

Que hacen los probióticos en el intestino del recién nacido

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Funciones de la microbiota en el
intestino

Factores que alteran la colonización
normal de los recién nacidos

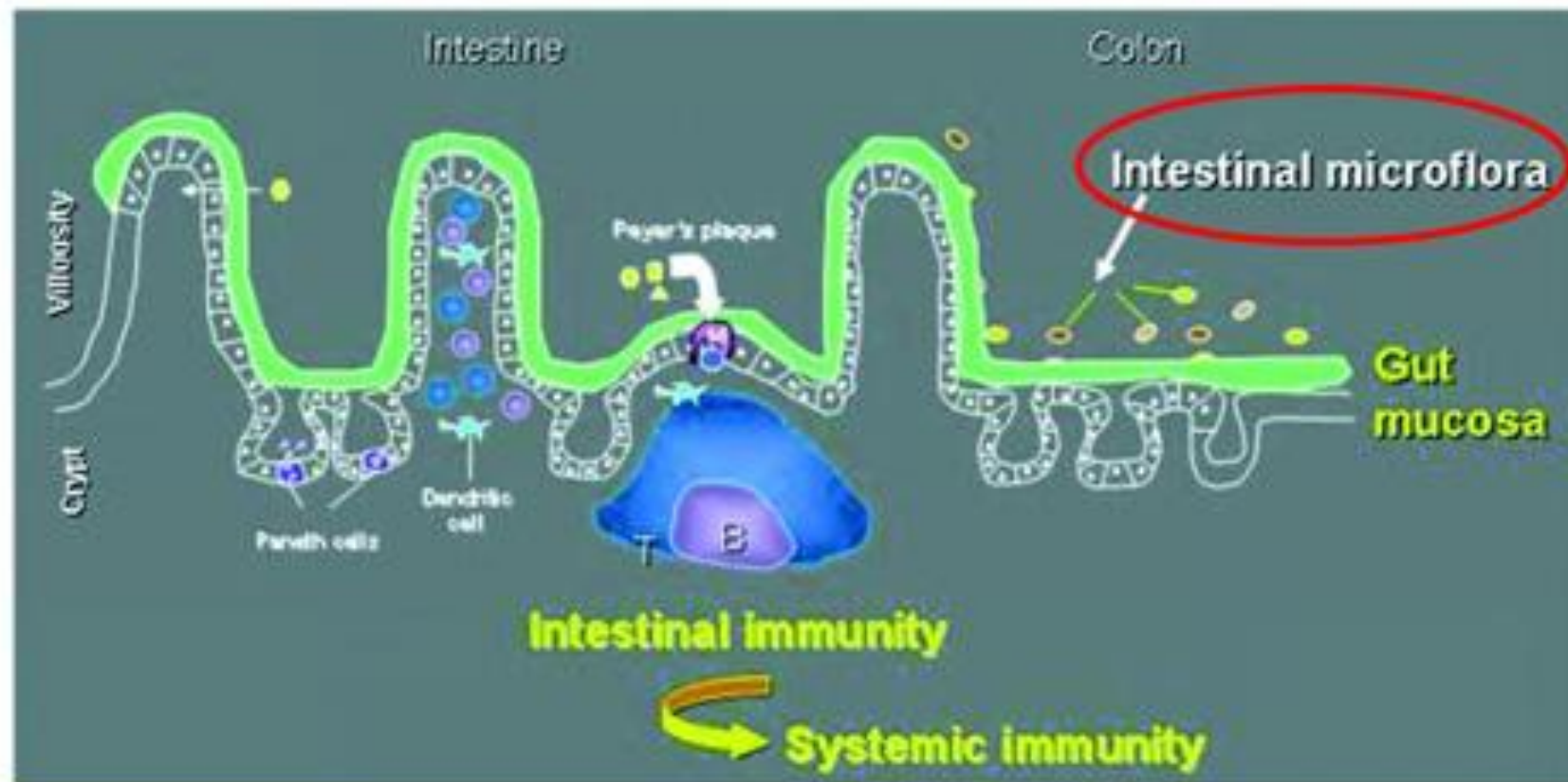
Que es un probiótico

Selección de probióticos

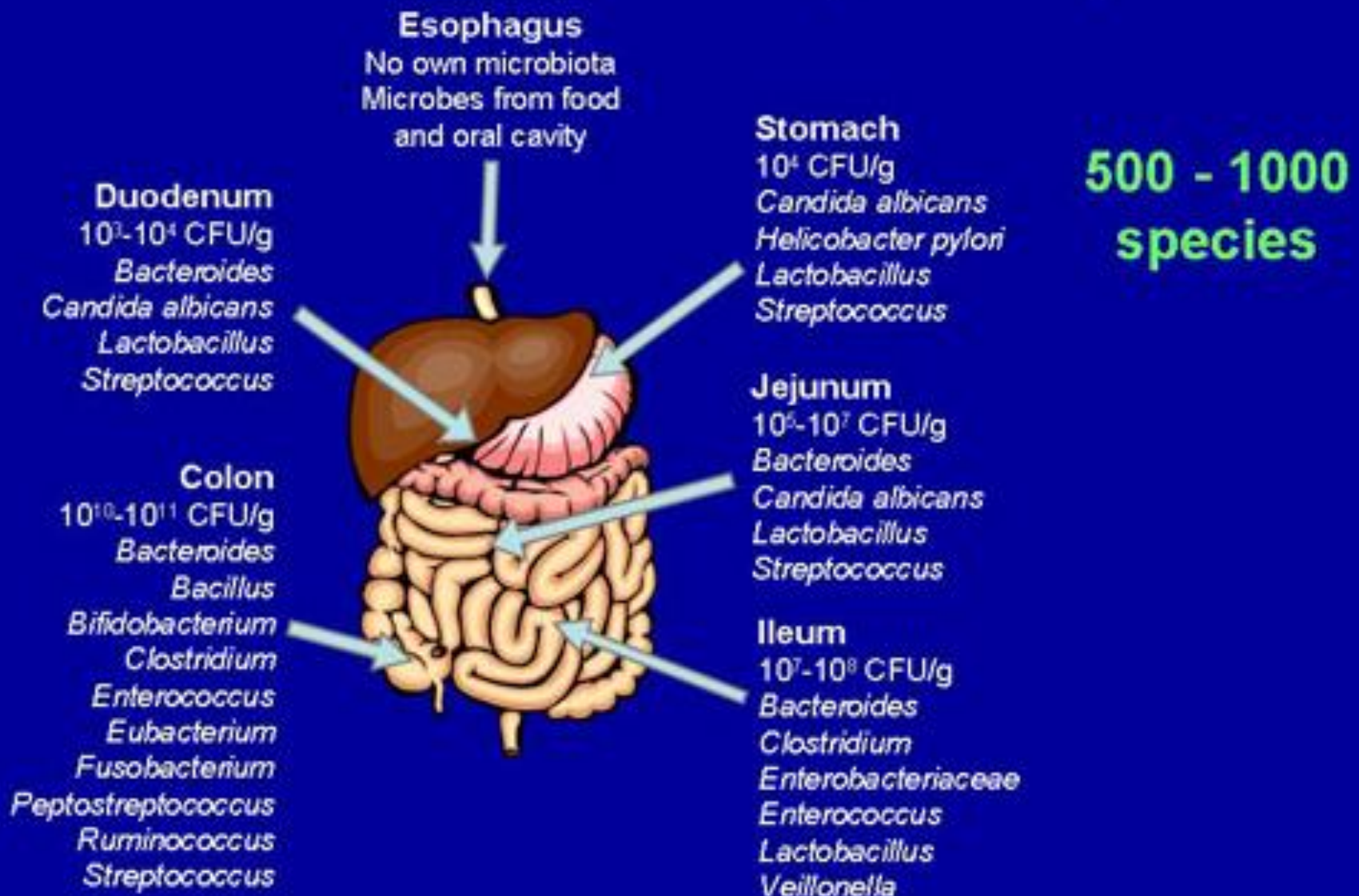


The intestine constitutes the largest interface between a person and his or her environment

The microbiota consists of $> 10^{13}$ microorganisms; more than the total number of cells in the human body



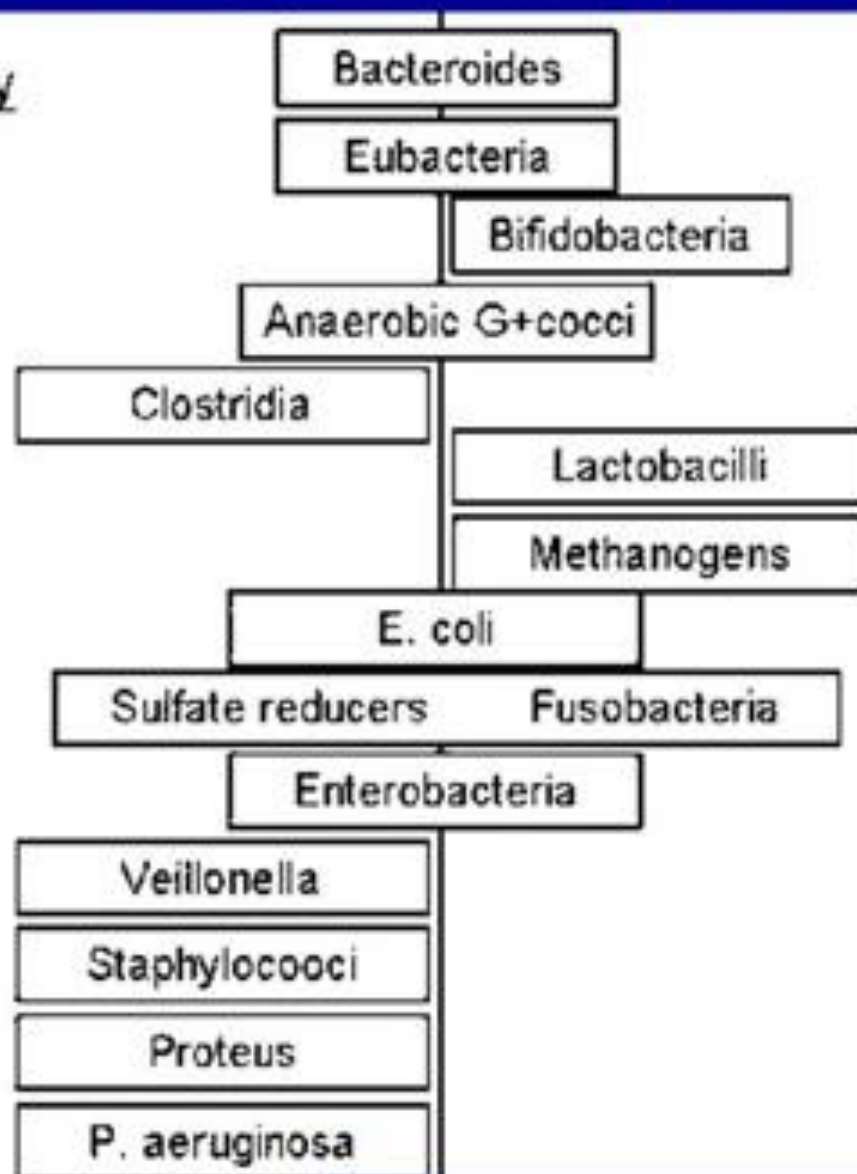
Microflora in the adult : Complex Ecosystem



