Food for the Healthy Gut

B Sesikeran

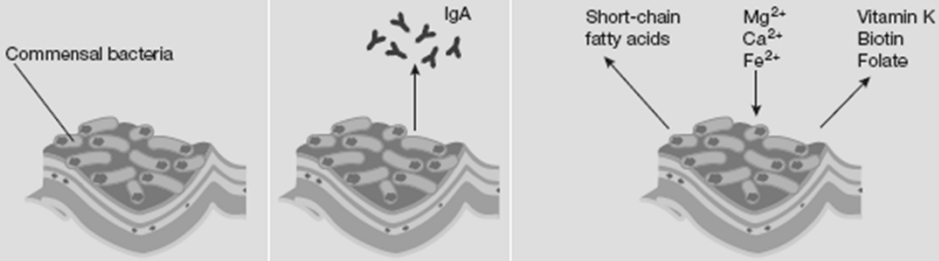
Novel advances in our understanding of the human microbiome

What are the findings ?

- The human body is home to far more than human cells
  - 100 trillion (10^{14}) microbial cells and a quadrallion viruses in and on us
  - Complex community contains taxa from across the tree of life
- Collectively the microbial associates that reside in and on the human body constitute our Microbiota and the genes they encode is known as our Microbiome

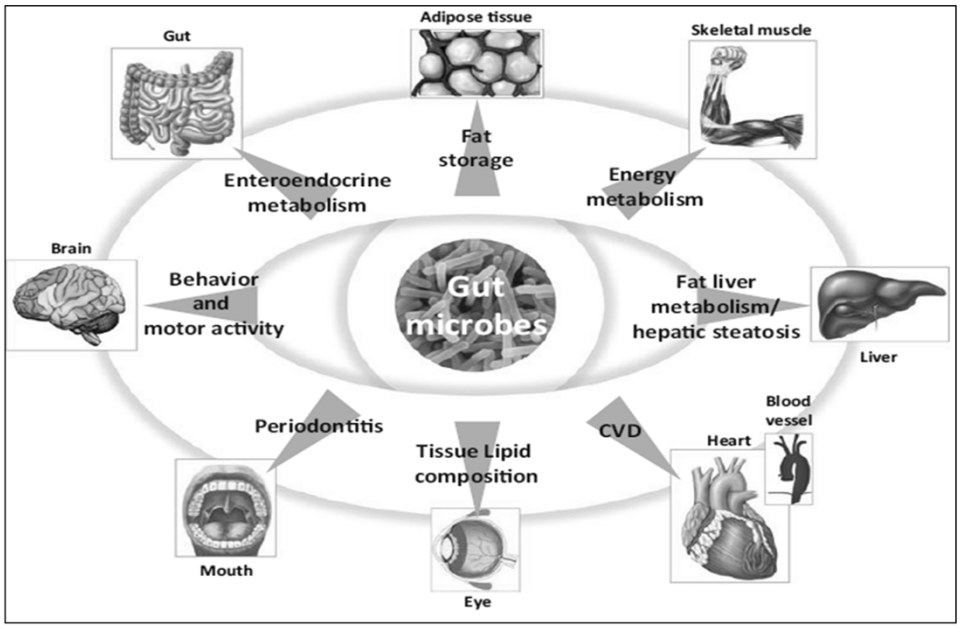
The Gut Microbiota and its influence on health

Protective functions	Structural functions	Metabolic functions	
Pathogen displacement	Barrier fortification	Control IEC differentiation and proliferation	Ferment non-digestible dietary residue and endogenous epithelial-derived mucus
Nutrient competition	Induction of IgA	Metabolize dietary carcinogens	Ion absorption
Receptor competition	Apical tightening of tight junctions	Synthesize vitamins e.g., biotin, folate	Salvage of energy
Production of anti-microbial factors e.g., bacteriocins, lactic acids	Immune system development		



O'Hara A.M. *et al.* EMBO reports 2006; 7: 688-693.

