



MILANO 2015

NUTRIRE IL PIANETA  
ENERGIA PER LA VITA

NOURRIR LA PLANETE  
ENERGIE POUR LA VIE

FEEDING THE PLANET  
ENERGY FOR LIFE



# Probiotics and human immune system

*Between innovative scientific evidence  
and regulatory challenges*

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*Probiotical S.p.A. - Novara*

**Milan, October 16<sup>th</sup>, 2015**

# **Bacteria fertilize the Earth and the Oceans...**

**Bacteria destroy every type of pollutants...**

**Most foods and drinks are prepared thanks to bacteria...**

**Bread, wine, beer, yogurt, kefir, cheese, salami, ham, sauerkraut, miso, soy sauce, tempeh and many other foods see the involvement of bacterial fermentation...**

**BUT ...**

# Selected bacteria have a big role also in the NUTRACEUTICAL area !

*"Let your food be your medicine  
and your medicine be your food."*

Hippocrates



# The functions of intestinal microbiota

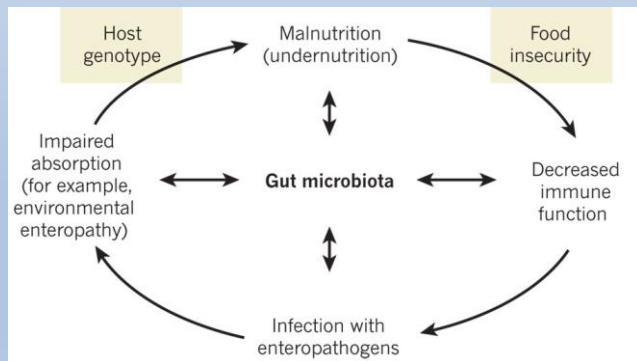
The composition of this ecosystem is unique to each individual, representing a kind of digital **fingerprint** to each of us.

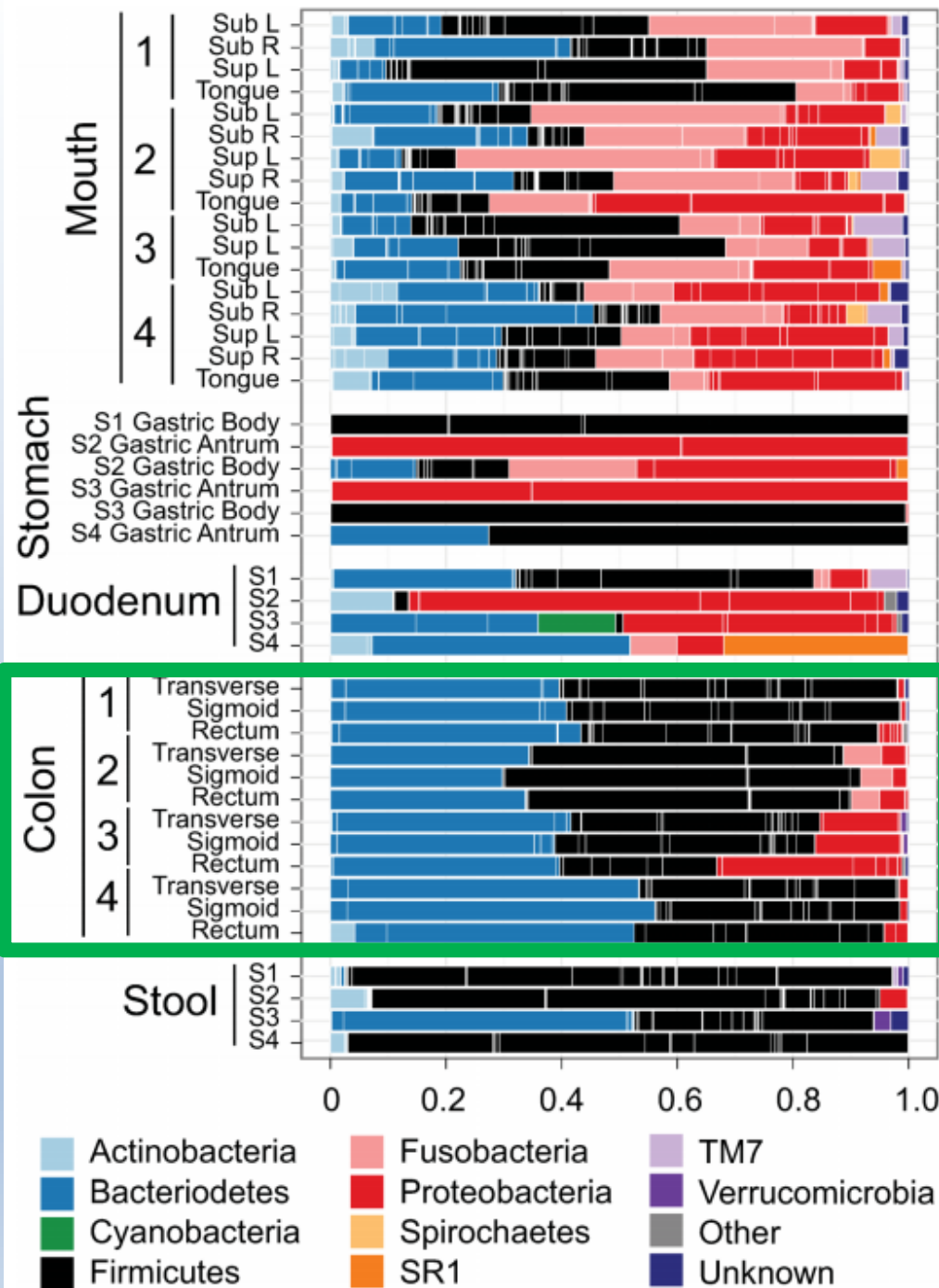
Despite some slight modifications over the years, the microbiota tends to **retain** its main features, regardless of any type of medical or surgical treatment involving the gut.



## MAIN FEATURES

- Synthesize nutrients and promote their consumption
- Maintain the integrity of the mucosal barrier
- Support and stimulate the immune system
- Inhibit the growth of pathogenic bacteria





Of the 70 known bacterial phyla (divisions) only 2 are most represented in the gastrointestinal tract.

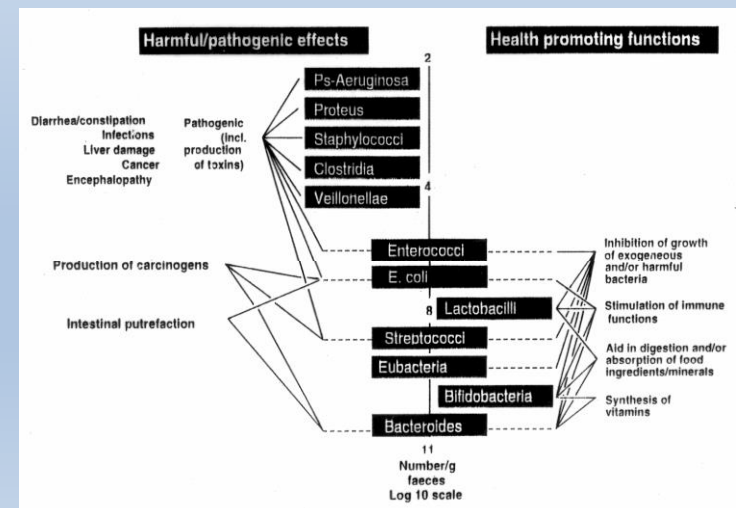
Basically similar composition between the various inhabitants of the world (same PHYLAs), some differences are detected in the relative proportions of the various subgroups (SPECIES and STRAIN)

1000-1500 different species in man, 160 species in each individual.

Distribution range of microbial species.

