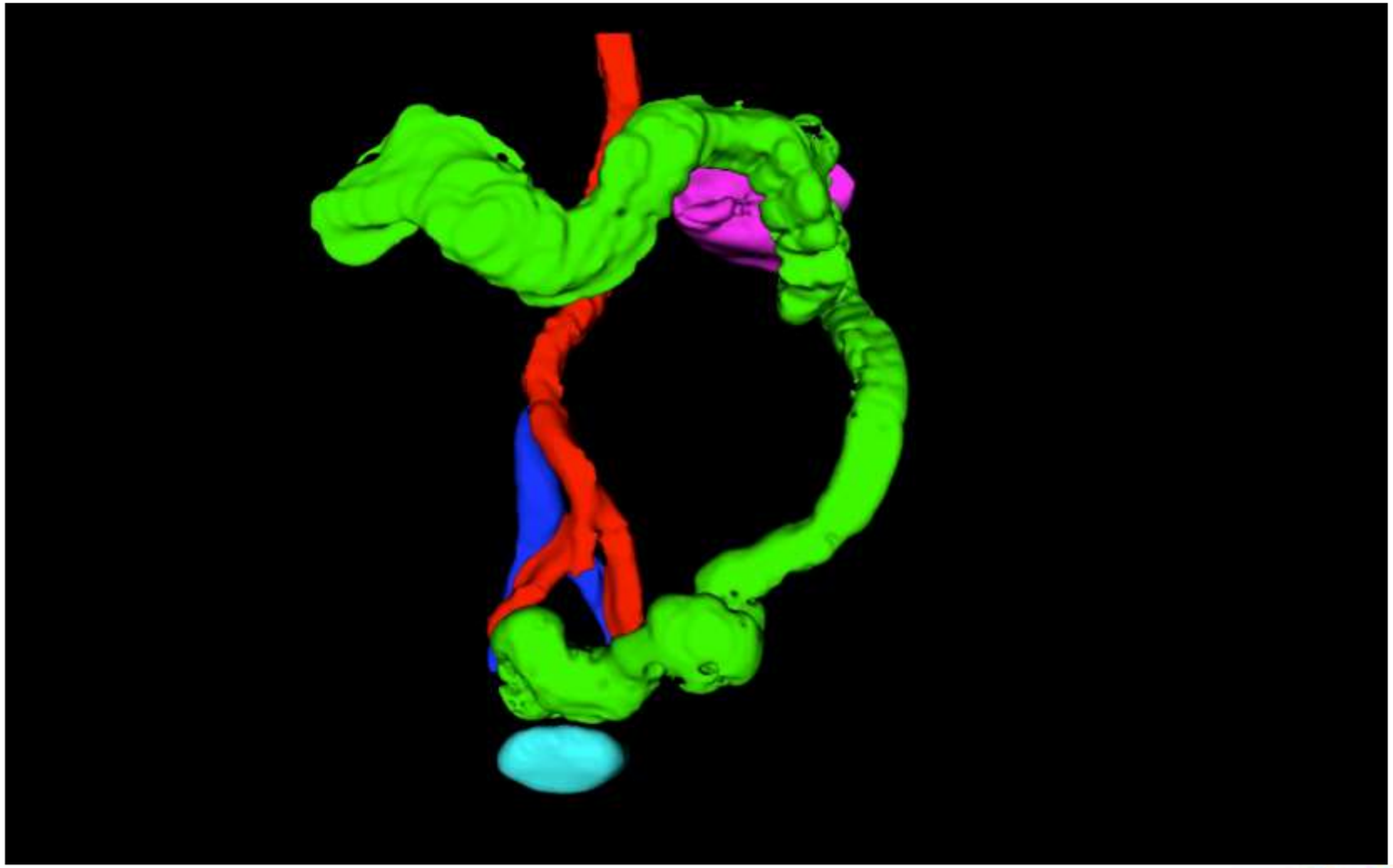
Source: Body Scan Intl., Irvine, CA

From Quantified Self to Quantified Surgery: Converting MRI Slices to 3D Organ Segmentation for Surgical Pre-Planning

High Resolution 3 Tesla MRI in UCSD's Center for Translational Imaging and Precision Medicine



Calit2's Dr. Jurgen Schulze Developed Software to Convert 150 2D MRI Slices to 3D Organs



MRI Radiology Team to Enable 3D:
Dr. Anders Dale, Dr. Stephen Dorros, Dr. Christine Chung, and Dr. Cynthia Santillan

Pre-Surgical Planning in QI Virtual Reality:
Using Virtual Reality As Input for Positioning The Two Resection Cuts



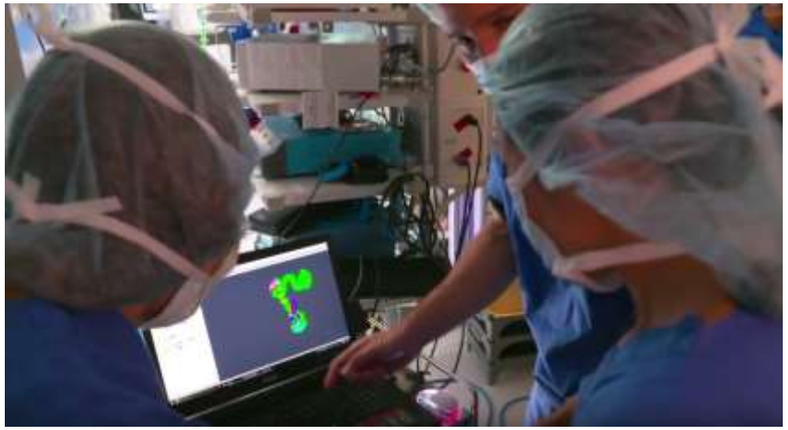
Surgeon Sonia Ramamoorthy, MD
in QI Virtual Reality CAVE



Colon Visualization by Jurgen Schulze, Calit2;
Photo Credit Tom DeFanti, Calit2

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

Dr. Ramamoorthy Using Interactive 3D Anatomy in the Operating Room During My Surgical Resection



Dr. William Sandborn Using Colonoscope in OR To Simultaneously Get Inside and Outside View of Reconnected Colon

