INTESTINAL MICROBIOLOGY IN EARLY LIFE

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ISAPP, 5th June 2018, Singapore

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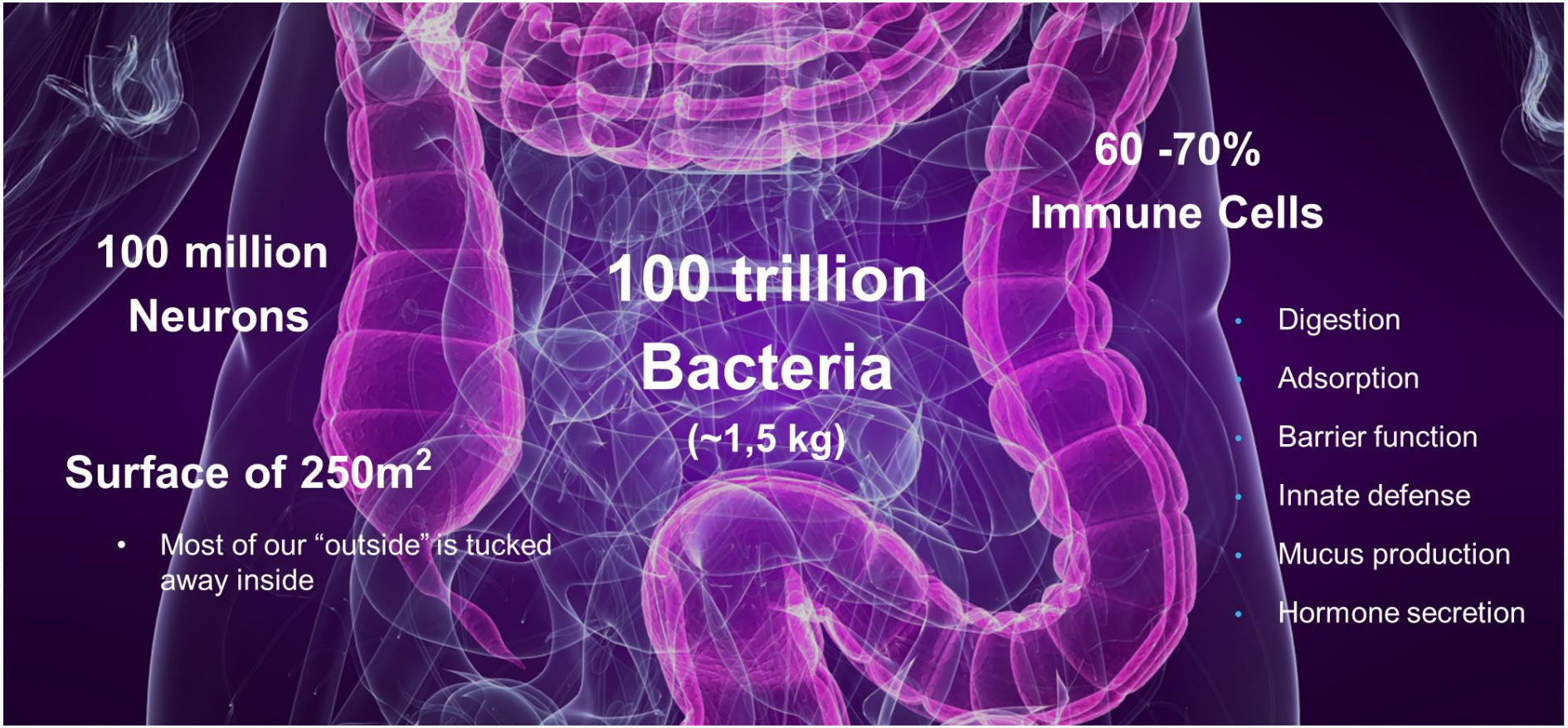
THE GUT MICROBIOTA



PATTERNS IN EARLY LIFE MICROBIOTA DEVELOPMENT

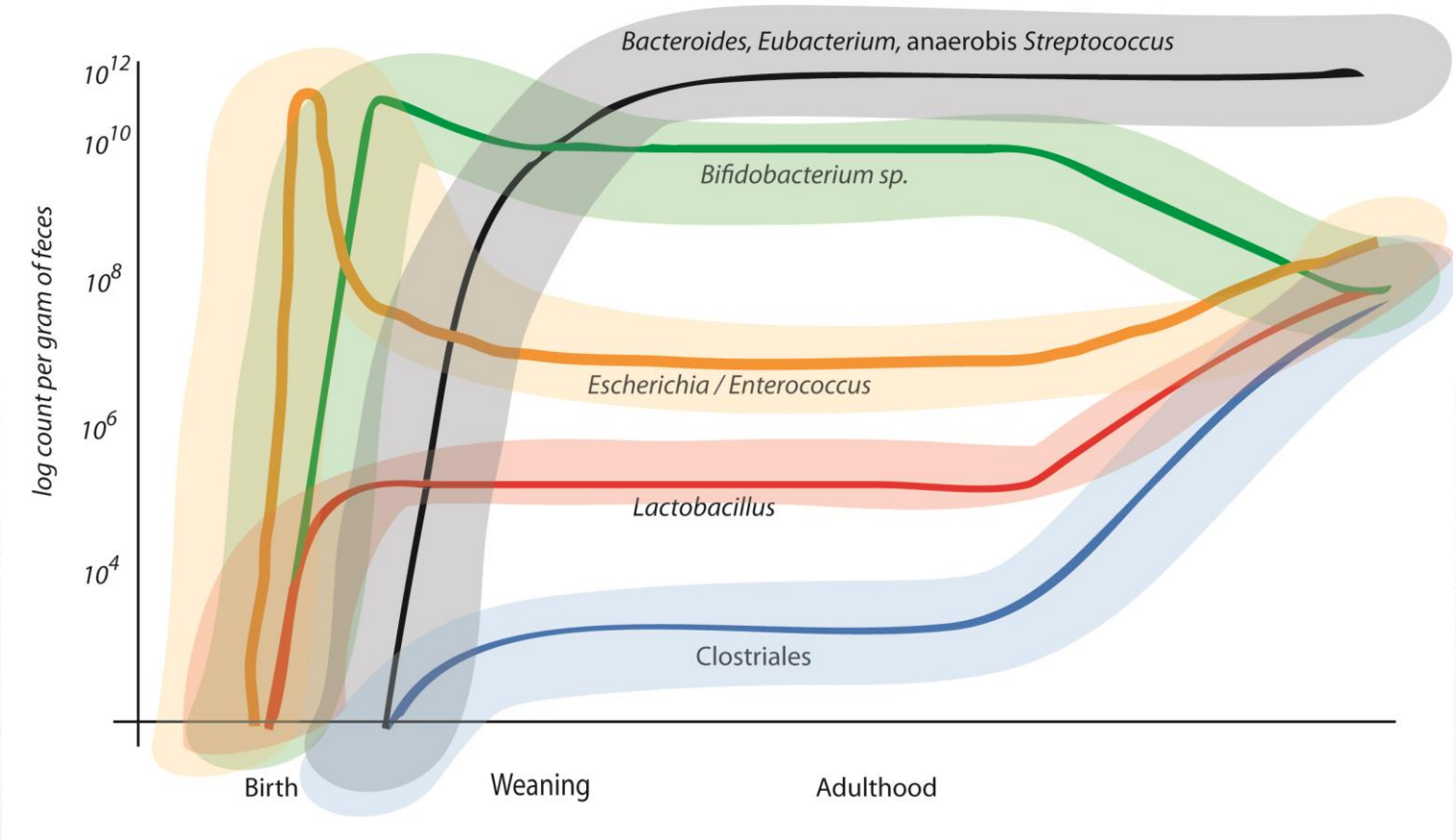
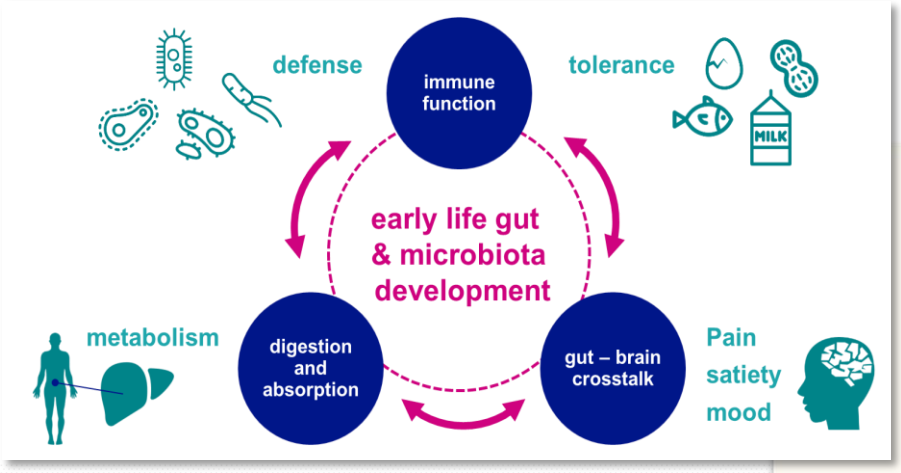
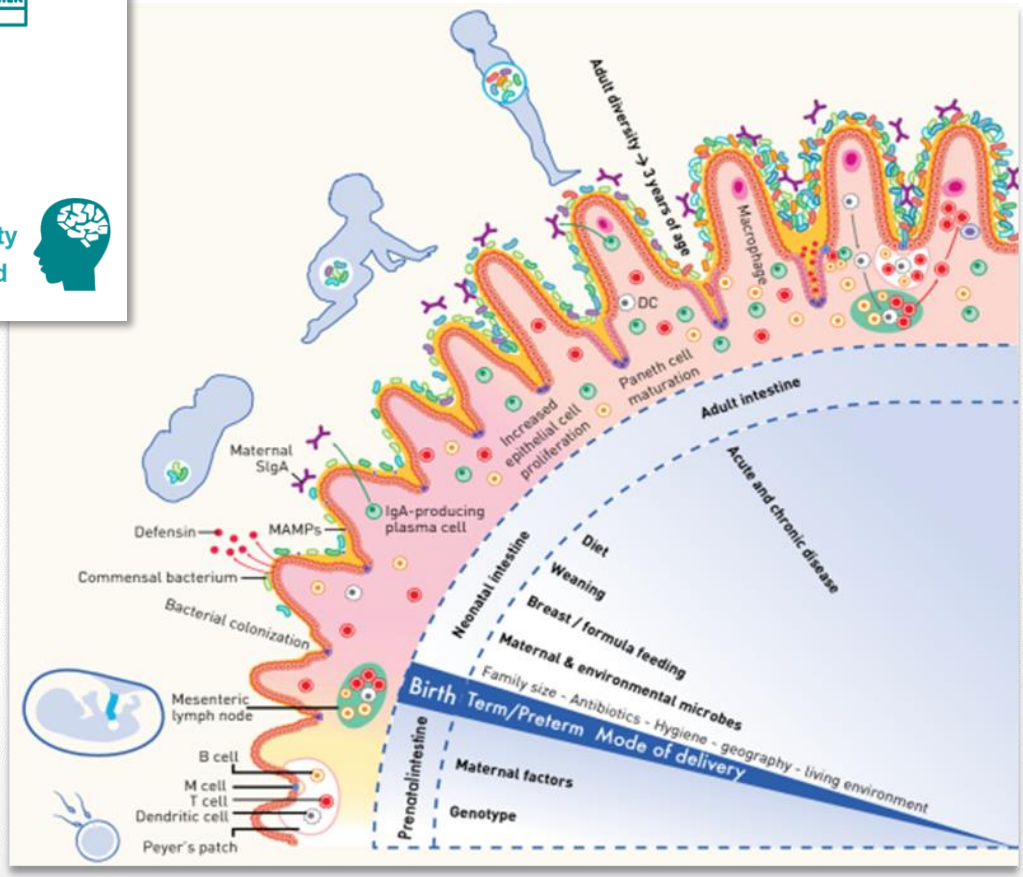


Figure based on Mitsuoka & Hayakawa (1973)
Die Zusammensetzung der Faekalflora der verschiedenen Altersgruppen.
Zbl Bakt Hyg I Orig 233: 333–342.

