Human Milk Oligosaccharides

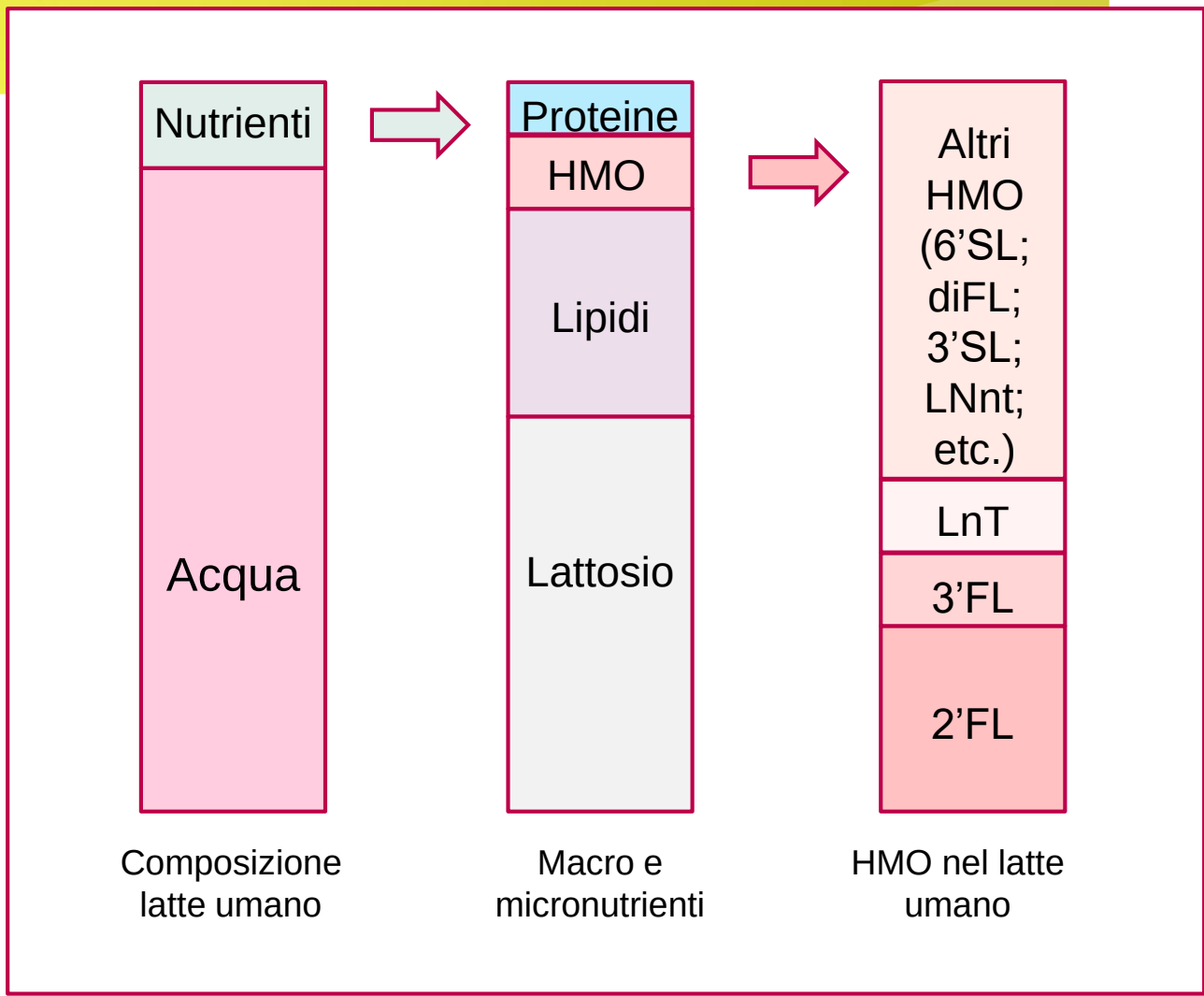
4-16 g/l LM, 20 g/l nel colostro

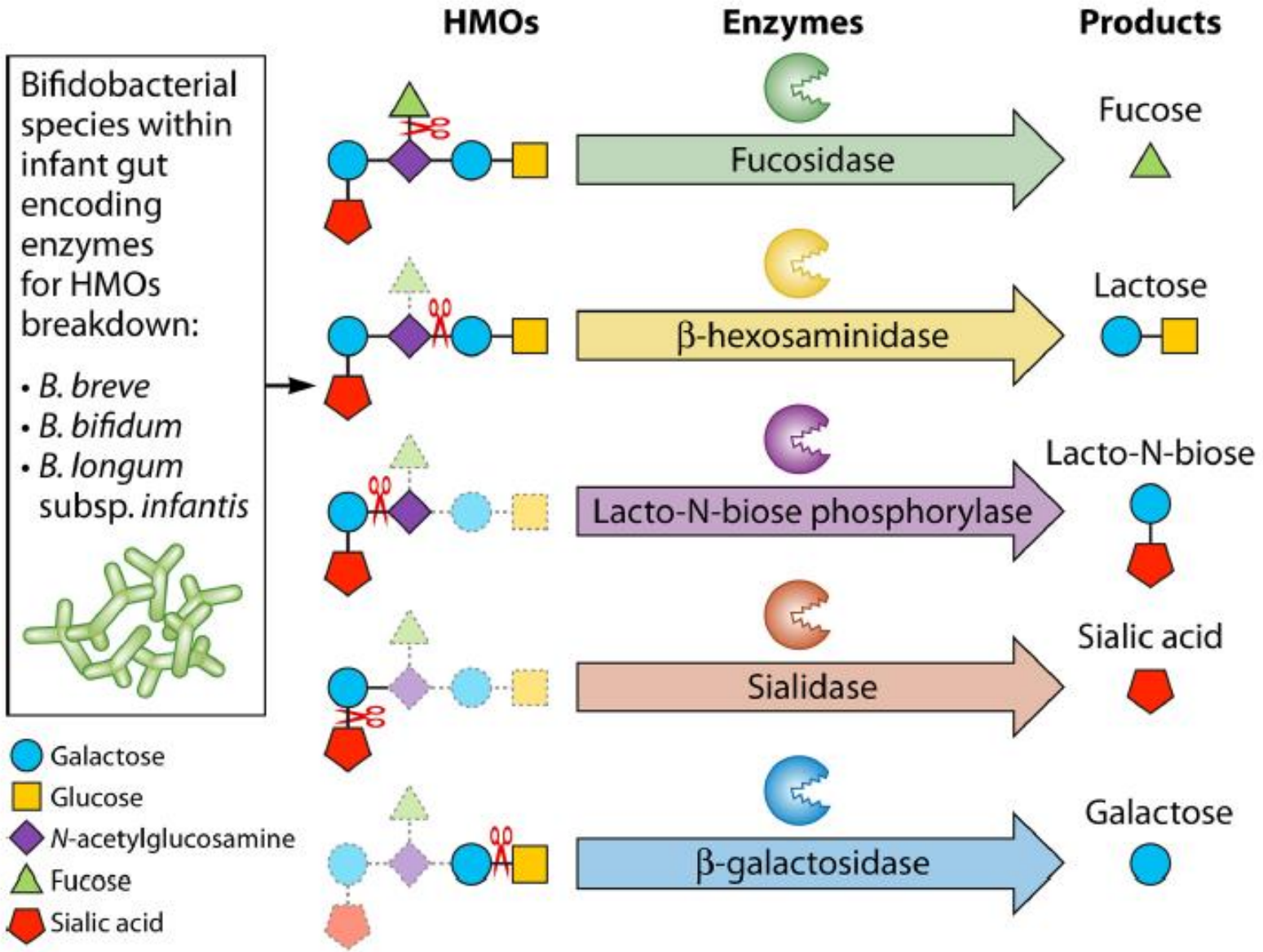
Più di 100 tipi

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

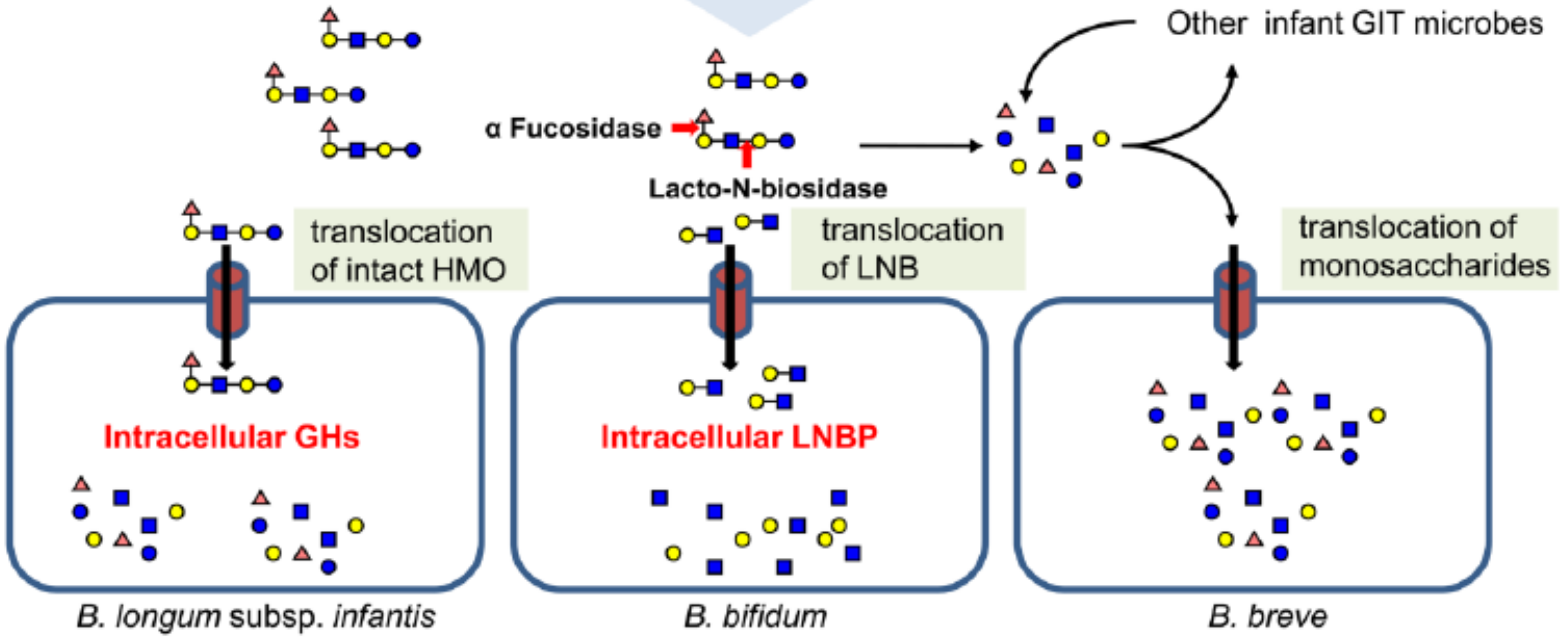
Funzione

- 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

Terapie

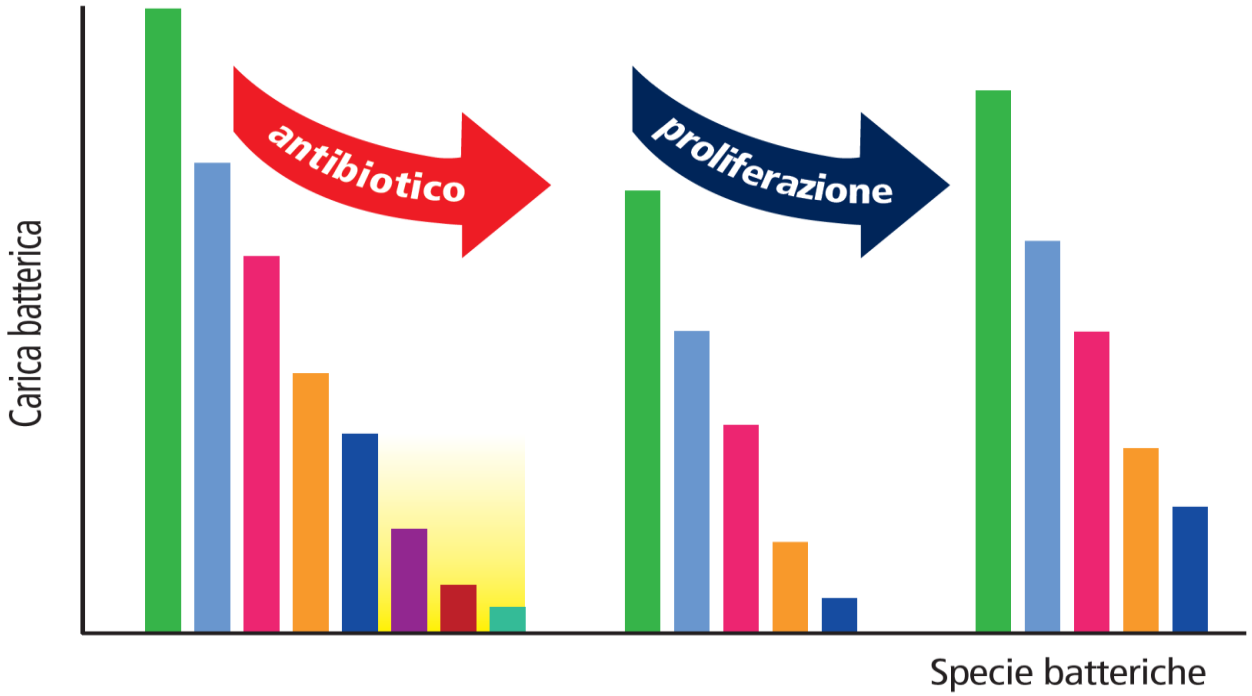