# Examples of functional disorders and bowel diseases associated with changes of intestinal microbiota

- **Post-infectious Irritable Bowel Syndrome (20-25% of cases of IBS)**
- **Functional constipation**
- *Clostridium difficile* colitis
- **Small Intestine Bacterial Overgrowth (SIBO)**
- **Diverticular disease**
- **Irritable Bowel Diseases (IBD)**



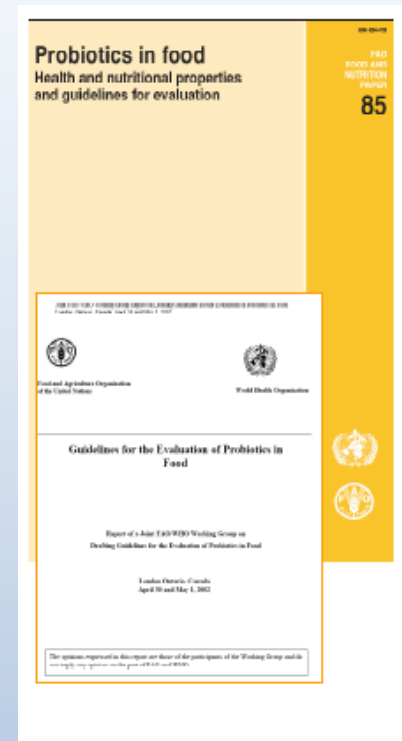
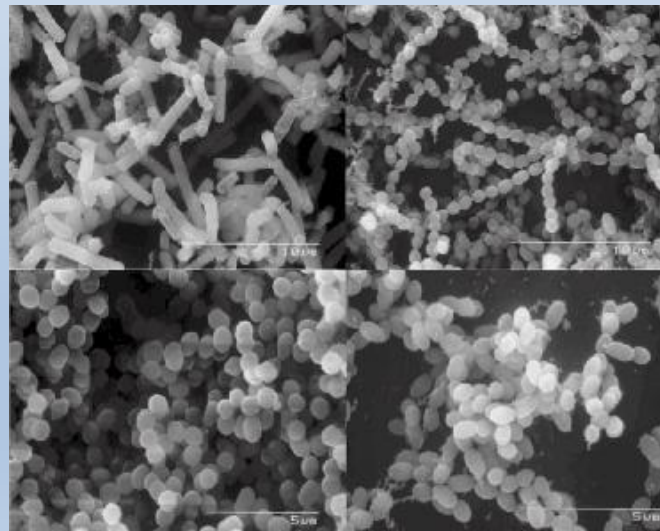
# Probiotics ... definition and main applications

Probiotics are defined as “live microorganisms which, when administered in adequate amounts and for a sufficient time, are able to exert at least one beneficial effect on the host.”

(Joint FAO/WHO Expert Consultation, October 2001)

## MARKET BOOM

*In recent years there has been an exponential growth of **functional foods** (e.g. fermented milk and foods, often of plant origin) and **food supplements containing probiotics**. A parallel increase in the interest of the average consumer for nutraceuticals has been registered as well.*



# What should a probiotic do ??

...

- ◆ Reach the gut alive, viable and in adequate numbers.
- ◆ Replicate rapidly and become numerically important ( $>10^8$ - $10^9$  CFU/g) **[concept of colonization]**, thus exerting at least a beneficial effect on the human organism through their metabolism.



## Microbiota of the lumen

### Production of:

- *Organic acids and short chain fatty acids (SCFA);*
- *Enzymes able to hydrolyze proteins and sugars;*
- *Vitamins;*
- *Antioxidant compounds;*
- *Molecules with antimicrobial activity.*

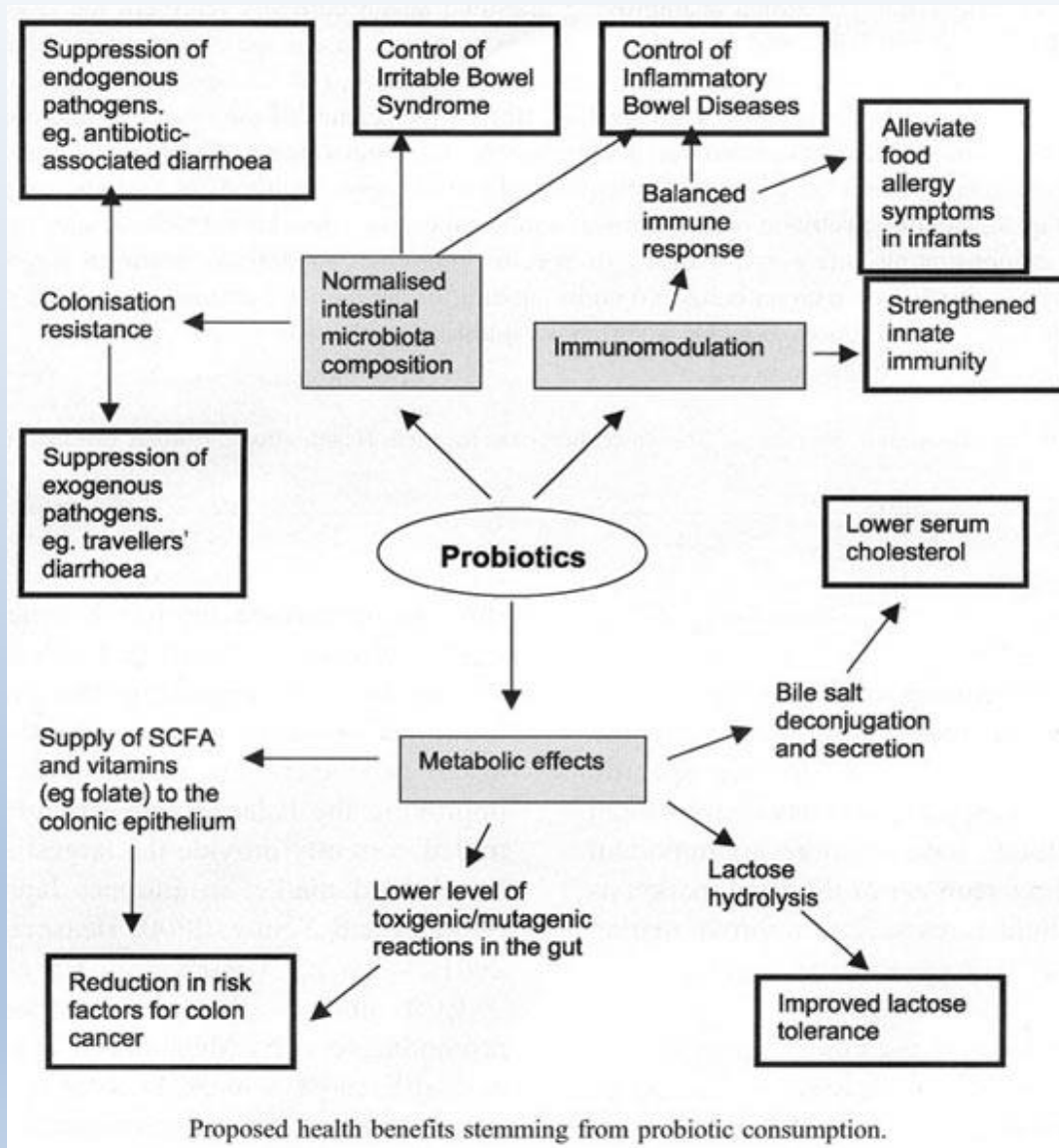
## Microbiota adhering to the mucosa

### Action of:

- *Adhesion to the mucosal surface;*
- ***Immunomodulation;***
- ***Competition and barrier effect towards pathogens;***
- *Restoration or maintenance of a proper permeability of the mucosa.*



# Well-recognized beneficial actions of probiotics

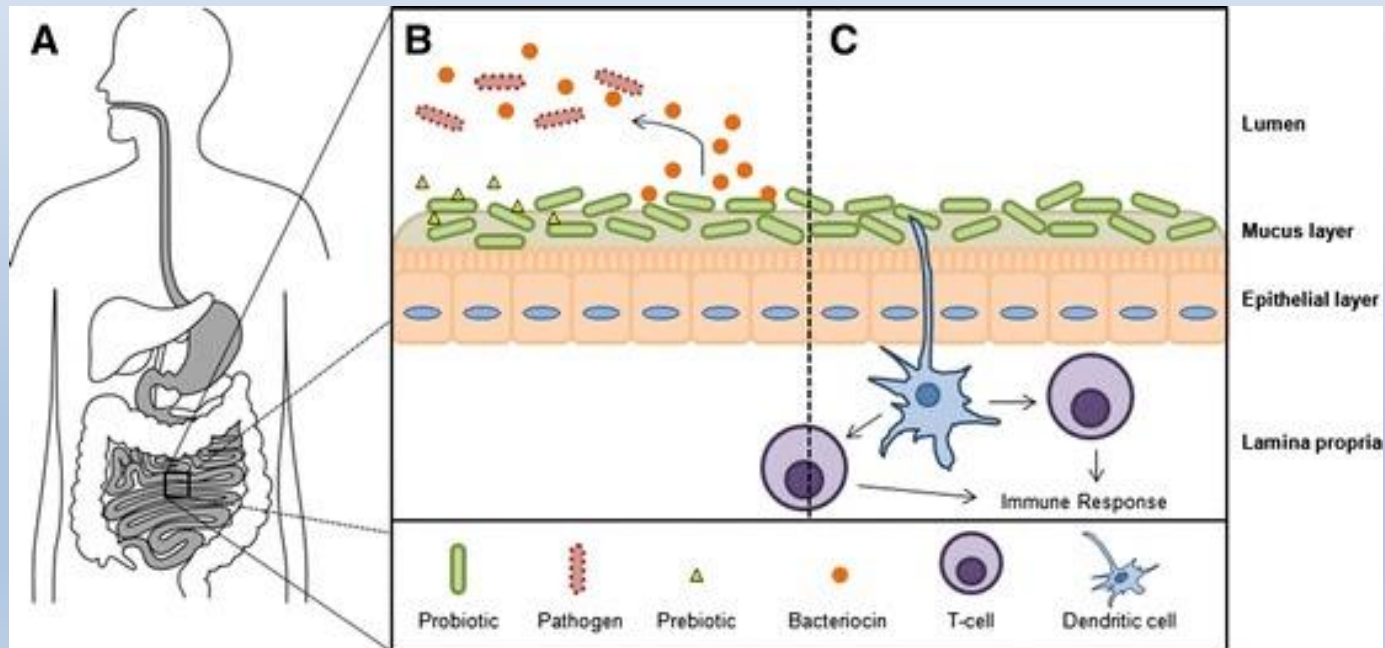


# Some data

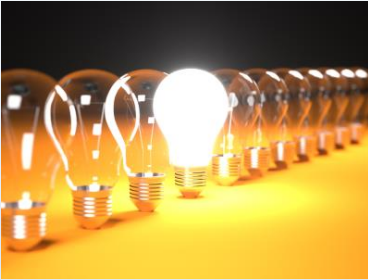
**80% of our immune system is located in the digestive tract**