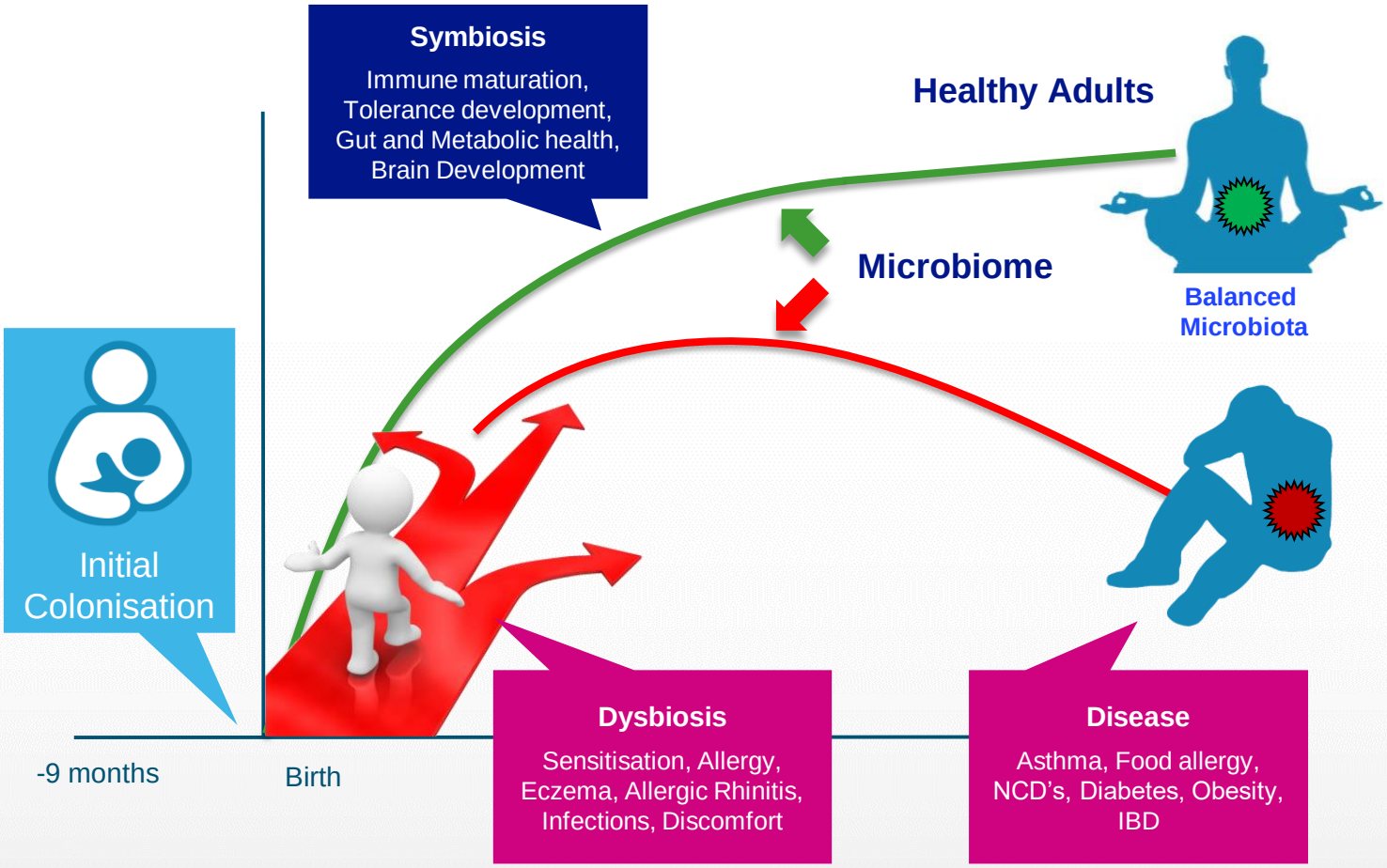
ESTABLISHING THE SYMBIOSIS





Wopereis H, et al. Pediatr Allergy Immunol 2014;25:428-438

MICROBIOTA IN EARLY LIFE
POWERFUL MEANS FOR IMPROVING OUR HEALTH



EARLY MICROBIOME ALTERATIONS & DISEASE RISK

Infant gut microbiota composition could be early allergy indicator: Danone

By Cheryl Tay

Elevated pathogen / bacteria ratio in infants could be an early microbiota biomarker for allergies, according to researchers in Singapore, the UK and the Netherlands.

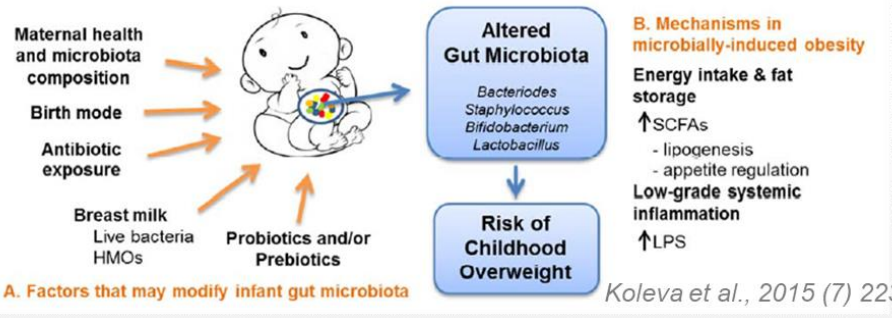
Korpela *et al. Microbiome* (2017) 5:26
DOI 10.1186/s40168-017-0245-y

Microbiome

RESEARCH Open Access

Childhood BMI in relation to microbiota in infancy and lifetime antibiotic use

K. Korpela[1*], M. A. C. Zijlmans[2], M. Kuitunen[3], K. Kukkonen[4], E. Savilahti[3], A. Salonen[1], C. de Weerth[2] and W. M. de Vos[1,5]



Koleva et al., 2015 (7) 2237-2260

MICROBIOME DIFFERENCES PRECEDE THE ONSET

Beneficial Microbes, 2017 online ARTICLE IN PRESS Wageningen Academic Publishers

Ratio of *Klebsiella*/*Bifidobacterium* in early life correlates with later development of paediatric allergy

J.S.Y. Low[1], S.-E. Soh[2,3#], Y.K. Lee[4], K.Y.C. Kwek[5#], J.D. Holbrook[2,6], E.M. Van der Beek[7,8], L.P. Shek[2,3#], A.E.N. Goh[5#], O.H. Teoh[5#], K.M. Godfrey[9#], Y.-S. Chong[2,10#], J. Knol[7,11] and C. Lay[1,3*]

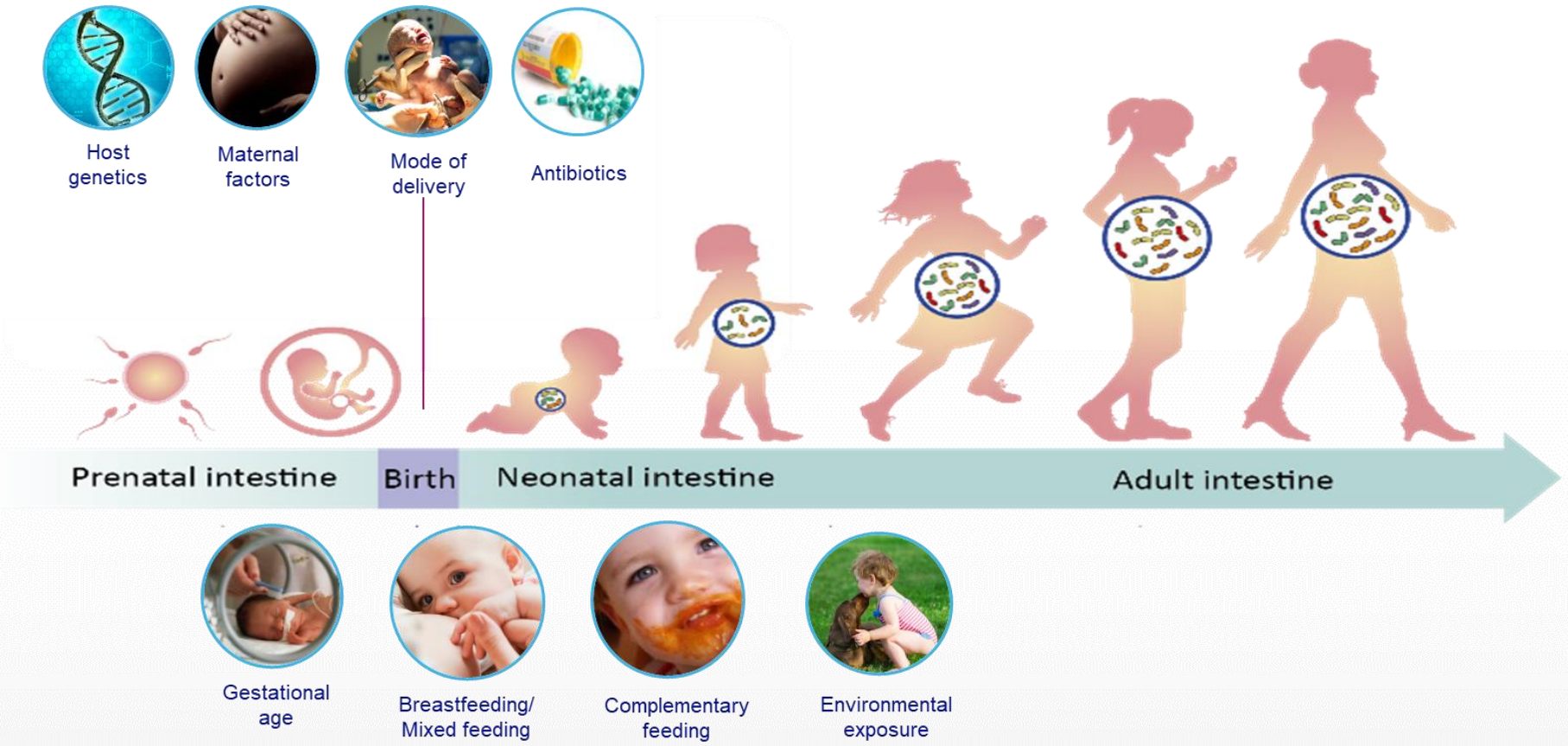
Table S2. Ratio of relative abundances of *Klebsiella* to *Bifidobacterium* (K/B ratio) of allergic and healthy infants at age 3 weeks, 3 months and 6 months respectively.

Timepoint	*Klebsiella/Bifidobacterium* ratio		
	Healthy controls	Allergic cases	*P*-value
Week 3	0.23 (0.01-213.07)	1.70 (0.01-1408.00)	0.12
Month 3	0.03 (0.00-0.68)	0.52 (0.00 – 2281.33)	*0.01
Month 6	0.01 (0.00-62.00)	0.05 (0.00-910.50)	0.26

The values were expressed in median (range). Differences in medians of *Klebsiella/Bifidobacterium* ratio between the two groups were performed using non-parametric Mann-Whitney U test. Single asterisk (*) indicate $P \leq 0.05$.