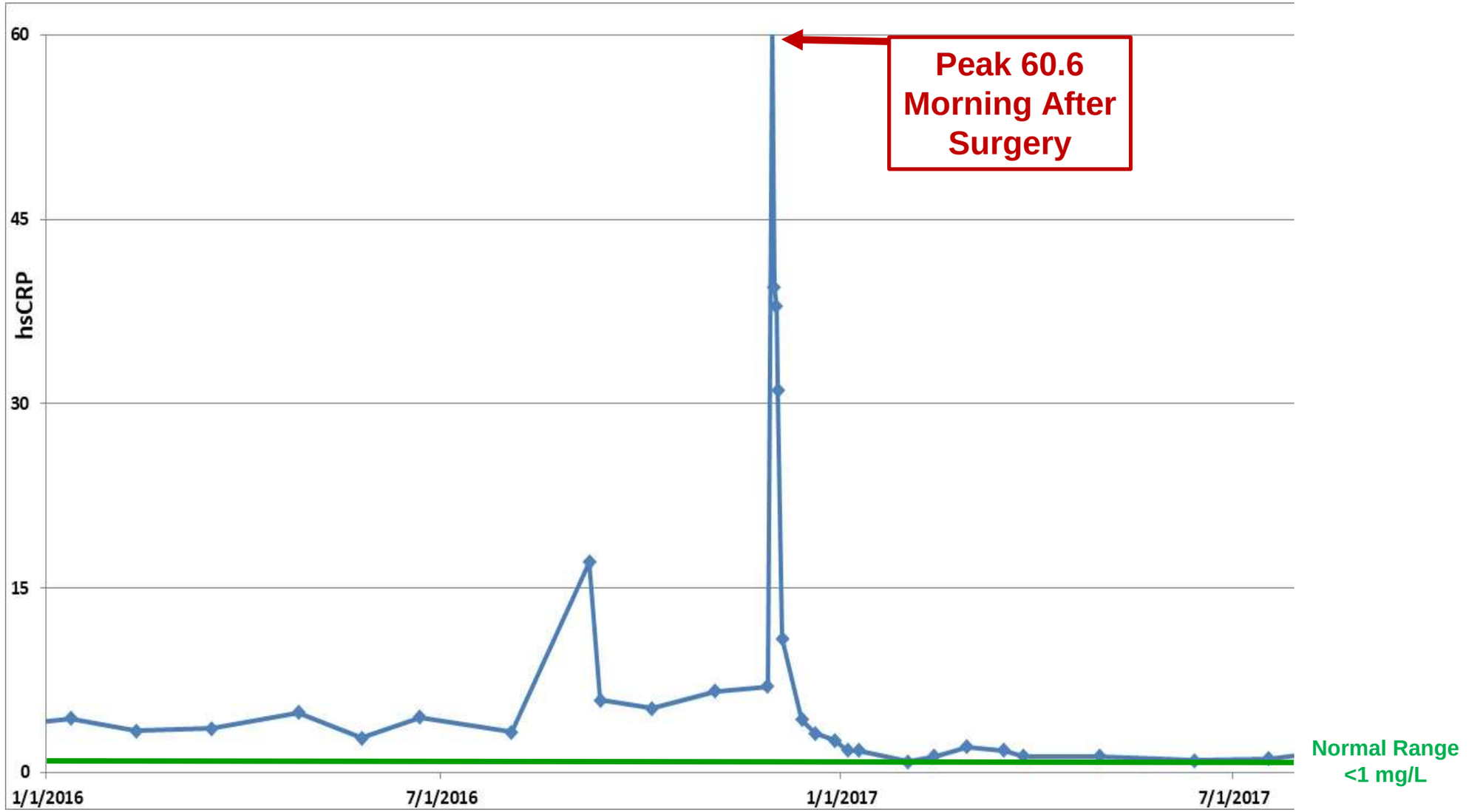


Dr. William Sandborn Performing Colonoscopy While da Vinci Observes from Inside Abdomen

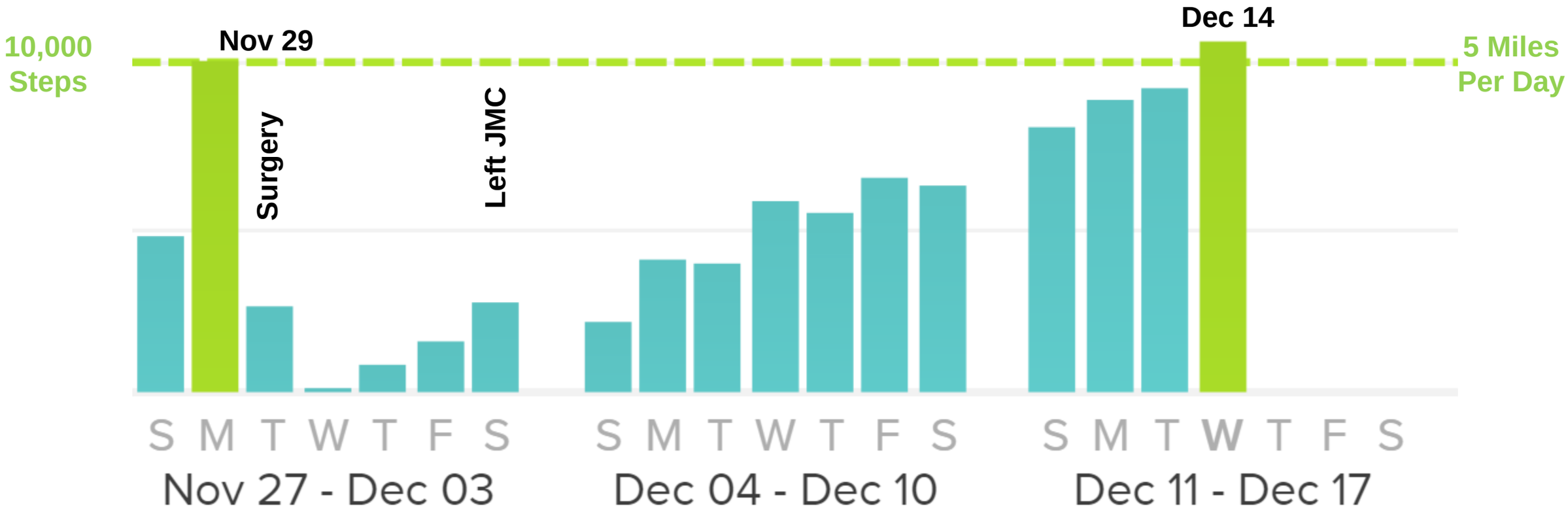


Dr. Santi Horgan, Director of Minimal Invasive Surgery, Pointing to Stapled Anastomosis

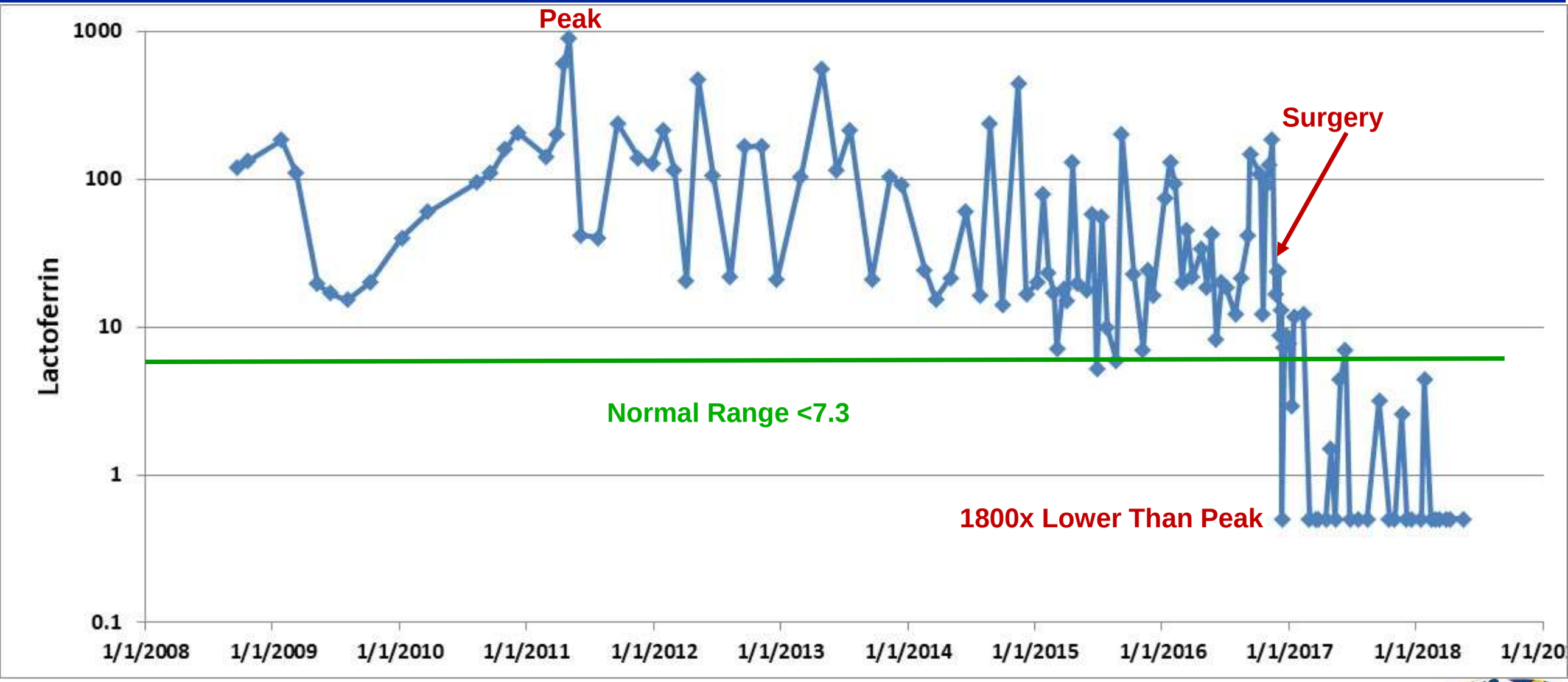
Using hsCRP to Track Inflammation Following Surgery to Detect Post-Surgical Complications



Quantified Recovery (Steps Walked Per Day) - Recovered to Pre-Surgery Level in Two Weeks



Colonic Inflammation:
Abrupt Shift to Healthy Following Surgical Resection



From N=1 Experiment to Clinical Tool: 3D Medical Imaging Pilot to Improve Surgical Outcomes for Patients with Crohn's Disease (CD)

