

# Microbiota Intestinal



# Contenido

- Microbiota hot topic
- Microbiota y enfermedades metabolicas
- ¿Como se puede cambiar la microbiota?



# Microbiota hot topic



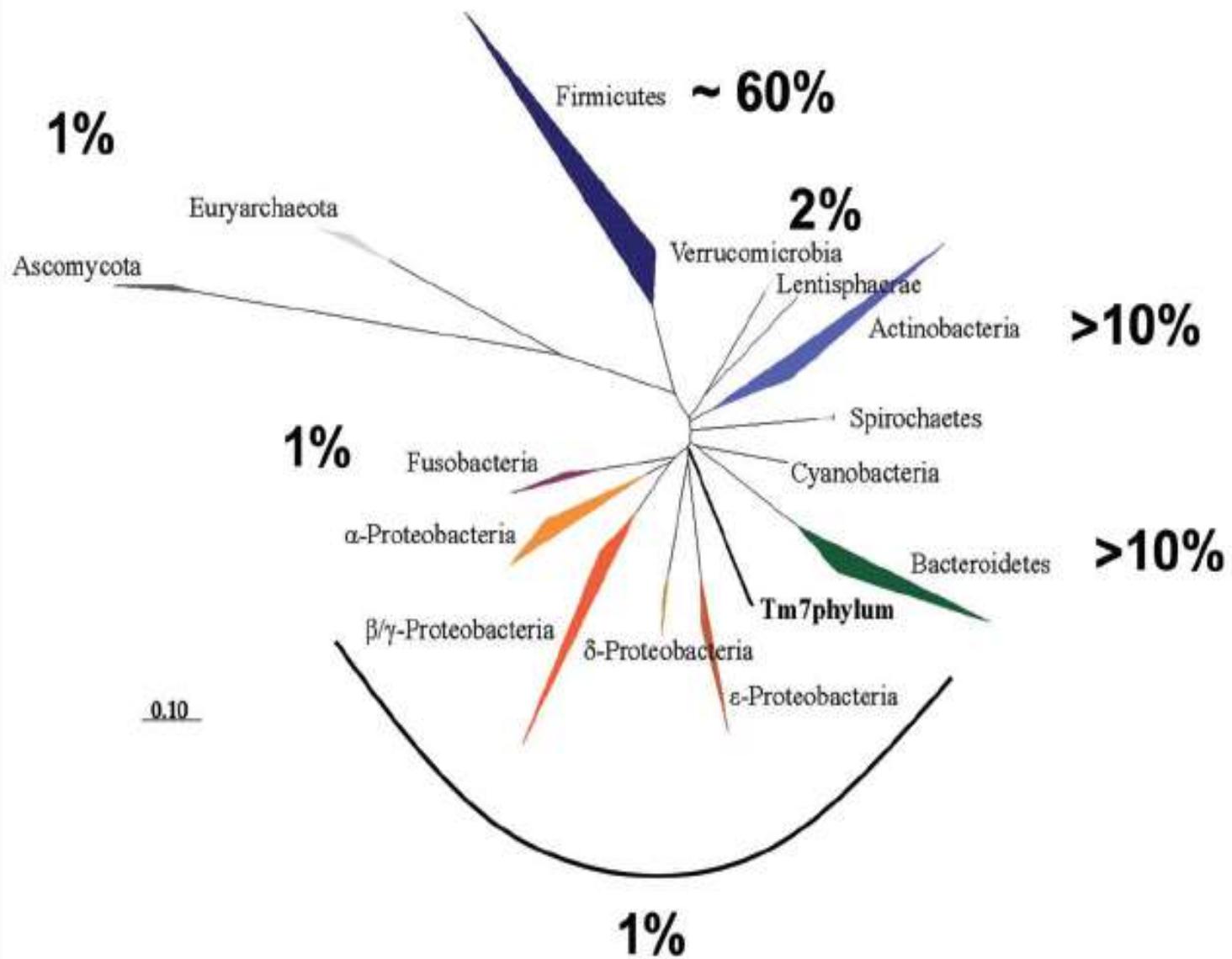
# *Publicaciones en las que aparece como tópico microbiota*



# *MICROBIOTA*

- Tienen un peso de 1.5 Kg.
- 10 veces más células que las células del ser humano
  - 100 billones de bacterias
    - 1000 especies
    - 150 veces mas genes que el genoma humano.





# *FUNCIÓNES DE LA MICROBIOTA*

## **FUNCIÓN INMUNE**

- Destrucción toxinas /carcinógenos
- Colonización por bacterias patógenas
  - Desarrollo del SI
- Modulación del estado inflamatorio

## **FUNCIÓN DIGESTIVA**

- Motilidad digestiva
- Síntesis micronutrientes
- Absorción electrolitos/ minerales
- Fermentación sustancias indigeribles

Gill, SR et al. Metagenomic analysis of the human distal gut microbiome. Science. 2006; 312 (5778): 1355-59.



*Está cambiando la microbiota en  
el ser humano en las últimas  
décadas*



# CAMBIOS EN ECOLOGÍA HUMANA AFECTAN A LA COMPOSICIÓN DE LA MICROBIOTA

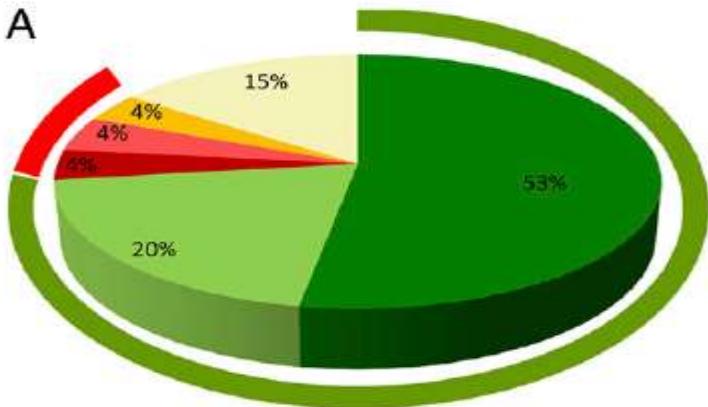
| CHANGE                                      | CONSEQUENCES                    |
|---|---------------------------------|
| Water sanitation                            | Fecal transmission decrease     |
| Cesarean surgery increase                   | Vaginal transmission decrease   |
| Increase of the antibiotic use in preterm   | Vaginal transmission decrease   |
| Lactation reduction                         | Cutaneous transmission decrease |
| Small families                              | Early contamination decrease    |
| Antibiotic use increase                     | Microbiota changes              |
| Antibacterial soaps and toiletries increase | Microbiota changes              |
| Mercury-amalgam dental filling increase     | Microbiota changes              |

*Nature Reviews Microbiology* | AOP, published online 9 November 2009;



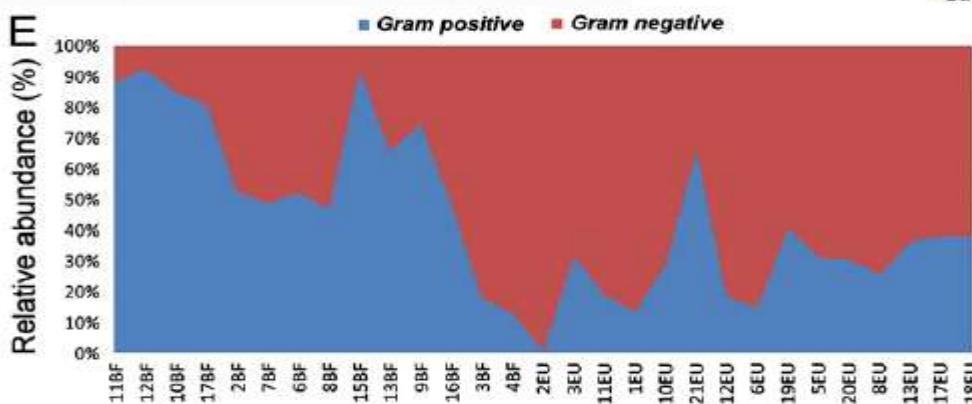
## B. FASO CHILDREN

A



BF

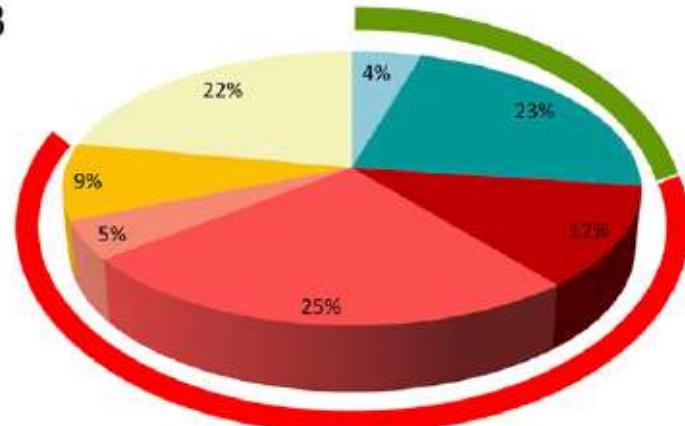
- Prevotella ] Bacteroidetes
- Xylanibacter ]
- Acetitomaculum ]
- Faecalibacterium ] Firmicutes
- Subdoligranulum ]
- Others ]



De Filippo et al.

## EUROPEAN CHILDREN

B

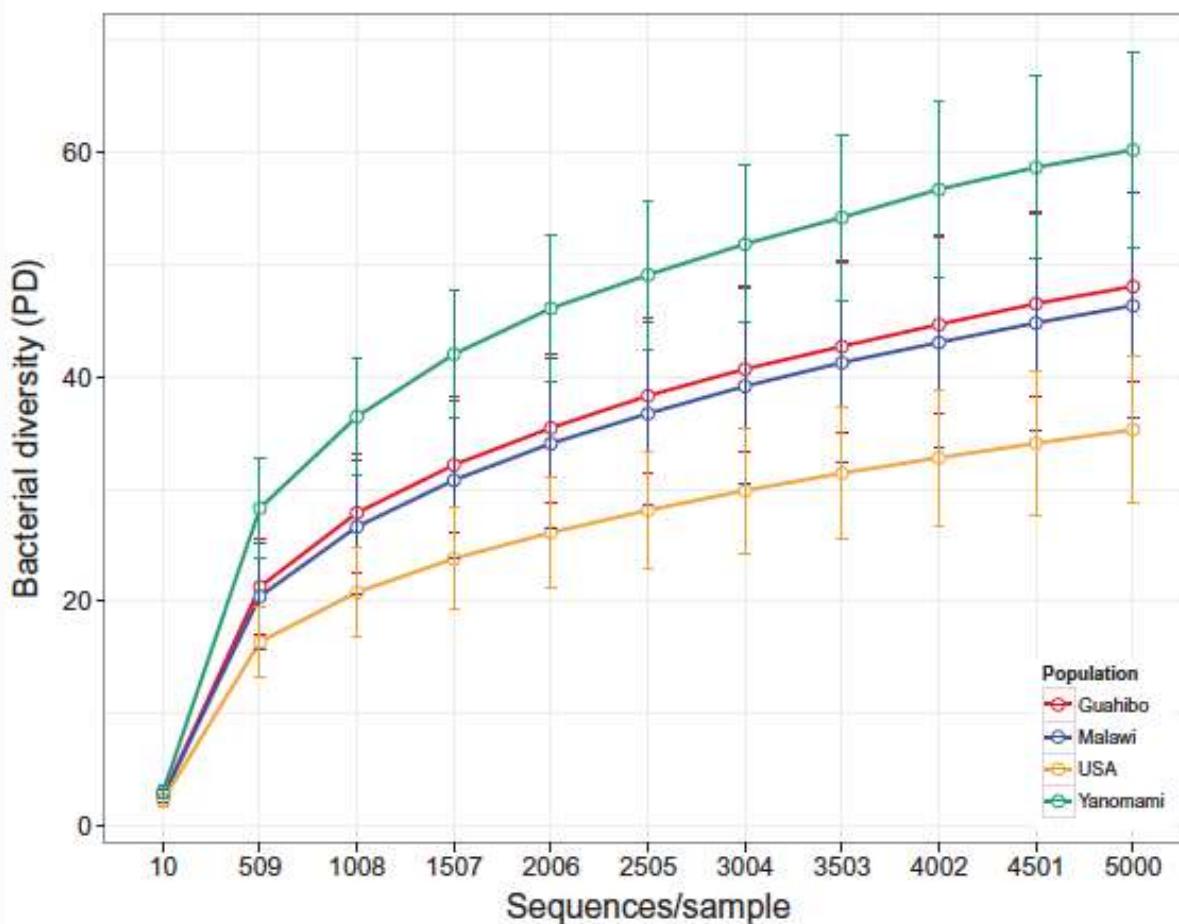


EU

- Alistipes ] Bacteroidetes
- Bacteroides ]
- Acetitomaculum ]
- Faecalibacterium ] Firmicutes
- Roseburia ]
- Subdoligranulum ]
- Others ]



