Microbiome and good bacteria – the future for health and food

Anja Wellejus, *Senior Research Scientist, Human Health Microbiome Innovation*

Anna Przewozna, *Commercial Manager , Diary Bioprotection*


Good bacteria
and the future of human health
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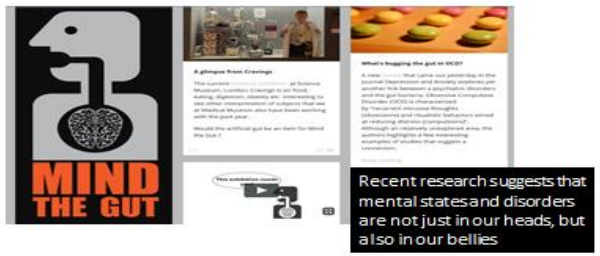
Awareness of the “microbiome” is rising

Scientific communities / general population

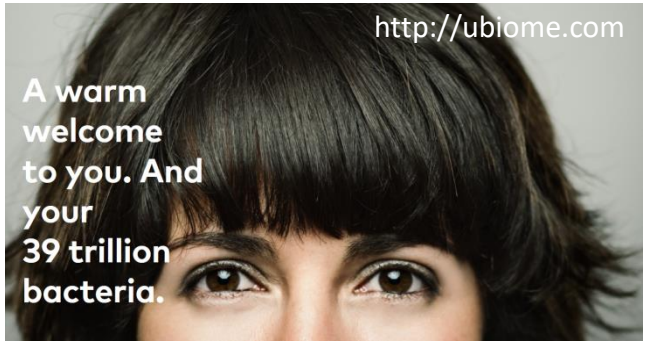
Exihibitions

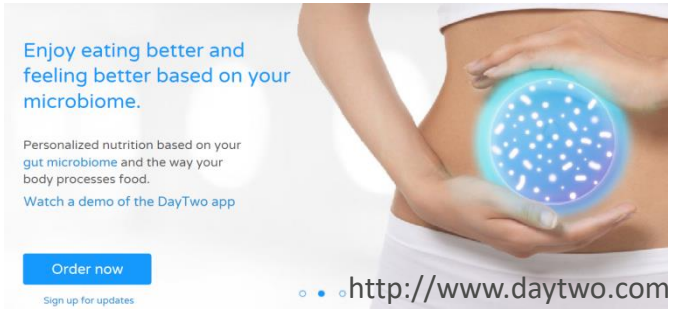
A Microbiome exhibition was set up at large scale in 2015 at the American Museum of Natural History in New York

Mind the Gut - an upcoming exhibition on the connections between the brain, gut and microbes



Microbiota profiling .. and how to modulate it





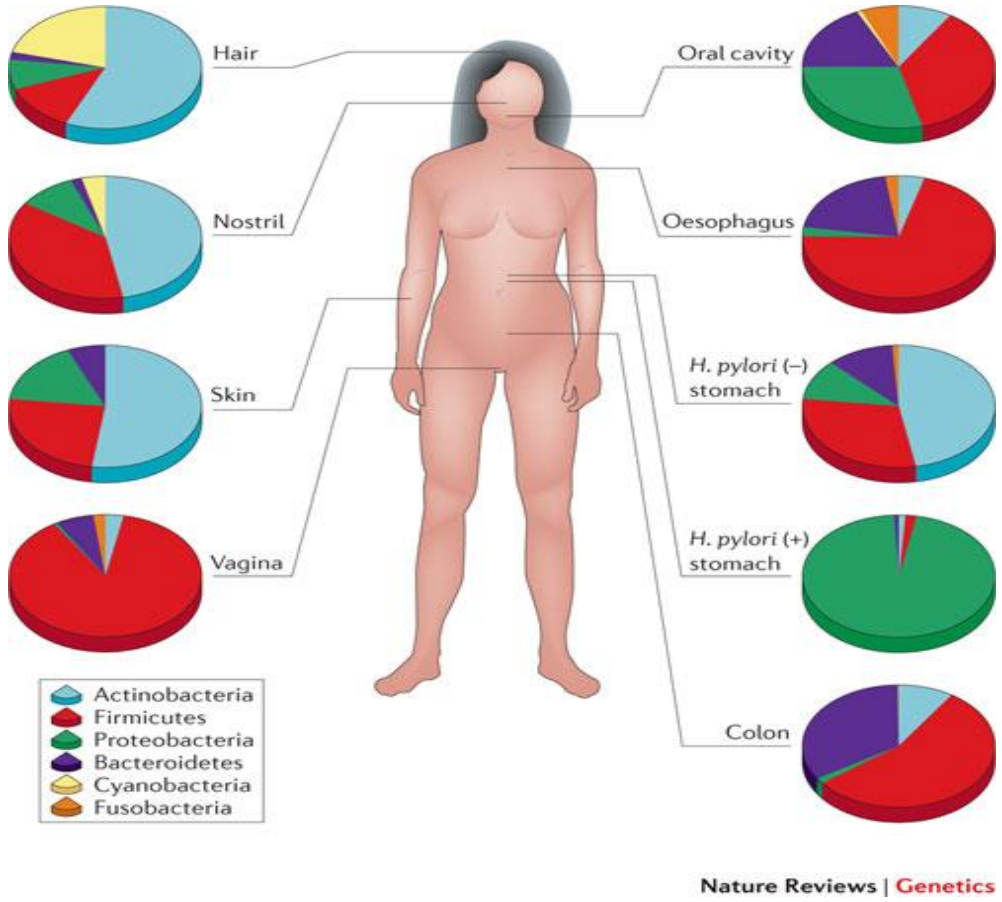
The human microbiome – a massive diversity

