

# Effects of controlled diet and prebiotics on the microbiome

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		<input type="checkbox"/> Protocol
<b>Registration date</b> 23/02/2018	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
<b>Last Edited</b> 12/12/2018	<b>Condition category</b> Nutritional, Metabolic, Endocrine	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

There is increasing interest in studying the relationship between disease and the microbial communities inhabiting the human gut. However, relatively little is known about the impact of dietary patterns and other environmental influences on gut microbial composition, making identification of disease-specific microbial signatures in patient populations with a variable diet problematic. In particular, it has been observed in both mice and humans that the composition of fecal microbiota differs in obese versus lean individuals, prompting the hope that interventions targeting the gut microbiota may offer a viable complementary strategy for combating obesity moving forward. However, it remains to be shown that these differences are not directly attributable to the dietary habits of the individuals in question. Indeed, previous studies in humans have contrasted the effects of certain types of dietary interventions (e.g. plant-based versus animal-based diets) on the gut microbiome, giving us a coarse-grained appreciation of the microbial patterns associated with diet. This study aims to probe the specifics of diet-related microbial signatures by observing the effect of different dietary supplements on the gut microbiota of health individuals. The effect of introducing particular dietary supplements, such as specific types of dietary fibers or omega-3 fats, will be compared between these two populations, and further examine whether diet-related changes can explain the differences between their microbial compositions. In addition, the information can be used to correct for strong correlations between diet and the microbiome in analyses aiming to identify gut microbial signatures involved in a variety of human diseases.

### Who can participate?

Adults aged 18-70 who have a BMI between 18-25 or above 30.

### What does the study involve?

Participants provide stool samples on two consecutive days as baseline, during which participants consume their ordinary diet, as desired. In the evening of the second day, participants perform a bowel cleanse with PEG, and the following morning begin a period of six days during which their diet is fixed. The diet of the first three days are common to all participants, and consists of water and a nutritional meal replacement (Ensure) ad libitum. This is then followed by a further three days during which participants consume the nutritional meal replacement in addition to a specific micronutrient supplement to which they were randomized

at the beginning of the study. Supplements considered include inulin, pectin, cellulose, fish oil, coconut oil and protein powder. Participants are then instructed to resume their normal diet after day 6, and follow up samples are collected one day and one week after resuming their ordinary diet. Stool samples are collected daily (or, failing that, as often as possible), and processed for 16S rRNA and metagenomics sequencing to assess the effect on the composition of the microbiota.

What are the possible benefits and risks of participating?

There are no anticipated benefits or risks to participants of the study.

Where is the study run from?

Massachusetts Institute of Technology (USA)

When is the study starting and how long is it expected to run for?

June 2015 to December 2017

Who is funding the study?

MIT Center for Microbiome Informatics and Therapeutics (USA)

Who is the main contact?

Professor Eric Alm (Public)

Dr Thomas Gurry (Scientific)

## Contact information

### Type(s)

Public

### Contact name

Prof Eric Alm

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### Type(s)

Scientific

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Dr Thomas Gurry

### Contact details

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## Additional identifiers

Protocol serial number  
123456

## Study information

### Scientific Title

Predictability and persistence of prebiotic dietary supplementation in a healthy human cohort

### Study objectives

The study is based on the hypothesis that controlling dietary background will allow for higher resolution in our ability to discern individual bacterial species that respond to prebiotics.

### Ethics approval required

Old ethics approval format

### Ethics approval(s)

MIT Committee on the Use of Humans as Experimental Subjects, 29/06/2015, ref#: 1504007066.

### Study design

Interventional non randomised study

### Primary study design

Interventional

### Study type(s)

Other

### Health condition(s) or problem(s) studied

Diet and the microbiome

### Interventions

This study aims to identify the microbial responders to specific micronutrients in the human diet. By placing a cohort of approximately 50 healthy human individuals on a diet consisting entirely of a nutritional meal replacement milkshake and water, and controlling for dietary background, and against this background, supplement the participants' diet with individual micronutrients. Stool samples are collected and the bacterial DNA in them are sequenced to quantify the bacterial communities and the abundances of specific bacteria in each sample. In this manner, we are able to measure the effect of specific prebiotic supplements on the composition of the human gut microbiome.

Participants are placed on a diet consisting entirely of a liquid nutritional meal replacement for three days, and then for three further days in addition to a prebiotic spike-in of choice; microbiome composition is measured throughout the course of the intervention.

The study involves comparing the effects of a controlled diet in contrast to a variable diet on the composition of the gut microbiota. The methodology involves obtaining stool samples on two consecutive days as baseline, during which participants consume their ordinary diet, as desired. In the evening of the second day, participants perform a bowel cleanse with PEG, and the following morning begin a period of six days during which their diet is fixed. The composition of the diet on the first three days are common to all participants, and consists of water and a nutritional meal replacement (Ensure) ad libitum. This is then followed by a further three days during which participants consume the nutritional meal replacement in addition to a specific micronutrient supplement to which they were randomized at the beginning of the study. Supplements considered include inulin, pectin, cellulose, fish oil, coconut oil and protein powder. Participants are then instructed to resume their normal diet after day 6, and follow up samples are collected one day and one week after resuming their ordinary diet. Stool samples are collected daily (or, failing that, as often as possible), and processed for 16S rRNA and metagenomics sequencing to assess the effect on the composition of the microbiota.

### **Intervention Type**

Supplement

### **Primary outcome(s)**

Gut microbiota composition is measured using the stool samples collected on the two first baseline days and on each day during the provided dietary regimen. This consists of a maximum of 10 stool samples (two baseline, six intervention, and two follow-up), which are sequenced for the 16S rRNA gene.

### **Key secondary outcome(s)**

The effect of the diet on the microbiota at the level of genes and bacterial strains are processed for metagenomics sequencing at the second baseline sample, day 3 sample, and day 6 sample.

### **Completion date**

31/12/2017

## **Eligibility**

### **Key inclusion criteria**

1. Individuals between 18-70 years of age
2. BMI between 18-25 or above 30
3. A waist-to-hip ratio of more than 0.9

### **Participant type(s)**

Healthy volunteer

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

18 years

**Upper age limit**

70 years

**Sex**

All

**Key exclusion criteria**

1. Food allergies
2. Inability to comply with study procedure
3. Suffer from IBS, IBD, Type-2 diabetes, kidney disease or intestinal obstruction
4. Allergic to polyethylene glycol
5. Have received antibiotics in the last 6 months
6. Have untreated, in situ colorectal cancer
7. Are currently pregnant, planning to get pregnant in the next 60 days, or currently breastfeeding

**Date of first enrolment**

01/07/2015

**Date of final enrolment**

01/12/2017

**Locations****Countries of recruitment**

United States of America

**Study participating centre**

**Massachusetts Institute of Technology**

500 Technology Square

Cambridge

United States of America

02139

**Sponsor information****Organisation**

MIT Center for Microbiome Informatics and Therapeutics

**ROR**

<https://ror.org/042nb2s44>

**Funder(s)**

**Funder type**

University/education

**Funder Name**

MIT Center for Microbiome Informatics and Therapeutics

## Results and Publications

**Individual participant data (IPD) sharing plan**

The datasets generated (16S and shotgun metagenomics) during and/or analysed during the current study are/will be available upon request from the corresponding author, Prof. Eric Alm. Only deidentified data will be shared.

**IPD sharing plan summary**

Available on request

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	23/08/2018		Yes	No
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes