Bifido-genesi e microbiota del latte materno

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BIFIDOBATTERIO… PROTAGONISTA!

International Journal of Surgery 61 (2019) 17–25

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.elsevier.com/locate/ijsu

Review

Bifidobacterium may benefit the prevention of necrotizing enterocolitis in preterm infants: A systematic review and meta-analysis

Xiu-Li Zhu[a,1], Xiao-Gang Tang[b,1], Fan Qu[a], Yu Zheng[a], Wen-Hao Zhang[a], Yu-Qiao Diao[b,*]

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5. Conclusion

This systematic review has shown that bifidobacteria may have a role in preventing NEC in preterm infants. Our meta-analysis has found that supplement of bifidobacteria could reduce the incidence of NEC Stage ≥ II (according to the Bell staging criteria) and death. And, what deserved to be mentioned is that the supplement of bifidobacteria does not increase the incidence of sepsis of preterm infants. On the basis of our analysis, bifidobacterium may have a beneficial effect and be safe in preventing NEC in preterm infants.

American Physiological Society
AMERICAN JOURNAL OF PHYSIOLOGY
Gastrointestinal and Liver Physiology

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Am J Physiol Gastrointest Liver Physiol. 2010 Nov; 299(5): G1118–G1127.
Published online 2010 Aug 12.
doi: 10.1152/ajpgi.00131.2010; 10.1152/ajpgi.00131.2010

PMCID: PMC2993641
PMID: 20705904

Bifidobacterium bifidum reduces apoptosis in the intestinal epithelium in necrotizing enterocolitis

Ludmila Khailova,[1] Sarah K. Mount Patrick,[1] Kelly M. Arganbright,[1] Melissa D. Halpern,[1] Toshi Kinouchi,[2] and Bohuslav Dvorak[1,3]

PEDIATRICS INTERNATIONAL Official Journal of the Japan Pediatric Society

Pediatrics International (2014) **56**, 714–719 doi: 10.1111/ped.12330

Original Article

Bifidobacterium and enteral feeding in preterm infants: Cluster-randomized trial

Satsuki Totsu,[1] Chika Yamasaki,[2] Masaki Terahara,[3] Atsushi Uchiyama[1] and Satoshi Kusuda,[1] on behalf of Probiotics Study Group in Japan

[1]*Maternal and Perinatal Center, Tokyo Women's Medical University,* [2]*Department of Neonatology, Aiiku Hospital, Tokyo and* [3]*Food Science Institute, Meiji Dairies Corporation, Odawara, Japan*

19 VLBW: 10 trattati con *B. bifidum,* 9 controlli

- Enteral feeding (= >100 ml/Kg/giorno) anticipato nel gruppo trattato (11d vs 12, p<0,05)
- Late-onset sepsis più bassa nel gruppo trattato (3,9 vs 10%, p<0,05)
- Mortalità non differente -> trattamento sicuro

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Sci Rep. 2019; 9: 3254.
Published online 2019 Mar 1. doi: 10.1038/s41598-018-35737-1

PMCID: PMC6397183
PMID: 30824845

Loading ceftriaxone, vancomycin, and *Bifidobacteria bifidum* TMC3115 to neonatal mice could differently and consequently affect intestinal microbiota and immunity in adulthood

RuYue Cheng,[1] JiaWen Guo,[1] FangFang Pu,[1] ChaoMin Wan,[2] Lei Shi,[3] HuaWei Li,[4] YuHong Yang,[4] ChengYu Huang,[1] Ming Li,[1] and Fang He[1]

Recent studies have demonstrated that antibiotics/or probiotics administration in early life play key roles on modulating intestinal microbiota and the alterations might cause long-lasting consequences both physiologically and immunologically. We investigated the effects of early life ceftriaxone, vancomycin and *Bifidobacterium bifidum* TMC3115 (TMC3115) treatment on intestinal microbiota and immunity both in neonates and adults even after termination of antibiotics exposure. We found that ceftriaxone and vancomycin, but not TMC3115, significantly altered the intestinal microbiota, serum total IgE level, and the morphology and function of the intestinal epithelium in the neonatal mice. In the adult stages, the diversity and composition of the intestinal microbiota were significantly different in the antibiotic-treated mice, and ceftriaxone-treated mice exhibited significantly higher serum total IgE and OVA-specific IgE levels. TMC3115 significantly mitigated the alteration of intestinal microbiota caused by ceftriaxone not vancomycin. Antibiotics and TMC3115 can differently modulate intestinal microbiota and SCFAs metabolism, affecting the development and function of the immunity and intestinal epithelium to different degrees in neonatal mice. Neonatal ceftriaxone-induced abnormal intestinal microbiota, immunity and epithelium could last to adulthood partly, which might be associated with the enhancement of host susceptibility to IgE-mediated allergies and related immune responses, TMC3115 may protect against the side effects of antibiotic treatment, at least partly.

Clinical Trial/Experimental Study

Medicine

OPEN

A low abundance of *Bifidobacterium* but not *Lactobacillus* in the feces of Chinese children with wheezing diseases

Zhang Liwen, MD[a], Wan Yu, PhD[a], Ma Liang, MD[b], Xu Kaihong, PhD[a,*], Cheng Baojin, PhD[a,*]

Abstract

Background: The intestinal microbiota is linked with allergic reaction diseases. However, the difference in the fecal microbiota composition between sensitized wheezy and nonsensitized subjects in Chinese children remains unknown. The aim of this study was to quantitate the amounts of fecal microbiota in wheezy children, and to explore the correlation between fecal microbiota and serum Th1/Th2/Th17-type cytokines and total IgE in these patients.

Methods: The amounts of *Bifidobacterium* and *Lactobacillus* were determined using a 16S-RNA real-time polymerase chain reaction (PCR) method in wheezy children (cases) and nonwheezy controls. Serum Th1/Th2/Th17-type cytokines levels were measured using flow a cytometric bead array assay. In addition, the concentrations of total serum IgE was also determined.

Results: In comparison with that in the healthy control (HC), significantly lower abundance of *Bifidobacterium* and lower levels of Th1 cytokines (IFN-γ and TNF-α), but higher levels of Th2-type cytokines (IL-4, IL-5) and Th17-type (IL-17A) cytokine were detected in children with bronchiolitis and asthma. But there was no significant difference in the amounts of *Lactobacillus*. Interestingly, the amounts of fecal *Bifidobacterium* were correlated positively with serum Th1 cytokines IFN-γ, and correlated negatively with serum Th17 cytokines IL-17A, Th2 cytokines IL-4 and serum total IgE in these patients.

Conclusions: Our findings demonstrated that lower quantity of *Bifidobacterium*, but not *Lactobacillus*, may be correlated with asthma and bronchiolitis in chinese children. These results also may provide guidance in choosing the proper probiotics for wheezing children.

Abbreviations: IFN-γ = interferon-γ, IL-17A = interleukin-17A, IL-4 = interleukin-4, IL-5 = interleukin-5, Th cell = helper T cell, TNF-α = tumor necrosis factor-α.

Keywords: asthma, *Bifidobacterium*, bronchiolitis, IgE, *Lactobacillus*, Th1/Th2/Th17-type cytokines

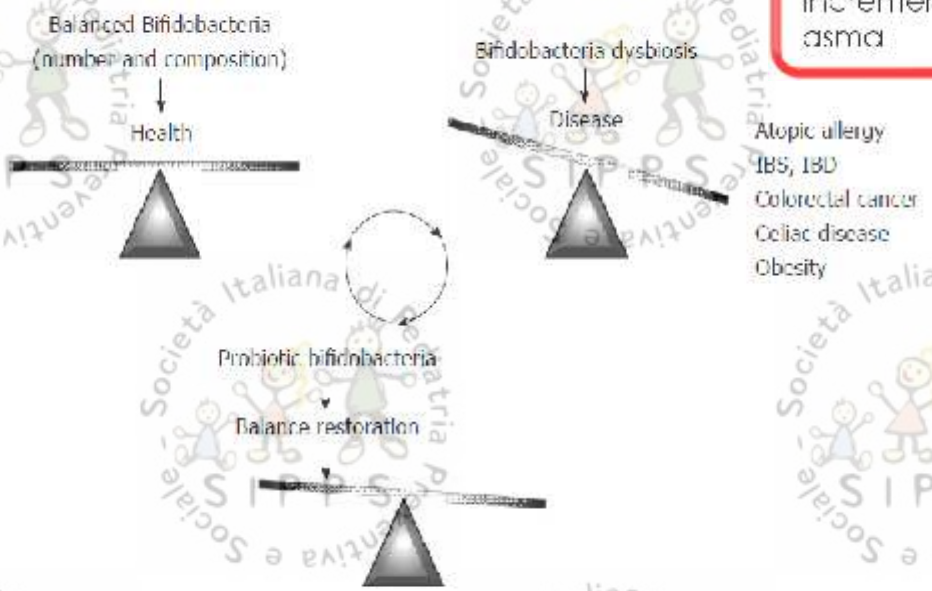
WJG 20th Anniversary Special Issues (17): Intestinal microbiota

Intestinal microbiota in health and disease: Role of bifidobacteria in gut homeostasis

Rafael Tojo, Adolfo Suárez, Marta G Clemente, Clara G de los Reyes-Gavilán, Abelardo Margolles, Miguel Gueimonde, Patricia Ruas-Madiedo

World Journal of Gastroenterology

Tojo R *et al*. Intestinal bifidobacteria in health and disease



Incremento del 20% del rischio di asma

8% obesità grave
64% sovrappeso

Figure 2 Bifidobacterial dysbiosis and its relationship with diseases: A target for probiotic intervention. IBD: Inflammatory bowel disease; IBS: Irritab syndrome.