Numbers

- Human body → 30 trillion cells
- Human genome → 23,000 genes

- Human microbiome → 100 trillion cells
- Microbial genome → 2 million genes

- 1100 bacterial species
- Large diversity across body sites
- Large interpersonal diversity
- Dominated by “unexploited” bacteria (often strict anaerobes)



Qin et al. 2010, Nature, 464, 59-65; Nielsen et al. *Nature Biotechnol*. doi:10.1038/nbt.2939; Cho and Blaser, 2010, Nature Reviews, 13, 260-270

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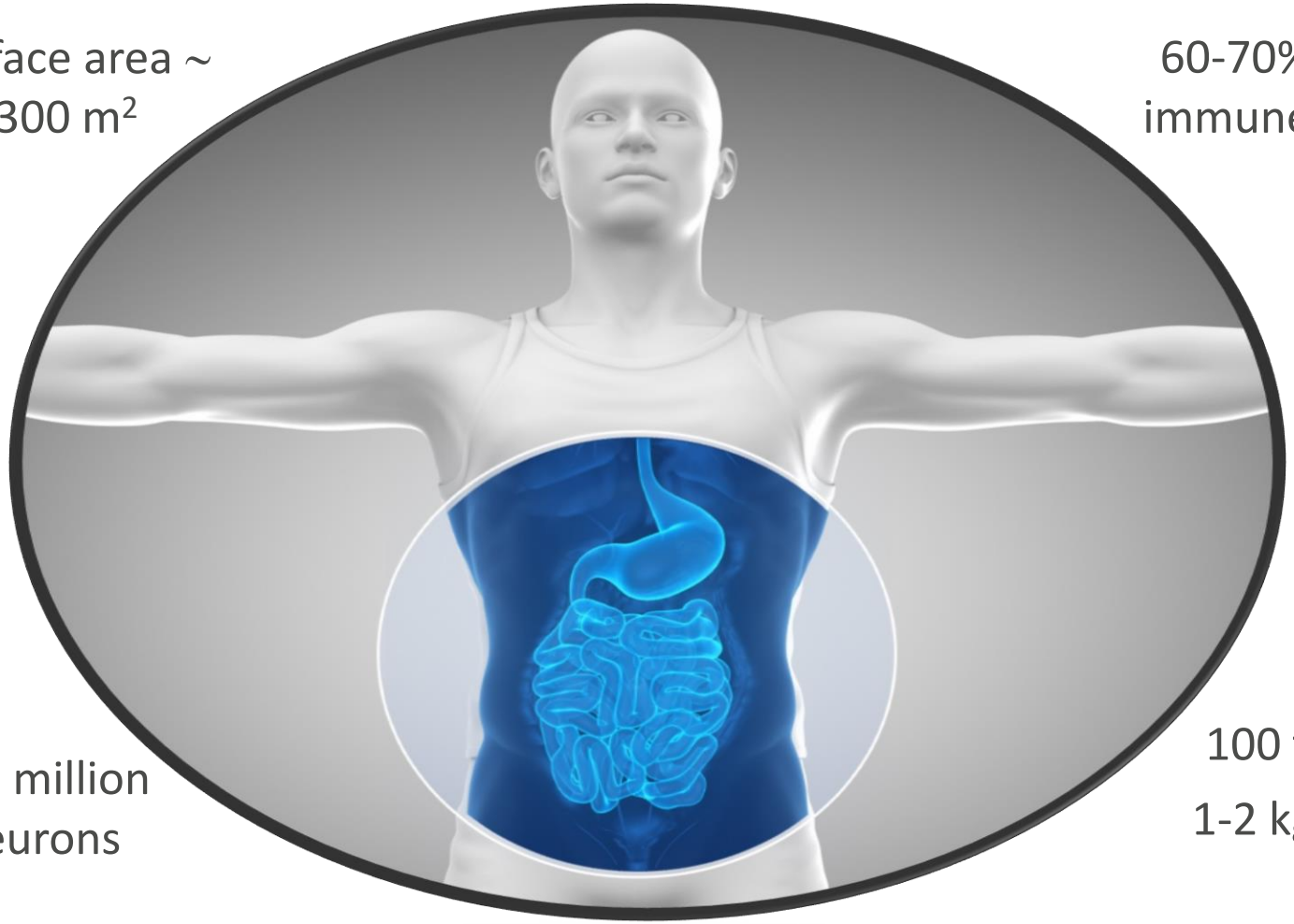
The intestine

