RELACIÓN ENTRE LA MICROBIOTA INTESTINAL Y LA SALUD Y CONTRIBUCIÓN DE LA FIBRA EN LA DIETA

Laboratorio de Ecología Microbiana, Nutrición y Salud.
MARINA ROMANÍ-PÉREZ
OVERVIEW

1. GUT MICROBIOTA
2. GUT MICROBIOTA & DISEASES. OBESITY
3. MICROBIOME-BASED INTERVENTIONS FOR PROMOTING METABOLIC HEALTH. PREBIOTICS & PROBIOTICS
4. MICROBIOTA-BY-DIET INTERACTION. SCFAs
5. GUT MICROBIOTA-HOST COMMUNICATION
6. GROUP OF MICROBIAL ECOLOGY, NUTRITION AND HEALTH. ‘On the way to evaluate new probiotics’
   6.1 Evaluation of the potential probiotic *Bacteroides uniformis* CECT 7771
   6.2 Evaluation of dietary fiber supplementation (WBE) combine with *B. uniformis* CECT 7771 intervention
39 trillion microbial cells
1-3% of body mass

10 times more cells than human cells
150 times more genes than human genes

Body habitat groups

The Human Microbiome Project Consortium
1. GUT MICROBIOTA

PHYLOGENY OF BACTERIAL PHYLA

**Firmicutes**
Clostridium, Enterococcus, Lactobacillus and Ruminococcus

**Bacteroidetes**
Bacteroides and Prevotella

**Actinobacteria**

**Proteobacteria**

**Host Phenotype Plasticity**

DIET

Dynamic microbial community structure among individuals

Synergy

HOST

Host genome

Gender

Drugs

Antibiotics

Stress

Aging

Delivery mode

1. GUT MICROBIOTA
1. GUT MICROBIOTA

Stability of metabolic pathways among individuals

Phyla

- Firmicutes
- Bacteroidetes

Gut microbiota

- Firmicutes
- Actinobacteria
- Bacteroidetes
- Proteobacteria
- Fusobacteria
- Tenericutes
- Spirochaetes
- Cyanobacteria
- Verrucomicrobi

CH metabolism

- Cofactor & Vitamin biosynthesis
- Oligosaccharide and polyol transport system
- Purine metabolism
- ATP synthesis
- Phosphate and amino acid transport system
- Aminocetyl tRNA
- Pyrimidine metabolism
- Ribosome
- Aromatic amino acid metabolism

The Human Microbiome Project Consortium

HOST

Gut microbiota

- Energy harvest
- Protection against pathogens
- Immunomodulation
- Energy metabolic status

Nutrients

Shelter
1. GUT MICROBIOTA & HOST

**SYMBIOSIS**

**HOST**

**SYMBOIONS**

**MUTUALISM**

**COMMENSALISM**

**PARASITISM**

**SYMBIONTS**

**PATHOSYMBIONTS**

**Eubiosis**

**Dysbiosis**

**Immune homeostasis**

**Healthy state**

**Intestinal and extra-inestinal inflammatory DISEASES**

**Proinflammatory state**

**DC**  
**T cells**  
**M1**  
**Treg**  
**M2**  
**B cells**
Dysbiosis

PATHOSYMBIONTS

SYMBIONTS

Chronic

Intestinal and extra-intestinal Inflammatory DISEASES
- Inflammatory bowel disease
- Celiac disease
- Cardiovascular diseases
- Mental diseases (emotional, cognitive-related diseases; anxiety, depression, autism, etc)
- Metabolic diseases: Diabetes (T1D or T2D), Obesity, metabolic syndrome

A Pyrosequencing Study in Twins Shows That Gastrointestinal Microbial Profiles Vary With Inflammatory Bowel Disease Phenotypes

Author's Accepted Manuscript

Psychosomatic Medicine

Article Title: Brain-gut-microbiota axis in psychiatry: novel paradigm or false dawn?

