UNIVERSITAT POLITÈCNICA DE CATALUNYA
BARCELONATECH

Centre de Recerca en Seguretat
i Control Alimentari

# MICROBIOTA Y SU RELACIÓN CON EL SISTEMA INMUNE. PAPEL DE LOS PROBIÓTICOS


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Consejo Superior de Investigaciones Científicas (CSIC). Madrid

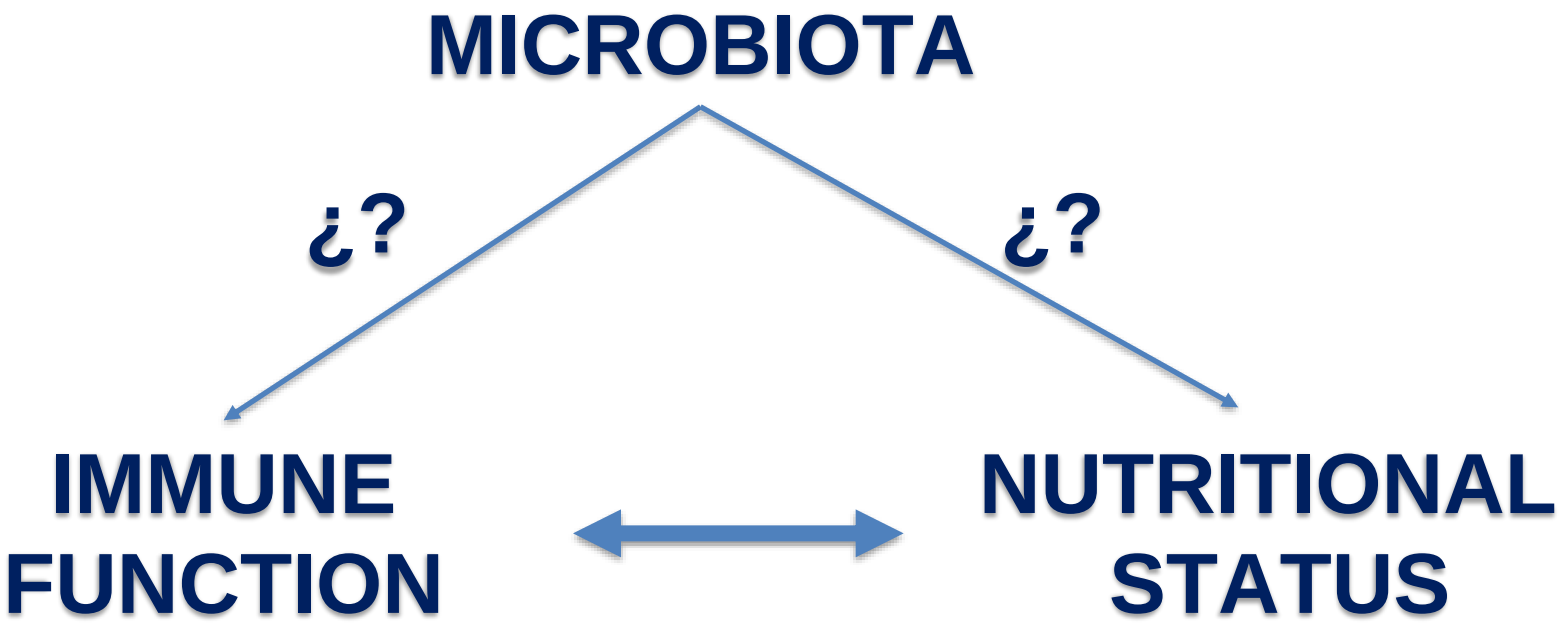

ictan

CSIC

http://www.inmunonutricion-csic.com/

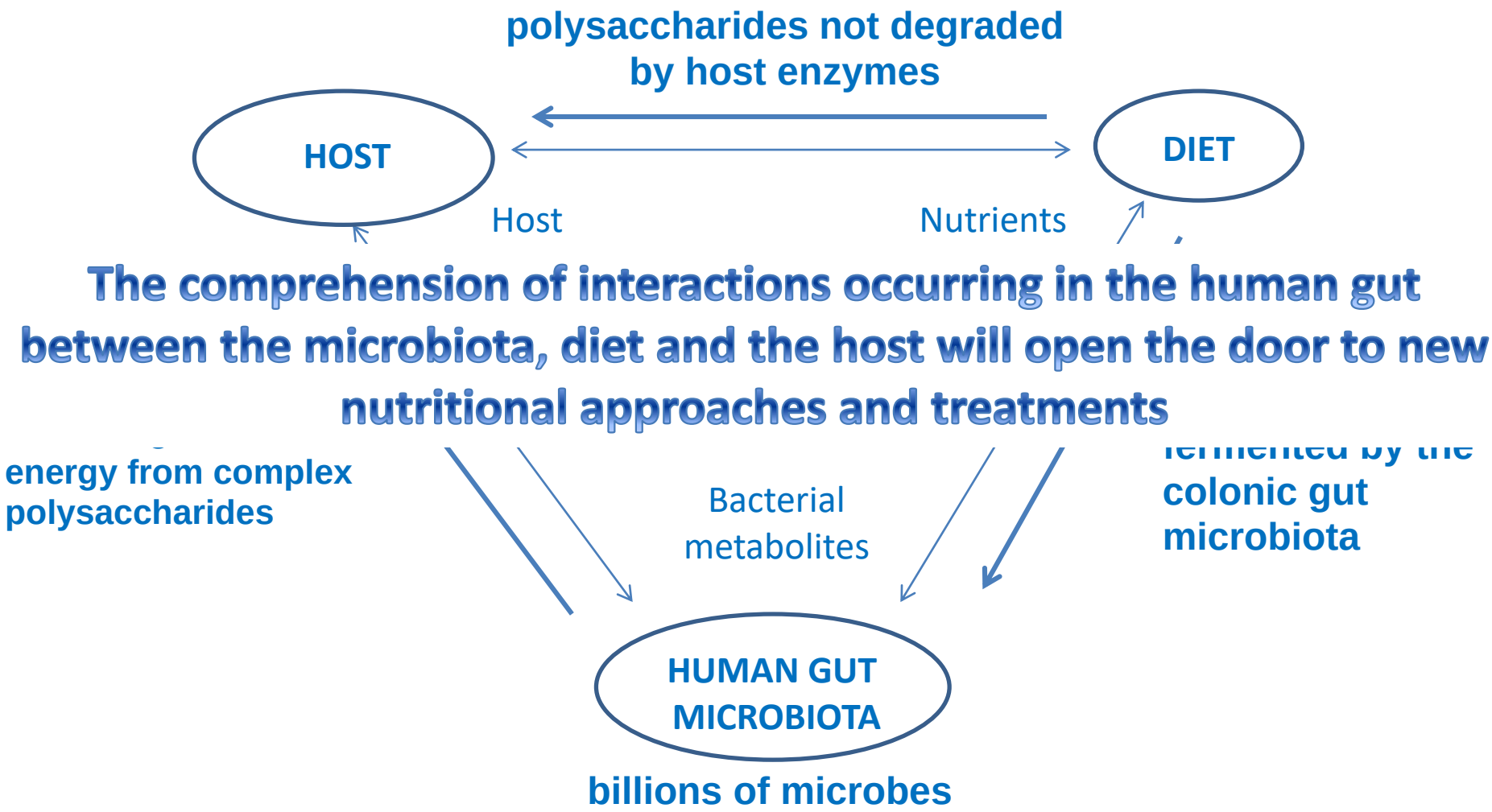
Grupo Inmunonutricion Ictan CSIC Madrid

InmunonutrIctanCsic @InmunonutriCSIC


MICROBIOTA
¿?
¿?
IMMUNE FUNCTION
NUTRITIONAL STATUS

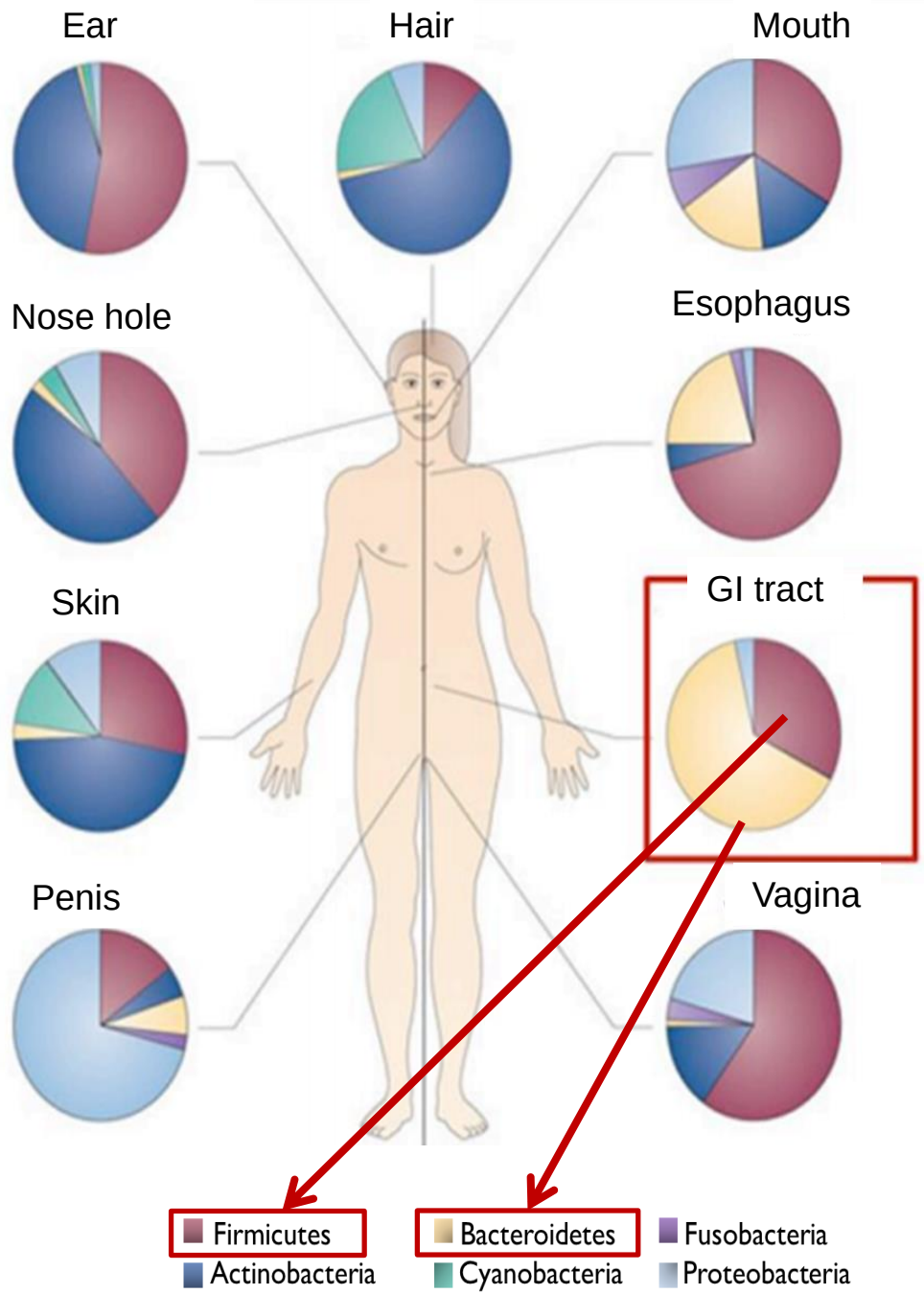
# ARE WE REALLY 100% HUMANS?