- **$1.2 M Grant From the Helmsley Charitable Trust**



- **UC San Diego Collaborative Team:**
  - PI Larry Smarr, PhD, Director Calit2
  - Jurgen Schulze, PhD, Virtual Reality Research Scientist, Calit2
  - Sonia Ramamoorthy, MD, Chief of Colorectal Surgery
  - Bill Sandborn, MD, Chief of Gastroenterology
  - Cynthia Santillan, MD, Chief of the Body Imaging

- **Pilot Will:**
  - Integrate 3D Medical Imaging Within Clinical Practice
  - Evaluate 10 CD Patients Having Small Bowel or Colonic Strictures Using 3D Imaging
  - Assess Software Usability in the UCSD IBD Clinic & Operating Room for Both Physician & Patient

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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

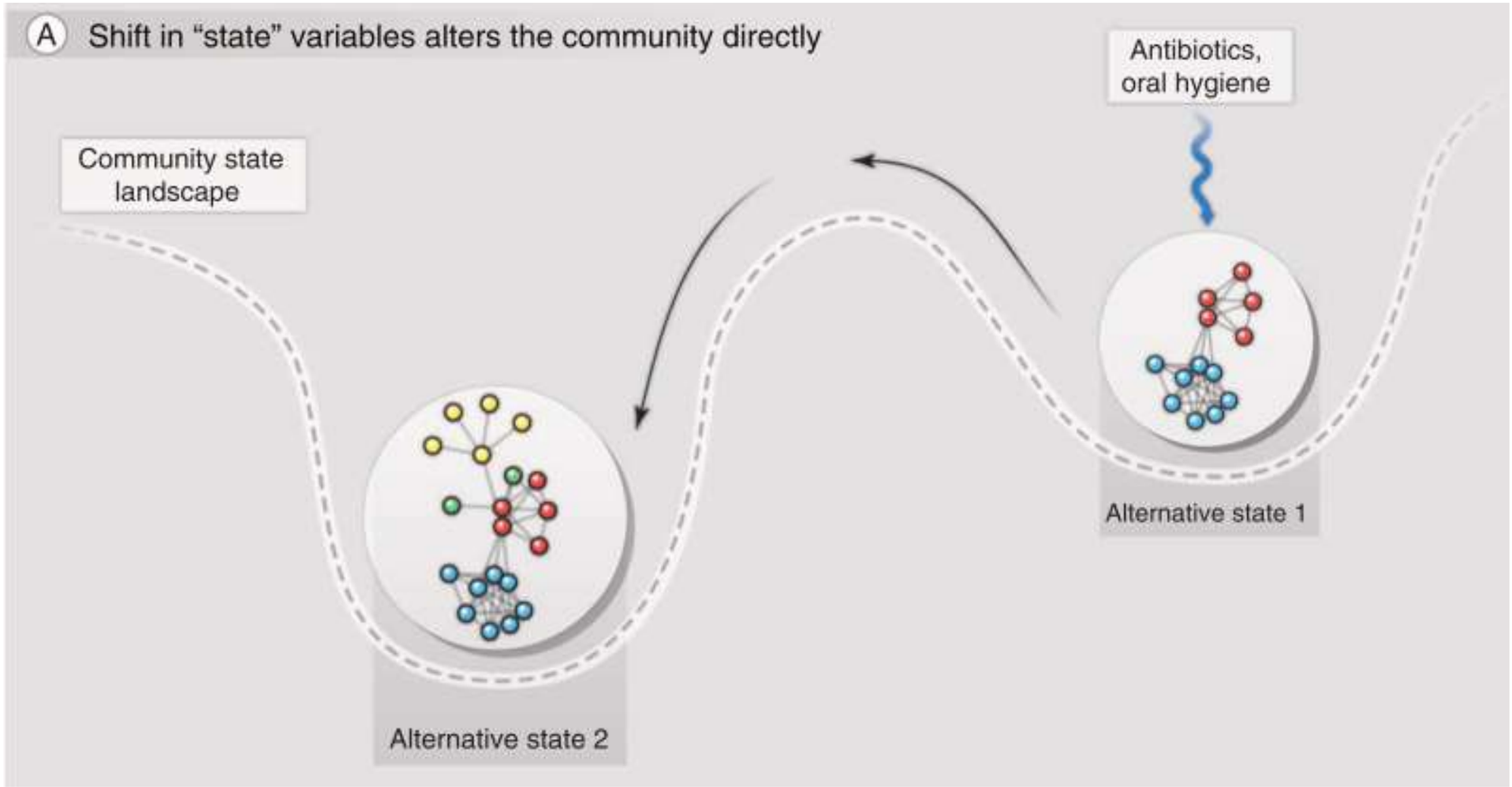
By Gary Robbins 1:30 P.M. JAN. 11, 2015 Updated 12:17 P.M. JAN. 12, 2015 PRINT COMMENTS 0





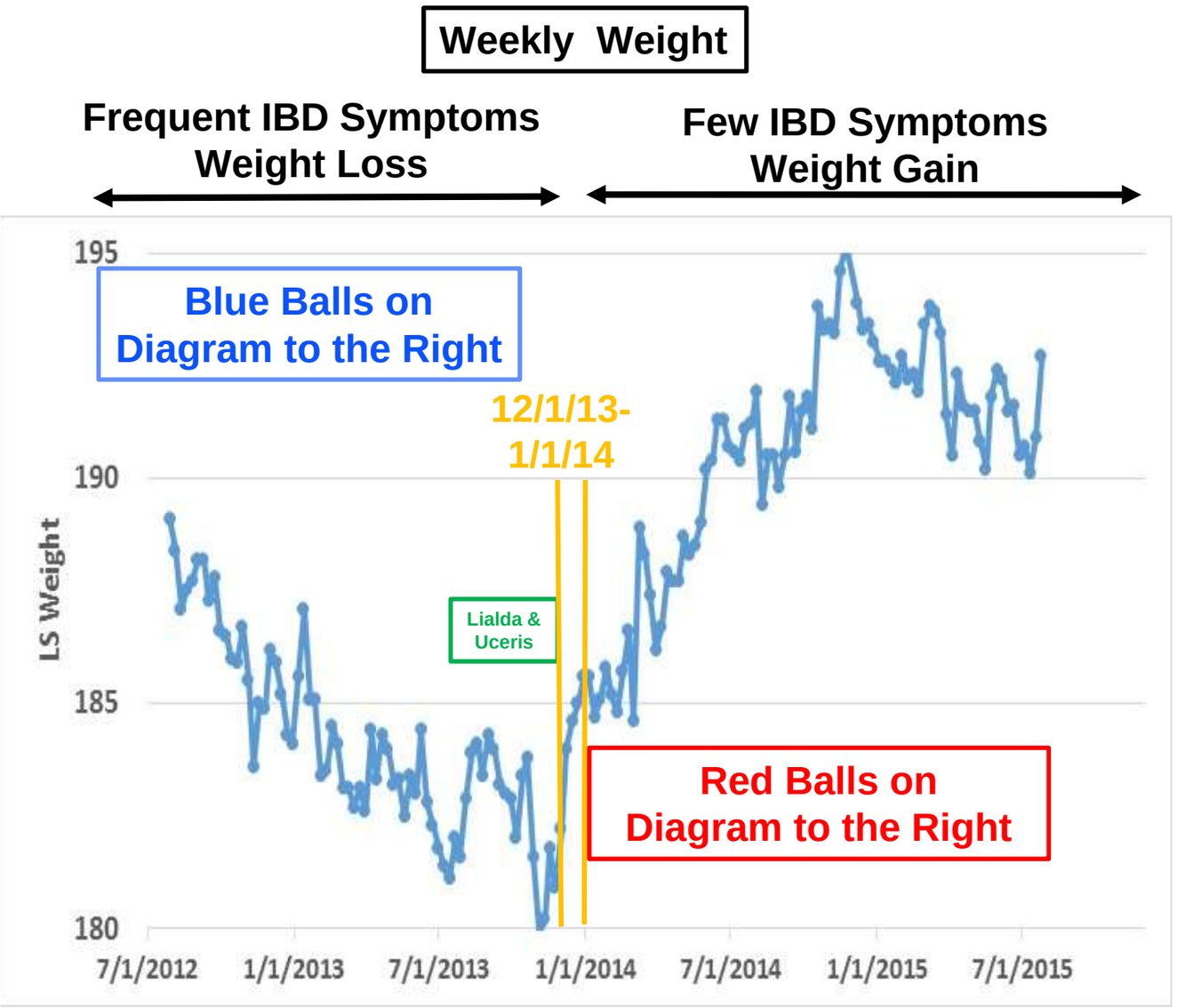
Larry's 40 Stool Samples Over 3.5 Years
to Rob's lab on April 30, 2015