Multiple site impact of Gut Microbiota on whole Host Metabolism

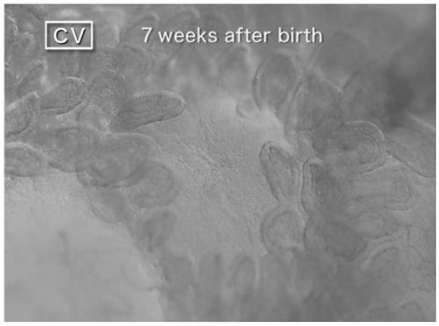


Burcelin R et al. Acta Diabetol. 2011

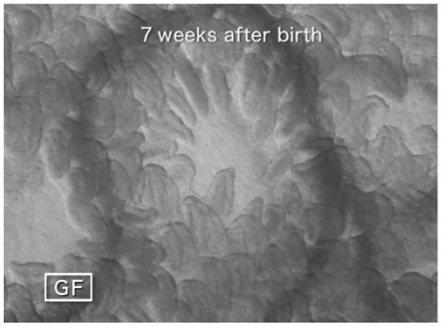
Microbiota plays important roles in the development of the Immune Response

In germ-free animals,
- hypoplasia of Peyer's patches 、
- the reduction in the number of Peyer's patches 、
- reduced IgA-producing cells
- Immature T-cells

have been observed.



Normal mouse



Germ-free mouse

Beginning of symbiosis
(Icum Co. Ltd.)

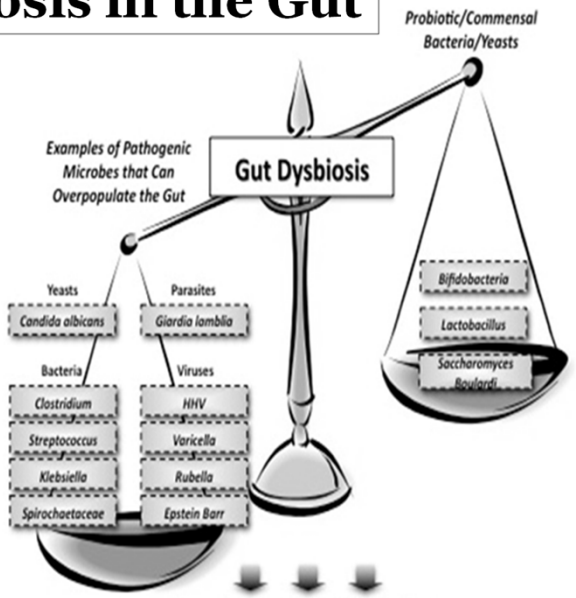
Is Dysbiosis of the gut microbiota responsible for disease?

Historically the influence of the gut microbiota on host health has foccussed on two extremes of relationship : pathogenesis and symbiosis. Latest scientific research has thrown light on the fact that various disease states are profoundly influenced by the levels of various bacteria present in the gut. Decreased microbial diversity in infancy is associated with an increase in atopic disease later in childhood.

Chronic autoimmune inflammatory diseases such as celiac disease, type 2diabetes and obesity may also be associated with an altered gut flora.

A recent study in twins revealed that reduced abundance of a particular commensal bacteria (*Fecalibacterium prausnitzii*) and an increased number of harmful bacteria(*Escherichia coli*) is in fact associated with chron's disease. Therefore a symbiotic or beneficial relationship between the various organisms found in the gut is imperative for the maintenance of health and well – being. An alteration in this balance leads to various diseases that may range from the less serious problems such as diarrhoea and constipation to the more complicated cancers especially that of the colon.

Dysbiosis in the Gut



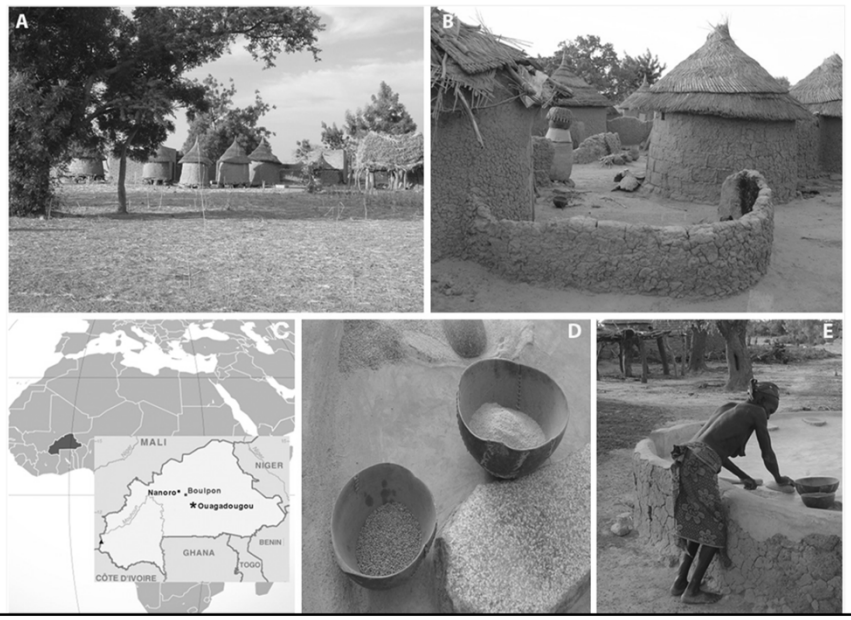
Increasingly recognized as a risk factor for human disease: Infections, Obesity, Diabetes, NEC, IBS, IBD