Langdon *et al. Genome Medicine* (2016) 8:39
DOI 10.1186/s13073-016-0294-z

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[1,3,4,5*]



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

Nutrients. 2018 Nov 10;10(11). pii: E1723. doi: 10.3390/nu10111723.

Therapeutic Microbiology: The Role of *Bifidobacterium breve* as Food Supplement for the Prevention/Treatment of Paediatric Diseases.

Bozzi Cionci N[1], Baffoni L[2], Gaggìa F[3], Di Gioia D[4].

Disbiosi

Dermatite atopica

Il microbiota dei pz atopici mostra stato disbiotico caratterizzato da aumento di *Faecalibacterium, Oscillospira, Bacteroides, Parabacteroides* e *Sutterella* e riduzione dei batteri produttiori di SCFA (bifidobatteri, *Blautia, Coprococcus, Eubacterium, Propionilbacterium*)

www.nature.com/scientificreports
21/3/2019

Gut microbiota profile in children affected by atopic dermatitis and evaluation of intestinal persistence of a probiotic mixture

Sofia Reddel[1], Federica Del Chierico[1], Andrea Quagliariello[1], Simona Giancristoforo[2], Pamela Vernocchi[1], Alessandra Russo[1], Alessandro Fiocchi[3], Paolo Rossi[4], Lorenza Putignani[5] & May El Hachem[2]