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

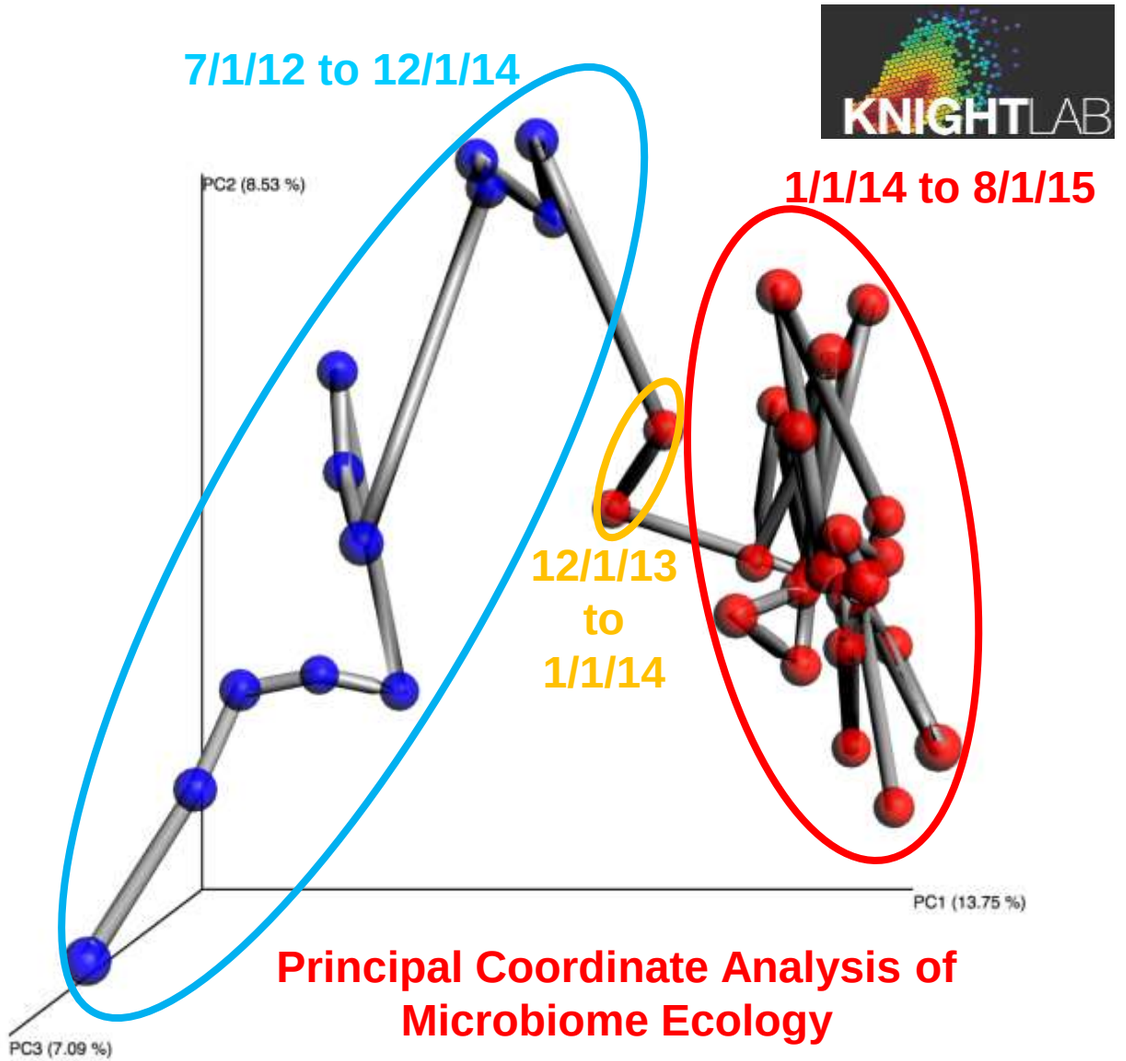


"The Application of Ecological Theory Toward an Understanding of the Human Microbiome," Elizabeth Costello, Keaton Stagaman, Les Dethlefsen, Brendan Bohannan, David Relman Science 336, 1255-62 (2012)

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



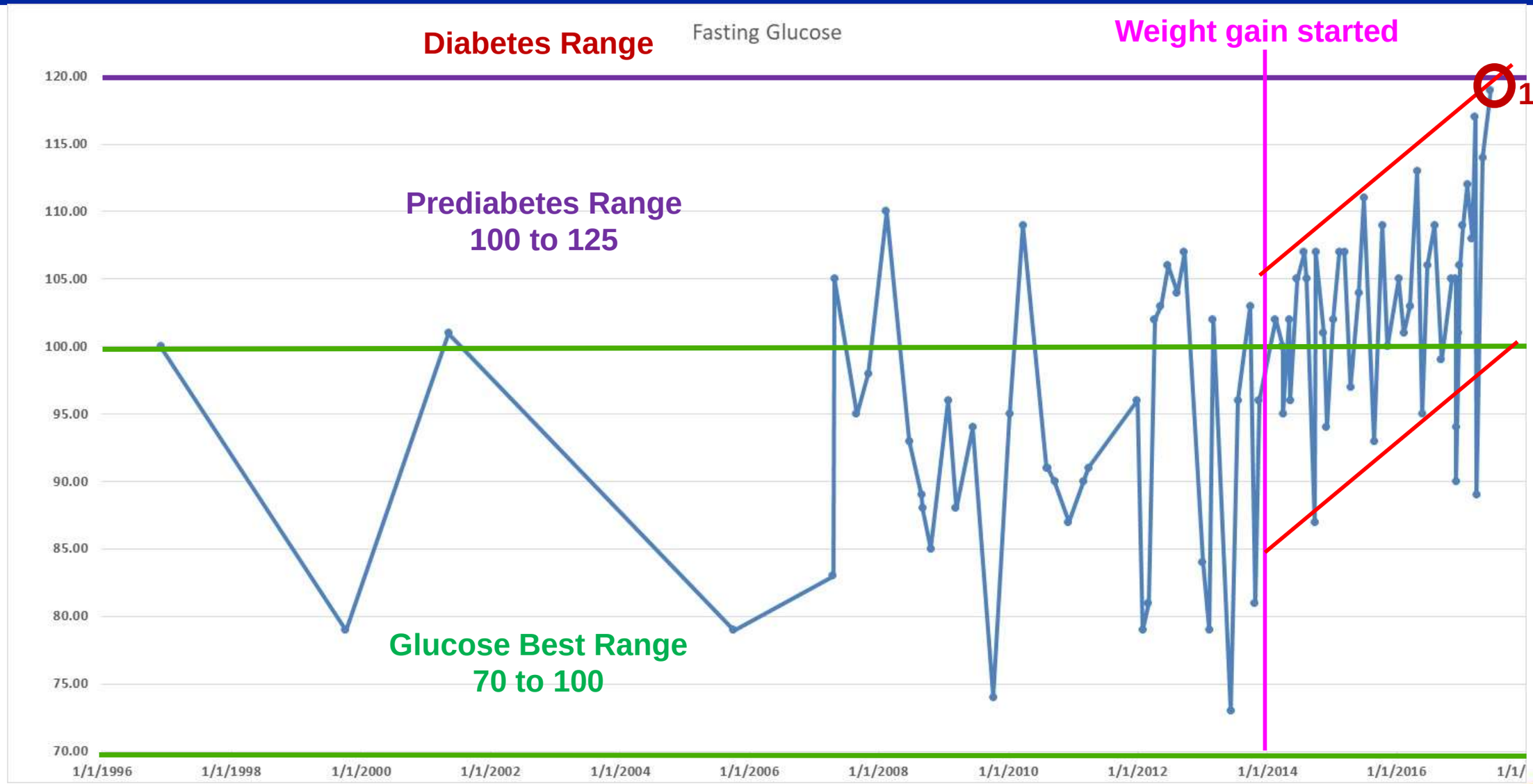
Weight Data from Larry Smarr, Calit2, UCSD