PNAS March 15, 2011 Suppl.

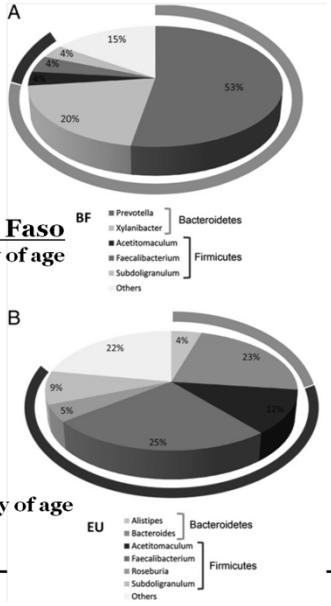
Implicated Microbiota	Changes in Microbiota Presence / Function	References
Allergies		
Lactobacillus spp↓ Bifidobacterium adolescentis ↓	Early colonization with Lactobacillus associated w/decreased allergies Early colonization with more diverse microbiota might prevent allergies	Round et al., 2011 Round and Mazmanian, 2009
Autism		
Bacteroidetes ↑ Proteobacteria ↑ Actinobacteria ↓ Firmicutes ↓	Increased bacterial diversity in feces of autistic children compared to controls	Robinson et al., 2010

Can Dietary Intervention Influence the Gut Microbiota

The rural village of Burkina Faso



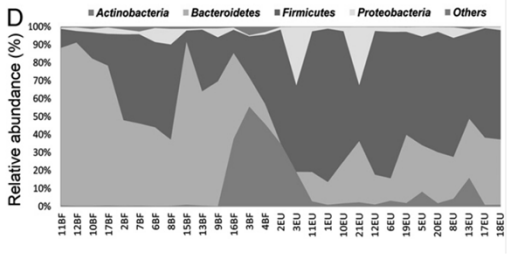
Pie charts of median values of bacterial genera present in fecal samples of BF and EU children



Burkina Faso
N=15, 1-6 y of age

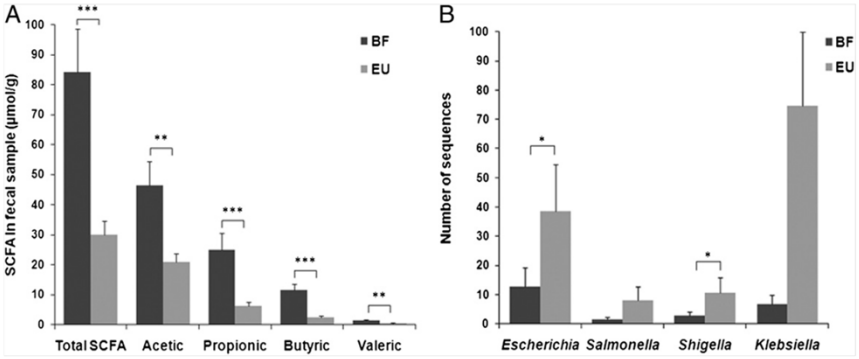
Italy
N=15, 1-6 y of age

Relative abundance of the four most abundant bacterial phyla in each individual among the BF and EU children



Flippo et al. (2010). PNAS. 107: 14691

SCFA-producing bacteria could help to prevent establishment of some potentially pathogenic intestinal flora



Gut microbiota coevolved with the polysaccharide-rich diet of BF individuals, allowing them to maximize energy intake from fibers while also protecting them from inflammations and noninfectious colonic diseases

Lesson learned

Diet has a dominant role over other variables such as ethnicity, sanitation, hygiene, geography, and climate in shaping the gut microbiota.