Candela et al. BMC Microbiology 2012, 12:95
http://www.biomedcentral.com/1471-2180/12/95

BMC Microbiology

RESEARCH ARTICLE Open Access

Unbalance of intestinal microbiota in atopic children

Marco Candela[1*], Simone Rampelli[1], Silvia Turroni[1], Marco Severgnini[2], Clarissa Consolandi[2], Gianluca De Bellis[2], Riccardo Masetti[3], Giampaolo Ricci[4], Andrea Pession[3] and Patrizia Brigidi[1]

Table 3 qPCR quantification of *F. prausnitzii*, *A. muciniphila*, *Enterobacteriaceae*, *Clostridium* cluster IV, *Bifidobacterium* and *Lactobacillus* group in the faecal microbiota of atopics and healthy controls

	16S rRNA gene copies/μg fecal DNA		
Bacterial species/group	Atopics	Controls	*P* value
Faecalibacterium prausnitzii	6.17E+06	2.03E+07	**0.0014**
Akkermansia muciniphila	3.01E+05	5.03E+05	**0.0190**
Enterobacteriaceae	3.86E+04	1.19E+04	0.3500
Clostridium cluster IV	4.46E+06	1.55E+07	**0.0035**
Bifidobacterium	1.08E+06	1.72E+06	0.0850

Differences in *Bifidobacterium* flora composition in allergic and healthy infants

Arthur C. Ouwehand, PhD[a]
Erika Isolauri, MD, PhD[b]
Fang He, PhD[a,c]
Hideo Hashimoto, PhD[c]
Yoshimi Benno, DVM, PhD[d]
Seppo Salminen, PhD[a]

J ALLERGY CLIN IMMUNOL
JULY 2001

TABLE I. *Bifidobacterium* composition in allergic and healthy age-matched infants

Bifidobacterium species	Percentage of isolates (frequency of isolation) Allergic	Healthy	*P* value*: healthy vs allergic
B adolescentis	50 (6/7)	0 (0/6)	.005
B bifidum	2 (1/7)	58 (5/6)	.029
B breve	15 (1/7)	27 (2/6)	>.05
B infantis	21 (4/7)	15 (1/6)	>.05
B longum	12 (1/7)	0 (0/6)	>.05

*Fisher exact test.

B. adolescentis: bifidobatterio dell'adulto

B. infantis: alti ma comportamento «selfish» e non favoriscono la biodiversità

Anti-inflammatory properties of intestinal *Bifidobacterium* strains isolated from healthy infants

Ekaterina V. Khokhlova[1], Vladimir V. Smeianov[3], Boris A. Efimov[1], Lyudmila I. Kafarskaia[1], Svetlana I. Pavlova[2] and Andrei N. Shkoporov[1]

[1]Department of Microbiology and Virology, [2]Department of Pharmacology, Russian State Medical University, Moscow, Russia and [3]Department of Biochemistry, University Wisconsin, Madison, WI, USA

Microbiol Immunol 2012; 56: 27–39
doi:10.1111/j.1348-0421.2011.00398.x

La presenza di ceppi esogeni (*Lactobacillus* e *Bifidobacterium*) riduce, soprattutto nel caso del bifidobatterio, la permeazione di LPS (liberato dai G- morti) e conseguente stato infiammatorio con presenza periferica di TNF a.

LPS in circolo viene legato da LBP. Il complesso viene legato da CD14 dei macrofagi che producono TNF a.

RESEARCH ARTICLE

Bifidobacterium bifidum PRL2010 alleviates intestinal ischemia/reperfusion injury

Sabrina Duranti[1&], Valentina Vivo[2&], Irene Zini[2&], Christian Milani[1], Marta Mangifesta[3], Rosaria Anzalone[1], Leonardo Mancabelli[1], Alice Viappiani[1], Anna Maria Cantoni[4], Elisabetta Barocelli[1], Douwe van Sinderen[5], Simona Bertoni[2*], Francesca Turroni[1,6]

1 Laboratory of Probiogenomics, Department of Chemical Sciences, Life Sciences, and Environmental Sustainability, University of Parma, Parma, Italy, 2 Food and Drug Department, University of Parma, Parma, Italy, 3 GenProbio srl, Parma, Italy, 4 Department of Veterinary Sciences, University of Parma, Parma, Italy 5 APC Microbiome Institute and School of Microbiology, Bioscience Institute, National University of Ireland, Cork, Ireland, 6 Microbiome Research Hub, University of Parma, Parma, Italy

PLOS | ONE

Il pretrattamento con PRL2010

- Riduce infiltrazione neutrofila
- Riduce stress ossidativo
- Riduce traslocazione batterica
- Riduce trascrizione TNF a e IL 10
- Aumenta trascrizione IL 12

In the present study, the transient occlusion of SMA triggered an extensive intestinal mucosal damage associated to an intense local and systemic inflammatory response: massive neutrophil infiltration in the gut and lung districts, marked increase of gut and lung vascular permeability and oxidative stress, remote bacterial translocation and TNFalpha and IL-10 up-regulation in liver and kidneys occurred. In these experimental conditions, we observed that a five-days treatment with *B.bifidum* PRL2010 was able to attenuate mesenteric I/R-induced changes: in fact, pre-treatment with probiotic dampened neutrophil infiltration, especially at the pulmonary level, moderately reduced oxidative stress and significantly decreased bacterial translocation and TNFalpha and IL-10 liver and kidneys transcription levels, while increasing those of IL-12 in kidneys. These findings are in line with Wang research, that recently demonstrated that 14 days oral pre-treatment with a pool of bifidobacteria was able to increase the expression of tight junctions proteins and to reduce bacterial translocation from gut to distant organs [30].

As concerns the evaluation of local inflammatory parameters, *B. bifidum* PRL2010 exerted a slight beneficial effect on neutrophils infiltration and lipid peroxidation in the gut after I/R injury, lowering MPO activity and driving MDA levels closer to the respective SO mice. *B. bifidum* PRL2010 previously showed immunomodulatory properties stimulating the host immune system during colonization and inducing different host genes expression. Among the main targeted genes, some chemokines and HSP encoding genes resulted down regulated, while defensin and tight junctions genes were up regulated [14, 17, 31]. On the basis of those immunomodulatory properties, the slight increase of neutrophil recruitment and lipid peroxidation observed in treated SO mice could be explained as a reinforcement of the innate system driven by the *B. bifidum* PRL2010, which might contribute to mitigate the degree of inflammation evoked by mesenteric I/R.

AEM
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Bifidobacterium bifidum PRL2010 Modulates the Host Innate Immune Response

Francesca Turroni,[a] Valentina Taverniti,[b] Patricia Ruas-Madiedo,[c] Sabrina Duranti,[d] Simone Guglielmetti,[b] Gabriele Andrea Lugli,[d] Laura Gioiosa,[e] Paola Palanza,[e] Abelardo Margolles,[c] Douwe van Sinderen,[a] Marco Ventura[d]

Alimentary Pharmabiotic Centre and Department of Microbiology, Biosciences Institute, National University of Ireland, Cork, Ireland[a]; Dipartimento di Scienze e Tecnologie Alimentari e Microbiologiche, Università degli Studi di Milano, Milan, Italy[b]; Departamento de Microbiología y Bioquímica de Productos Lácteos (IPLA-CSIC), Villaviciosa, Asturias, Spain[c]; Laboratory of Probiogenomics, Department of Life Sciences, University of Parma, Parma, Italy[d]; Department of Evolutionary and Functional Biology, University of Parma, Parma, Italy[e]

PRL 2010 stimola il sistema immune ed al contempo attenua la risposta proinfiammatoria downregolando certe chemochine e le HSP, upregolando defensine e geni delle tight junctions

Conclusions. A large body of data pertaining to modulated genes in *B. bifidum* PRL2010 upon contact with human cell lines (6) or during colonization of animal models (12) was previously obtained. However, very little was known about the transcriptional response of the host as a consequence of the presence of PRL2010 cells. Here, through the use of high-throughput gene expression technology and by employing both an *in vitro* cell line model and a murine model, we assayed the host gene response triggered by *B. bifidum* PRL2010 cells. Comparison of transcriptome changes following *B. bifidum* PRL2010 exposure with the identified murine transcriptome changes upon colonization of mice with PRL2010 cells revealed intriguing similarities with regard to transcription profiles involving HSP-encoding genes and genes involved in tight junctions, as well as Adamts-encoding genes. Such findings involving two different models (e.g., a rather simple HT29 model and a complete eukaryotic organism) clearly support the possibility of a specific effect of *B. bifidum* PRL2010 on the human immune system. The data presented also confirm and extend previous published results achieved from Caco-2 cell monolayers. Interestingly, the overall host response scenario driven by PRL2010 cells may be summarized as a stimulatory response to prime the immune system, while it, at the same time, attenuates the proinflammatory response by downregulating certain chemokines and HSPs and upregulating defensin and tight junction genes (Fig. S2). Overall, these results suggest that PRL2010 exerts an immunomodulatory activity as well as a reinforcement of the innate defense toward its host during gut colonization. Future comparative studies involving *B. bifidum* PRL2010 as well as other bifidobacterial strains belonging to different species will be carried out in order to evaluate the existence of specific strain/species immune-modulatory activities.

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Bifidobacterium Abundance in Early Infancy and Vaccine Response at 2 Years of Age

M. Nazmul Huda, Shaikh M. Ahmad, M. Jahangir Alam, Afsana Khanam, Karen M. Kalanetra, Diana H. Taft, Rubhana Raqib, Mark A. Underwood, David A. Mills and Charles B. Stephensen

Pediatrics 2019;143;
DOI: 10.1542/peds.2018-1489 originally published online January 23, 2019;

L'abbondanza di Bifidobatteri nella prima infanzia si associa alla risposta CD4 a vaccini quali BCG, TT, HBV

BACKGROUND: The intestinal microbiome in early infancy affects immunologic development and thus may affect vaccine memory, though few prospective studies have examined such associations. We examined the association of *Bifidobacterium* levels in early infancy with memory responses to early vaccination measured at 2 years of age.

