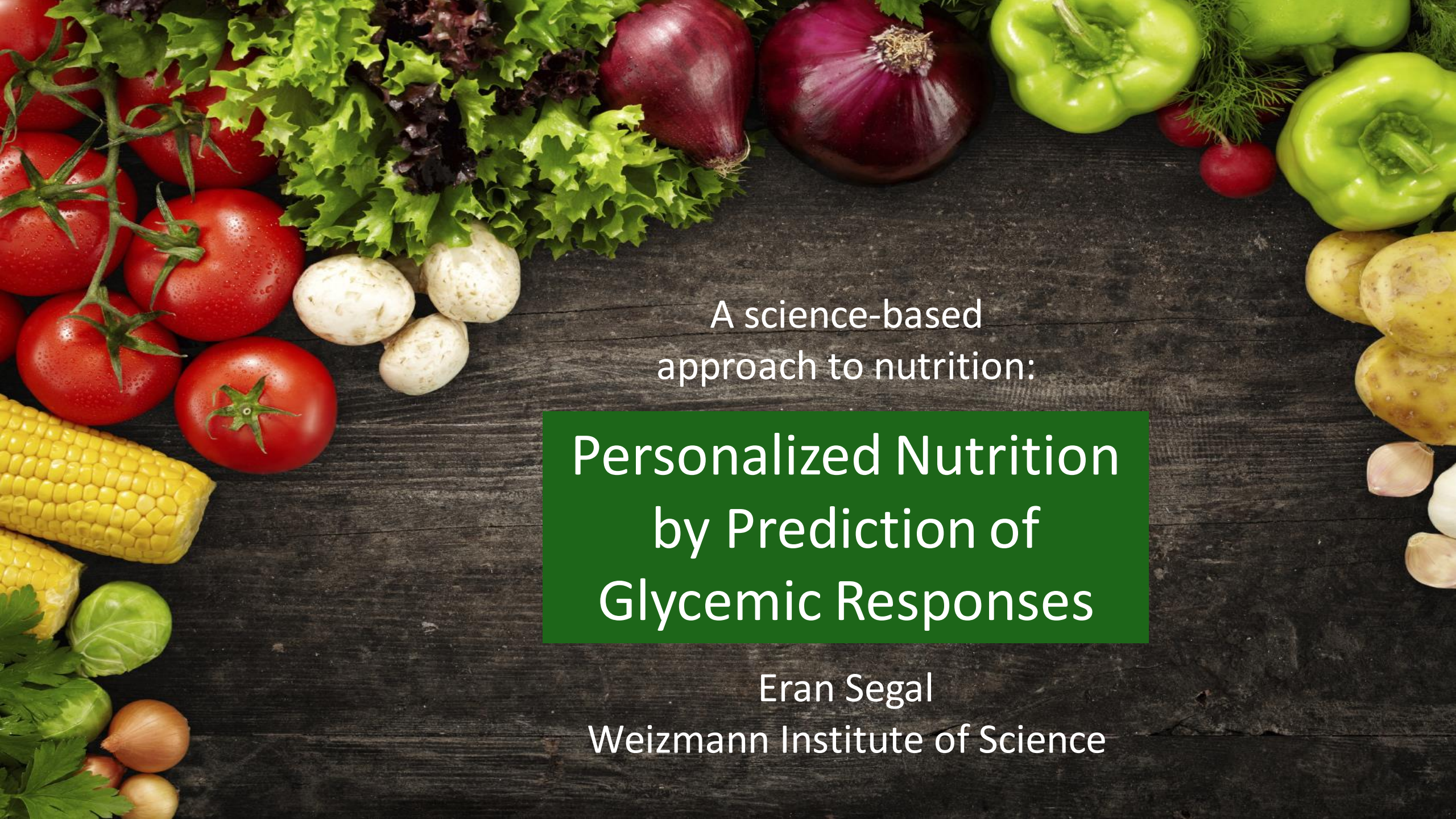


Microsoft Research
Faculty
Summit
2016

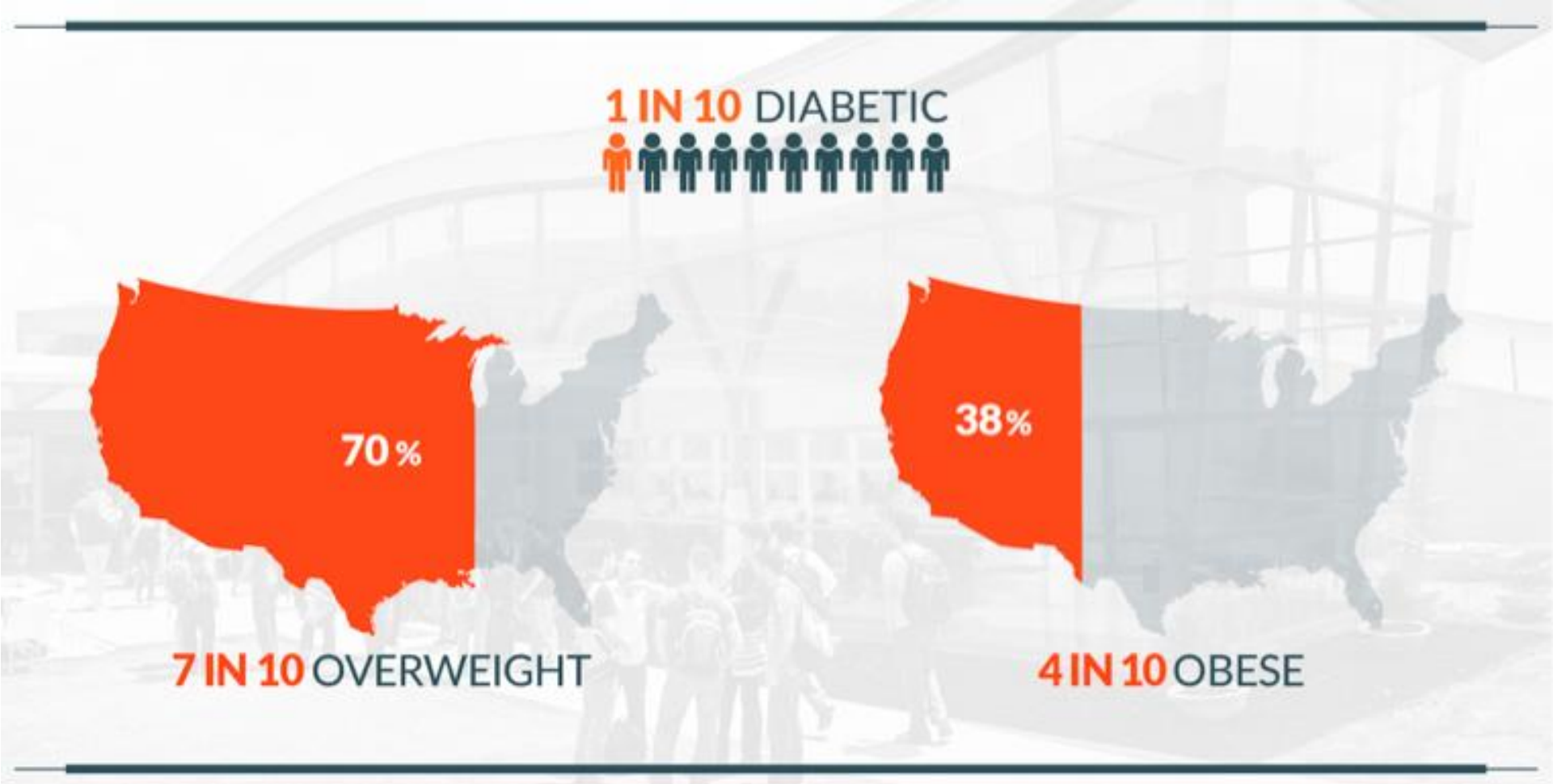


A science-based
approach to nutrition:

Personalized Nutrition by Prediction of Glycemic Responses

Eran Segal
Weizmann Institute of Science

The metabolic disease epidemic



**Changes in our nutrition greatly contributed
to the recent metabolic syndrome epidemic**

Changes in our nutrition greatly contributed to the recent metabolic syndrome epidemic



Reduced fat consumption and increased carbohydrates consumption



Increased consumption of added sugar



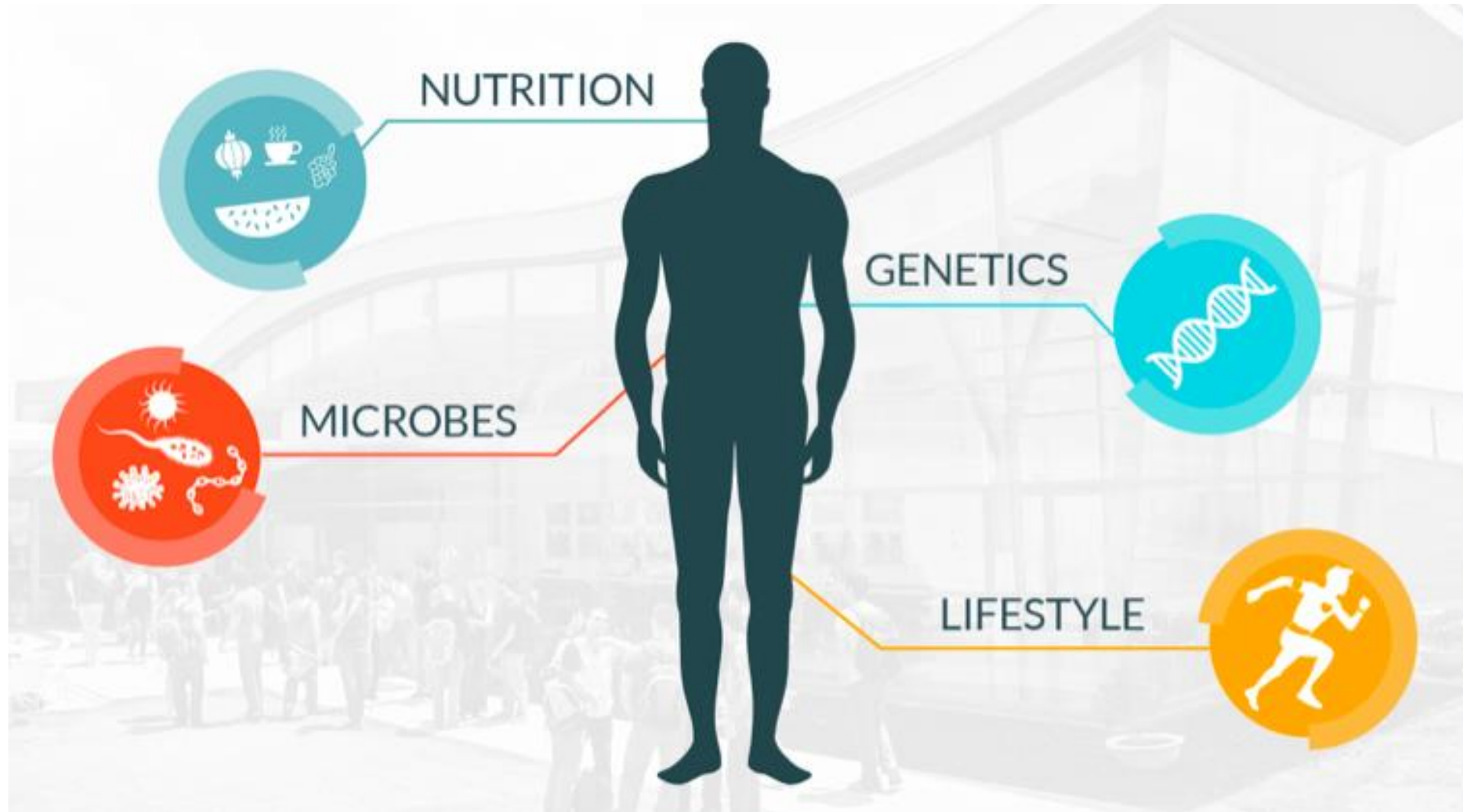
Increased consumption of food additives and artificial sweeteners



Changed meal times and introduced shift working

If nutritional changes drove the metabolic syndrome epidemic, can it be treated by restoring healthy nutrition?

Studying the link between nutrition, lifestyle, genetics, and microbiome



How can we take a science-based approach to nutrition?



Tal Korem

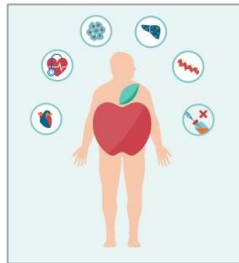


Dudi Zeevi

Science based approach to nutrition: What should a marker of healthy nutrition satisfy?



Relevant for weight management

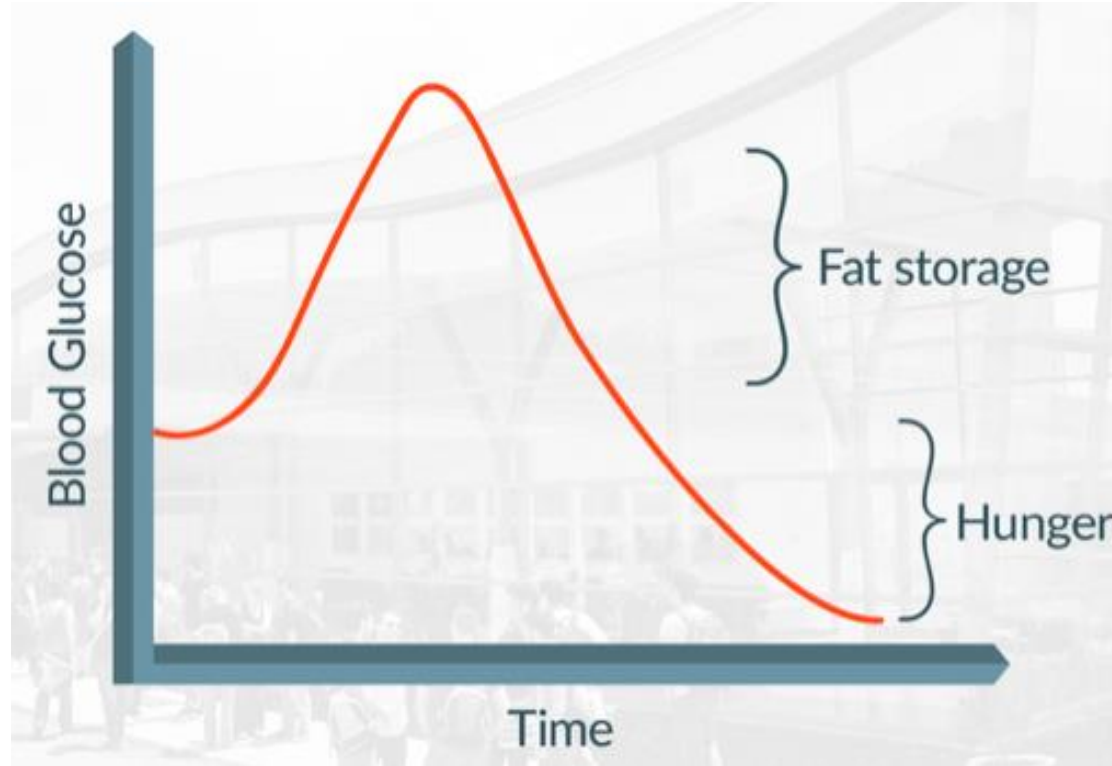


Relevant for metabolic disease



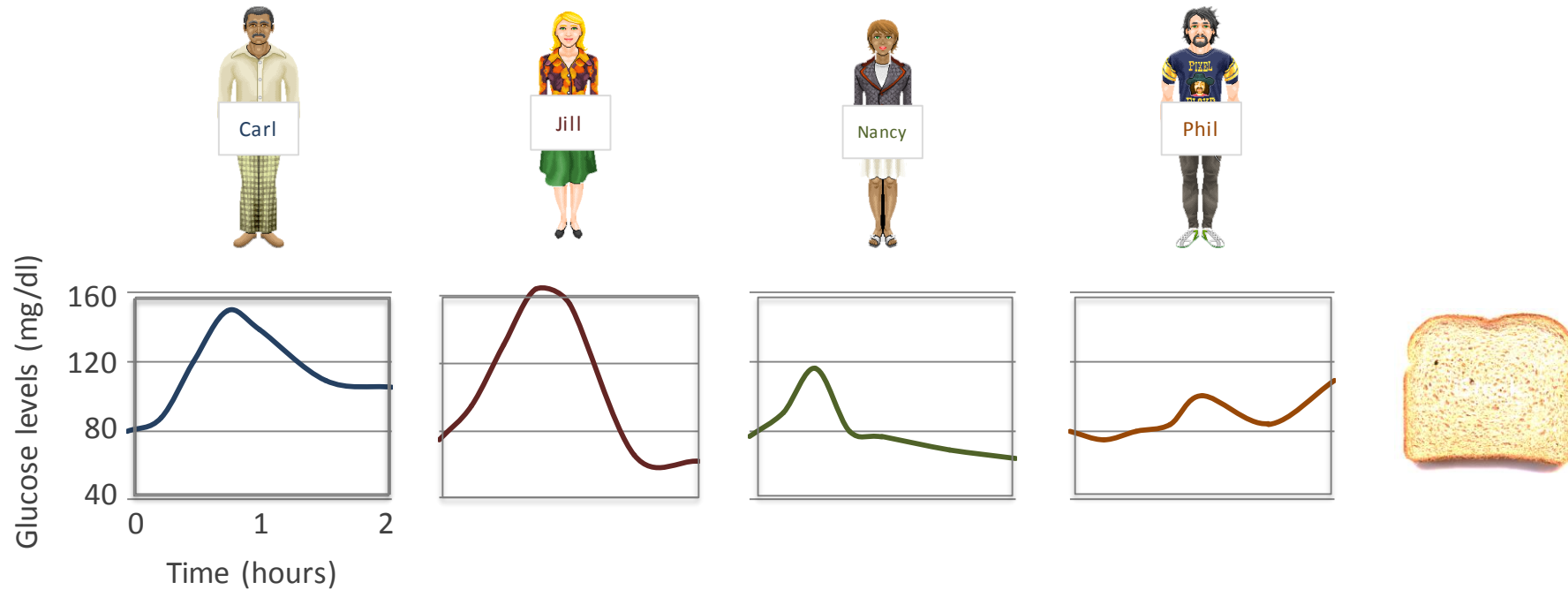
Easily measurable quantitatively

Postprandial (Post-meal) glucose response as a measure of healthy nutrition



- Directly affects fat storage, weight gain, and hunger
- Strongly associated with obesity, diabetes, CVD
- Easily measurable quantitatively