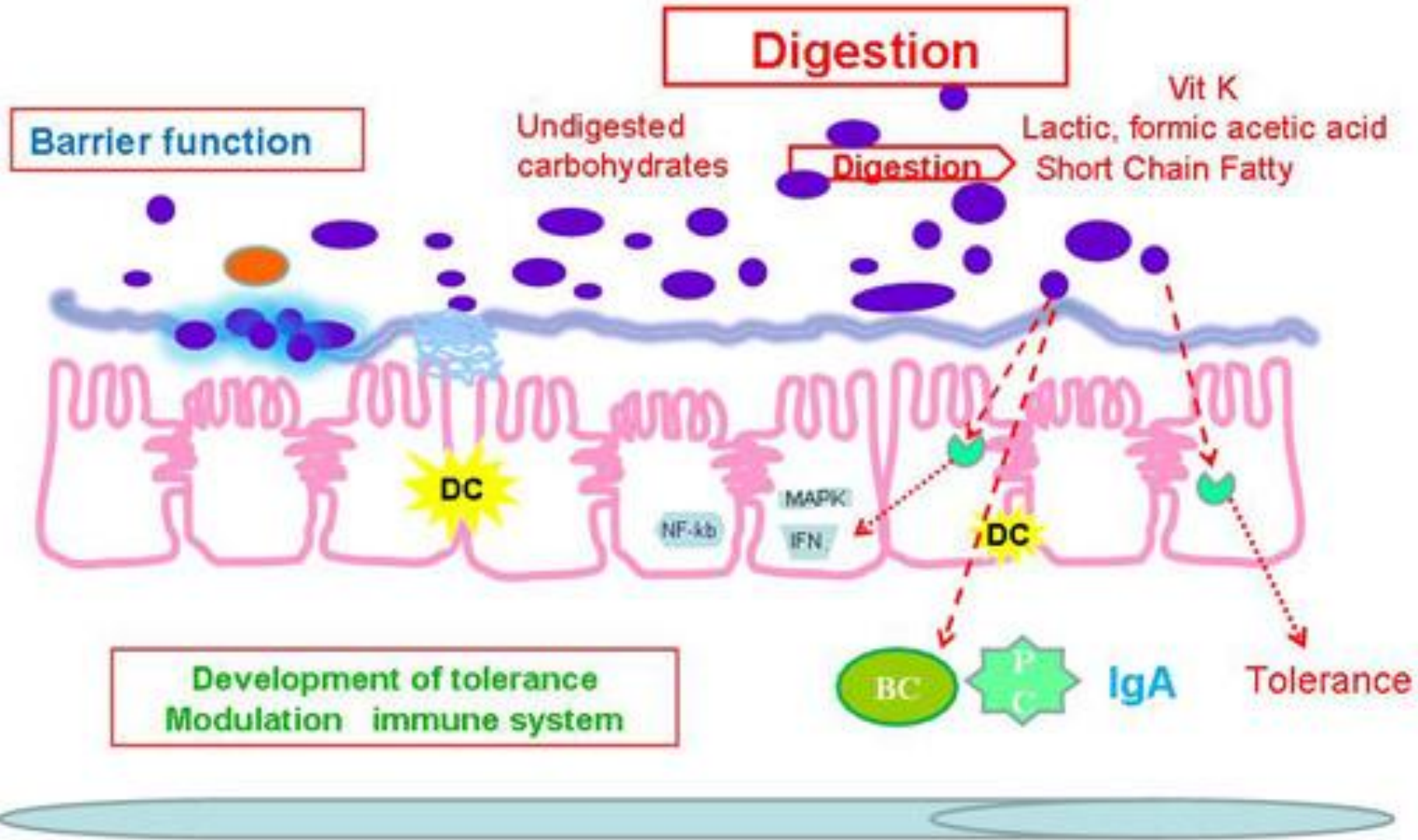
Intestinal / Ecosystem

Potentially
harmful

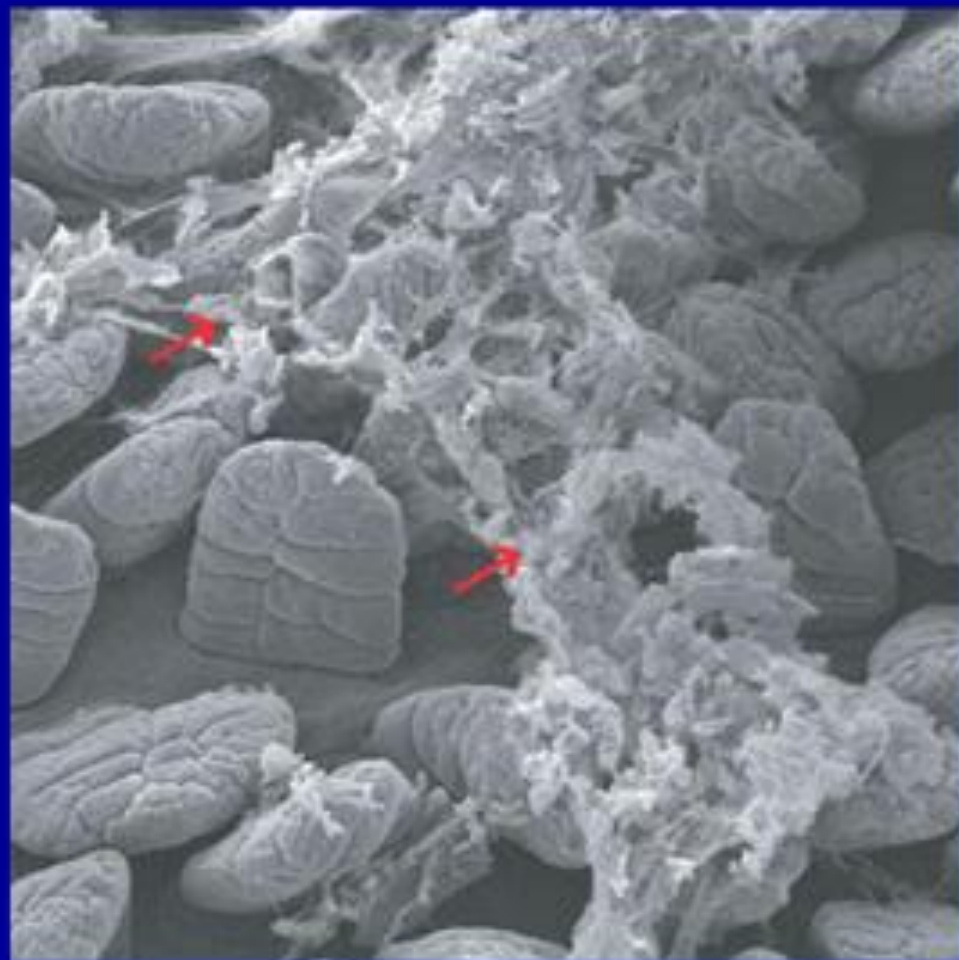
Potentially
beneficial



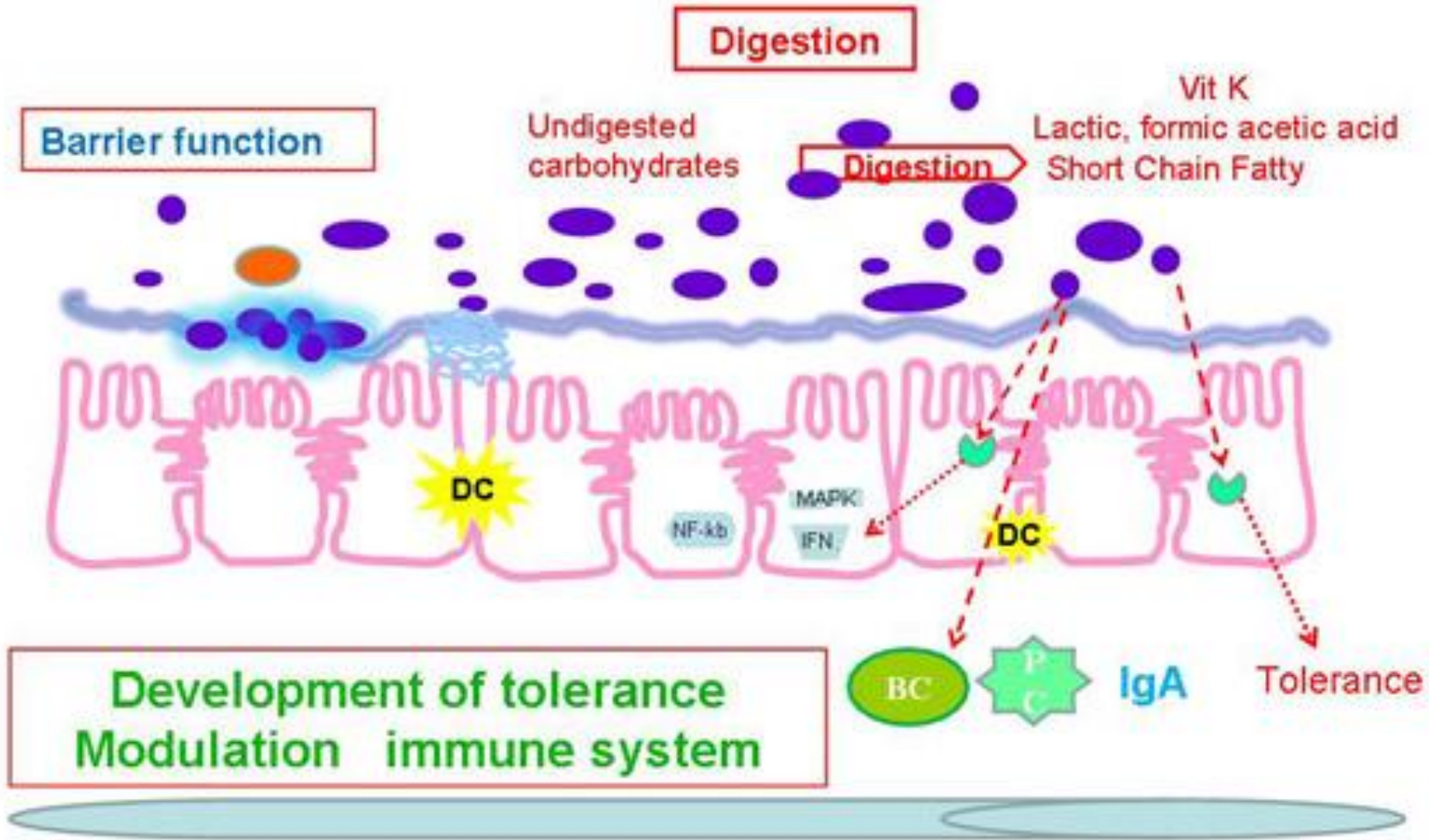
ROLE OF MICROBIOTIA IN THE IMMATURE INTESTINE