Authors: Timothy G. Dinan and John Cryan

Intermittent Fasting Promotes White Adipose Browning and Decreases Obesity by Shaping the Gut Microbiota

Author Manuscript In Press
2. GUT MICROBIOTA & OBESITY

KEY FACTS OF OBESITY

• \(\uparrow\) prevalence from 1975 (x3)
• In 2016:
  • ADULTS: 39% overweight and 13% obese.
  • CHILDREN & ADOLESCENTS: 18% overweight or obese
• Obesity ranks fifth in risk of global deaths in the general population
• \(\uparrow\) prevalence in low and middle-income countries
• OBESITY IS PREVENTABLE
2. GUT MICROBIOTA & OBESITY

PATHOPHYSIOLOGY OF OBESITY

BMI: Kg/m² (body mass index)

Overweight: 25 ≥ BMI ≤ 30
Obesity: BMI ≥ 30

Insulin resistance

Metabolic comorbidities
T2D, NAFLD, dyslipidaemia, cardiovascular disease, etc

State of Chronic low-grade of inflammation

Metabolic profile

Energy intake
Energy expenditure

Energy imbalance

GUT MICROBIOTA & OBESITY PATHOPHYSIOLOGY OF OBESITY

www.who.int
2. GUT MICROBIOTA & OBESITY

- **ENERGY IMBALANCE**
  - Over-eating
  - Adiposity
  - Glucose intolerance
  - Insulin resistance

- **ENERGY BALANCE**
  - Restoration of gut-brain communication

Genetic factors: 30-40% (30-40%) vs. 70-60%

Environmental factors:
- Sedentary lifestyle
- DIET: Energy-dense foods
- Gut microbiota

Brain-Hypothalamus-Gut-brain-periphery axis

Anti-obesity interventions
An obesity-associated gut microbiome with increased capacity for energy harvest

Peter J. Turnbaugh¹, Ruth E. Ley¹, Michael A. Mahowald³, Vincent Magrini³, Elaine R. Mardis¹,² & Jeffrey I. Gordon¹

Gut microbial communities

Extraction and storage of energy from diet

Individual predisposition to obesity

Gut microbiota is an environmental factor of obesity
2. GUT MICROBIOTA & OBESITY

Gut Microbiota from Twins Discordant for Obesity Modulate Metabolism in Mice
Vanessa K. Ridaura et al.
Science 341, (2013);
DOI: 10.1126/science.1241214

Discordant Twins
Lean GF mice
Obese GF mice

Microbiota invasion depends on microbiota-by-diet interaction
LoSF-HiFV
HiSF-LoFV
Gut microbiota invasion linked to leaness

Cohousing
Bacteroidetes invasion

Lean (Ln) Obese (Ob)
2. GUT MICROBIOTA & OBESITY

**Human gut microbes associated with obesity**
Ley et al, Nature 2006

- **FAT-R**, fat restricted
- **CARB-R**, carbohydrate restricted

**Obesity alters gut microbial ecology**
Ruth E. Ley¹, Fredrik Bäckhed¹, Peter Turnbaugh⁷, Catherine A. Lozupone⁸, Robin D. Knight⁹, and Jeffrey I. Gordon¹⁰

**Firmicutes**
Clostridium, Enterococcus, Lactobacillus and Ruminococcus

**Bacteroidetes**
Bacteroides and Prevotella

**Actinobacteria**

**Proteobacteria**

Ob/ob 50% fewer Bacteroidetes

**Manipulation of microbial community structure**

**MICROBIOME-BASED interventions for promoting metabolic health**

**PREBIOTICS**

**PROBIOTICS**

**FECAL TRANSFER**
3. MICROBIOME-BASED INTERVENTIONS FOR PROMOTING METABOLIC HEALTH

**Microbiome-based interventions**

- Alter composition/activity of host gut microbiota
- Health benefit
- Metabolic Health

**Next generation of Probiotics**
(Live microorganisms)

**Prebiotics**
(Food grade component)

**Microbiota replacement**
(FMT, microbiota community transfer)

- **Akkermansia muciniphila**
  - ↓ Fat mass
  - ↓ AT inflammation
  - ↑ GLP-1, PYY
  - ↑ inflammation (INFγ)
  - ↑ acylglycerols

- **Bacteroides acidifaciens**
  - ↓ Food intake

- **Eubacterium hallii**
  - ↑ GLP-1, PYY
  - ↑ inflammation (INFγ)

- **SCFAs**
  - Acetate
  - Propionate
  - Butyrate
  - FFAR2, FFAR3

- **GLP-2**
  - ↑ Gut barrier integrity
  - ↓ Inflammation

- **Butyrate**
  - ↑ Thermogenesis

- **Acetate**
  - ↑ Thermogenesis

- **Propionate**
  - ↑ Thermogenesis

- **SCFAs**
  - ↑ Thermogenesis

- **Lean healthy donor**

- **Brain**
  - ↓ Food intake

- **OST**
  - ↑ TGR5

- **α**
  - ↑ TGR5

- **β**
  - ↑ TGR5

- **γ**
  - ↑ TGR5

- **PPAR**
  - ↑ TGR5

- **Browning**
  - ↑ Thermogenesis

- **Gut barrier integrity**
  - ↑ Thermogenesis

- **Microbiota replacement**
  - (FMT, microbiota community transfer)