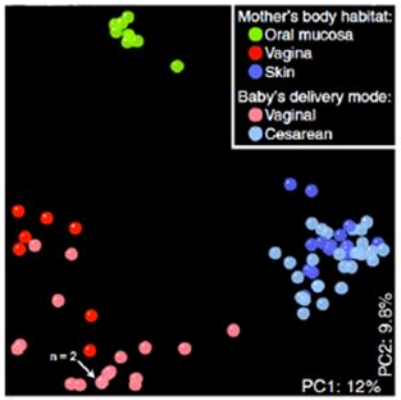
Differences precede the onset

FACTORS IMPACTING EARLY COLONIZATION

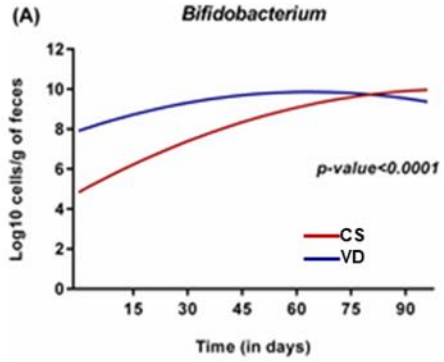


ACQUISITION OF THE MICROBIOME IN EARLY LIFE BY VERTICAL TRANSMISSION

Infants born by C-section have a delayed colonization



Dominguez-Bello et al., 2010, PNAS 107:11971-11975



Martin et al., 2016, PlosONE 11 (6)

Gonzalez et al., (2011) EMBO reports

ASSOCIATIONS BETWEEN FACTORS IMPACTING EARLY COLONIZATION AND HEALTH OUTCOMES

http://www.dailymail.co.uk/home/index.html

Babies delivered by Caesarean section at higher risk of asthma and allergies

C. Roduit et al., 2009, Thorax, 64(2):107-13

Asthma at 8 years of age in children born by caesarean section

http://www.healio.com/dermatology/dermatitis/news/

Cesarean delivery showed link with gut microbiota, atopic dermatitis

News · Science

Children born by c-section far more likely to be obese by aged five, major study suggests

Citation: Keag OE, Norman JE, Stock SJ (2018) Long-term risks and benefits associated with cesarean delivery for mother, baby, and subsequent pregnancies: Systematic review and meta-analysis. PLoS Med 15(1): e1002494. https://doi.org/10.1371/journal.pmed.1002494

JAMA Pediatrics | Original Investigation

Association Between Use of Acid-Suppressive Medications and Antibiotics During Infancy and Allergic Diseases in Early Childhood

JAMA Pediatr. doi:10.1001/jamapediatrics.2018.0315 Published online April 2, 2018.

Edward Mitre, MD; Apryl Susi, MS; Laura E. Kropp, MPH; David J. Schwartz, MD; Gregory H. Gorman, MD; Cade M. Nylund, MD

Clin Exp Allergy. 2017 February ; 47(2): 236–244. doi:10.1111/cea.12807.

Early Life Antibiotic Use and Subsequent Diagnosis of Food Allergy and Allergic Diseases

Annemarie G. Hirsch, PhD, MPH[1], Jonathan Pollak, MPP[2,3], Thomas A. Glass, PhD[4], Melissa N. Poulsen, PhD[1,2], Lisa Bailey-Davis, DEd, RD[1], Jacob Mowery, BS[1], and Brian S. Schwartz, MD, MS[1,2,4]

Ann Allergy Asthma Immunol 119 (2017) 54–58

Influence of antibiotic use in early childhood on asthma and allergic diseases at age 5

Kiwako Yamamoto-Hanada, MD, PhD*; Limin Yang, MD, PhD*; Masami Narita, MD, PhD*; Hirohisa Saito, MD, PhD†; Yukihiro Ohya, MD, PhD*

Obesity (Silver Spring). 2017 February ; 25(2): 438–444. doi:10.1002/oby.21719.

Associations of Prenatal and Childhood Antibiotic Use with Child Body Mass Index at Age Three Years

Melissa N. Poulsen, PhD, MPH[1,2], Jonathan Pollak, MPP[1], Lisa Bailey-Davis, DEd, RD[2], Annemarie G. Hirsch, PhD, MPH[2], Thomas A. Glass, PhD[3], and Brian S. Schwartz, MD[1,2,3,4]

COMPROMISING THE MATERNAL MICROBIOTA DURING PREGNANCY HAS LONG TERM HEALTH CONSEQUENCES ON THE OFFSPRING

Clin Exp Allergy. 2014 Jun 18. doi: 10.1111/cea.12356. [Epub ahead of print]

Prenatal and Postnatal Exposure to Antibiotics and Risk of Asthma in Childhood.

Metsälä J[1], Lundqvist A, Virta LJ, Kaila M, Gissler M, Virtanen SM.

Maternal antibiotic use and childhood asthma: the missing link?

Lancet Respir Med 2014
Published Online
July 25, 2014
http://dx.doi.org/10.1016/
S2213-2600(14)70122-5

Use of Antibiotics during Pregnancy Increases the Risk of Asthma in Early Childhood

Lone Graff Stensballe, MD, PhD[1,2], Jacob Simonsen, MSc, PhD[2], Signe M. Jensen, MSc[1], Klaus Bønnelykke, MD, PhD[1], and Hans Bisgaard, MD, DMSc[1]

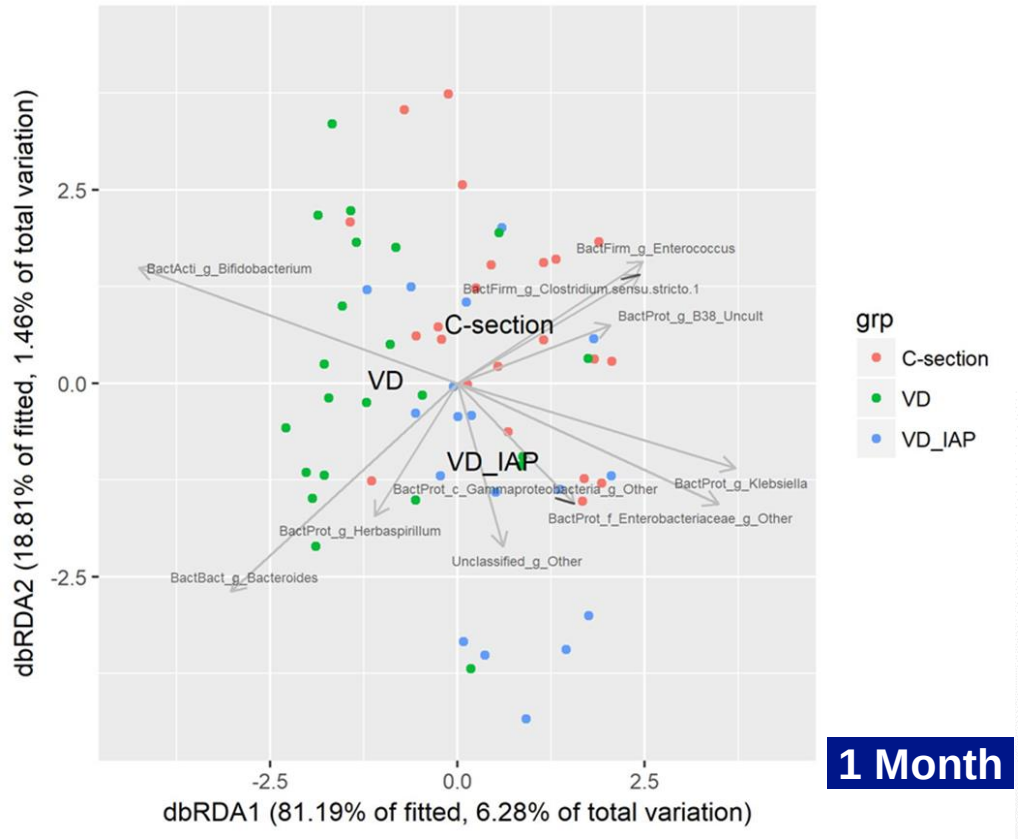
Lancet Respir Med. 2014 Aug;2(8):631-7. doi: 10.1016/S2213-2600(14)70152-3. Epub 2014 Jul 24.

Maternal propensity for infections and risk of childhood asthma: a registry-based cohort study.

Stokholm J[1], Sevelsted A[2], Bønnelykke K[2], Bisgaard H[3].

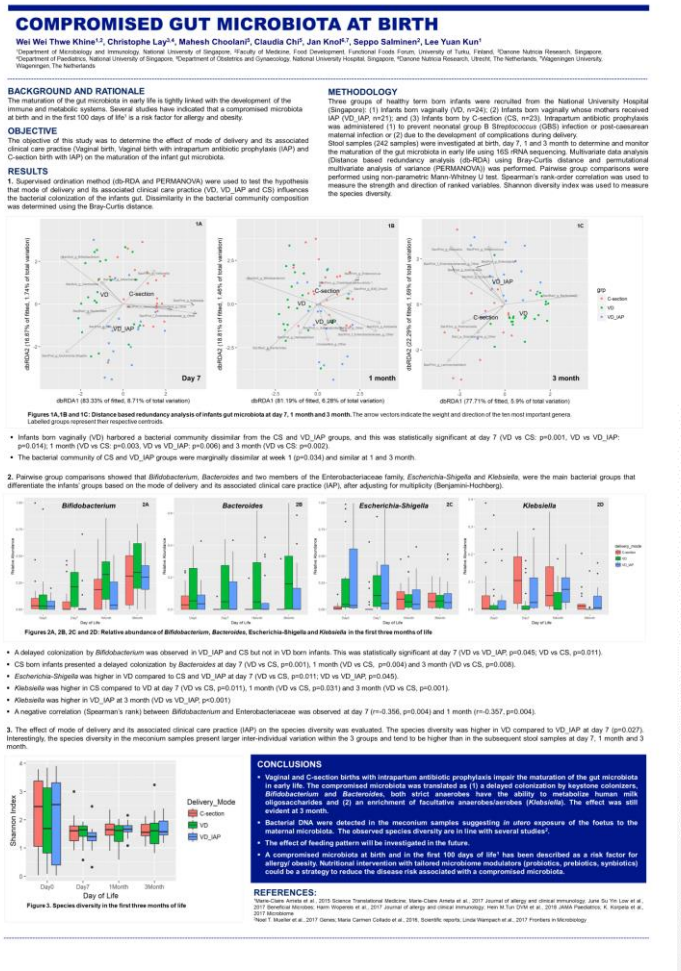
INTRAPARTUM ANTIBIOTIC PROPHYLAXIS AND C-SECTION DISRUPT THE EARLY COLONIZATION PROCESS

Poster 7833



1 Month

time point	VD vs VD_IAP	VD vs CS	CS vs VD_IAP
Day 0	0.561	0.023	0.044
Day 7	0.014	0.001	0.034
1 Month	0.006	0.003	0.550
3 Month	0.047	0.002	0.193



COMPROMISED GUT MICROBIOTA AT BIRTH

Wei Wei Thwe Khine[1,2], Christophe Lay[3,4], Mahesh Choolani[5], Claudia Chi[2], Jan Knol[6,7], Seppo Salminen[2], Lee Yuan Kun[1]

[1]Department of Microbiology and Immunology, National University of Singapore, [2]Faculty of Medicine, Food Development, Functional Foods Forum, University of Turku, Finland, [3]Danone Nutricia Research, Singapore, [4]Department of Paediatrics, National University of Singapore, [5]Department of Obstetrics and Gynaecology, National University Hospital, Singapore, [6]Danone Nutricia Research, Utrecht, The Netherlands, [7]Wageningen University, Wageningen, The Netherlands

BACKGROUND AND RATIONALE

The maturation of the gut microbiota in early life is tightly linked with the development of the immune and metabolic systems. Several studies have indicated that a compromised microbiota at birth and in the first 100 days of life[1] is a risk factor for allergy and obesity.