People have widely different glucose responses to the same food



Diets that maintain normal blood glucose levels must be personally tailored

THE PERSONALIZED NUTRITION PROJECT

1,000 PARTICIPANTS



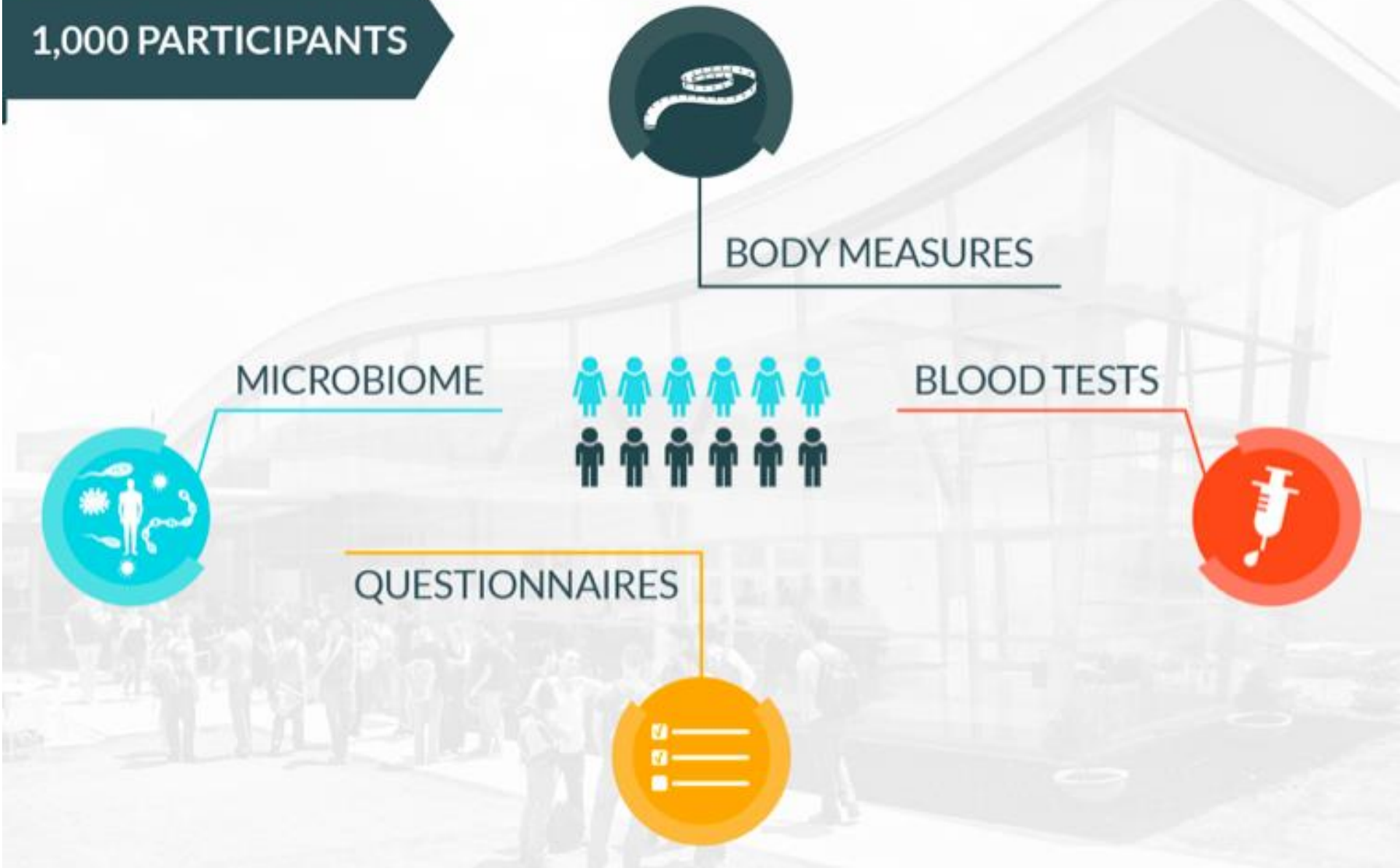
50,000 MEALS



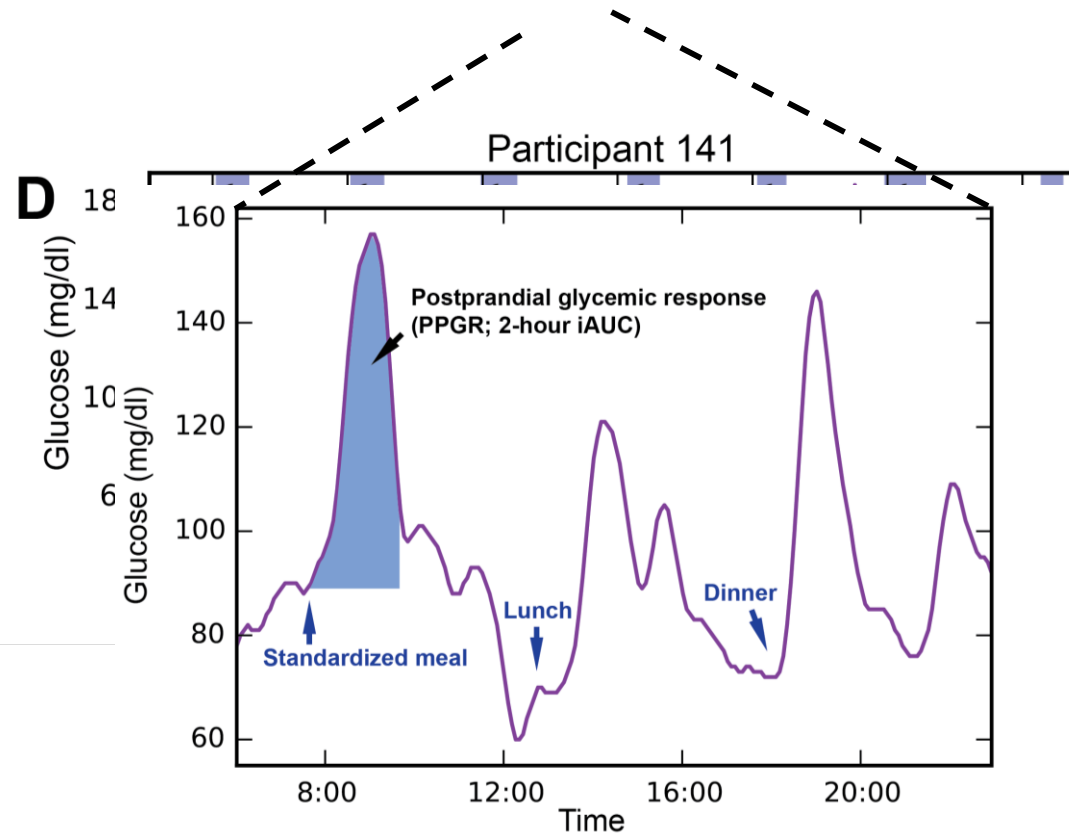
2,000,000 GLUCOSE MEASUREMENTS



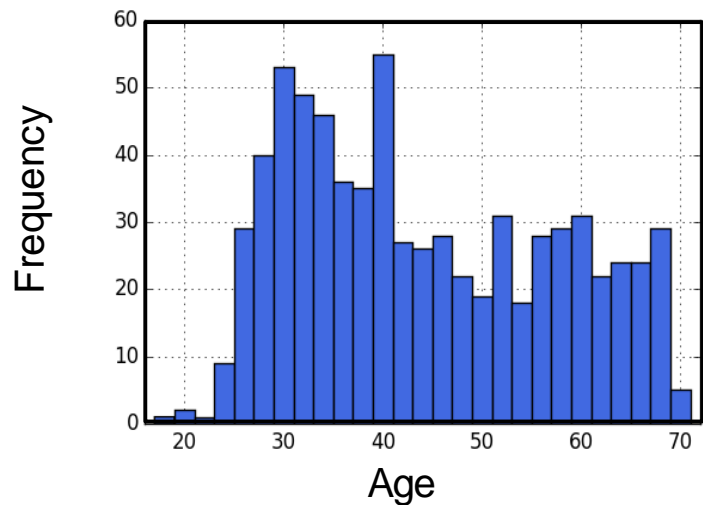
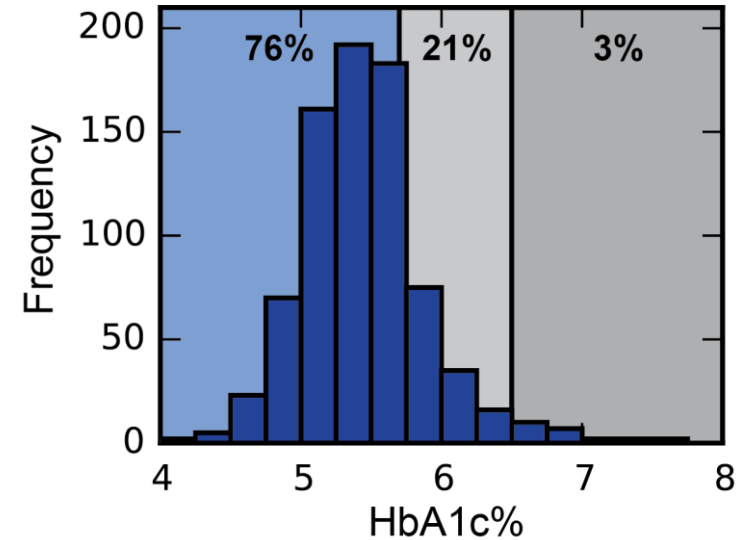
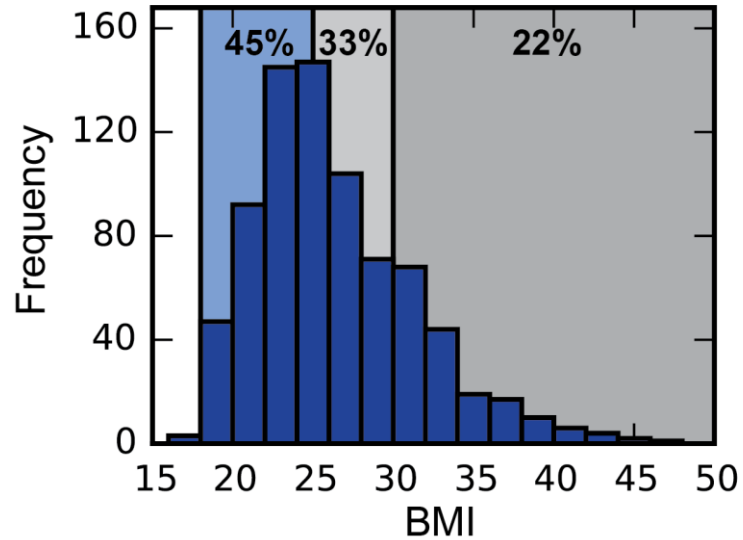
1,000 PARTICIPANTS



Continuous glucose monitoring



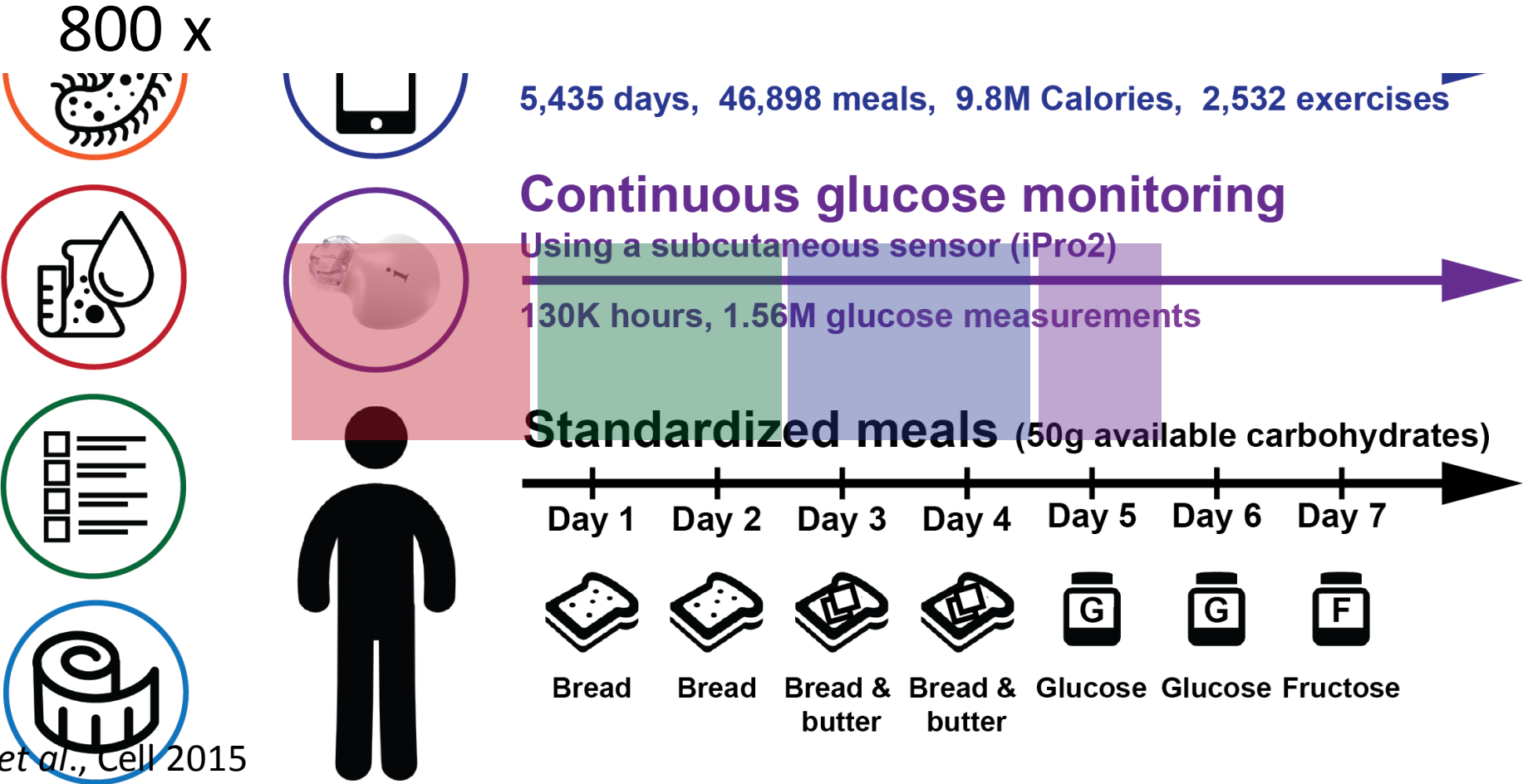
The Personalized Nutrition Project: Cohort statistics



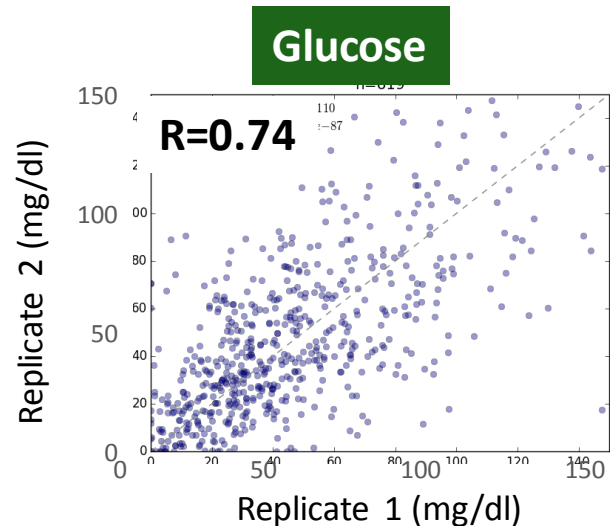
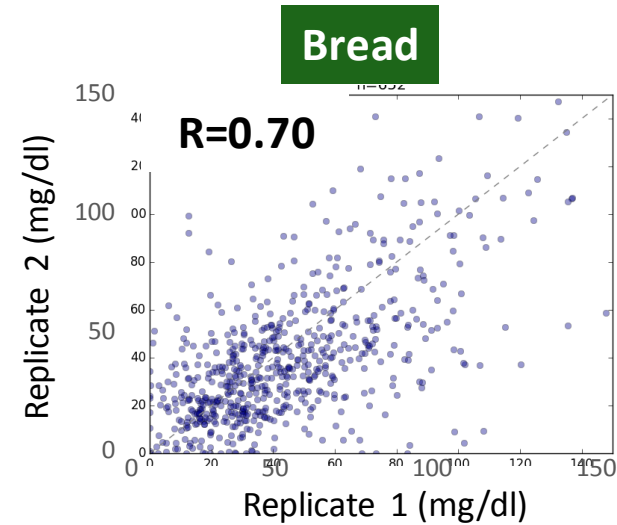
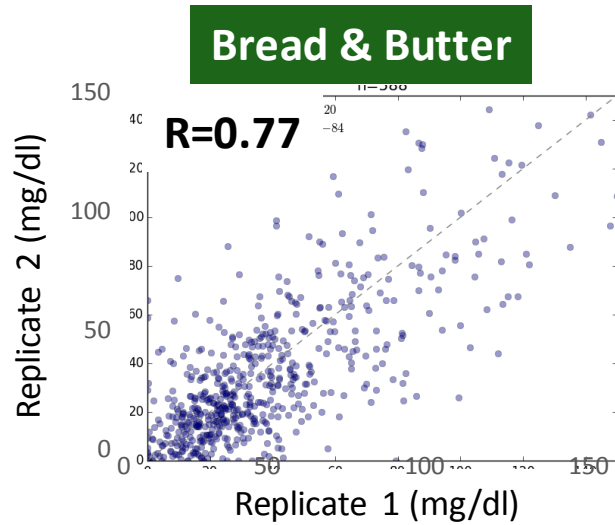
- 25-70 years of age
- 55% overweight
- 22% obese
- 21% pre-diabetic