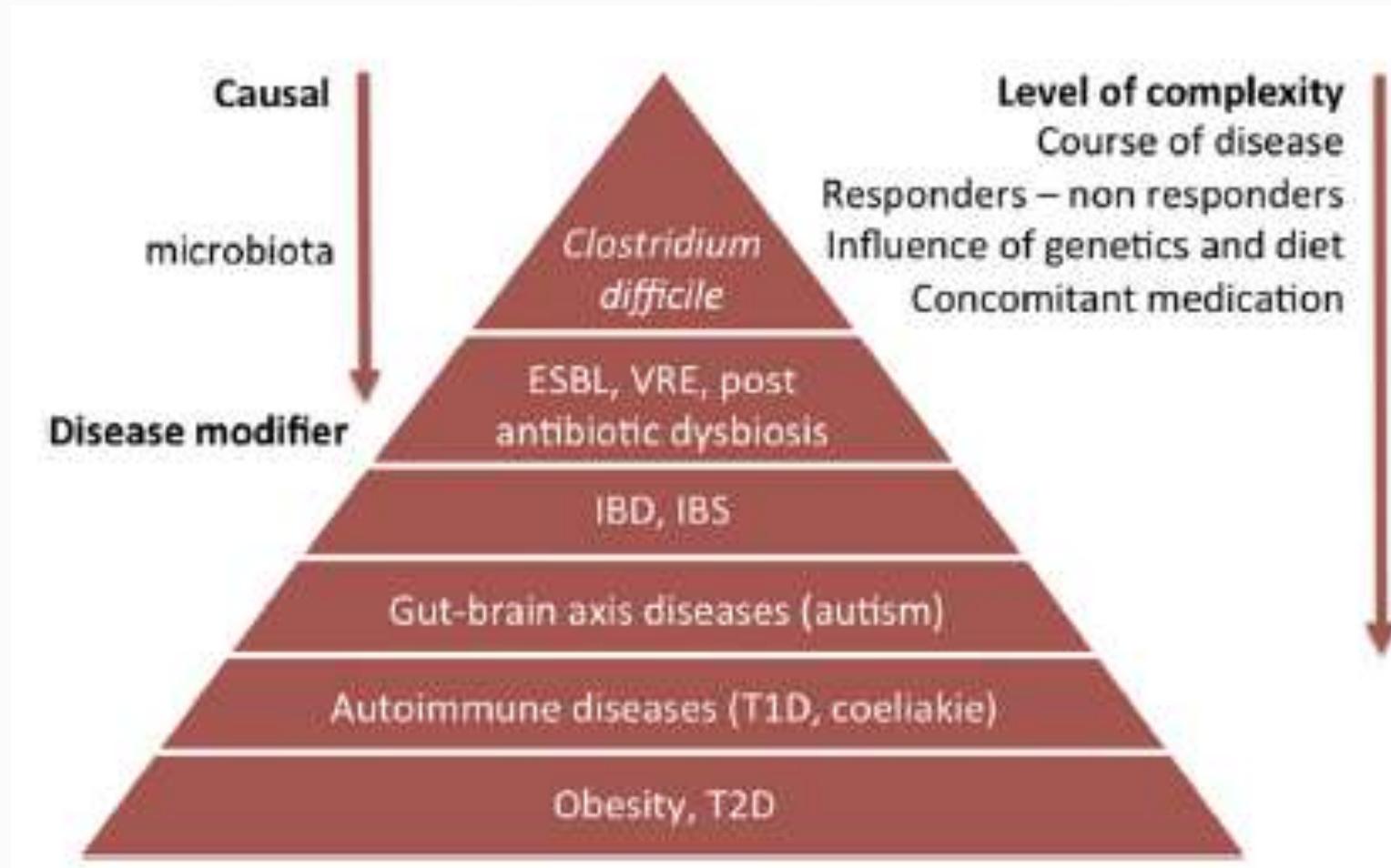
# The microbiome of uncontacted Amerindians



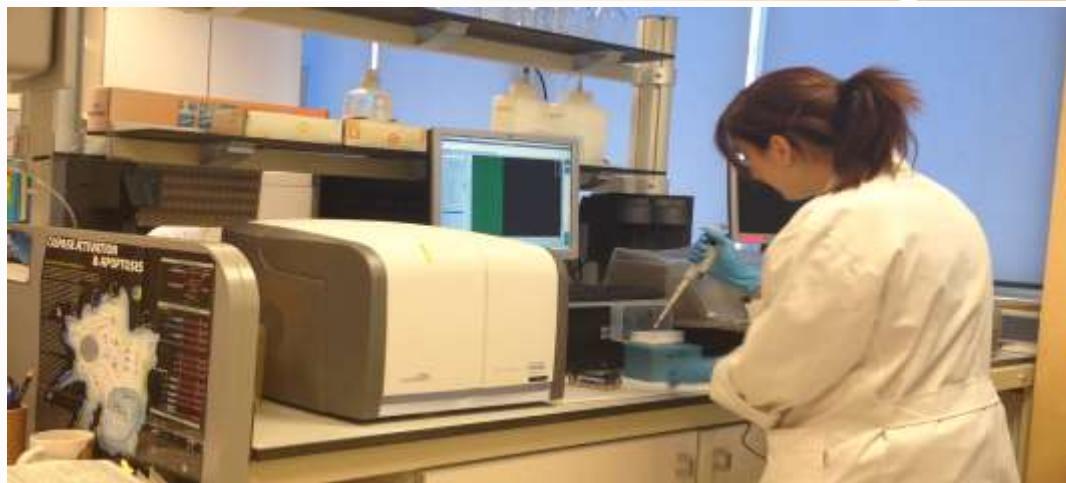
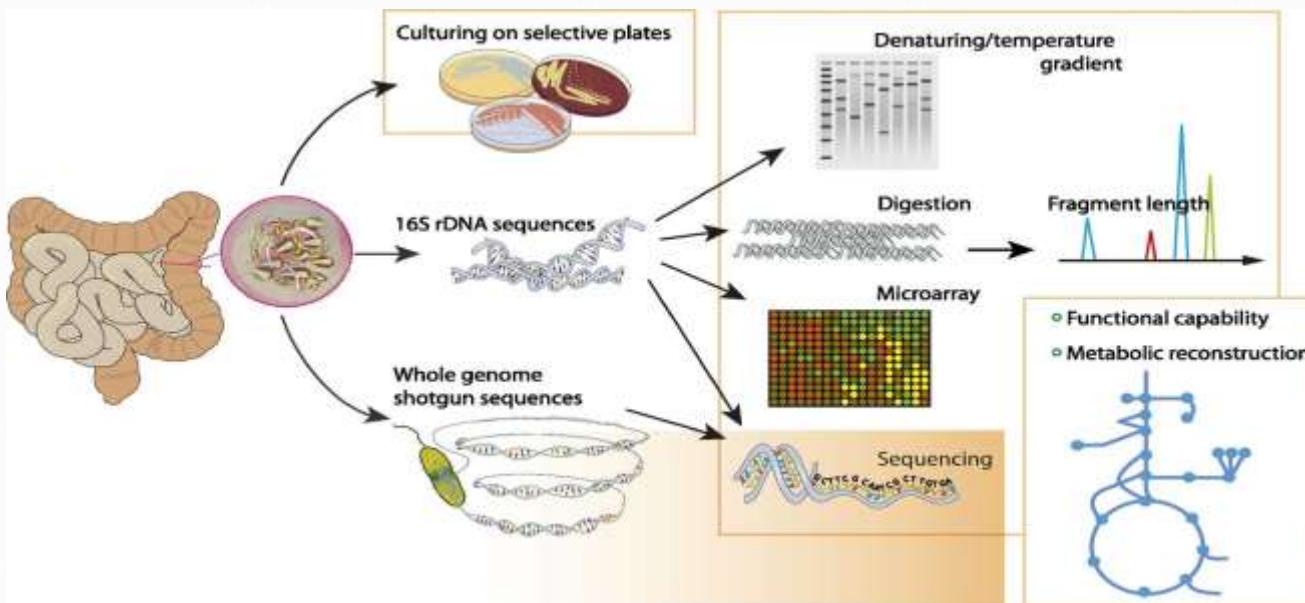
Clemente et al. Sci. Adv. 2015;1:e1500183



# *PAPÉL HOLÍSTICO DE LA MICROBIOTA*



# METODOS DE DETERMINACION DE LA MICROBIOTA



# ¿ Que le ocurre al modelo animal que no tiene gérmenes en su intestino?

↓ Expresión de proteínas intestinales

relacionadas con la saciedad  
PLoS One 2012; 7: e39748



↑ Incrementan consumo energía y soluciones dulces.  
Br J Nutr 2012; 107: 621–30.

↓ Son más delgados que los controles a pesar de consumir más calorías

Proc Natl Acad Sci USA 2004

↑ Incrementan resistencia a padecer enfermedades metabólicas

con consumo dietas grasas

Proc Natl Acad Sci USA 2007

Tienen respuestas exageradas al estrés y alteraciones de la conducta  
J Physiol 2017



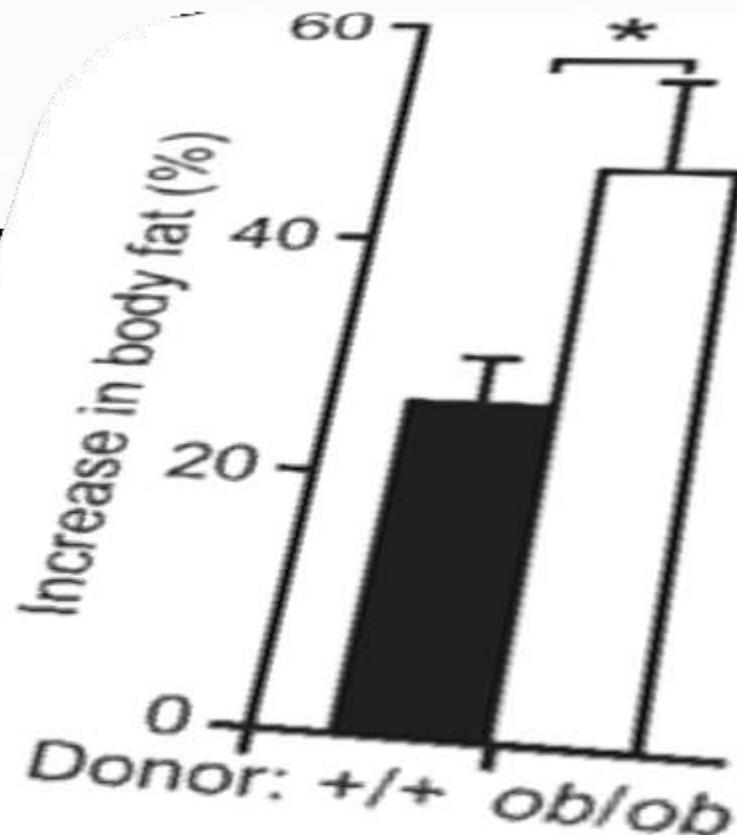
# Microbiota y enfermedades metabolicas





## MICROBIOTA OBESIDAD





Turnbaugh, PJ et al. Nature. 2006; 444 (7122):



## Gut Microbiota from Twins Discordant for Obesity Modulate Metabolism in Mice

Vanessa K. Ridaura *et al.*

Science 341, (2013);

DOI: 10.1126/science.1241214

delgado



Ln



Ob

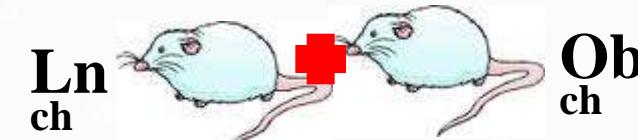


## Gut Microbiota from Twins Discordant for Obesity Modulate Metabolism in Mice

Vanessa K. Ridaura *et al.*

Science 341, (2013);

DOI: 10.1126/science.1241214

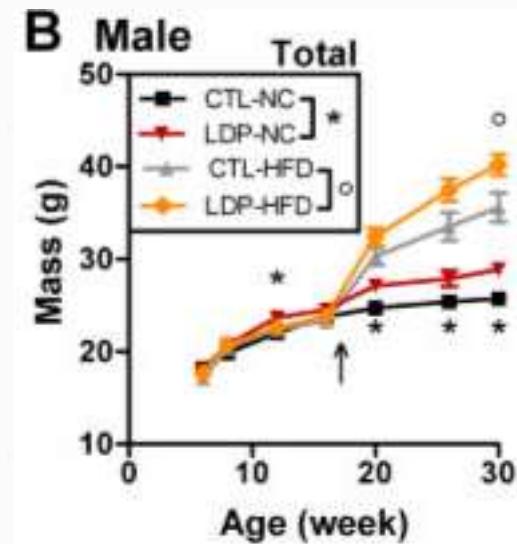
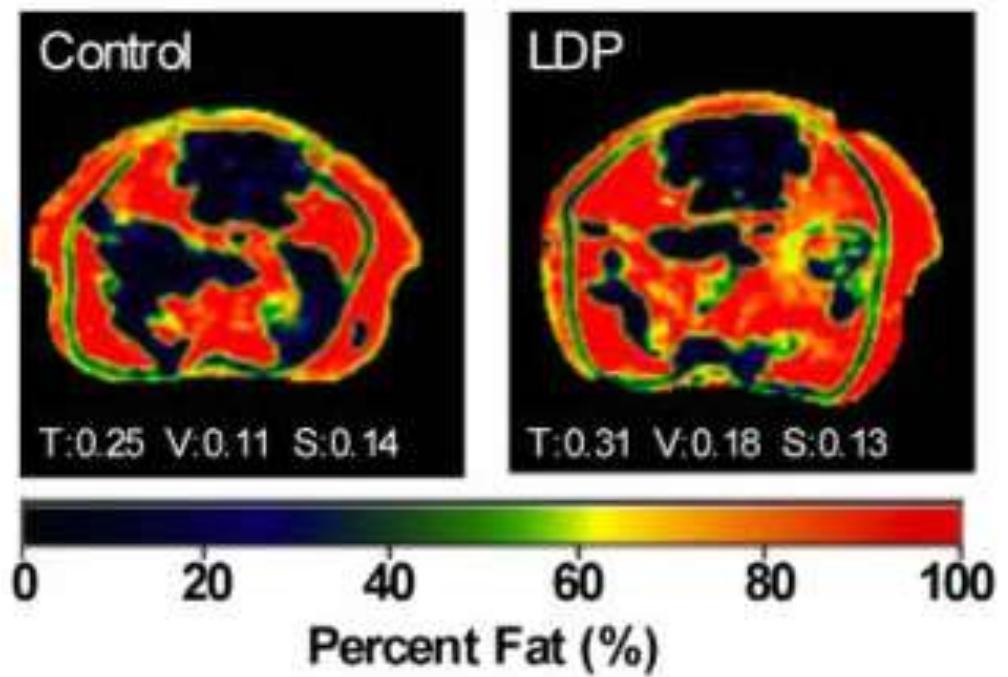


Ob<sup>ch</sup> : Menor aumento de la adiposidad que el Ob  
(similar a Ln o Ln<sup>ch</sup>)

**Conclusión: Las interacciones modificables y transmisibles entre la dieta y la microbiota influyen en la biología del hospedador.**



# Tratamiento antibiotico tras el nacimiento en modelos animales



Cell. 2014 August 14; 158(4): 705–721.