**Particularly prevalent in the small intestine**

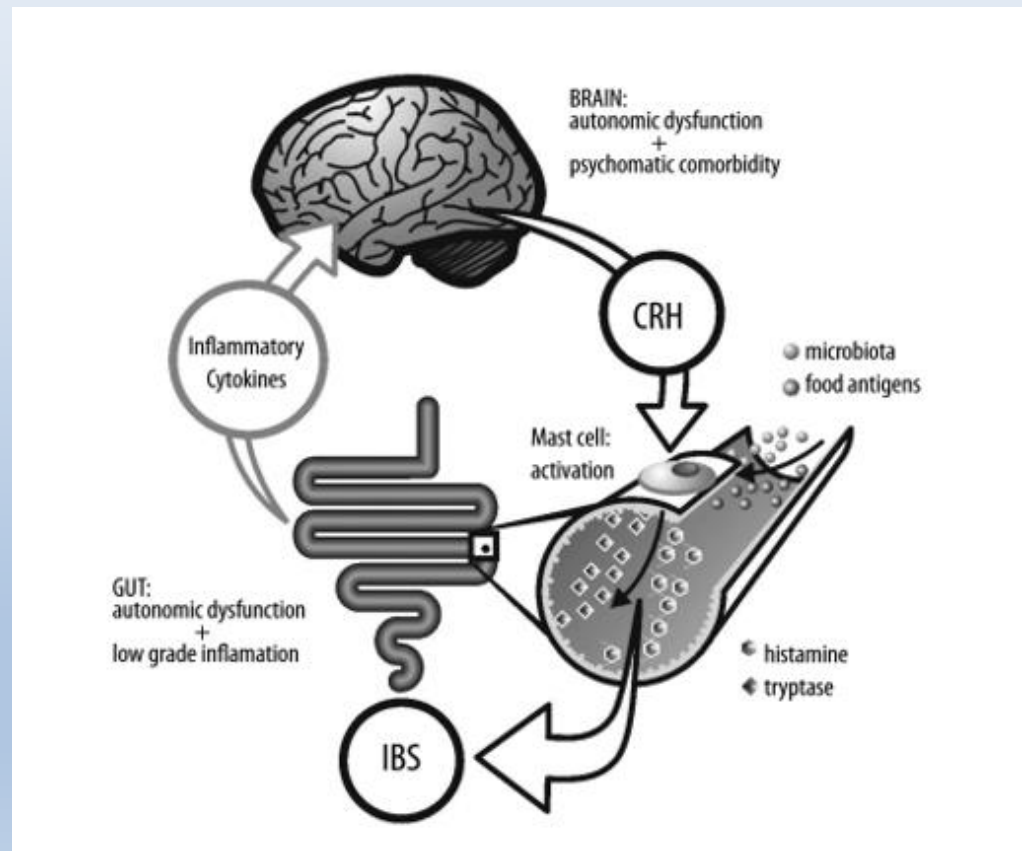
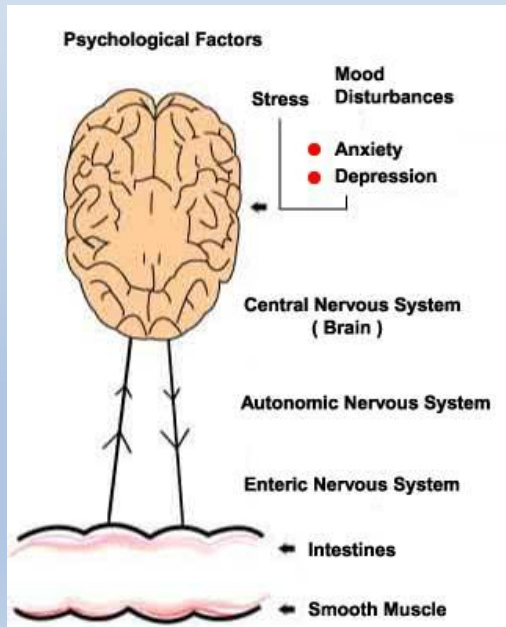
**The overall area of the gut surface is approximately 200 m<sup>2</sup>**



# The brain-gut axis: a key element

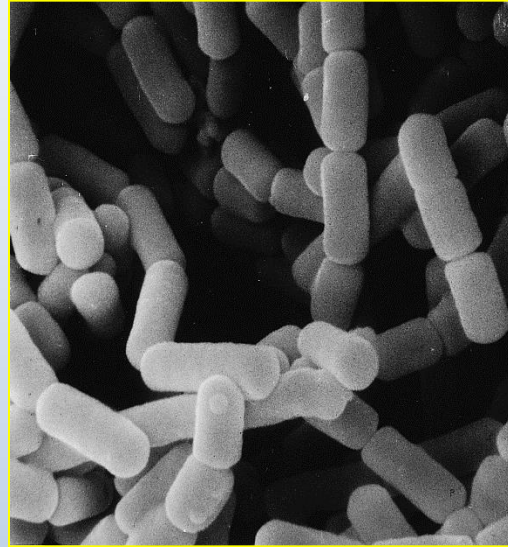


More than **500** million neurons located along the 9 meters of the digestive system ... a real **second brain**!



# Probiotics, immunity and pathogens

**Production of  
adhesins and  
exopolysaccharides  
(EPS)**

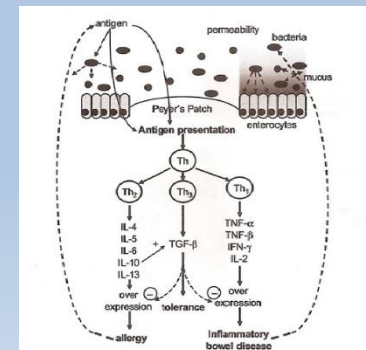
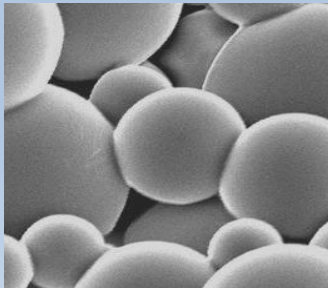


**Synthesis of  
antimicrobial  
substances**

**Transmigration  
from the gut to  
vagina**

**Stimulation of  
non specific and  
specific immune  
responses to  
pathogens**

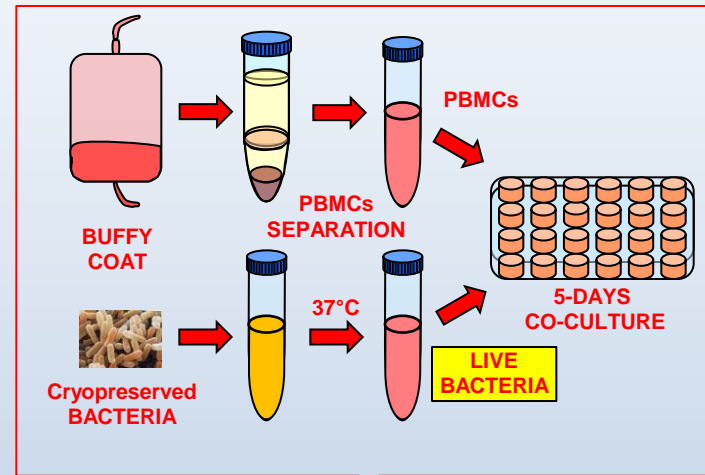
**Competitive  
inhibition of  
pathogens  
adhesion**