Principal Coordinate Analysis of Microbiome Ecology

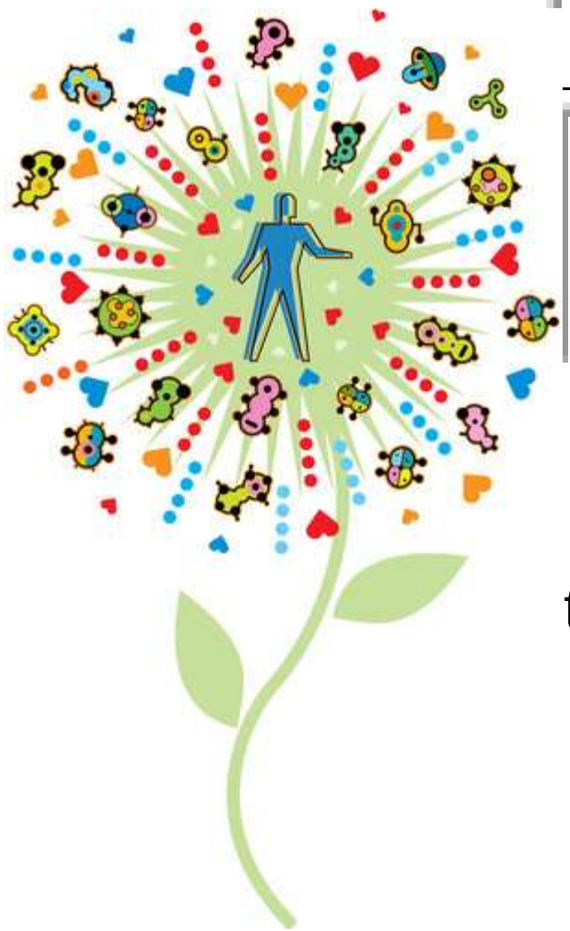
PCoA by Justine Debelius and Jose Navas, Knight Lab, UCSD

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

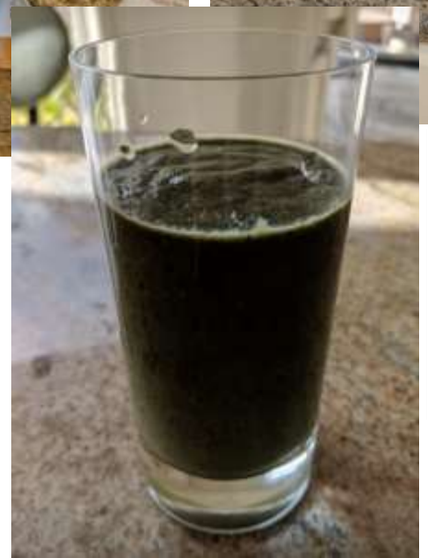
The more different types of plants a person eats, the higher their gut microbiome diversity.

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

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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

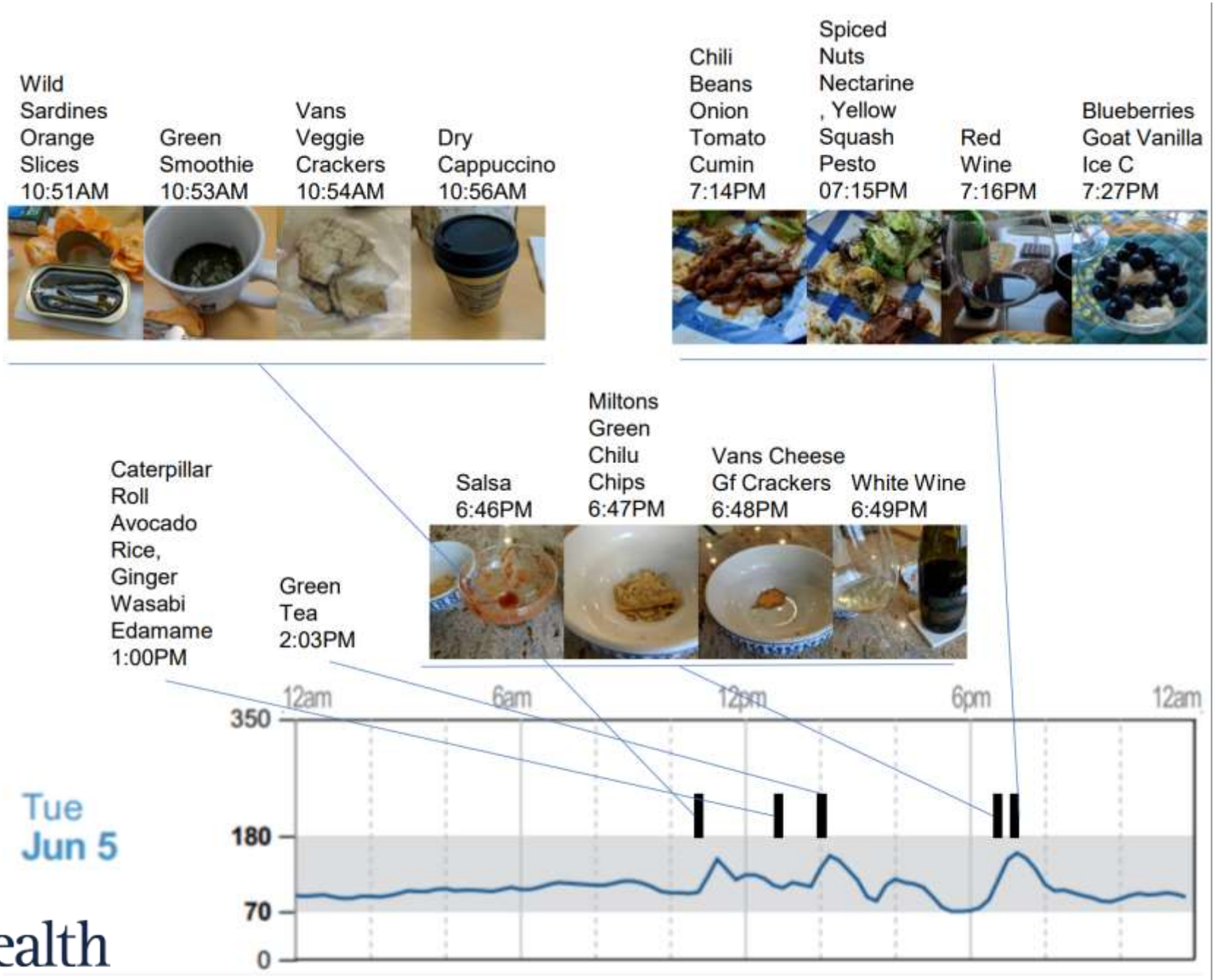
Correlating Time Stamped Annotated Food Intake Against Continuous Blood Glucose Readings

salk
Where cures begin.

