

# Relationship between hormones that decrease blood glucose and the resident bacterial content of the intestine

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|--|---|---|
| <b>Submission date</b><br>25/09/2020   | <b>Recruitment status</b><br>No longer recruiting | <input type="checkbox"/> Prospectively registered<br><input type="checkbox"/> Protocol            |
| <b>Registration date</b><br>01/10/2020 | <b>Overall study status</b><br>Completed          | <input type="checkbox"/> Statistical analysis plan<br><input checked="" type="checkbox"/> Results |
| <b>Last Edited</b><br>06/12/2021       | <b>Condition category</b><br>Digestive System     | <input type="checkbox"/> Individual participant data  |

## Plain English summary of protocol

### Background and study aims

The gut microbiome is made up of trillions of bacteria, fungi and other microbes. The gut microbiome plays a very important role in health by helping control digestion and benefiting the immune system and many other aspects of health. In obese people, the diversity of the gut microbiome is reduced. Also, there are changes in chemical messenger substances (hormones) that communicate between the gut and fat cells in the body.

In this study, we plan to investigate the effect of weight loss in moderately obese patients on intestinal hormones, gut microbial composition, and the effect on the fat tissue.

### Who can participate?

Subjects with a body mass index (BMI) between 30 and 40 kg/m<sup>2</sup> with no known previous diseases, as well as a group of healthy control participants of a similar age range with BMI between 18 and 25 kg/m<sup>2</sup>

### What does the study involve?

Patients with obesity will be recruited and subjected to a reduced-calorie diet for six months, after which the initial assessments will be repeated to verify the effect of effective weight reduction on fat tissue.

### What are the possible benefits and risks of participating?

The benefits of participating in the study may be related to improvement associated with weight loss. Although it may be that no benefits are obtained.

### Where is the study run from?

Joan XXIII University Hospital in Tarragona (Spain).

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

June 2015 to June 2017

Who is funding the study?  
Carlos III Health Institute (Spain)

Who is the main contact?  
Prof. Joan J. Vendrell, jvo@comt.es

## Contact information

**Type(s)**  
Scientific

**Contact name**  
Prof Joan Josep Vendrell

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## Additional identifiers

**EudraCT/CTIS number**  
Nil known

**IRAS number**

**ClinicalTrials.gov number**  
Nil known

**Secondary identifying numbers**  
PI14/00228

## Study information

**Scientific Title**  
Incretin mediation on microbiome, metainflammation and adipose tissue plasticity. Functional study in an obese cohort after a dietary intervention

**Acronym**  
IncMic

**Study objectives**

The activity of glucagon-like peptides (GLPs) and gastric inhibitory polypeptide (GIP) on adipose tissue can influence the adipogenic, proliferative and functional capacity of human adipose-derived mesenchymal cells (hADSCs). Thus, differences in the dynamics of the GLPs/GLPRs and GIP/GIPR axis may influence the pattern of insulin resistance and metal inflammation associated with obesity and type 2 diabetes.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

Approved 03/11/2014, Hospital Universitari Joan XXIII ethics committee (Avda Mallafrè Guasch, 4, 43005 Tarragona, Spain; +34 977759394; no email provided), ref: 83/2014

### **Study design**

Interventional non randomized

### **Primary study design**

Interventional

### **Secondary study design**

Non randomised study

### **Study setting(s)**

Hospital

### **Study type(s)**

Other

### **Participant information sheet**

Not available in web format, please use the contact details below to request a patient information sheet

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

Relationship between hormones that decrease blood glucose and the resident bacterial content of the intestine

### **Interventions**

Equal numbers of non-morbidly obese and age-matched healthy controls will be recruited.

All participants will be prescribed a six-month low-calorie Mediterranean type Diet (20 Kcal/Kg baseline body weight), with 4 daily meals for 6 months (50% carbohydrates, 25- 30% lipids, and 20 to 25% protein) and will be encouraged to increase their physical activity. Monthly visits by a dietitian with a health status review and diet reminder recommendations will be scheduled.

Assessment will be carried out as follows:

Collection of clinical and anthropometric variables (age, sex, weight, height, BMI, BP). Analytical determination of complete blood count, glycemia, HbA1c, insulin, C peptide, total cholesterol, HDL and LDL and triglycerides, creatinine, MDRD, basic biochemistry. HOMA index ( $\text{glucose [mmol/l]} \times \text{insulin [mIU/l]} / 22.5$ ). Serum and plasma samples that will be frozen at -80C and stored in the HUJ23 Biobank for the subsequent determination of low-grade inflammation

markers (ultrasensitive C-reactive protein (PCRus), interleukin-6 (IL-6) and adiponectin. Stool collection. Biopsy of subcutaneous adipose tissue in obesity group.