# FUNCIONES DIGESTIVAS DE LA MICROBIOTA

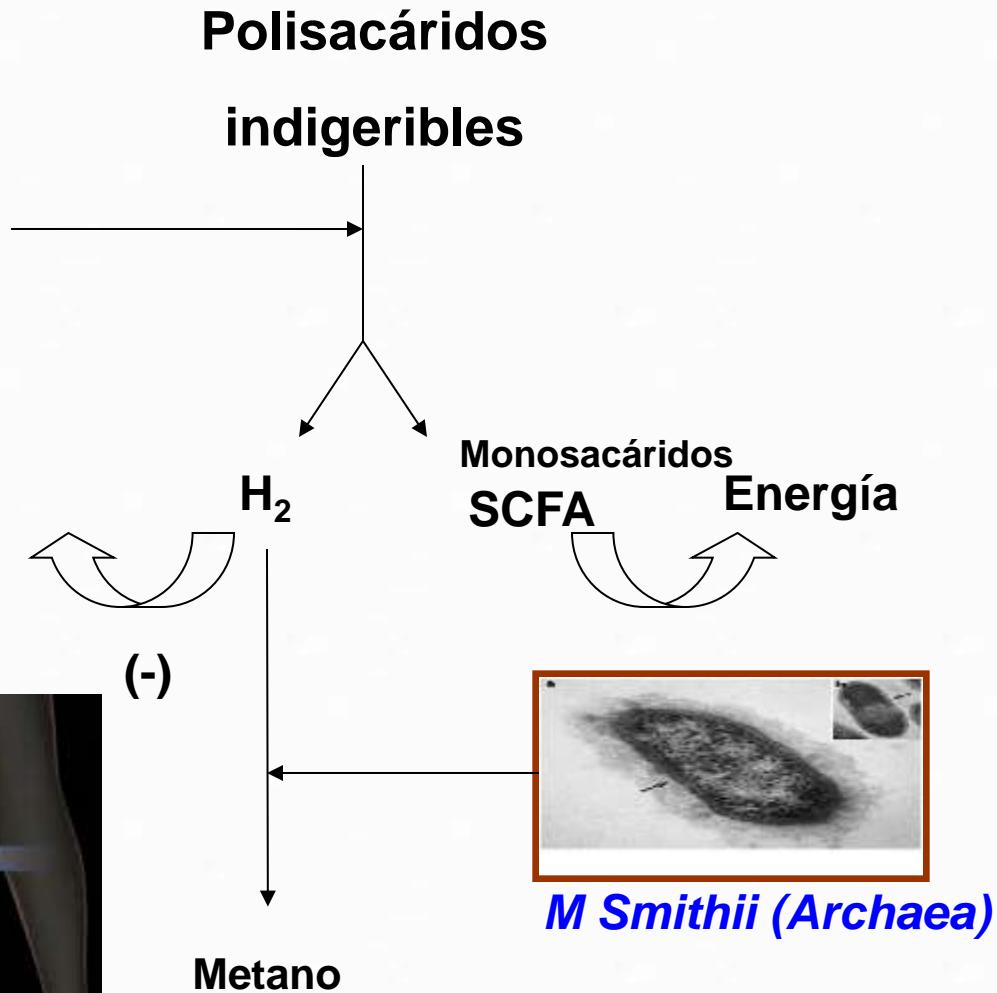
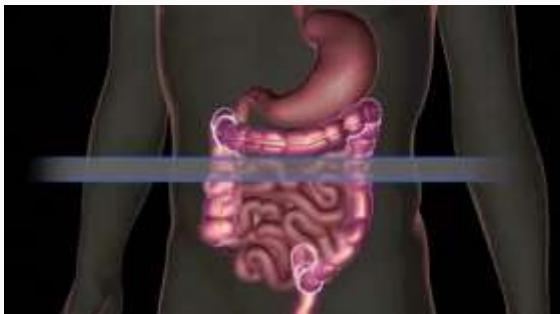
| Region   | pH  | Function  | Bacteria  | Density (cells/g)  | Oxygen / antimicrobial substances |
|----------|-----|---|---|--------------------|-----------------------------------|
| Duodenum | 5-7 | Digestion of proteins, monosaccharides, SCFAs; Immunomodulation | Lactobacillaceae, Enterobacteriaceae  | $10^3\text{-}10^4$ |                                   |
| Jejunum  | 7-9 | Absorption of FFAs, Calcium, Vitamin A, D, E, K                 | Lactobacillaceae, Enterobacteriaceae  | $10^4\text{-}10^5$ |                                   |
| Ileum    | 7-8 | Absorption of vitamin B12, bile acids                           | Lactobacillaceae, Enterobacteriaceae  | $10^8$             |                                   |
| Colon    | 5-7 | Absorption of water, SCFAs                                      | Bacteroidaceae, Prevotellaceae, Rikenellaceae, Lachnospiraceae, Ruminococcaceae | $10^{11}$          |                                   |



# Fermentación sustancias indigeribles



*Firmicutes  
intestinales*



# REGULACION BALANCE ENERGETICO

20  
KILOCALORIAS  
MAS AL DIA

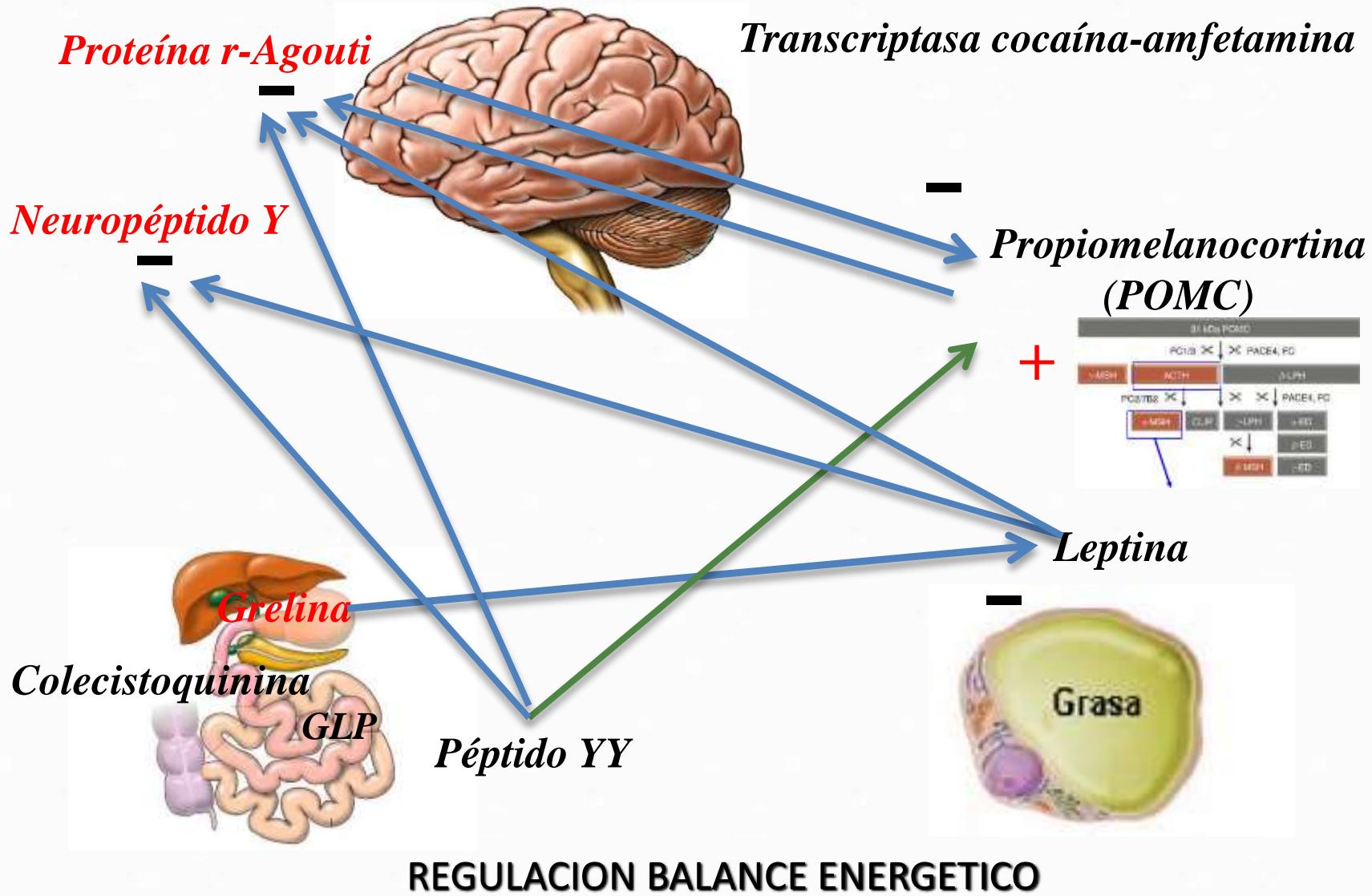


20 KILOS  
MAS



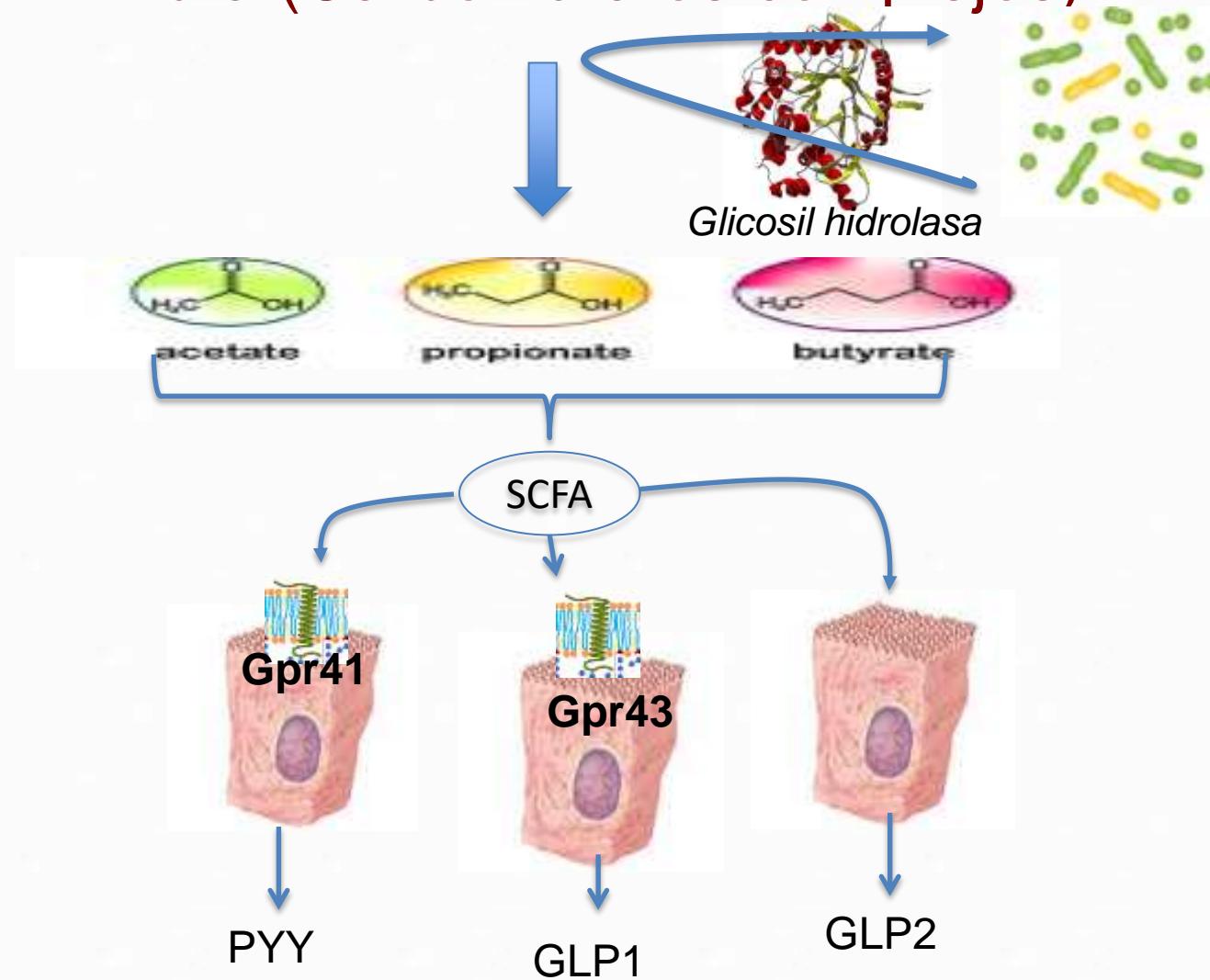
# Modificación de la secreción de incretinas



