Personalized Dietary Treatment Based on the Gut Microbiome

A journey to better health with Microbiome Solutions.

Conflict of Interest Disclosure Statement

Susan Yake is a paid consultant for DayTwo
## Objectives

<table>
<thead>
<tr>
<th>Objective 1:</th>
<th>Discuss the degree of variation in personal glycemic response to meals among different individuals</th>
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<td>Objective 2:</td>
<td>Describe the role the gut microbiome plays in the development and management of diabetes and other diseases</td>
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<td>Objective 3:</td>
<td>Explain that machine learning algorithms can be used to personalize diets to normalize blood glucose levels in people with diabetes and pre-diabetes</td>
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“If you think you are too small to make a difference, try sleeping in a closed room with a **mosquito**.”

*(African Proverb)*
Andromeda Galaxy Compared to Microbes in the Gut

There are 100 Billion Stars in the Andromeda Galaxy

There are 390 x as many microbes in the human body - 39 Trillion

This is 1.3 x more than the 30 Trillion human cells in the human body

It is estimated that 3 to 4 lbs. of our weight is from bacteria

https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.1002533

Intervention Study

Can you guess the good diet?
Intervention Study

Can you guess the good diet?

Initial Intervention Results

Spiking Diet

Non-Spiking Diet
Weizmann Institute Research

Choose the foods that are right for you!

Discover the right foods for you, by measuring your genetics, microbes, and personal glucose response to food

Join Study

Eran Elinav, M.D. Ph.D
Prof. Eran Segal, Ph.D

What is the best diet for humans?

An apple a day keeps the doctor away?
The metabolic disease epidemic

1 IN 10 DIABETIC

7 IN 10 OVERWEIGHT

NUTRITION

GENETICS

MICROBES

LIFESTYLE
Post-Prandial Glucose Response as a Measure of Healthy Nutrition

The Personalized Nutrition Project: Clinical and Microbiome Data Collected

1,000 PARTICIPANTS

BODY MEASURES

MICROBIOME

BLOOD TESTS

QUESTIONNAIRES
People Have a Widely Different Glucose Response to the Same Food
People Have a Widely Different Glucose Response to the Same Food

Zeevi et al., Cell, in press

Therapeutic Potential of The Microbiome

Microbiome was important in explaining the difference in meal glucose responses

Glucose responses were modifiable by changing what was eaten

This lead to exploring if the microbiome could accurately predict glucose response for a food or meal
How do we use trends to make predictions?

Machine Learning Process

**Inputs**
- Measure personal features

**AI & ML**
- Design personalized diet to lower glycemic responses

**Output**
- Predict personal glycemic responses

- Microbiome
- Blood tests and CGMS
- Questionnaires / Lifestyles
- Anthropometrics
- Food diary

**Personalized Nutrition Predictor**
Dietary interventions targeting post-meal glucose responses induce consistent changes in microbiota

- **Bifidobacterium adolescentis** decreases following the ‘good’ diet week
  - Low levels associate with greater weight loss (Santacruz et al., 2009)

- **Roseburia inulinivorans** increases following the ‘good’ diet week
  - Low levels associate with T2DM (Qin et al., 2012)
Glycemic Index vs Glycemic Response

Glycemic Index is an **Average**

- Original study was done with **10 people**
- Score is **0 to 100**
- Score of **55 or lower is good**
- Score based on **single food item**
- Amount of food scored is **set**
- Glycemic response **varies by an average of 20 percent**

Glycemic Response is **Personal**

- First study has **1000+ individuals**
- Score is **1 to 9.9**
- Score of **7 or higher is good**
- Score can be based on **single food or a combination of foods**
- Score **changes with amount** for meal or snack
- Results of score **reproducible**


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**Glucose response to bread is highly personalized and degree of personalization increases with food complexity**

*Korem et al., Cell Metabolism, 2017*
Mayo Clinic Study

Different glycemic response from Participants after eating a bagel and cream cheese.

Carbohydrate sensitivity is measured as the correlation between carbohydrates (in grams) in the meal consumed and the computed postprandial glycemic response.

Intervention Impact on Time-In-Range....Interim Results

Pre-Diabetes RCT in Weizmann

Algorithm Diet
60% avg reduction of time spent >140 mg/dl

Mediterranean Diet
10% avg reduction of time spent >140 mg/dl

*** P<0.0001

N=93 participants; Based on CGM Data
Intervention Impact on HbA1c...Interim Results

HbA1c average reduction of 0.62% in 3 months and 0.92% in 6 months

Algorithm diet reduces average glucose levels

*** P<0.0001
US Studies of the Microbiome Using Machine Learning

UCSD hires star biologist Rob Knight

Microbiome Test Samples Ready for Full Spectrum Sequencing

Major State Shifts in Microbial Ecology Phyla Between Healthy and Three Forms of IBD
The Adult Healthy Gut Microbiome Is Remarkably Stable Over Time

- Average of 200 species in the human gut
- Between 300 and 1000 species
- Most estimate there are 500

Source: Eric Alm, MIT

NASA’s Human Research Program

The Twins Study was the first study of its kind to compare molecular profiles of identical twin astronauts with one in space and another on Earth.

The Twins Study is a supplemental study built upon the framework of the One-Year Mission research investigations.

The Twins Study explores space through you by using omics (DNA, Gene Expression, Microbiome) to look more closely at individual health.

DR. MICHAEL SCHMIDT

CHRISTOPHER E. MASON, PH.D.
"The gut and its interrelationship with its microbiome is a fundamental arsenal of defense at first line that helps to protect us from everyday stuff out there that in the absence of it, we would not make it a day."
- Dr. Jeffrey Bland

Northwest Biologist with a Ph.D. in chemistry
Founder of the Institute for Functional Medicine
Leads the Personalized LifeStyle Medicine Institute
First member of the Board of Trustees of Bastyr University
Over 40 years researching nutrition at the cell level and 35 years as a recognized international leader in nutritional medicine

Hyperinsulinemia and Obesity

• High insulin levels are associated with increased risk of obesity
• Hyperinsulinemia increases the risk of weight regain after weight loss
• Higher glucose variability and insulin levels can result in increased hunger level making weight loss difficult

Karel A. Erion and Barabara E Corkey
Hyperinsulinemia: a Cause of Obesity
Current Obesity Reports 2017 May 2 6(2): 178-186
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5487935/
• 1/2 of pts with HTN are insulin resistant and have hyperinsulinemia

• High insulin levels linked to very-low-density lipoprotein synthesis and plasma triglyceride levels.

• Atherosclerotic Heart Disease and Rise in CHF is associated with high insulin levels


Hyperinsulinemia and Heart Disease

Hyperinsulinemia

Diabetes doubles the risk of developing cancers of the liver, pancreas and endometrium

Clear but smaller increase in risk for colon and breast cancers in people who have diabetes

Sources:
Hyperinsulinemia & Alzheimer’s Disease

After Insulin has lowered the glucose level, it must be degraded by the insulin-degrading (IDE) enzyme to prevent hypoglycemia.

IDE also degrades amyloid, the protein fragment found in synapse-destroying plaques in Alzheimer’s Disease.

IDE cannot degrade amyloid when the insulin is being degraded.

Hyperinsulinemia increased the risk of Alzheimer’s Disease.
Thank you!

Questions?
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