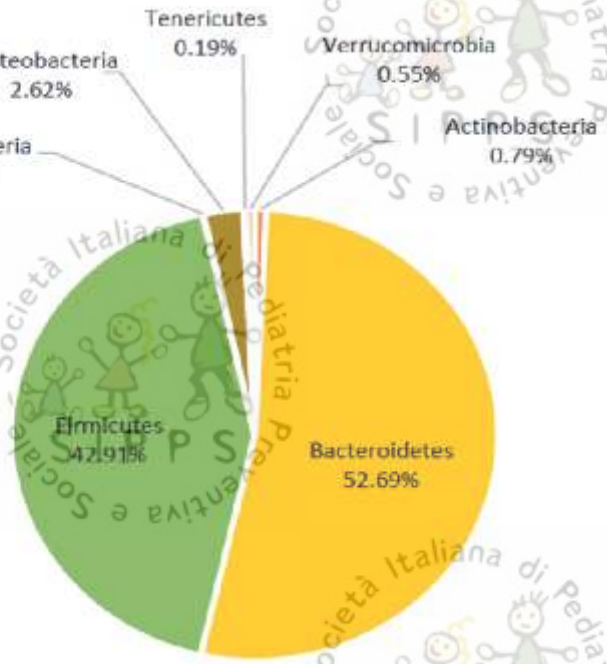
METHODS: In this prospective observational study, we examined the association of *Bifidobacterium* abundance in the stool of healthy infants at 6 to 15 weeks of age, near the time of vaccination, with T-cell and antibody responses measured at 6 weeks, 15 weeks, and 2 years of age. Infants were vaccinated with *Bacillus* Calmette-Guérin (BCG) (at birth), oral polio virus (at birth and at 6, 10, and 14 weeks), tetanus toxoid (TT) (at 6, 10, and 14 weeks), and hepatitis B virus (at 6, 10, and 14 weeks). Fecal *Bifidobacterium* was measured at 6, 11, and 15 weeks. *Bifidobacterium* species and subspecies were measured at 6 weeks.

RESULTS: Mean *Bifidobacterium* abundance in early infancy was positively associated with the CD4 T-cell responses to BCG, TT, and hepatitis B virus at 15 weeks, with CD4 responses to BCG and TT at 2 years, and with plasma TT-specific immunoglobulin G and stool polio-specific immunoglobulin A at 2 years. Similar associations were seen for the predominant subspecies, *Bifidobacterium longum* subspecies *infantis*.

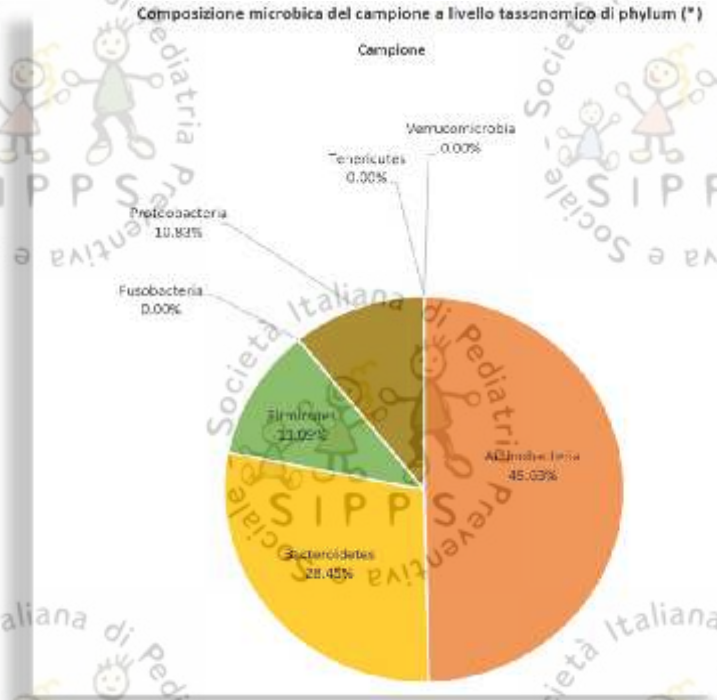
CONCLUSIONS: *Bifidobacterium* abundance in early infancy may increase protective efficacy of vaccines by enhancing immunologic memory. This hypothesis could be tested in clinical trials of interventions to optimize *Bifidobacterium* abundance in appropriate populations.

Microbiota adulto vs lattante

adulto

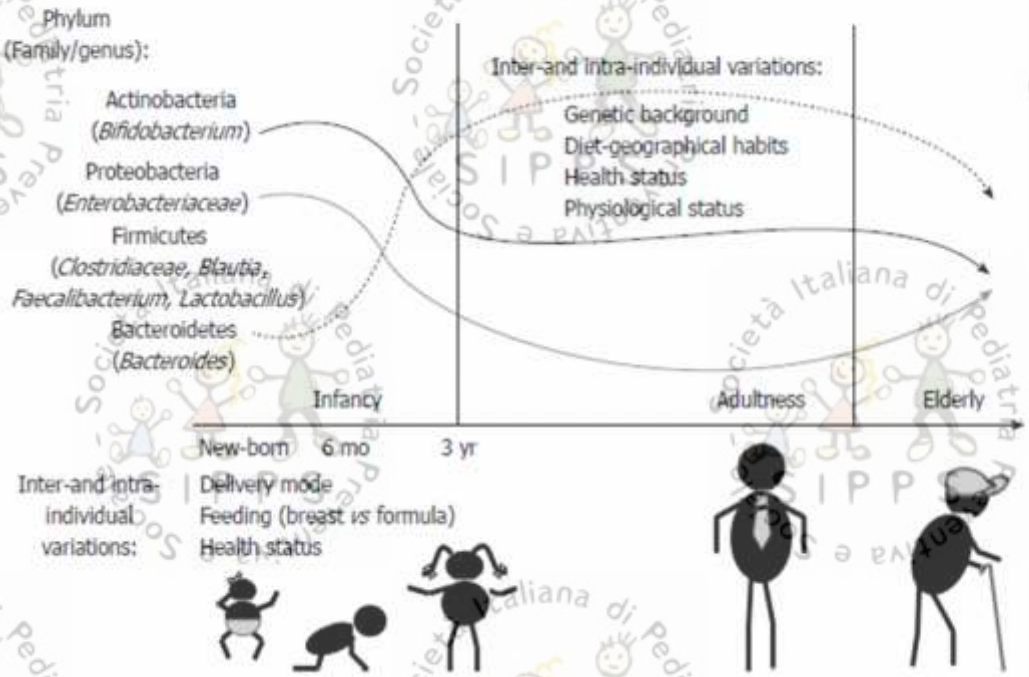


Lattante nato da PS allattato al seno



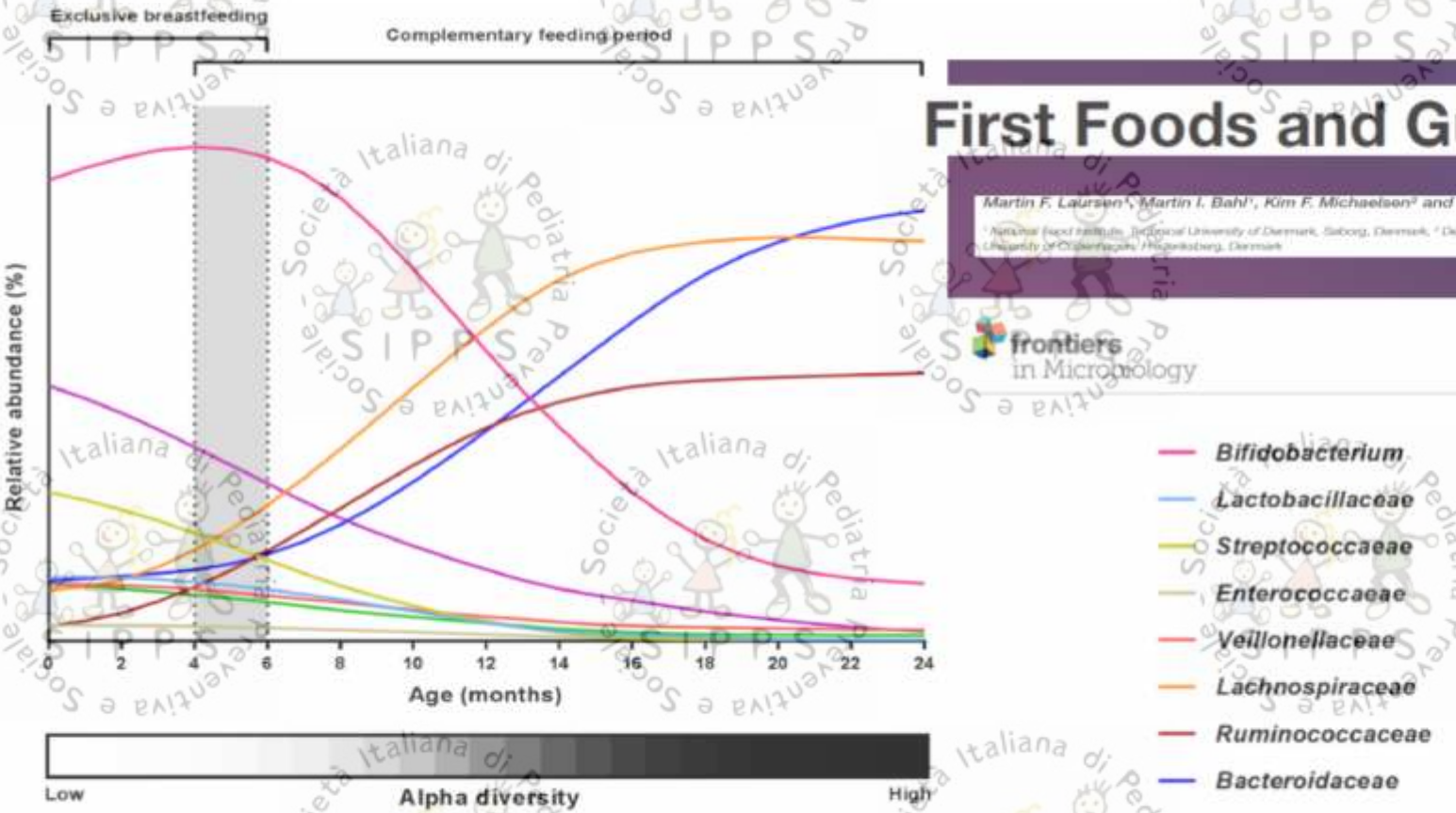
Variazioni in base all'età

Tojo R *et al*. Intestinal bifidobacteria in health and disease



Immediatamente dopo il parto Enterobatteriaceae, Stafilococcaceae, Lactobacillus iniziano a creare le condizioni di microaerofilia necessarie alla sopravvivenza di Bifidobacterium