# SCHEMATIC ECOLOGICAL INTERACTIONS OCCURRING IN THE HUMAN COLON



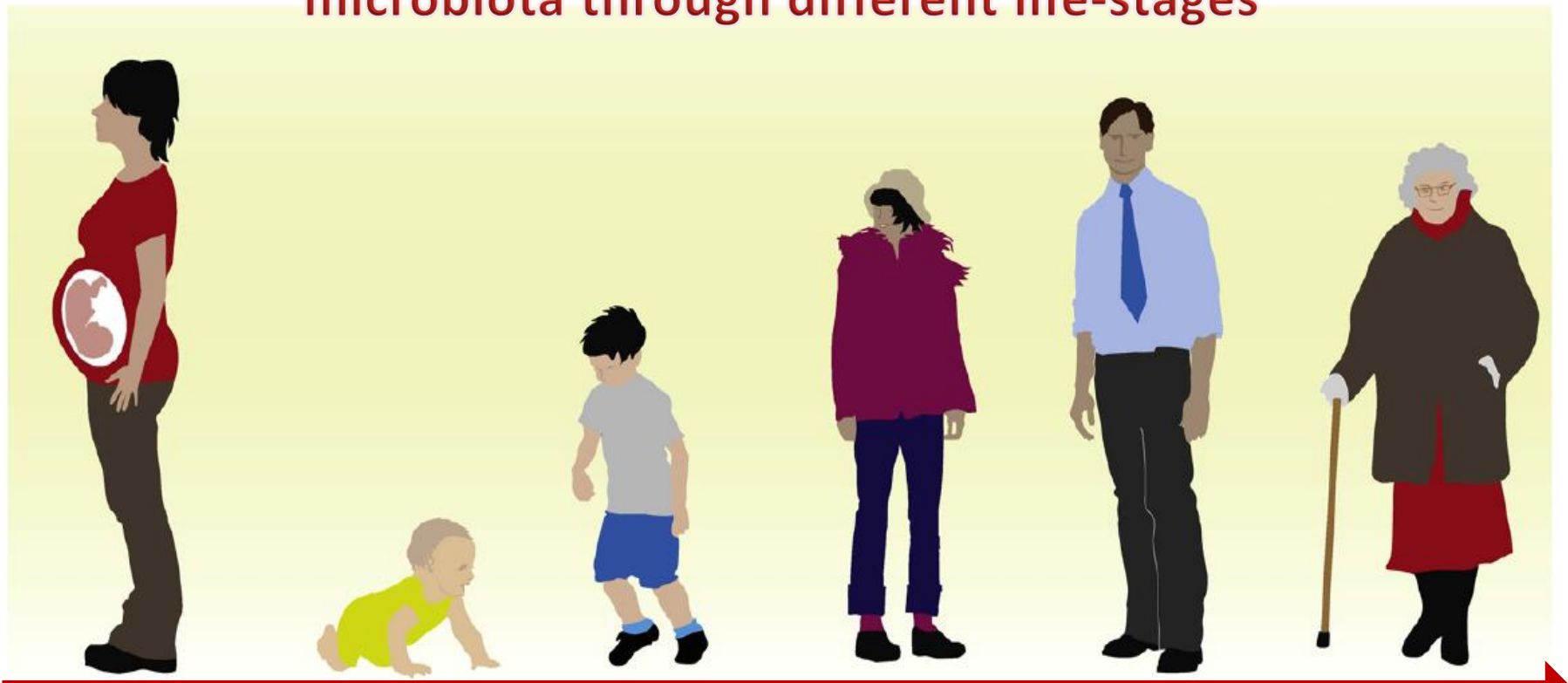

*Chassard &Lacroix. Curr Opin Clin Nutr Metab Care 2013, 16:453–460*

# HUMAN MICROBIOTA

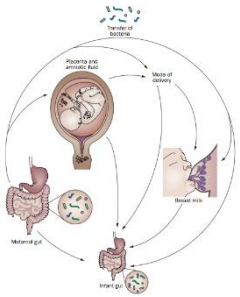



*Etxeberria, et al., 2016*

# Schematic summarising changes in the composition of the gut microbiota through different life-stages

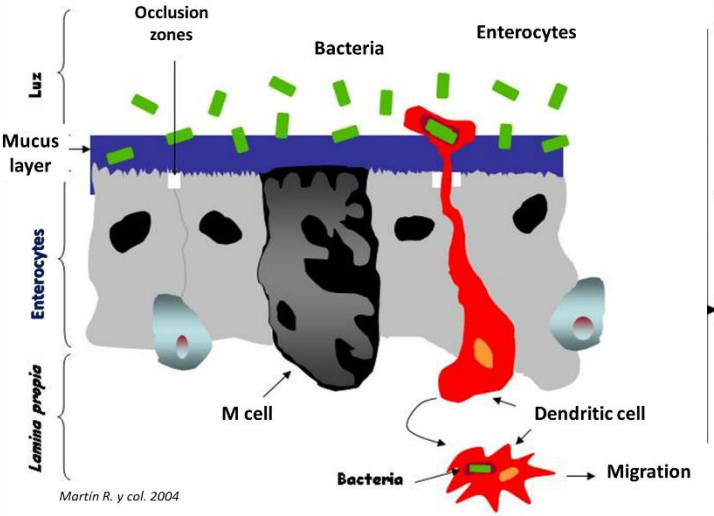


| FOETUS | BABY | CHILD | ADULTS | ELDERLY |
|---|---|---|---|---|
| Usually sterile | **Breast-fed-** bifidobacteria usually dominate<br><br>**Bottle fed-** more diverse with more Bacteroidetes, and less bifidobacteria | Increase in microbial diversity following weaning and intake of solids | **Dominant phyla** Firmicutes, Bacteroidetes, Actinobacteria<br>**Less dominant phyla** Proteobacteria, Verrucomicrobia | **Compared to healthy adults-** Reduction in Firmicutes and bifidobacteria. Increase in Bacteroidetes and Proteobacteria |



*Duncan and Flint. Maturitas. 2013;75(1):44-50.*

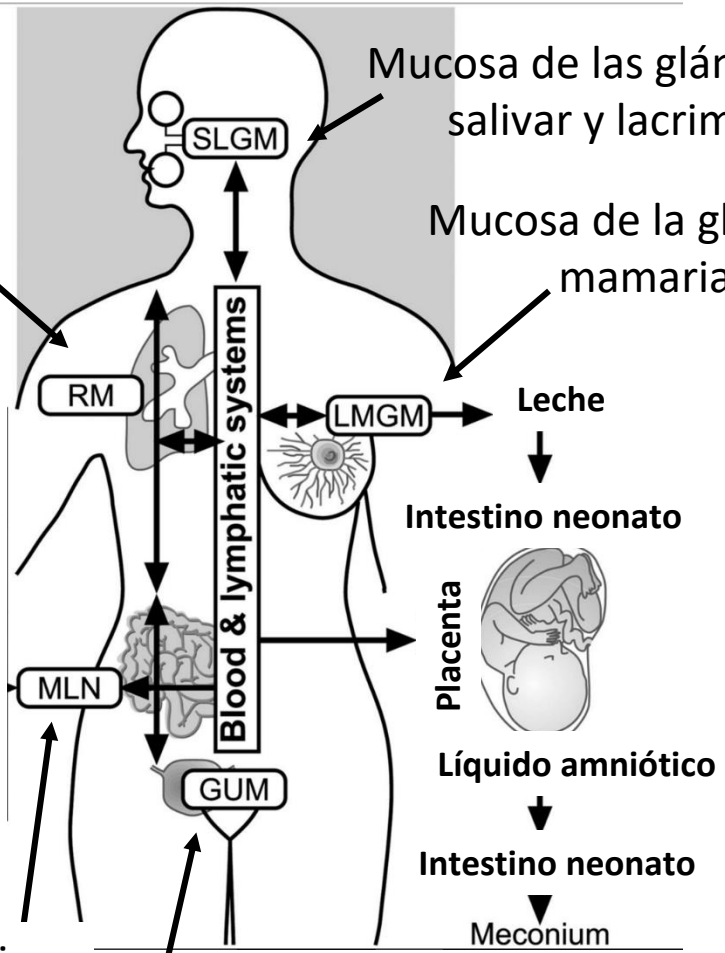
# LA MODULACIÓN NUTRICIONAL DE LA MICROBIOTA INTESTINAL MATERNA INFLUYE EL DESARROLLO DEL TRACTO GASTROINTESTINAL INFANTIL