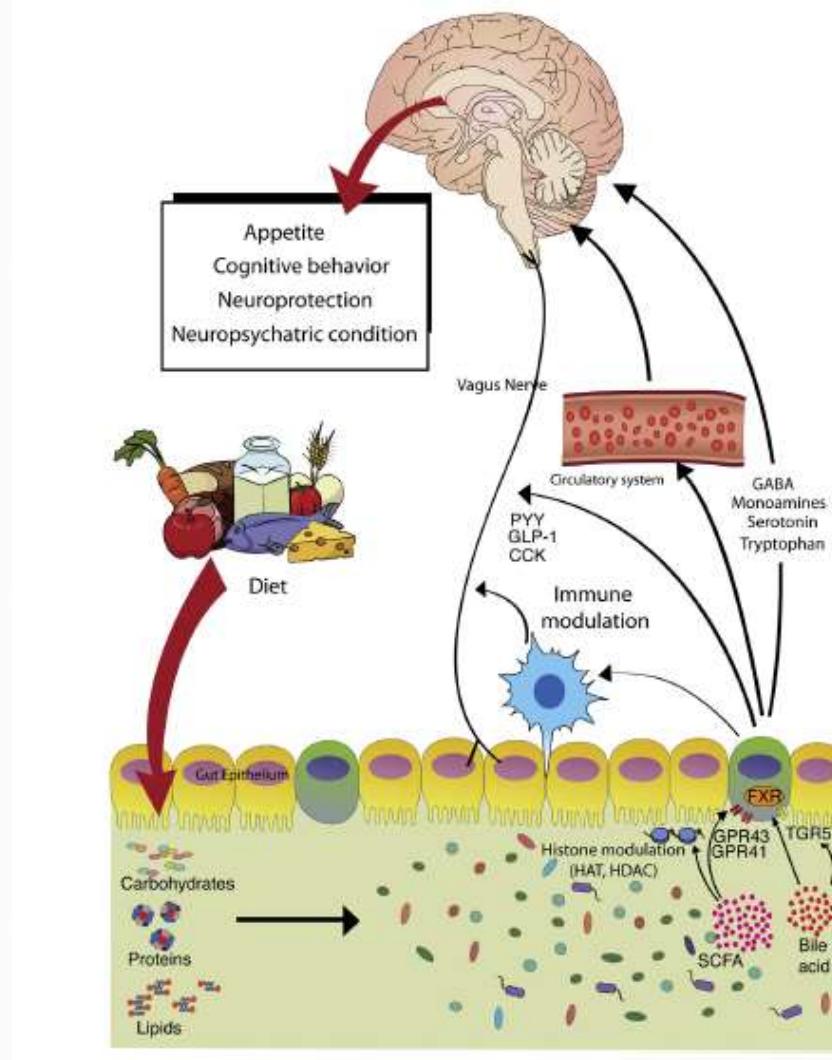


# INCRETINAS

## Fibra (Carbohidratos complejos)



# Algo mas que señales anorexigénicas





## DIABETES MICROBIOTA



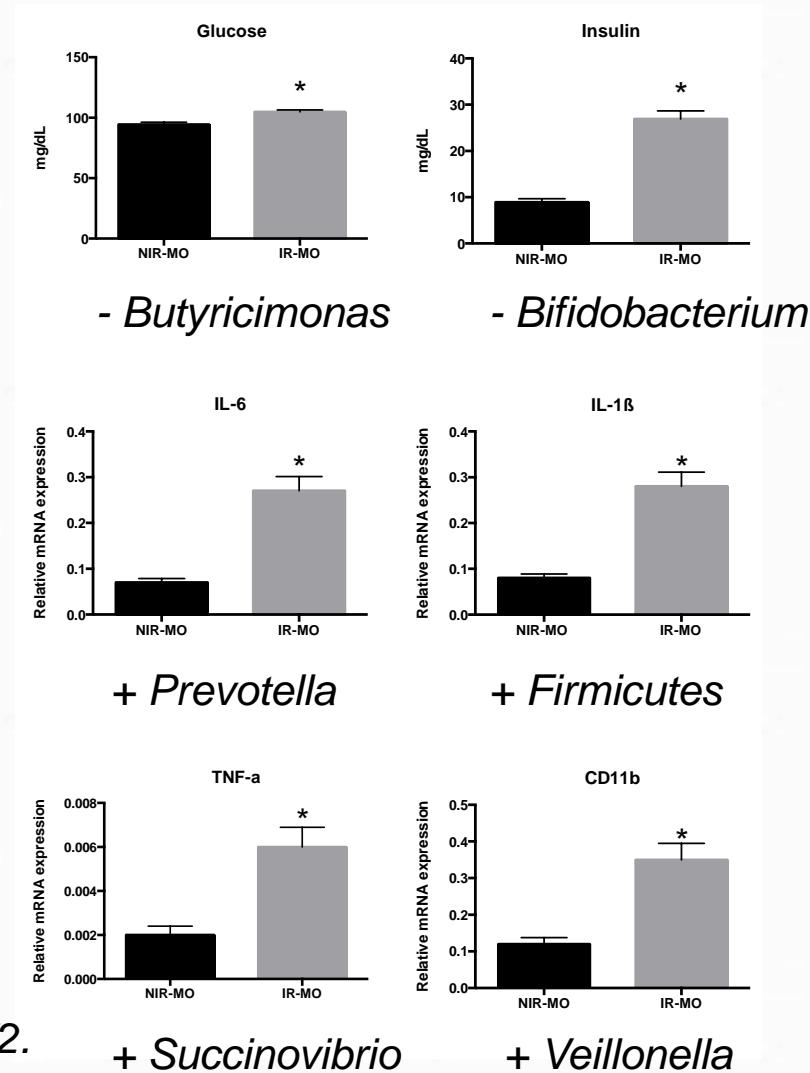
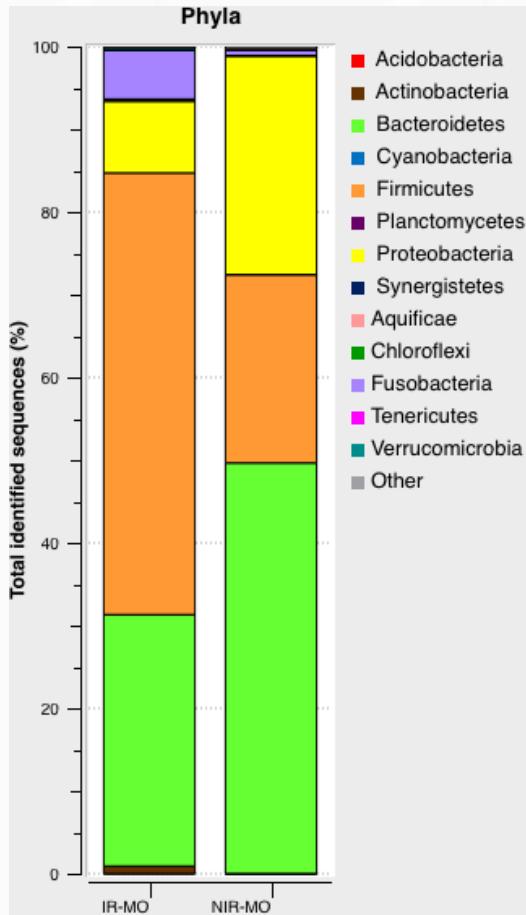
# Hallazgos mayores en el análisis del metagenoma en diabetes tipo 2

- Descenso de bacterias productoras de butirato como *Roseburia intestinalis* and *Faecalibacterium prausnitzii*
- *Lactobacillus gasseri* and *Streptococcus mutans* y ciertos Clostridiales mas elevados en T2D
- Proteobacteria más alta en T2D
- Incremento de expresión de genes de la microbiota envueltos en estrés oxidativo e inflamación

Tilg H et al. Gut. 2014 Sep;63(9):1513-21



# La microbiota está relacionada con la insulino-resistencia



Moreno-Indias et al. 2016. Am J Transl Res 8:5672.