# How to study immunomodulation?

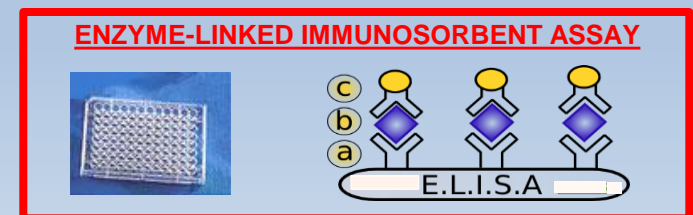
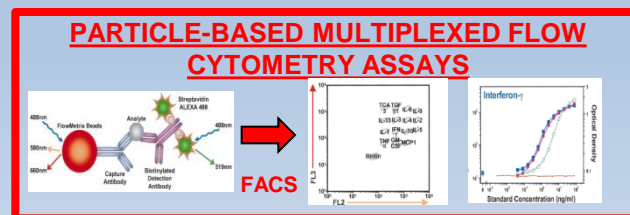
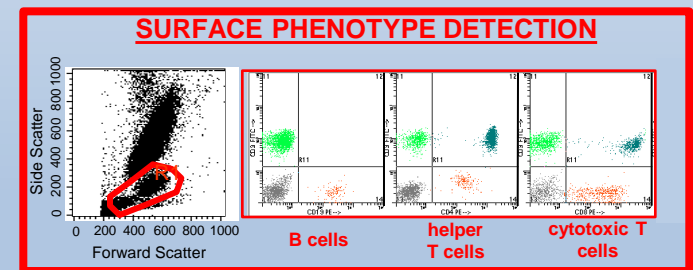
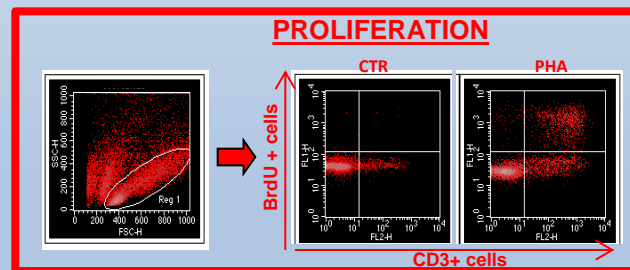
PBMCs are isolated from human peripheral blood and co-cultured with two selected probiotic strains LP01 and LPS01.

The specific stimulation of different immune cell populations and cytokines secretion could be monitored by monoclonal fluorescent antibody staining (FACS) and by enzyme-linked immunosorbent assay (E.L.I.S.A.), respectively.



FACS analysis

Cytokine assay

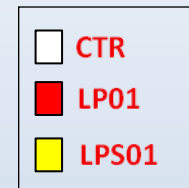
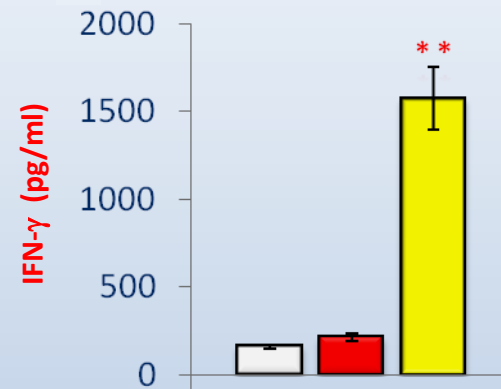
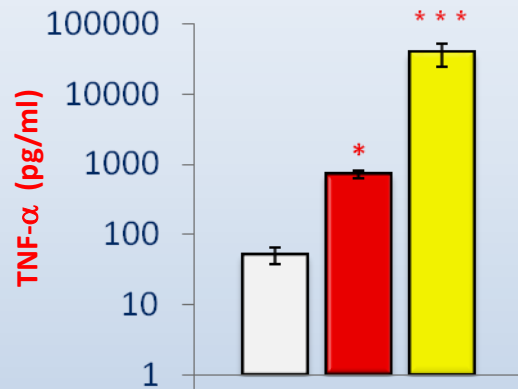


# *In vitro* data

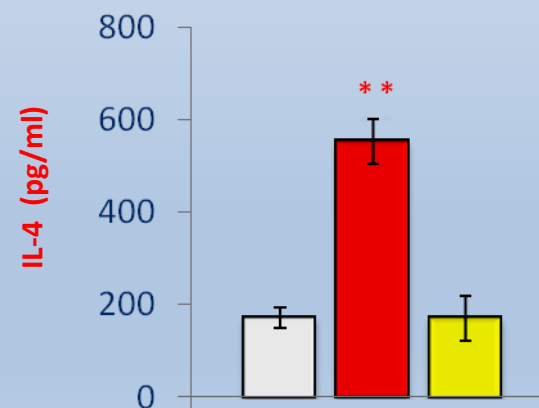
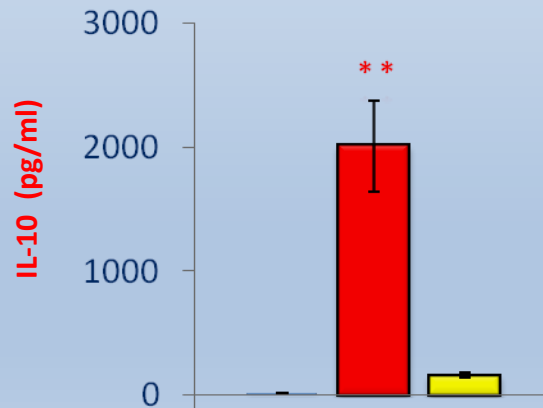
**LP01 = *Lactobacillus plantarum* LP01**

**LPS01 = *Lactobacillus pentosus* LPS01**

**Th1- TYPE  
POLARIZED  
CYTOKINES**



**Th2- TYPE  
POLARIZED  
CYTOKINES**



**Production of cytokines by PBMCs in response to probiotic bacteria LP01 and LPS01 after 5 days of co-culture.**

Data are mean  $\pm$  SEM values of 14 healthy controls. P values calculated using the paired-samples *t* test (\*: 0.01 to 0.05; \*\*: 0.001 to 0.01; \*\*\*: <0.001).

# *In vitro* data



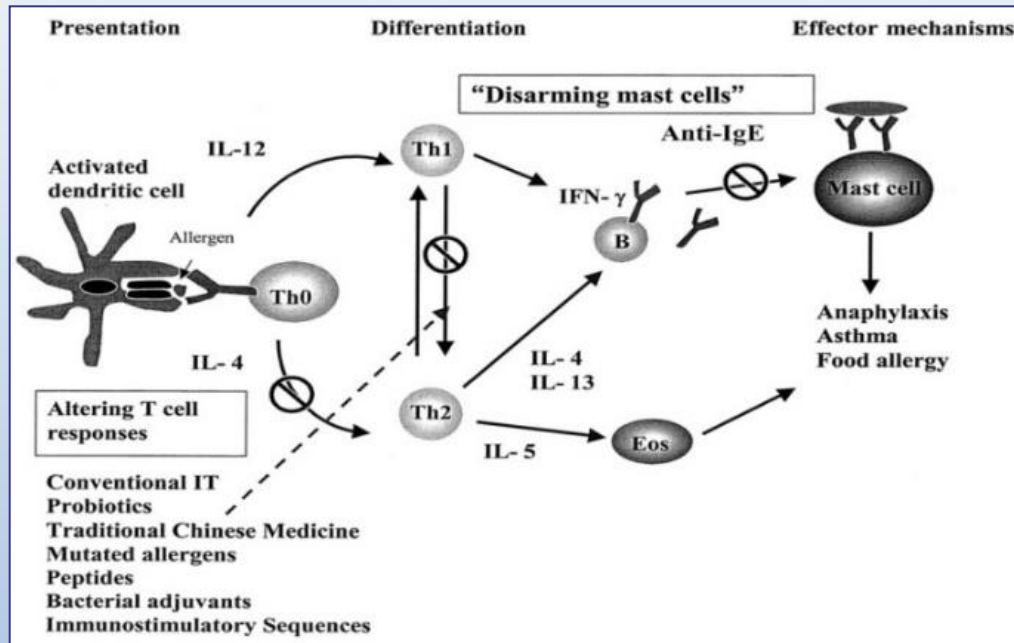
	IFN- $\gamma$ / IL-4	IFN- $\gamma$ / IL-10	TNF- $\alpha$ / IL-4	TNF- $\alpha$ / IL-10	
LP 01	0.38	0.11	1.28	0.35	Th2
LPS 01	9.23	9.70	219.84	231.17	Th1

Data presented at the 5<sup>th</sup> Probiotics, Prebiotics & New Foods, Rome, September 2009.



# The Th1/Th2 paradigm

The Th1/Th2 paradigm implied the existence of two different, mutually regulated, CD4(+) T helper subsets.



A third member of the T helper set, IL-17-producing CD4(+) T cells, now called Th17 cells, was recently described as a distinct lineage that does not share developmental pathways with either Th1 or Th2 cells.



# The importance of human clinical trials

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An efficacy trial with a proper protocol is the basis for the demonstration of efficacy of a probiotic strain and to be hopefully able to get a health claim approved.