Mucosa del tracto respiratorio

Mucosa de las glándulas salivar y lacrimal

Mucosa de la glándula mamaria

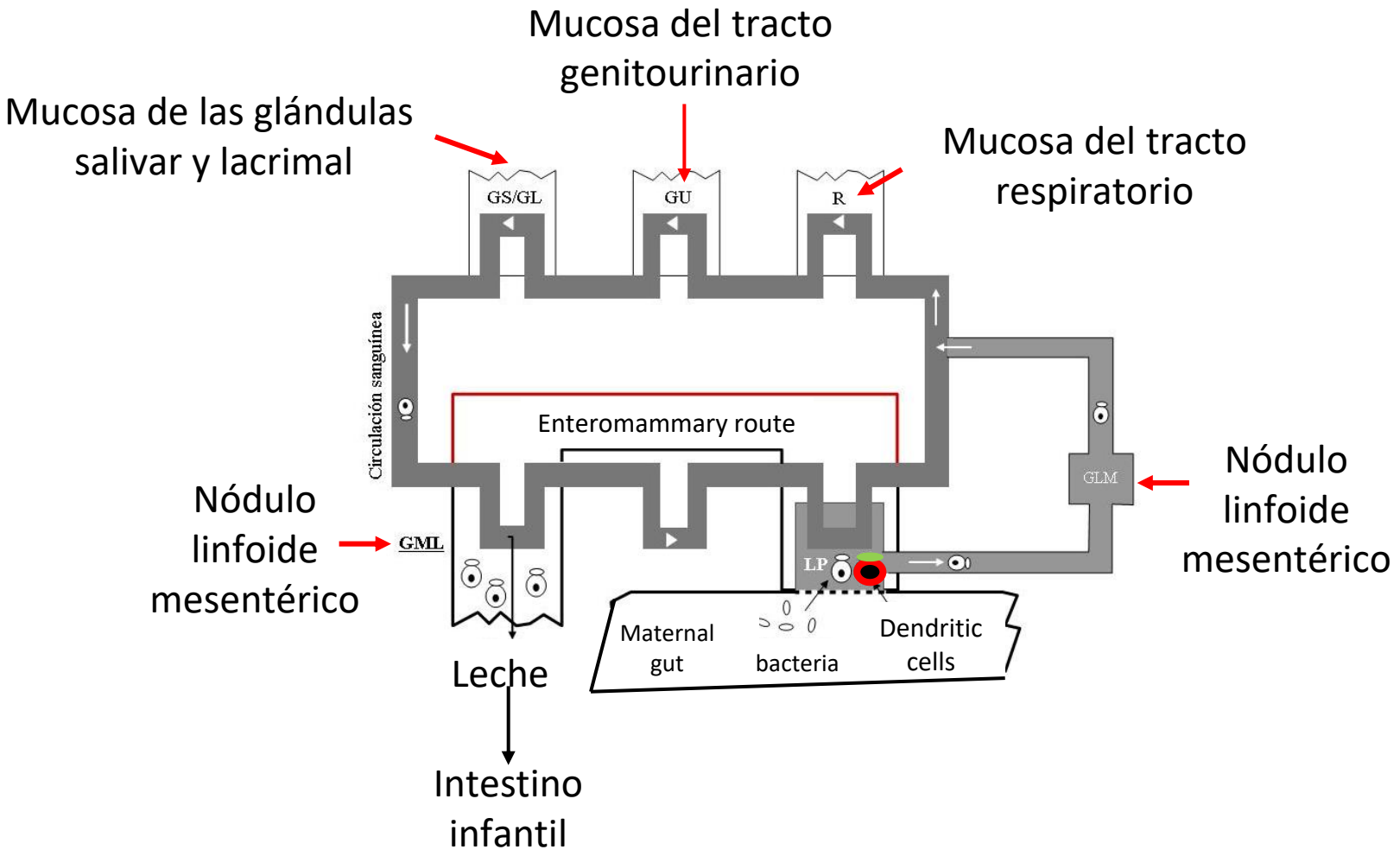



Nódulo linfoide mesentérico

Mucosa del tracto genitourinario

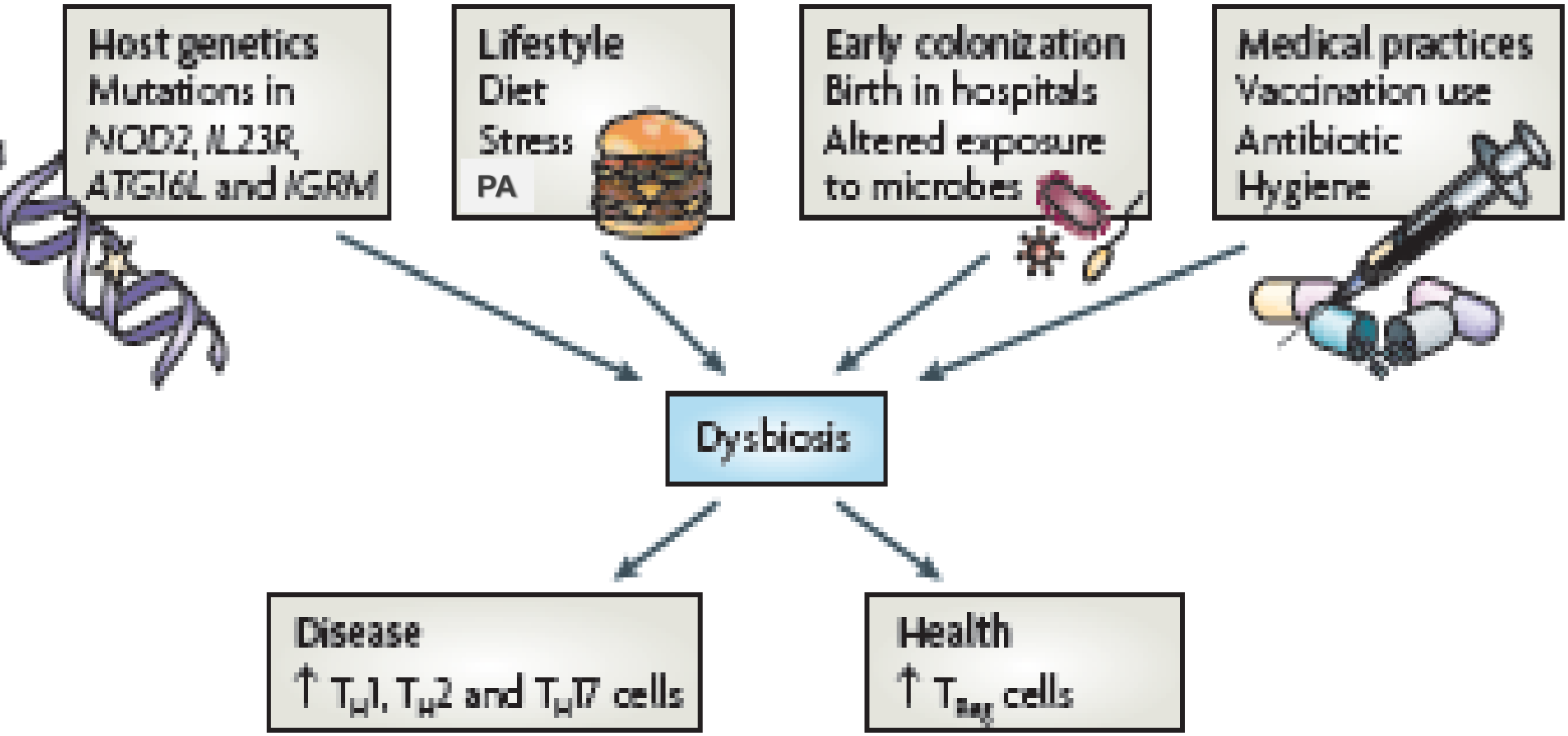
*Thum et al., J. Nutr. 2012;142:1921-1928*

# RUTA ENTEROMAMARIA



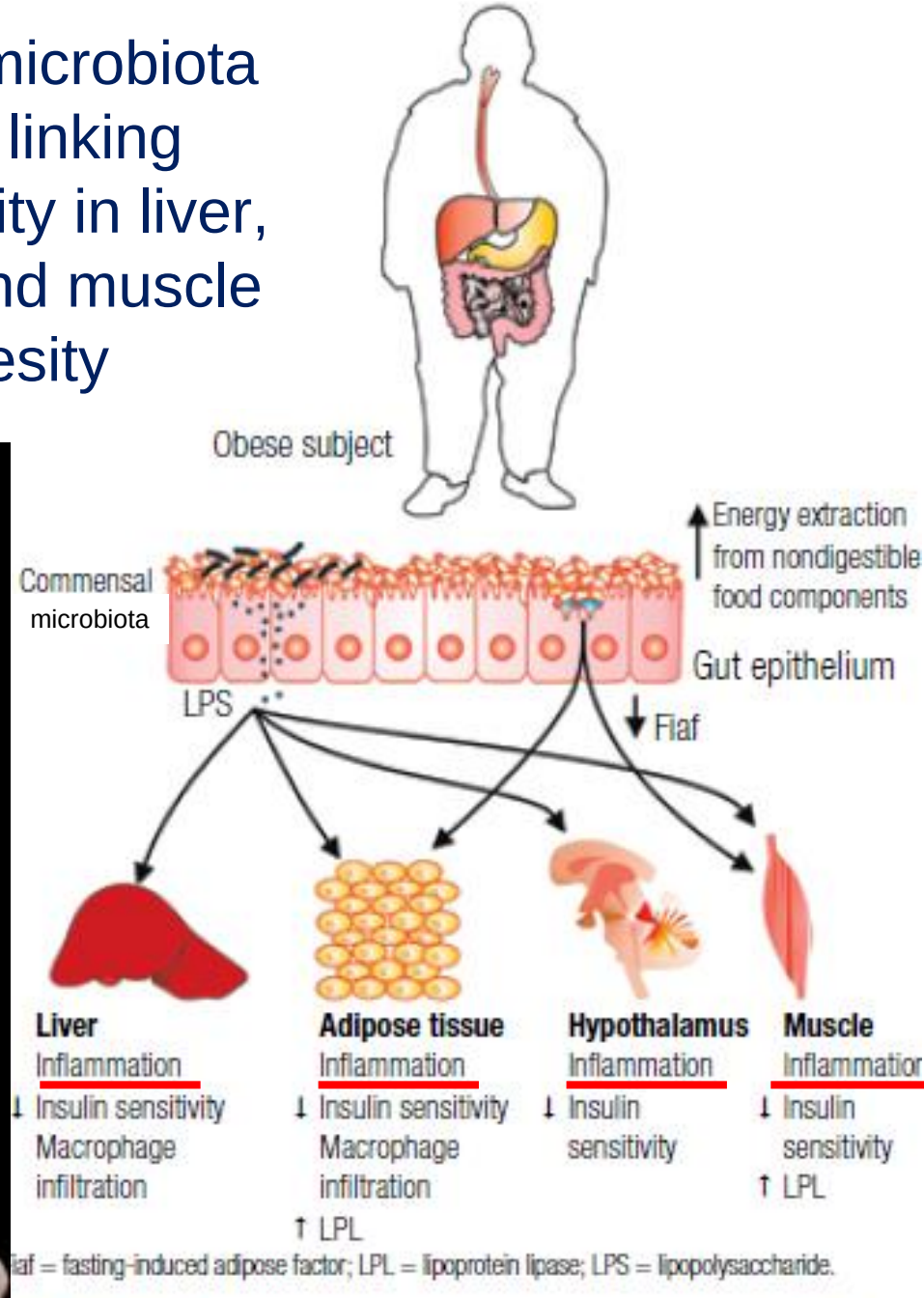

## Acceso de la bacteria intestinal a la leche materna

# THE COMPOSITION OF THE MICROBIOTA CAN SHAPE A HEALTHY IMMUNE RESPONSE OR PREDISPOSE TO DISEASE




**Deviations from the normal development of the microbiota may alter the outcome of immune development and potentially predispose individuals to various inflammatory diseases later in life**