**What is the variability across people in
the response to the same food?**

Testing the cohort response to standardized meals

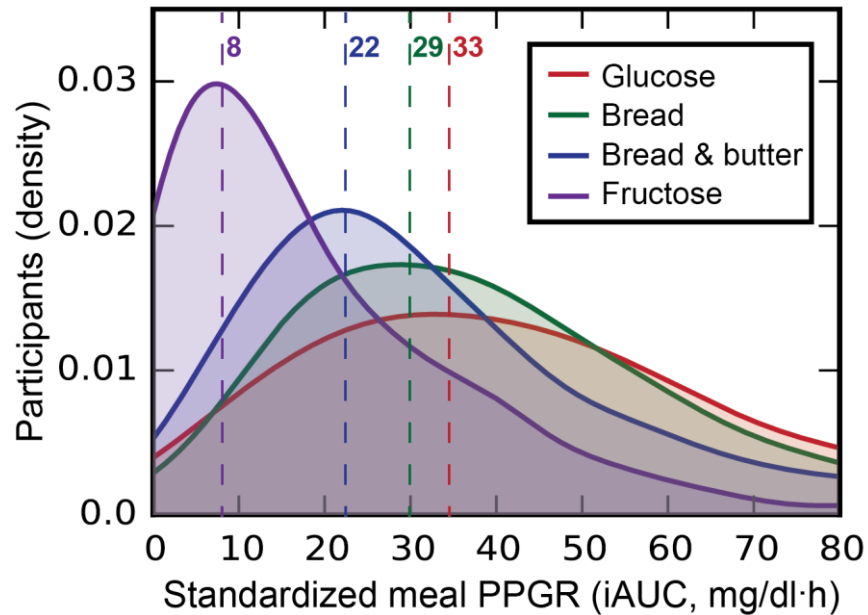


The same person has a highly similar post-meal response to the same standardized meal across different days

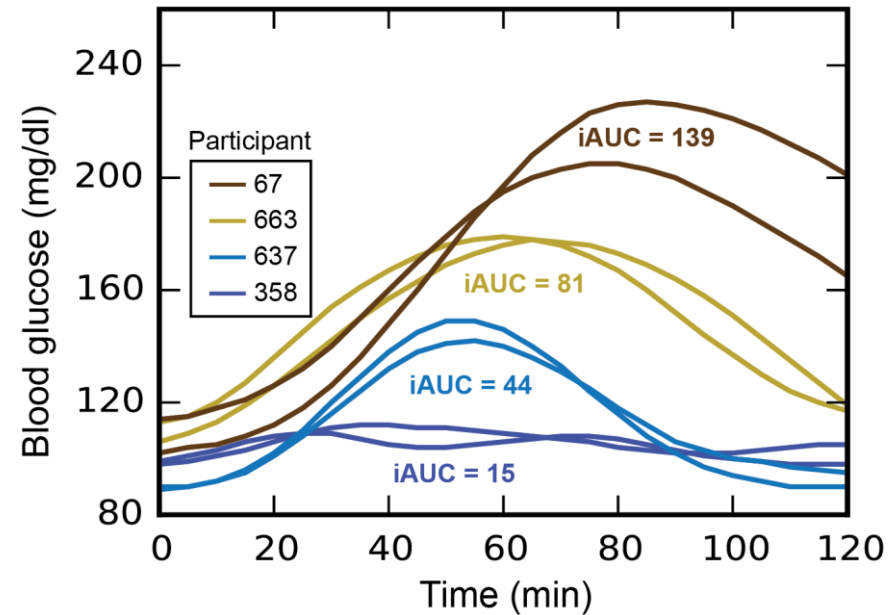


Different people have widely different post-meal responses to the same standardized meal

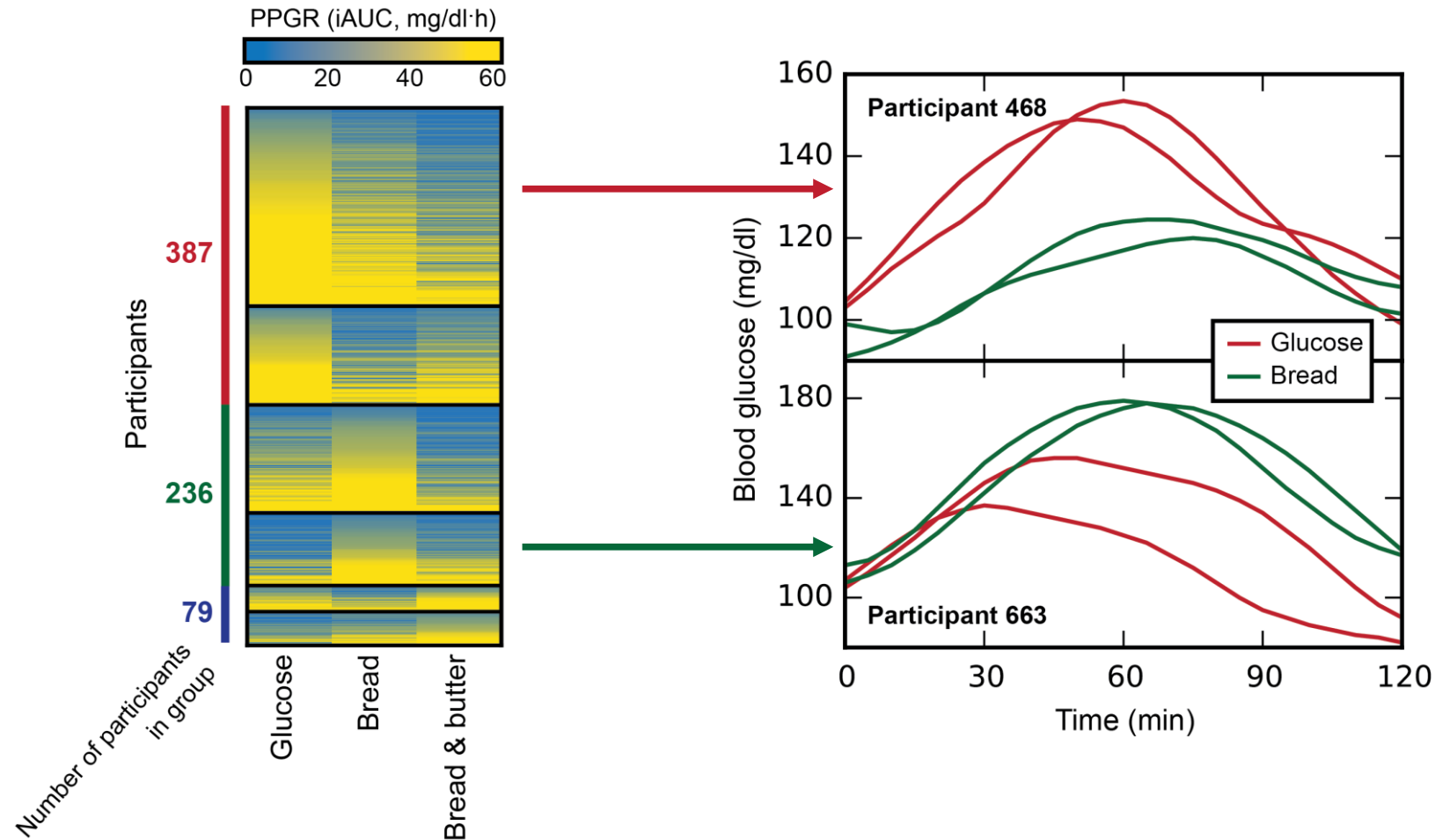
Population Responses to Standardized Meals



Four Individual Responses to Bread

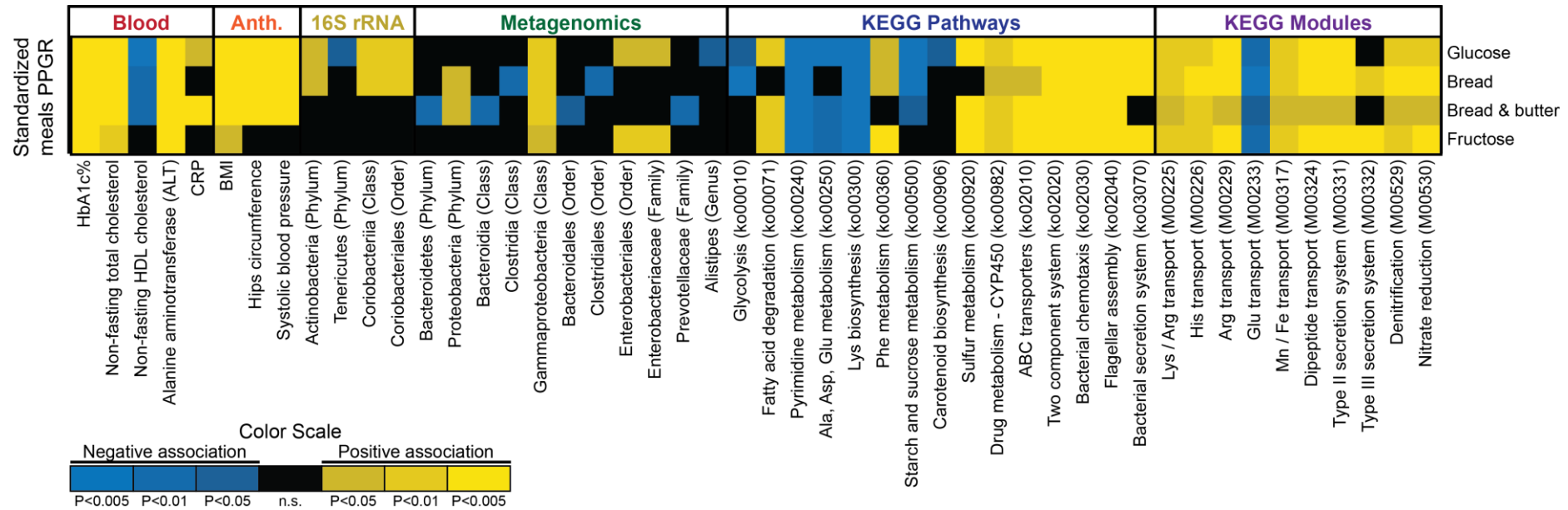


Different people have widely different post-meal responses to the same standardized meal

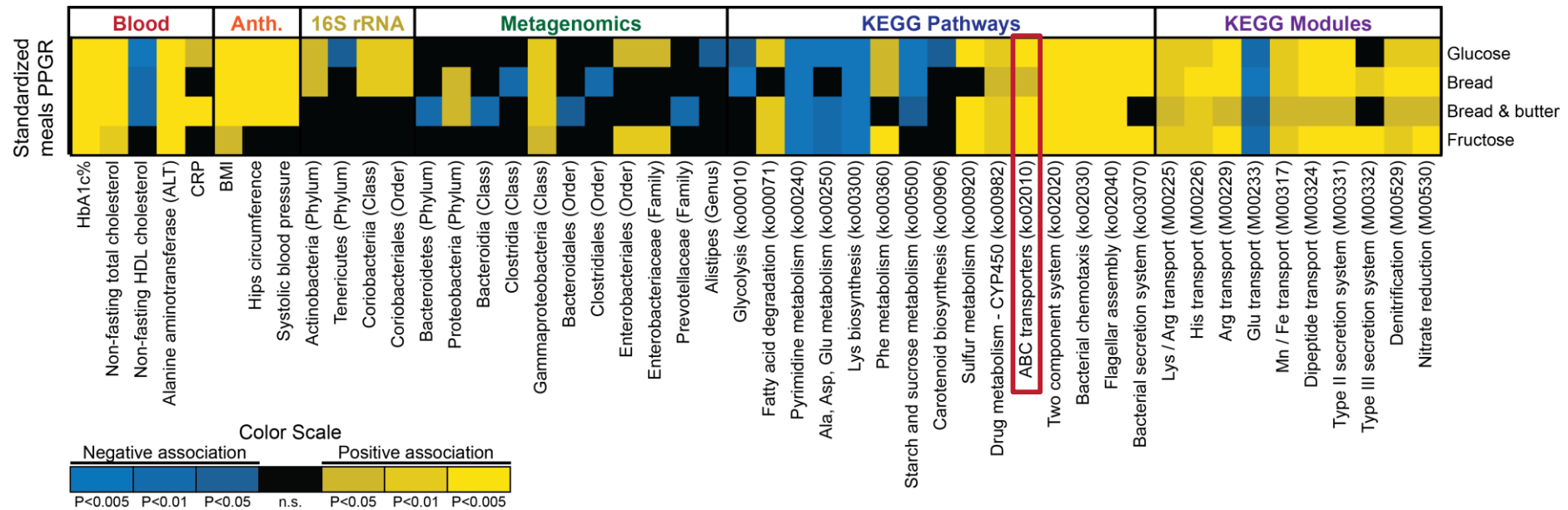


**What explains the variability in
people's response to the same food?**

Variability in post-meal glucose response across people associates with microbiota composition and function



Positive association between ABC transporters and post-meal glucose response to all standardized meals



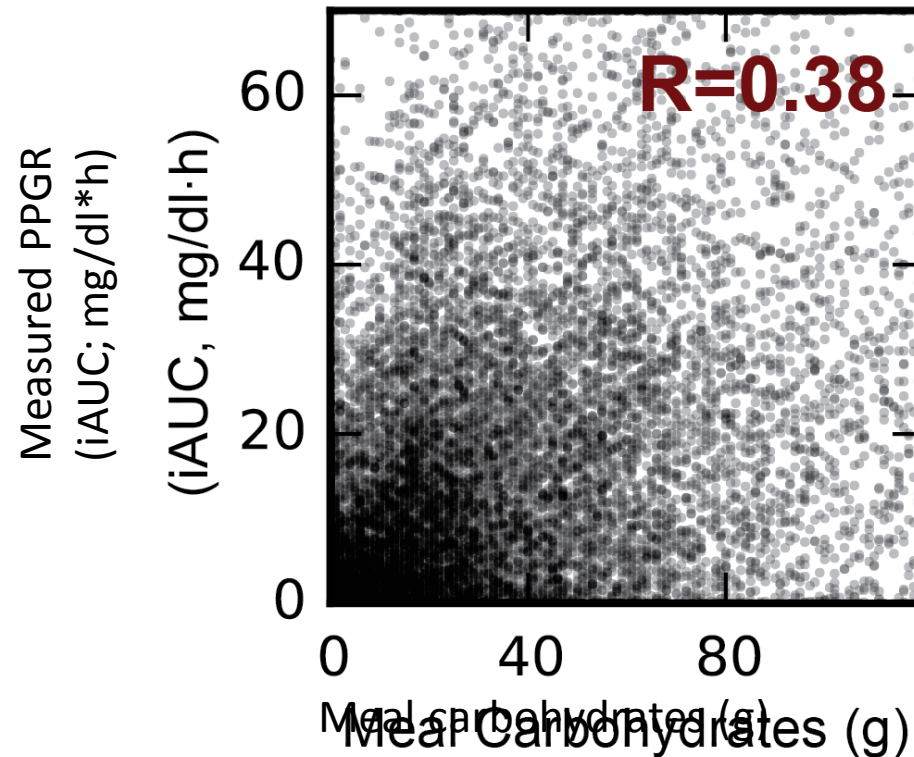
- Positive association with **TIIDM** (Karlsson et al., 2013)
- Positive association with **western high-fat/high-sugar diet** (Turnbaugh et al., 2009)

**Can we predict the personal post-prandial
glucose response to any complex meal?**

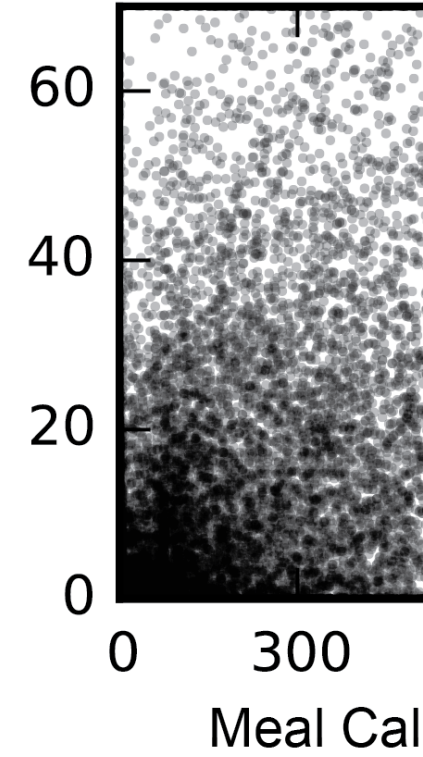
Meal Carbohydrates: State of the art in predicting post-meal glucose responses