- **Lean healthy donor**

- **Microbiota replacement**
  - (FMT, microbiota community transfer)

- **Next generation of Probiotics**
  - (Live microorganisms)

- **Prebiotics**
  - (Food grade component)

- **Microbiome-based interventions**
  - Alter composition/activity of host gut microbiota
  - Health benefit
  - Metabolic Health
### 3.1 PREBIOTICS

**DIETARY FIBER:** indigestible plant polysaccharides

<table>
<thead>
<tr>
<th>NUTRIENT</th>
<th>Natural SOURCE</th>
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<tbody>
<tr>
<td><strong>Water-insoluble dietary fibers</strong></td>
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<tr>
<td>Cellulose</td>
<td>Cereals, Fruit, Vegetables</td>
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<tr>
<td>Hemicellulose</td>
<td>Cereals, Bran, Legumes</td>
</tr>
<tr>
<td>Lignin</td>
<td>Cereals, Garden beans</td>
</tr>
<tr>
<td>Resistant starch</td>
<td>Corn, Wheat, Barley</td>
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</table>

<table>
<thead>
<tr>
<th>NUTRIENT</th>
<th>Natural SOURCE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Water-soluble dietary fibers</strong></td>
<td></td>
</tr>
<tr>
<td>Inulin</td>
<td>Chicory root, Onion</td>
</tr>
<tr>
<td>Fructooligosaccharides (FOS)</td>
<td>Leek, Banana</td>
</tr>
<tr>
<td>Arabinoxylan (Hemicellulose)</td>
<td></td>
</tr>
<tr>
<td>Arabinoxylan oligosaccharides (AXOS)</td>
<td></td>
</tr>
<tr>
<td>Pectin</td>
<td>Fruits, Corn, Carrots</td>
</tr>
<tr>
<td>Non-starch polysaccharide (NSP)</td>
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</tr>
</tbody>
</table>
3.2 PROBIOTICS

‘Classical’ probiotics

- Currently commercialized probiotics
- Lactic acid bacteria and bifidobacteria
- Biological samples or derived from fermented foods

Next Generation of Probiotics (NGP)

- Massive use of DNA sequencing in controlled (16S rRNA gene-based approach, whole-genome shotgun-based approach) epidemiological studies
- NGP: Selected functionally distinct indigenous bacteria with potential higher efficacy of current probiotic formulation
- Evaluation of the administration of A. muciniphila on parameters of Metabolic Syndrome

Probiotic for FOOD

Strain identification

Functional characterization → Safety assessment → Efficacy

Phase 2 human trial (DBPC). Probiotic vs placebo

Phase 3 human trial. Probiotic vs standard treatment

ClinicalTrials.gov Identifier: NCT02637115

Sponsor: Patrice D. Cani

Romani-Pérez M et al, 2017
Different diets in human population

**Burkina Faso children**
DIET: high in FIBER and low in fat

**European children**
DIET: high in animal PROTEIN, SUGAR and FAT. Low in fiber

Metabolic phenotype plasticity

4. MICROBIOTA-BY-DIET INTERACTION. SCFAs

De Filippo et al, PNAS 2010
4. MICROBIOTA-BY-DIET INTERACTION. SCFAs

**DIETARY FIBER**

- Gut microbiota metabolic routes
- **SHORT CHAIN FATTY ACIDS**

**Bacteroides**
Resistant starches (1, 4), arabinoyxylans, pectin, inulin, FOS, mucin, mucopolysaccharides

**Fermentations**

- Non digestible CHO
- Oxalacetate → Pyruvate → Formate or H₂ + CO₂ → Acetyl-CoA → Acetate
- Butyrogenic cross-feeding
- Butyrate
- Lactate to propionate cross-feeding

**Acetate Producers:**
- Bacteroides (B. thetaotaomicron)
- Proteobacteria (Desulfovibrio pigren)
- Ruminococcus
- Bifidobacteria
- Clostridia
- Eubacteria
- Fusobacteria
- Peptococci
- Peptostreptococci
- Propionibacteria
- Veillonella

**Butyrate Producers:**
- Mainly Clostridium clusters
- X/IV and X: *P. prausnitzii*
- E. rectale
- E. hallii
- R. bromide
- Roseburia spp.
- Aecetobutylicum