# Bacterial LPS derived from gut microbiota may act as a triggering factor linking inflammation and insulin sensitivity in liver, adipose tissue, hypothalamus and muscle to high-fat diet-induced obesity




Daniela M. Tsukumo[1], Bruno M. Carvalho[1], Marco A. Carvalho-Filho[1], Mário J. A. Saad[1] Arq Bras Endocrinol Metab. 2009;53/2

# LA ALTA CANTIDAD DE GRASA Y EL BAJO APORTE DE FIBRA EN LA DIETA PUEDEN FOMENTAR LA DISBIOSIS, CON PREDISPONSICIÓN A LA OBESIDAD

FLUCTUACIONES PONDERALES

COMPORTAMIENTO ALIMENTARIO

CALIDAD& CANTIDAD DE SUEÑO

DIETA

↑ *BACTEROIDETES*

*FIRMICUTES* ↑

ACTIVIDAD FÍSICA

HÁBITOS SEDENTARIOS

**ESTRÉS**

*(Kotzampassi et al ., 2014)*

# Richness of Human Gut Microbiome correlates with Metabolic Markers

| | LGC | HGC | p |
|---|---|---|---|
| N (men/women) | 68 (23/45) | 224 (113/111) | |
| Age (yrs) | 56 ± 7.5 | 57 ± 7.3 | 0.86 |
| BMI (kg/m$^2$) | 32 (29 - 34) | 30 (23 - 33) | 0.035 |
| Weight (kg) | 95 (75 - 100) | 86 (71 - 100) | 0.019 |
| Fat % | 37 (29 - 42) | 31 (25 - 39) | 0.0069 |
| S-Adiponectin (mg/l) | 7.5 (5.5 – 12.9) | 9.6 (6.7 – 13.7) | 0.006 |
| B-leucocytes (10$^9$/l) | 6.4 (5.2 - 7.8) | 5.6 (4.8 - 6.9) | 0.0021 |
| P-CRP (mg/l) | 2.3 (1.1 - 5.7) | 1.4 (0.6 - 2.7) | 0.00088 |
| S-FIAF (µg/l) | 88 (72 - 120) | 78 (60 - 100) | 0.0047 |

**LGC is characterized by more marked overall adiposity, insulin resistance and dyslipidaemia and a more pronounced inflammatory phenotype than HGC**

Le Chatellier et al, Nature 2013

Comprehensive intervention (Diet+Physical Activity+Psychology) to treat adolescents (13-16 years old) with overweight and obesity (the EVASYON study)

nature publishing group

EVASYON

ARTICLES

INTERVENTION AND PREVENTION

Recorte rectangular

# Interplay Between Weight Loss and Gut Microbiota Composition in Overweight Adolescents

Arlette Santacruz[1], Ascensión Marcos[2], Julia Wärnberg[2,3], Amelia Martí[4,5], Miguel Martin-Matillas[6], Cristina Campoy[6], Luis A. Moreno[7], Oscar Veiga[8], Carlos Redondo-Figuero[9], Jesús M. Garagorri[10], Cristina Azcona[5], Manuel Delgado[11], Miguel García-Fuentes[9], Maria C. Collado[1] and Yolanda Sanz[1]; the EVASYON Study Group

# Comprehensive intervention (Diet+Physical Activity+Psychology) to treat adolescents (13-16 years old) with overweight and obesity (the EVASYON study)


EVASYON

WEIGHT LOSS < 2 KG

INTENSIVE PHASE

2 MONTHS

WEIGHT LOSS > 4 KG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# BACTERIAL COUNTS IN FECAL SAMPLES OF LOW-WEIGHT LOSS (<2KG) GROUP OF ADOLESCENTS, BEFORE AND AFTER INTERVENTION

| | Bacterial counts[a] (log cells/g fecal sample), $n = 13$ | | | | | | | | Mann–Whitney *U*-test |
|---|---|---|---|---|---|---|---|---|---|
| | Before Intervention | | | | After Intervention | | | | |
| Bacterial group | Pr[b] | Mean | Median | IQR | Pr[b] | Mean | Median | IQR | *P* value |
| Total bacteria | 13 | 13.2 | 12.9 | 12.8–13.9 | 13 | 13.2 | 13.1 | 12.8–13.4 | 0.975 |
| *Bacteroides* | 13 | 6.2 | 6.2 | 5.8–7.0 | 13 | 6.3 | 6.2 | 5.8–6.9 | 0.957 |
| *Clostridium coccoides* | 13 | 10.0 | 10.0 | 9.8–10.2 | 13 | 9.9 | 10.0 | 9.7–10.2 | 0.978 |
| *Clostridium leptum* | 13 | 8.2 | 8.0 | 7.9–8.5 | 13 | 8.4 | 8.3 | 7.9–8.8 | 0.446 |
| *Lactobacillus* | 13 | 7.9 | 7.8 | 7.6–8.1 | 13 | 7.9 | 7.9 | 7.7–8.1 | 0.723 |
| *Escherichia coli* | 13 | 6.7 | 6.5 | 6.0–7.7 | 13 | 6.6 | 6.5 | 6.0–7.1 | 0.624 |
| *Bifidobacterium* | 13 | 9.2 | 9.2 | 8.8–9.5 | 13 | 8.9 | 9.0 | 8.4–9.6 | 0.514 |
| *Bifidobacterium longum* | 13 | 7.1 | 7.0 | 6.8–7.4 | 13 | 7.0 | 6.9 | 6.3–7.7 | 0.644 |
| *Bifidobacterium breve* | 13 | 4.8 | 4.8 | 4.4–5.2 | 13 | 4.5 | 4.5 | 4.3–4.7 | 0.110 |
| *Bifidobacterium bifidum* | 13 | 9.1 | 9.0 | 8.8–9.4 | 13 | 8.9 | 8.9 | 8.3–9.7 | 0.640 |
| *Bifidobacterium adolescentis* | 13 | 8.1 | 8.0 | 7.8–8.4 | 13 | 8.0 | 7.9 | 7.3–8.7 | 0.650 |
| *Bifidobacterium catenulatum* | 13 | 5.8 | 5.8 | 5.5–6.2 | 13 | 5.5 | 5.5 | 5.3–5.7 | 0.103 |

[a]Data are shown as medians and interquartile range (IQR) of cell number per gram of fecal samples. [b]Prevalence (Pr) reflects the number of positive amplifications by quantitative real-time PCR from total samples ($n = 13$).

*Statistical differences between bacterial counts before and after intervention were calculated by using the Mann–Whitney *U*-test and established at $P < 0.050$.

EVASYON

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# BACTERIAL COUNTS IN FECAL SAMPLES OF LOW-WEIGHT LOSS (>4KG) GROUP OF ADOLESCENTS, BEFORE AND AFTER INTERVENTION

| | Bacterial counts[a] (log cells/g fecal sample), *n* = 23 | | | | | | | | Mann–Whitney *U*-test |
|---|---|---|---|---|---|---|---|---|---|
| | Before intervention | | | | After intervention | | | | |
| Bacterial group | Pr[b] | Mean | Median | IQR | Pr | Mean | Median | IQR | *P* value |
| Total bacteria | 23 | 14.8 | 14.6 | 14.0–15.6 | 23 | 14.5 | 14.8 | 13.1–16.1 | 0.450 |
| *Bacteroides* | 23 | 7.5 | 7.6 | 6.7–8.2 | 23 | 8.6 | 8.6 | 8.1–9.3 | 0.001* |
| *Clostridium coccoides* | 23 | 8.7 | 8.6 | 8.3–9.0 | 23 | 7.9 | 7.7 | 7.4–8.5 | 0.001* |
| *Clostridium leptum* | 23 | 9.5 | 9.6 | 8.7–9.9 | 21 | 9.5 | 9.7 | 9.1–10.0 | 0.666 |
| *Lactobacillus* | 23 | 6.4 | 6.4 | 5.9–6.9 | 23 | 6.9 | 7.0 | 6.3–7.1 | 0.007* |
| *Escherichia coli* | 23 | 6.3 | 6.3 | 5.8–6.8 | 23 | 6.4 | 6.3 | 6.1–7.0 | 0.231 |
| *Bifidobacterium* | 23 | 8.3 | 8.1 | 7.7–8.6 | 23 | 8.2 | 8.2 | 7.4–8.6 | 0.692 |
| *Bifidobacterium longum* | 23 | 7.1 | 7.2 | 6.3–7.9 | 23 | 6.4 | 6.2 | 5.3–7.3 | 0.044* |
| *Bifidobacterium breve* | 15 | 3.5 | 3.3 | 3.0–3.6 | 11 | 3.2 | 3.1 | 3.0–3.5 | 0.237 |
| *Bifidobacterium bifidum* | 19 | 5.9 | 5.6 | 4.5–7.1 | 17 | 5.6 | 5.6 | 4.3–7.1 | 0.490 |
| *Bifidobacterium adolescentis* | 23 | 7.6 | 7.9 | 6.8–8.8 | 23 | 6.9 | 7.0 | 6.0–8.1 | 0.092 |
| *Bifidobacterium catenulatum* | 22 | 7.6 | 7.7 | 6.7–8.5 | 23 | 7.2 | 7.6 | 6.3–8.4 | 0.594 |

[a]Data are shown as medians and interquartile range (IQR) of cell number per gram of fecal samples. [b]Prevalence (Pr) reflects the number of positive amplifications by quantitative real-time PCR from total samples (*n* = 23).