State of the art

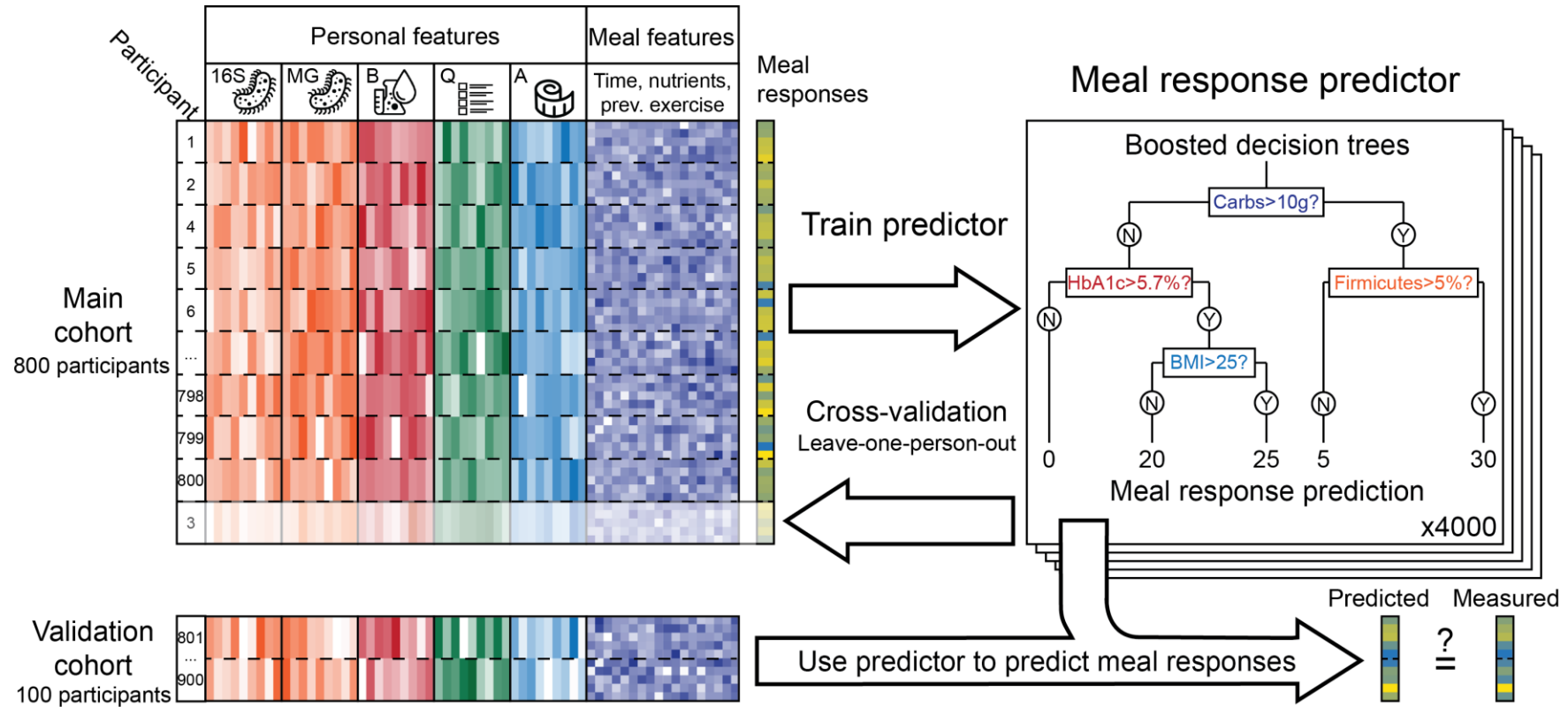
Carbohydrate-only prediction



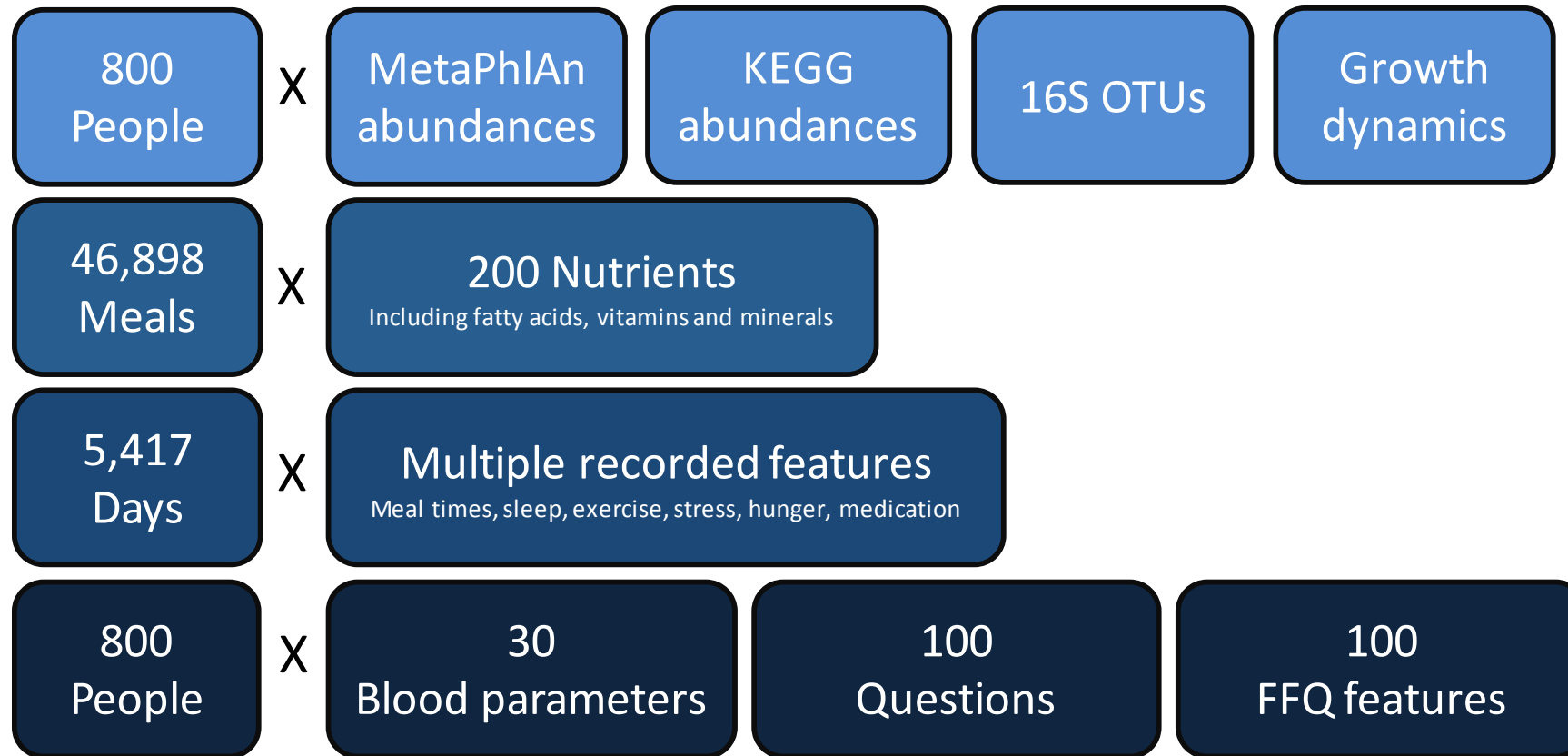
Calorie prediction



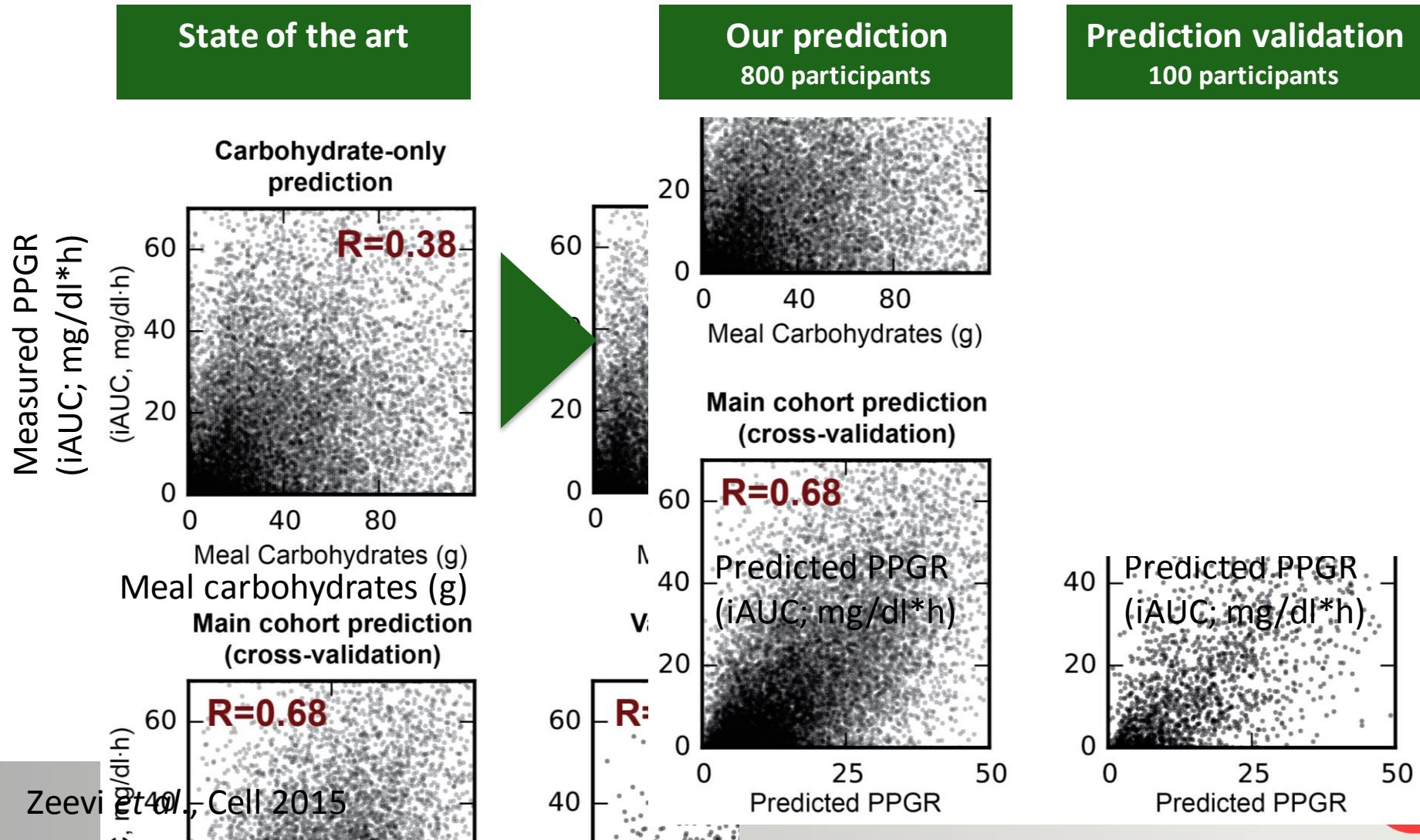
Prediction scheme



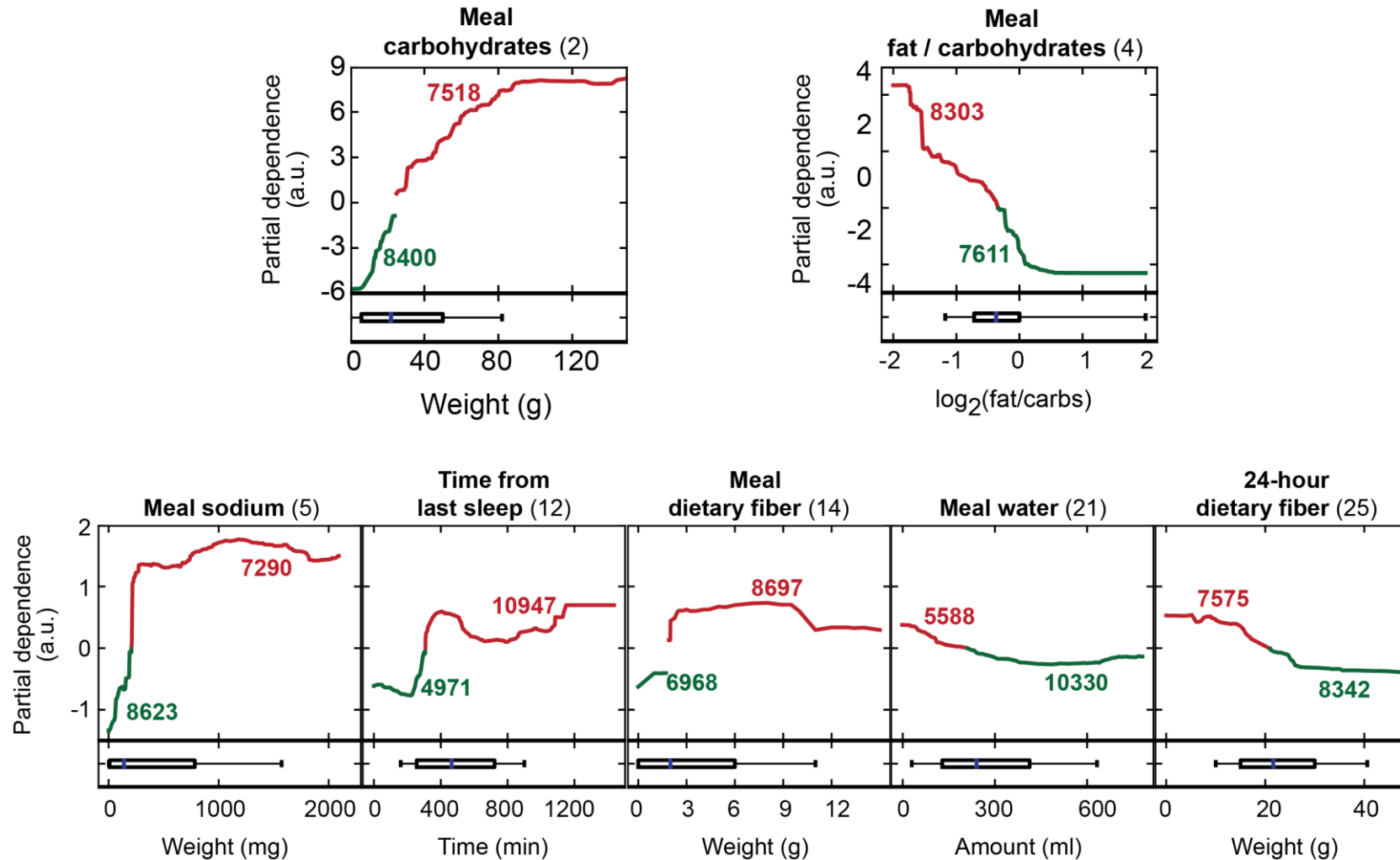
Model features



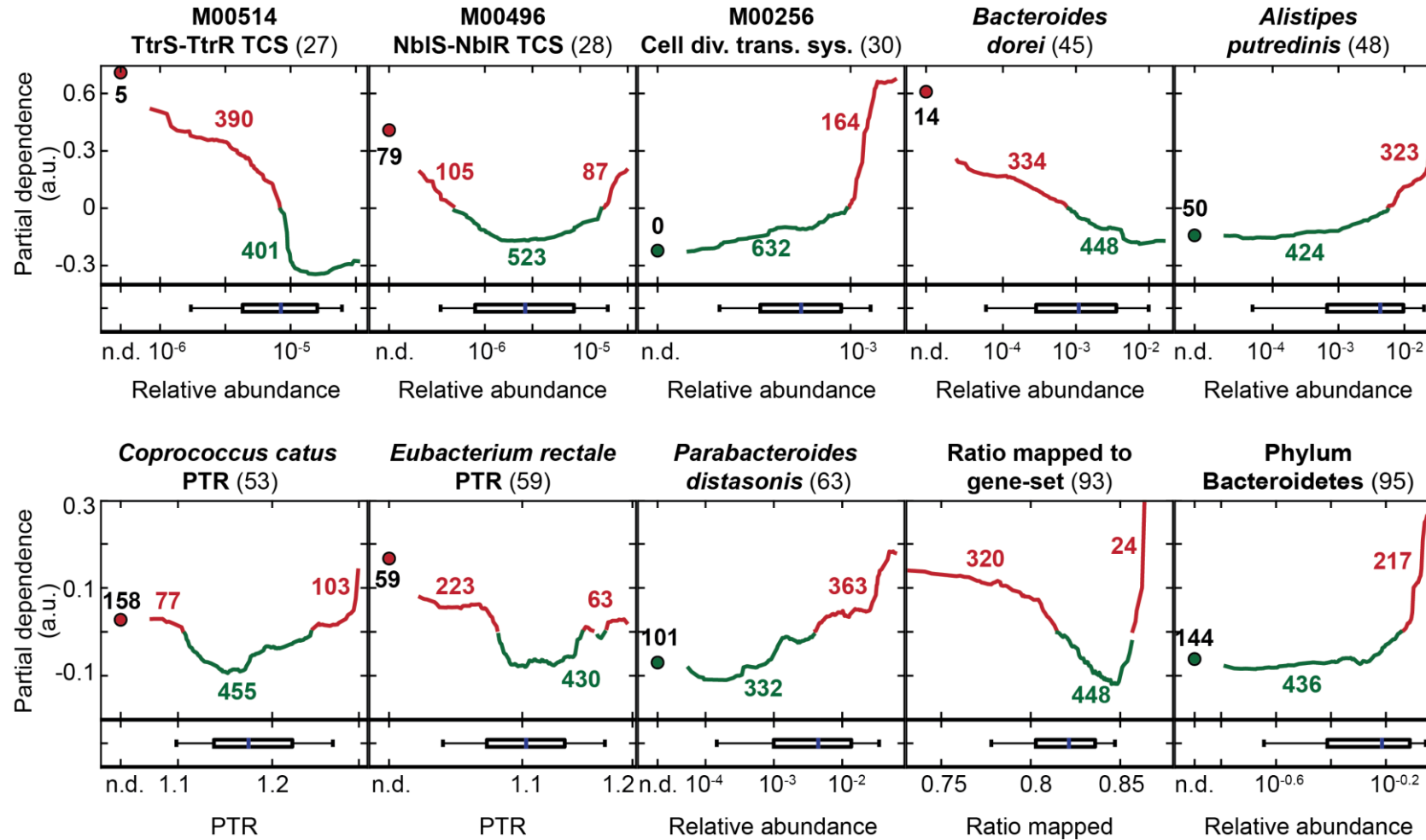
Accurate predictions of personalized glucose responses



Meal and lifestyle factors affect the post-meal glucose response



Microbiome features affect the post-meal glucose response



Can personally tailored dietary interventions improve post-prandial glucose responses?