PNAS

Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa

Carlotta De Filippo[a], Duccio Cavalieri[a], Monica Di Paola[b], Matteo Ramazzotti[c], Jean Baptiste Poullet[d], Sebastien Massart[d], Silvia Collini[b], Giuseppe Pieraccini[e], and Paolo Lionetti[b,1]

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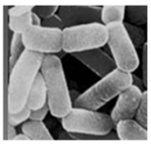
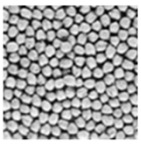
Edited* by Daniel L. Hartl, Harvard University, Cambridge, MA, and approved June 30, 2010 (received for review April 29, 2010)

De Filippo *et al.* (2010). PNAS. 107: 14691

Mechanisms for favorable modification of the gut flora



Probiotics
Live microorganisms which when administered in adequate amounts confer a health benefit on the host
FAO/WHO (2001)

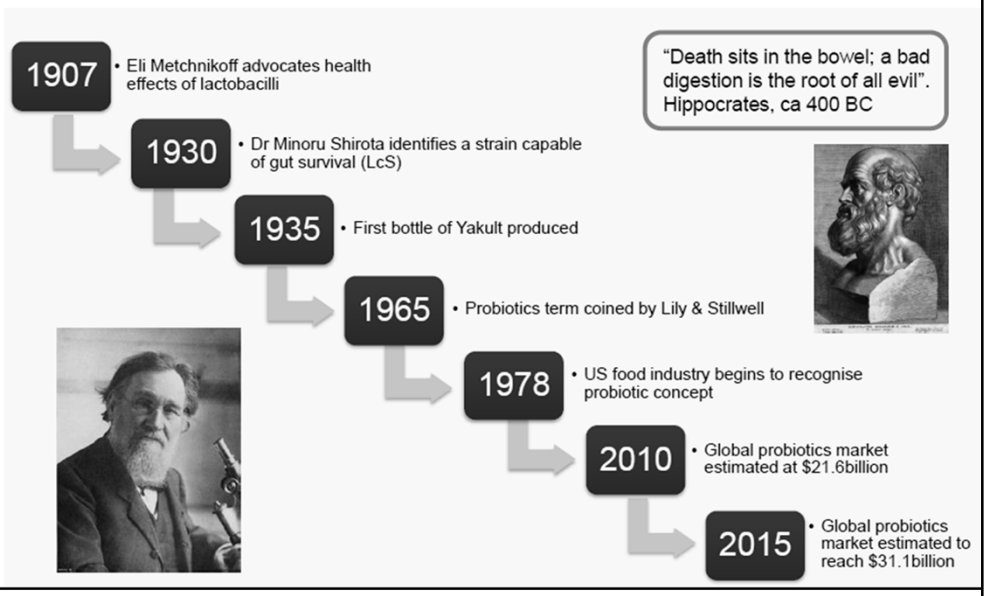


Prebiotics
Prebiotics are non-digestible substances that when consumed provide a beneficial physiological effect on the host by selectively stimulating the favourable growth or activity of a limited number of indigenous bacteria
Gibson GR & Roberfroid MB (1995)

Synbiotics
Probiotic + prebiotic (synergy?)

Role of Probiotics in modulating the Gut Microbiota and preventing Disease?

Probiotic Timeline



Amerian Córdoba Park Hotel,
Córdoba, Argentina
1-4 October 2001

Food and Agriculture Organization
of the United Nations

World Health Organization

Health and Nutritional Properties of Probiotics in Food including Powder Milk with Live Lactic Acid Bacteria