*Statistical differences between bacterial counts before and after intervention were calculated by using the Mann–Whitney *U*-test and established at $P < 0.050$.

EVASYON

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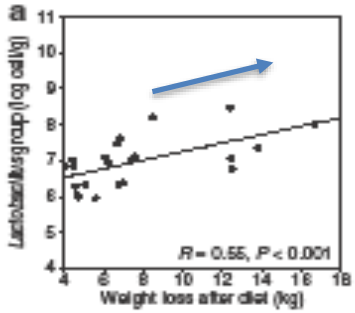
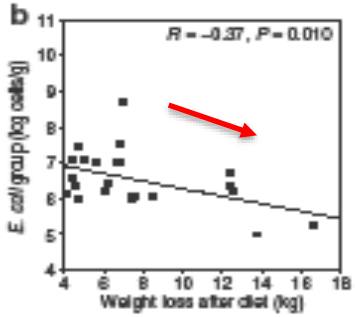
# Correlations between fecal bacteria counts and weight lost after intervention in responder adolescents (n=23; >4.0 kg weight lost)

EVASYON

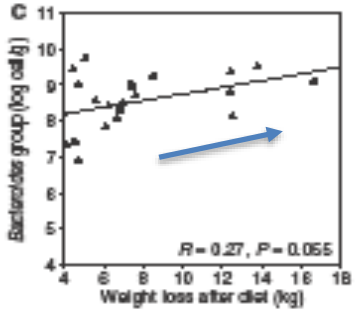
**LACTOBACILLUS GROUP**




**E. COLI GROUP**




**BACTEROIDES GROUP**

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# BACTERIAL COUNTS IN FECAL SAMPLES OF LOW AND HIGH-WEIGHT LOSS GROUPS OF ADOLESCENTS, BEFORE AND AFTER INTERVENTION

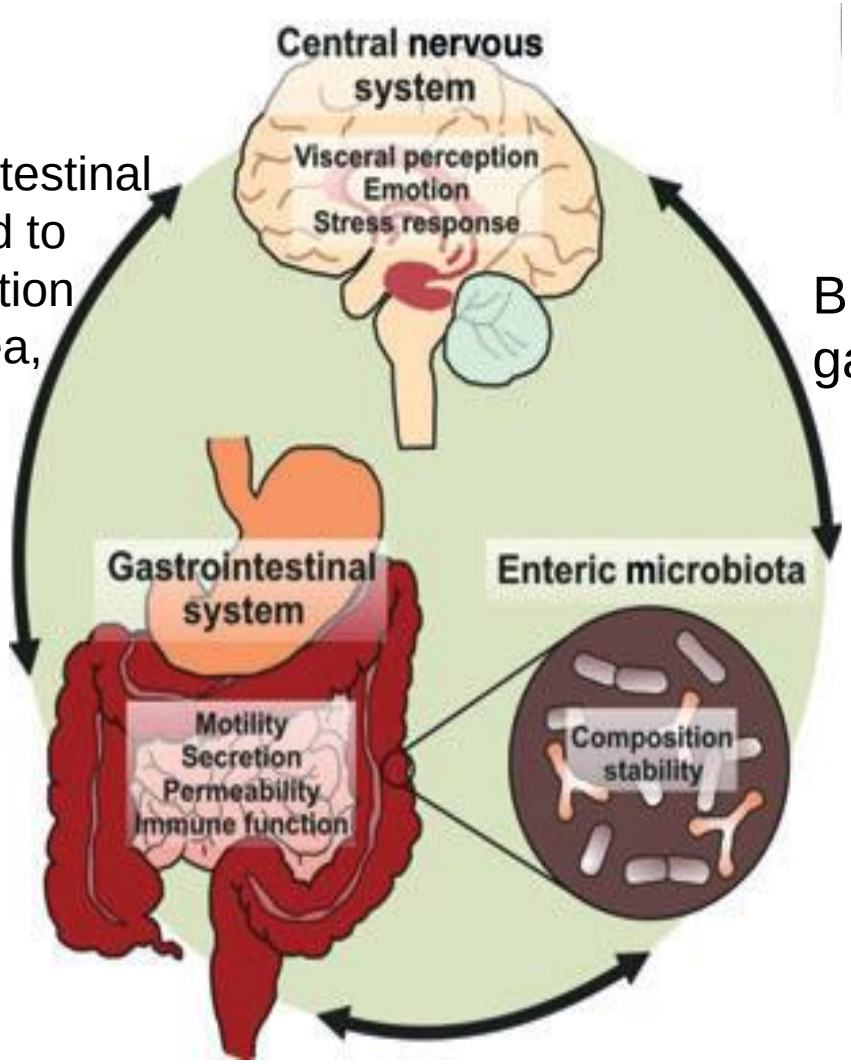
| | Low weight–loss group (<2.0 kg) (*n* = 13) | | | | High weight–loss group (>4.0 kg) (*n* = 23) | | | | Mann–Whitney *U*-test |
|---|---|---|---|---|---|---|---|---|---|
| Bacterial group | Pr* | Mean | Median | IQR | Pr | Mean | Median | IQR | *P* value |
| Bacterial counts† before intervention (log cells/g fecal sample) | | | | | | | | | |
| Total bacteria | 13 | 13.2 | 12.9 | 12.8–13.9 | 23 | 14.8 | 14.6 | 14.0–15.6 | <0.001* |
| *Bacteroides* | 13 | 6.2 | 6.2 | 5.8–7.0 | 23 | 7.5 | 7.6 | 6.7–8.2 | 0.004* |
| *Clostridium coccoides* | 13 | 10.0 | 10.0 | 9.8–10.2 | 23 | 8.7 | 8.6 | 8.3–9.0 | <0.001* |
| *Clostridium leptum* | 13 | 8.2 | 8.0 | 7.9–8.5 | 23 | 9.5 | 9.6 | 8.7–9.9 | <0.001* |
| *Lactobacillus* | 13 | 7.9 | 7.8 | 7.6–8.1 | 23 | 6.4 | 6.4 | 5.9–6.9 | <0.001* |
| *Escherichia coli* | 13 | 6.7 | 6.5 | 6.0–7.7 | 23 | 6.3 | 6.3 | 5.8–6.8 | 0.123 |
| *Bifidobacterium* | 13 | 9.2 | 9.2 | 8.8–9.5 | 23 | 8.3 | 8.1 | 7.7–8.6 | 0.001* |
| *Bifidobacterium longum* | 13 | 7.1 | 7.0 | 6.8–7.4 | 23 | 7.1 | 7.2 | 6.3–7.9 | 0.845 |
| *Bifidobacterium breve* | 13 | 4.8 | 4.8 | 4.4–5.2 | 15 | 3.5 | 3.3 | 3.0–3.6 | 0.001* |
| *Bifidobacterium bifidum* | 13 | 9.1 | 9.0 | 8.8–9.4 | 19 | 5.9 | 5.6 | 4.5–7.1 | <0.001* |
| *Bifidobacterium adolescentis* | 13 | 8.1 | 8.0 | 7.8–8.4 | 23 | 7.6 | 7.9 | 6.8–8.8 | 0.468 |
| *Bifidobacterium catenulatum* | 13 | 5.8 | 5.8 | 5.5–6.2 | 22 | 7.6 | 7.7 | 6.7–8.5 | 0.030* |
| Bacterial counts† after intervention (log cells/g fecal sample) | | | | | | | | | |
| Total bacteria | 13 | 13.2 | 13.1 | 12.8–13.4 | 23 | 14.5 | 14.8 | 13.1–16.1 | 0.015* |
| *Bacteroides* | 13 | 8.3 | 8.2 | 5.8–8.9 | 23 | 8.6* | 8.6 | 8.1–9.3 | 0.001* |
| *C. coccoides* | 13 | 9.9 | 10.0 | 9.7–10.2 | 23 | 7.9* | 7.7 | 7.4–8.5 | <0.001* |
| *C. leptum* | 13 | 8.4 | 8.3 | 7.9–8.8 | 21 | 9.5 | 9.7 | 9.1–10.0 | <0.001* |
| *Lactobacillus* | 13 | 7.9 | 7.9 | 7.7–8.1 | 23 | 6.9* | 7.0 | 6.3–7.1 | <0.001* |
| *E. coli* | 13 | 6.6 | 6.5 | 6.0–7.1 | 23 | 6.4 | 6.3 | 6.1–7.0 | 0.972 |
| *Bifidobacterium* | 13 | 8.9 | 9.0 | 8.4–9.6 | 23 | 8.2 | 8.2 | 7.4–8.6 | 0.008* |
| *B. longum* | 13 | 7.0 | 6.9 | 6.3–7.7 | 23 | 6.4* | 6.2 | 5.3–7.3 | 0.062 |
| *B. breve* | 13 | 4.5 | 4.5 | 4.3–4.7 | 11 | 3.2 | 3.1 | 3.0–3.5 | <0.001* |
| *B. bifidum* | 13 | 8.9 | 8.9 | 8.3–9.7 | 17 | 5.6 | 5.6 | 4.3–7.1 | <0.001* |
| *B. adolescentis* | 13 | 8.0 | 7.9 | 7.3–8.7 | 23 | 6.9 | 7.0 | 6.0–8.1 | 0.063 |
| *B. catenulatum* | 13 | 5.5 | 5.5 | 5.3–5.7 | 23 | 7.2 | 7.6 | 6.3–8.4 | 0.036* |