Daphna Rothschild



Orly Ben-Yaacov



Michal Rein

Constructing personally tailored diets that achieve normal post-prandial glucose responses

One week profiling
(26 participants)

Dietitian prescribed meals

Day	1	2	3	4	5	6
Breakfast	B ₁	B ₂	B ₃	B ₄	B ₅	B ₆
Lunch	L ₁	L ₂	L ₃	L ₄	L ₅	L ₆
Snack	S ₁	S ₂	S ₃	S ₄	S ₅	S ₆
Dinner	D ₁	D ₂	D ₃	D ₄	D ₅	D ₆

Personal features



Color-coded response
(blue - low; yellow - high)

L₆ Text meal identifier

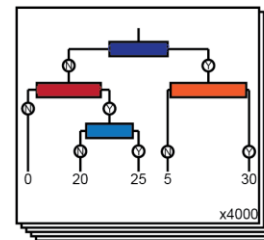
Choose meals for dietary intervention weeks

Expert-based



14 participants
(E1, E2, ..., E14)

Predictor-based



12 participants
(P1, P2, ..., P12)

Find best
and worst meals
for each row

'Good' diet

B ₄	L ₂	S ₅	D ₂
B ₆	L ₅	S ₆	D ₃

'Bad' diet

B ₁	L ₃	S ₁	D ₁
B ₂	L ₆	S ₂	D ₅

'Good' diet

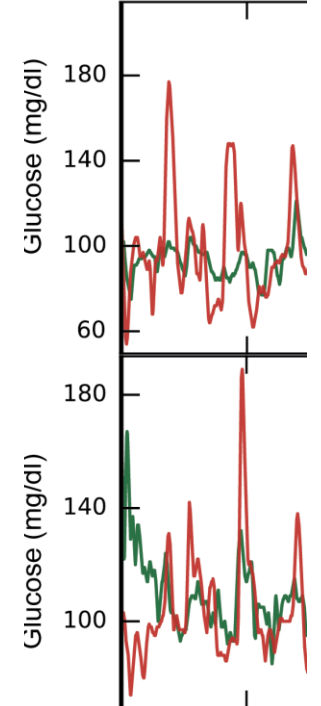
B ₄	L ₄	S ₅	D ₂
B ₅	L ₅	S ₆	D ₄

'Bad' diet

B ₁	L ₁	S ₁	D ₁
B ₃	L ₆	S ₂	D ₆











Measure α

Day 1 2



Can you distinguish between the good and bad menus?



	“Bad” Diet	“Good” Diet ?	“Bad” Diet	“Good” Diet ?
Breakfast		Muesli		Egg with bread and coffee
Lunch		Sushi		Hummus and pita
Snack		Marzipan		Edamame
Dinner		Corn and nuts		Vegetable noodles with tofu
Night snack		Toblerone and coffee		Ice cream

Can you distinguish between the good and bad menus?



**Bad
Diet**

**Good
Diet**

Breakfast



Muesli



**Egg with
bread and
coffee**

Lunch



Sushi



**Hummus
and pita**

Snack



Marzipan



Edamame

Dinner



**Corn and
nuts**



**Vegetable
noodles
with tofu**

Night snack

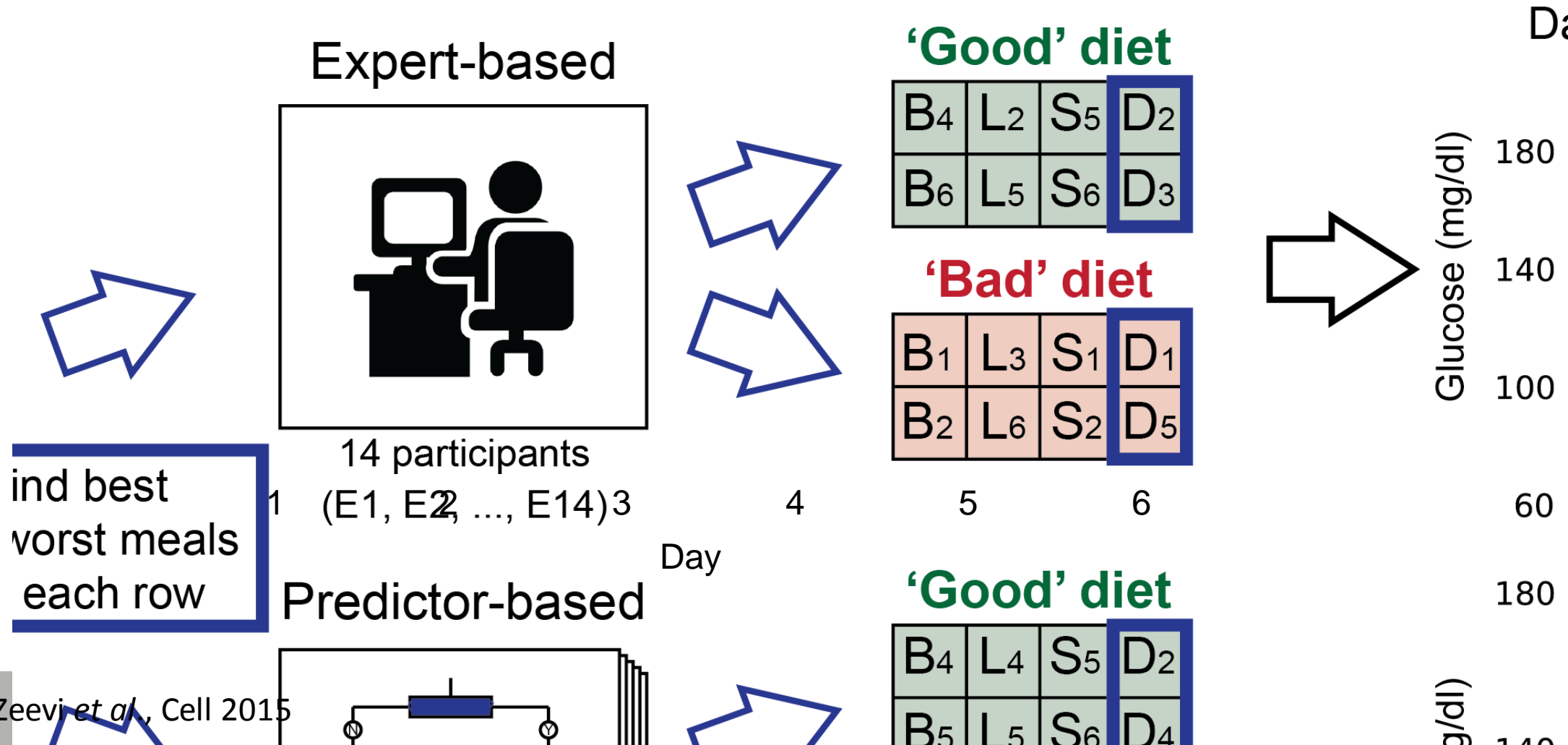


**Toblerone
and coffee**



Ice cream

Personally tailored diets reduce the post-prandial glucose response



Can you distinguish between the good and bad menus?



Breakfast

Lunch

Snack

Dinner

Night snack

**“Bad”
Diet**

**“Good”
Diet** ?



Orange juice



Schnitzel



Peach



Bread with
butter



Grapes

**“Bad”
Menu**

**“Good”
Diet** ?



Croissant



Goulash
with rice



Halva



Hummus



Red wine

Can you distinguish between the good and bad menus?



**Bad
Diet**

**Good
Diet**

Breakfast



Orange juice



Croissant

Lunch



Schnitzel



Goulash
with rice

Snack



Peach



Halva

Dinner



Bread with
butter



Hummus

Night snack

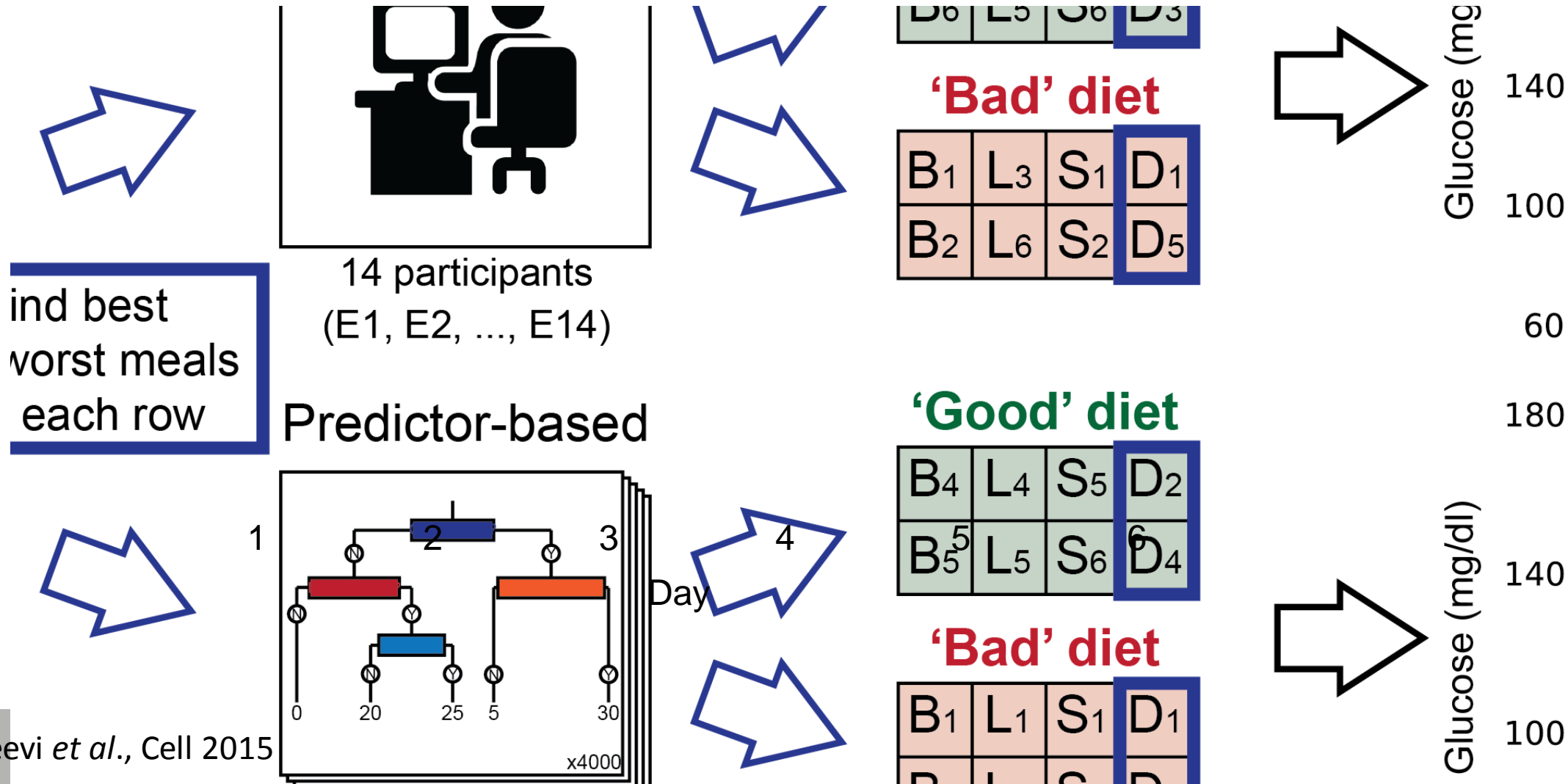


Grapes

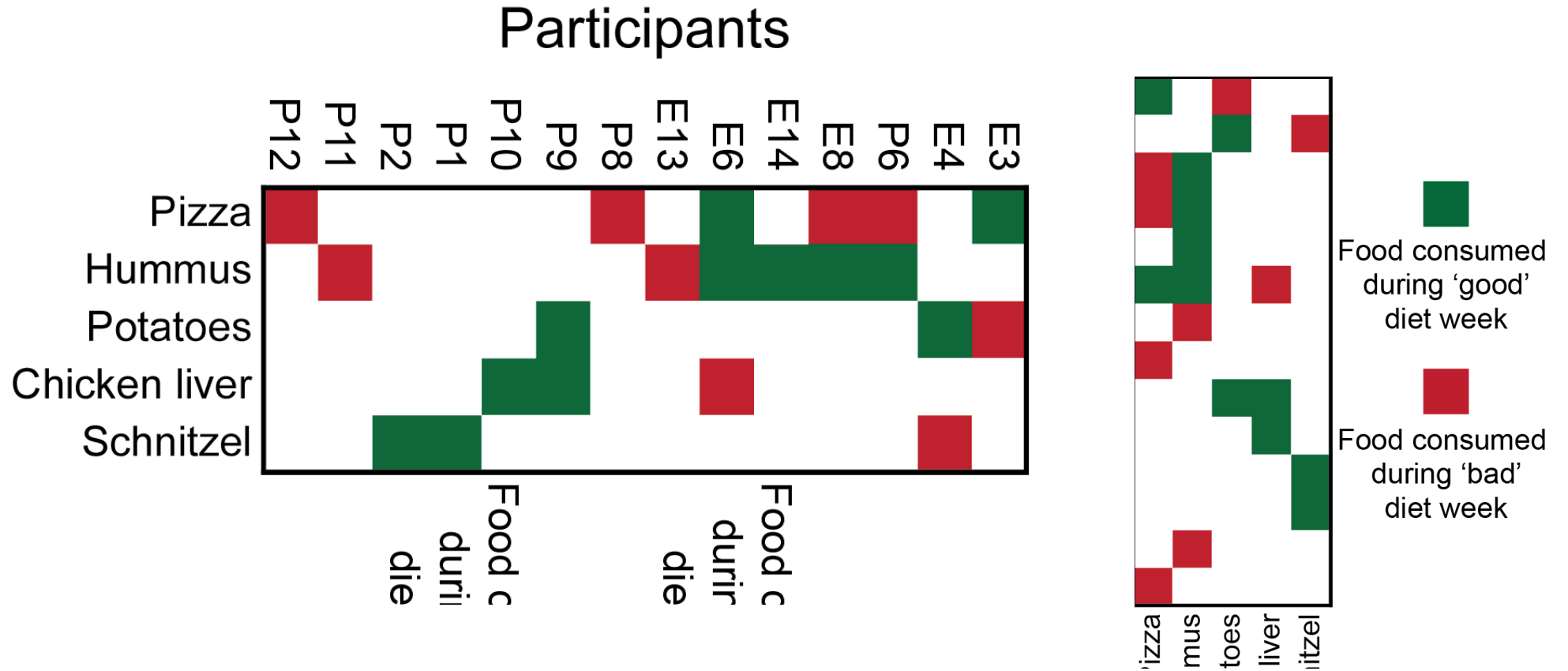


Red wine

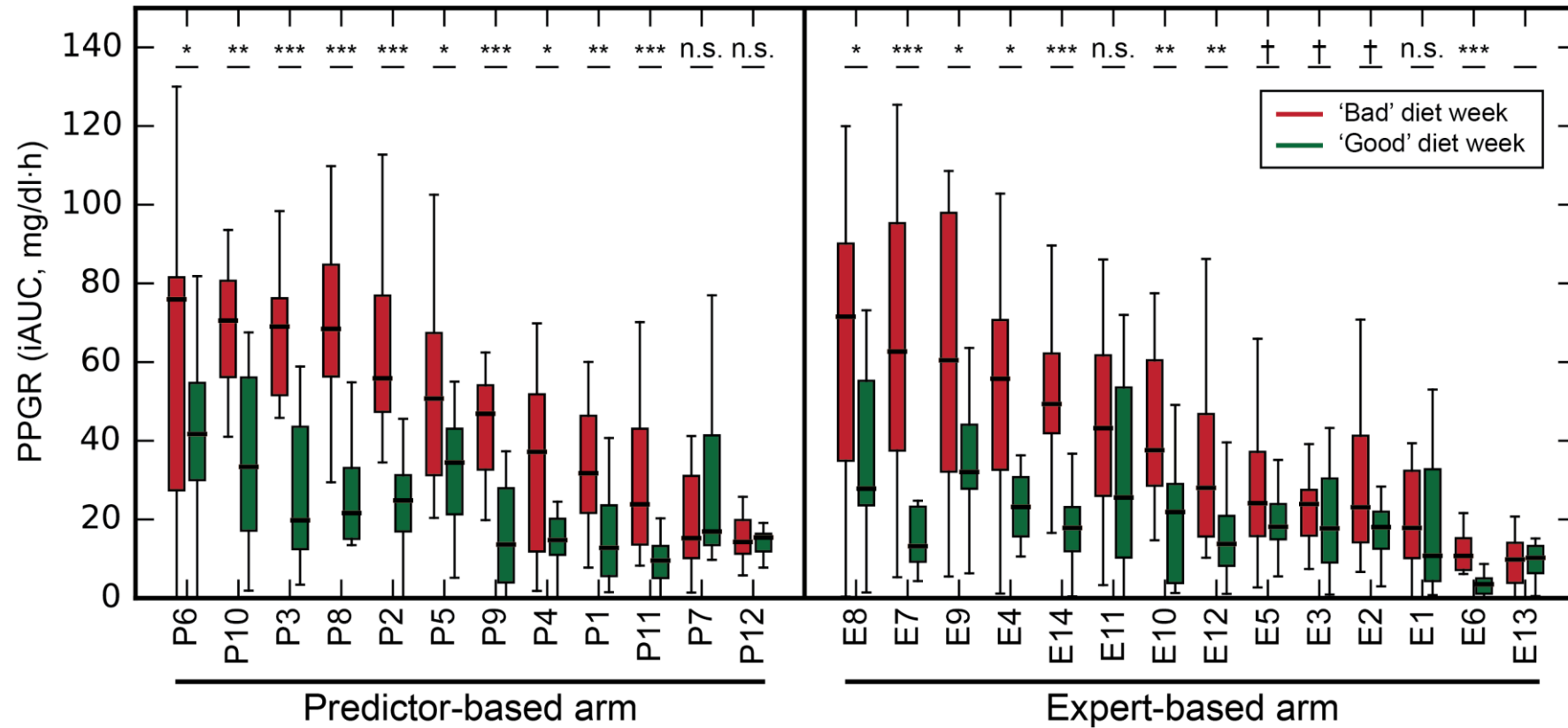
Personally tailored diets reduce the post-prandial glucose response