## Protocol definition for human clinical trials



- Randomized, double-blind, placebo controlled (DBPC)
- Group dimensions calculated for each *clinical output*
- Protocol set able to register possible adverse effects

# Probiotics in Irritable Bowel Syndrome (IBS)

## Abdominal pain

**Group A** : *Lactobacillus plantarum* LP01 (LMG P-21021) + *Bifidobacterium breve* BR03 (DSM 16604) [5 billion/strain/day]

**Group B** : *Lactobacillus plantarum* LP01 (LMG P-21021) + *Lactobacillus acidophilus* LA02 (DSM 21717) [5 billion/strain/day]

**Gruppo PI** : placebo

A score between 0 and 3 is assigned to each parameter:

0 = no pain or symptoms;

1, 2, 3 = pain or symptom of weak, moderate or strong intensity, respectively.

Pain scores at different locations in the RLQ and LLQ of the abdomen at day 0						
Pain location		Day 0			P (A vs. B)	P (A vs. PI)
		A (24)	B (26)	PI (20)		
RLQ	total score	42	41	43	0.530	0.167
	average	1.75	1.58	2.15		
LLQ	total score	61	64	46	0.724	0.278
	average	2.54	2.46	2.30		
Epigastrium	total score	41	40	37	0.511	0.603
	average	1.71	1.54	1.85		
Back	total score	32	34	32	0.862	0.136
	average	1.33	1.31	1.60		
Other sites	total score	21	20	22	0.577	0.268
	average	0.88	0.77	1.10		
Overall	total score	197	199	180	0.306	0.159
	average	1.64	1.53	1.80		

Pain scores at different locations in the RLQ and LLQ of the abdomen and percentages of decrease after 28 days of treatment with probiotics						
Pain location		Day 28			P (A vs. B)	P (A vs. PI)
		A (21)	B (23)	PI (16)		
RLQ	total score	19	24	35	0.496	<0.001
	% decrease	48.3	33.8	-1.7		
	average	0.90	1.04	2.19		
LLQ	total score	19	24	35	0.582	<0.001
	% decrease	64.4	57.6	4.9		
	average	0.90	1.04	2.19		
Epigastrium	total score	18	20	33	0.956	<0.001
	% decrease	49.8	43.5	-11.5		
	average	0.86	0.87	2.06		
Back	total score	17	18	20	0.912	0.105
	% decrease	39.3	40.2	21.9		
	average	0.81	0.78	1.25		
Other sites	total score	17	16	20	0.519	0.059
	% decrease	7.5	9.6	-13.6		
	average	0.81	0.70	1.25		
Overall	total score	90	102	143	0.766	<0.001
	% decrease	47.8	42.1	0.7		
	average	0.86	0.89	1.79		

# Probiotics in Irritable Bowel Syndrome (IBS)

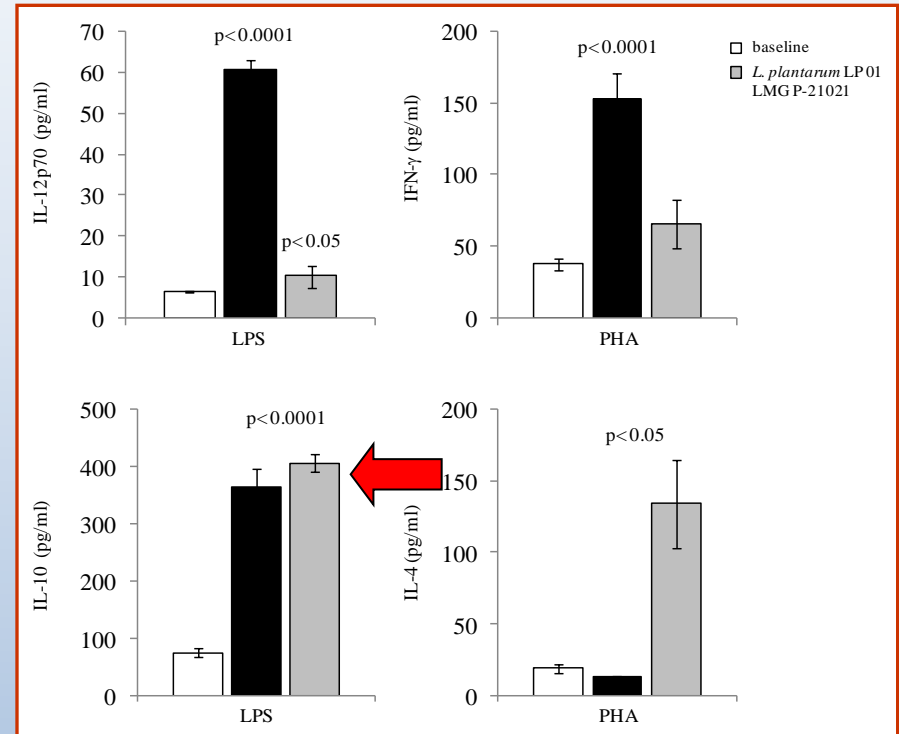
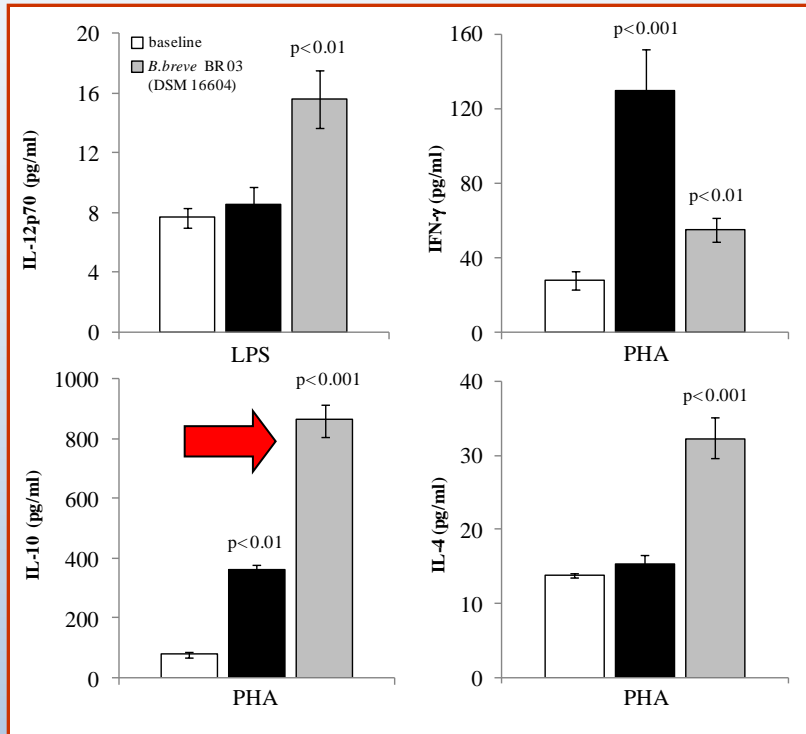
## Other symptoms related to IBS

Overall symptoms scores and percentages of decrease after 28 days of treatment with probiotics									
Symptoms		Day 0			Day 28			p ( $\Delta_A$ vs. $\Delta_B$ )	p ( $\Delta_A$ vs. $\Delta_{PI}$ )
		A (24)	B (26)	PI (20)	A (21)	B (23)	PI (16)		
Constipation	total score	17	18	23	14	15	19	0.590	0.712
	% decrease				5.9	5.8	-3.3		
	average	0.71	0.69	1.15	0.67	0.65	1.19		
Diarrhoea	total score	54	55	58	18	21	41	0.370	0.001*
	% decrease				61.9	56.8	11.6		
	average	2.25	2.12	2.90	0.86	0.91	2.56		
Bloating	total score	47	40	44	15	20	41	0.048	<0.001
	% decrease				63.5	43.5	-16.5		
	average	1.96	1.54	2.20	0.71	0.87	2.56		
Flatulence	total score	51	46	45	16	18	36	0.174	<0.001*
	% decrease				64.1	55.8	0.0		
	average	2.13	1.77	2.25	0.76	0.78	2.25		
Nausea	total score	19	18	21	12	14	18	0.591	0.066
	% decrease				27.8	12.1	-7.1		
	average	0.79	0.69	1.05	0.57	0.61	1.13		
Cephalaea	total score	27	26	26	14	17	18	0.278	0.257
	% decrease				27.8	12.1	13.5		
	average	1.13	1.00	1.30	0.67	0.74	1.13		
Dyspepsia	total score	38	34	33	22	24	31	0.030	<0.001
	% decrease				33.8	20.2	-17.4		
	average	1.58	1.31	1.65	1.05	1.04	1.94		
Overall	total score	253	237	250	111	129	204	0.023	<0.001
	% decrease				49.9	38.5	-2.0		
	average	1.51	1.30	1.79	0.76	0.80	1.82		

# A selection criterion: the anti-inflammatory activity

## *Bifidobacterium breve* BR03

## *Lactobacillus plantarum* LP01



Averages ± S.E.M. of 20 independent experiments

### Positive controls

PHA = phytohemagglutinin

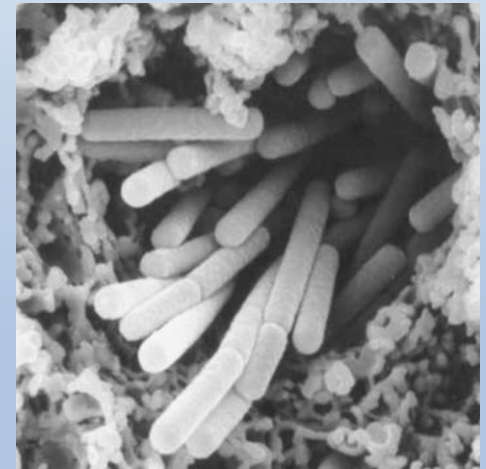
LPS = lipopolysaccharide

# Prevention of winter diseases

This is shown by a study performed by the University of Milan by **Dr. Fabrizio Pregliasco**, virologist at the Department of Public Health, Microbiology and Virology.