World Journal of Gastroenterology



First Foods and Gut Microbes

Martin F. Laursen[1], Martin I. Bahl[1], Kim F. Michaelsen[2] and Tine R. Licht[1]*

[1] National Food Institute, Technical University of Denmark, Søborg, Denmark, [2] Department of Nutrition, Exercise and Sports, University of Copenhagen, Frederiksberg, Denmark

frontiers in Microbiology

PERSPECTIVE
published: 06 March 2017
doi: 10.3389/fmicb.2017.00356

FIGURE 2 | Changes in the major gut microbial taxa during the first 24 months of life. Relative abundance estimates and curve shapes are based on average values from available literature (Arrieta et al., 2014; Bäckhed et al., 2015; Kostic et al., 2015; Laursen et al., 2016; Yassour et al., 2016). Individual abundances were normalized to an abundance sum for all bacterial families at each month, and curve smoothing was performed with GraphPad Prism. Dashed lines and gray background indicate the period of introduction to solid foods. Alpha diversity development is shown by a grayscale gradient (white = low diversity, black = high diversity).

Variazione dei bifidobatteri per età

Con gli ultimi 6 (*Figura 1*) identificati nel 2018 dal gruppo di ricerca del Prof. Marco Ventura[4], se ne conoscono oggi almeno 67 specie diverse identificate come in Tabella 1. Di l'intestino umano solo il *B. adolescentis*, il *B. bifidum*, il *B. pseudocatenulatum*, il *B. dentium*, il *B. gallinarum*, il *B. pullorum*, *B. minimum* e il *B. mongoliense*. L'analisi delle feci coloniche

Table 3. The frequency of *Bifidobacterium spp.* by PCR-DGGE during the first 6 months of life.

	3th week	12th week	6th month
B. breve	29% (10/34)	35% (12/34)	25% (9/36)
B. adolescentis	9% (3/34)	6% (2/34)	14% (5/36)
B. bifidum	12% (4/34)	24% (8/34)	42% (15/36)
B. angulatum	N.D.	3% (1/34)	N.D.
B. longum	44% (15/34)	59% (20/34)	72% (26/36)
B. catenulatum group*	18% (6/34)	18% (6/34)	31% (11/36)

ADULTO

B. animalis lactis

1. *B. longum longum*
2. *B. adolescentis*
3. *B. catenolatum*
4. *B. pseudocatenolatum*
5. *B. dentium*
6. *B. gallinarum*
7. *B. pullorum*
8. *B. saeculare*
9. *B. minimum*
10. *B. mongoliense*

Variazioni inter- ed intra-individuali

- Microbiota materno
- Tipo di parto
- Profilassi intrapartum
- Ambiente
- Terapie
- Allattamento

Microbiota materno

- Microbiota individuale

- Il latte di mamme di pretermine è meno ricco di Bifidobatteri
- Il latte di mamme allergiche ha meno Bifidobatteri
- Il latte di mamme celiache ha meno Bifidobatteri e meno Bacteroides
- Il latte di mamme obese ha meno Bifidobatteri ma più stafilococchi

Microbiota materno

- Trattamenti in gravidanza

Expert Opin Drug Saf. 2019 Mar;18(3):173-185. doi: 10.1080/14740338.2019.1579795. Epub 2019 Feb 22.

REVIEW

The role of antimicrobial treatment during pregnancy on the neonatal gut microbiome and the development of atopy, asthma, allergy and obesity in childhood

Sarah Milliken[a], Ruridh M. Allen[b] and Ronald F. Lamont[c,d]

ABSTRACT

Introduction: The use of antibiotics prenatally, during pregnancy, or neonatally may have adverse effects on the neonatal gut microbiome, and adversely affect the development of the infant immune system, leading to childhood atopy, asthma, allergy and obesity.

Areas covered: Vaginal eubiosis and dysbiosis from molecular-based, cultivation-independent techniques, and how this affects the neonatal gut microbiome and early development of the immune system, the association between maternal antibiotics and the beneficial role of vitamin D in the development of atopy, asthma, allergy and obesity, efforts to reduce the use of antibiotics in pregnancy and therapeutic interventions such as vaginal 'seeding', probiotics, breastfeeding and neonatal dietary supplementation.

Expert opinion: Currently available research gives insufficient attention to confounding variables. There remains uncertainty as to whether it is relevant that the mother suffered from the same condition as the purported infant outcome variable, for which she may have received antibiotics. In most studies, there is a lack of control for the number of antibiotic courses administered, the timing of use, the use of broad spectrum or narrow range antibiotics, the indication for antibiotics, the dose-dependent nature of the effect, the class of antibiotics used, or a varying degree of risk.

Tipo di parto

The mode of delivery affects the diversity and colonization pattern of the gut microbiota during the first year of infants' life: a systematic review

Erigene Rutayisire[1], Kun Huang[1,2], Yehao Liu[3] and Fangbiao Tao[1,2*]

Results: Seven out of 652 retrieved studies met inclusion criteria, were included in systematic analysis. Caesarean Section (CS) was associated with both lower abundance and diversity of the phyla Actinobacteria and Bacteroidetes, and higher abundance and diversity of the phylum Firmicute from birth to 3 months of life. At the colonization level, *Bifidobacterium*, and *Bacteroides* genera seems to be significantly more frequent in vaginally delivered infants compared with CS delivered. These infants were more colonized by the *Clostridium*, and *Lactobacillus* genera. From the reports, it is tempting to say that delivery mode has less effect on colonization and diversity of *Bifidobacteria*, *Bacteroides*, *Clostridium*, and *Lactobacillus* genera from the age of 6 to 12 months of life.

Profilassi intrapartum

Early Gut Microbiota Perturbations Following Intrapartum Antibiotic Prophylaxis to Prevent Group B Streptococcal Disease

Giuseppe Mazzola[1*], Kiera Murphy[2,3,4*], R. Paul Ross[4], Diana Di Gioia[1*], Bruno Biavati[1], Luigi T. Corvaglia[5], Giacomo Faldella[5], Catherine Stanton[2,4]

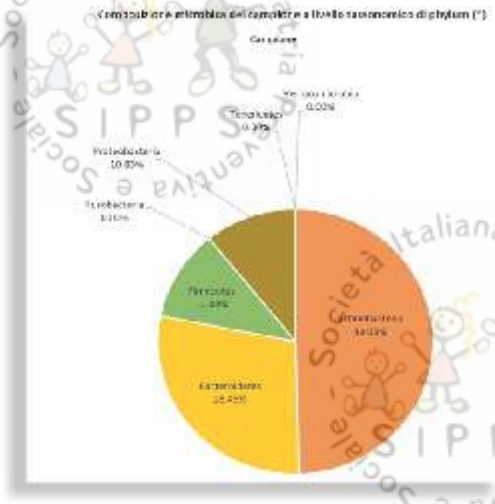
PLOS ONE | DOI:10.1371/journal.pone.0157527 June 22, 2016

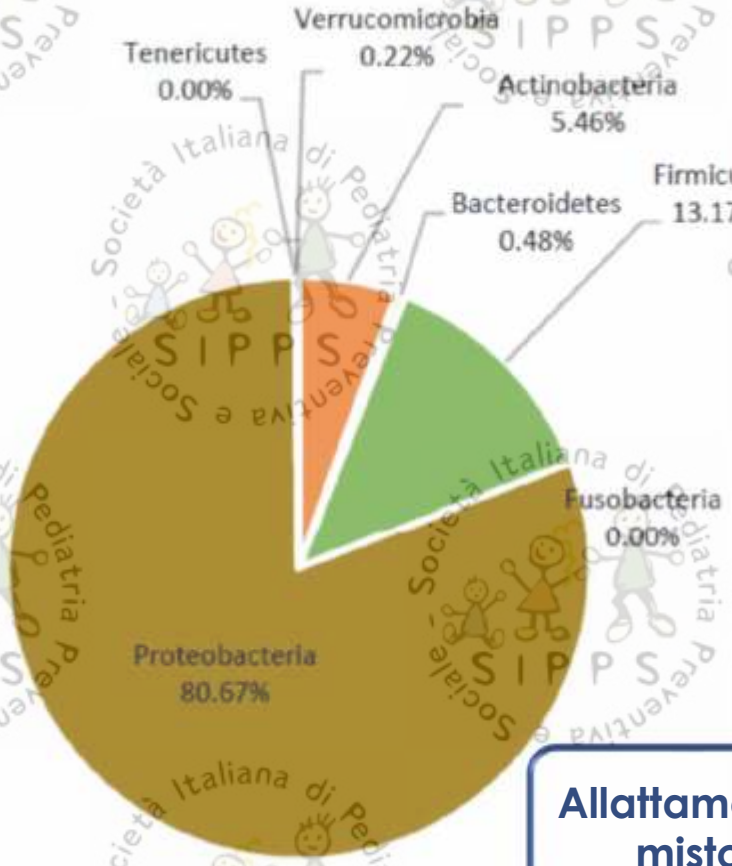
Abstract

The faecal microbiota composition of infants born to mothers receiving intrapartum antibiotic prophylaxis with ampicillin against group B *Streptococcus* was compared with that of control infants, at day 7 and 30 of life. Recruited newborns were both exclusive breastfed and mixed fed, in order to also study the effect of dietary factors on the microbiota composition. Massive parallel sequencing of the V3-V4 region of the 16S rRNA gene and qPCR analysis were performed. Antibiotic prophylaxis caused the most marked changes on the microbiota in breastfed infants, mainly resulting in a higher relative abundance of Enterobacteriaceae, compared with control infants (52% vs. 14%, $p = 0.044$) and mixed-fed infants (52% vs. 16%, $p = 0.13$ NS) at day 7 and in a lower bacterial diversity compared to mixed-fed infants and controls. Bifidobacteria were also particularly vulnerable and abundances were reduced in breastfed ($p = 0.001$) and mixed-fed antibiotic treated groups compared to non-treated groups. Reductions in bifidobacteria in antibiotic treated infants were also confirmed by qPCR. By day 30, the bifidobacterial population recovered and abundances significantly increased in both breastfed ($p = 0.025$) and mixed-fed ($p = 0.013$) antibiotic treated groups, whereas Enterobacteriaceae abundances remained highest in the breastfed antibiotic treated group (44%), compared with control infants (16%) and mixed-fed antibiotic treated group (28%). This study has therefore demonstrated the short term consequences of maternal intrapartum antibiotic prophylaxis on the infant faecal microbial population, particularly in that of breastfed infants.