# Mecanismos microbiota diabetes



# Microbiota/Diabetes

PRODUCCION DE BUTIRATO

Permeabilidad intestinal

Incretinas

ENDOTOXEMIA

ACIDOS BILIARES



# Microbiota/Diabetes

**PRODUCCION DE BUTIRATO  
Permeabilidad intestinal  
Incretinas**

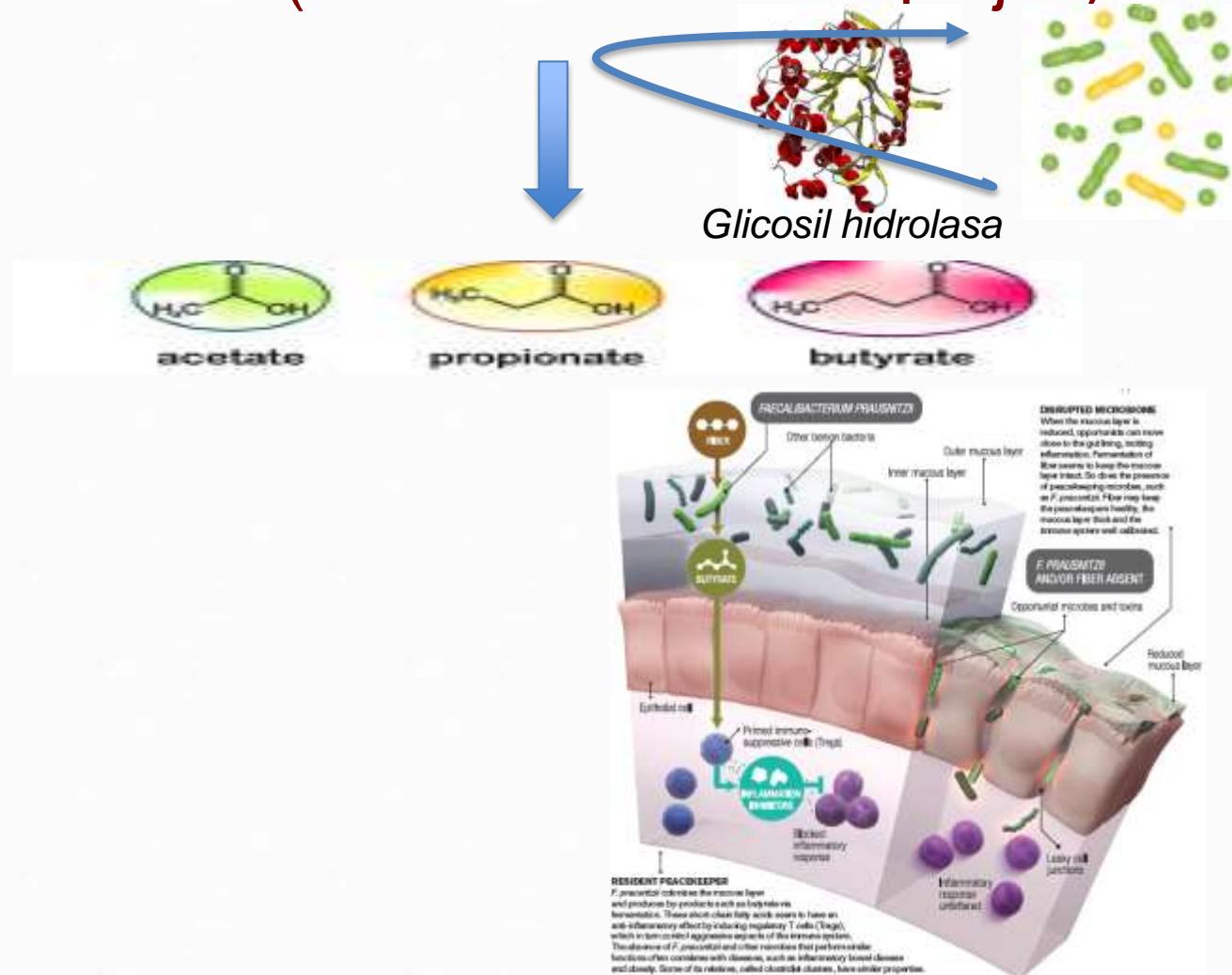
ENDOTOXEMIA

ACIDOS BILIARES



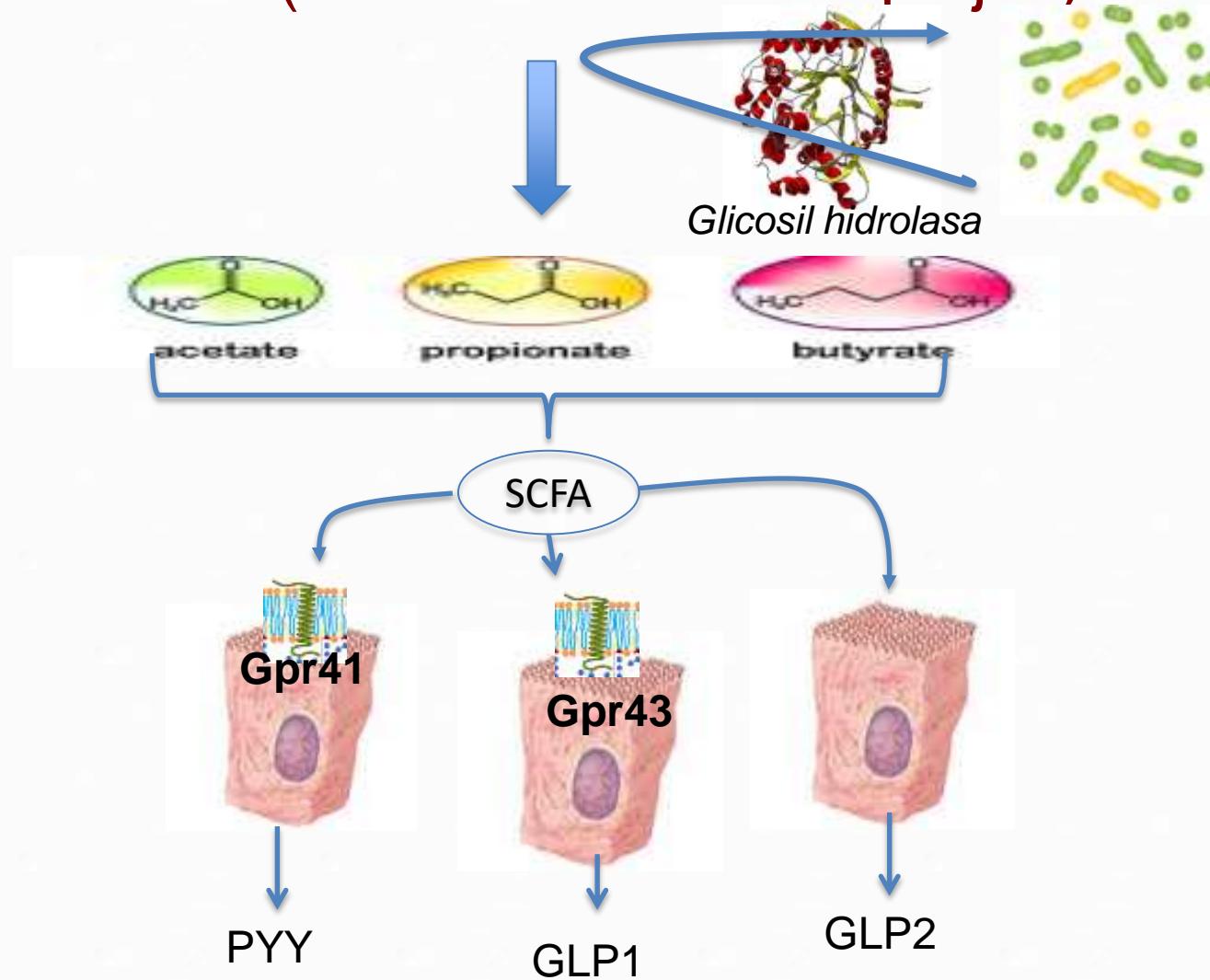
# PERMEABILIDAD

## Fibra (Carbohidratos complejos)



# INCRETINAS

## Fibra (Carbohidratos complejos)



# Microbiota/Diabetes

PRODUCCION DE BUTIRATO  
Permeabilidad intestinal  
Incretinas

**ENDOTOXEMIA**

ACIDOS BILIARES

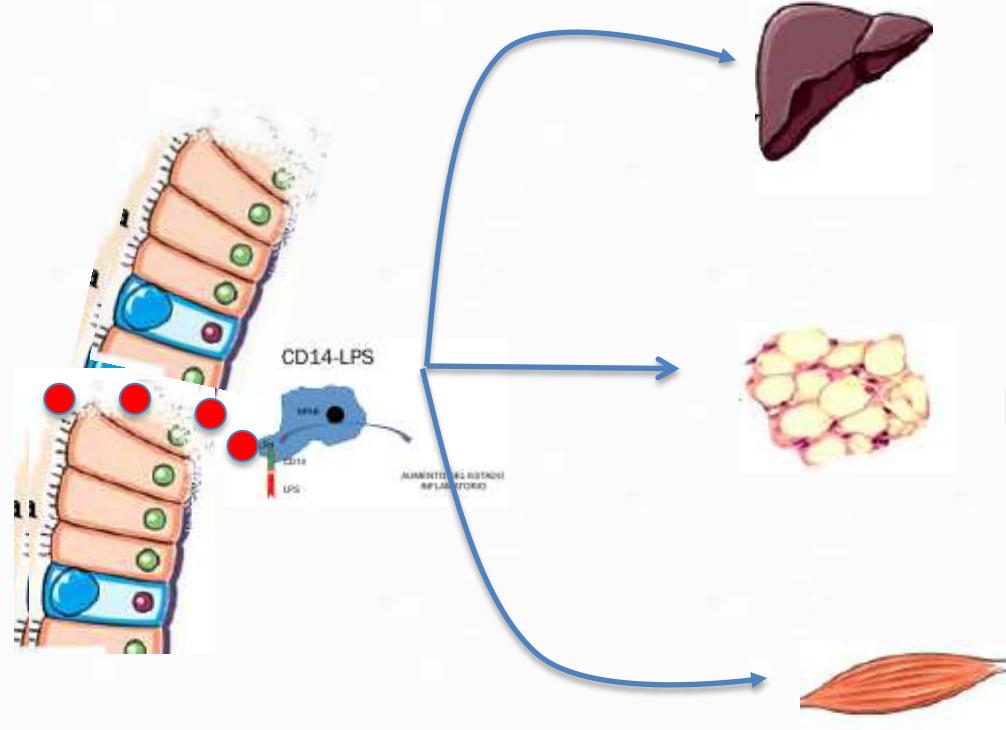


# ENDOTOXEMIA

- ⬇ Roseburia
- ⬇ Bifidobacterias
- ⬆ GRAM negativas



LPS

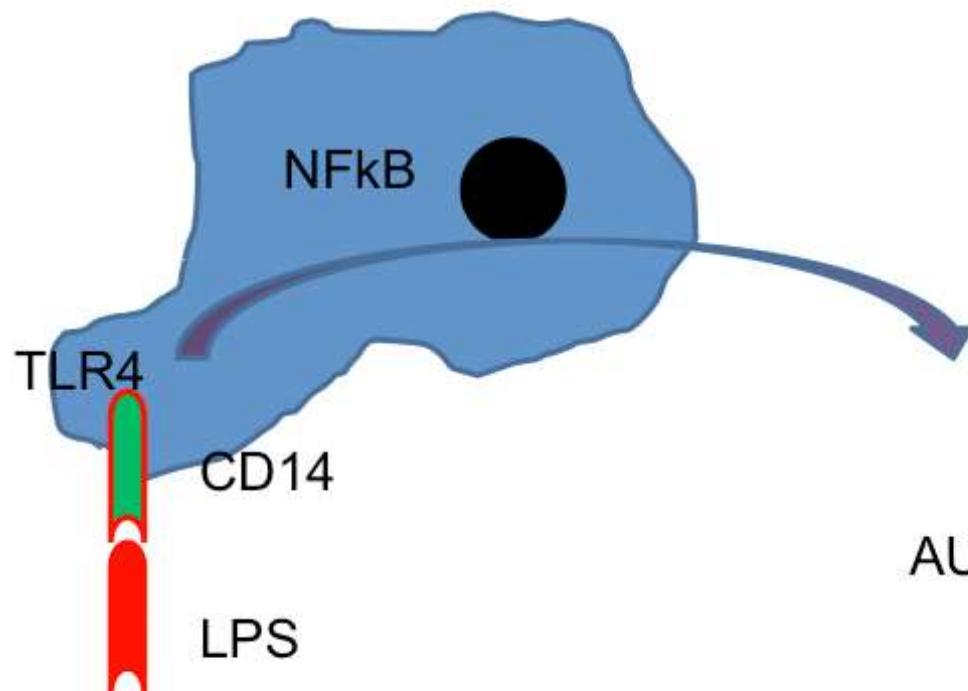


Inflamación  
Resistencia a  
insulina



# ENDOTOXEMIA

## CD14-LPS

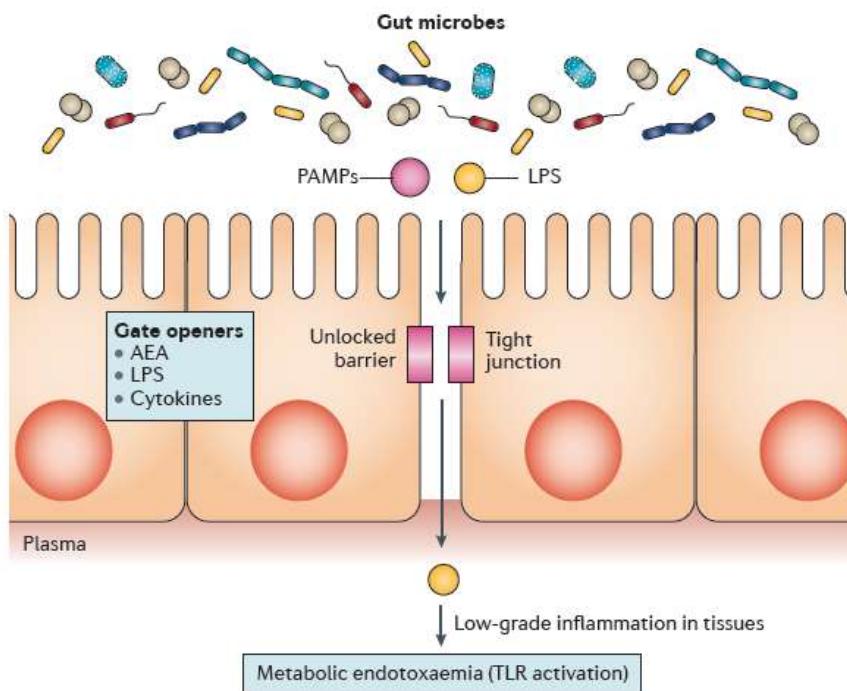


AUMENTO DEL ESTADO  
INFLAMATORIO

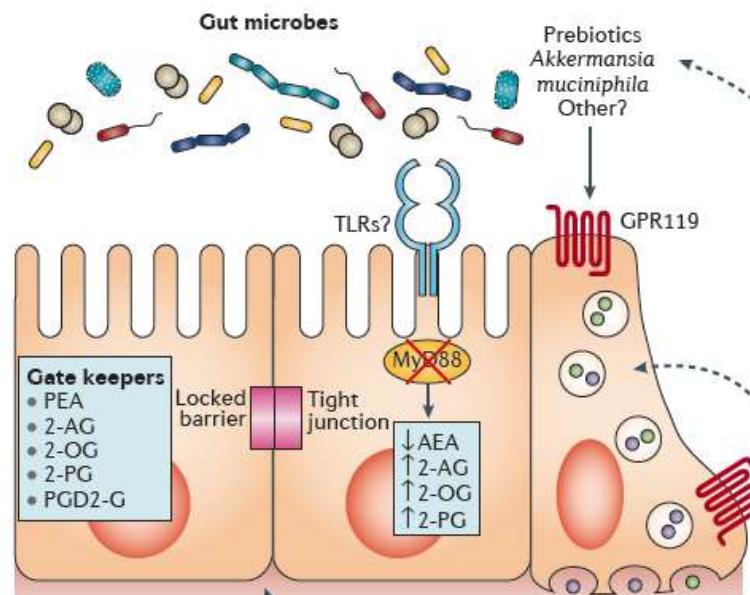


# Los que abren y los que cierran

ABREN



CIERRAN



Cani P. Nature Reviews Endocrinology. 2016



# Microbiota/Diabetes

PRODUCCION DE BUTIRATO  
Permeabilidad intestinal  
Incretinas

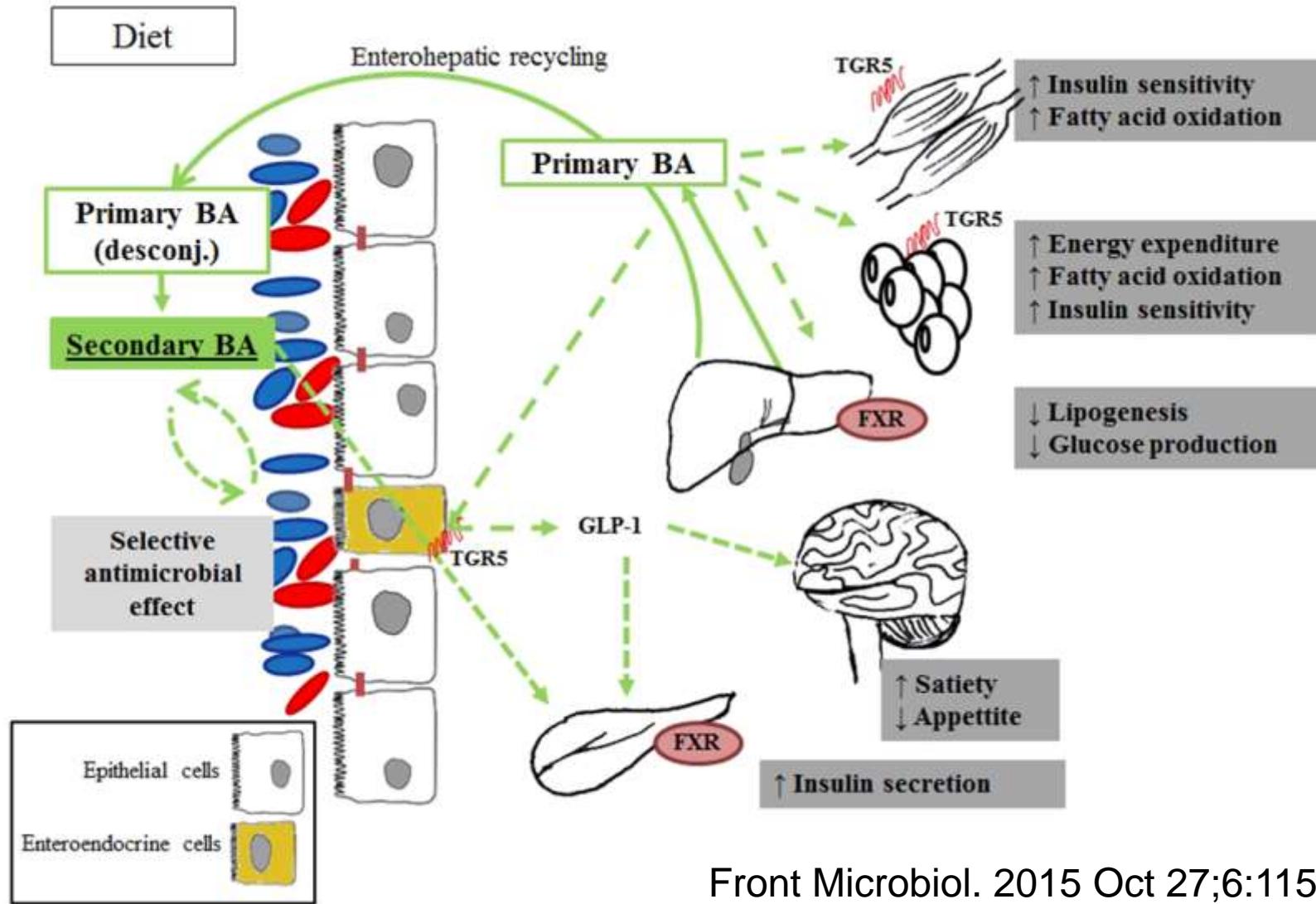
ENDOTOXEMIA

**ACIDOS BILIARES**

TEJIDO ADIPOSO MARRON



# ACIDOS BILIARES



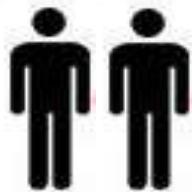
Front Microbiol. 2015 Oct 27;6:1151.