†Prevalence (Pr) reflects the number of positive amplifications by quantitative real-time PCR from total samples (*n* = 13 or 23). ‡Data are shown as medians and interquartile range (IQR) of cell number per gram of fecal samples.
*Statistical differences between bacterial counts for each group (high- and low-weight adolescent groups) before and after intervention were calculated by using

# THE ENTERIC MICROBIOTA-GUT-BRAIN AXIS

(BI-DIRECTIONAL COMMUNICATION SYSTEM)

Any alteration in gastrointestinal function is communicated to the brain with the perception of visceral events (nausea, satiety, pain)

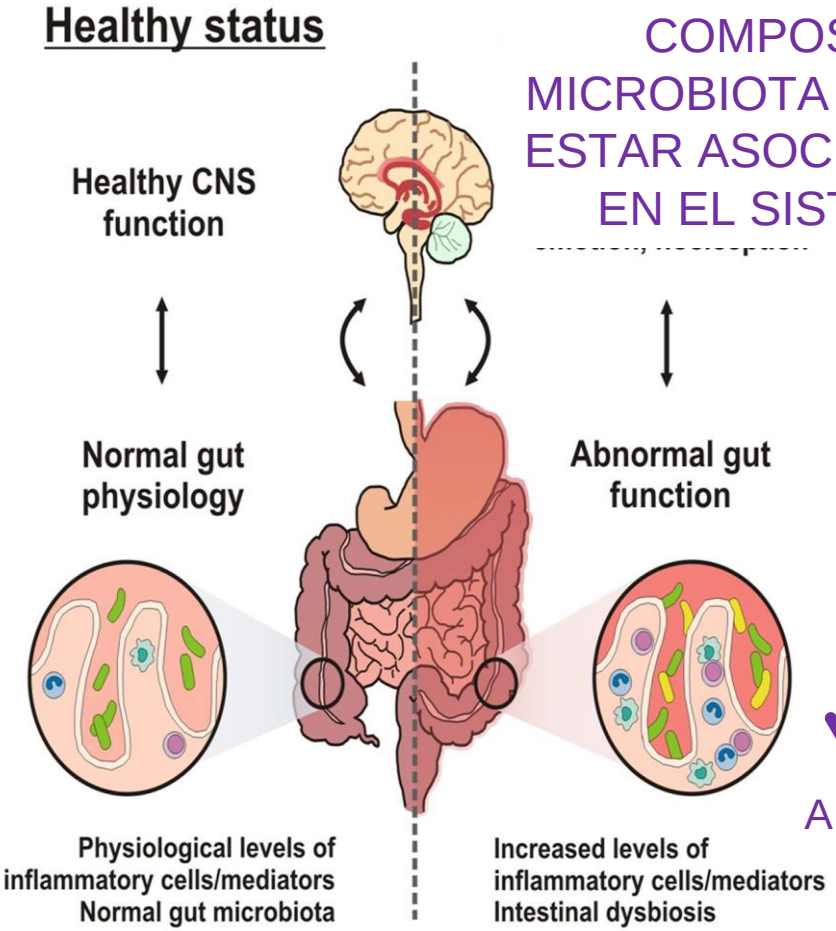



Brain modulates gastrointestinal function

**NEURAL PATHWAYS AS WELL AS IMMUNE AND ENDOCRINE MECHANISMS**

*Cryan JF & O'Mahony SM. Neurogastroenterol Motil. 2011;23(3):187-92*

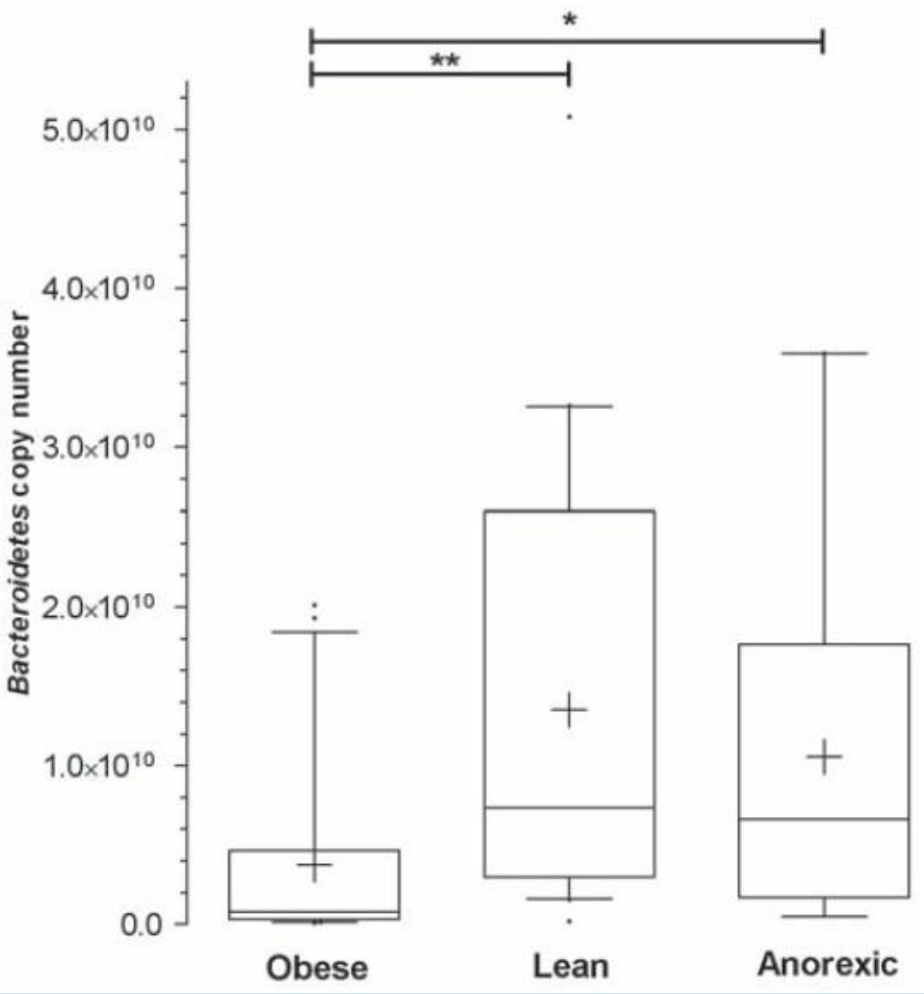
# COMUNICACIÓN MICROBIOTA INTESTINAL-CEREBRO EN LA SALUD Y LA ENFERMEDAD




COMPOSICIÓN DE LOS MICROBIOTA INTESTINAL PUEDE ESTAR ASOCIADA CON CAMBIOS EN EL SISTEMA NERVIOSO

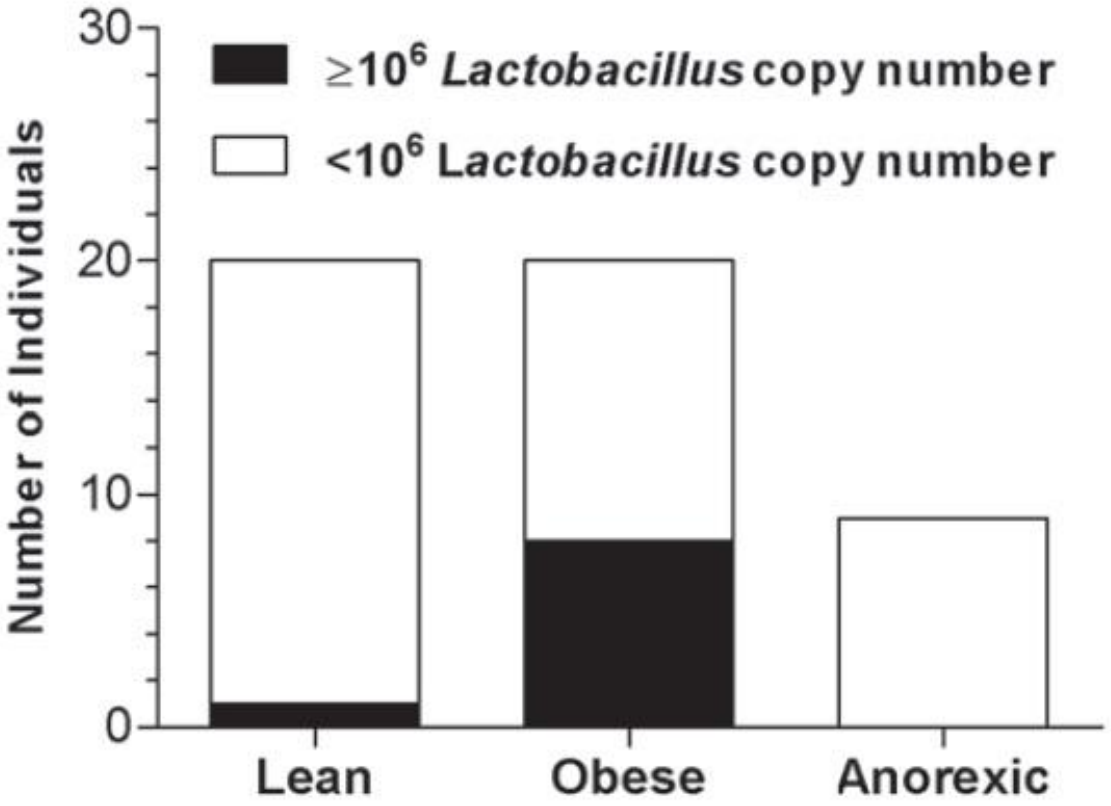
ALTERACIONES PSIQUIÁTRICAS ?