Plasma concentrations of active GLP-1 (7-36 and 7-37) plasma levels of GLP-2 and Glucagon  
Standard food test (Meal test): Administration of 200ml of EDANEC (Abott Laboratories; 101kcal /100ml, of which 54% are carbohydrates, 16% proteins and 30% lipids). Extraction at 0, 15, 30, 60 and 120min. Determination of plasma concentrations of glucose, insulin, GLP-1, GLP-2.

Lipid overload test (Lipid test): Administration of a preparation (Patent No P201030776) that contains a total of 50g of fat (100ml) of which 30% is saturated, 49% monounsaturated and 21% polyunsaturated. unsaturated. Blood will be drawn at 0, 60, 120 and 180 min for the determination of plasma concentrations of GLP-1, GLP-2 and triglycerides.  
The two tests will be carried out on two different days (at least 3 days apart) and after a fasting period of 12 hours.

Intestinal permeability study: Administration of a solution with 10g of Lactulose and 5g of Mannitol in 100ml of water. Urine collection for 5h. The permeability index (lactulose/mannitol ratio) will be analyzed by HPLC.

Microbiota study: Extraction of both microbial and host genomic DNA using the PowerFecal DNA Isolation Kit (MOBIO) system. Mesenchymal ADSCs from patients with different degrees of obesity will be obtained before and after weight loss.

## **Intervention Type**

Behavioural

## **Primary outcome measure**

Measured at every visit at baseline and every month until the end of the study:

1. Bodyweight (kg)
2. Height (m)
3. Waist circumference (cm)
4. Blood pressure (mmHg)

At baseline and 6 month follow up:

5. Meal Tolerance Test (MTT) (blood will be taken before meal ingestion (time 0 min) and at 15, 30, 60, and 120 min after meal ingestion)
  - 5.1. GLP-1 and GLP-2 assessed using ELISA methods
  - 5.2. Glucose, cholesterol, and triglycerides determined using standard enzymatic methods
  - 5.3. Plasma insulin analyzed by immunoassay
6. A study of the intestinal microbiome-related with the incretin response will be determined using shotgun sequencing of stool DNA for whole metagenome analysis

## **Secondary outcome measures**

There are no secondary outcome measures

## **Overall study start date**

01/06/2015

## **Completion date**

30/06/2017

# Eligibility

## Key inclusion criteria

- 1.1. Obese group: Non-morbid obese subjects with a body mass index (BMI) range  $\geq 30$  to  $\leq 40$  kg/m<sup>2</sup>
- 1.2. Control group:
  2. Aged  $>18$  and  $<65$  years
  3. Absence of acute or chronic systemic disease (other than obesity)
  4. Absence of any pharmacological treatment and weight stability at least during the 3 previous months before entry in the study
  5. Informed consent signed
  6. BMI range  $\geq 18$  to  $\leq 25$  kg/m<sup>2</sup>

## Participant type(s)

Mixed

## Age group

Adult

## Lower age limit

18 Years

## Sex

Both

## Target number of participants

20

## Total final enrolment

36

## Key exclusion criteria

Both groups:

1. Active smokers
2. Alcohol intake  $>40$ gr/day
3. Presence of other cardiovascular risk factors except obesity (arterial hypertension, dyslipidemia, diabetes mellitus or history of disease cardiovascular disease)
4. Moderate-severe chronic liver disease or chronic renal failure
5. Chronic inflammatory diseases
6. Surgery or recent hospital admission ( $<3$  months)
7. Glucocorticoid treatment in the last 6 months
8. Neoplasia in the previous 5 years
9. Pregnancy or lactation

## Date of first enrolment

01/06/2016

## Date of final enrolment

30/01/2017

# Locations

## Countries of recruitment

Spain

## Study participating centre

Hospital Universitari Joan XXIII

Mallafre Guasch, 4

Tarragona

Spain

43005

# Sponsor information

## Organisation

Institut d'Investigació Sanitària Pere Virgili

## Sponsor details

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## Sponsor type

Research organisation

## Website

[http://www.iispv.cat/en\\_index.html](http://www.iispv.cat/en_index.html)

## ROR

<https://ror.org/01av3a615>

# Funder(s)

## Funder type

Government

## Funder Name

Instituto de Salud Carlos III

**Alternative Name(s)**

SaludISCI, Instituto de Salud Carlos III, Instituto de Salud Carlos III | Madrid, Spain, Carlos III Institute of Health, Institute of Health Carlos III, Carlos III Health Institute, ISCI

**Funding Body Type**

Government organisation

**Funding Body Subtype**

National government

**Location**

Spain

## Results and Publications

**Publication and dissemination plan**

Planned publication in a high-impact journal.

**Intention to publish date**

01/04/2021

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

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

**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> |         | 06/11/2021   | 06/12/2021 | Yes            | No              |