OBJECTIVE

The objective of this study was to determine the effect of mode of delivery and its associated clinical care practice (Vaginal birth, Vaginal birth with intrapartum antibiotic prophylaxis (IAP) and C-section birth with IAP) on the maturation of the infant gut microbiota.

METHODOLOGY

Three groups of healthy term born infants were recruited from the National University Hospital (Singapore): (1) infants born vaginally (VD, n=24); (2) Infants born vaginally whose mothers received IAP (VD_IAP, n=21); and (3) Infants born by C-section (CS, n=23). Intrapartum antibiotic prophylaxis was administered (1) to prevent neonatal group B *Streptococcus* (GBS) infection or post-caesarean maternal infection or (2) due to the development of complications during delivery.
Stool samples (242 samples) were investigated at birth, day 7, 1 and 3 month to determine and monitor the maturation of the gut microbiota in early life using 16S rRNA sequencing. Multivariate data analysis (Distance based redundancy analysis (db-RDA) using Bray-Curtis distance and permutational multivariate analysis of variance (PERMANOVA)) was performed. Pairwise group comparisons were performed using non-parametric Mann-Whitney U test. Spearman's rank-order correlation was used to measure the strength and direction of ranked variables. Shannon diversity index was used to measure the species diversity.

RESULTS

1. Supervised ordination method (db-RDA and PERMANOVA) were used to test the hypothesis that mode of delivery and its associated clinical care practice (VD, VD_IAP and CS) influences the bacterial colonization of the infants gut. Dissimilarity in the bacterial community composition was determined using the Bray-Curtis distance.

Figures 1A,1B and 1C: Distance based redundancy analysis of infants gut microbiota at day 7, 1 month and 3 month. The arrow vectors indicate the weight and direction of the ten most important genera. Labelled groups represent their respective centroids.

- Infants born vaginally (VD) harbored a bacterial community dissimilar from the CS and VD_IAP groups, and this was statistically significant at day 7 (VD vs CS: p=0.001, VD vs VD_IAP: p=0.014); 1 month (VD vs CS: p=0.003, VD vs VD_IAP: p=0.006) and 3 month (VD vs CS: p=0.002).
- The bacterial community of CS and VD_IAP groups were marginally dissimilar at week 1 (p=0.034) and similar at 1 and 3 month.

2. Pairwise group comparisons showed that *Bifidobacterium*, *Bacteroides* and two members of the Enterobacteriaceae family, *Escherichia-Shigella* and *Klebsiella*, were the main bacterial groups that differentiate the infants' groups based on the mode of delivery and its associated clinical care practice (IAP), after adjusting for multiplicity (Benjamini-Hochberg).

Figures 2A, 2B, 2C and 2D: Relative abundance of *Bifidobacterium*, *Bacteroides*, *Escherichia-Shigella* and *Klebsiella* in the first three months of life

- A delayed colonization by *Bifidobacterium* was observed in VD_IAP and CS but not in VD born infants. This was statistically significant at day 7 (VD vs VD_IAP: p=0.045; VD vs CS, p=0.011).
- CS born infants presented a delayed colonization by *Bacteroides* at day 7 (VD vs CS, p=0.001), 1 month (VD vs CS, p=0.034) and 3 month (VD vs CS, p=0.008).
- *Escherichia-Shigella* was higher in VD compared to CS and VD_IAP at day 7 (VD vs CS, p=0.011; VD vs VD_IAP, p=0.045).
- *Klebsiella* was higher in CS compared to VD at day 7 (VD vs CS, p=0.011), 1 month (VD vs CS, p=0.031) and 3 month (VD vs CS, p=0.001).
- *Klebsiella* was higher in VD_IAP at 3 month (VD vs VD_IAP, p<0.001)
- A negative correlation (Spearman's rank) between *Bifidobacterium* and Enterobacteriaceae was observed at day 7 (r=-0.356, p=0.004) and 1 month (r=-0.357, p=0.004).

3. The effect of mode of delivery and its associated clinical care practice (IAP) on the species diversity was evaluated. The species diversity was higher in VD compared to VD_IAP at day 7 (p=0.027). Interestingly, the species diversity in the meconium samples present larger inter-individual variation within the 3 groups and tend to be higher than in the subsequent stool samples at day 7, 1 month and 3 month.

Figure 3. Species diversity in the first three months of life

CONCLUSIONS

- Vaginal and C-section births with intrapartum antibiotic prophylaxis impair the maturation of the gut microbiota in early life. The compromised microbiota was translated as (1) a delayed colonization by keystone colonizers, *Bifidobacterium* and *Bacteroides*, both strict anaerobes have the ability to metabolize human milk oligosaccharides and (2) an enrichment of facultative anaerobes/aerobes (*Klebsiella*). The effect was still evident at 3 month.
- Bacterial DNA were detected in the meconium samples suggesting *in utero* exposure of the foetus to the maternal microbiota. The observed species diversity are in line with several studies[2].
- The effect of feeding pattern will be investigated in the future.
- A compromised microbiota at birth and in the first 100 days of life[1] has been described as a risk factor for allergy/ obesity. Nutritional intervention with tailored microbiome modulators (probiotics, prebiotics, synbiotics) could be a strategy to reduce the disease risk associated with a compromised microbiota.

REFERENCES:

[1]Marie-Claire Arrieta et al., 2015 Science Translational Medicine; Marie-Claire Arrieta et al., 2017 Journal of allergy and clinical immunology; June Su Yin Low et al., 2017 Beneficial Microbes; Harm Wopereis et al., 2017 Journal of allergy and clinical immunology; Hein M.Tun DVM et al., 2018 JAMA Paediatrics; K. Korpela et al., 2017 Microbiome
[2]Noel T. Mueller et al., 2017 Genes; Maria Carmen Collado et al., 2016, Scientific reports; Linda Wampach et al., 2017 Frontiers in Microbiology

Unpublished

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FROM A PROTECTED ENVIRONMENT…

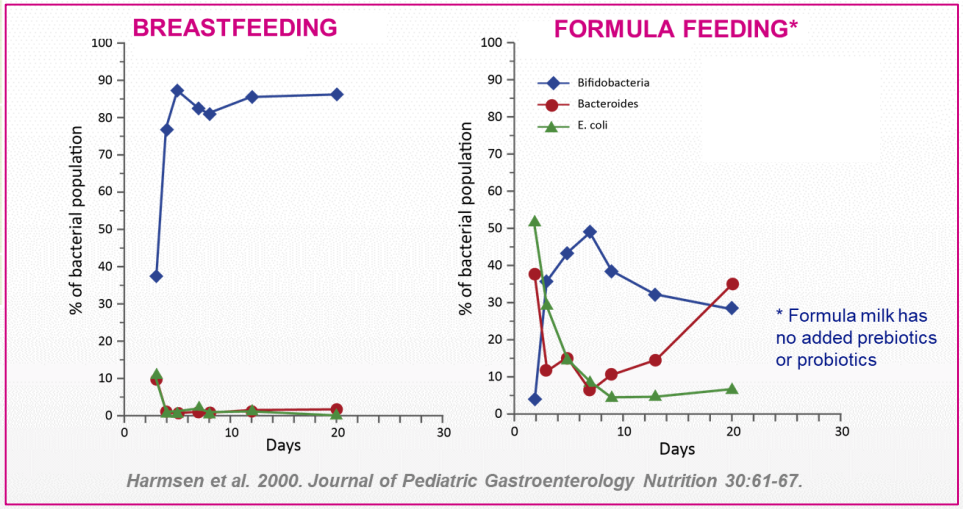
…TO A CHALLENGING EXTRA-UTERINE WORLD…

…Breast feeding is important for optimal development of infants

HUMAN MILK CONTAINS MULTIPLE BIOACTIVE COMPOUNDS THAT IMPACT IMMUNE & MICROBIOTA DEVELOPMENT

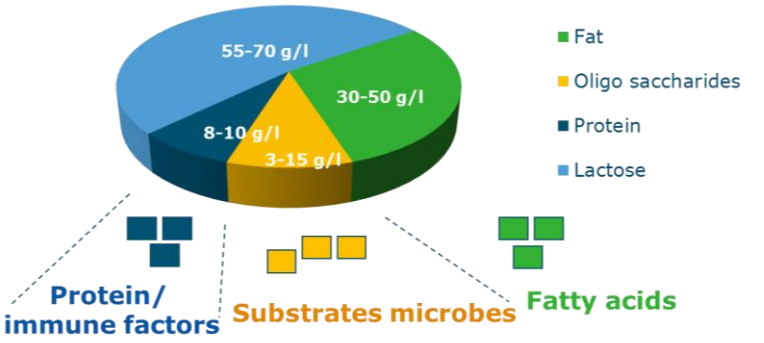
Milk Constituent	Bioactive Component
Cells	Lymphocytes, Macrophages, Granulycytes
Proteins	Antibodies, Growth Factors, Cytokines
Bacteria	*Bifidobacterium,* Lactobacilli,
Oligosaccharides	(HMOs) ~1000 different
Fatty Acids	Saturated (45%), MUFA (40%), PUFA (15%): 0.35% DHA 0.60% ARA
Protein, carbohydrates, others, macromolecules	Allergens, Lactose, Nucleotides
Minerals, Vitamins	Mg, Zn, Fe, Se, Vit A, C, E

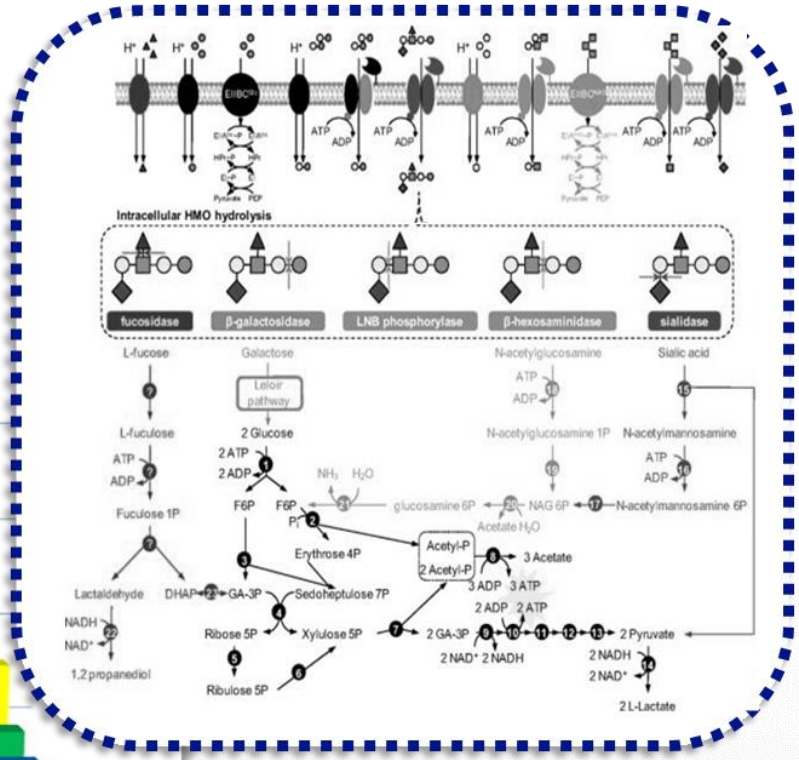
Effect on microbiota composition- *Bifidobacterium* dominated microbiota in breastfed infants