Atopic dermatitis (AD) has been hypothesised to be associated with gut microbiota (GM) composition. We performed a comparative study of the GM profile of 19 AD children and 18 healthy individuals aimed at identifying bacterial biomarkers associated with the disease. The effect of probiotic intake (*Bifidobacterium breve* plus *Lactobacillus salivarius*) on the modulation of GM and the probiotic persistence in the GM were also evaluated. Faecal samples were analysed by real-time PCR and 16S rRNA targeted metagenomics. Although the probiotics, chosen for this study, did not shape the entire GM profile, we observed the ability of these species to pass through the gastrointestinal tract and to persist (only *B. breve*) in the GM. Moreover, the GM of patients compared to CTRLs showed a dysbiotic status characterised by an increase of *Faecalibacterium*, *Oscillospira*, *Bacteroides*, *Parabacteroides* and *Sutterella* and a reduction of short-chain fatty acid (SCFA)-producing bacteria (i.e., *Bifidobacterium*, *Blautia*, *Coprococcus*, *Eubacterium* and *Propionibacterium*). Taken togheter these results show an alteration in AD microbiota composition with the depletion or absence of some species, opening the way to future probiotic intervention studies.

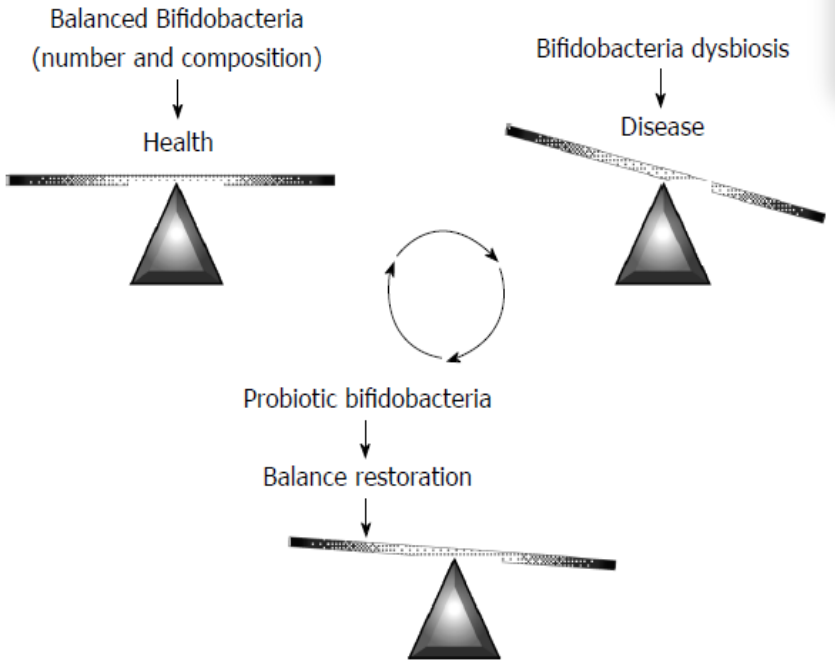
TOPIC HIGHLIGHT

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

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.

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

	Percentage of isolates (frequency of isolation)		
***Bifidobacterium* species**	**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

Dysbiosis Anticipating Necrotizing Enterocolitis in Very Premature Infants

Kathleen Sim,[1,a] Alexander G. Shaw,[1,a] Paul Randell,[1] Michael J. Cox,[2] Zoë E. McClure,[1] Ming-Shi Li,[1] Munther Haddad,[3] Paul R. Langford,[1] William O. C. M. Cookson,[2] Miriam F. Moffatt,[2] and J. Simon Kroll[1]

Departments of [1]Medicine, Section of Paediatrics, [2]Molecular Genetics and Genomics, National Heart and Lung Institute, and [3]Paediatric Surgery, Imperial College London, United Kingdom

Background. Necrotizing enterocolitis (NEC) is a devastating inflammatory bowel disease of premature infants speculatively associated with infection. Suspected NEC can be indistinguishable from sepsis, and in established cases an infant may die within hours of diagnosis. Present treatment is supportive. A means of presymptomatic diagnosis is urgently needed. We aimed to identify microbial signatures in the gastrointestinal microbiota preceding NEC diagnosis in premature infants.