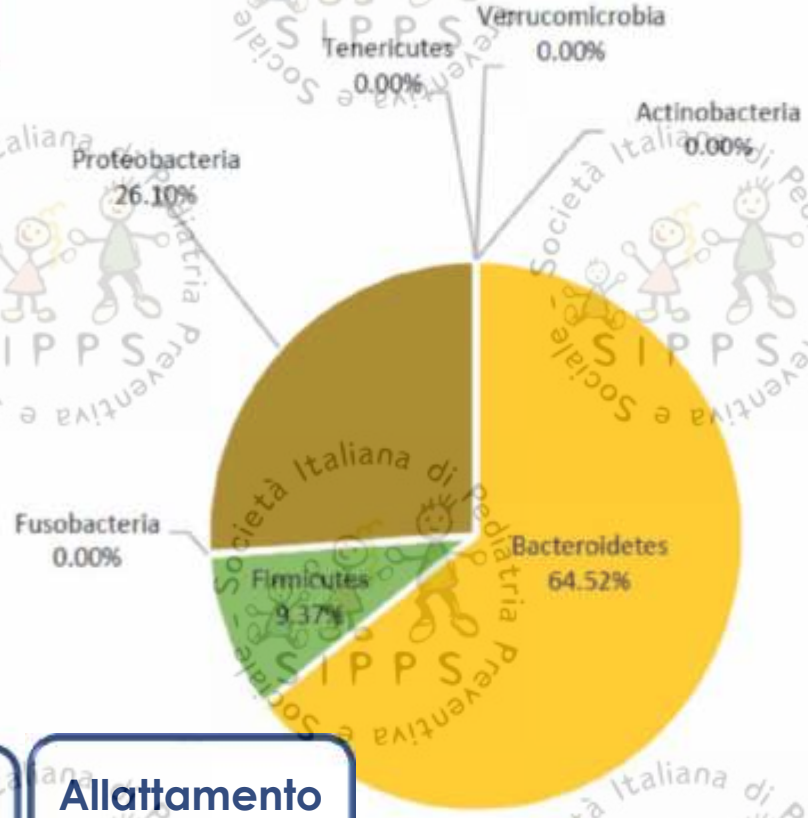
Ambiente

Allattamento





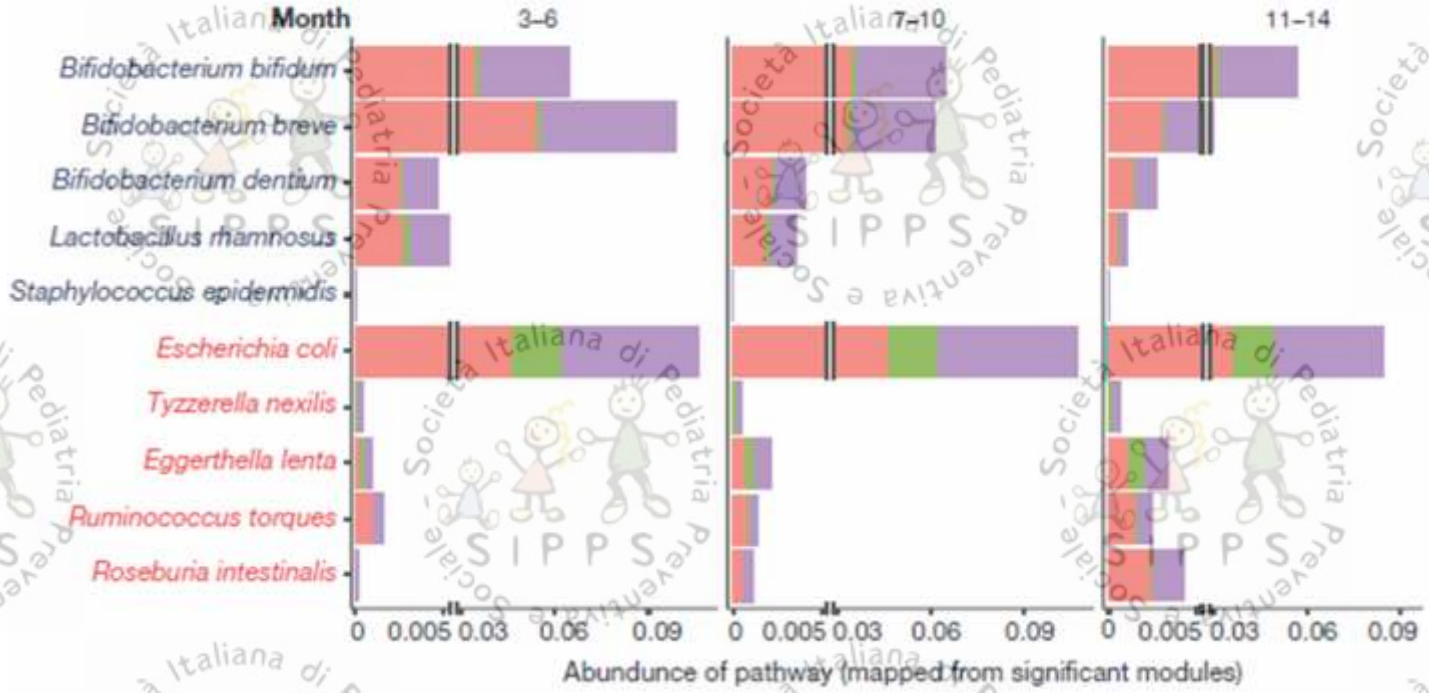
Allattamento misto



Allattamento artificiale

Temporal development of the gut microbiome in early childhood from the TEDDY study

Christopher J. Stewart[1,2,18]*, Nadim J. Ajami[1,18], Jacqueline L. O'Brien[1], Diane S. Hutchinson[1], Daniel P. Smith[1], Matthew C. Wong[1], Matthew C. Ross[1], Richard E. Lloyd[1], HarshaVardhan Doddapaneni[1], Ginger A. Metcalf[1], Donna Muzny[1], Richard A. Gibbs[1], Tommi Vatanen[3], Curtis Huttenhower[4], Ramnik J. Xavier[4], Marian Rewers[5], William Hagopian[6], Jorma Toppari[7,8], Anette-G. Ziegler[9,10,11], Jin-Xiong She[12], Beena Akolkar[13], Ake Lernmark[14], Heikki Hyoty[15,16], Kendra Vehik[17], Jeffrey P. Krischer[17] & Joseph F. Petrosino[1]*



903 pz
3-14 mesi

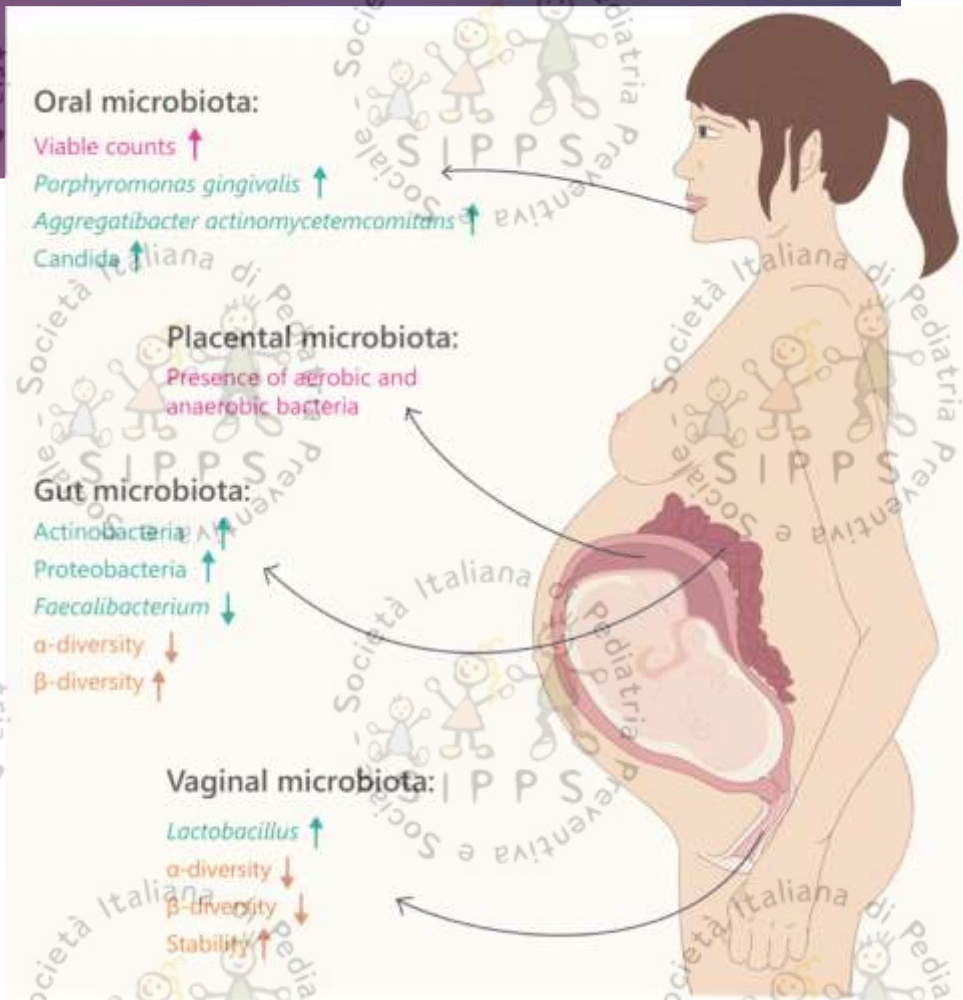
25 OCTOBER 2018 | VOL 562 | NATURE | 583

Come avviene l'impianto del microbiota nel bambino?