# BACTEROIDETES



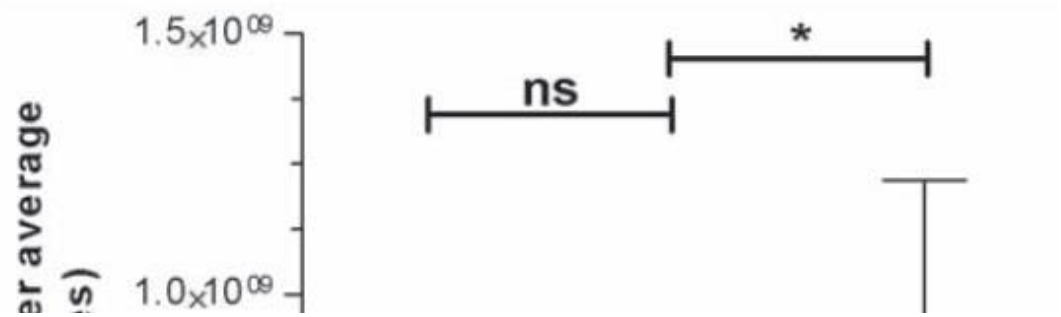

*Armougom et al., 2009. Plos One, 4, 9, e7125*

# LACTOBACILLUS



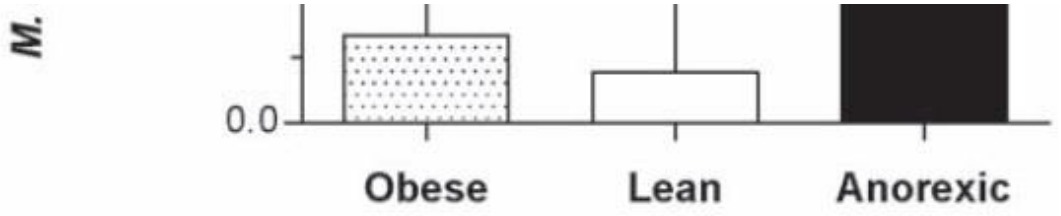

*Armougom et al., 2009. Plos One, 4, 9, e7125*

# METHANOGENS SMITHII



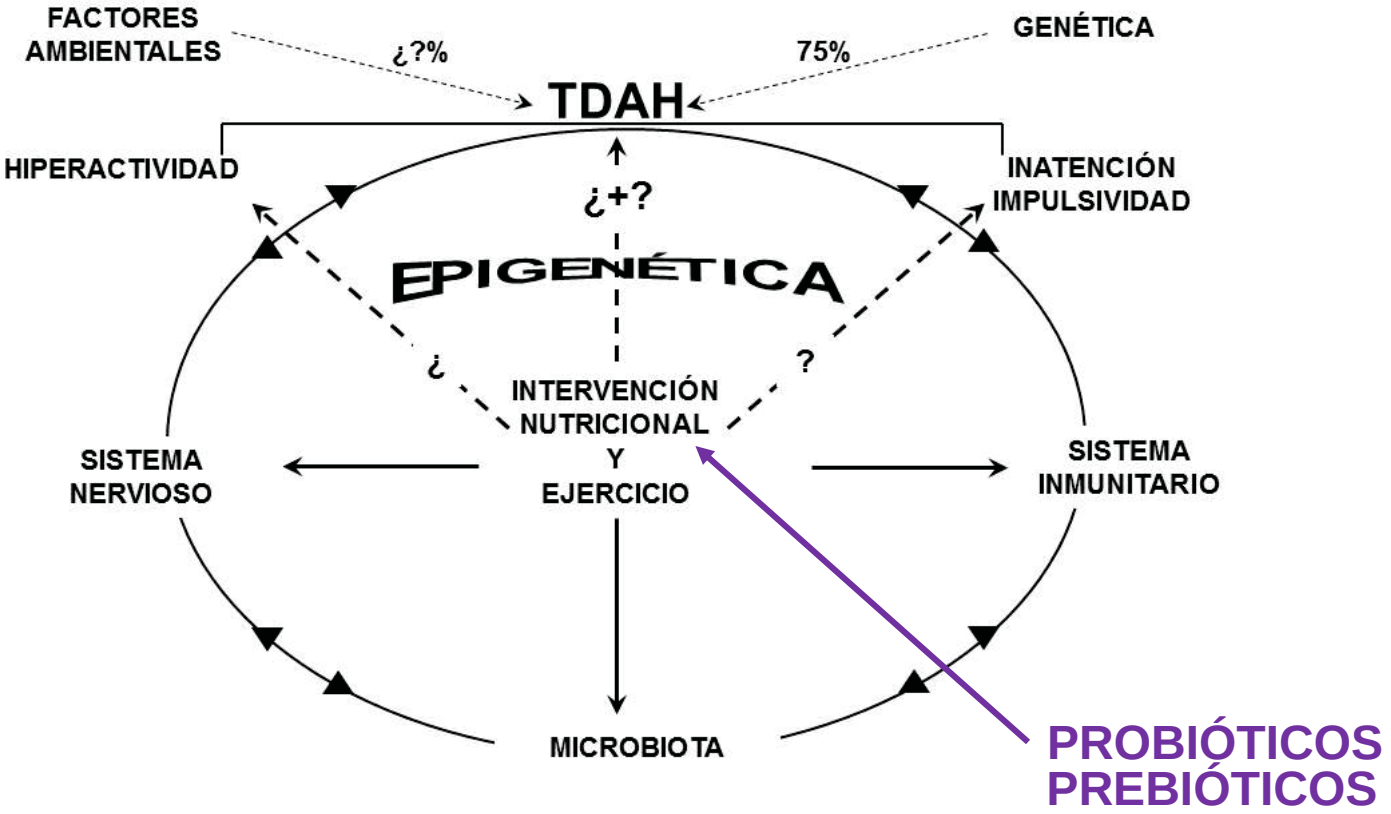

M. smithii recicla el hidrógeno en metano, permitiendo un incremento en la transformación de nutrientes en calorías

Estas bacterias podrían estar asociadas a una adaptación del organismo de forma óptima a la dieta tan baja en calorías consumida por la AN




*Armougom et al., 2009. Plos One, 4, 9, e7125*

# FACTORES LIGADOS AL EJE MICROBIOTA INTESTINAL-CEREBRO




# Sociedad Española de Probióticos y Prebióticos

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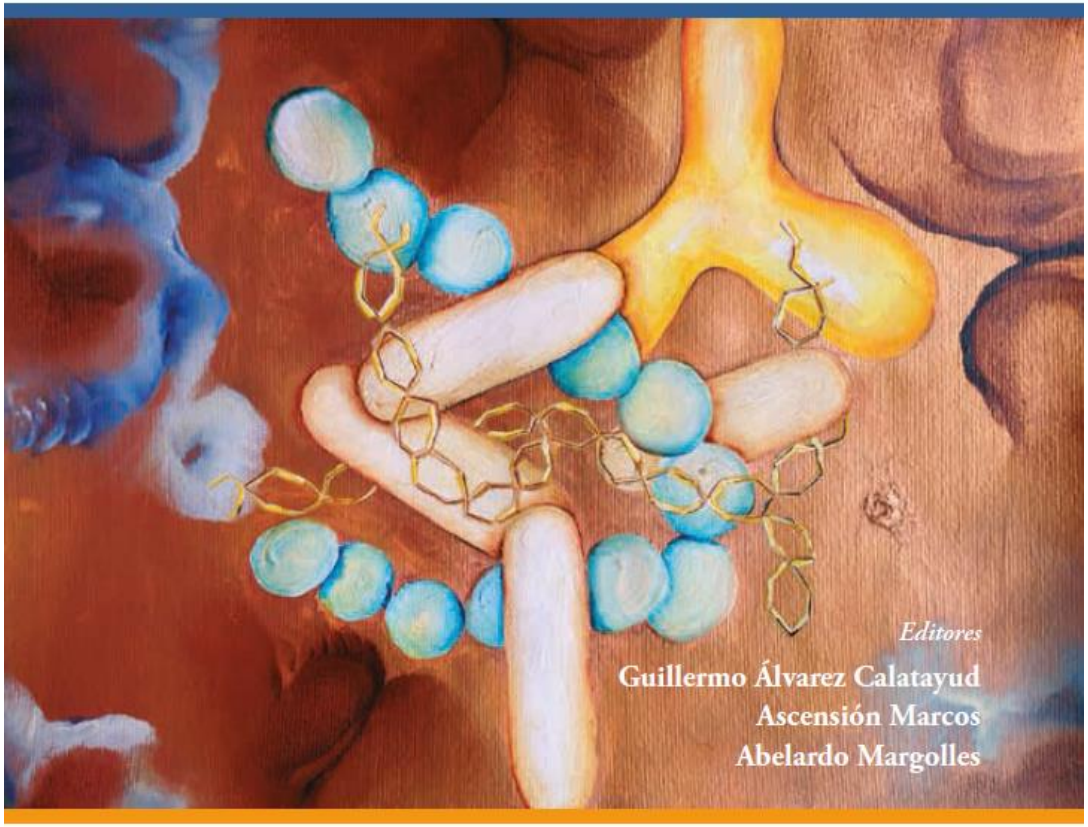
# Probióticos, prebióticos y salud: Evidencia científica



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SOCIEDAD ESPAÑOLA DE PROBIÓTICOS Y PREBIÓTICOS

# Declaraciones consensuadas del Workshop "PROBIÓTICOS Y SALUD. EVIDENCIA CIENTÍFICA"

Madrid, 18 de diciembre de 2009

# PROBIOTICOS COMO TERAPIA ALTERNATIVA

## Inmunomodulación

**Prevención cáncer**

**Diarrea**

**Helicobacter pílori**

**Enterocolitis necrotizante**

**Alergia**

**Enfermedad inflamatoria intestinal**

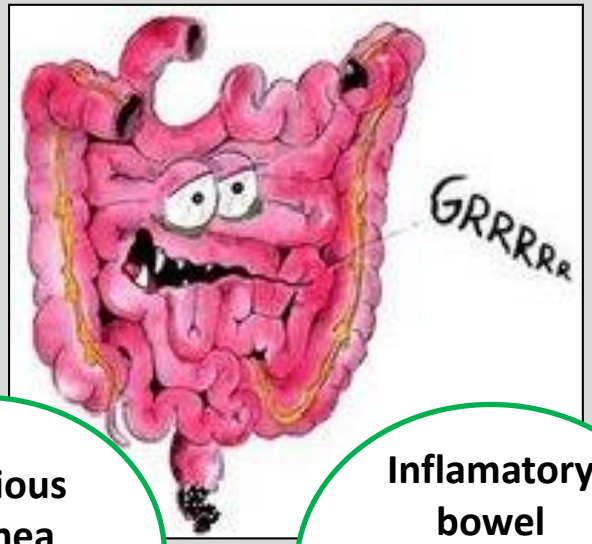
**Metabolismo lipídico**

# What is a probiotic?

*"Live microorganisms which, when administered in adequate amounts, confer a health benefit to the host"* (FAO/WHO )