The **incidence, severity and duration of episodes** of respiratory infections (cough, flu, bronchitis, pharyngitis, cold) and sick days can also be reduced by half thanks to prolonged use of selected probiotic bacteria.

This also means a reduction  
in the use of antibiotics and  
overall better health.



### Stage 3 (Synbiotic C Versus Synbiotic D Versus Placebo)

In the stage 3 study, enrollment took place between the third week of January and the second week of February 2007, involving an overall number of 250 people. There were no differences between the 84 subjects in the active group C (average age,  $42 \pm 15.3$ ), the 84 in the active group D (average age,  $45 \pm 16.3$ ) and the 82 belonging to the placebo group (average age,  $42 \pm 19.5$ ).

**TABLE 8.** Analysis of Data Regarding the Number of Episodes, Severity, and Duration of Respiratory System Diseases in the 3 groups in the Stage 3 Study, Based on the Information Provided in the Diaries

	Placebo	Synbiotic C (GOS)	Synbiotic D (FOS)	<i>P</i> (Synbiotic C Versus Placebo)	<i>P</i> (Synbiotic D Versus Placebo)	<i>P</i> (Synbiotic C Versus Synbiotic D)
Episodes						
Total IRA	62	35	37	< 0.001	< 0.001	0.992
Cold	31	19	20	0.005	0.059	0.925
Cough	15	12	14	0.644	0.907	0.887
ILI	16	4	3	0.008	0.002	0.972
Severity						
Total IRA	3.65 (62)	2.77 (35)	2.70 (37)	< 0.001	< 0.001	0.726
Cold	3.55 (31)	2.89 (19)	2.85 (20)	0.008	0.004	0.864
Cough	3.07 (15)	2.58 (12)	2.43 (14)	0.174	0.047	0.673
ILI	4.38 (16)	2.75 (4)	3.00 (3)	0.003	0.018	0.437
Duration						
Total IRA	6.10 (62)	4.71 (35)	4.59 (37)	< 0.001	< 0.001*	0.684
Cold	5.97 (31)	4.95 (19)	4.65 (20)	0.019	0.001	0.461
Cough	7.33 (15)	4.25 (12)	4.50 (14)	< 0.001	< 0.001	0.586
ILI	5.19 (16)	5.00 (4)	4.67 (3)	0.837	0.561	0.809

All statistical analyses were performed applying the ANOVA method.

\*Statistical analysis according to Kruskal-Wallis.

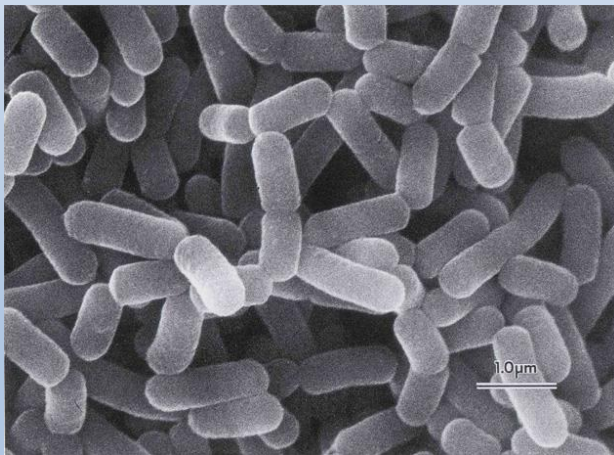
FOS indicates fructooligosaccharides; GOS, galactooligosaccharides; ILI, influenza-like illness.

# A new field: the first evidence of efficacy in sport

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After an intense exercise a significant reduction in immune Natural Killer (NK) cells has been reported.

A fermented milk containing a probiotic belonging to *Lactobacillus casei* species has been particularly effective in preventing the reduction in activity of NK cells normally found in athletes after a particularly stressful exercise.

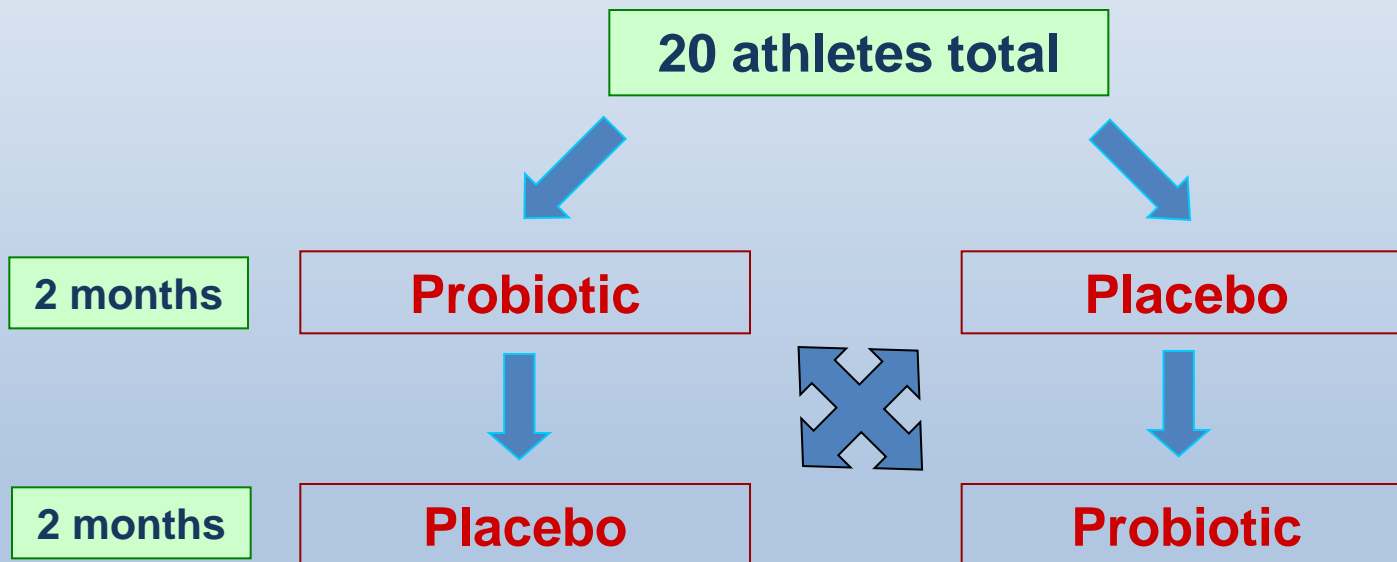




# The important contribution of AIS in 2003

The Australian Institute of Sport (AIS) conducted a study using a strain belonging to the species *Lactobacillus fermentum* in highly trained runners.

The study was conducted during the intensive program of winter training, when colds and other infectious respiratory diseases achieve maximum impact.



**Placebo:** 72 total days with symptoms or disease

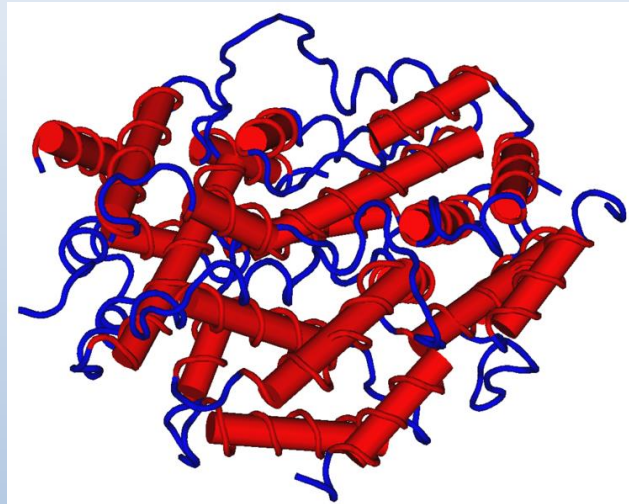
**Probiotic:** 30 total days with symptoms or disease



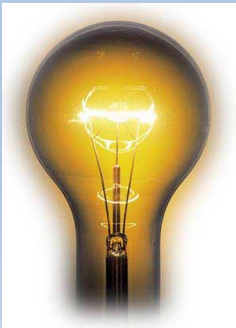
# Interferon- $\gamma$ : a pivotal role?