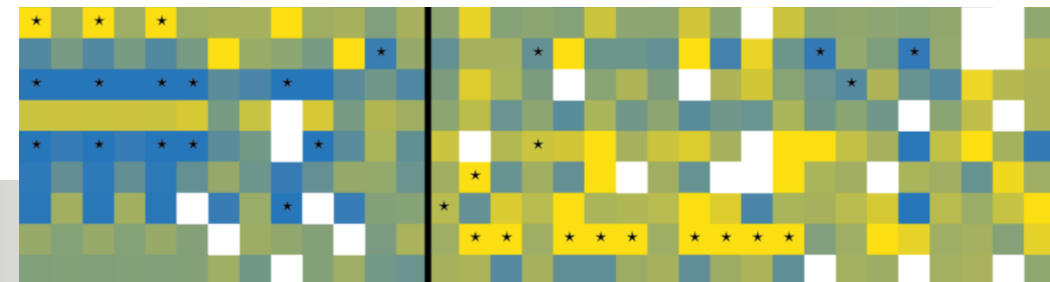
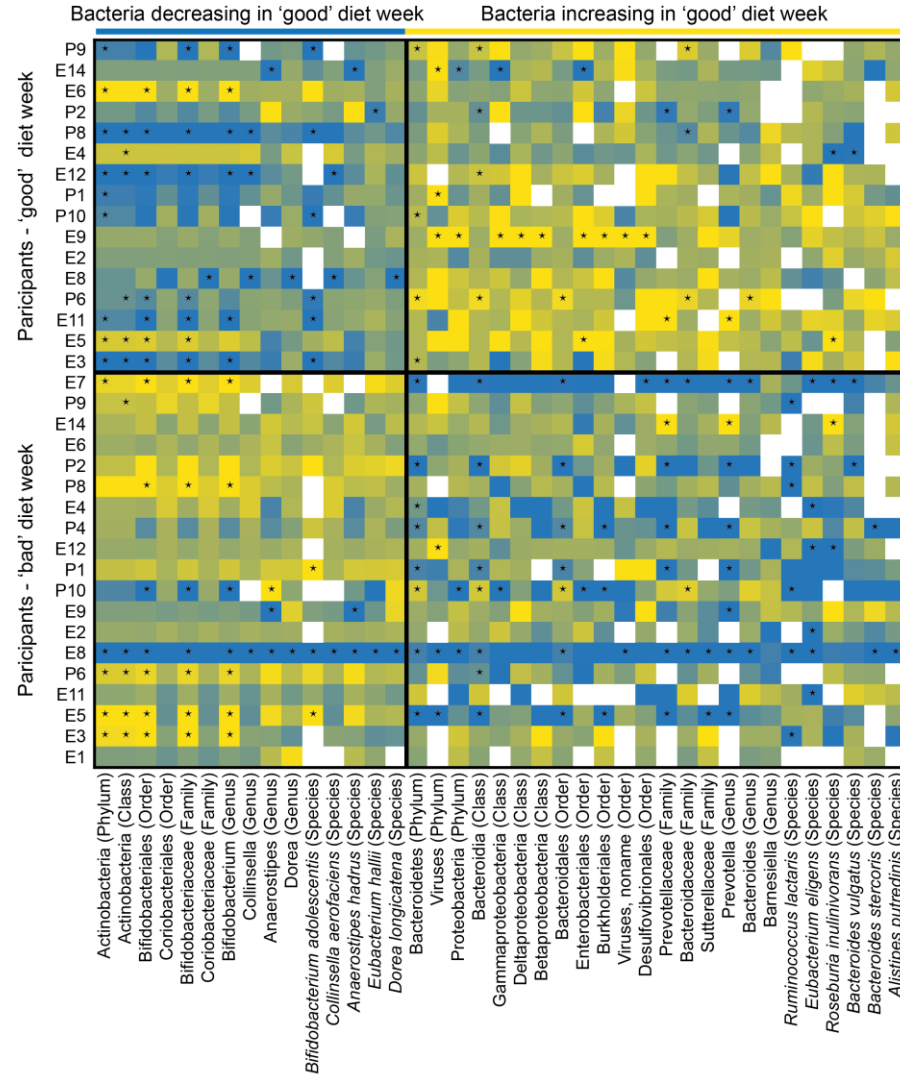
Foods that appear in the 'good' diet of one person may appear in the 'bad' diet of another



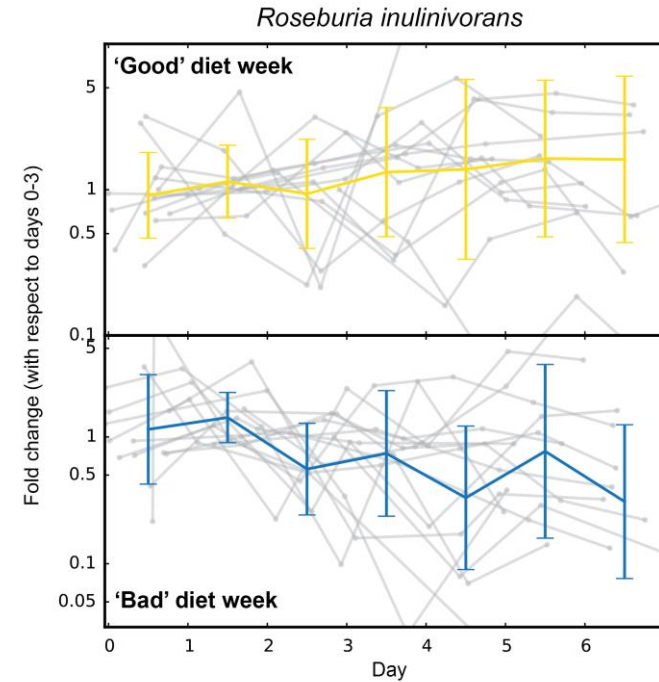
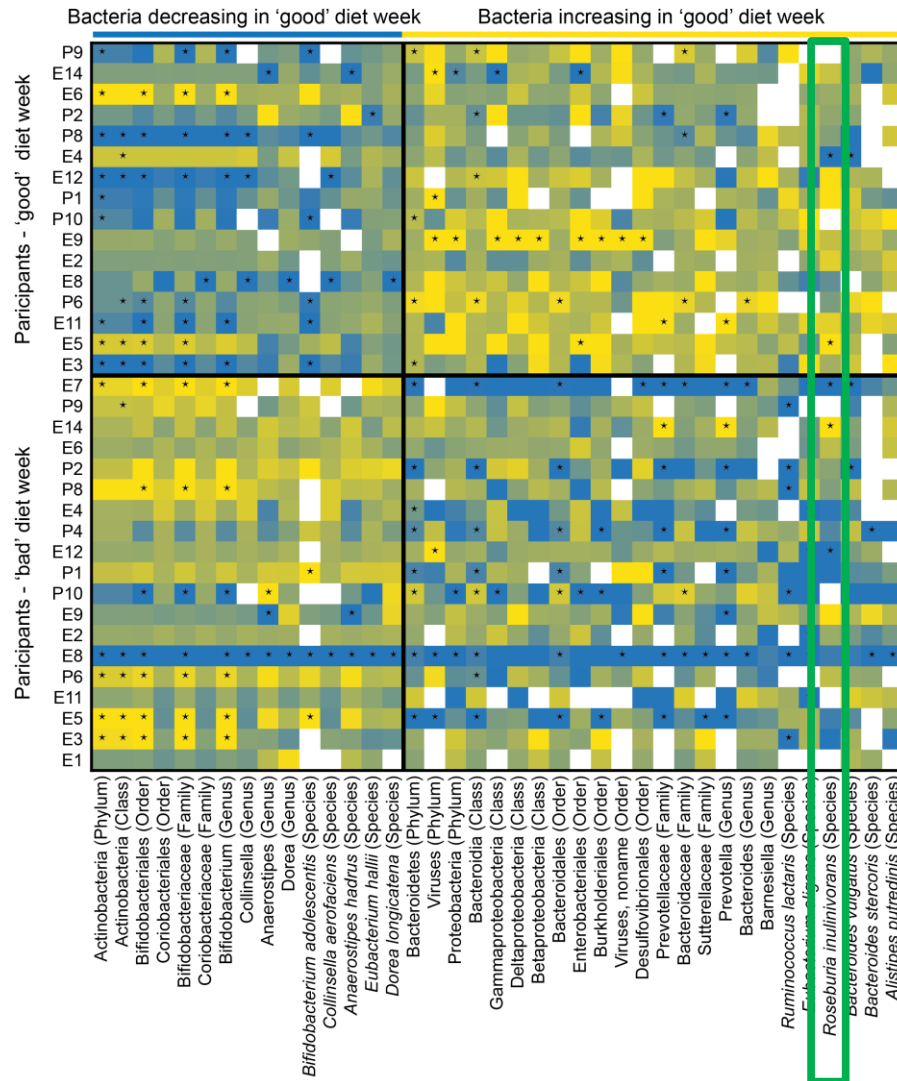
Personally tailored diets improve post-meal responses



Dietary interventions targeting post-meal glucose responses induce consistent changes in microbiota

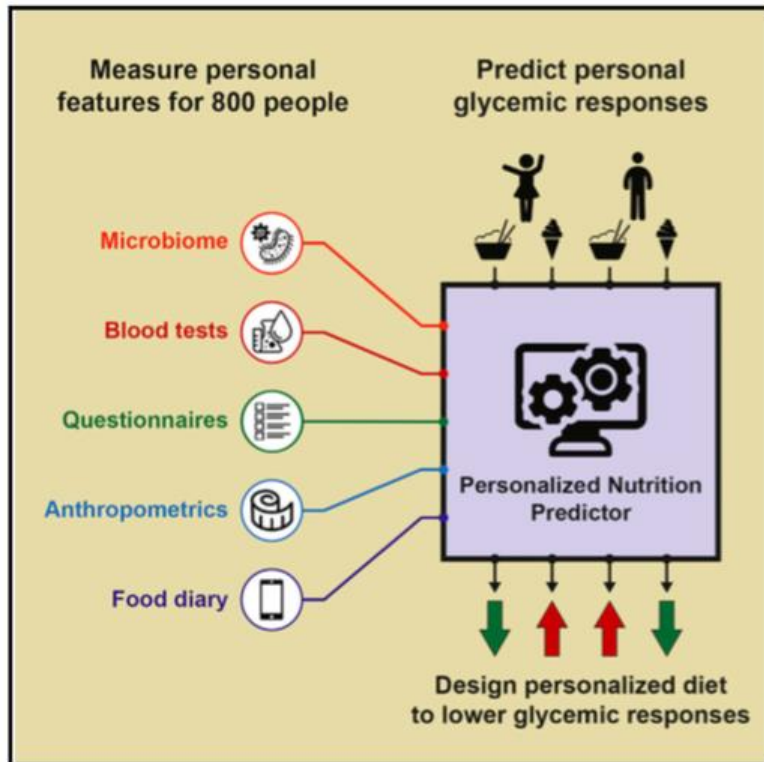


Dietary interventions targeting post-meal glucose responses induce consistent changes in microbiota



- *Roseburia inulinivorans* increases following the 'good' diet week
- Low levels associate with T1DM (Qin et al., 2012)

Personalized nutrition project summary



- High interpersonal variability in post-meal glucose response to identical meals
- Personal and microbiome features enables accurate glucose response prediction
- Short term personalized dietary interventions successfully lower post-meal glucose

Why can't we maintain our weight after dieting?



Christoph Thaiss

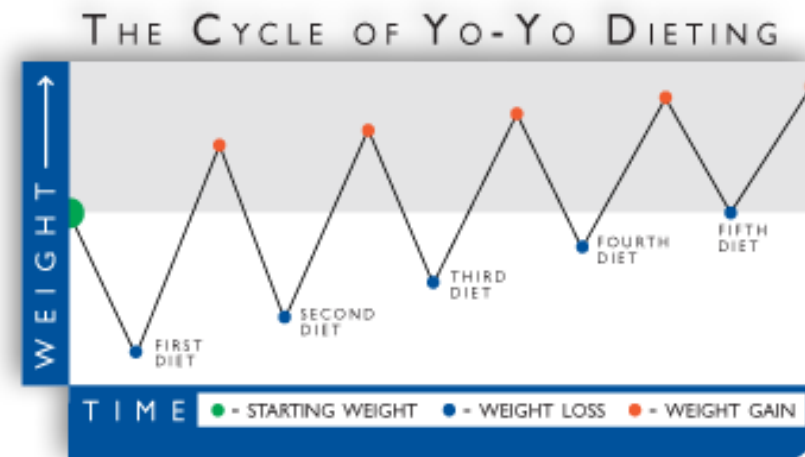


Shmulik Motola

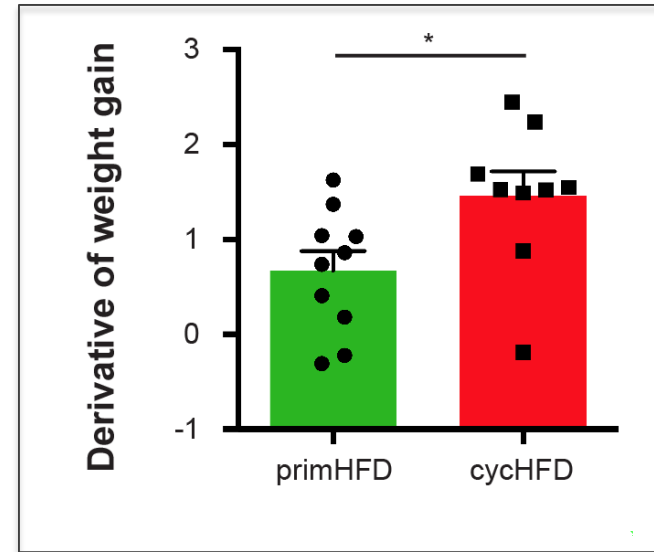
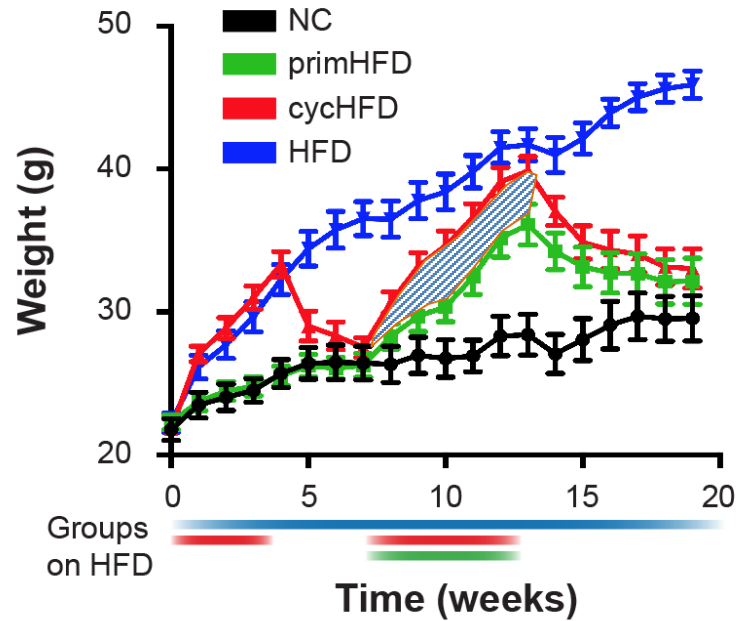