## Disease

**Treatment and reducing morbidity**



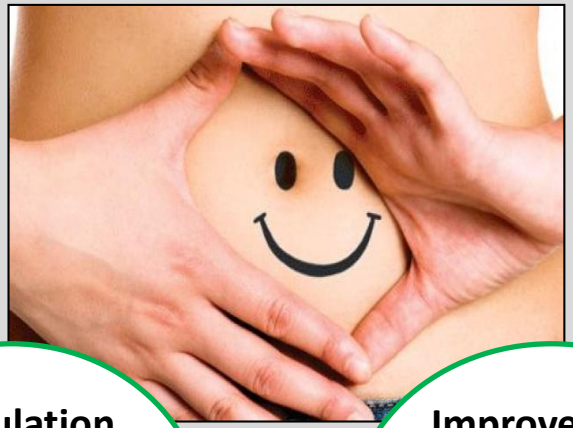

**Infectious diarrhea** (*Preidis et al. 2011)*

**Lactose intolerance** *(Pelletier et al. 2001).*

**Inflamatory bowel diseases** (*Sood et al. 2009*)

## Health

**Prevention of disease risk**



**Modulation of intestinal microbiota** *(Matsumoto et al. 2010*)

**Reduction of intestinal symptoms** *(Guyonet et al. 2009*)

**Improvement of constipation** *(Matsumoto et al. 2006*)

# PREVENTIVE ROLE OF LGG

n=62

Atopic history

LGG

(2-4 wk)

LGG

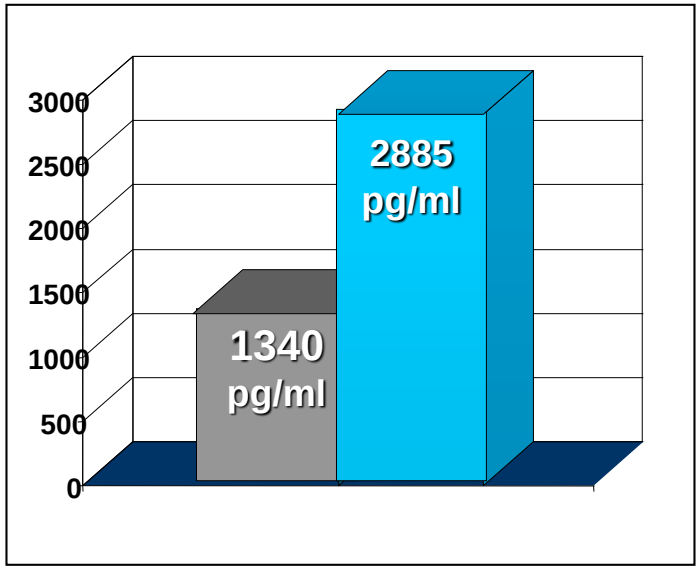
(6 months)

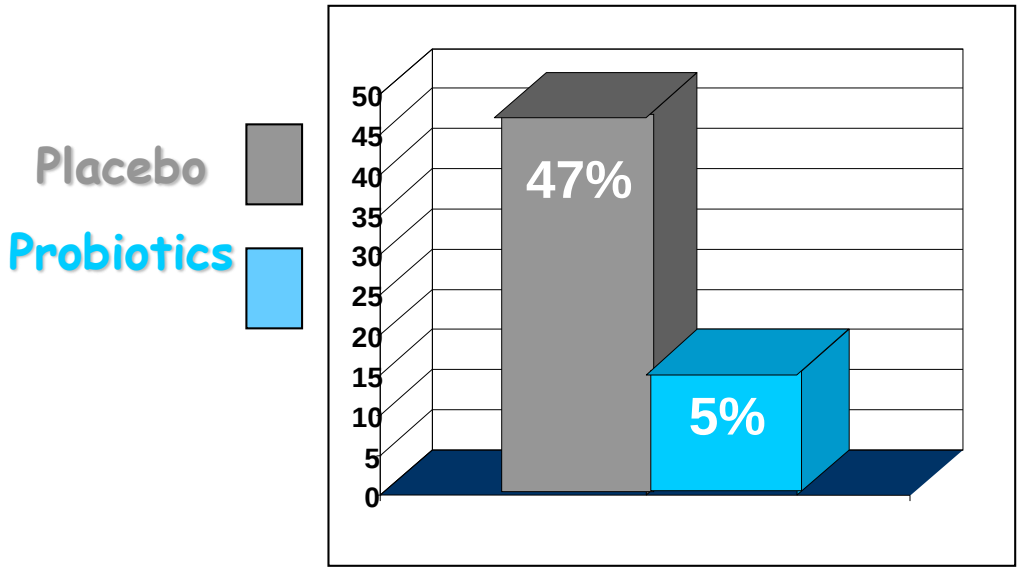

breast-feeding

with formula

Risk of developing atopic eczema during the first 2 years

TGF-β2
in breast milk



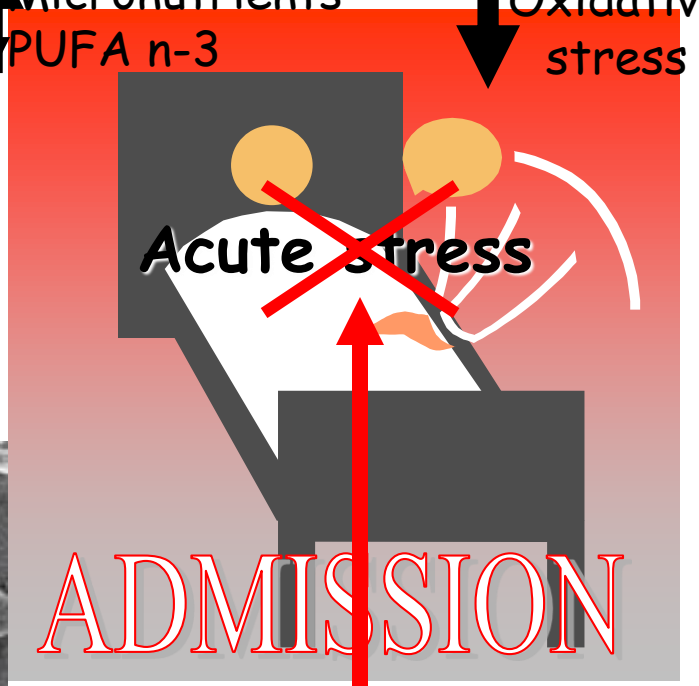



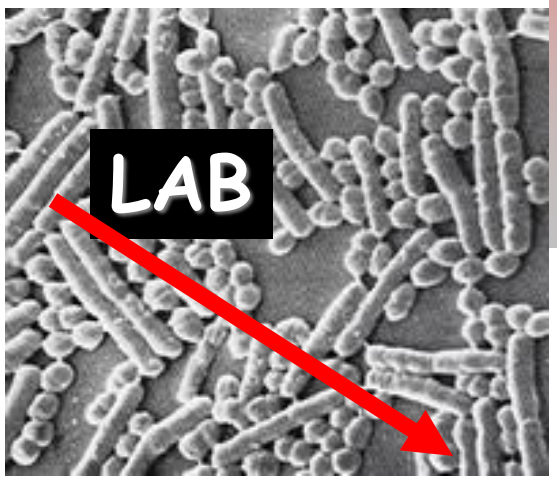

*Isolauri et al. Lancet. 2001 Apr 7;357(9262)*

MAJOR DEPRESSIVE DISORDER (MDD)

Micronutrients
PUFA n-3

Oxidative stress



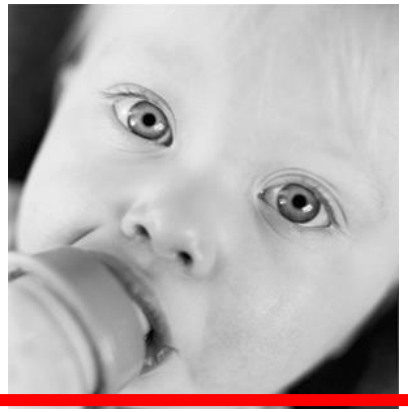

Altered GI function

Lactobacillus
Bifidobacterium

Cortisol

Proinflammatory Cytokines

*Logan A & Katzman M. (2005)*

# PROMOVER CALIDAD DE VIDA

# MEDIANTE LA PREVENCIÓN DE

# MECANISMOS INFLAMATORIOS

CSIC
Consejo Superior de Investigaciones Científicas

# MENSAJES PARA LLEVAR A CASA

**La microbiota intestinal ejerce un alto impacto en el estado nutricional y la salud del huésped a través de la modulación del sistema inmune**

**Los probióticos pueden ejercer un importante papel en el microambiente intestinal cambiando la composición de la microbiota y probablemente**

# ¿RECOMENDACIONES FUTURO?

**No obstante, son necesarios más estudios para demostrar cual es la dosis de probiótico/s más adecuada para ejercer un determinado efecto en una determinada población dependiendo de su estado nutricional**

**DOSIS, CEPA, PERIODO DE TIEMPO DE CONSUMO, EDAD, SEXO, ESTADO NUTRICIONAL**

FACTORES

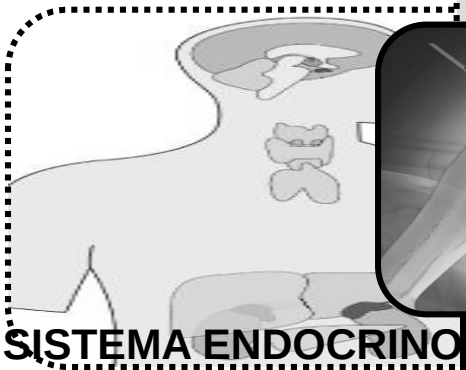
# INMUNONUTRICIÓN Y ESTILO DE VIDA

CONFUSIÓN

Estrés

Sueño

**SISTEMA INMUNE**



MICROBIOTA

**SISTEMA ENDOCRINO**

**SISTEMA NERVIOSO**

**NUTRICIÓN**

Actividad física

Comportamiento alimentario

Sedentarismo

**GRACIAS POR VUESTRA ATENCIÓN**

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