Desarrollo y regulación de la barrera intestinal



ROLE OF MICROBIOTIA IN THE IMMATURE INTESTINE



Maderación óptima de la repuesta inmune de la mucosa

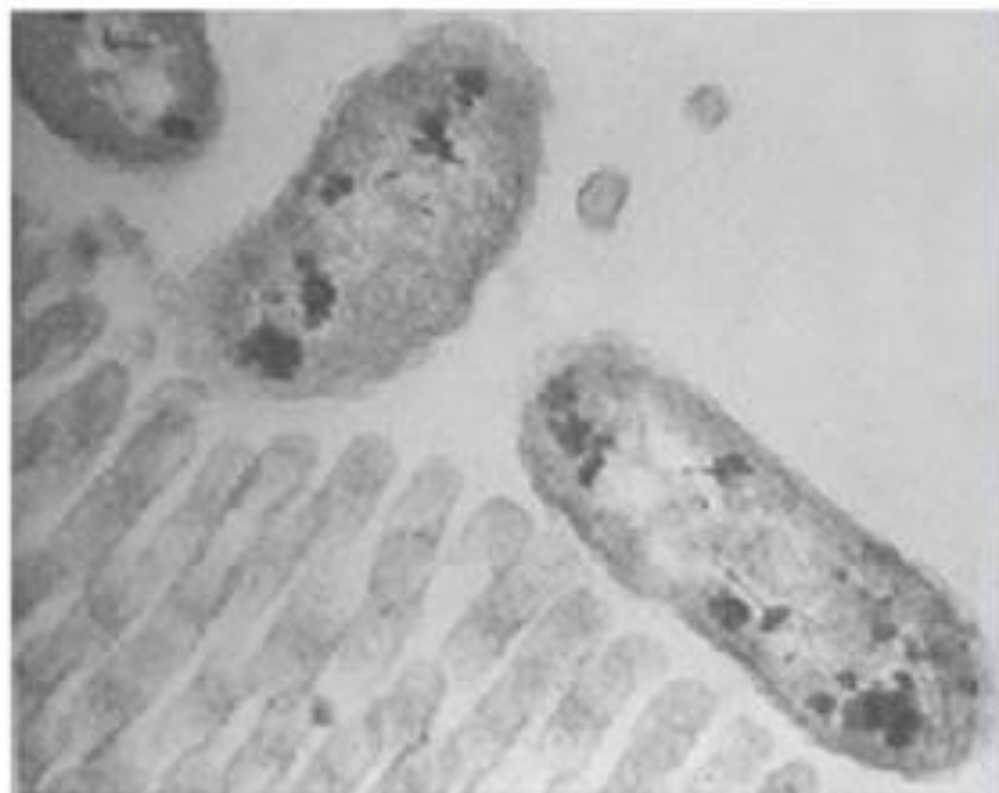
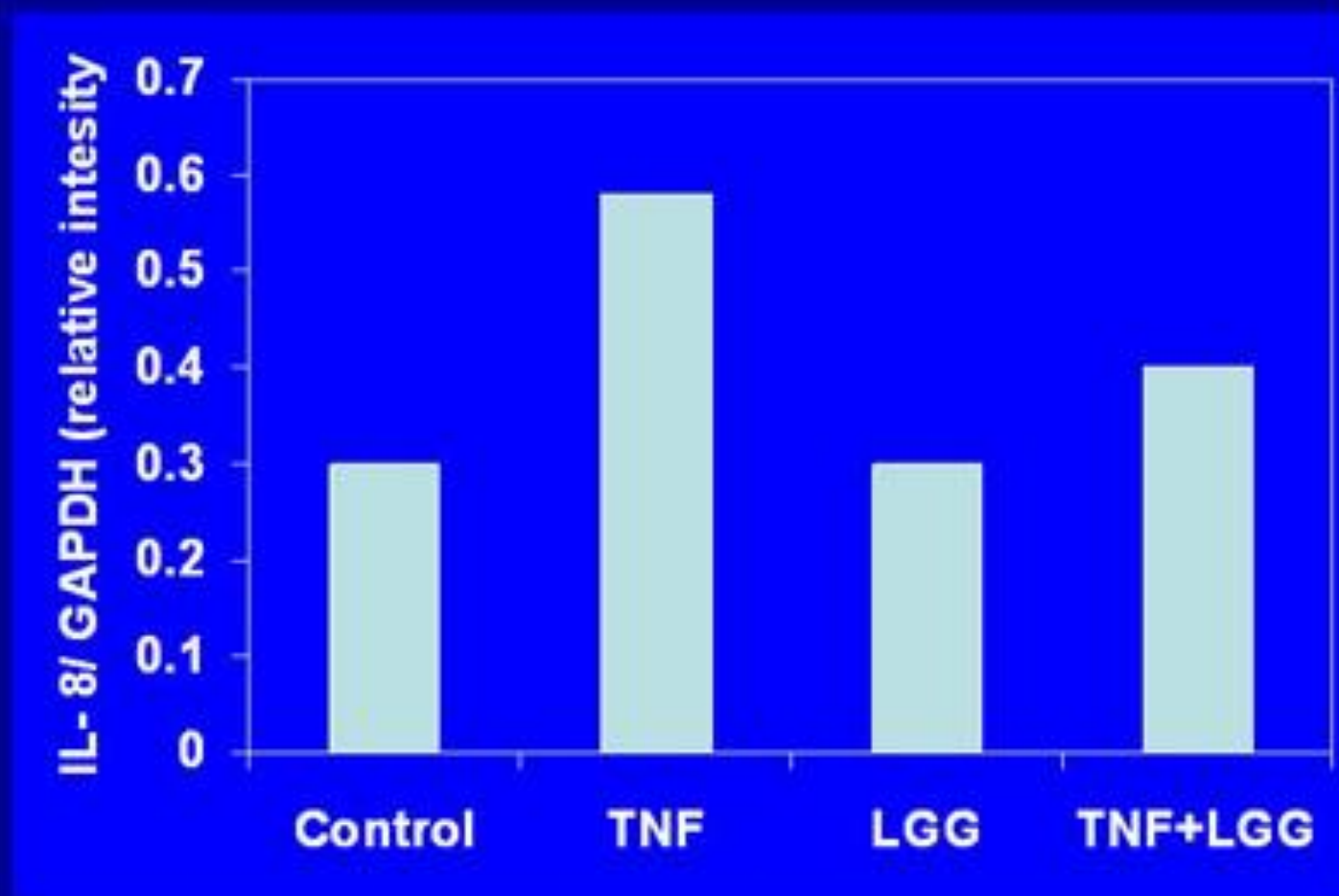
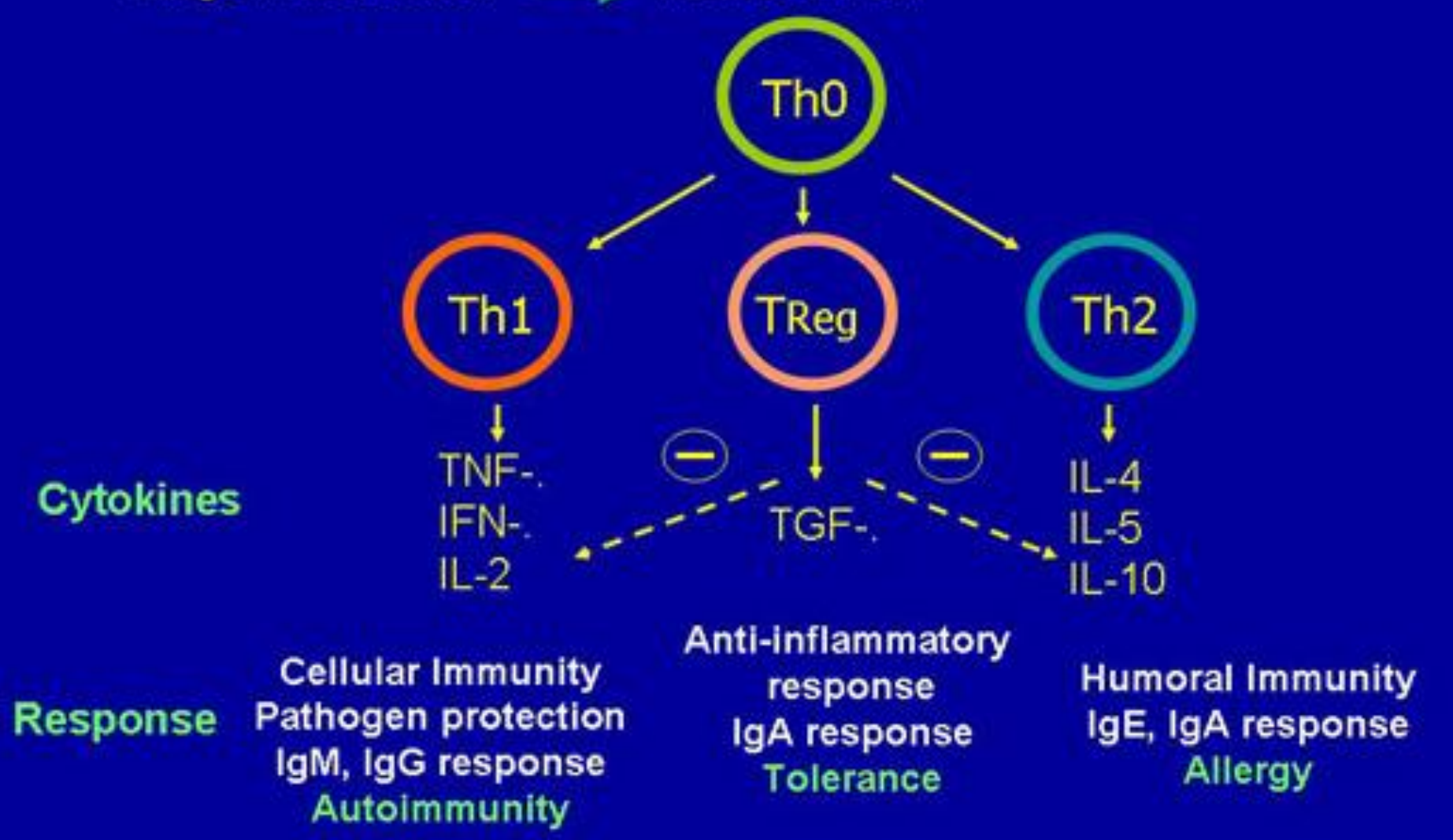
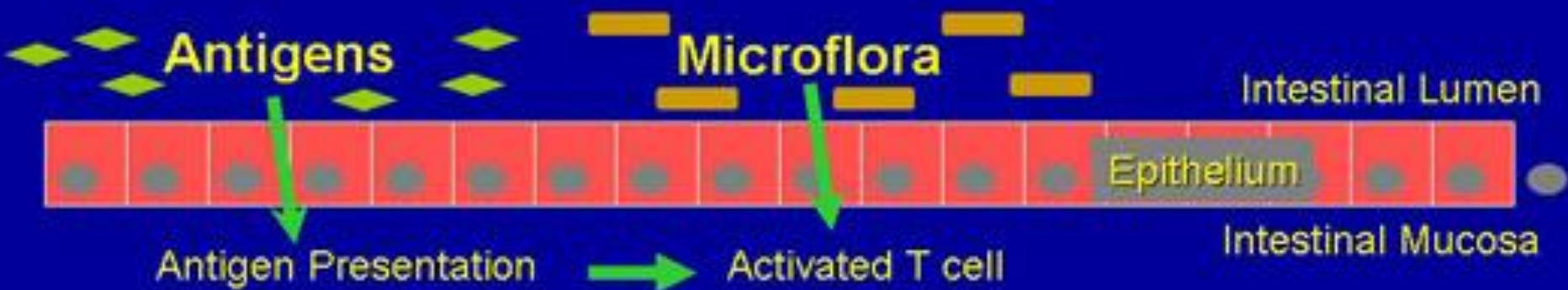


Figure 1. An electron microscopic view of an enteric bacterium interacting with the microvillus surface of the small intestine—microbial-epithelial "crosstalk".