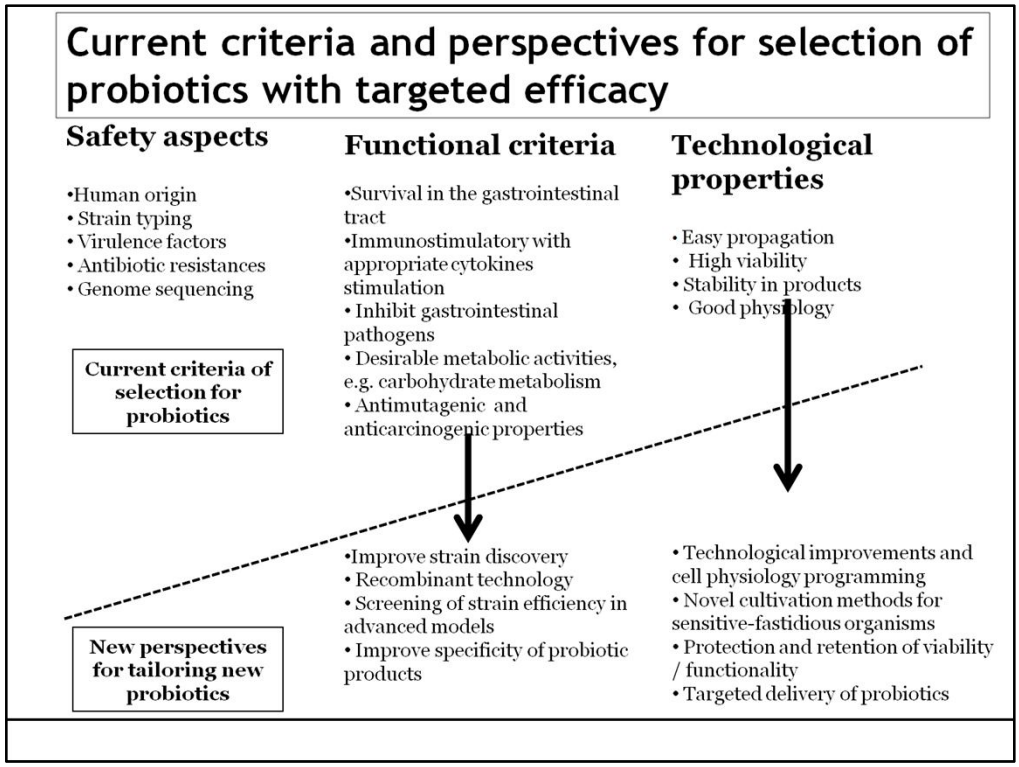
Report of a Joint FAO/WHO Expert Consultation on
Evaluation of Health and Nutritional Properties of Probiotics in Food Including
Powder Milk with Live Lactic Acid Bacteria

'Live micro-organisms which,
when administered in adequate amounts,
confer a health benefit on the host'

Probiotic Selection

- Non toxic and Non Pathogenic, Generally Regarded As Safe (GRAS)
- Resistant to Gastric acid, Bile and Pancreatic juices
- Reaches the target site (small intestine/ large intestine) live in large numbers
- Just as pills and drugs are not the same- all probiotics are not the same
- Strain Specificity of Probiotics – Defined by Genus, Species and Strain
  - Strains differ widely in Genotype and Functionality
  - Single / Multi strain ?
  - Quantities – Vary depending on the strain of bacteria
- Elicits a health benefit that is scientifically proven

Current criteria and perspectives for selection of probiotics with targeted efficacy



Product Criteria

- Safety
- Stability
- Survival
- Efficacy

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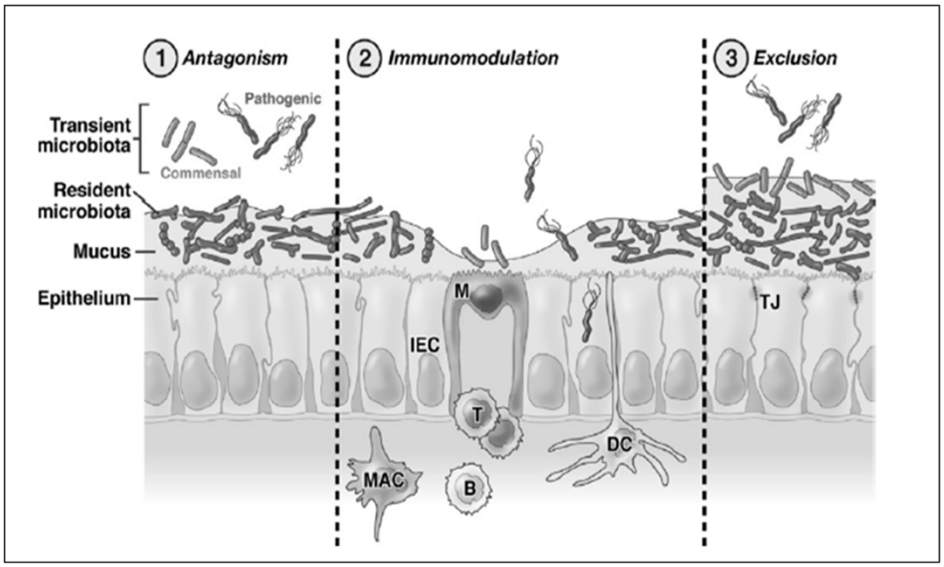
From Mimics to Mechanisms