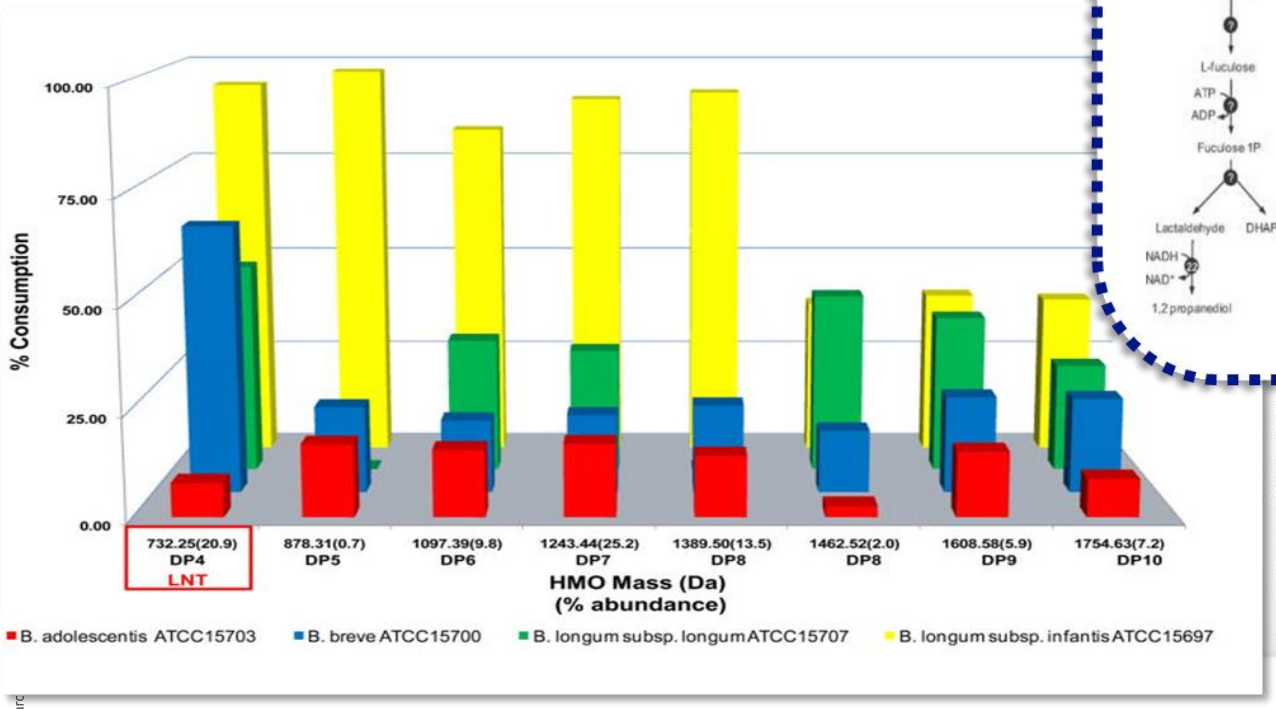


Harmsen et al. 2000. Journal of Pediatric Gastroenterology Nutrition 30:61-67.

MILK CONTAINS GROWTH SUBSTRATES FOR BIFIDOBACTERIA







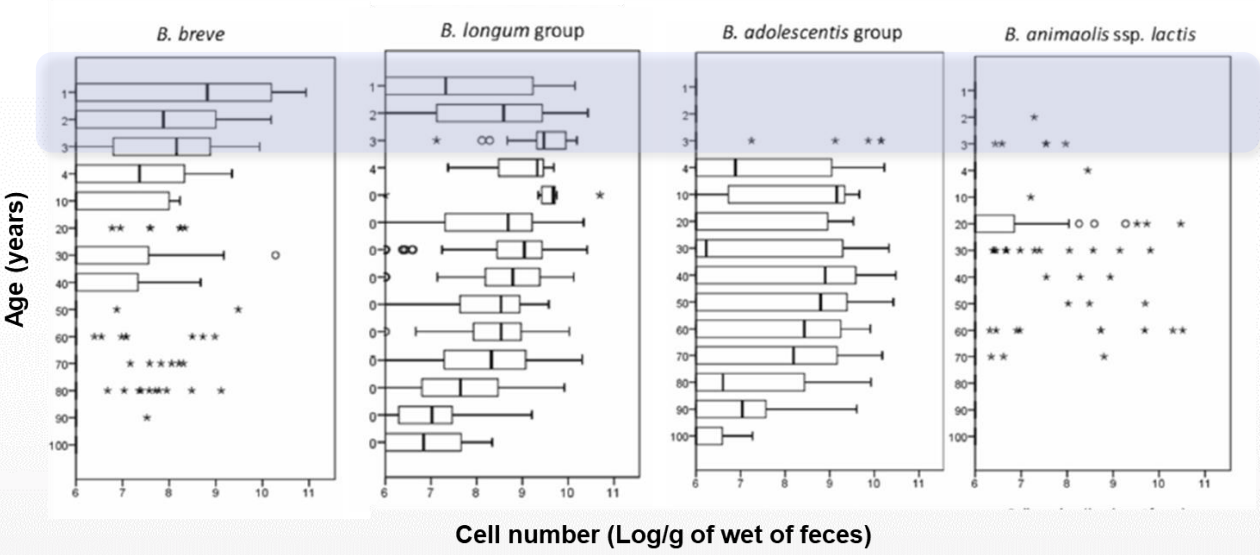
BIFIDOBACTERIA-DOMINATED COMMUNITY- BUT NOT ALL SPECIES ARE NATURALLY PRESENT IN THE INFANT GUT

Curr Microbiol (2017) 74:987–995
DOI 10.1007/s00284-017-1272-4

CrossMark

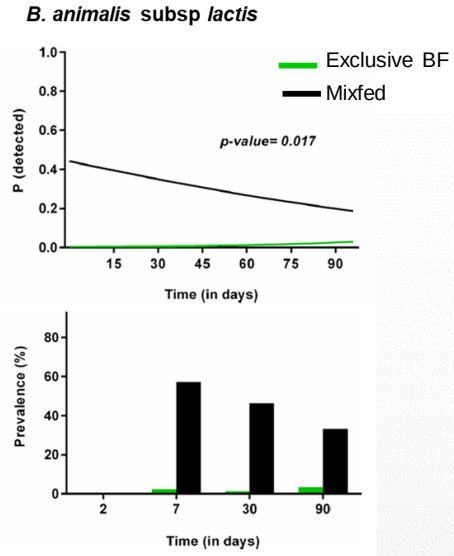
Age-Related Changes in the Composition of Gut *Bifidobacterium* Species

Kumiko Kato[1] · Toshitaka Odamaki[1] · Eri Mitsuyama[1] · Hirosuke Sugahara[1] · Jin-zhong Xiao[1] · Ro Osawa[2]



Early-Life Events, Including Mode of Delivery and Type of Feeding, Siblings and Gender, Shape the Developing Gut Microbiota

Rocio Martin[1]**, Hiroshi Makino[2], Aysun Cetinyurek Yavuz[1], Kaouther Ben-Amor[1], Mieke Roelofs[1], Eiji Ishikawa[2], Hiroyuki Kubota[2], Sophie Swinkels[1], Takafumi Sakai[2], Kenji Oishi[2], Akira Kushiro[2], Jan Knol[1,3]



Supplemented B. longum subsp. infantis EVC001 (Frese et a;., 2017) and B. breve M-16V (Chua et al., 2017) could stably colonize the infant gut- detected >1 month after the supplementation ceased

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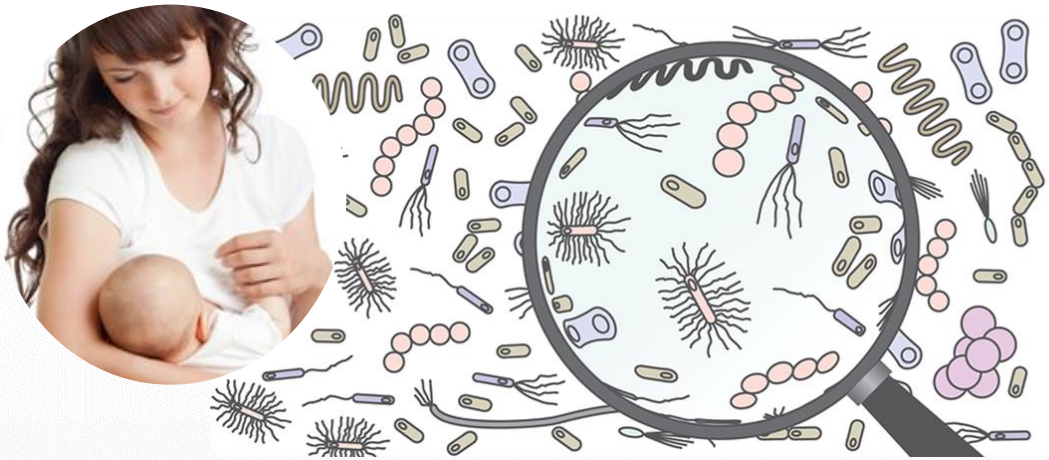
HUMAN MILK CONTAINS BACTERIA

Human milk contains between 10^3 -10^5 bacterial cells/ml



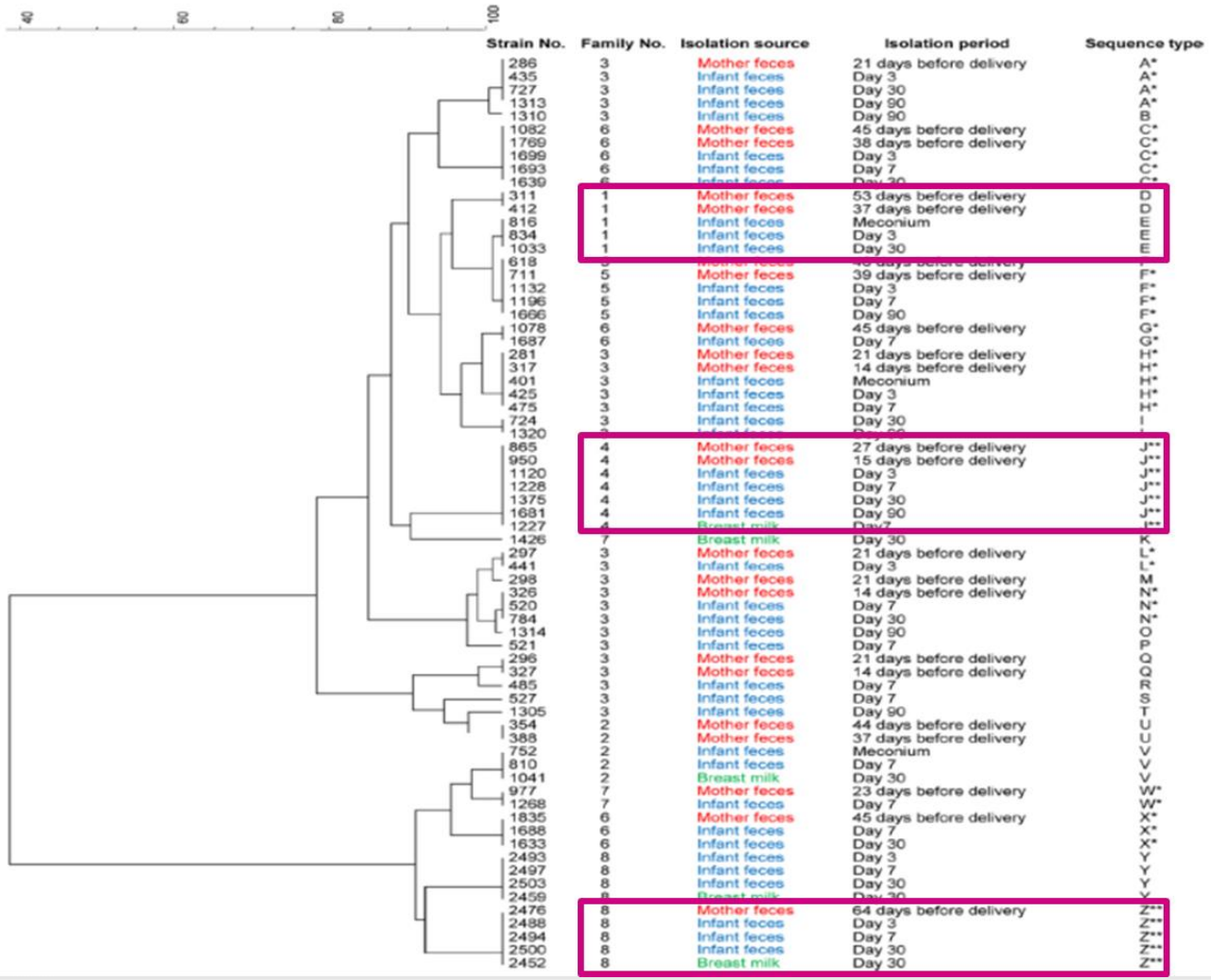
Milk microbiota is dominated by

- *Staphylococcus*
- *Streptococcus*
- *Propionibacterium*
- *Bifidobacterium*
- *Lactobacillus*