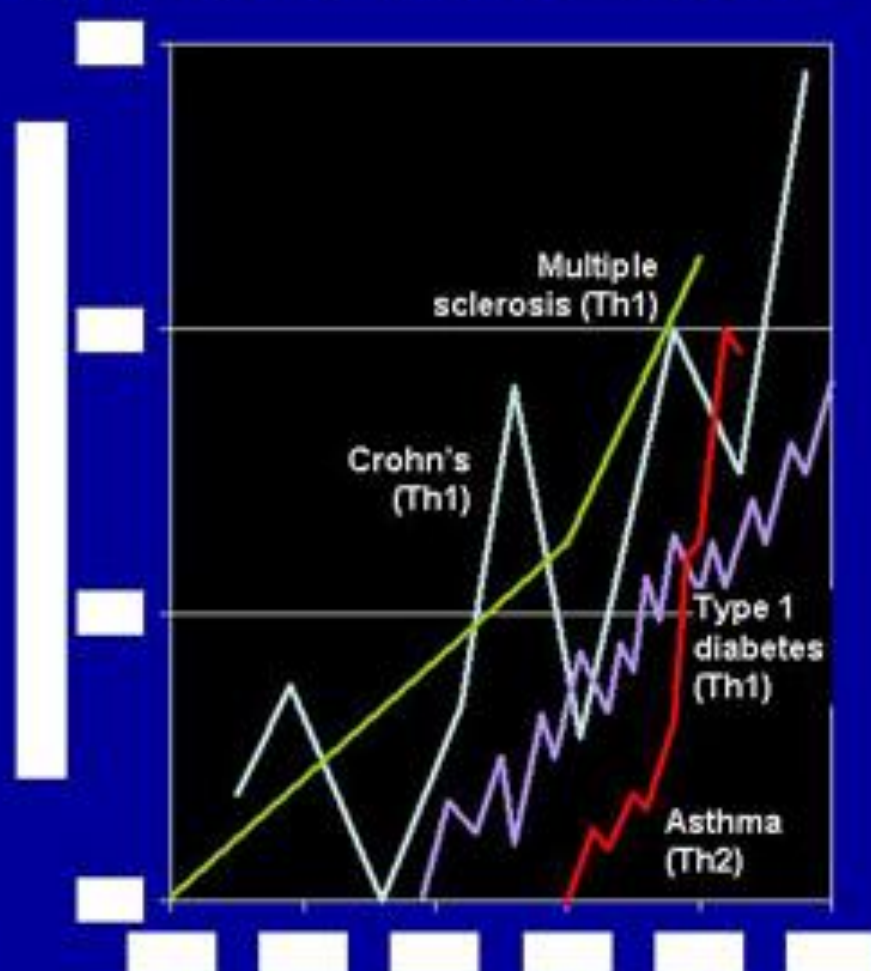
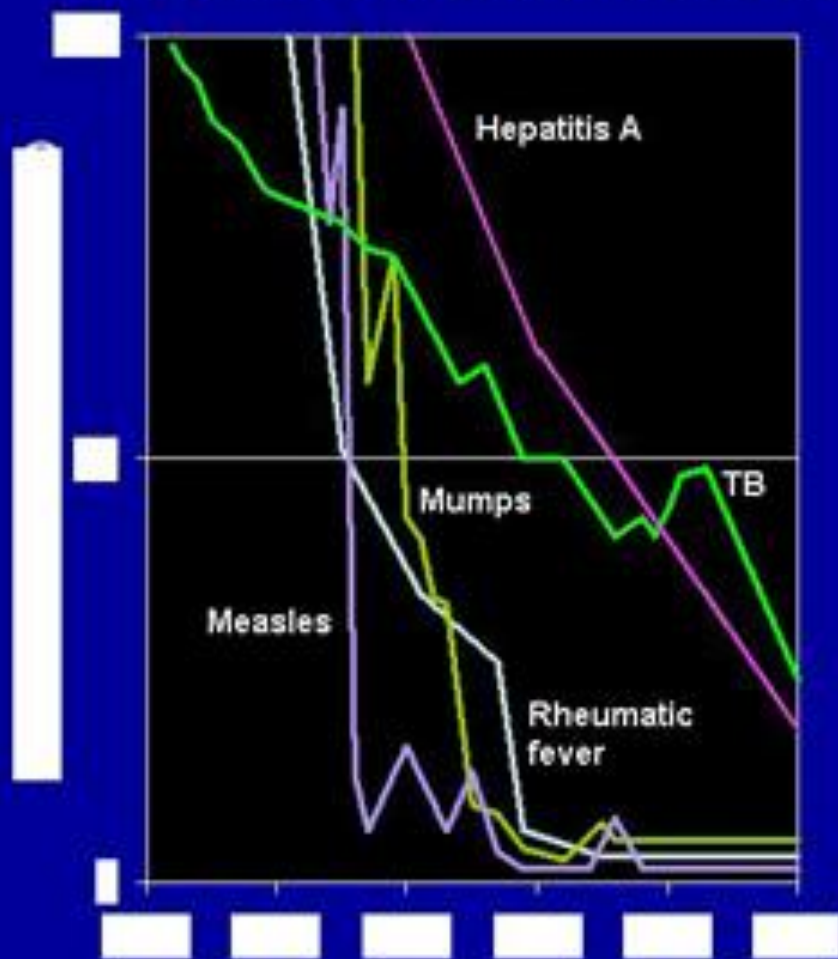
Alive and Dead Lactobacillus rhamnosus GG
decrease TNF- α -Induced Interleukine-8 Production
in Caco-2 Cells





Chronic Disease Prevalence in the Last 50 Years

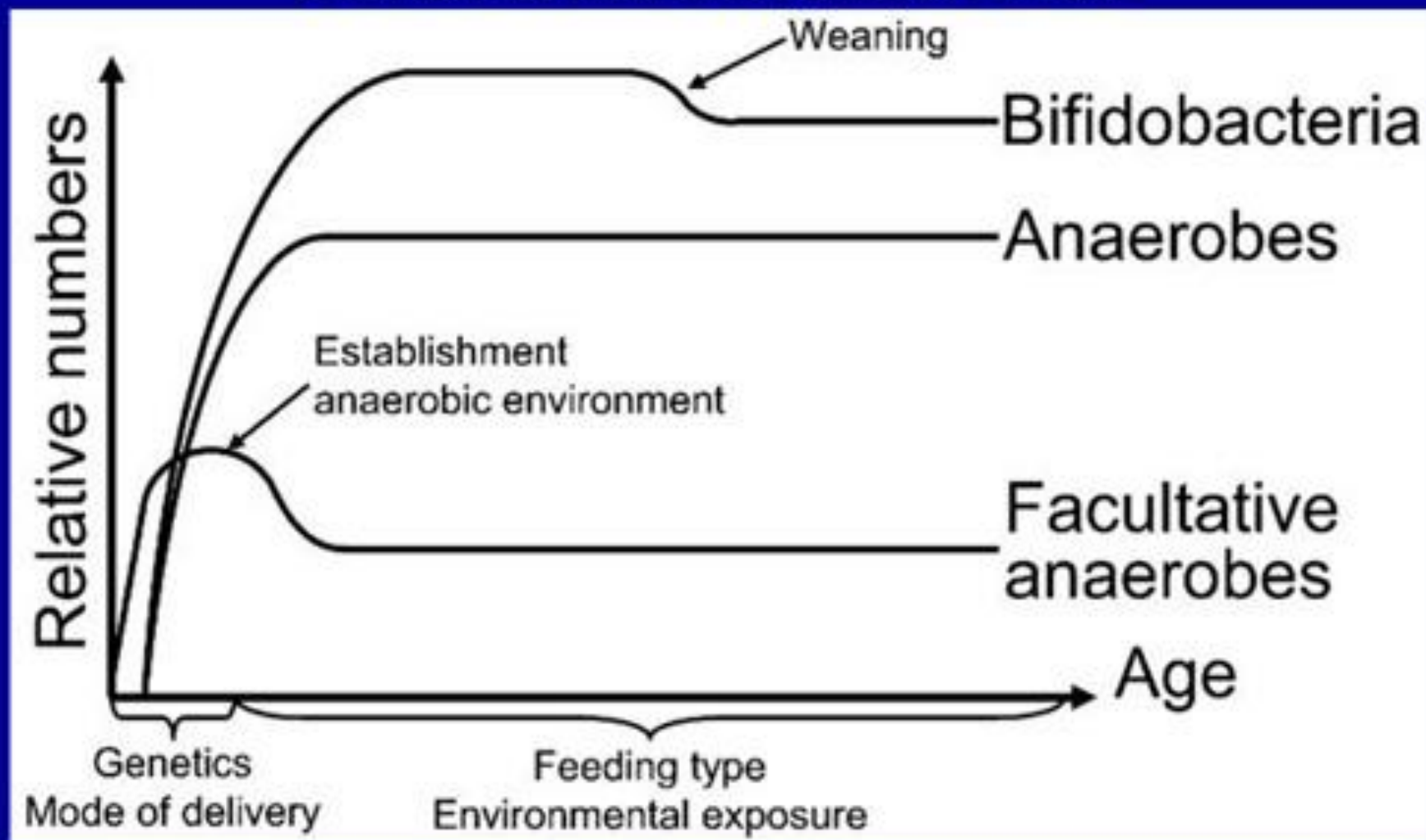
Decrease in infections is associated with increase immune disorders



- Descripción del microbioma / metagenoma
- Significación del microbioma
- Interacción entre ambos
- Manipulación de microbioma
- Salud esta asociada con diversidad

Alteración de la microbiota en recién nacidos

The postnatal period is crucial because the initial colonization will determine the final composition of the permanent microbiota in the adult



Influence of maternal bifidobacteria on the establishment of bifidobacteria colonizing the Gut in Infants (n=110) (Mikani 2009)

	C-section	Vaginal	p value
# counts	8.8 (5.0 - 9.3)	9.4 (8.4 - 9.8)	0.064
# species	0.3 \pm 0.5	1.3 \pm 1.0	0.006

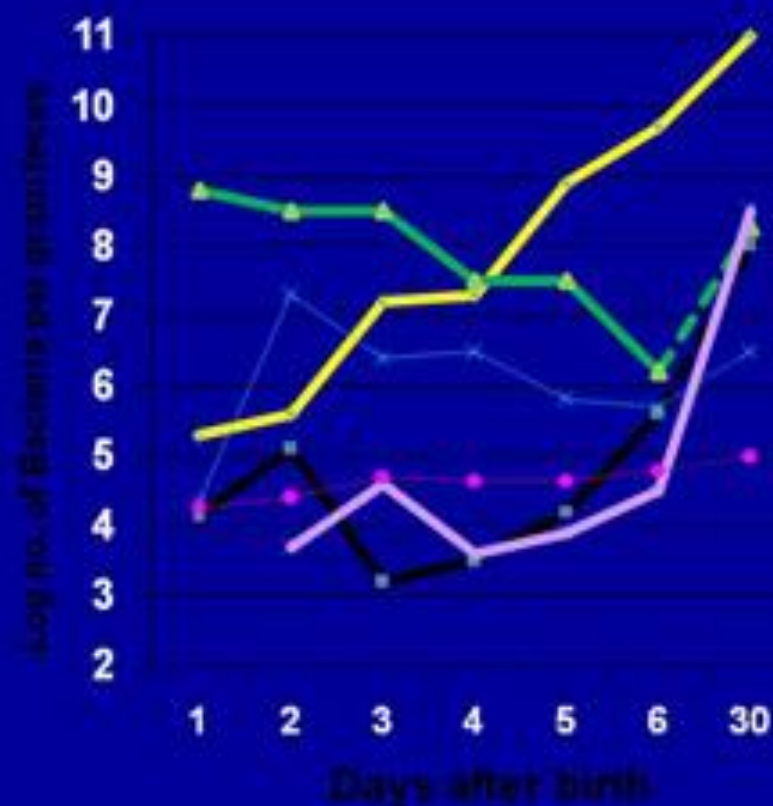
Development of the Normal Intestinal Flora and Its Clinical Significance in Infants and Children

	<u>FT</u>	<u>PT</u>
• Bifidobacteria first appeared (day)	1	8
• Become predominant (day)	5	19
• Bifidobacteria / Enterobacteria	1000/1	10/1
• Amount of human milk intake		
– When bifidobacteria appeared	69 \pm 29 ml/kg	
– When bifidobacteria become predominant	118 \pm 29ml/kg	

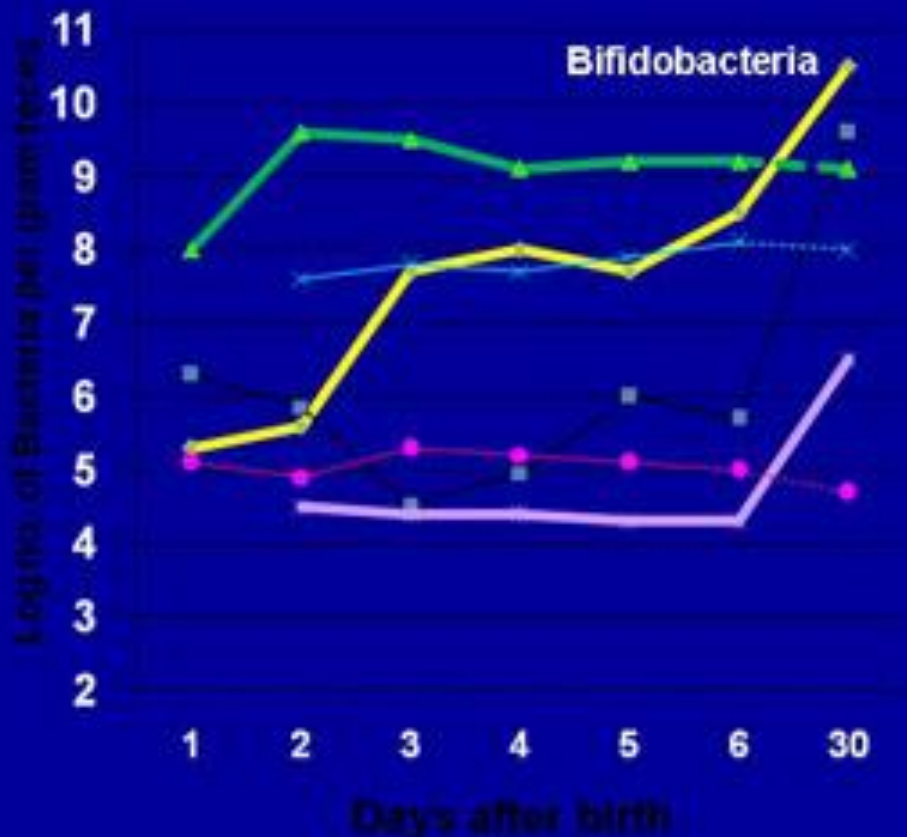
(Yoshioka 1991)