**Propionate Producers:**
- Mainly Bacteroidetes* (Bacteroides)
- Clostridia (Clostridium cluster IX)
- Propionibacteria*
- Valiella*

**Succinate Producers:**
- Bacteroides fragilis
- Propionibacterium spp., and Veillonella spp.
  - Produce both succinate and propionate

**Lactate Degraders:**
- *E. rectale and Roseburia* to generate butyrate

**Butyrate Degraders:**
- Sulfate- or nitrate-reducing anaerobic bacteria
- Aecetobutylicum
- Aecetagecum,
- Eubacterium, and Clostridium species degrade butyrate and propionate into acetate

SCFAs: biactive molecules

In the gut, short-chain fatty acids (SCFAs) act as biactive molecules, influencing various cellular responses. These include:

- Enteroendocrine cells
- Neurons
- Immune cells

The Microbial Metabolites, Short-Chain Fatty Acids, Regulate Colonic Treg Cell Homeostasis

5. GUT MICROBIOTA-HOST COMMUNICATION

Wheat-derived arabinoxylan oligosaccharides with prebiotic effect increase satietogenic gut peptides and reduce metabolic endotoxemia in diet-induced obese mice

Inulin-type fructans modulate gastrointestinal peptides involved in appetite regulation (glucagon-like peptide-1 and ghrelin) in rats

In immune homeostasis, SCFAs interact with immune cells, promoting a balanced immune response.

In colonic transit, SCFAs regulate motility, influencing the release of neurotransmitters such as ACh.

Energy homeostasis is maintained through the interaction of gut hormones with the central nervous system and the enteric nervous system.
Obesity → State of Chronic low-grade of inflammation

Adipose tissue

Increased M1/M2 ratio

Cytotoxic T cells

Th1 and Th17

B cells

Insulin resistance

Systemic Insulin resistance

Metabolic endotoxemia

Systemic inflammation

IL-6, TNF-α, IL-1β

Leptin

Dysbiosis

High fat diet

TLRs

Intestinal immunity

Gut microbiota

Gut permeability

Inflammatory mediators

Innate immunity

Adaptive immunity

CD4+

CD8+

MCHI

MCHII

MLN

DC

T cells

M1

Treg

M2

B cells

DNA

PGN

LPS

SCFAs

MLN

NOD

IFN-γ

Ab

Wire et al. Cell Metabolism 2016
Evaluation of probiotics for food

- Strain identification
- Functional characterization
- Safety assessment

Phase 2 human trial (DBPC)
Probiotic vs placebo

Phase 3 human trial
Probiotic vs standard treatment

Probiotic for FOOD

Pathophysiology of metabolic and inflammatory diseases
6.1 ‘On the way to evaluate new probiotics’

**In vitro functional characterization of Bacteroides uniformis CECT 7771**

- Higher abundance in breast-fed than in formula-fed infants.
- **B. uniformis CECT 7771** isolated from stools of healthy breast-fed infants.

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**Table 2. Effect of different Bacteroides strains on cytokine production by RAW264.7 macrophages.**

<table>
<thead>
<tr>
<th>Bacteroides strains</th>
<th>Cytokine production</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TNF-α (pg/ml)</td>
</tr>
<tr>
<td>DEMEN</td>
<td>491.2(112.1)</td>
</tr>
<tr>
<td>LPS</td>
<td>1425.6(37.6)</td>
</tr>
<tr>
<td>B. dorei SS1</td>
<td>3765.5(150.0)</td>
</tr>
<tr>
<td>B. ovatus SU2</td>
<td>4515.7(211.3)</td>
</tr>
<tr>
<td>B. distasonis CAY3</td>
<td>4462.4(173.9)</td>
</tr>
<tr>
<td>B. uniformis CECT 7771</td>
<td>2998.4(50.4)</td>
</tr>
<tr>
<td>B. thetaiotamicron SAC4</td>
<td>2931.2(464.5)</td>
</tr>
<tr>
<td>B. fragilis SK3</td>
<td>6657.3(278.3)</td>
</tr>
<tr>
<td>B. caccae SV3</td>
<td>11622.8(318.3)</td>
</tr>
<tr>
<td>B. firegoldii SX2</td>
<td>6535.8(62.2)</td>
</tr>
</tbody>
</table>