These bacteria are anticipated to protect the infant against infections and contribute to the maturation of the immune system

Alba Boix-Amorós et al., 2016

TRANSMISSION OF MATERNAL MICROBIAL HERITAGE AT BIRTH AND DURING BREASTFEEDING



Strain No.	Family No.	Isolation source	Isolation period	Sequence type
286	3	Mother feces	21 days before delivery	A*
435	3	Infant feces	Day 3	A*
727	3	Infant feces	Day 30	A*
1313	3	Infant feces	Day 90	A*
1310	3	Infant feces	Day 90	B
1082	6	Mother feces	45 days before delivery	C*
1769	6	Mother feces	38 days before delivery	C*
1699	6	Infant feces	Day 3	C*
1693	6	Infant feces	Day 7	C*
1639	6	Infant feces	Day 30	C*
311	1	Mother feces	53 days before delivery	D
412	1	Mother feces	37 days before delivery	D
816	1	Infant feces	Meconium	E
834	1	Infant feces	Day 3	E
1033	1	Infant feces	Day 30	E
618	5	Mother feces	45 days before delivery	F*
711	5	Mother feces	39 days before delivery	F*
1132	5	Infant feces	Day 3	F*
1196	5	Infant feces	Day 7	F*
1666	5	Infant feces	Day 90	F*
1078	6	Mother feces	45 days before delivery	G*
1687	6	Infant feces	Day 7	G*
281	3	Mother feces	21 days before delivery	H*
317	3	Mother feces	14 days before delivery	H*
401	3	Infant feces	Meconium	H*
425	3	Infant feces	Day 3	H*
475	3	Infant feces	Day 7	H*
724	3	Infant feces	Day 30	I
1320	3	Infant feces	Day 90	I
865	4	Mother feces	27 days before delivery	J**
950	4	Mother feces	15 days before delivery	J**
1120	4	Infant feces	Day 3	J**
1228	4	Infant feces	Day 7	J**
1375	4	Infant feces	Day 30	J**
1681	4	Infant feces	Day 90	J**
1227	4	Breast milk	Day7	J**
1426	7	Breast milk	Day 30	K
297	3	Mother feces	21 days before delivery	L*
441	3	Infant feces	Day 3	L*
298	3	Mother feces	21 days before delivery	M
326	3	Mother feces	14 days before delivery	N*
520	3	Infant feces	Day 7	N*
784	3	Infant feces	Day 30	N*
1314	3	Infant feces	Day 90	O
521	3	Infant feces	Day 7	P
296	3	Mother feces	21 days before delivery	Q
327	3	Mother feces	14 days before delivery	Q
485	3	Infant feces	Day 7	R
527	3	Infant feces	Day 7	S
1305	3	Infant feces	Day 90	T
354	2	Mother feces	44 days before delivery	U
388	2	Mother feces	37 days before delivery	U
752	2	Infant feces	Meconium	V
810	2	Infant feces	Day 7	V
1041	2	Breast milk	Day 30	V
977	7	Mother feces	23 days before delivery	W*
1268	7	Infant feces	Day 7	W*
1835	6	Mother feces	45 days before delivery	X*
1688	6	Infant feces	Day 7	X*
1633	6	Infant feces	Day 30	X*
2493	8	Infant feces	Day 3	Y
2497	8	Infant feces	Day 7	Y
2503	8	Infant feces	Day 30	Y
2459	8	Breast milk	Day 30	Y
2476	8	Mother feces	64 days before delivery	Z**
2488	8	Infant feces	Day 3	Z**
2494	8	Infant feces	Day 7	Z**
2500	8	Infant feces	Day 30	Z**
2452	8	Breast milk	Day 30	Z**

Makino H et al. Applied and Environmental Microbiology, 2011; 77 (19): 6788-6793

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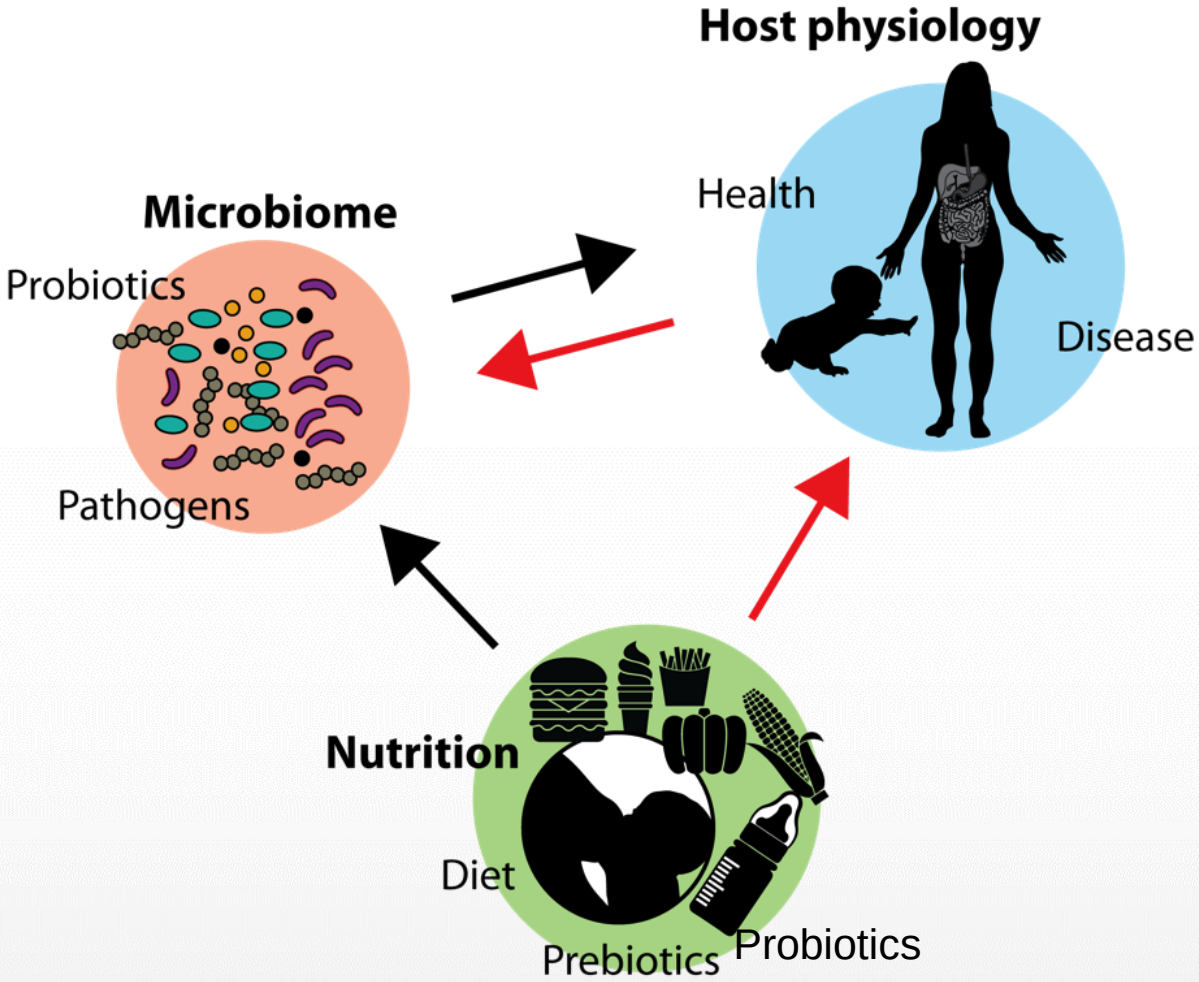
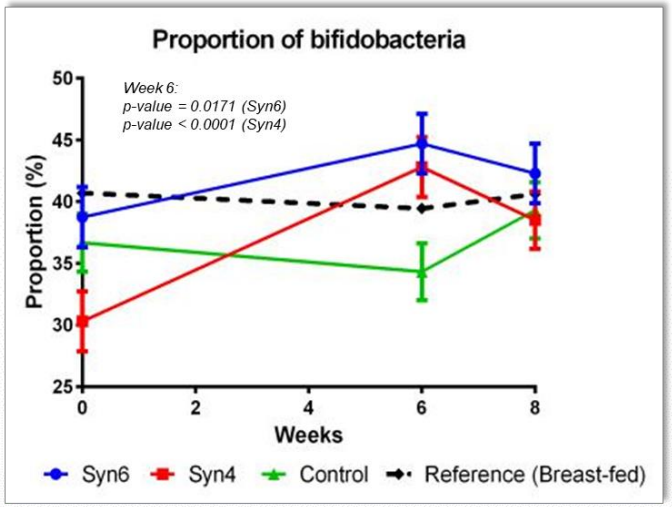
CAUSE AND EFFECT- THE ROLE OF NUTRITION TO REBALANCE AND SHAPE THE MICROBIOTA



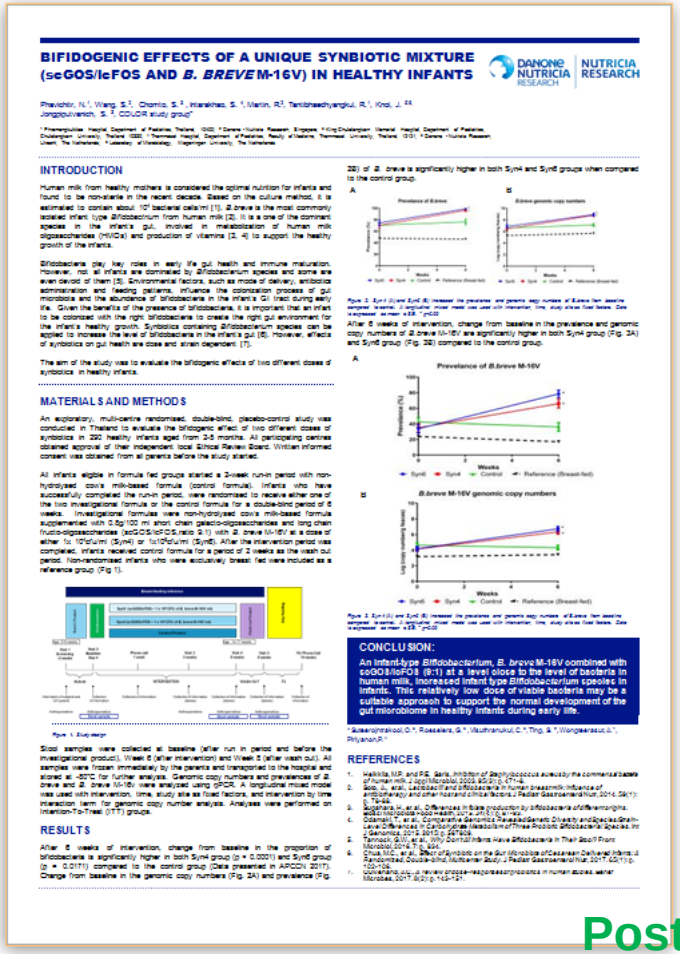
COLOR STUDY: SYNBIOTIC SUPPLEMENTATION INCREASES BIFIDOBACTERIA AND REDUCES *C. DIFFICILE* IN INFANTS

N= 290 Healthy infants, 6-19 weeks of a

*Synbiotics: scGOS/lcFOS + *B. breve* M-16V at a dos



Abundance of bifidobacteria in early life is a microbial indication of immune fitness and gut health
(Hong PY et al, 2010).