Daphna Rothschild

People tend to regain their weight after a successful diet

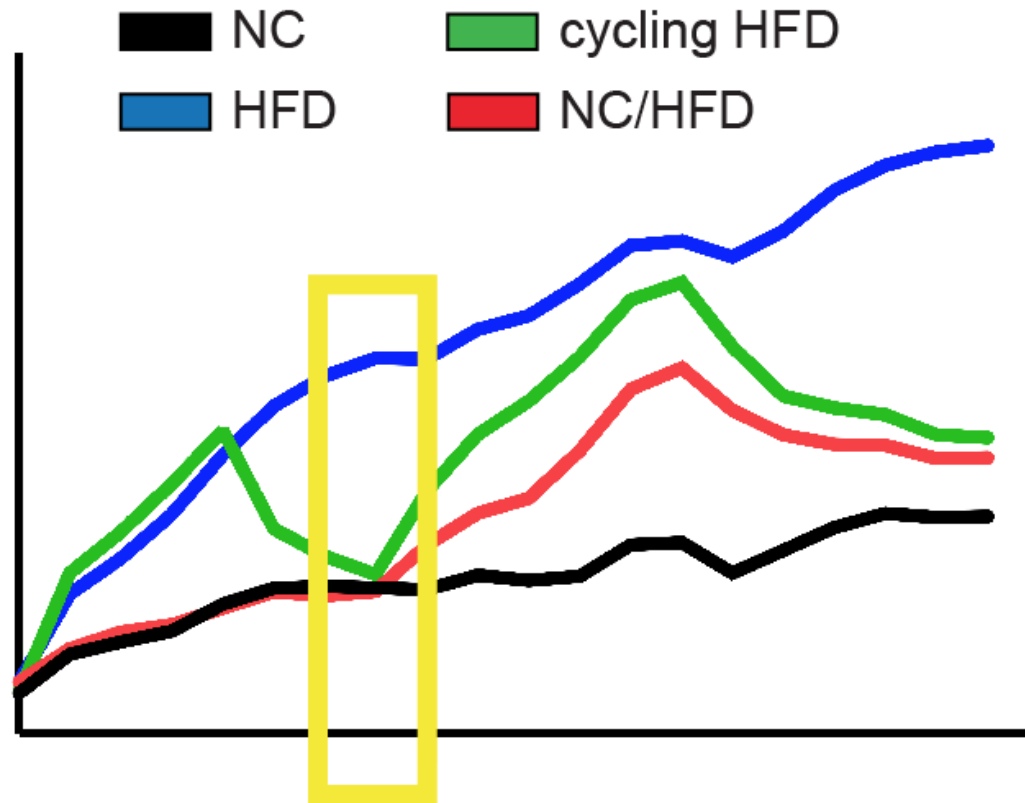


A mouse model of recurring obesity

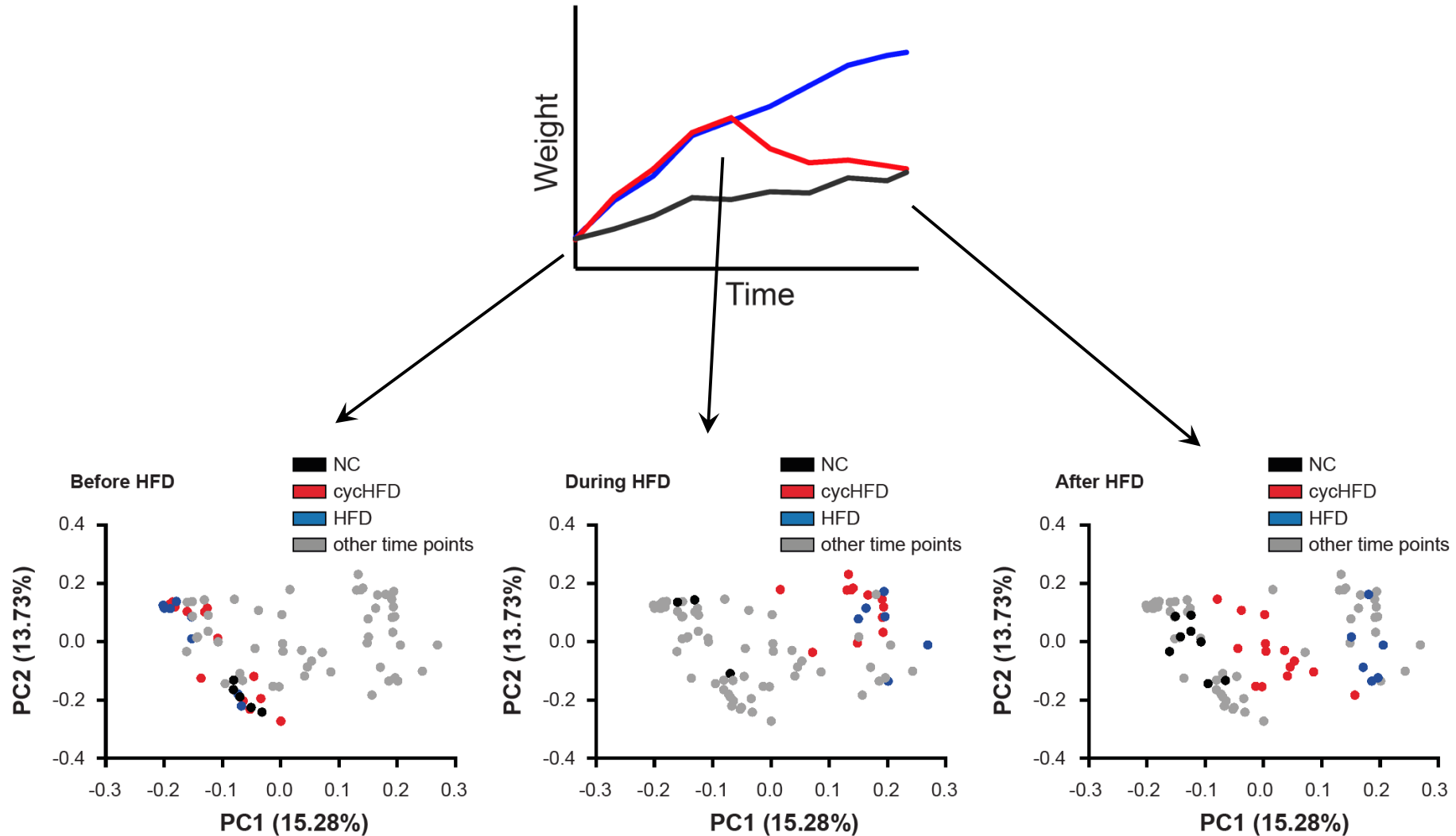


**Is there a “memory”
of previous obesity?**

Is there a memory of previous obesity?

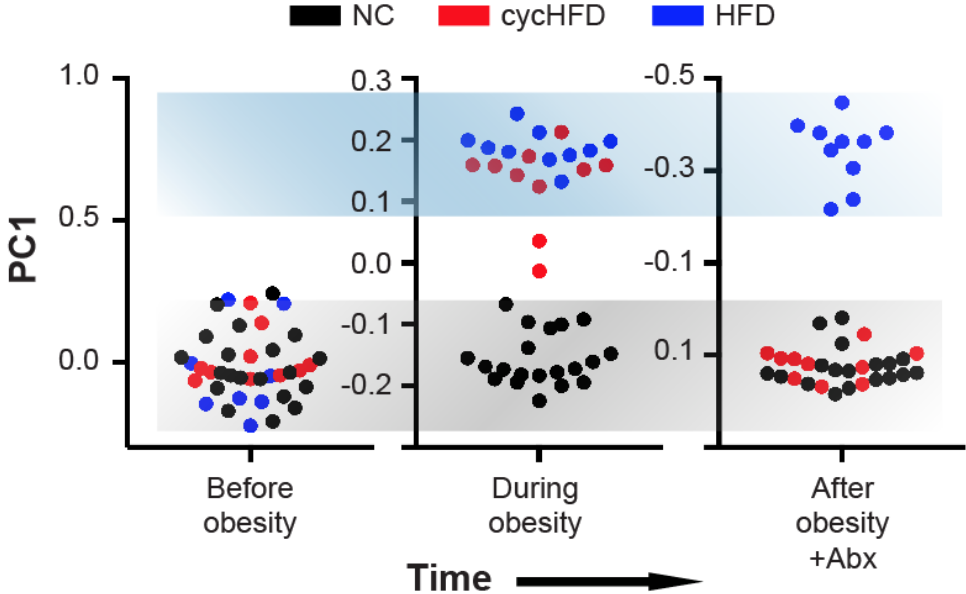
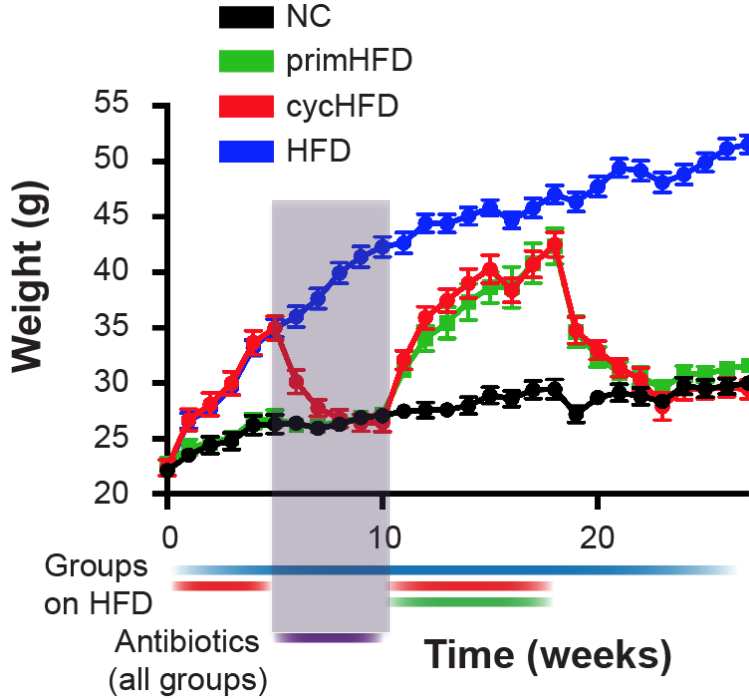


Some differences in 16S microbiome composition are retained after weight loss

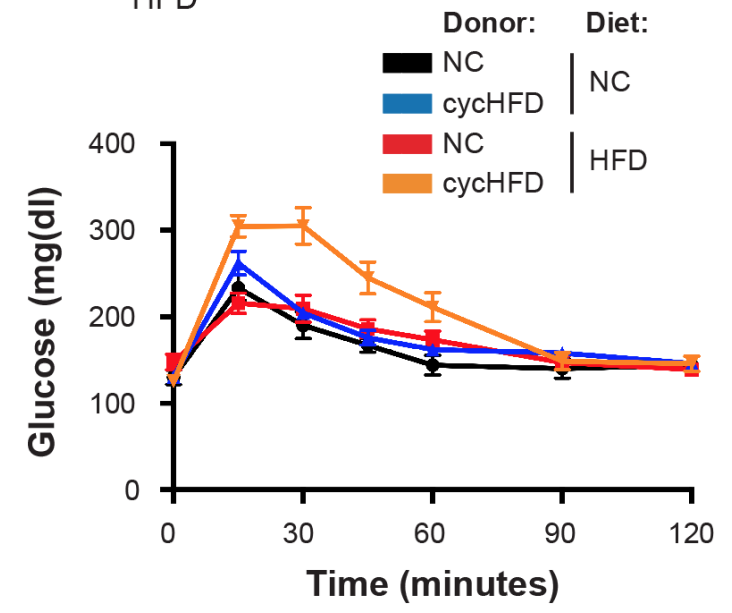
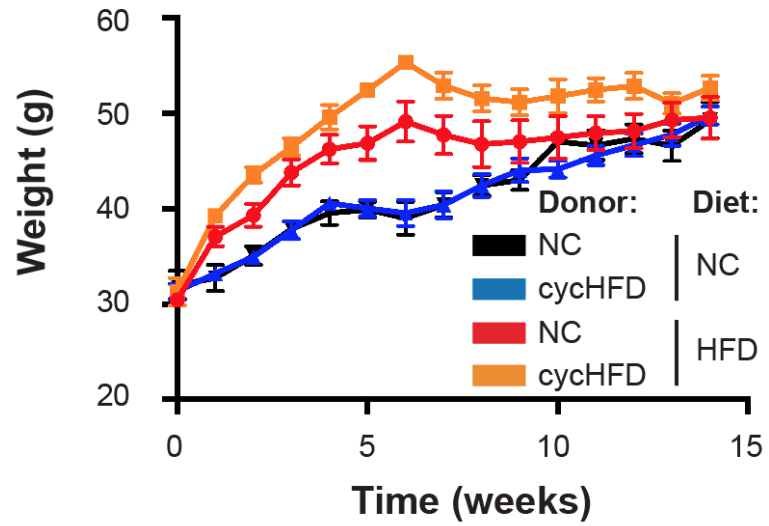
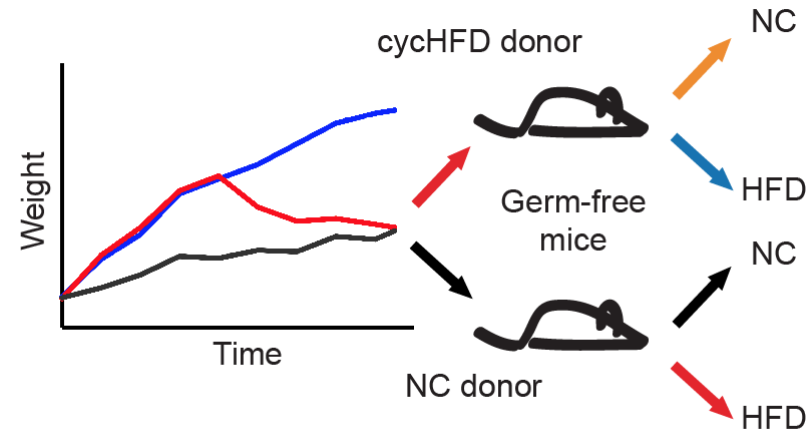


**Does the microbiome have a causal
role in enhanced weight regain?**

Antibiotic treatment abolishes effect of previous obesity

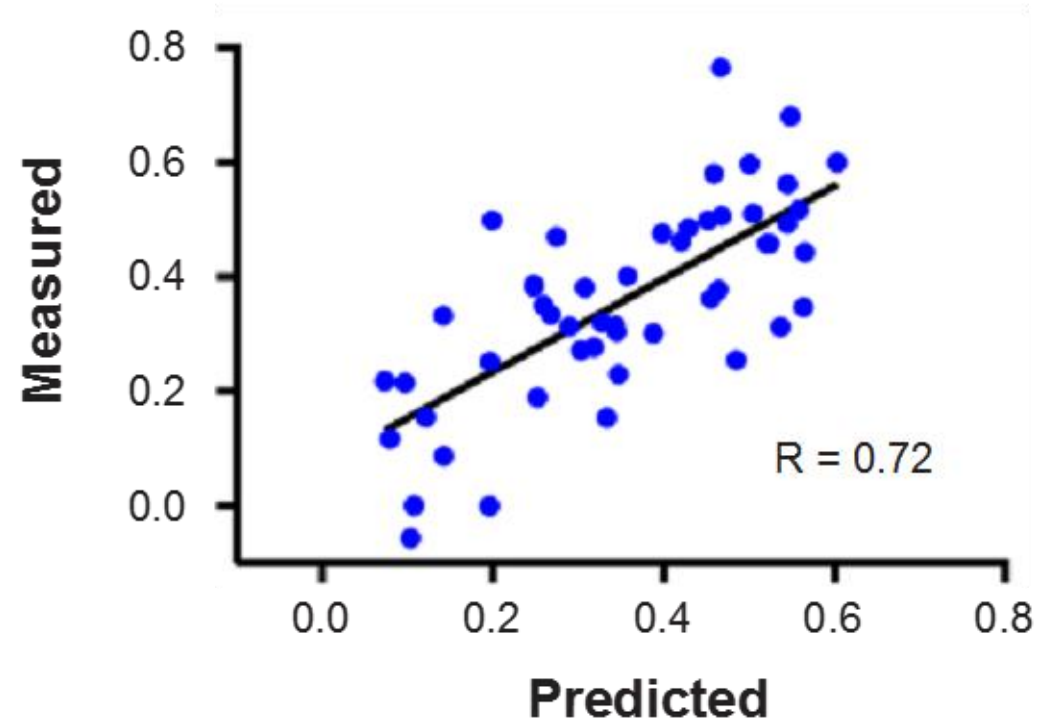
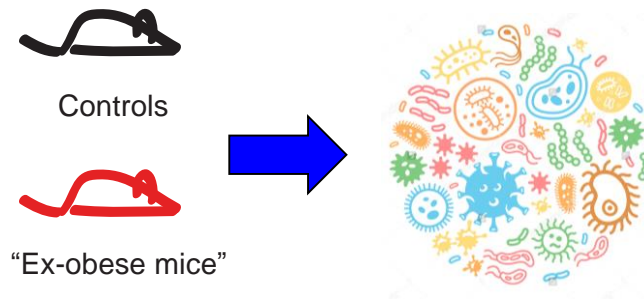