# Modificando la microbiota con dieta y probioticos



## STUDY DESIGN



**10 volunteers with cardiovascular risk factors**



**Crossover, randomized, controlled**

Washout

**1st Intervention  
20 days  
272 ml RED WINE**



**2nd Intervention  
20 days  
272 ml RED WINE**



**3rd Intervention  
20 days  
272 ml RED WINE**



**1st Intervention  
20 days  
272 ml DEALCOHOLIZED  
RED WINE  
(Polyphenol Control)**



**2nd Intervention  
20 days  
272 ml DEALCOHOLIZED  
RED WINE  
(Polyphenol Control)**



**3rd Intervention  
20 days  
272 ml DEALCOHOLIZED  
RED WINE  
(Polyphenol Control)**



**1st Intervention  
20 days  
100 ml GIN  
(Alcohol Control)**



**2nd Intervention  
20 days  
100 ml GIN  
(Alcohol Control)**



**3rd Intervention  
20 days  
100 ml GIN  
(Alcohol Control)**



HECES

HECES

HECES

HECES

# EFFECTS OF MODERATE WINE CONSUMPTION IN SUBJECTS WITH CARDIOVASCULAR RISK ON THE MICROBIAL COMPOSITION IN FECES

## RESULTS



*Firmicutes* (

*Bacteroidetes*

*Fusobacteri*

*Enterococc*

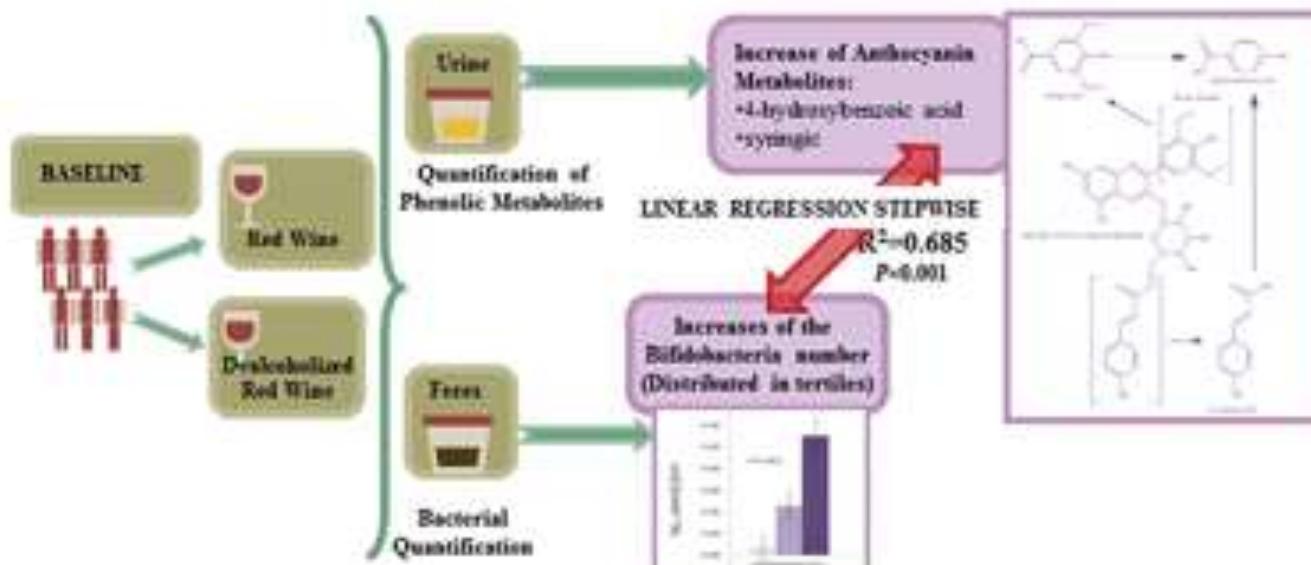
*Bacteroides*

*Prevotella s*

*Clostridium*

*Bifidobacterium spp*

*Lactobacillus spp*

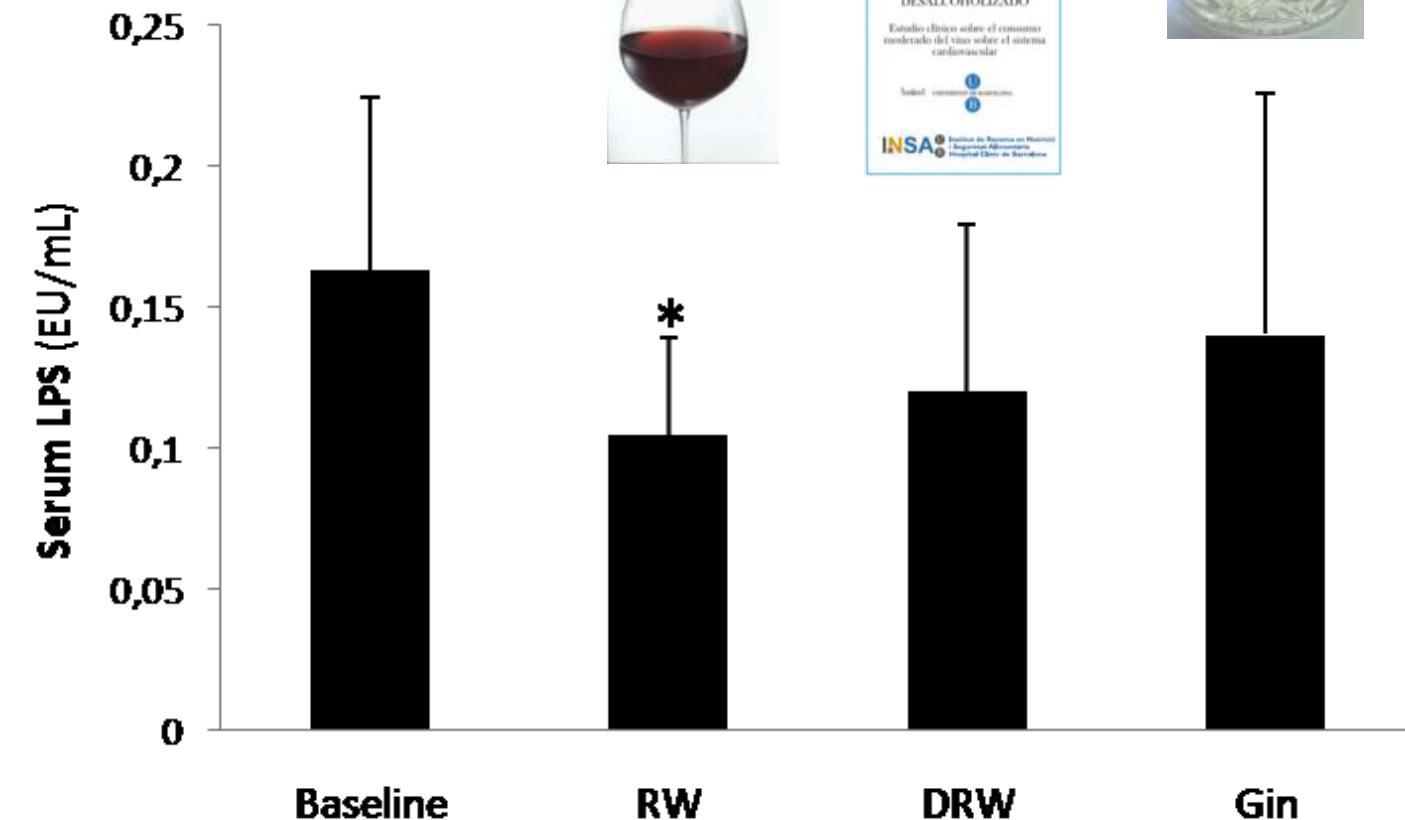


T

T

Boto M et al Food Funct. 2014 Aug;5(8):1932-8.

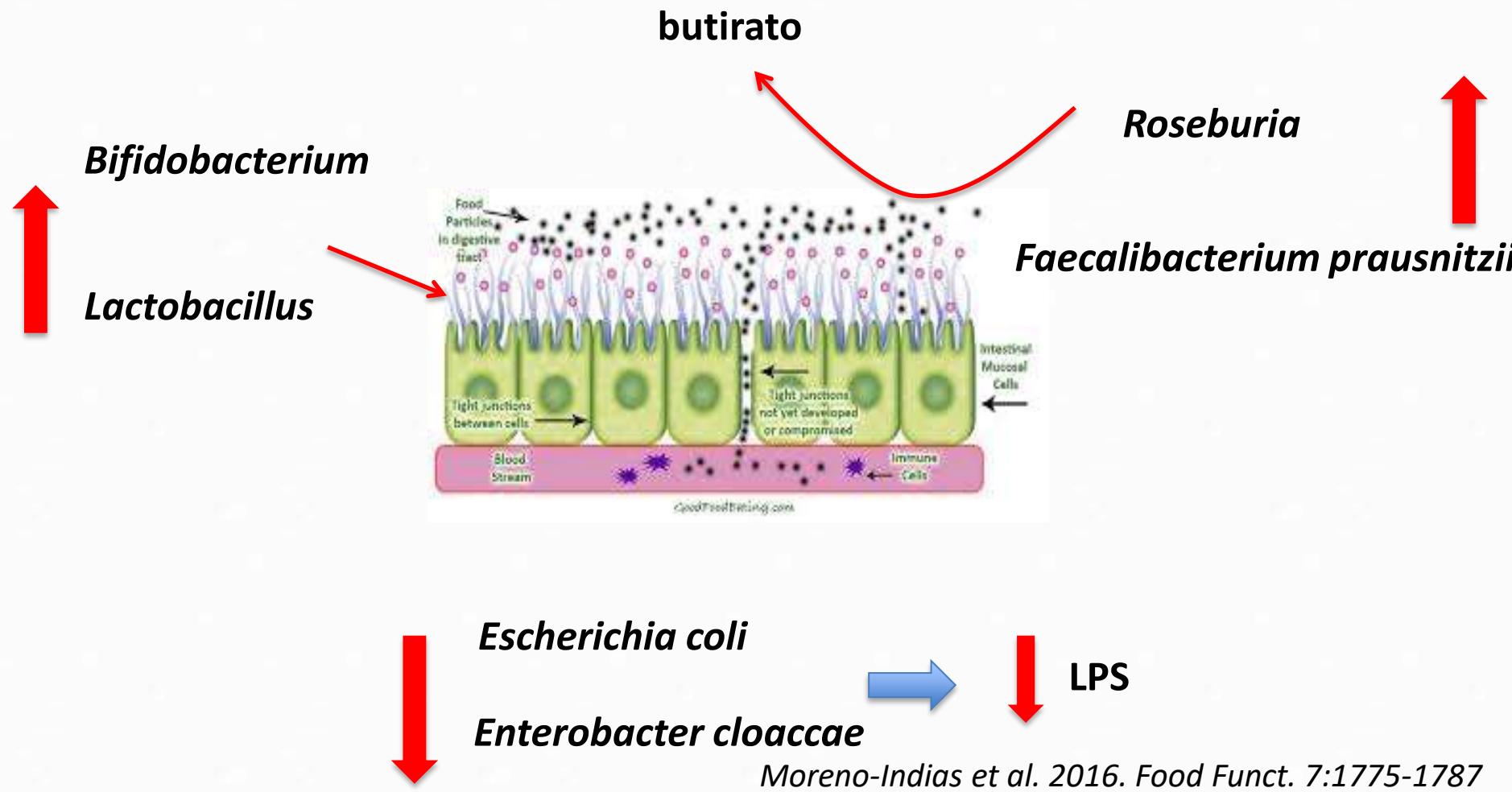
# Vino y LPS



Clemente M et al. Am J Clin Nutr 2013

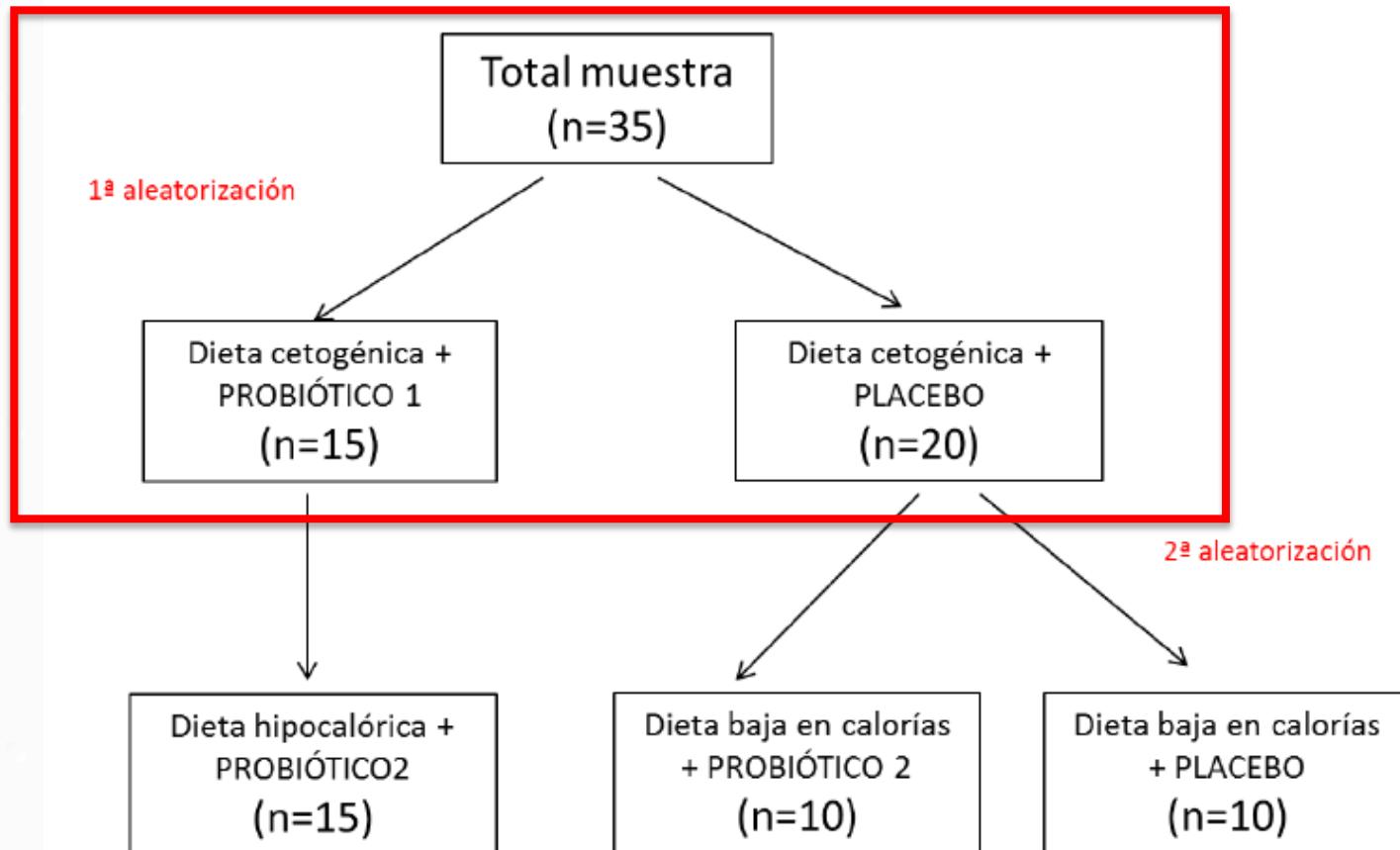


# El componente prebiótico del vino tinto mejora el síndrome metabólico a través de la microbiota intestinal



# Estudio MICROBIOTA

Estudio sobre los efectos de la dieta cetogénica baja en grasas en la microflora intestinal y su restitución mediante el uso de probióticos en pacientes obesos en tratamiento de pérdida de peso con Método PnK®