Scientific Evidence

- In vitro studies
- In vivo animal studies
- Human observational/epidemiology studies
- Human experimental studies
- Randomised Double Blind Placebo Controlled Trials with validated biomarkers (RDBPCT)

Number of peer-reviewed article (PubMed Central)

>200	>100	>25	>10
L. casei Shirota	*B. lactis* BB-12	*L. acidophilus* NSFM	*L. casei* CRL 431
L. rhamnosus GG (LGG)	*E. coli* strain Nissle 1917	*L. plantarum* 299V	*L. paracasei* F19
S. boulardii	VSL#3†	*L. johnsonii* LA-1	*B. bifidum* Yakult
		L. rhamnosus GR-1	*L. acidophilus* LA5
		B. breve Yakult	*L. rhamnosus* LCR-35
		L. acidophilus CERELA	*L. rhamnosus* R0011
		B. longum BB536	*L. gasseri* OLL2716
		L. rhamnosus HN001	*L. acidophilus* NCFB1748
		B. lactis HN019	*P. freudenreichii* ET-3
		L. salivarius UCC118	*L. casei* DN 114001
		L. rhamnosus Lcr35	*B. lactis* DN-173 010
		L. rhamnosus LC705	

† VSL#3 is a composite probiotic containing multiple strains of three viable lyophilized bacteria species: three strains of *Bifidobacterium* (*B. longum, B. infantis and B. brev* e); four strains of *Lactobacillus* (*L. acidophilus, L. casei, L. bulgaricus and L. plantarum*); and one strain of *Streptococcus* (*S. salivarius subspecies thermophilus*)

March 2012

Health-related benefits of Probiotics

Gastrointestinal Disorders	▪ ***Prevention and treatment infectious diarrhoea*** ▪ ***Prevention and alleviation of antibiotic-associated diarrhoea*** ▪ ***Constipation*** ▪ ***Irritable bowel syndrome*** ▪ ***Ulcerative Colitis***
Immune Modulation	▪ ***Increase in NK cell activity*** ▪ ***Prevention of Upper Respiratory Disorders*** ▪ ***Prevention or Alleviation of Allergies and Atopic Diseases in children*** ▪ ***Prevention of Bladder and Colorectal Cancers***

Epidemiol. Infect., Page 1 of 8. © Cambridge University Press 2010
doi:10.1017/S0950268810001780

Role of probiotic in preventing acute diarrhoea in children: a community-based, randomized, double-blind placebo-controlled field trial in an urban slum

D. SUR[1]*, B. MANNA[1], S. K. NIYOGI[1], T. RAMAMURTHY[1], A. PALIT[1], K. NOMOTO[2], T. TAKAHASHI[2], T. SHIMA[2], H. TSUJI[2], T. KURAKAWA[2], Y. TAKEDA[3], G. B. NAIR[1] AND S. K. BHATTACHARYA[4]