Intestinal Flora and Mode of Feeding

Breast feeding



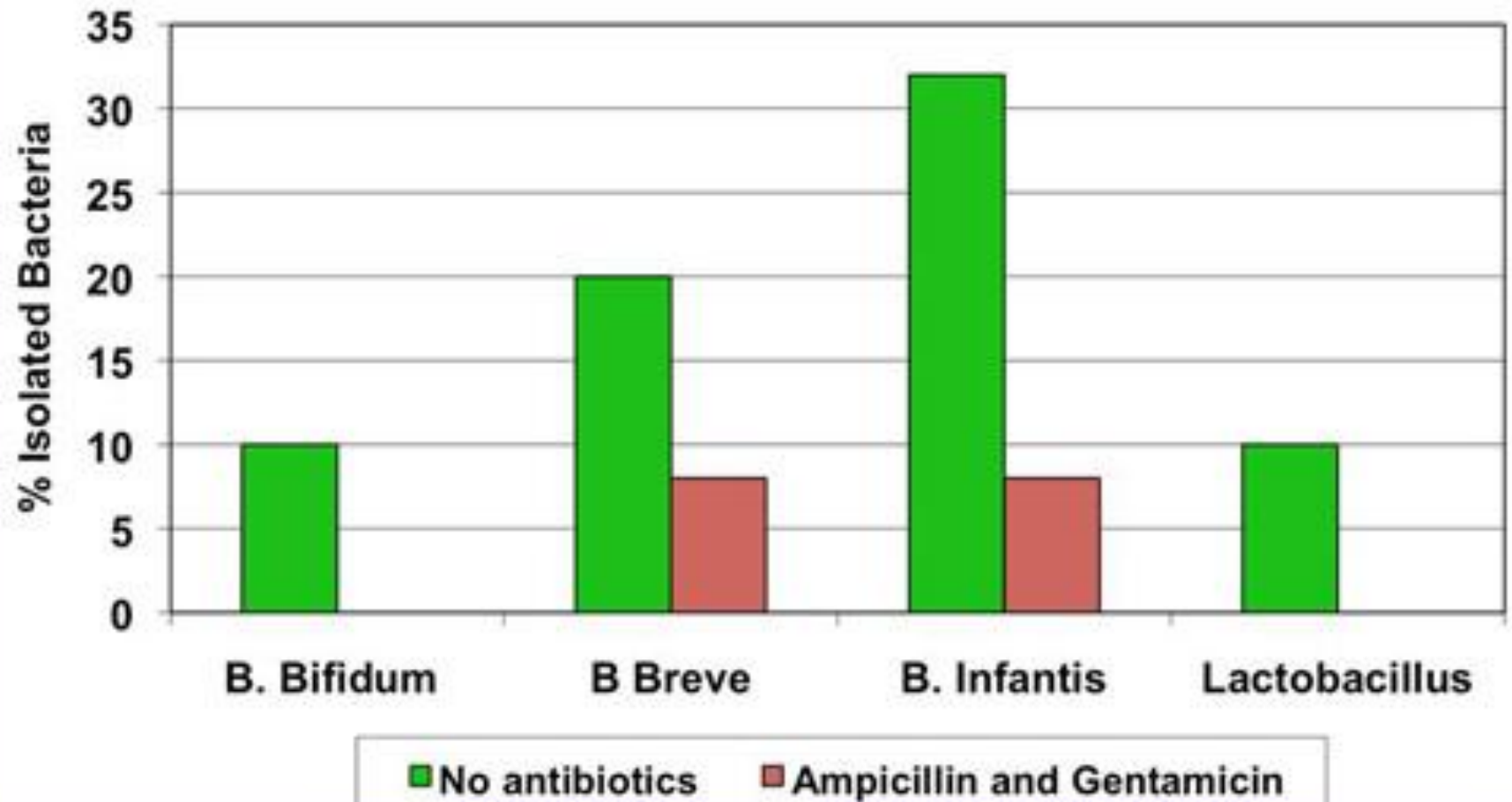
Formula feeding



— Bifidobacteria
 — Bacteroides
 — Enterobacteria
 — Enterococci
 — Lactobacilli
 — Staphylococci

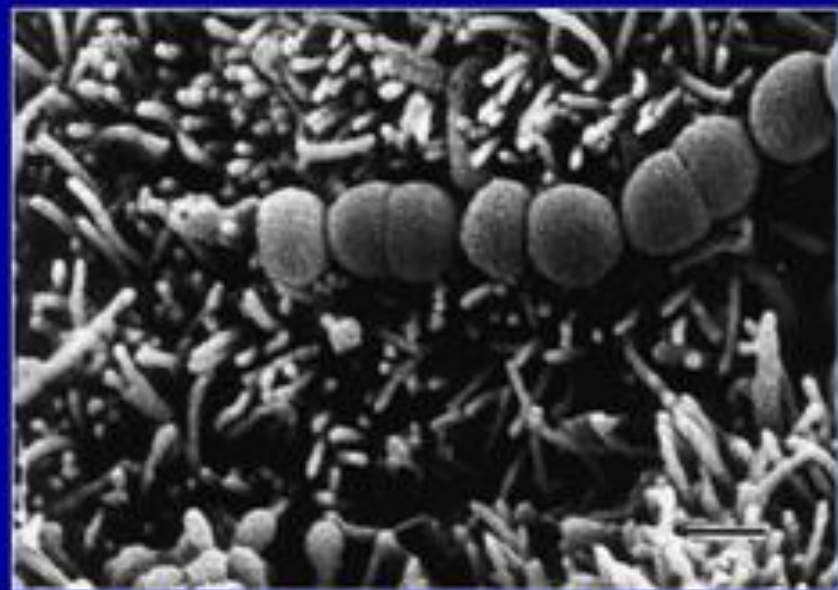
Use of antibiotics microecology of the gut

(Zetterstrom 1994)

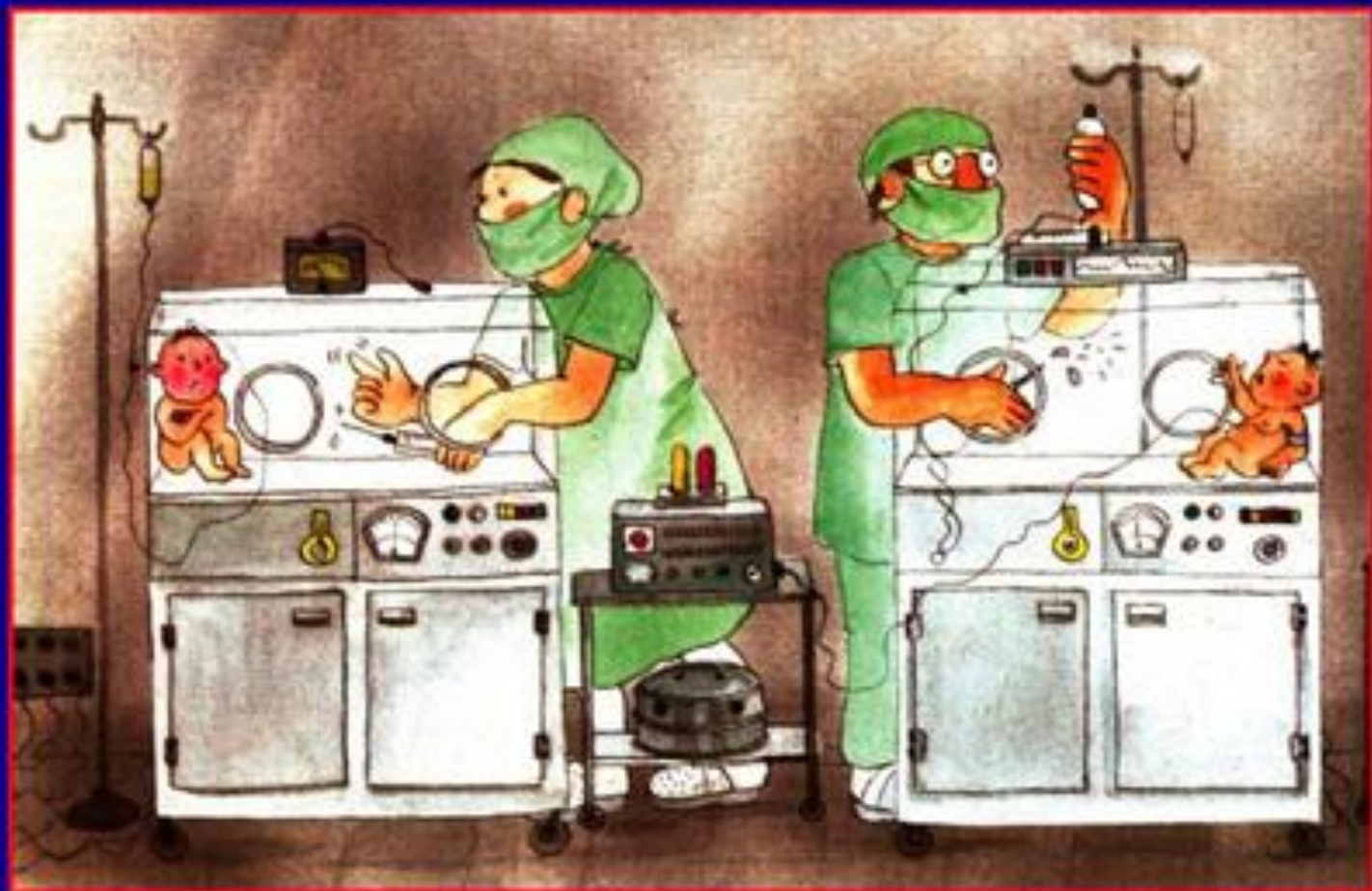


Intestinal Colonization

- Age —————→
- Type of delivery ———→
- Maternal flora ———→
- Environment ———→
- Diet —————→
- Use of antibiotics ———→
- Genes receptors ———→



GUT MICROFLORA



Podemos optimizar la microbiota del recién nacido con la administración de probióticos ?