Impianto del microbiota

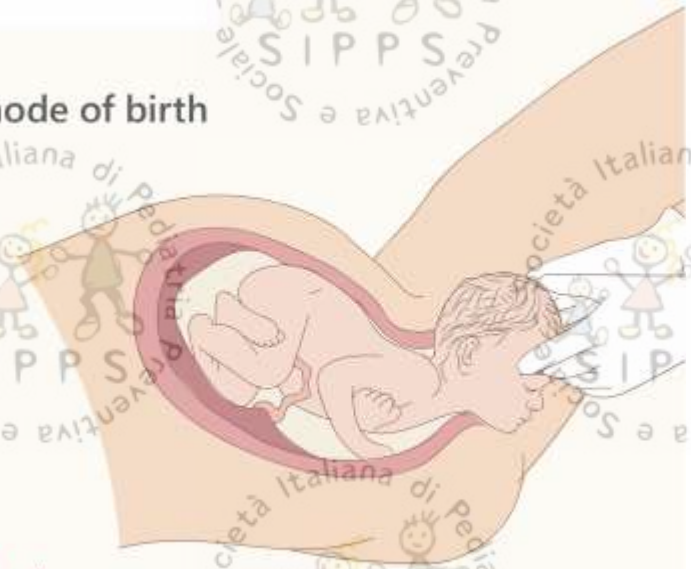
Microbial Changes during Pregnancy, Birth, and Infancy

*Meital Nuriel-Ohayon †, Hadar Neuman † and Omry Koren **



A. Changes associated with mode of birth (vaginal vs. C-section)

Prevotella ↑
Lactobacillus ↑
Propionibacterium ↓
Corynebacterium ↓
Enterobacteriaceae ↓
Streptococcus ↓
Earlier colonization of Bacteroidetes
Antibiotic resistance bacterial genes ↓
Resemblence to mother's gut microbiota ↑
Viable counts ↑
β-diversity ↓



B. Changes associated with feeding (breast milk vs. formula)

Bacteroides fragilis ↓
Bifidobacterium infantis ↑
Sneathia ↑
Staphylococcus ↓
α-diversity ↓

Microbiota del latte materno

- Il LM contiene diverse centinaia di tipi di batteri, circa 1000 UFC/ml
- Ogni bambino ingerisce circa 800.000 batteri/giorno
- C'è condivisione di ceppi di Bifidobatteri, Stafilococchi, Lattobacilli, Enterococchi tra LM e feci di lattante
- Durante il primo mese di allattamento, le feci del neonato condividono il 28% dei batteri con il microbiota del latte materno

Microbiota del latte materno

3 componenti

1. microbiota residente della ghiandola mammaria(proteobatteri)

AEM
Journals.ASM.org

Microbiota of Human Breast Tissue

was *Proteobacteria*. The most abundant taxa in the Canadian samples were *Bacillus* (11.4%), *Acinetobacter* (10.0%), *Enterobacteriaceae* (8.3%), *Pseudomonas* (6.5%), *Staphylococcus* (6.5%), *Propionibacterium* (5.8%), *Comamonadaceae* (5.7%), *Gammaproteobacteria* (5.0%), and *Prevotella* (5.0%). In the Irish samples the most abundant taxa were *Enterobacteriaceae* (30.8%), *Staphylococcus* (12.7%), *Listeria welshimeri* (12.1%), *Propionibacterium* (10.1%), and *Pseudomonas* (5.3%). None of the subjects had signs or symptoms of infection, but the presence of viable bacteria was confirmed in some samples by culture. The extent to

Microbiota del latte materno

2. <u>microbiota orale del bambino (flusso retrogrado)</u>

Scambi di batteri tra i due microbioti (indagini US sul flusso del latte dimostrano un flow back)…

Stafilococchi, Streptococchi

Dal mese anche Veilonella, Leptotrichia, Prevotella

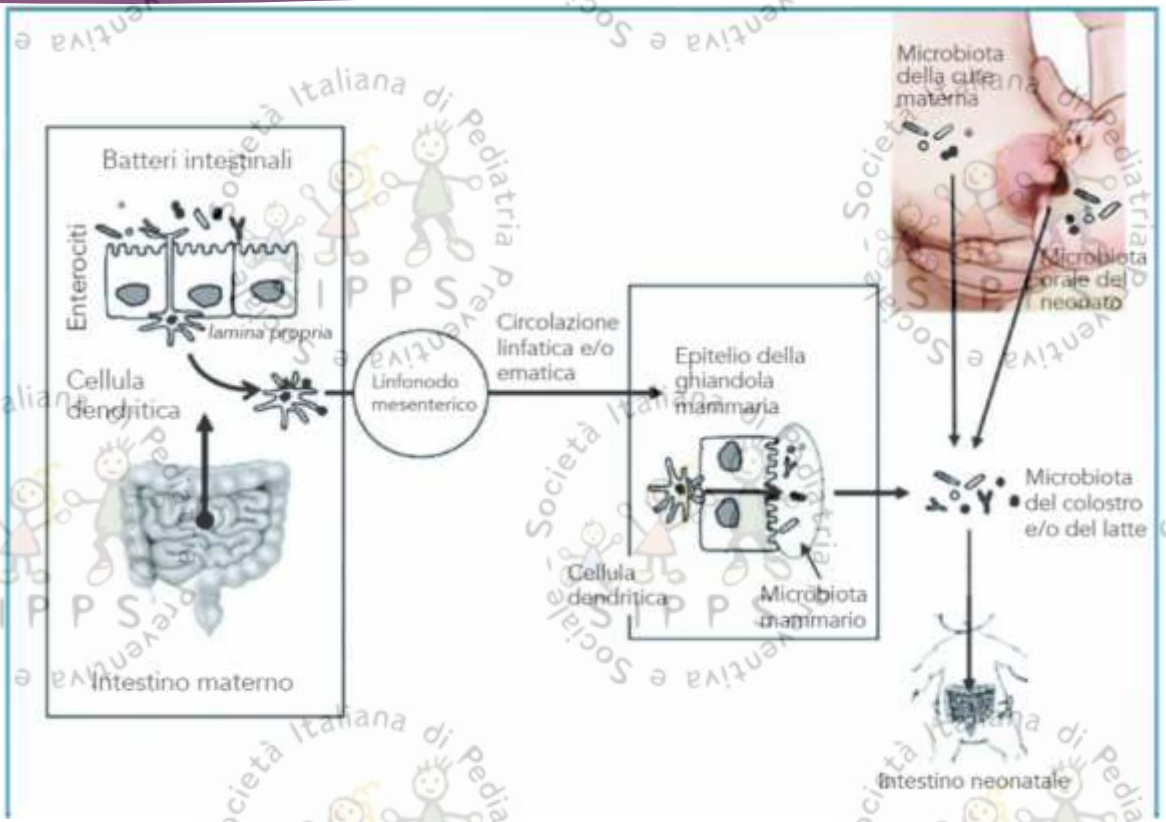
Microbiota del latte materno

3. circolazione entero-mammaria

batteri intestinali (Bifidobacterium, Bacteroides, Parabacteroides, Blautia, Coprococcus)

The Origin of Human Milk Bacteria: Is There a Bacterial Entero-Mammary Pathway during Late Pregnancy and Lactation?[1–4]

Juan M. Rodriguez*
Department of Nutrition, Food Science and Food Technology, Complutense University of Madrid, Madrid, Spain



Microbiota del latte materno

- CLUSTERING IN BASE AL CORE:

C1: Moraxellaceae, Enterobacteriaceae, Pseudomonadacaea

C2: Streptococcaceae, Staphylococcaceae, Oxalobacteriaceae

C3: Oxalobacteriaceae, Comamonadaceae

C4: Streptococcaceae, Comamonadaceae

VARIAZIONI DURANTE L'ALLATTAMENTO

- Nel colostro presenti Weissella, Leuconostoc, Staphylococcus, Streptococcus, Lactococcus
- Dal mese presenti Veillonella, Leptotrichia, Prevotella