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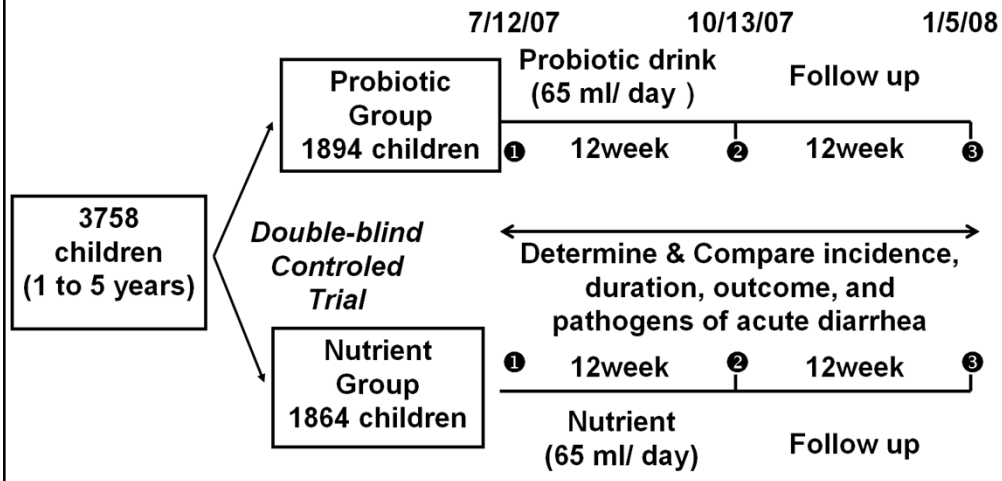
[4] *Indian Council of Medical Research, New Delhi, India*

Schematic Diagram of Probiotic Trial for Prevention of Acute Diarrhea in Children



- Nutritional assessment (height, weight and mid-arm circumference) done at the ❶,❷ and ❸ (beginning, after 12weeks, and at the end of follow-up)

frontiers in
ENDOCRINOLOGY

REVIEW ARTICLE
published: 07 April 2014
doi: 10.3389/fendo.2014.00047

The role and influence of gut microbiota in pathogenesis and management of obesity and metabolic syndrome

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Review Article

Management of metabolic syndrome through probiotic and prebiotic interventions

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ABSTRACT

Metabolic syndrome is a complex disorder caused by a cluster of interrelated factors that increases the risk of cardiovascular diseases and type 2 diabetes. Obesity is the main precursor for metabolic syndrome that can be targeted in developing various therapies. With this view, several physical, psychological, pharmaceutical and dietary therapies have been proposed for the management of obesity. However, dietary strategies found more appropriate without any adverse health effects. Application of probiotics and prebiotics as biotherapeutics is the new emerging area in developing dietary strategies and many people are interested in learning the facts

Genes, Brain and Behavior

Official publication of the International Behavioural and Neural Genetics Society

Genes, Brain and Behavior (2014) **13:** *69–86*

doi: 10.1111/gbb.12109

Review

Microbial genes, brain & behaviour – epigenetic regulation of the gut–brain axis

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Since their emergence, the evolution of multicellular eukaryotic organisms has taken place in the presence of prokaryotes and a plethora of diverse micro-organisms now colonize virtually all body surfaces of animal hosts, residing as beneficial symbionts, harmless commensals or pathogenic parasites (Dave *et al.* 2012; Schloissnig *et al.* 2013; Turnbaugh *et al.* 2007) most prominently within the gastrointestinal tract. An understanding of the importance of these

MEETING REPORT

Gut Microbes 5:1, 74–82; January/February 2014; © 2014 Landes Bioscience

Can prebiotics and probiotics improve therapeutic outcomes for undernourished individuals?

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Keywords: prebiotics, probiotics, microbiota, malnutrition, undernutrition, ISAPP

It has become clear in recent years that the human intestinal microbiota plays an important role in maintaining health and thus is an attractive target for clinical interventions. Scientists and clinicians have become increasingly interested in assessing the ability of probiotics and prebiotics to enhance the nutritional status of malnourished children, pregnant women, the elderly, and individuals with non-communicable

This report is the result of discussion during an expert workshop titled "How do the microbiota and probiotics and/or prebiotics influence poor nutritional status?" held during the 10th Meeting of the International Scientific Association for Probiotics and Prebiotics (ISAPP) in Cork, Ireland from October 1–3, 2012. The complete list of workshop attendees is shown in Table 1.

Recent evidences

- Infants consuming formula with Bb12 produced feces with detect- able presence of Bb12 and augmented sIgA concentration.

Bifidobacterium lactis (B_L):
Good Samaritan of intestinal microbiota

- Prevention of acute diarrhea, including antibiotics-associated diarrhea

For healthcare professionals only

fewer and shorter episodes of diarrhea, with no effect on respiratory illnesses. These effects were more prominent with *L reuteri*, which was also the only supplement to improve additional morbidity parameters.