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Effects of controlled diet and prebiotics on the microbiome

Submission date	Recruitment status
02/02/2018	No longer recruiting
Registration date	**Overall study status**
23/02/2018	Completed
Last Edited	**Condition category**
12/12/2018	Nutritional, Metabolic, Endocrine

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] 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

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
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

Secondary study design
Non randomised study

Study setting(s)
Other

Study type(s)
Other

Participant information sheet
No participant information sheet available

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 measure
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.

Secondary outcome measures
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.

Overall study start date
29/06/2015

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

Age group
Adult

Lower age limit
18 Years

Upper age limit
70 Years

Sex
Both

Target number of participants
75

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

Sponsor details
500 Technology Square
Cambridge
United States of America
02139

Sponsor type
Research organisation

Website
microbiome.mit.edu

ROR
https://ror.org/042nb2s44

Funder(s)

Funder type
University/education

Funder Name
MIT Center for Microbiome Informatics and Therapeutics

Results and Publications

Publication and dissemination plan
We are currently undergoing peer-review and anticipate publication in a peer reviewed journal in early to mid-2018. No additional documents are available.

Intention to publish date
01/06/2018

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?
Results article	results	23/08/2018		Yes	No