BIFIDOGENIC EFFECTS OF A UNIQUE SYNBIOTIC MIXTURE (scGOS/lcFOS AND *B. BREVE* M-16V) IN HEALTHY INFANTS

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INTRODUCTION

MATERIALS AND METHODS

RESULTS

CONCLUSION:
An infant-type *Bifidobacterium*, *B. breve* M-16V combined with scGOS/lcFOS (9:1) at a level close to the level of bacteria in human milk, increased infant type *Bifidobacterium* species in infants. This relatively low dose of viable bacteria may be a suitable approach to support the normal development of the gut microbiome in healthy infants during early life.

REFERENCES

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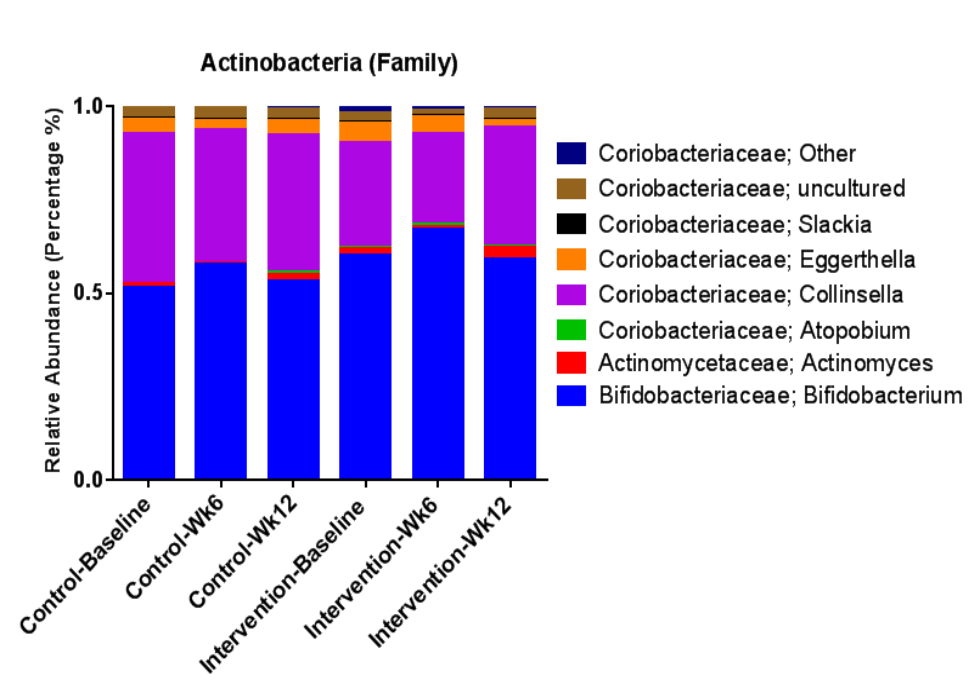
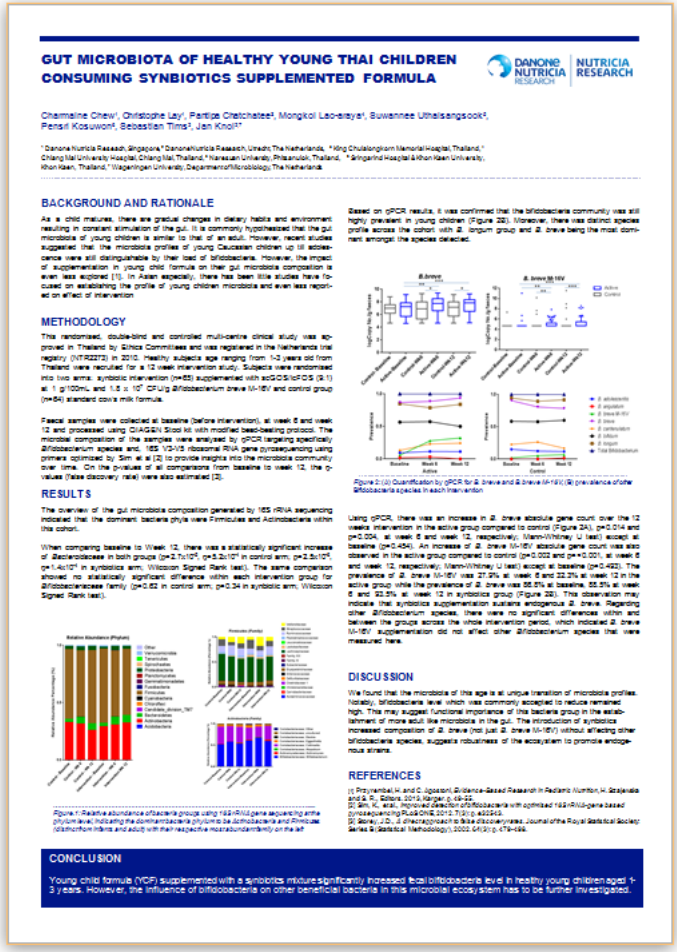
YCF SUPPLEMENTED WITH A SYNBIOTICS MIXTURE SIGNIFICANTLY INCREASED FECAL BIFIDOBACTERIA LEVEL IN HEALTHY YOUNG CHILDREN AGED 1-3 YEARS

N= 129 Healthy young children, 1-3 years





GUT MICROBIOTA OF HEALTHY YOUNG THAI CHILDREN CONSUMING SYNBIOTICS SUPPLEMENTED FORMULA

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Charmaine Chew[1], Christophe Lay[2], Pantipa Chatchatee[3], Mongkol Lao-araya[4], Suwannee Uthaisangsook[5], Pensiri Kosuwon[6], Sebastian Tims[2], Jan Knol[2,7]

[1] Danone Nutricia Research, Singapore; [2] Danone Nutricia Research, Utrecht, The Netherlands; [3] King Chulalongkorn Memorial Hospital, Thailand; [4] Chiang Mai University Hospital, Chiang Mai, Thailand; [5] Naresuan University, Phitsanulok, Thailand; [6] Srinagarind Hospital & Khon Kaen University, Khon Kaen, Thailand; [7] Wageningen University, Department of Microbiology, The Netherlands

BACKGROUND AND RATIONALE

METHODOLOGY

RESULTS

DISCUSSION

REFERENCES

CONCLUSION

Young child formula (YCF) supplemented with a synbiotics mixture significantly increased fecal bifidobacteria level in healthy young children aged 1-3 years. However, the influence of bifidobacteria on other beneficial bacteria in this microbial ecosystem has to be further investigated.

Kosuwon et al., Beneficial Microbes 2018 Apr 10:1-12. doi: 10.3920/BM2017.0110.

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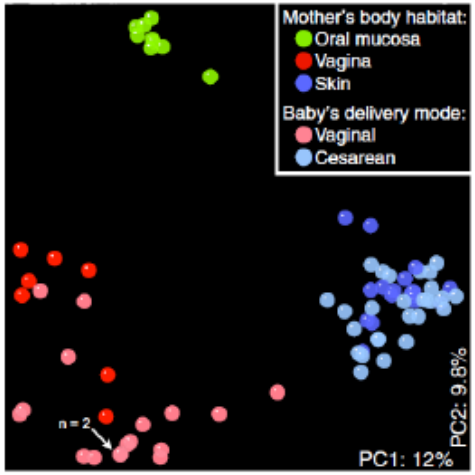
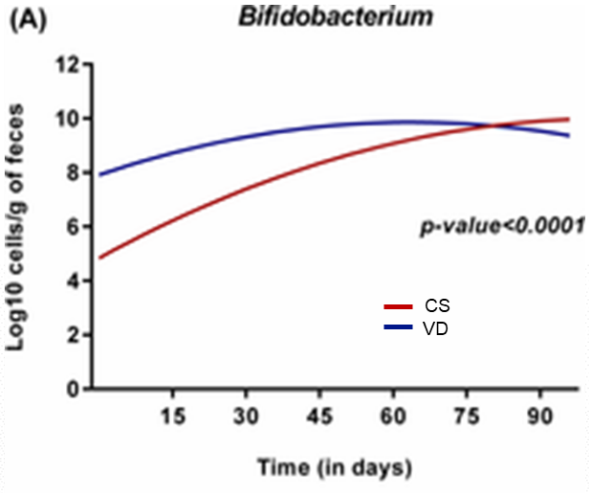
DIFFERENT MICROBIOTA COMPOSITION IN C-SECTION BORN INFANTS MAY EXPLAIN HIGHER RISK OF ALLERGY



Dominguez-Bello et al, 2010, PNAS 107: 11971-11975



Martin et al., 2016, PlosONE 2016, 11(6)

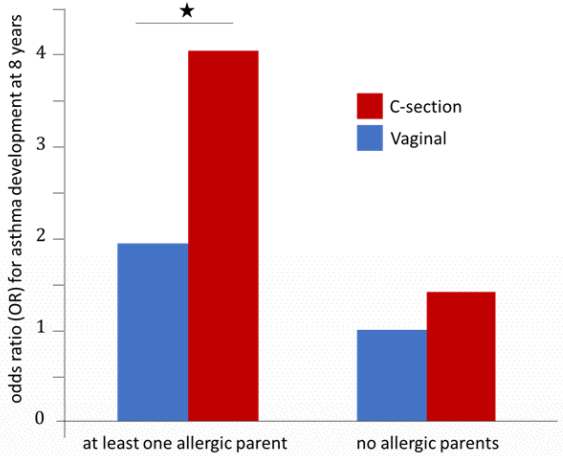
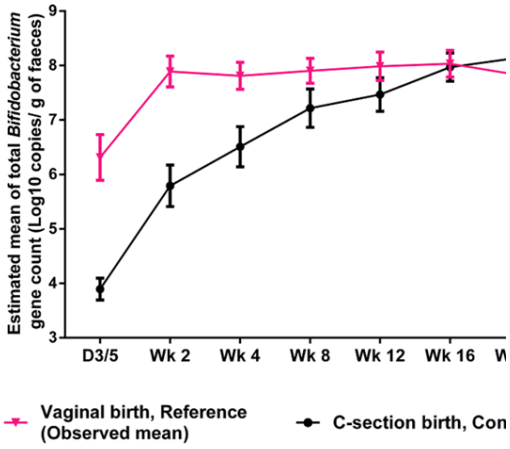
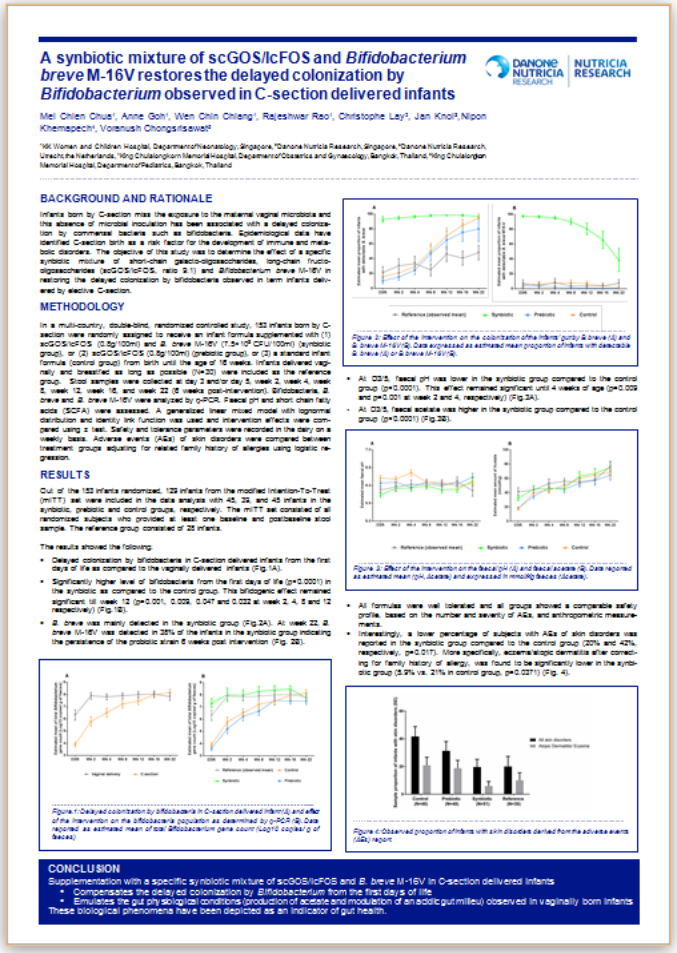