**6.1 ‘On the way to evaluate new probiotics’ in vivo functional characterization of *Bacteroides uniformis* CECT 7771**

**In vivo Functional characterization of *Bacteroides uniformis* CECT 7771**

**DIET INDUCED OBESITY (DIO)**

<table>
<thead>
<tr>
<th>DIET</th>
<th>PROTEINS (% of Kcal)</th>
<th>CH (% of Kcal)</th>
<th>FAT (% of Kcal)</th>
<th>FRUCTOSE (% of Kcal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SD</td>
<td>23</td>
<td>64</td>
<td>13 (corn oil)</td>
<td>0</td>
</tr>
<tr>
<td>HFHFD</td>
<td>18</td>
<td>34</td>
<td>48 (palm oil)</td>
<td>20</td>
</tr>
</tbody>
</table>

**Placebo (10% skimmed milk)**

- B. *uniformis* CECT 7771 (1X10⁹ CFU)

**Placebo (10% skimmed milk)**

- B. *uniformis* CECT 7771 (1X10⁹ CFU)

**weeks**

- 10
- 14

**OGTT**

**IMMUNOMETABOLIC PARAMETERS**

- Peyer’s Patches
- Blood
- Fecal samples
- Gut microbiota

**Lympoid cells**: B cells and T cells

**Myeloid cells**: macrophages

**Cytokines**

**Blood**

- Triglycerides
- Cholesterol
- Glucose
- Leptin
6.1 ‘On the way to evaluate new probiotics’

in vivo functional characterization of *Bacteroides uniformis* CECT 7771
Mechanistic understanding of how *B. uniformis* promote anti-obesity effects

6.1 ‘On the way to evaluate new probiotics’ *in vivo* functional characterization of *Bacteroides uniformis* CECT 7771

**ANTIINFLAMMATORY RESPONSE**

**PROINFLAMMATORY STATE**

Dendritic cells (DC)

Cytotoxic T cell (cyt T)

regulatory T cells (Treg)

Lean phenotype

Obese phenotype

**Blood**

Peyer’s Patches

**Adipose tissue**
6.1 ‘On the way to evaluate new probiotics’ in vivo functional characterization of Bacteroides uniformis CECT 7771

PROTEINS (% of Kcal)
CH (% of Kcal)
FAT (% of Kcal)
FRUCTOSE (% of Kcal)
SD 23 64 13 (corn oil)
HFHFD 18 34 48 (palm oil)

DIET

PROINFLAMMATORY STATE

ANTIINFLAMMATORY STATE

On the way to evaluate new probiotics...
TLRs

6.1 ‘On the way to evaluate new probiotics’ *in vivo* functional characterization of *Bacteroides uniformis* CECT 7771

**ileum**

**Peyer’s Patches**

**Adipose tissue**

Lean phenotype

Obese phenotype

TLR2

TLR4

TLR5

SD

HFHFD

**PROTEINS** (% of Kcal)

**CH** (% of Kcal)

**FAT** (% of Kcal)

**FRUCTOSE** (% of Kcal)

SD 23 64 13 (corn oil)

0

HFHFD 18 34 48 (palm oil)

20

**Diet**

**B cells (%)**

placebo B. uniformis

HFHFD

SDa b b b

B cells (%)
6.1 ‘On the way to evaluate new probiotics’ in vivo functional characterization of *Bacteroides uniformis* CECT 7771
6.1 ‘On the way to evaluate new probiotics’

*in vivo* functional characterization of *Bacteroides uniformis* CECT 7771

**Summary**

Pro-inflammatory state  →  Insulin resistance  →  obese-like phenotype

Anti-inflammatory effects  →  Insulin sensitivity  →  lean-like phenotype

**TLR5?**

**Adipose tissue**

- M1/M2
  - IL-33
  - IL-10
- TNF-α
- IL-6
- IL-1α
- IL-10

**Peyer’s Patches**

- M1/M2
  - IL-33
  - IL-10
- IFN-γ

**TLR5**

- TLR4
- TLR2

**dc**

- IFN-γ

**B. uniformis CECT 7771**

- LPS

**Helicobacter**

**HFHFD**

**T5KO mice**  →  metabolic syndrome

*Vijay-Kumar et al. 2010*
Normal general health status: activity and behavior
- No difference in body weight gain or loss
- No bacterial translocation (blood, liver or mesenteric lymph nodes)

Normal kidney function

Normal liver function

Normal pancreatic function

Normal Gut mucosa integrity
Normal gut integrity
Immunosupression reduced:
- globet cells and villus height/crypt depth ratio in jejunum.
- crypt width in the colon.
- *B. uniformis* CECT 7771 reversed the reduced height/crypt depth ratio in jejunum