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Blood tests conducted on athletes under study have shown doubled levels of interferon- $\gamma$ , a molecule directly involved in innate immune responses, suggesting that probiotics can somehow help the body's natural defenses.



<http://www.ncbi.nlm.nih.gov/Structure/>



An improvement in the resistance to common infections is a major benefit that enables athletes to undergo training at high level.

# A second important clinical trial

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A collaborative study between AIS and the University of Newcastle, published in 2006, indicated that fatigued athletes with lowered immune responses may benefit from supplementation with probiotics.

In particular, intense training in athletes was associated with an increased **reactivation of Epstein Barr virus (EBV)**, to a **reduced concentration of Immunoglobulin A (IgA)** in saliva and to a **significantly reduced secretion of interferon- $\gamma$**  by T cells.

The administration of a *Lactobacillus acidophilus* strain for 1 month at a dose of 20 billion viable cells/day significantly increased the secretion of interferon- $\gamma$  up to levels normally found in healthy athletes.

# A recent study in cyclists

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A group of 99 competitive cyclists were randomized to take a strain of *Lactobacillus fermentum* at a dose of 1 billion cells/day or a placebo for 11 weeks.

- Increase of 7.7 times in the title of fecal lactobacilli in male cyclists;
- Slight reduction of the severity of gastrointestinal discomfort at an average level of training intensity, more marked at higher training intensity;
- Reduction in the duration and severity of symptoms of respiratory infectious diseases, but only in males;
- Reduction in the size of the changes in the levels of certain cytokines normally induced by acute exercise.



# The positive implications of immunomodulation

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- ◆ **Protection against harmful or pathogenic bacteria**
- ◆ **Relief of troublesome symptoms related to inflammatory gut conditions and diseases**
- ◆ **Reduction of the incidence, duration and severity of Acute Respiratory infections (ARI)**
- ◆ **Lowering the incidence and severity of allergies and beneficial changes in response to allergens**
- ◆ **Usefulness in people who play sports and in competitive athletes**

# What about regulatory aspects?

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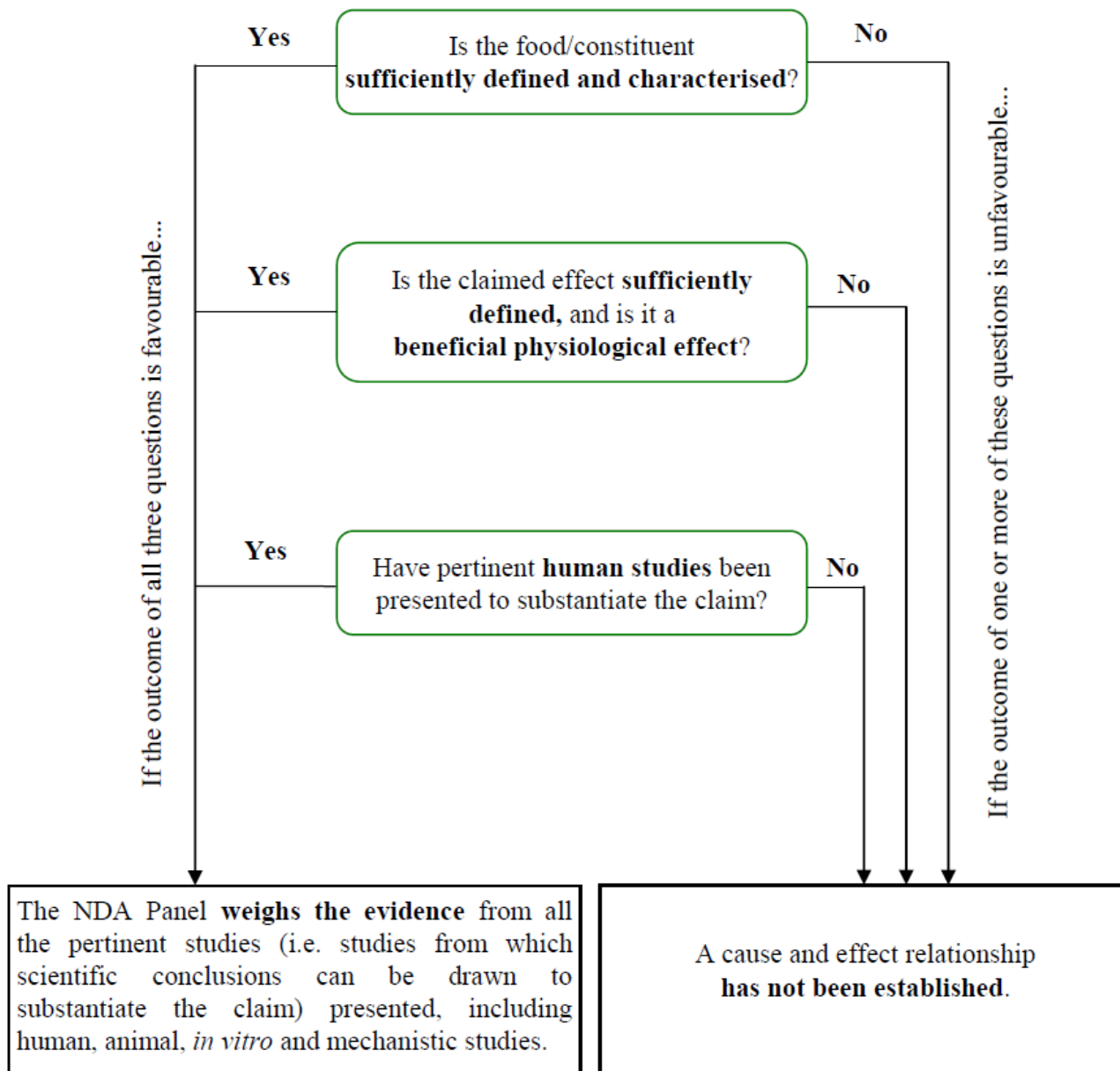
**A health claim is any statement about a relationship between food and health.**

The European Commission authorizes different health claims provided they are based on scientific evidence and can be easily understood by consumers.


The European Food Safety Authority (EFSA) is responsible for evaluating the scientific evidence supporting health claims.

## **EC Regulation 1924/2006**

- *Regulation 1924/2006/EC developed in order to:*
  - *Protect consumers from misleading claims*
  - *Encourage innovation in the food industry*
  - *Harmonise rules on claims in the EU allowing free trade*



# The Eu register of health claims



FOOD

Legal notice | Contact | Search | English (en)

European Commission > Food Safety > Food > Labelling and nutrition > Health and nutrition claims

Food Safety | RASFF | Labelling & Nutrition | Biological Safety | Genetically Modified Food & Feed | Chemical Safety | Food Improvement Agents | Novel Foods | Animal Nutrition | Food Waste

Health & Nutrition Claims

EU Register On Nutrition & Health Claims

Overview



Health claims

Nutrition claims

## EU Register on nutrition and health claims

The search tool only allows searches for health claims\*, and not [nutrition claims](#).

\* **Health claims for which protection of proprietary data is granted** (and for which the right of use of the claim is restricted to the benefit of the applicant) are **only** listed [here](#).

You can also download the complete dataset of nutrition and health claims in the following formats:  

Search the register

Claim status:

Type of claim:

EFSA Opinion reference:

Status

Claim type

EFSA opinion reference

Legislation:

Commission Regulation

Search:

Match entire phrase:

☐

The table will automatically refresh based upon the selections you make.

Clear filters

Showing 1 to 10 of 2,283 results

Show  results

First

Previous

1

2

3

4

5


Next

Last

Claim type	Nutrient, substance, food or food category	Claim	Conditions of use of the claim / Restrictions of use / Reasons for non-authorisation	Health relationship	EFSA opinion reference / Journal reference	Commission Regulation	Status	Entry ID
Art.13(1)	Activated charcoal	Activated charcoal contributes to reducing excessive flatulence after eating	The claim may be used only for food which contains 1 g of activated charcoal per quantified portion. In order to bear the claim information shall be given to the consumer that the beneficial effect is obtained with 1 g which should be taken at least 30 minutes before and 1 g shortly after the meal.	reduction of excessive intestinal gas accumulation	2011;9(4):2049	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	1938
Art.13(1)	Alpha-linolenic acid (ALA)	ALA contributes to the maintenance of normal blood cholesterol levels	The claim may be used only for food which is at least a source of ALA as referred to in the claim SOURCE OF OMEGA 3 FATTY ACIDS as listed in the Annex to Regulation (EC) No 1924/2006. Information shall be given to the consumer that the beneficial effect is obtained with a daily intake of 2 g of ALA.	maintenance of normal blood cholesterol concentrations	2009;7(9):1252, 2011;9(6):2203	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	493, 568

<http://ec.europa.eu/nuhclaims/?event=search&CFID=1841686&CFTOKEN=1785084a6fb18bd6-6B169C59-D566-A440-4DB8B5C31EED98BD&jsessionid=9312c3904fc97c624eaf6724659146d28796TR>

# No probiotic bacteria in the register !!



FOOD

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European Commission > Food Safety > Food > Labelling and nutrition > Health and nutrition claims



Food Safety | RASFF | Labelling & Nutrition | Biological Safety | Genetically Modified Food & Feed | Chemical Safety | Food Improvement Agents | Novel Foods | Animal Nutrition | Food Waste

**Health & Nutrition Claims**  
**EU Register On Nutrition & Health Claims** ▼  
Overview  
Health claims  
Nutrition claims

## EU Register on nutrition and health claims

The search tool only allows searches for health claims\*, and not [nutrition claims](#).