**Que es un
probiótico ?**

“Los probióticos son un suplemento dietético de bacterias vivas que tiene efectos beneficiosos en el huésped mejorando el balance de la flora intestinal ”

Productos que contienen probioticos

Bifidobacterium breve
Lactobacillus acidophilus
Bifidobacterium longum
Lactobacillus plantarum
Bifidobacterium infantis
Lactobacillus paracasei
Streptococcus thermophilus
Lactobacillus bulgaris



Recommended dose from 450 - 1,800 billion

An evaluation of nine probiotics available in South Africa

Table 1. Results of the culture-independent analyses of 9 South African probiotic products in August 2003

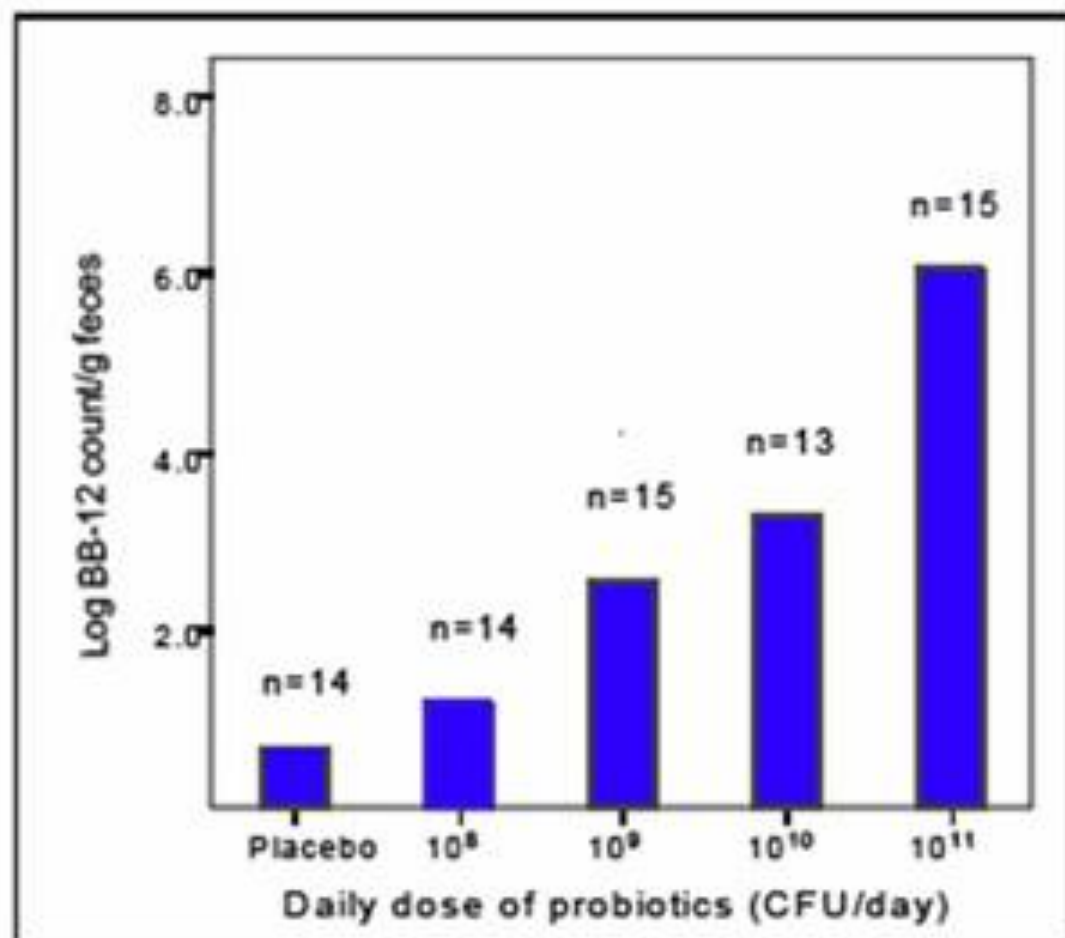
Product	Expiry date	Organism on label	Detected using DGGE	Conclusion
BioPro Reuteri straws	Aug 04	<i>Lactobacillus reuteri</i>	<i>Lactobacillus reuteri</i>	Product = label
BioPro Reuteri tablets	Sep 04	<i>Lactobacillus reuteri</i>	<i>Lactobacillus reuteri</i>	Product = label
Combiforte capsules	Mar 05	<i>Lactobacillus acidophilus</i> <i>Bifidobacterium bifidus</i> <i>Bifidobacterium longum</i>	<i>Lactobacillus acidophilus</i> <i>Bifidobacterium infantis</i>	Partial correlation of label and product
Cultunette sachets	Jun 04	<i>Bifidobacterium longum</i> <i>Lactobacillus acidophilus</i> <i>Streptococcus thermophilus</i>	<i>Bifidobacterium lactis</i> <i>Lactobacillus paracasei</i> <i>Enterococcus faecium</i>	Mislabelling Poor identification
Culturelle tablets	Jun 06	<i>Bifidobacterium longum</i> <i>Lactobacillus rhamnosus</i>	<i>Bifidobacterium lactis</i> <i>Lactobacillus paracasei</i>	Poor correlation of product and label
Infantiforte capsules	Jun 04	<i>Bifidobacterium infantis</i>	<i>Bifidobacterium infantis</i>	Product = label
Lactool Forte capsules	Jan 06	<i>Lactobacillus acidophilus</i>	DNA from heat-killed bacteria not detectable	Not measurable
Lactool Forte sachets	Feb 05	<i>Lactobacillus acidophilus</i>	DNA from heat-killed bacteria not detectable	Not measurable
Lactovita capsules	Aug 04	Lactic acid bacillus	<i>Saccharomyces cerevisiae</i>	No bacteria present

DGGE = denaturing gradient gel electrophoresis

Identificar un probiotico verdadero

No todos los “cultivos de bacteria viva” son probioticos

- LACTIC ACID BACTERIA INDUSTRY PLATAFORM (LABIP) Dunne 2001
 - Origen humano /bacteria autóctona
 - Resistencia al proceso tecnológico (forma de administración)
 - Resistencia a la degradación de ácidos gastricos y sales biliares
 - Que no sea patógena o invasiva
 - Colonización Adherencia a las células humanas



Recovery of BB-12 in feces immediately after cessation of bacterial supplementation (*Imm Med Microbiol* 2006)

Assessment of adhesion properties of novel probiotics strains to human intestinal mucus (Ouwehand 2000)

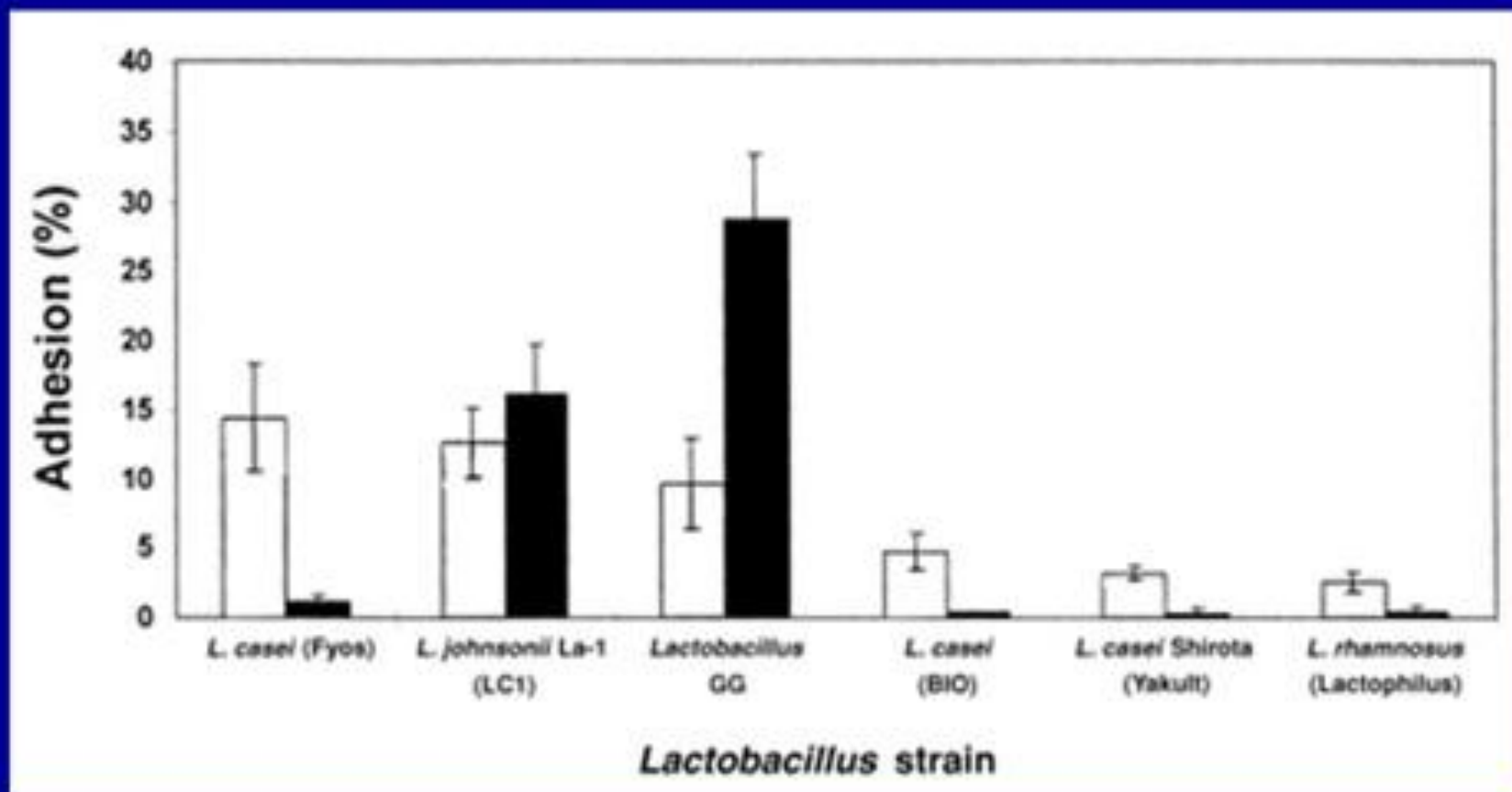


FIGURE 3. Adhesion of commercial probiotic strains in 2 in vitro models of the intestinal mucosa. , adhesion to a differentiated Caco-2 cell monolayer; , adhesion to intestinal mucins.

Quantitative Approach in the Study of Adhesion of Lactic Acid Bacteria to Intestinal Cells and Their Competition with Enterobacteria
(Lee

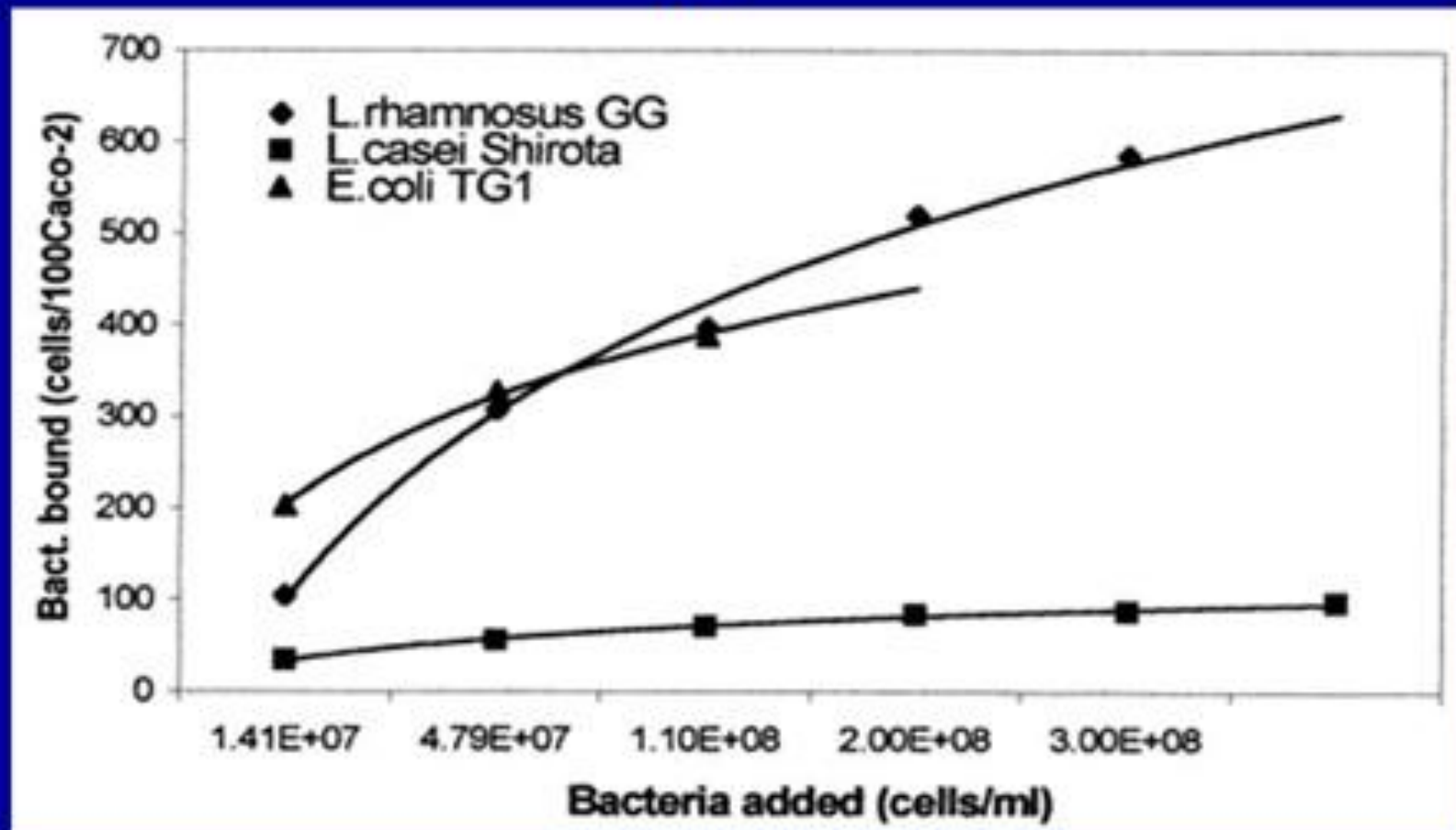
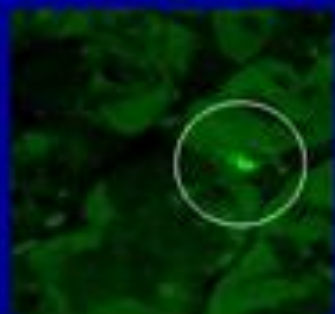


FIG. 1. Adhesion of *L. rhamnosus* GG, *L. casei* Shirota, and *E. coli* TG1 to human intestinal cell line Caco-2, presented as the number of bacteria bound per 100 Caco-2 cells versus the concentration of bacteria added (CFU per milliliter).