Graph Created by Emily Manoogian, Panda Lab, Salk Institute



UC San Diego Health



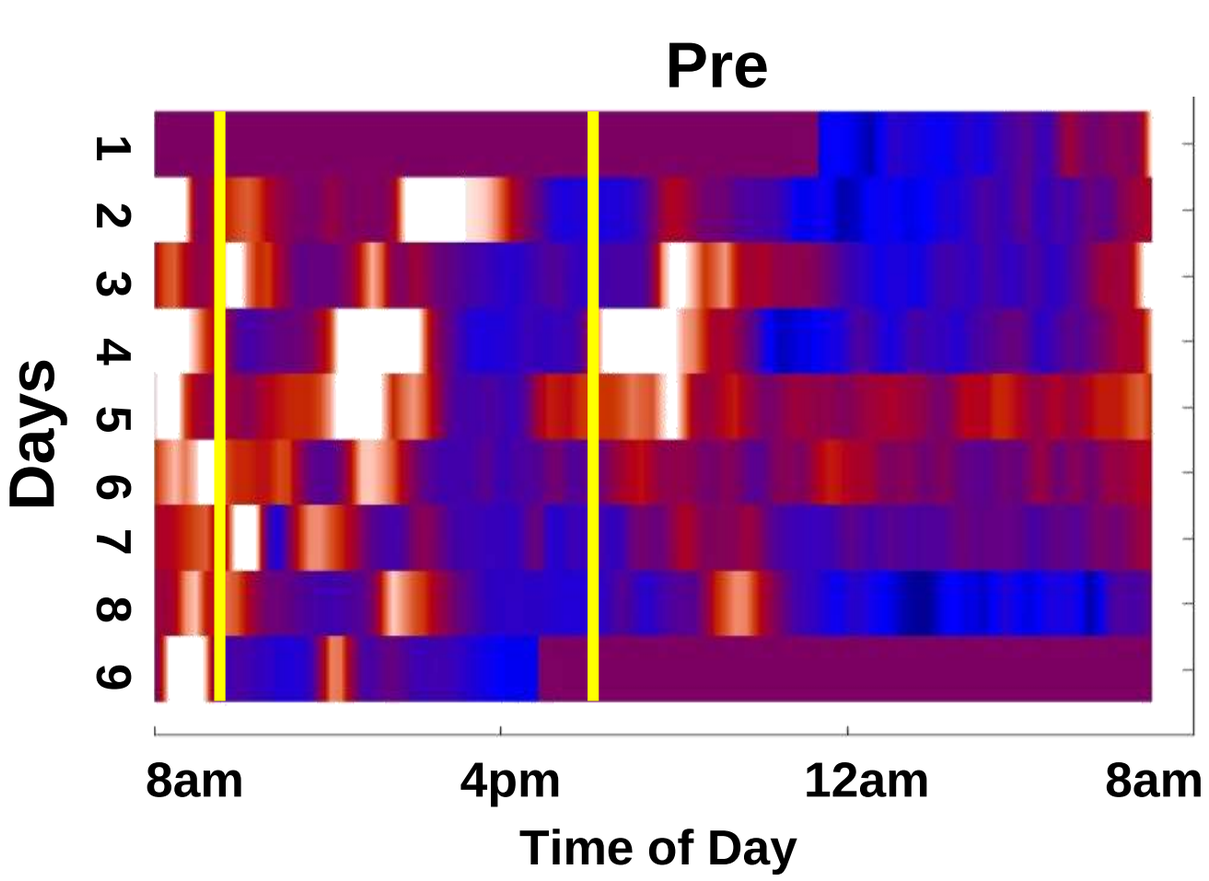
Panda/Taub Clinical Trial

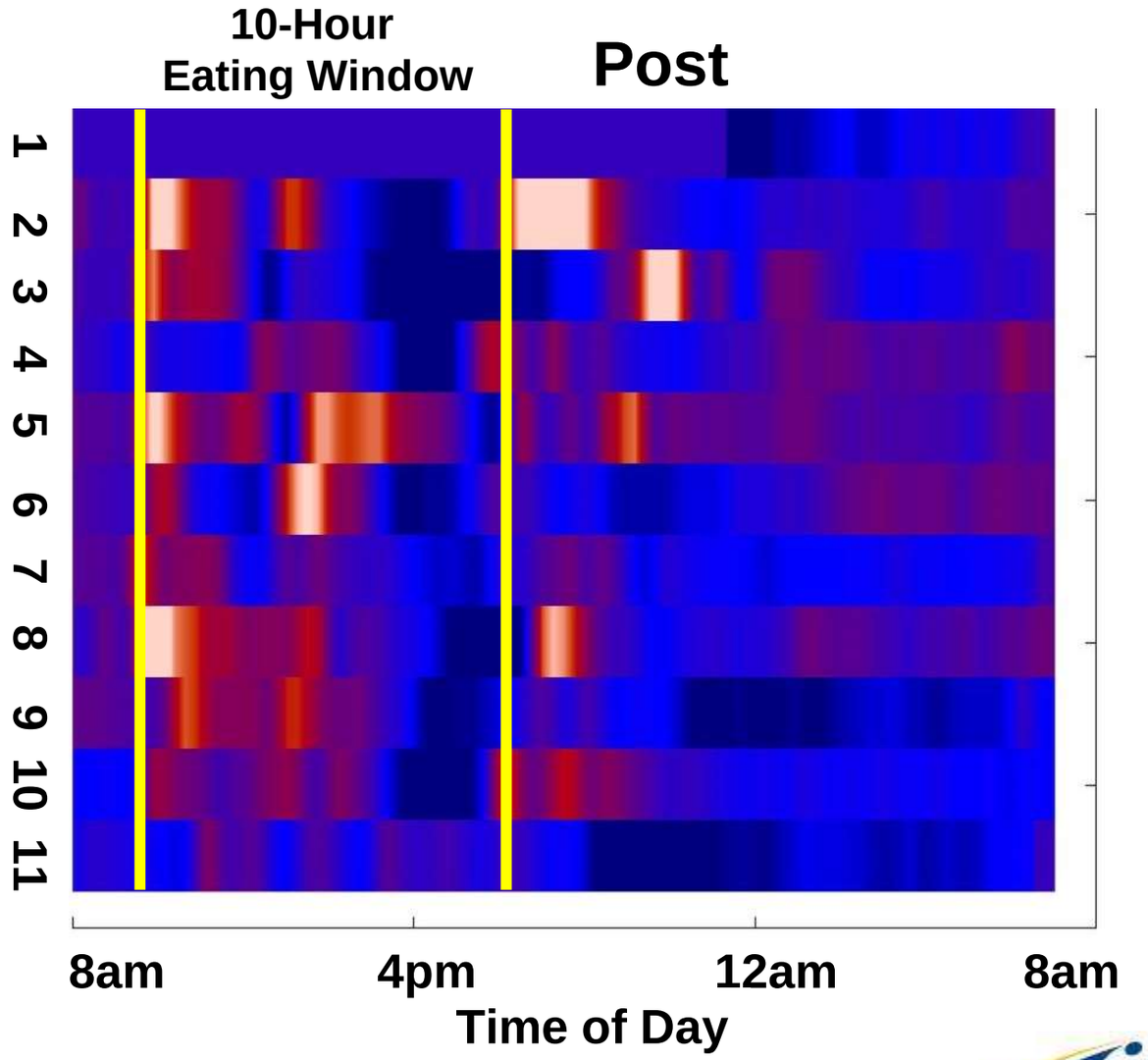
All Food/ Drink Photo/ Time-Stamped/ Annotated For 100-Days