47

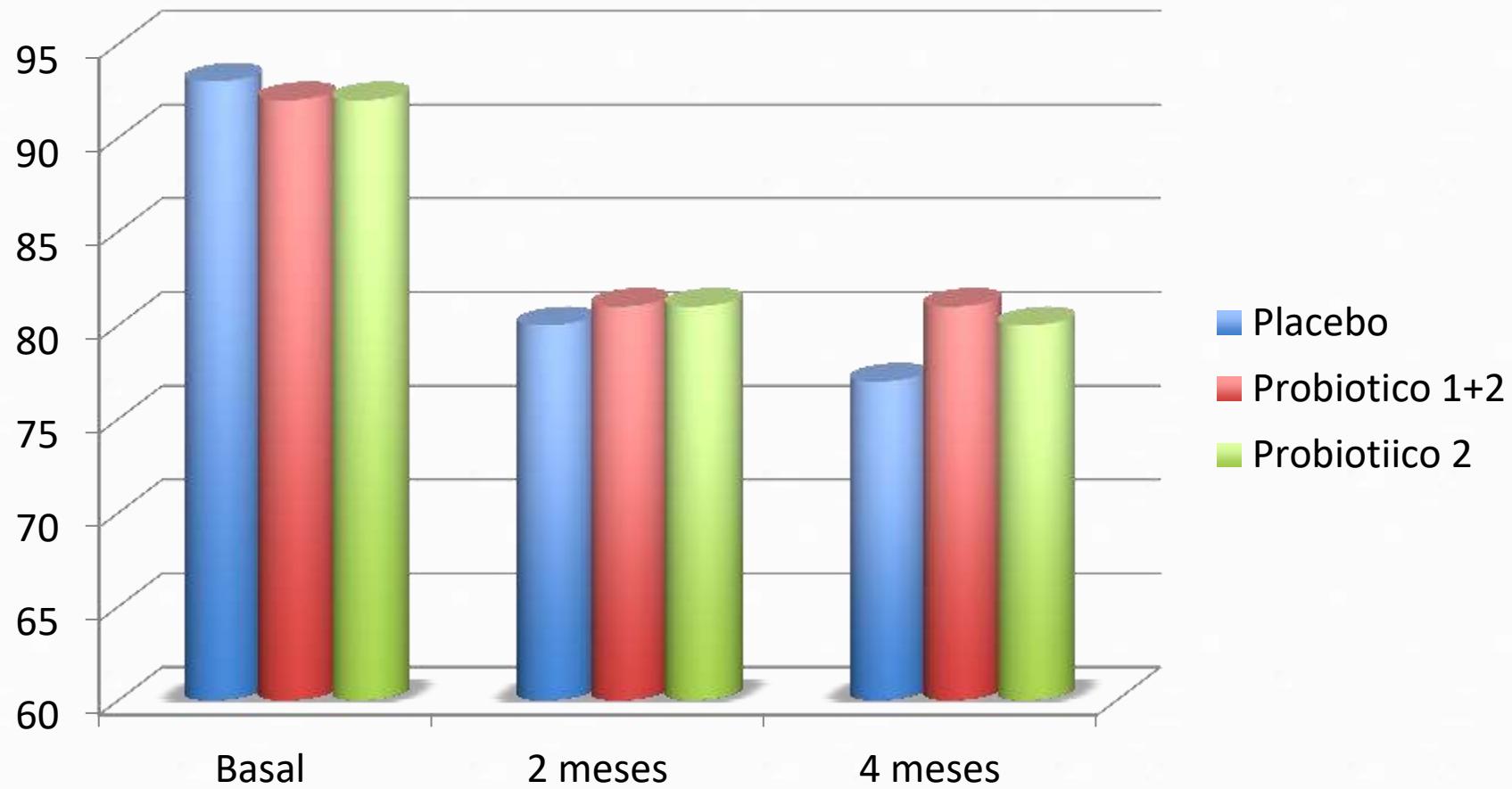
# Probioticos

- Probiotico 1: Bifidobacterium Longum ES1  
(Actinobacterias) y fibra prebiótica.
- Probiotico 2: Bifidobacterium animalis Subsp Lactis (Firmicutes) y Fibra prebiótica  
(maltodextrina)



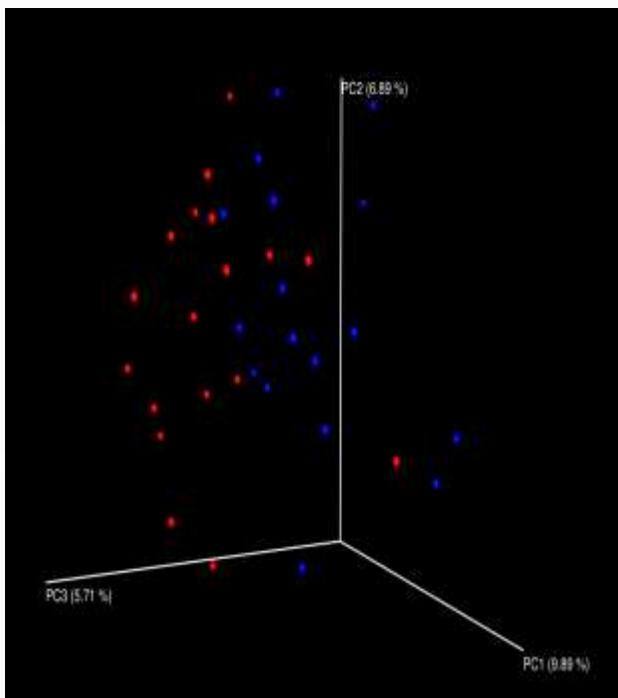
48

# Efecto sobre el peso

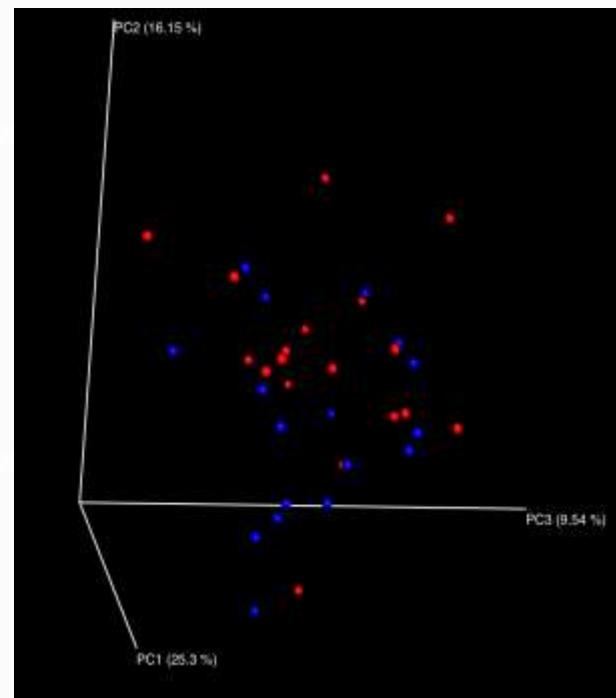


# La dieta cetogénica cambia la microbiota intestinal

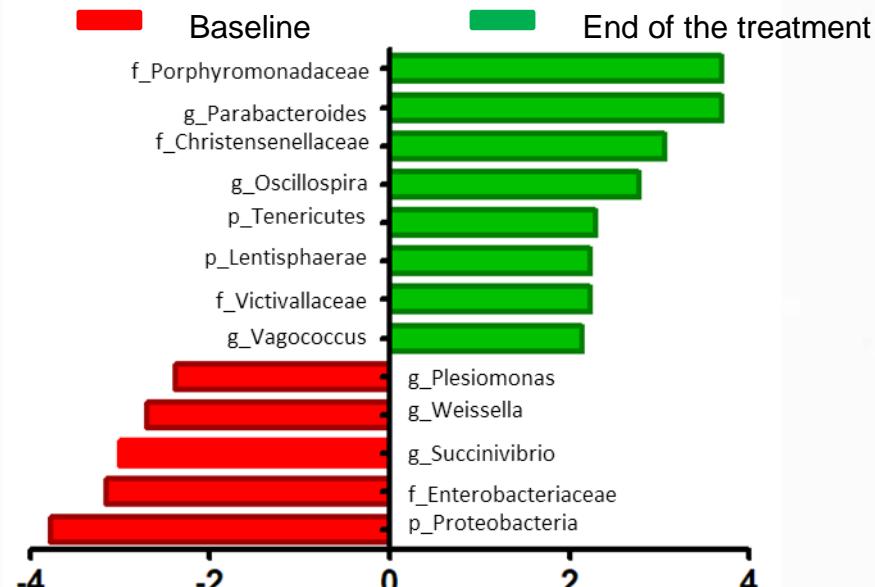
DIETA



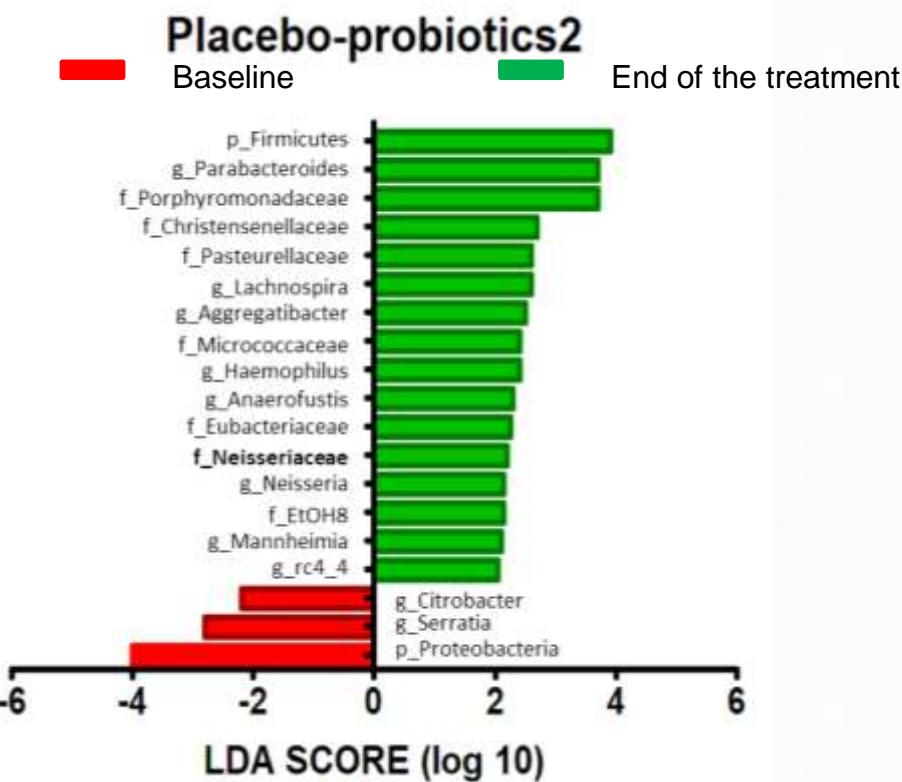
PROBIOTICO



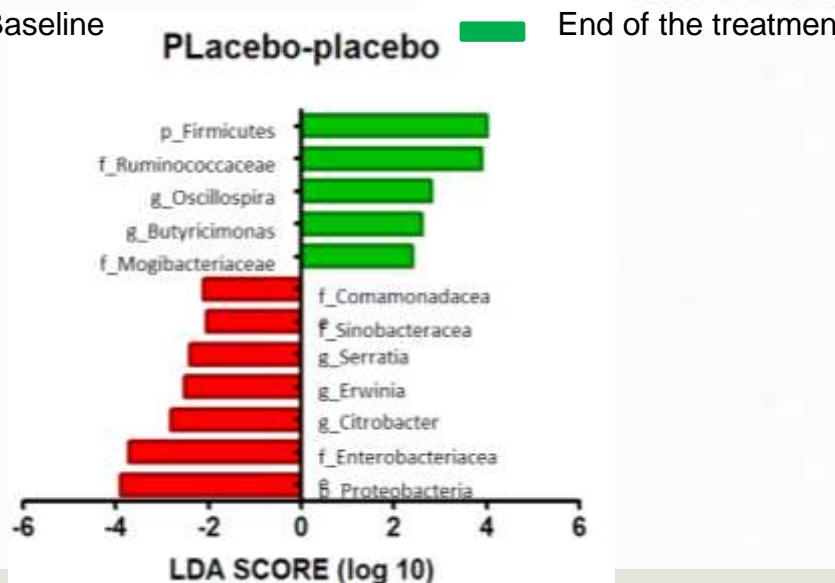
## Probiotics1-Probiotics2



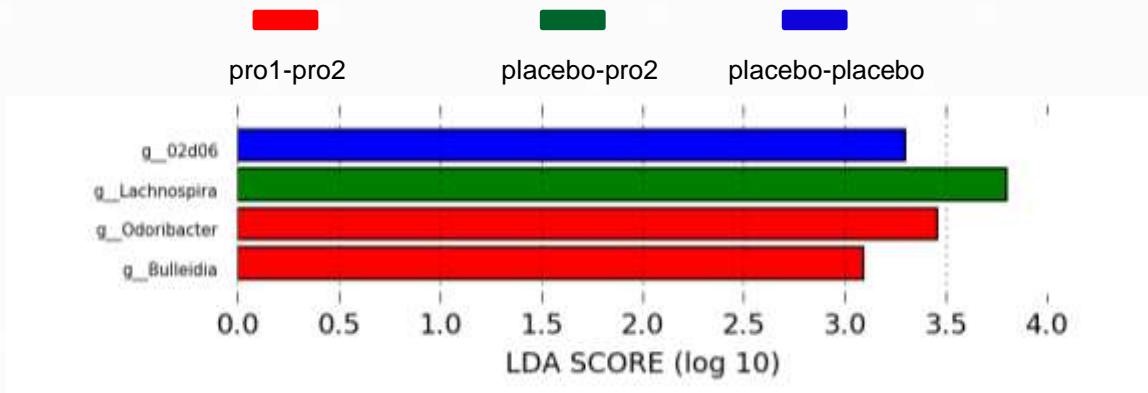
## Placebo-probiotics2



## PLacebo-placebo



# Hay cambios específicos de cada intervención



**Figure 1:** Histogram of the linear discriminant analysis (LDA) scores for differentially abundant bacterial groups in fecal samples between the three treatments. Red bars represent bacterial groups over-abundant in the pro1-pro2. Green bar represents the bacterial group over-abundant in the placebo-pro2. Blue bar represents the bacterial group over-abundant in placebo-placebo group.