Figure based on Roduit et al., 2009, Thorax 64:107-113

SYNBIOTIC RESTORE THE DELAYED COLONIZATION BY *BIFIDOBACTERIUM* IN CS BORN INFANTS FROM THE FIRST DAYS OF LIFE

Restores the numb
Restores the delayed colonis





A synbiotic mixture of scGOS/lcFOS and *Bifidobacterium breve* M-16V restores the delayed colonization by *Bifidobacterium* observed in C-section delivered infants

Mei Chien Chua[1], Anne Goh[1], Wen Chin Chiang[1], Rajeshwar Rao[1], Christophe Lay[2], Jan Knol[2], Nipon Khemapech[3], Voranush Chongsrisawat[4]

[1]KK Women and Children Hospital, Department of Neonatology, Singapore, [2]Danone Nutricia Research, Singapore, [3]Danone Nutricia Research, Utrecht, the Netherlands, [4]King Chulalongkorn Memorial Hospital, Department of Obstetrics and Gynaecology, Bangkok, Thailand, [5]King Chulalongkorn Memorial Hospital, Department of Pediatrics, Bangkok, Thailand

BACKGROUND AND RATIONALE

METHODOLOGY

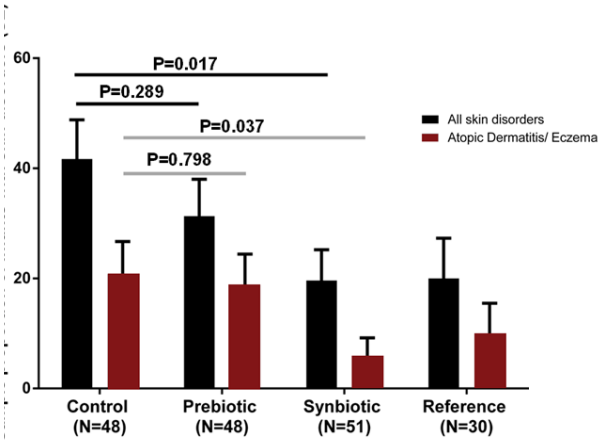
RESULTS

CONCLUSION

Supplementation with a specific synbiotic mixture of scGOS/lcFOS and *B. breve* M-16V in C-section delivered infants
- Compensates the delayed colonization by *Bifidobacterium* from the first days of life
- Emulates the gut physiological conditions (production of acetate and modulation of an acidic gut milieu) observed in vaginally born infants

These biological phenomena have been depicted as an indicator of gut health

tential protective effect* on skin rash especially eczema in early life



Less Incidence of reported skin related disorders & eczema during the study

Chua MC et al.. JPGN 2017;65: 102–106

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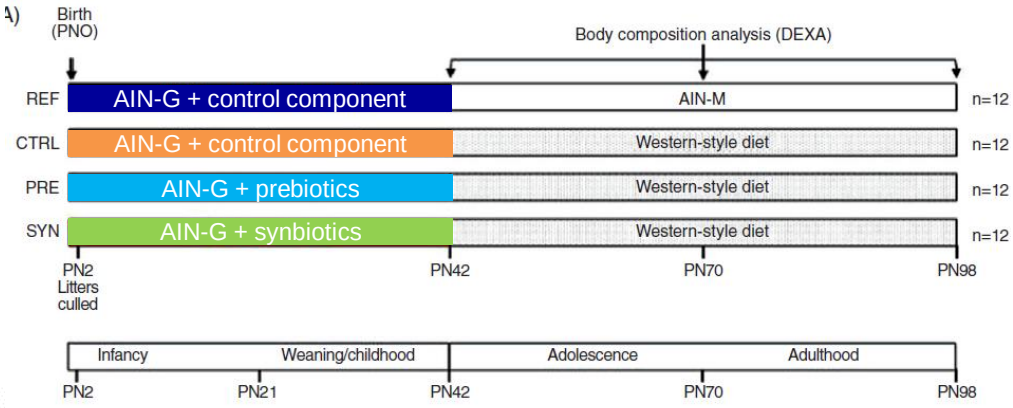
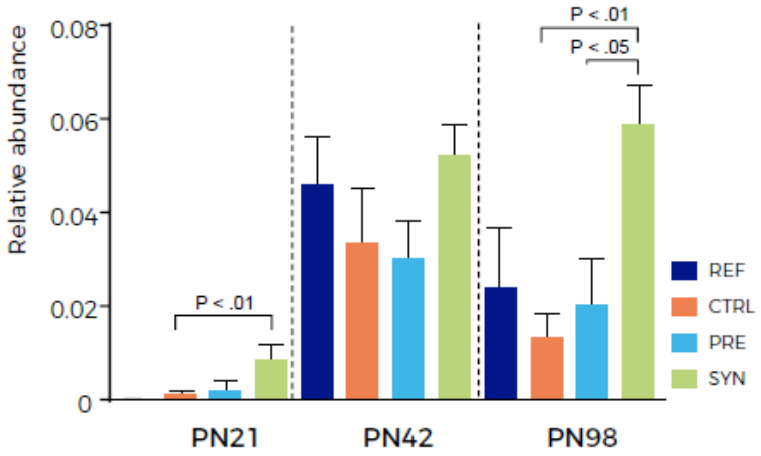
EARLY LIFE SYNBIOTIC SUPPLEMENTATION PROTECT AGAINST DIET-INDUCED OBESITY IN ADULT MICE



Different interventions → **Challenged with HF WSD 8wks**

Synbiotic supplementation increased the abundance of *Bifidobacterium*



*REF and CTRL: AIN-G**
PRE: AIN-G + prebiotics (scGOS/lcFOS, 9:1)
SYN : AIN-G + synbiotics (scGOS/lcFOS, 9:1 + B. breve M-16V)

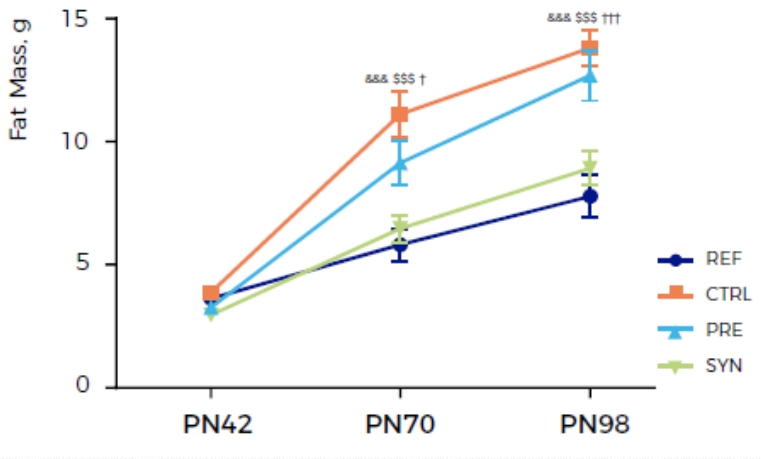
**AIN-G (standard semi-synthetic diet appropriate for breeding) plus control component (maltodextrin)*

Food intake did not differ between groups

Mischke M et al. Diabetes Obes Metab. 2018 Feb 20. doi: 10.1111/dom.13240.

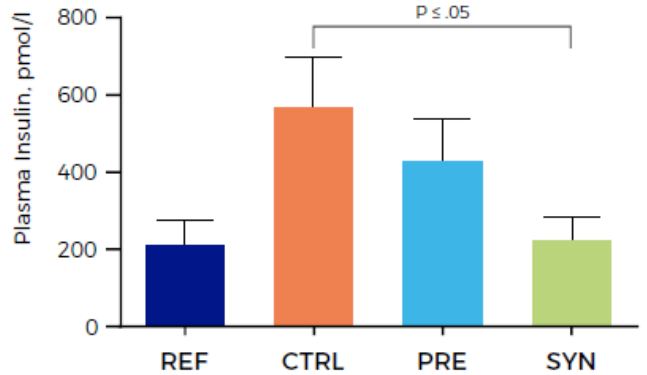
EARLY LIFE SYNBIOTIC SUPPLEMENTATION PROTECT AGAINST DIET-INDUCED OBESITY IN ADULT MICE

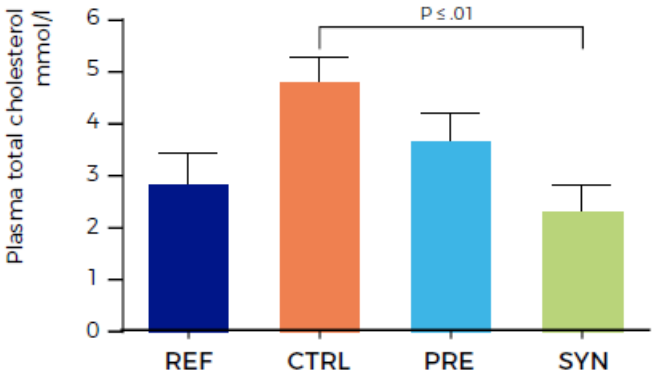
Provided long-term protection against diet-induced excessive fat accumulation



&&&P ≤ .001 indicates significance for REF vs CTRL.
††P ≤ .01, †††P ≤ .001 indicate significance for PRE vs SYN.
$P ≤ .05, $$P ≤ .01, $$$P ≤ .001 indicate significance for CTRL vs SYN.

Improved insulin sensitivity and dyslipidaemia in adulthood





Mischke M et al. Diabetes Obes Metab. 2018 Feb 20. doi: 10.1111/dom.13240.

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TAKE HOME MESSAGE

- Microbial colonization following birth, is essential for establishing a symbiosis with our immune system and profoundly influences health throughout life
- Breastfeeding and C-section delivered are key factors in early life that my impact long life health
- Dysbiosis or altered microbial colonization is associated with the development of allergies
- Nutrition represents a fundamental basis of the strong relationship between the gut microbiota, the immune system and health
- Specific pre, pro and synbiotic interventions in early life successfully modulate the early microbial colonization and influences immune development.