Human Milk Oligosaccharides

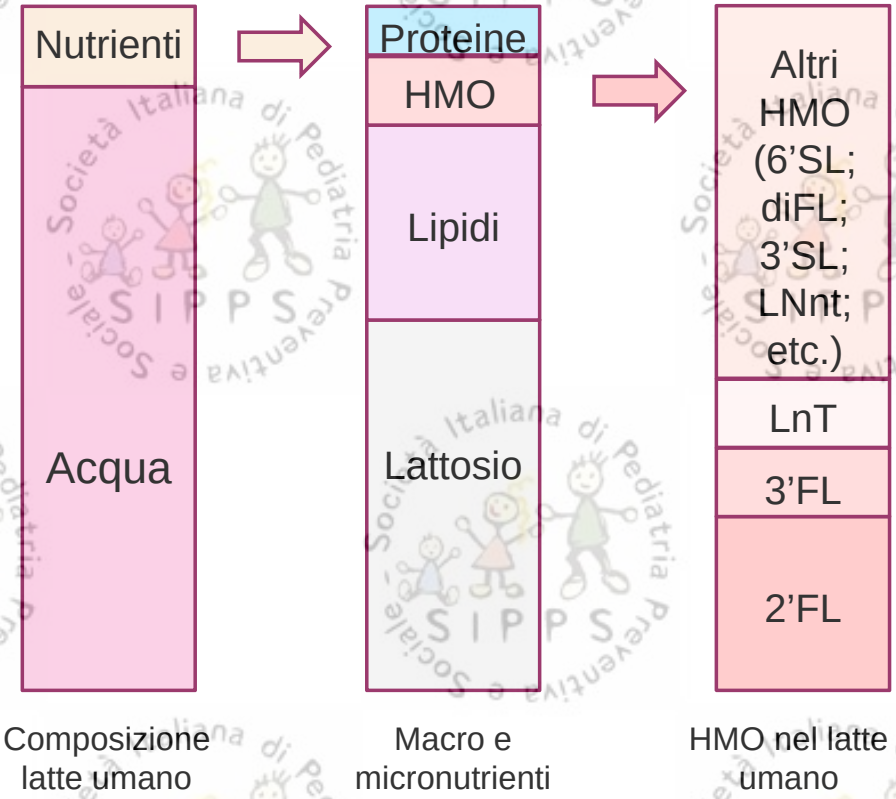
4-16 g/l LM, 20 g/l nel colostro

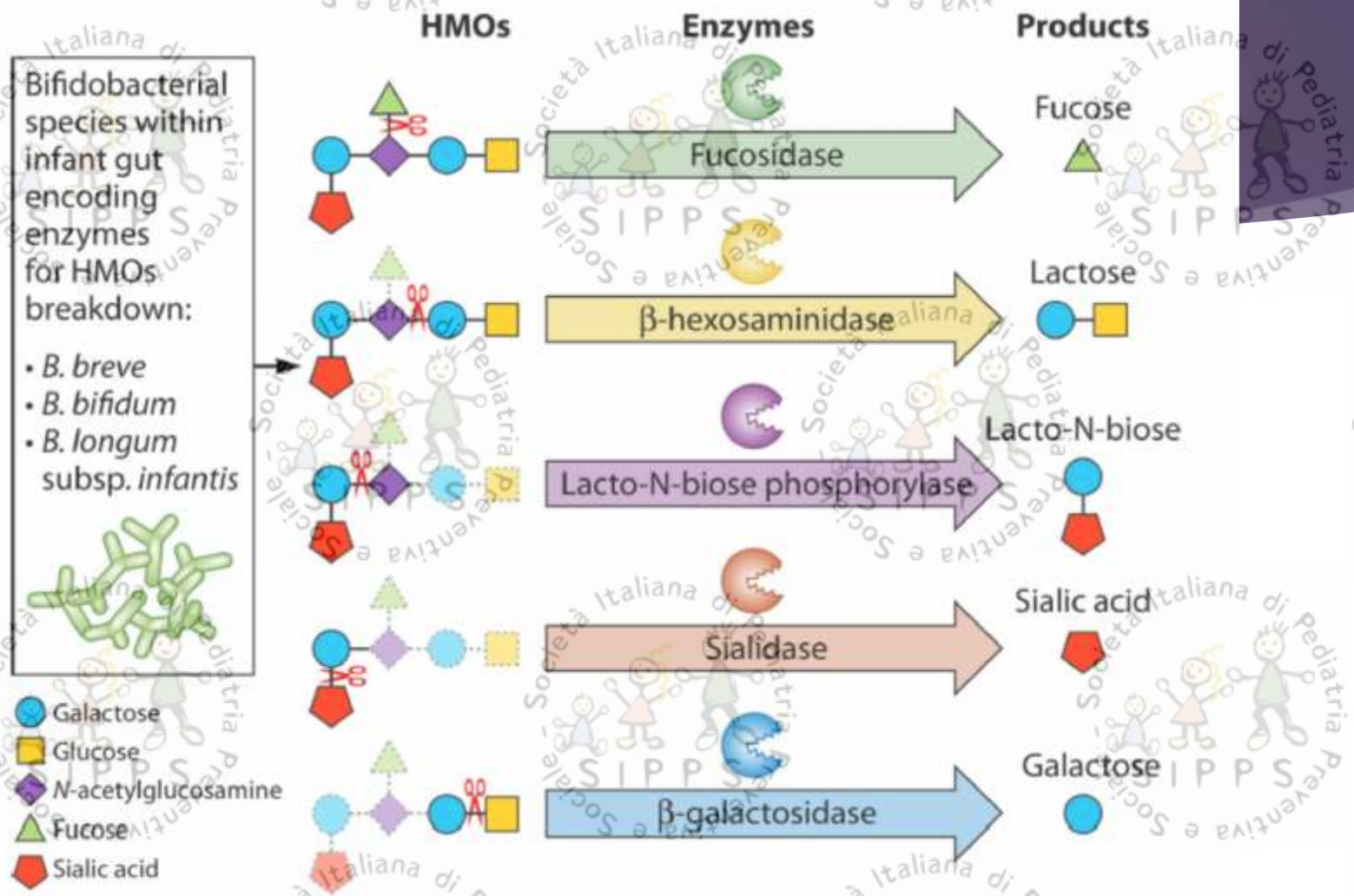
Più di 100 tipi

Non degradati nell'intestino, raggiungono intatti il tenue distale ed il colon

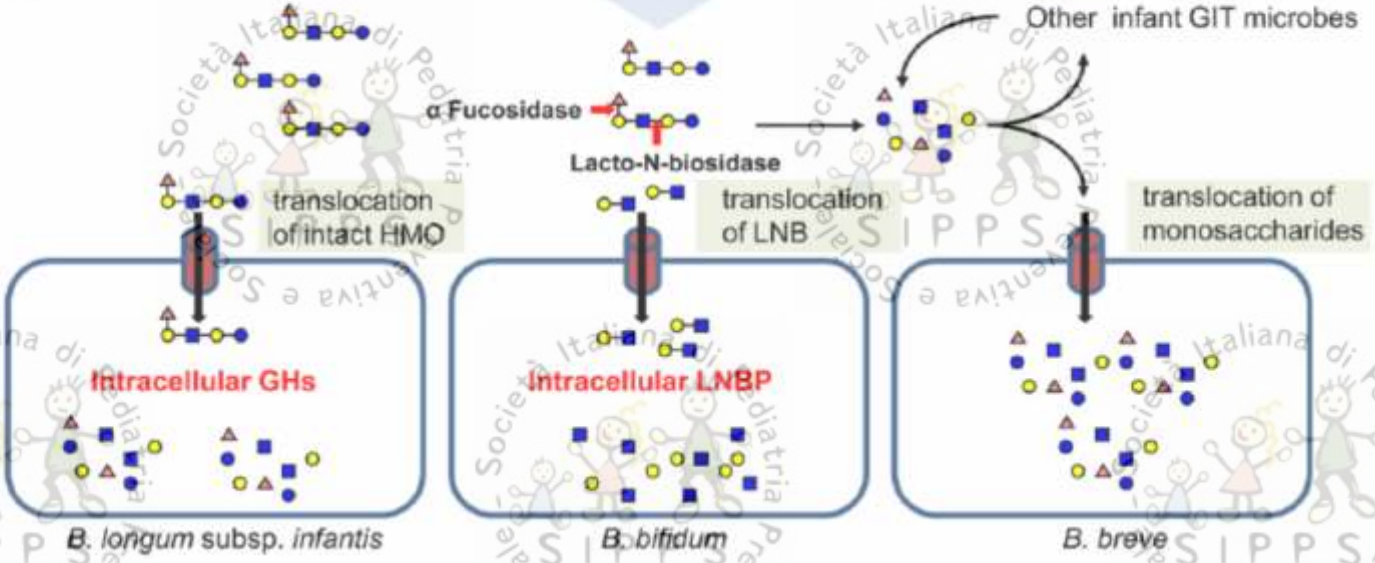
Funzione

- probiotica: per *Bifidobacterium, Bacteroides* (performance minore, quindi in assenza di *Bifidobacterium*)
- anti-adesiva: dimostrata per *C. jejuni, E. coli, E. hystolytica*
- antimicrobica: dimostrata per *S. agalactiae* e *C. albicans*




HMOs
Enzymes
Products
Bifidobacterial species within infant gut encoding enzymes for HMOs breakdown:
• B. breve
• B. bifidum
• B. longum subsp. infantis
Fucosidase
Fucose
β-hexosaminidase
Lactose
Lacto-N-biose phosphorylase
Lacto-N-biose
Sialidase
Sialic acid
β-galactosidase
Galactose
Galactose
Glucose
N-acetylglucosamine
Fucose
Sialic acid