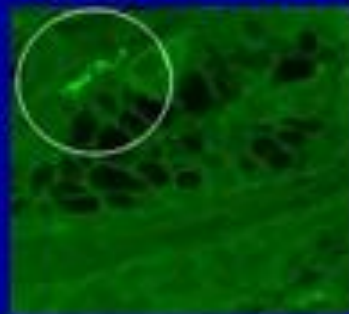
Lactobacillus reuteri grows in the human GI tract

Supplementation for 1 month

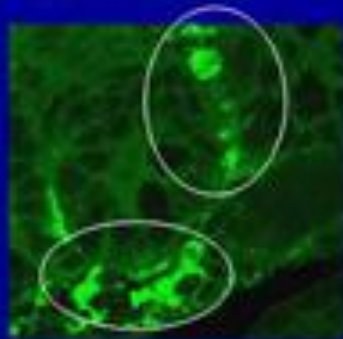
Gastric corpus



Gastric antrum



Duodenum



Ileum

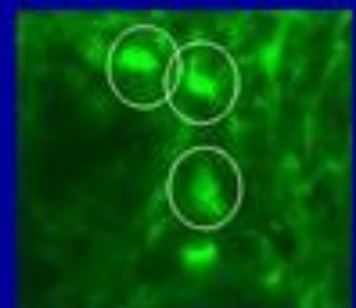


Supplementation for 6 months

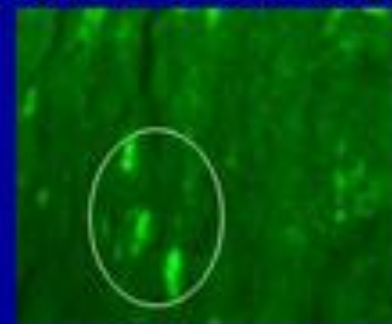
Gastric corpus



Gastric antrum



Gastric incisur angularis



Criterios tradicionales



Criterios actuales

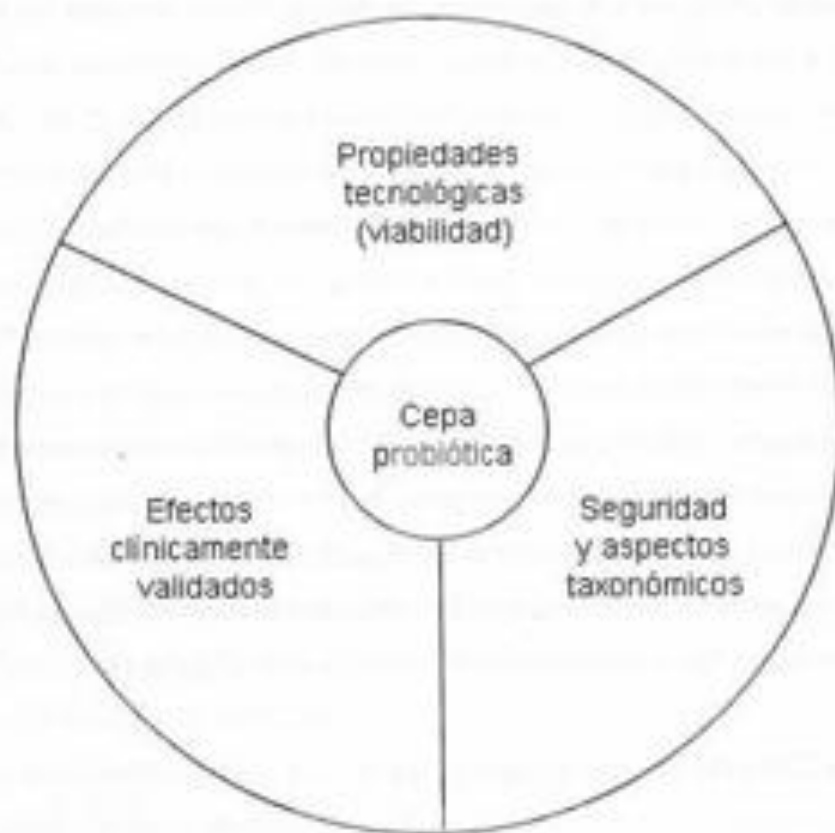


Figura 1. Evolución de los criterios para la selección de bacterias probióticas.

Probiotics RCT in Preterm Infants

<u>Author</u>	<u>Probiotics</u>	<u>Primary outcomes</u>
Reuman (USA)	<i>L. acidophilus</i>	Gut colonisation
Stansbridge (UK)	<i>L. GG</i>	Gut colonisation
Kitajima (Japan)	<i>B. breve</i>	Gut colonisation by BB
Uhlemann (Germany)	Bifidobacteria	Gut colonisation
Dani (Italy)	<i>L. GG</i>	UTI, Sepsis, NEC
Costalos (Greece)	<i>S. Boulardi</i>	Gut function/ stool col
Agarwal (India)	<i>L. GG</i>	
Bin Nun (Israel)	<i>B. inf/bifi, S. Therm</i>	NEC
Lin (Taiwan)	<i>L. acidophillus, B. Inf</i>	NEC
Indrio	<i>L reuteri</i>	Sepsis
Manzoni (Italy)	<i>L. Casei</i>	Gut col by <i>Candida</i> species
Mohan (Germany)	Bifidobat -Lact	Gut col by BB-L, enteric p.
Lin (Taiwan)	<i>L. acidophillus, B. Bifi</i>	NEC

Should the use of probiotics in the preterm be routine?

- Cual es el mecanismo de acción ?
- Es un probiótico tan efectivo como cualquier otro ?
- Es una intervención estandarizada?
- Cuales son las consecuencias a largo plazo ?
- Administración rutinaria producirá colonización cruzada a otros individuos?

Identificar un probiotico
adecuado para recién nacidos

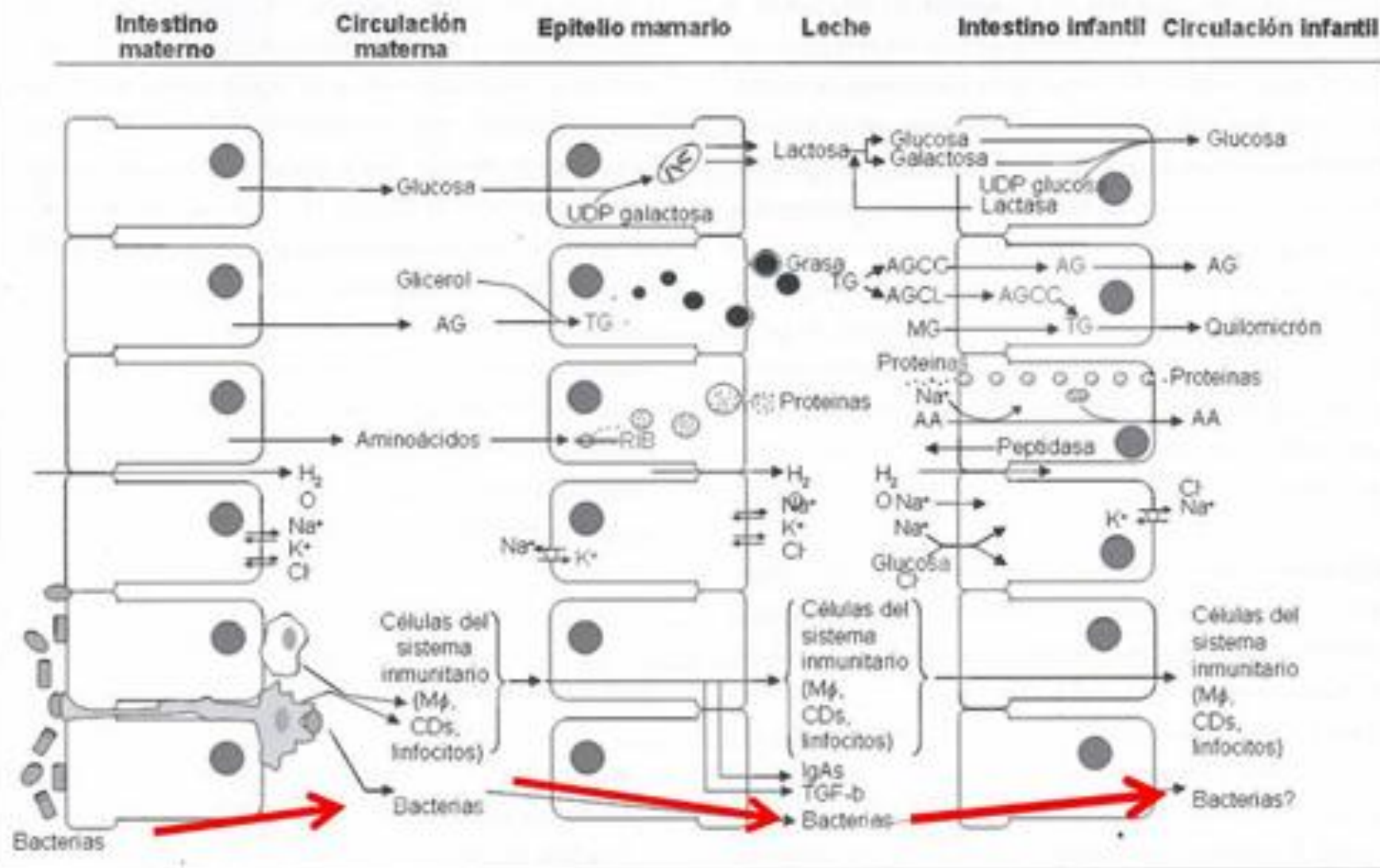


Figura 1. Complementariedad entre la estructura y función de los epitelios del intestino (materno e infantil) y el de la glándula mamaria lactante, ilustrando la síntesis, transferencia, utilización y/o absorción de algunos de los componentes de la leche materna. AA: aminoácidos; AG: ácidos grasos; AGCC: ácidos grasos de cadena corta; AGCL: ácidos grasos de cadena larga; MG: monoacilglicéridos; RIB: ribosomas; TG: triacilglicéridos.

Adaptado de Weaver (1992).