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

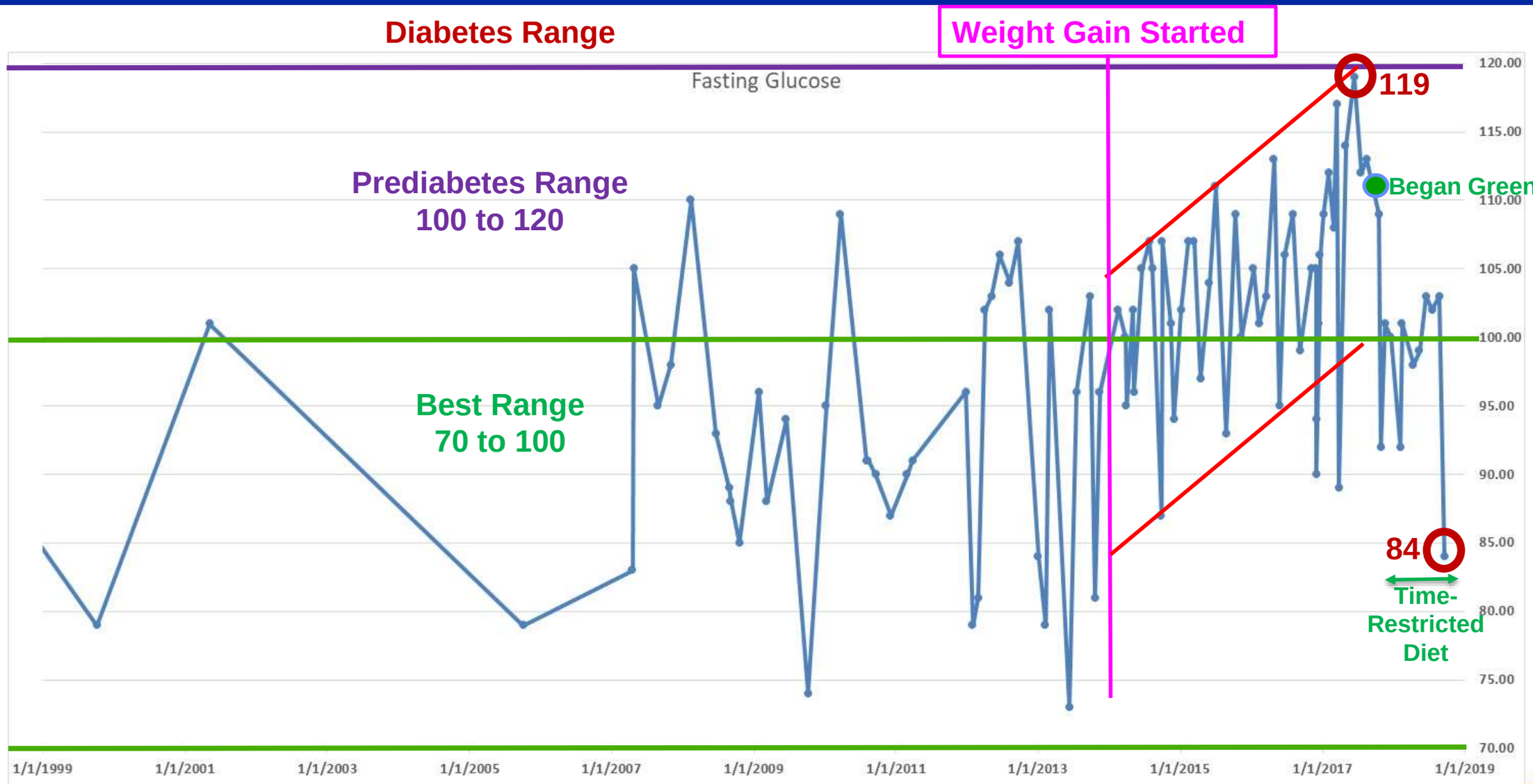




- **Other Improvements:**
  - **Waist 108cm to 102 cm**
  - **Weight 197 to 189**
  - **Blood Pressure 140/74 to 130/69**

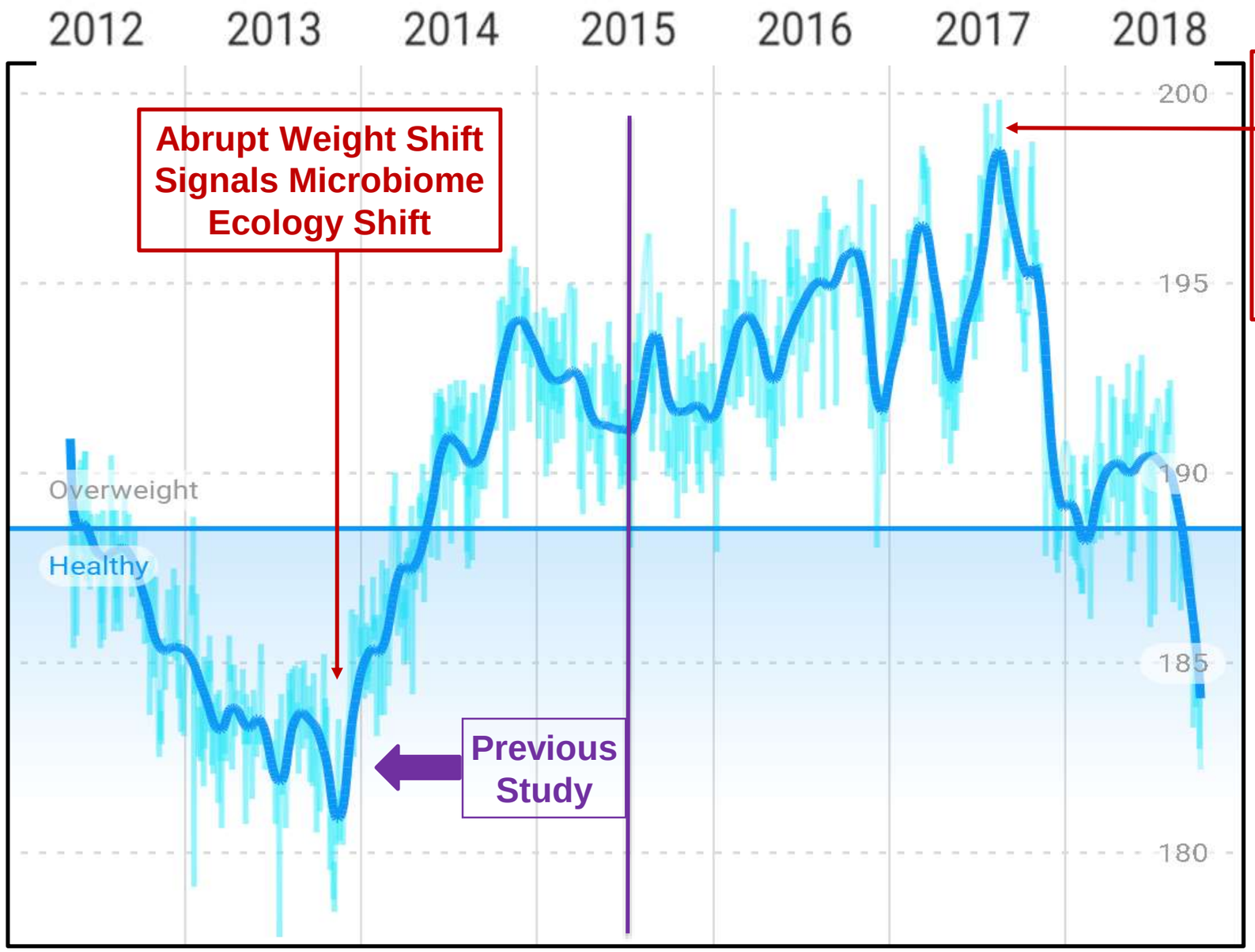
Data from Taub/Panda Clinical Trial
Graphics by Azure Grant, UC Berkeley

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

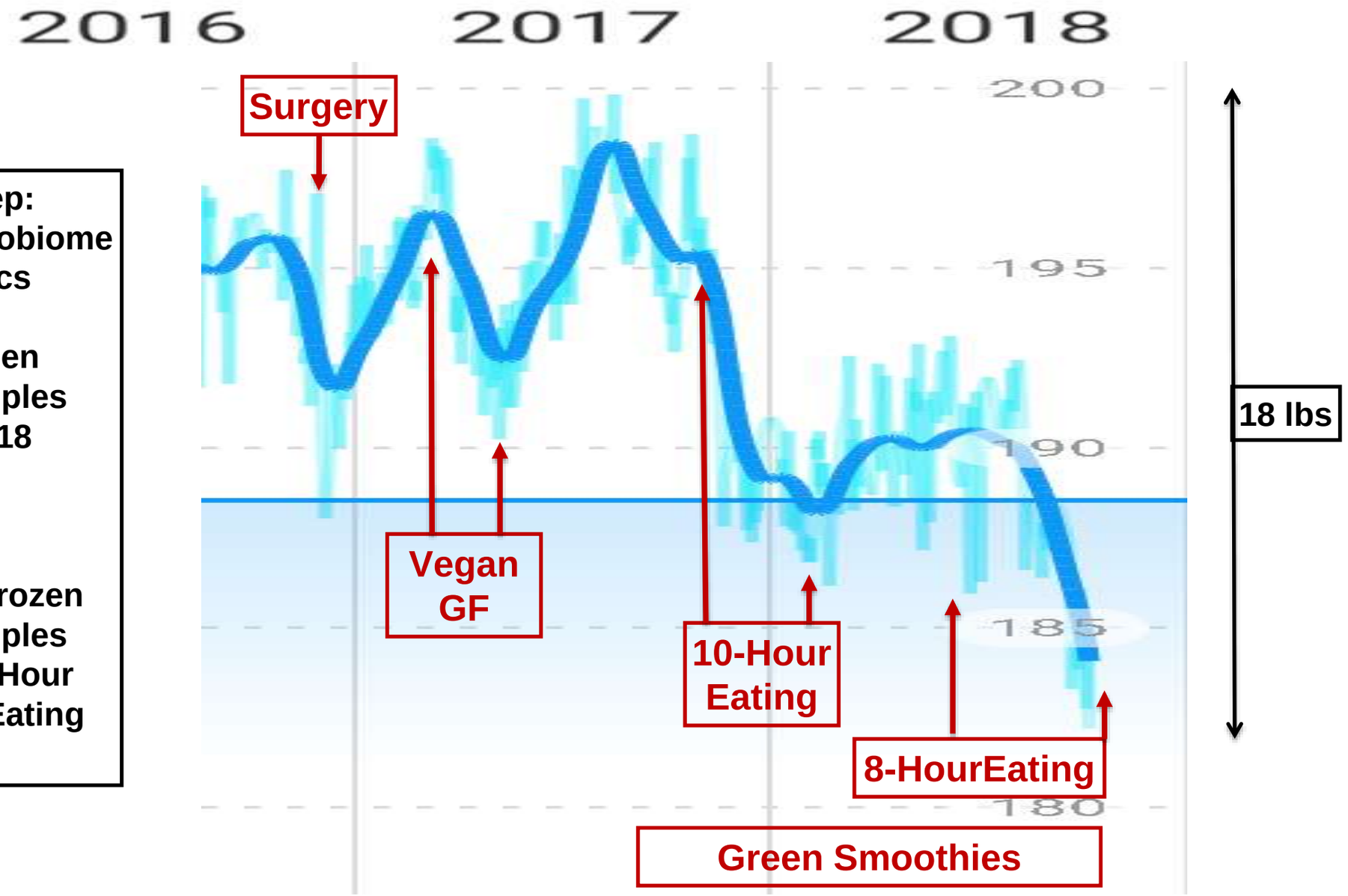
Diet Timing and Content
Can Have a Major Impact on Metabolic Syndrome