Microbiome transfer to germ free mice transmits enhanced weight regain phenotype

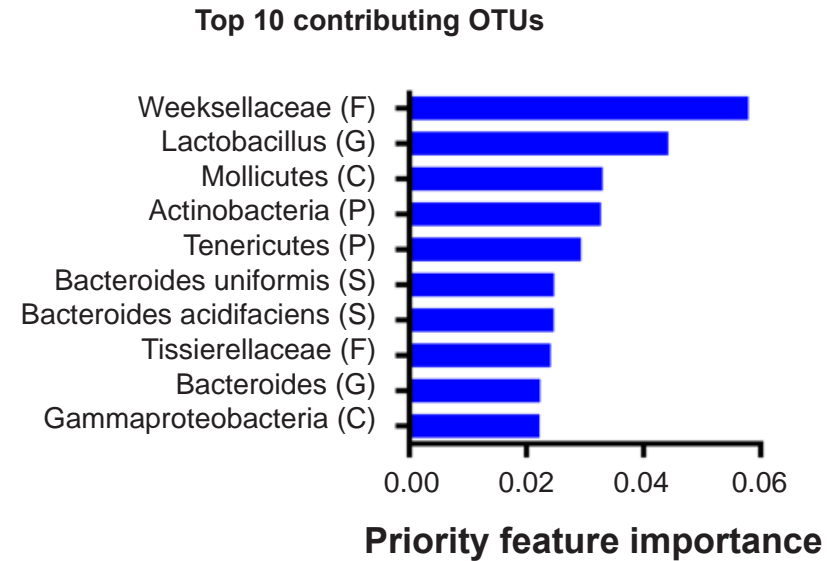
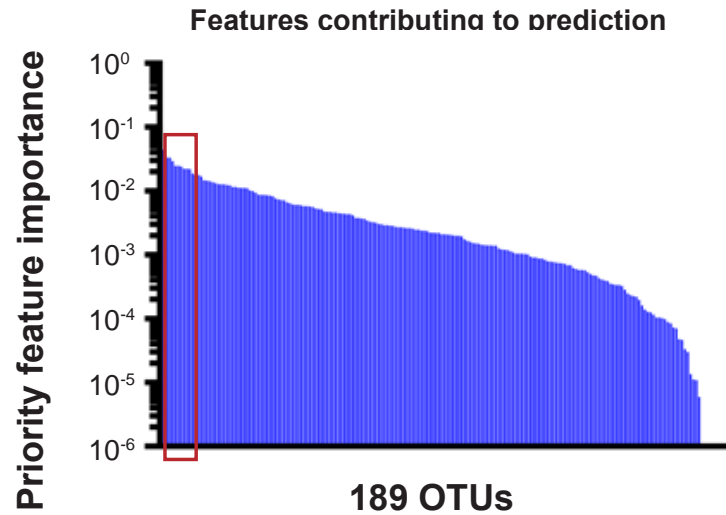


**Can we predict weight regain
using only microbiome composition?**

A microbiome-based predictor accurately predicts the degree of future weight gain

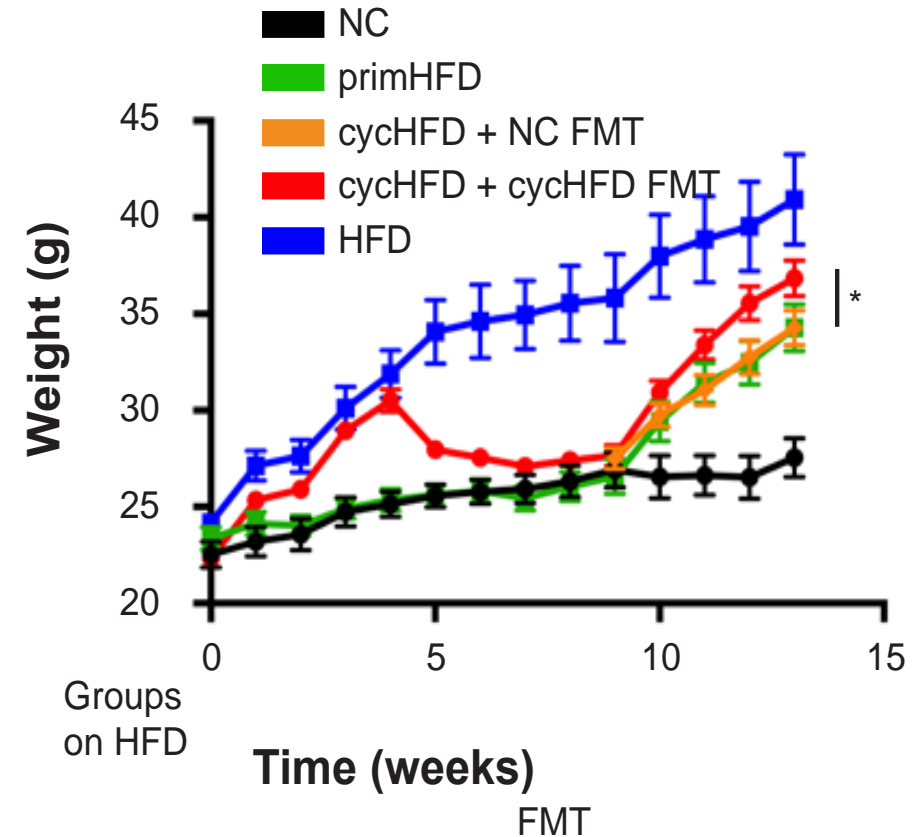
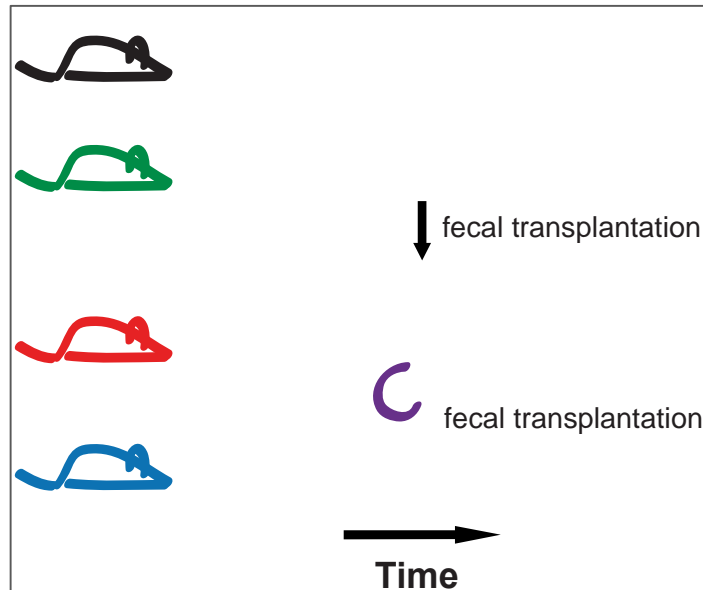


Multiple microbiome factors contribute to predictions

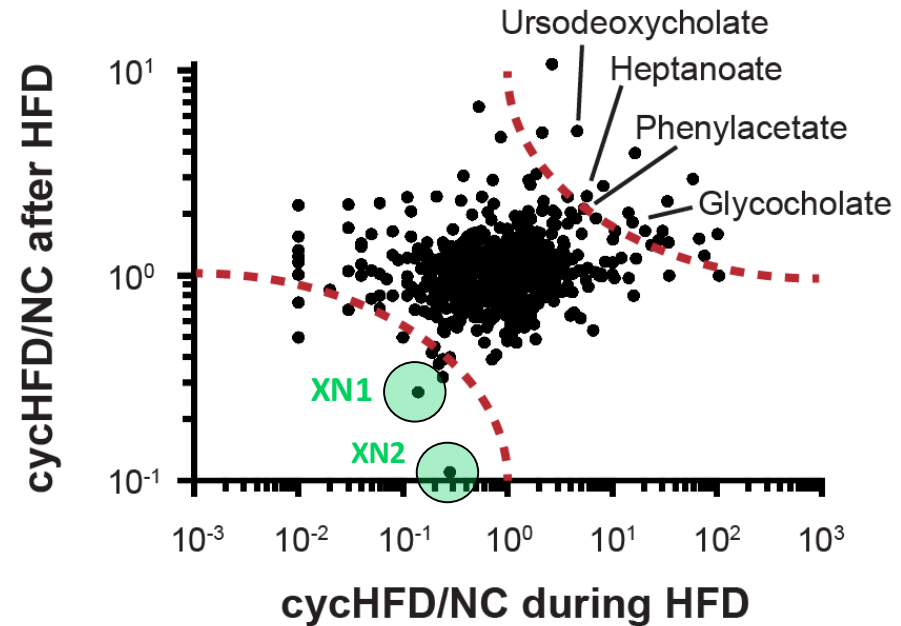
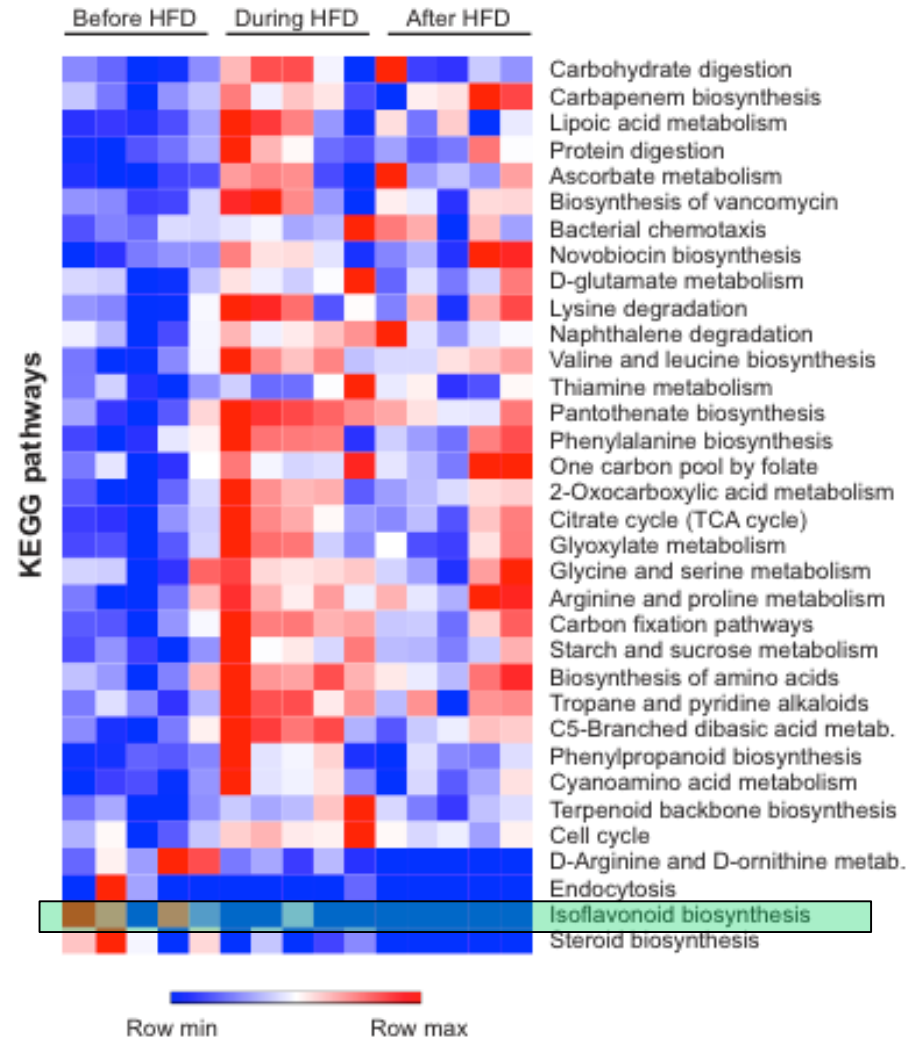


**Can we treat relapsing obesity
by targeting the microbiome?**

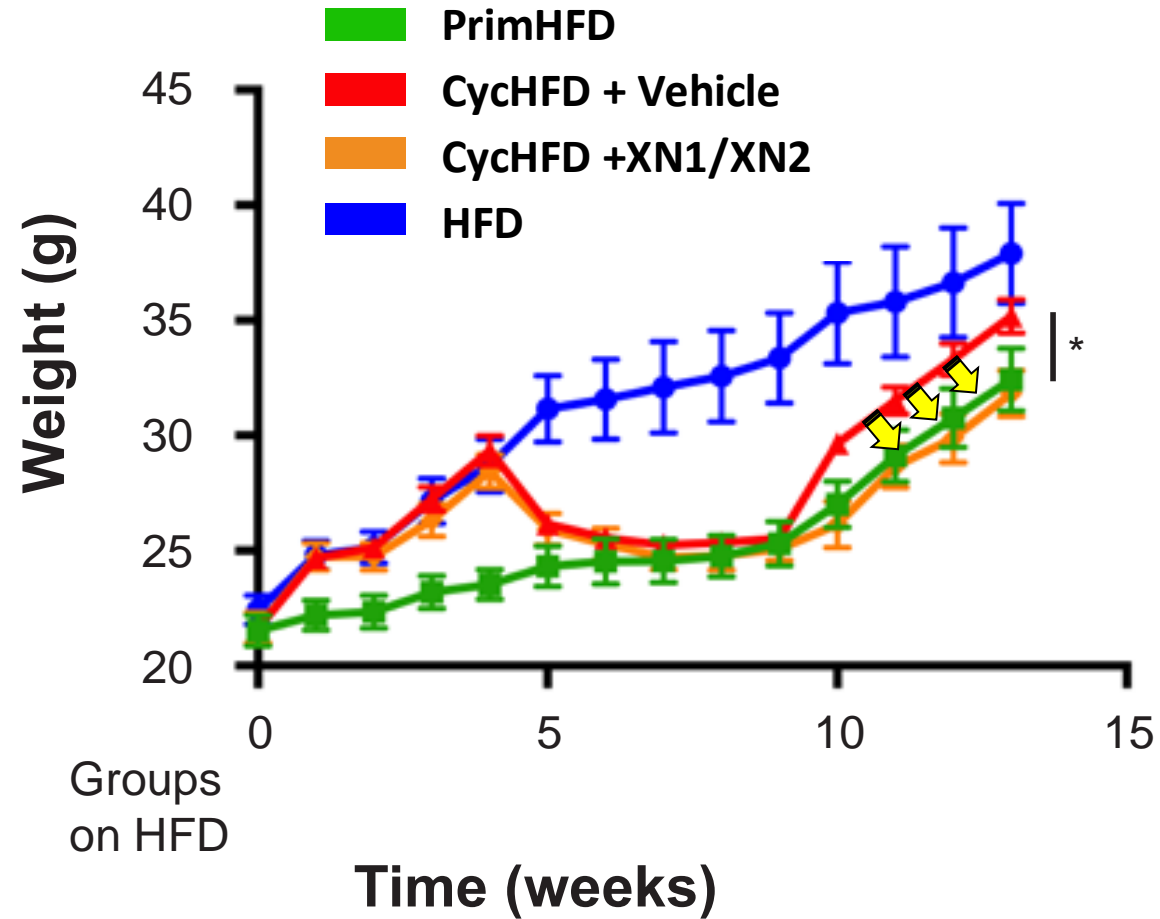
Fecal Microbiome Transplantation (FMT) abolishes microbiome-driven metabolic memory



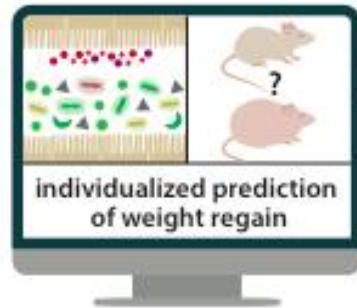
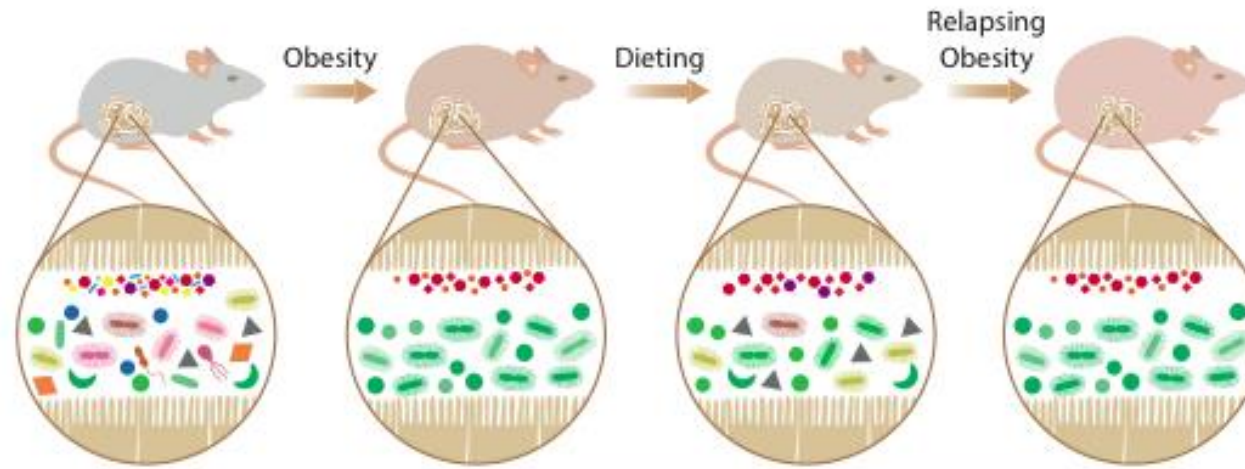
'Post-biotic' therapy abolishes microbiome-driven metabolic memory



'Post-biotic' therapy abolishes microbiome-driven metabolic memory



Relapsing obesity summary





David Zeevi

Tal Korem

Adina Weinberger

Dafna Rothschild

Nastya Godneva

Tali Avnit-Sagi

Maya Pompan-Lotan

Elad Matot

Dar Lador

Michal Rein

Orly Ben Yaakov

Rony Bikovsky

Izhak Levi

Hadas Elisar

Neta Levkovich

Noa Kossower

Gal Malka

Martin Mikl

Shira Gabbay

Eran Kotler

Leeat Keren

Ronit Nir

Yaara Unger

Iris Kalka

Niv Zmora

Jotham Suez

Jamel Abu-Mahdi

Gili Zilberman-Schapira

Lenka Dohnalová

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Christoph Thaiss

Hagit Shapiro

Shmulik Motola

Maayan Levy

Kfar Shaul Medical Center

Dr. David Israeli

Tel-Aviv Sourasky Medical Center

Prof. Zamir Halpern