BIFIDOBACTERIA

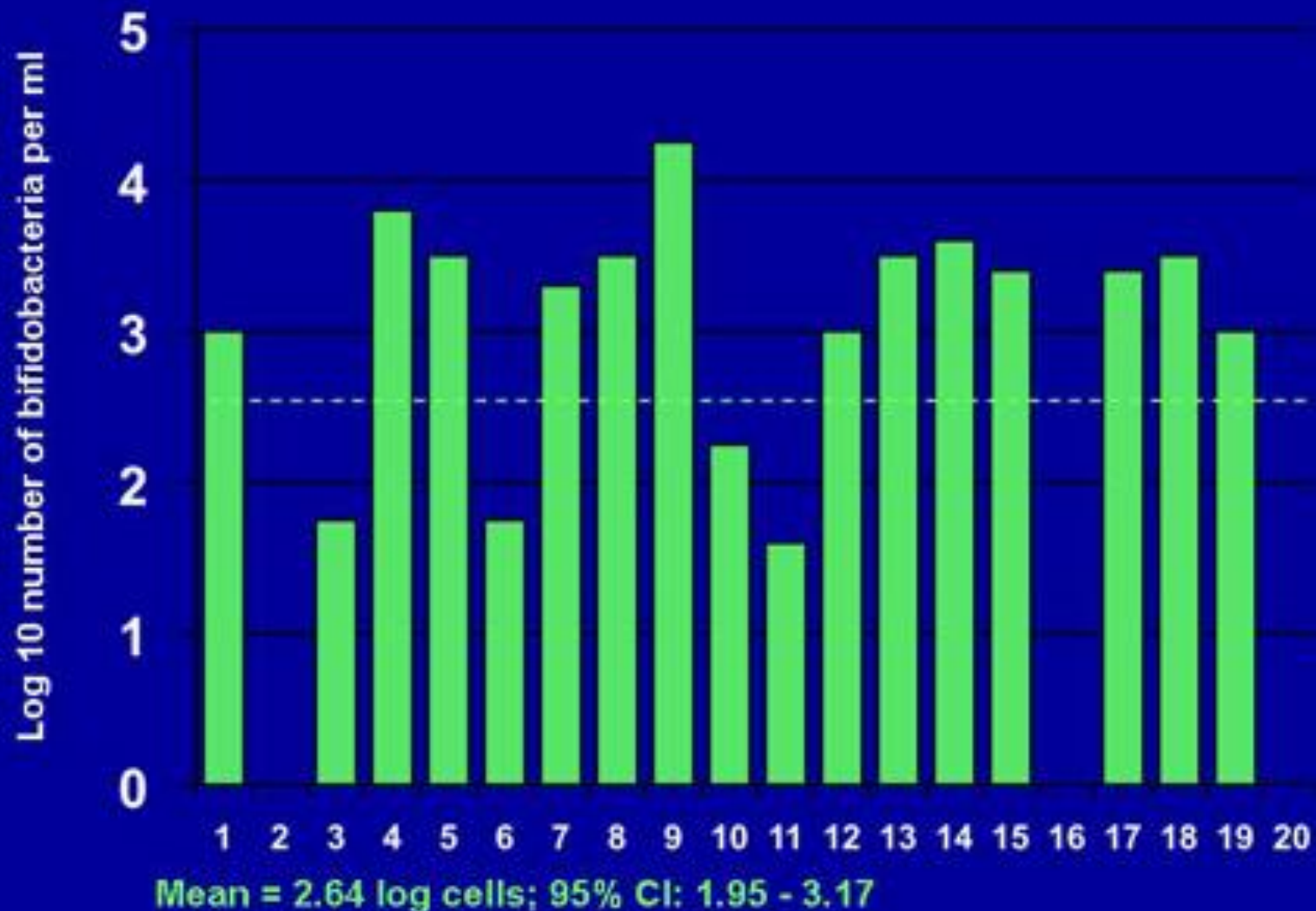


Bifidobacterium Lactis
Bifidobacterium Infantis
Bifidobacterium Breve
Bifidobacterium Adolescentis
Bifidobacterium Longum

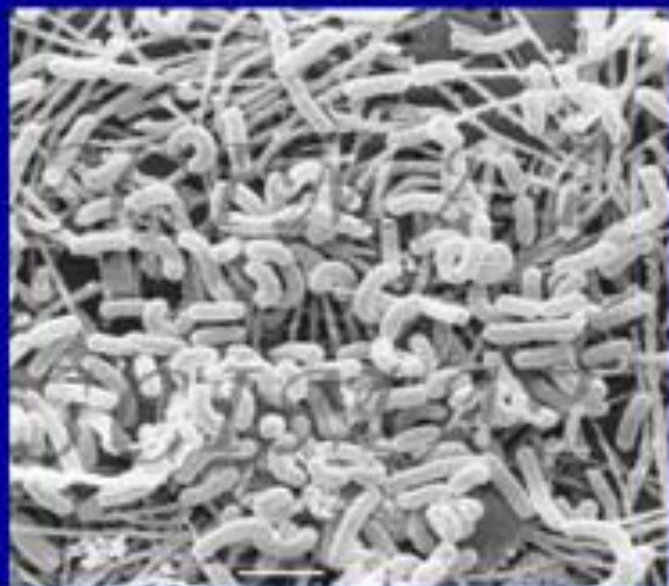


Constitute most of the microflora of breastfed infants

Bifidobacterial Counts in Breast Milk



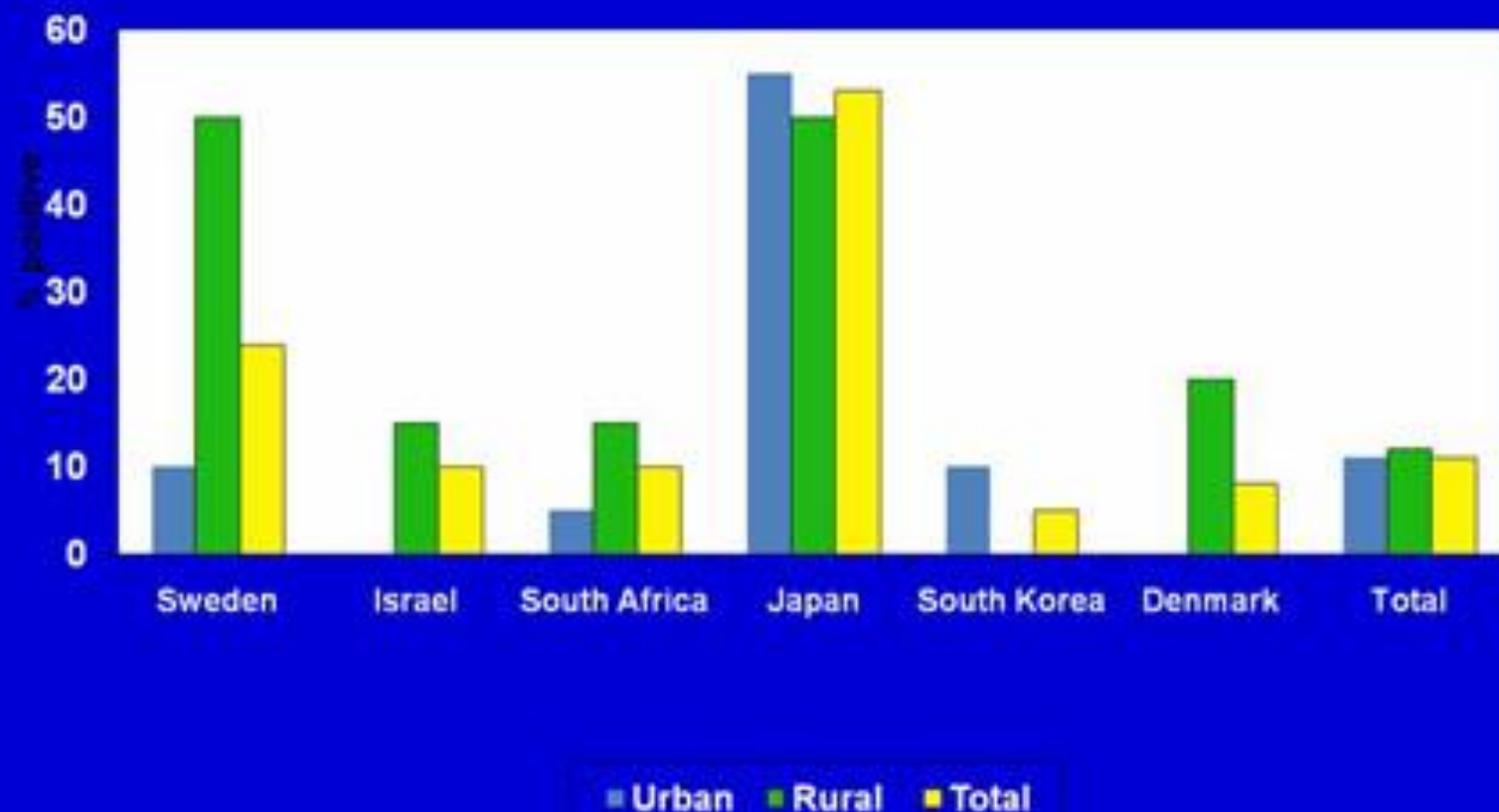
LACTOBACILLI



Lactobacillus reuteri
Lactobacillus rhamnosus
Lactobacillus acidophilus
Lactobacillus salivarius

Survey of *Lactobacillus reuteri* in human breast milk

Frequency of *L.reuteri* in breast milk
(220 mothers 6-32 days after delivery)





-They are live microorganisms/ Infections

Occasional cases of bacteremia associated with probiotics therapy have been reported

However No serious adverse effects have been reported in any of the RTC in newborn infants

-Interaction with gut cellular and metabolic functions / Digestive intolerance

-Translocation / Drug resistance

Long term effects on immune and gastrointestinal systems should be evaluated

Identificar probiótico efectivo

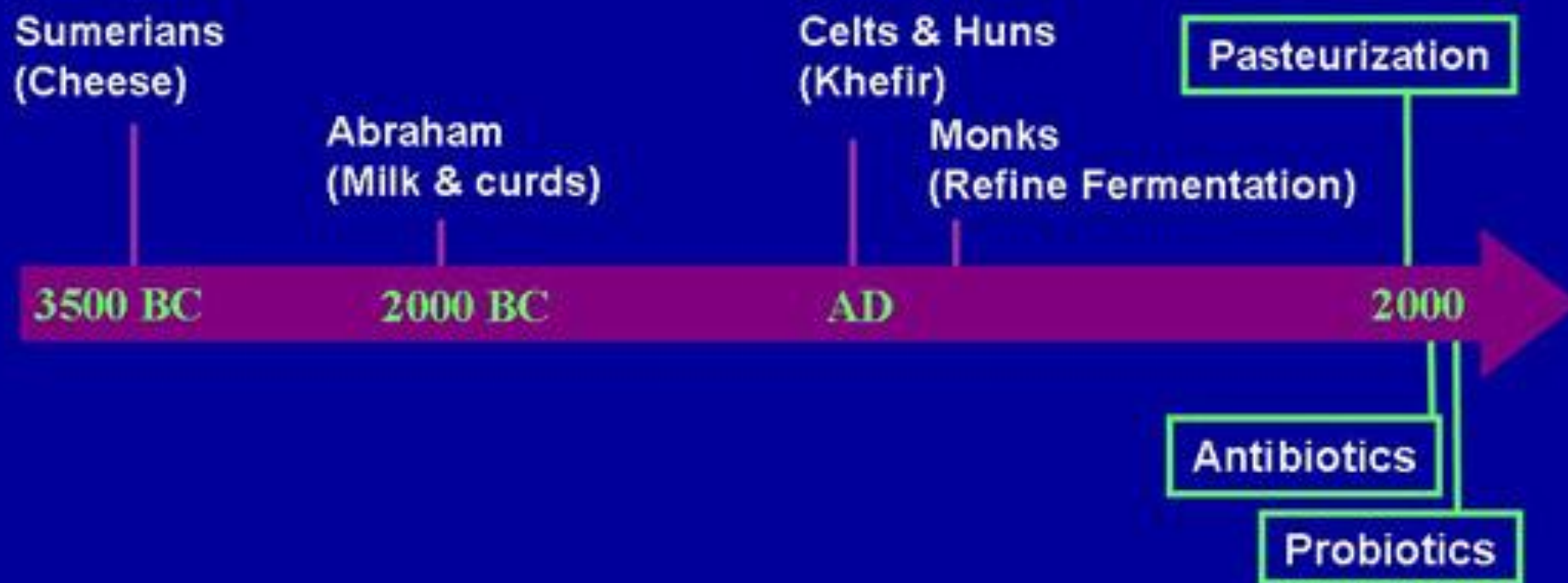
Se deben de usar productos bien caracterizados incluido la cepa

En los que mecanismos de acción y efectos específicos se hayan probado

Los resultados de uno no se pueden extrapolar a otros probióticos

•Guidelines for the evaluation of Probiotics in Food (FAO/WHO 2002)

Ingestion of Bacteria



In the last 100 years, we drastically changed our ingestion of microbes and our microbial environment.



GRACIAS