Methods. Fecal samples and clinical data were collected from a 2-year cohort of 369 premature neonates. Next-generation sequencing of 16S ribosomal RNA gene regions was used to characterize the microbiota of prediagnosis fecal samples from 12 neonates with NEC, 8 with suspected NEC, and 44 controls. Logistic regression was used to determine clinical characteristics and operational taxonomic units (OTUs) discriminating cases from controls. Samples were cultured and isolates identified using matrix-assisted laser desorption/ionization–time of flight. Clostridial isolates were typed and toxin genes detected.

Results. A clostridial OTU was overabundant in prediagnosis samples from infants with established NEC ($P = .006$). Culture confirmed the presence of *Clostridium perfringens* type A. Fluorescent amplified fragment-length polymorphism typing established that no isolates were identical. Prediagnosis samples from NEC infants not carrying profuse *C. perfringens* revealed an overabundance of a *Klebsiella* OTU ($P = .049$). Prolonged continuous positive airway pressure (CPAP) therapy with supplemental oxygen was also associated with increased NEC risk.

Conclusions. Two fecal microbiota signatures (*Clostridium* and *Klebsiella* OTUs) and need for prolonged CPAP oxygen signal increased risk of NEC in presymptomatic infants. These biomarkers will assist development of a screening tool to allow very early diagnosis of NEC.

International Immunopharmacology 65 (2018) 328–341

Contents lists available at ScienceDirect

International Immunopharmacology

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

Review

Antibiotics and autoimmune and allergy diseases: Causative factor or treatment?☆

Anna Strzępa[a], Francis M. Lobo[b], Monika Majewska-Szczepanik[a], Marian Szczepanik[a,*]

[a] Department of Medical Biology, Faculty of Health Sciences, Jagiellonian University Medical College, ul. Kopernika 7a, 31-034 Krakow, Poland
[b] Section of Allergy and Clinical Immunology, Department of Internal Medicine, Yale University School of Medicine, New Haven, CT, USA

La colonizzazione batterica è essenziale per spostare la risposta del neonato dal Tipo Th2, favorente l'allergia, verso il Tipo Th1, essenziale per l'eliminazione dei patogeni. Lo squilibrio tra le risposte di Tipo-1 e Tipo-2 può favorire l'autoimmunità.

Le malattie autoimmuni e allergiche sono comunemente associate a una composizione alterata dei batteri residenti, nota come disbiosi.

Forse la causa più comune di alterazione della colonizzazione batterica dei neonati è l'uso di antibiotici

Clinical Trial/Experimental Study

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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

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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.

Terapia batterica

BIOPROTICA

PROBIOTICI: *micro-organismi vivi che, somministrati in quantità adeguata, apportano un beneficio alla salute dell'ospite* (WHO, FAO)

Somministrazioni di ceppi altamente specifici per il paziente

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.

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[a,*]

[a] Department of Pediatric, The Fourth Hospital of Hebei Medical University, Shijiazhuang, 050000, China
[b] Department of Gastroenterology, Tiantai People's Hospital, Zhejiang Provincial, 317200, C

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.

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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] HuaWen 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.

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.

Take home messages:

Il microbiota si plasma nelle prime età della vita

Il microbiota del lattante è costituito per il 50% da Bifidobatteri

La disbiosi nel bambino si accompagna ad aumentato rischio di patologia (obesità, allergia, asma, sindrome metabolica…)

I driver disbiotici possono essere molteplici (microbiota materno, terapie antibiotiche, tipo di parto, allattamento al biberon…)

E' possibile, identificando la presenza dei driver, contrastare la disbiosi (terapia batterica)