\* **Health claims for which protection of proprietary data is granted** (and for which the right of use of the claim is restricted to the benefit of the applicant) are **only** listed [here](#).

You can also download the complete dataset of nutrition and health claims in the following formats:  

Search the register

Claim status:  
Authorised ▼

Type of claim:  
Claim type ▼

EFSA Opinion reference:  
EFSA opinion reference ▼

Legislation:  
Commission Regulation ▼

Search:  
probiotic

Match entire phrase:  
☒

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Showing 0 to 0 of 0 results (filtered from 2,283 total results)

Show 10 ▼ results

First

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Next

Last

Claim type	Nutrient, substance, food or food category	Claim	Conditions of use of the claim / Restrictions of use / Reasons for non-authorisation	Health relationship	EFSA opinion reference / Journal reference	Commission Regulation	Status	Entry ID
No matching records found								

Showing 0 to 0 of 0 results (filtered from 2,283 total results)

FirstPreviousNextLast



# Relation with the immune system approved only for vitamins and minerals

Show 10 results

First Previous 1 2 Next Last

Claim type	Nutrient, substance, food or food category	Claim	Conditions of use of the claim / Restrictions of use / Reasons for non-authorisation	Health relationship	EFSA opinion reference / Journal reference	Commission Regulation	Status	Entry ID
Art.13(1)	Copper	Copper contributes to the normal function of the immune system	The claim may be used only for food which is at least a source of copper as referred to in the claim SOURCE OF [NAME OF VITAMIN/S] AND/OR [NAME OF MINERAL/S] as listed in the Annex to Regulation (EC) No 1924/2006.	Maintenance of the normal function of the immune system	2009;7(9):1211, 2011;9(4):2079	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	264, 1725
Art.13(1)	Folate	Folate contributes to the normal function of the immune system	The claim may be used only for food which is at least a source of folate as referred to in the claim SOURCE OF [NAME OF VITAMIN/S] AND/OR [NAME OF MINERAL/S] as listed in the Annex to Regulation (EC) No 1924/2006.	function of the immune system	2009;7(9):1213	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	91
Art.13(1)	Iron	Iron contributes to the normal function of the immune system	The claim may be used only for food which is at least a source of iron as referred to in the claim SOURCE OF [NAME OF VITAMIN/S] AND/OR [NAME OF MINERAL/S] as listed in the Annex to Regulation (EC) No 1924/2006.	function of the immune system	2009;7(9):1215	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	252, 259
Art.13(1)	Selenium	Selenium contributes to the normal function of the immune system	The claim may be used only for food which is at least a source of selenium as referred to in the claim SOURCE OF [NAME OF VITAMIN/S] AND/OR [NAME OF MINERAL/S] as listed in the Annex to Regulation (EC) No 1924/2006.	maintenance of the normal function of the immune system	2009;7(9):1220, 2010;8(10):1727	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	278, 1750
Art.13(1)	Vitamin A	Vitamin A contributes to the normal function of the immune system	The claim may be used only for food which is at least a source of vitamin A as referred to in the claim SOURCE OF [NAME OF VITAMIN/S] AND/OR [NAME OF MINERAL/S] as listed in the Annex to Regulation (EC) No 1924/2006.	maintenance of the normal function of the immune system	2009;7(9):1221, 2011;9(4):2021	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	14, 200, 1462
Art.13(1)	Vitamin B12	Vitamin B12 contributes to the normal function of the immune system	The claim may be used only for food which is at least a source of vitamin B12 as referred to in the claim SOURCE OF [NAME OF VITAMIN/S] AND/OR [NAME OF MINERAL/S] as listed in the Annex to Regulation (EC) No 1924/2006.	function of the immune system	2009;7(9):1223	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	107
Art.13(1)	Vitamin B6	Vitamin B6 contributes to the normal function of the immune system	The claim may be used only for food which is at least a source of vitamin B6 as referred to in the claim SOURCE OF [NAME OF VITAMIN/S] AND/OR [NAME OF MINERAL/S] as listed in the Annex to Regulation (EC) No 1924/2006.	function of the immune system	2009;7(9):1225	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	68
Art.13(1)	Vitamin C	Vitamin C contributes to maintain the normal function of the immune system during and after intense physical exercise	The claim may be used only for food which provides a daily intake of 200 mg vitamin C. In order to bear the claim information shall be given to the consumer that the beneficial effect is obtained with a daily intake of 200 mg in addition to the recommended daily intake of vitamin C.	function of the immune system during and after extreme physical exercise	2009;7(9):1226	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	144
Art.13(1)	Vitamin C	Vitamin C contributes to the normal function of the immune system	The claim may be used only for food which is at least a source of vitamin C as referred to in the claim SOURCE OF [NAME OF VITAMIN/S] AND/OR [NAME OF MINERAL/S] as listed in the Annex to Regulation (EC) No 1924/2006.	maintenance of the normal function of the immune system	2009;7(9):1226, 2010;8(10):1815	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	134, 4321
Art.13(1)	Vitamin D	Vitamin D contributes to the normal function of the immune system	The claim may be used only for food which is at least a source of vitamin D as referred to in the claim SOURCE OF [NAME OF VITAMIN/S] AND/OR [NAME OF MINERAL/S] as listed in the Annex to Regulation (EC) No 1924/2006.	Normal function of immune system and inflammation response	2010;8(2):1468	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	154, 159

# In summary ...

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More than 75% of probiotics dossiers submitted to the European Food Safety Authority (EFSA) had health claims that were regarded as “beneficial” or “possibly beneficial”, however the evidence to show that strains had these effects was lacking.

**General guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims<sup>1</sup>**

**EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)<sup>2</sup>**

European Food Safety Authority (EFSA), Parma, Italy

- ❖ specific statements on what exactly the microorganism affects;
- ❖ scientific substantiation of the particular health claim should be based on the general population.

## **What is a health benefit? Researchers issue probiotic guidance for EFSA applications**

By [Nathan Gray+](#), 11-Sep-2013

An evaluation of all EFSA opinions relating to probiotics will help industry players better understand what sort of claims are accepted as a health benefit and which claims are not, say researchers.

<http://www.nutraingredients.com/Research/What-is-a-health-benefit-Researchers-issue-probiotic-guidance-for-EFSA-applications>

# The specific guidance issued by EFSA in 2015

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*“...the health effects of microorganisms (e.g. bacteria and yeast) are species and strain specific, unless the contrary is demonstrated, and thus the **correct identification** of the bacterium’s and yeast’s species and strain for which the claim is proposed is of critical importance.”*

*“...the **suitability of the study population** for the scientific substantiation of a claim has to be considered in the context of the specific claim and the target population for which the claim is intended”.*

*“Examples of claims which were not considered by the NDA Panel as **sufficiently defined** for a scientific evaluation include “gut health”, “natural defences”, “strengthen the immune system”, “maintenance of a normal immune system”, “normal development of gut function”, “normal digestion”.*

*“In order to allow a scientific evaluation by the NDA Panel, the claimed effect needs to refer to a **function of the body** and be **specific** enough to be testable and measurable in vivo in humans by generally accepted methods.”*

European Food Safety Authority. Outcome of a public consultation on the discussion paper for the revision of the guidance on the scientific requirements for health claims related to gut and immune function. EFSA supporting publication 2015:EN-758.

# Conclusions

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- ❖ Probiotic bacteria can modulate the immune system in different ways, thus delivering a selected beneficial effect to the host.
- ❖ The conduction of clinical trials in humans is crucial to assess the real effectiveness of the probiotics intended to be used.
- ❖ To date there are no approved health claims on probiotics in general and, more specifically, on bacteria and immune system.
- ❖ A much more specific approach is needed in order to get a health claim approved by EFSA, especially if related to the gastrointestinal tract, the immune system, and defence against pathogenic microorganisms.



**Thank you very much  
for your attention !!**