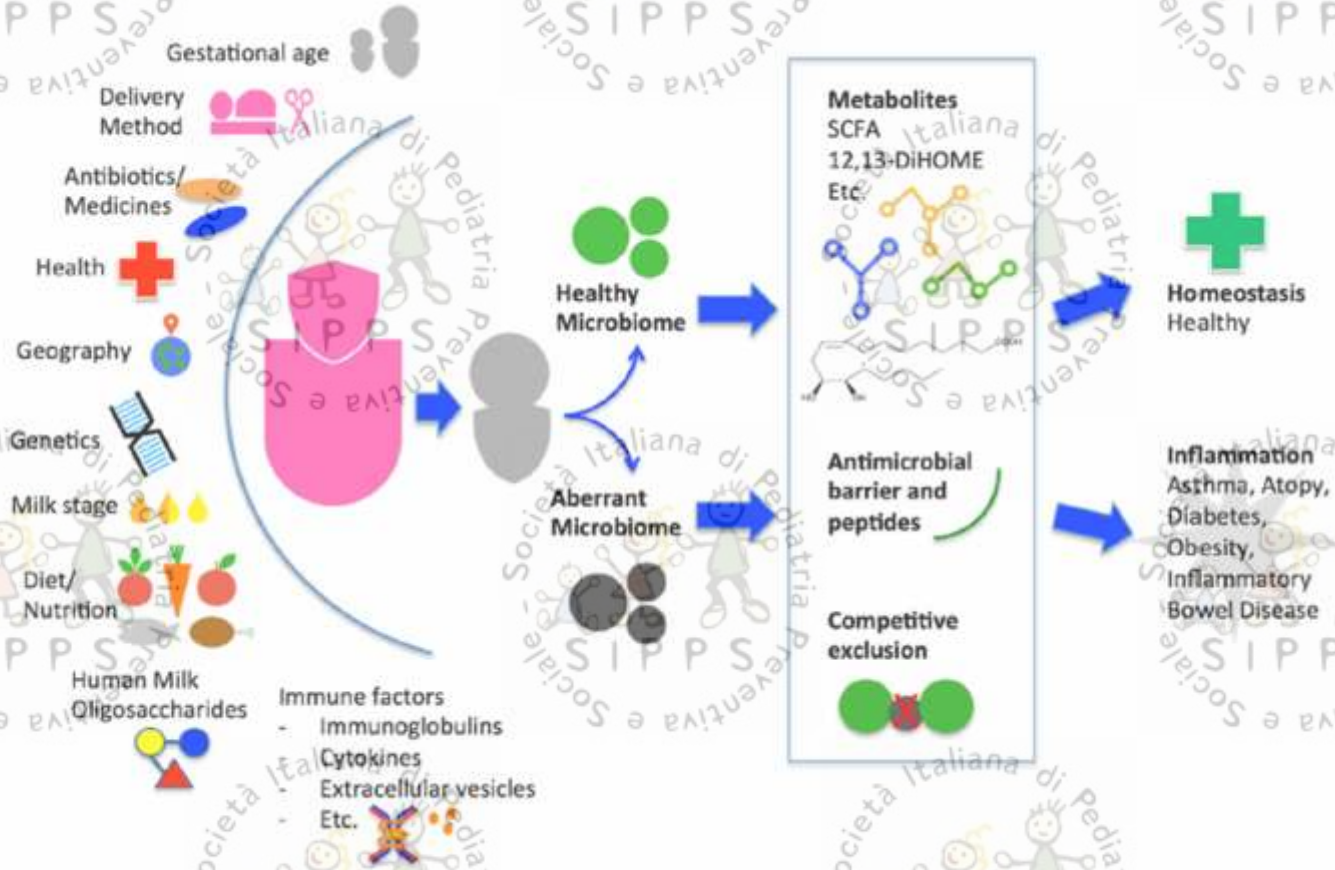
HMO


Other infant GIT microbes
α Fucosidase
Lacto-N-biosidase
translocation of intact HMO
translocation of LNB
translocation of monosaccharides
Intracellular GHs
Intracellular LNBP
B. longum subsp. infantis
B. bifidum
B. breve

Mother's Milk: A Purposeful Contribution to the Development of the Infant Microbiota and Immunity

Kirsty Le Doare[1,2,3,4], Beth Holder[1,2], Aisha Bassett[5] and Pia S. Pannaraj[5,6]*

frontiers in Immunology



Influenze sul microbiota del LM

- MODALITA' DI ALLATTAMENTO: LM estratto è più ricco di contaminanti potenziali patogeni e meno ricco di bifidobatteri (i bambini alimentati direttamente al seno sono quelli che hanno minore rischio di asma)
- SALUTE DELLA MAMMA: alterazioni del microbiota materno si riflettono nel neonato (disbiosi predisponenti all'allergia, alla sindrome metabolica, all'obesità…)
- TIPO DI PARTO: il latte di mamme che partoriscono per TC è meno ricco di bifidobatteri

Langdon et al. Genome Medicine (2016) 8:39
DOI 10.1186/s13073-016-0294-z

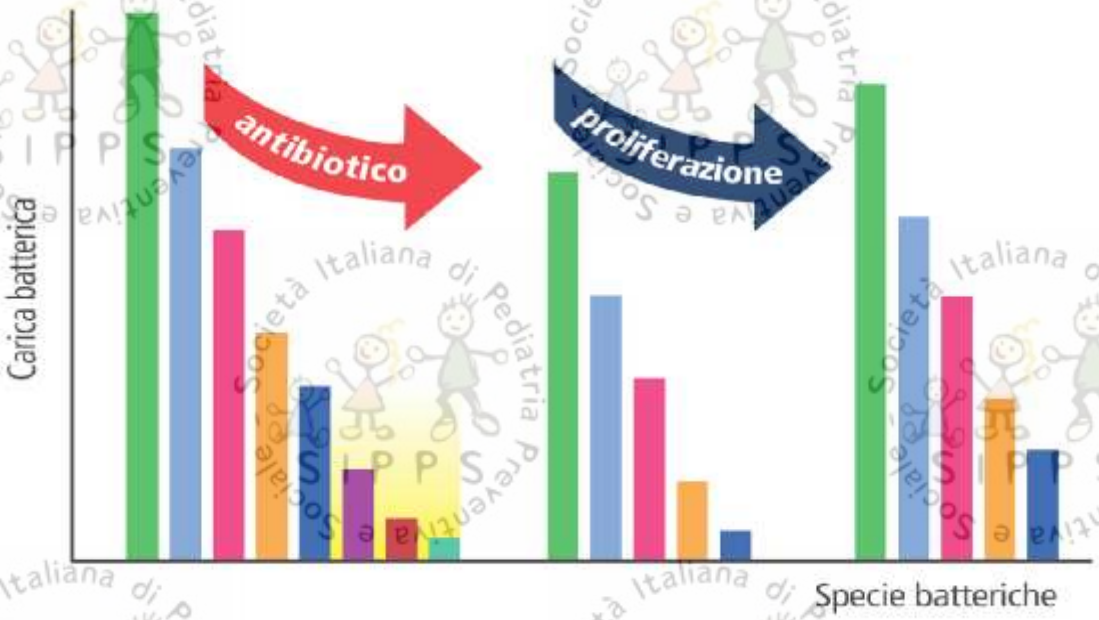
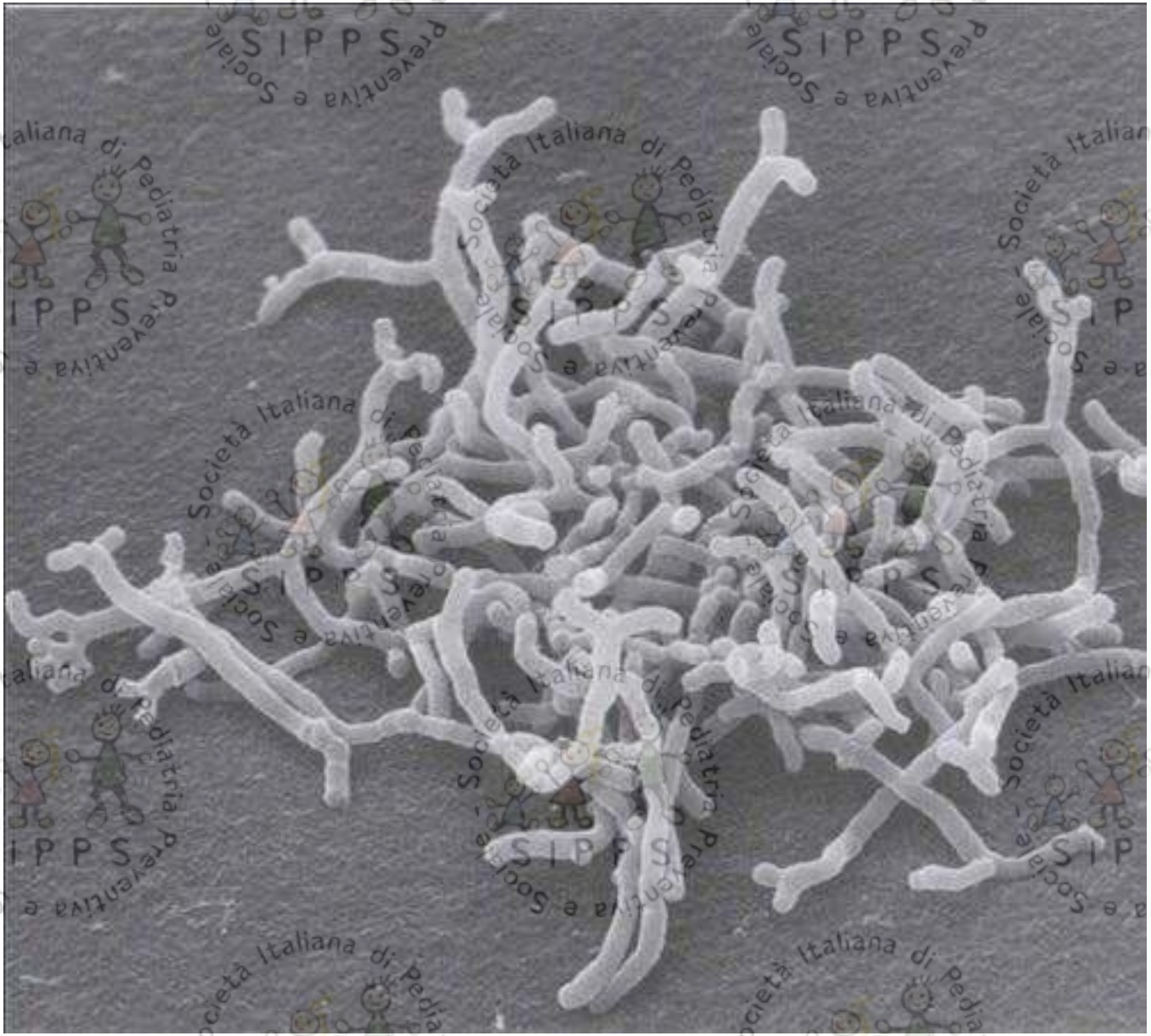
Genome Medicine

REVIEW Open Access

The effects of antibiotics on the microbiome throughout development and alternative approaches for therapeutic modulation

Amy Langdon[1,2†], Nathan Crook[1,3†] and Gautam Dantas[1,4,5*]

Antibiotic use further shifts the composition of the gut microbiota toward an increased abundance of *Proteobacteria* by depressing *Bifidobacterium* populations [41]. More generally, bacteriocidal drugs decrease the overall diversity of the infants' gut microbiota and select for drug-resistant microbes [42, 43]. Alternative strategies are needed to prevent and treat infections in premature infants.



La terapia antibiotica riduce la biodiversità intestinale, la specie meno rappresentate corrono il rischio di non poter più proliferare e con loro si perde il loro materiale genetico