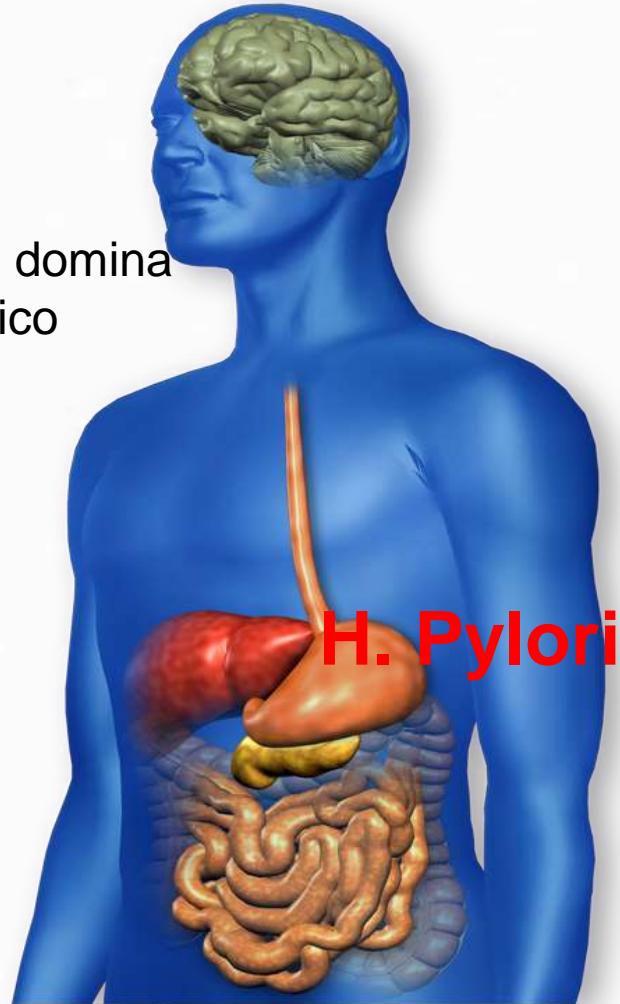


# Cambiando la microbiota con antibioticos

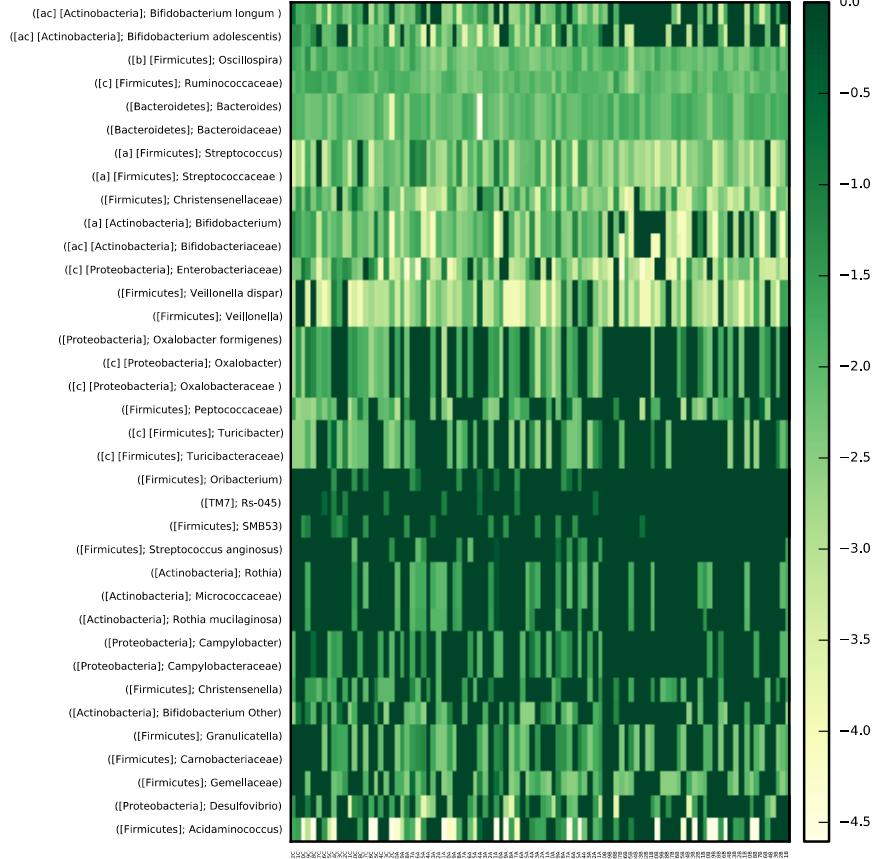
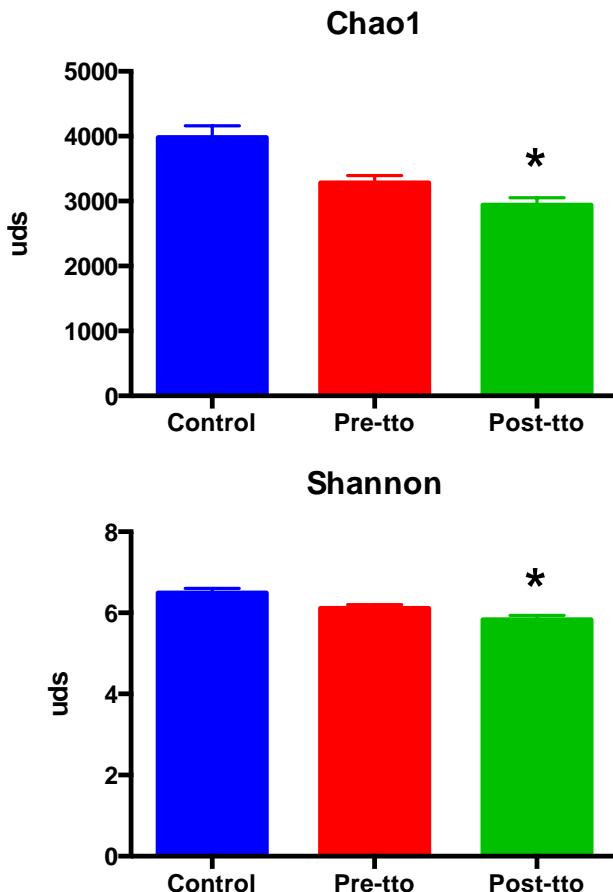


# ANTIBIOTICOS

H Pylori microbiota que domina  
en el nicho gástrico



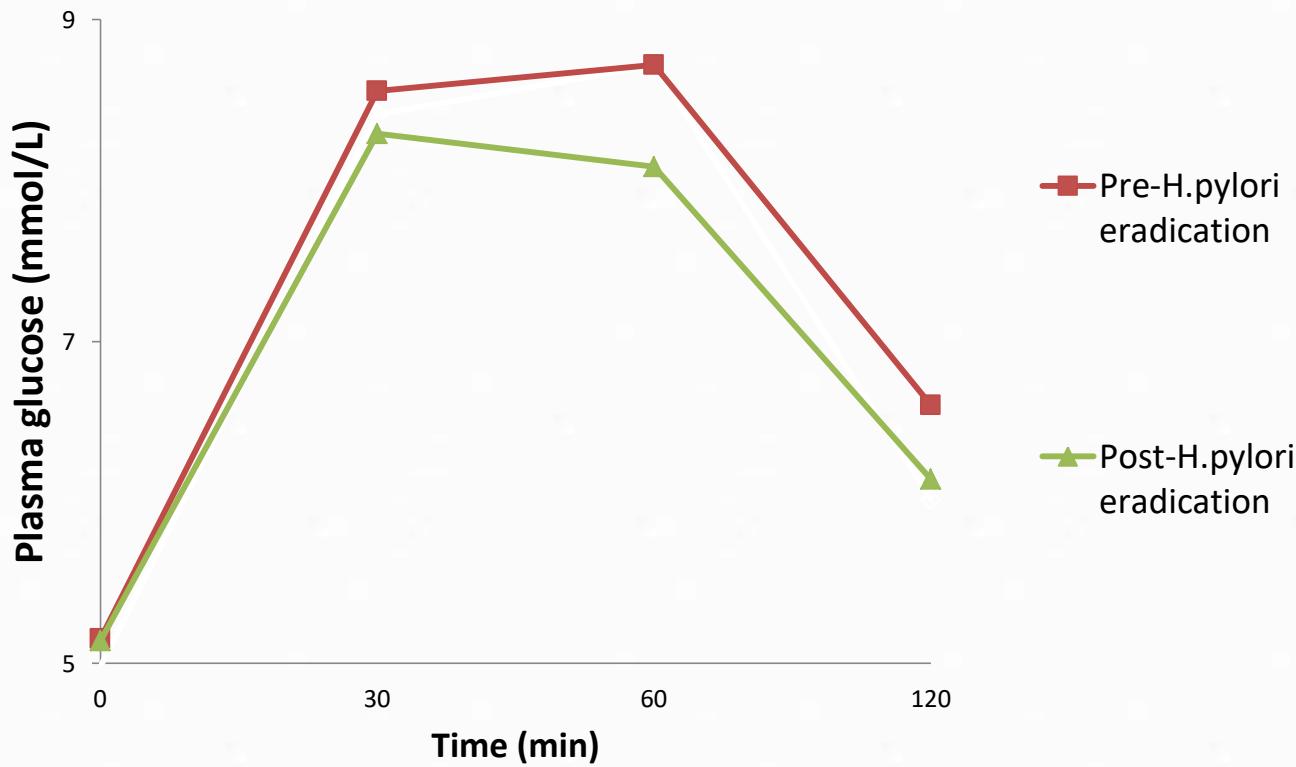
# Las terapias antibióticas modulan la microbiota intestinal



Martín-Núñez et al. 2016. Submitted



# La modulación de la microbiota intestinal por las terapias antibióticas, pueden tener efectos beneficiosos

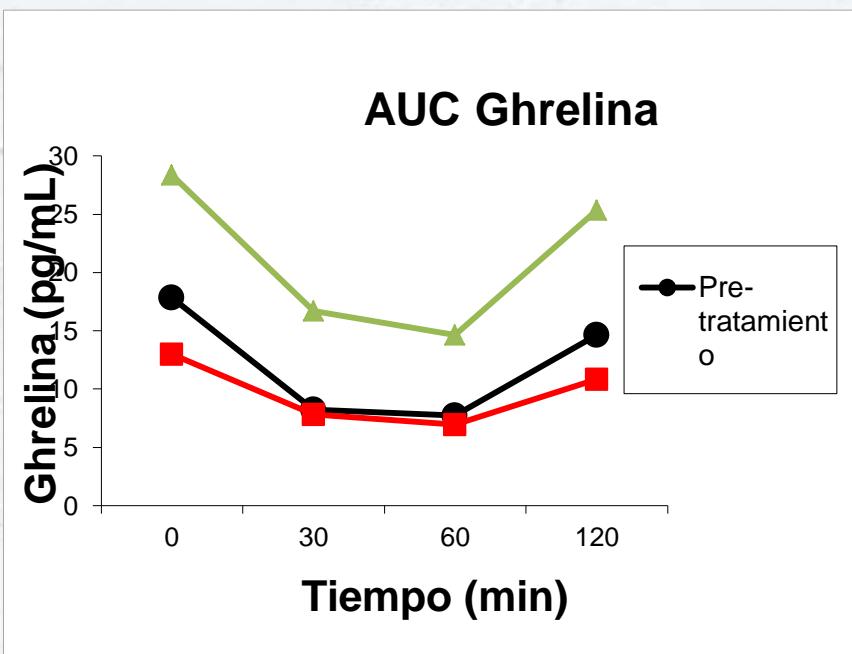


Roca MM et al. Diabetes Metabolism 2016

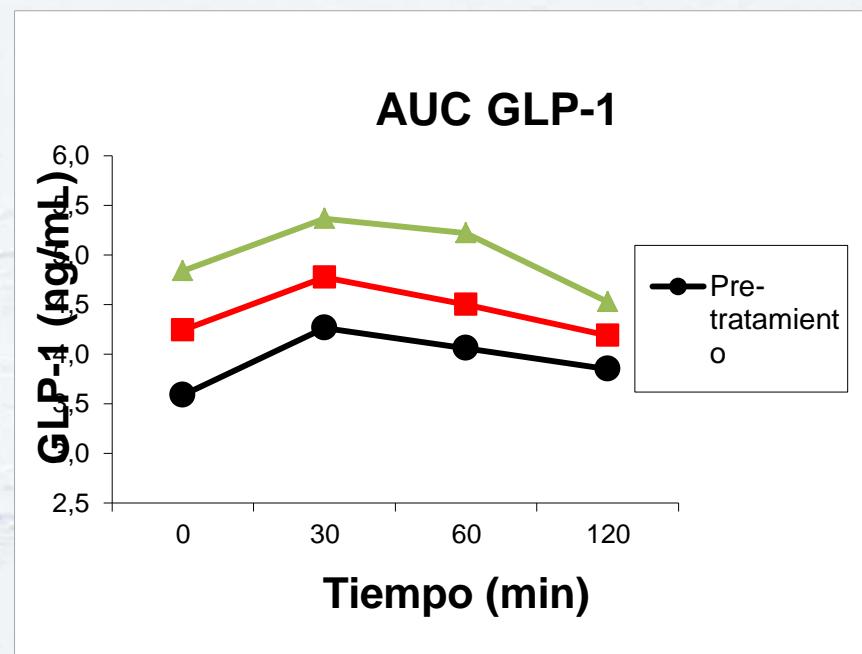


# EFECTO ATB ESTATUS GLUCÉMICO

## AUC GHRELINA tras SOG



## AUC GLP-1 tras SOG



# EL MERCADO POR DELANTE DE LA CIENCIA

The image displays three separate web pages side-by-side:

- Naturalinea.com**: A Mexican naturalist store. The header includes links for Contactanos, Quienes Somos, Cómo Comprar, Publicidad, and Condiciones Generales. Below the header, a banner reads "Sé natural, Naturalinea tu tienda naturista en México." It features a testimonial about Angelina Jolie's weight loss using a method that clears the colon, followed by social media links for Facebook, Twitter, and Google+.
- My Perfect Colon**: A website for a natural hydro-therapy system. The main menu includes Home, Sistema My Perfect Colon, Productos, FAQ, Testimonios, Video, Dónde comprar, and Tienda. A testimonial from Eficaz claims rapid weight loss through colon hydrotherapy.
- HIDROTERAPIA DE COLON VALENCIA**: A diet and health blog. The sidebar lists BENEFICIOS, QUIENES SOMOS, CONTACTENOS, SISTEMA DIGESTIVO, SALUD INTESTINAL, and INFORMACIÓN EN DIGESTIVO. The main content area features a blog post titled "Mi blog" with the subtitle "dieta, adelgazar,rápido,limpieza de colon,hidroterapia,bikini,aprender a comer".



**Nutrition & Food Science Department.**

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**Joan Vendrell-Tarragona**  
**Montse Fito-Barcelona**  
**Jordi Salas-Reus**  
**Albert Goday-Barcelona**  
**Jose M Gonzalez-Clemente-Sabadell**

[\*\*Universidad de Córdoba\*\*](#)  
Manuel Tena  
Francisco Pérez Jiménez

[\*\*Hospital of Girona 'Dr Josep Trueta'\*\*](#)  
José Manuel Fernández-Real