Antiinflammatory response
*B. uniformis* CECT 7771 reduced pro-inflammatory cytokines
*B. uniformis* CECT 7771 restored inflammatory cytokines of immunosuppressed mice

Ongoing experiment

Chronic toxicity assay: 3 months
6.2 ‘On the way to evaluate new probiotics’

*In vitro* functional characterization of WBE and *B. uniformis* CECT 7771 intervention

**Prebiotic & Probiotic intervention for FOOD**

- Anti-obesity strategies
- *Bacteroides* spp: glycan enriched environments

**Carbon source (0.5% w/v)**
- Glucose
- Inulin
- Wheat Bran Extract (WBE)
- Gum arabic
- Pectin
- Type II mucin

**Growth fitness of *B. uniformis* CECT 7771 in different dietary fibers**

- Growth phenotypes
- Doubling time in the log phase

- *Doubling time (mins)*
  - Glucose
  - Gum arabic
  - WBE
  - Inulin
  - Mucin
  - Pectin

- *Non-digestible carbohydrates: Arabinoxylans*
- Arabinoxylan-degrading enzymes
- Arabinoxylan oligosaccharides (AXOS)
- SCFA (propionate)

**Analysis**

- Optical Density (600 nm)
- Time (hours)

**Metabolic health**
6.2 ‘On the way to evaluate new probiotics’

**Functional characterization**

*in vitro*  *in vivo*

**DIET INDUCED OBESITY (DIO)**

<table>
<thead>
<tr>
<th>Kcal(%)</th>
<th>Proteins</th>
<th>CH</th>
<th>Sucrose</th>
<th>Fat</th>
<th>WBE</th>
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<tbody>
<tr>
<td>SD</td>
<td>20</td>
<td>70</td>
<td>0</td>
<td>10</td>
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</tr>
<tr>
<td>HFHS</td>
<td>20</td>
<td>35</td>
<td>20</td>
<td>45</td>
<td>0</td>
</tr>
<tr>
<td>HFHS+WBE</td>
<td>20</td>
<td>35</td>
<td>20</td>
<td>45</td>
<td>5</td>
</tr>
</tbody>
</table>

- Placebo (10% skimmed milk)
- B. uniformis CECT 7771 (1X10^7 CFU)

**weeks**

- 14
- 17

OGTT  IMMUNOMETABOLIC PARAMETERS

**Prebiotic & Probiotic intervention for FOOD**

**Anti-obesity strategies**

**in vivo** functional characterization of WBE and *B. uniformis* CECT 7771 intervention

**Functional characterization on metabolic phenotype of WBE+B. uniformis CECT 7771 intervention**
6.2 ‘On the way to evaluate new probiotics’ in vitro functional characterization of WBE and B. uniformis CECT 7771 intervention

Preliminary results

**Graph 1:** Body weight gain (g) over time for different groups: SD-Vehicle, HFHS, HFHS+WBE, HFHS B. uniformis

**Graph 2:** Glycemia (mg/dL) over time for different groups: SD, HFHS, HFHS+WBE, B. uniformis

**Legend:**
- SD
- HFHS
- HFHS+WBE
- B. uniformis

**Significance Levels:**
- * p at least <0.05
- ** p at least <0.01
- *** at least p<0.001
- **** at least p<0.0001

**Note:** At least p<0.05 indicates a statistically significant difference.
6.2 ‘On the way to evaluate new probiotics’

In vitro functional characterization of WBE and B. uniformis CECT 7771 intervention

ONGOING EXPERIMENTS

IMMUNOMETABOLIC PARAMETERS

ENERGY HOMEOSTASIS

Lamina propria

Epithelium

WAT

BAT

Lympoid cells: B cells, T cells, IEL

Myeloid cells: macrophages, ILCs

Cytokines

Fecal samples

Gut microbiota composition

Blood

Triglycerides

Cholesterol

Glucose

Leptin

Insulin

Gut hormones

Hypothalamus

Hypotalamic neuropeptides

Duodenum

ILEum

Colon

WAT

Liver

Energy metabolism

SCFA receptors

DUODENUM

ILEUM

COLON

Liver

Triglycerides

Cholesterol

Glucose

Leptin

Insulin

Gut hormones

Hypothalamus

Hypotalamic neuropeptides

Duodenum

Ileum

Colon

WAT

Liver

Energy metabolism

SCFA receptors

Duodenum

Ileum

Colon
THANK YOU FOR YOUR ATTENTION