Next Step:
Analyze Microbiome Dynamics

135 Frozen Stool Samples 2012-2018

Plus

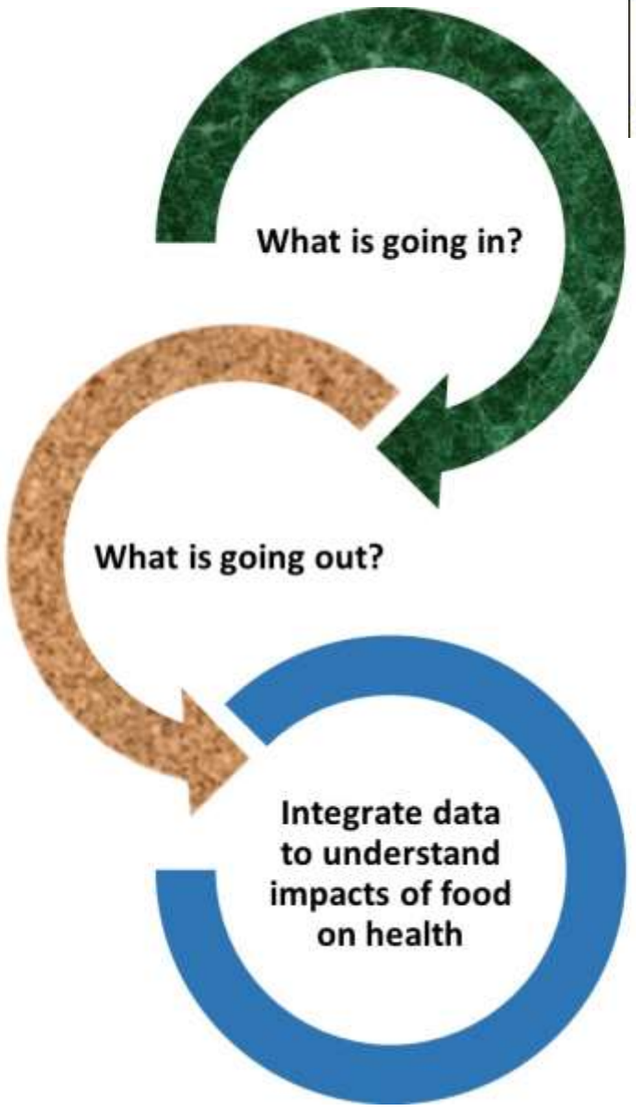
100 Daily Frozen Stool Samples During 10-Hour Restricted Eating Trial



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

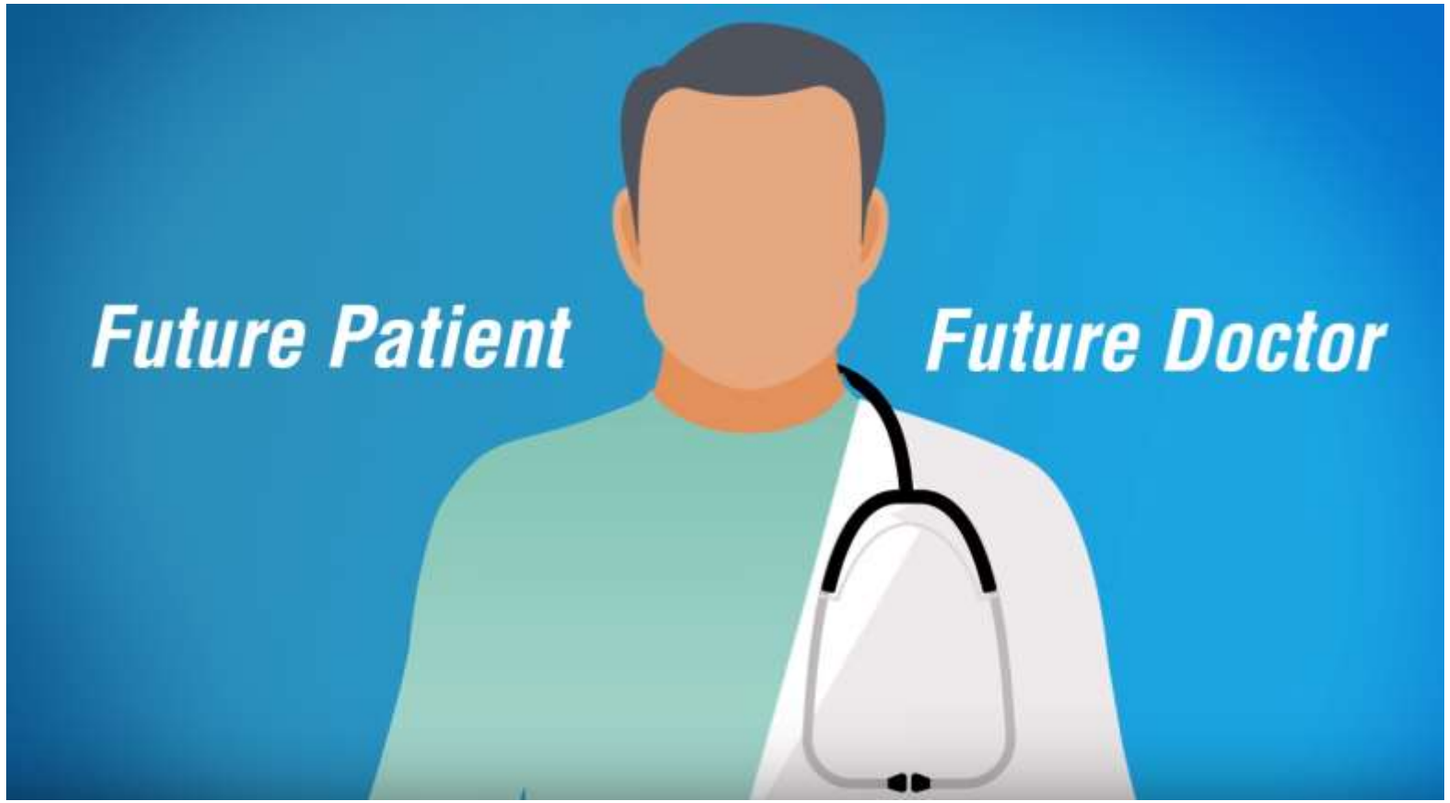
THE DUTTON LAB @ UCSD

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

From Digitally-Enabled Future Patient to Digitally-Enabled Future Doctor







University of California Television (UCTV)
Published on Jun 8, 2018

www.youtube.com/watch?v=FZK7JllMPLM

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



JCVI Team

Karen Nelson
Shibu Yooseph
Manolito Torralba

Ayasdi

Devi Ramanan
Pek Lum

UCSD Metagenomics Team

Weizhong Li
Sitao Wu

SDSC Team

Michael Norman
Mahidhar Tatineni
Robert Sinkovits

Dell/R Systems

Brian Kucic
John Thompson

UCSD Health Sciences Team

David Brenner, Dean
Rob Knight Lab
William J. Sandborn Lab
Sonia Ramamoorthy
Mike Kurisu/Hollis King DOs
Radiology Department

UCSD Bioengineering

Todd Coleman Lab
Bernhard Palsson Lab