Surface area ~ 300 m^2

60-70% of our immune system



100 million neurons

100 trillion bacteria

1-2 kg bacteria/adult

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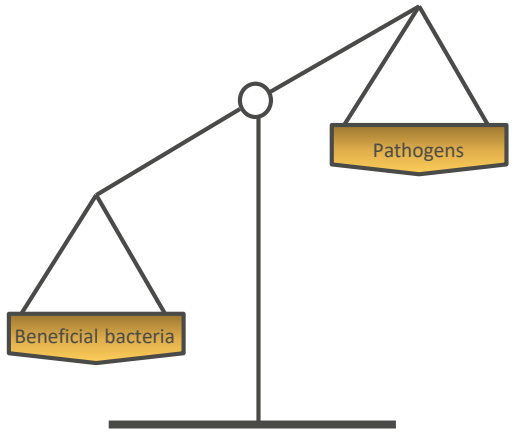
The gut microbiome

Microbial homeostasis

- Strengthen gut integrity
- Shape intestinal epithelium
- Harvest energy
- Protect against pathogens
- Develop and regulate host immunity



Dysbiosis

- Altered neurotransmitter production
- Inflammation
- Oxidative stress
- Increased permeability
- Endotoxin exposure

Infections
Obesity
Atopic disease
Autoimmunity
Type 1 diabetes

Thursby & Juge, 2017, Biochem J, 474, 1823-1836.

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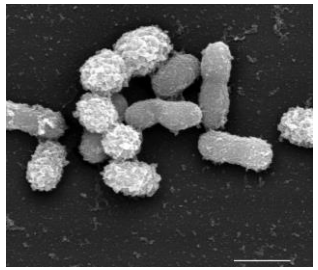
Areas of research where **microbial composition** seem crucial

Metabolic health

- *Akkermansia municiphila*



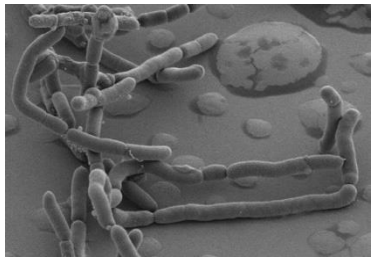
Derrien et al. 2017, Microb pathog, 106, 171-181

Infant health

Microbiota

Inflammatory Bowel Disease

- *Faecalibacterium prausnitzii*



https://presse.inserm.fr/en/treating-intestinal-pain-with-bacteria/22063/

Necrotizing EnteroColitis

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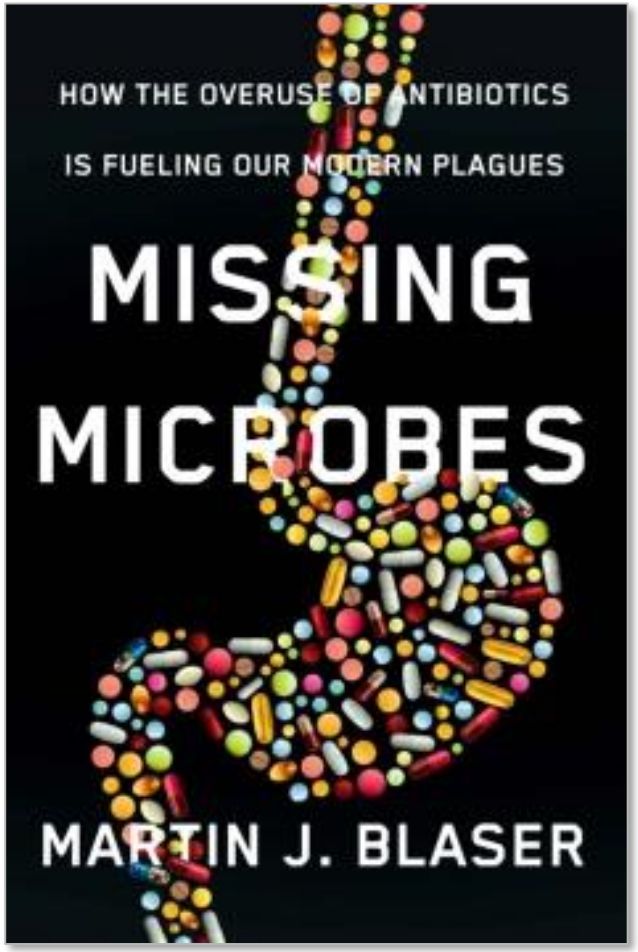
Rather than being invaded by enemies
- we may have lost some friends



Examples of missing microbes and activities
- often fueled by lifestyle

Infant gut:

- Early colonization by Bifidobacteria

Adult gut:

- Loss of Specific anti-inflammatory taxa
- Reduced SCFA production
- Low-grade inflammation and barrier impairment

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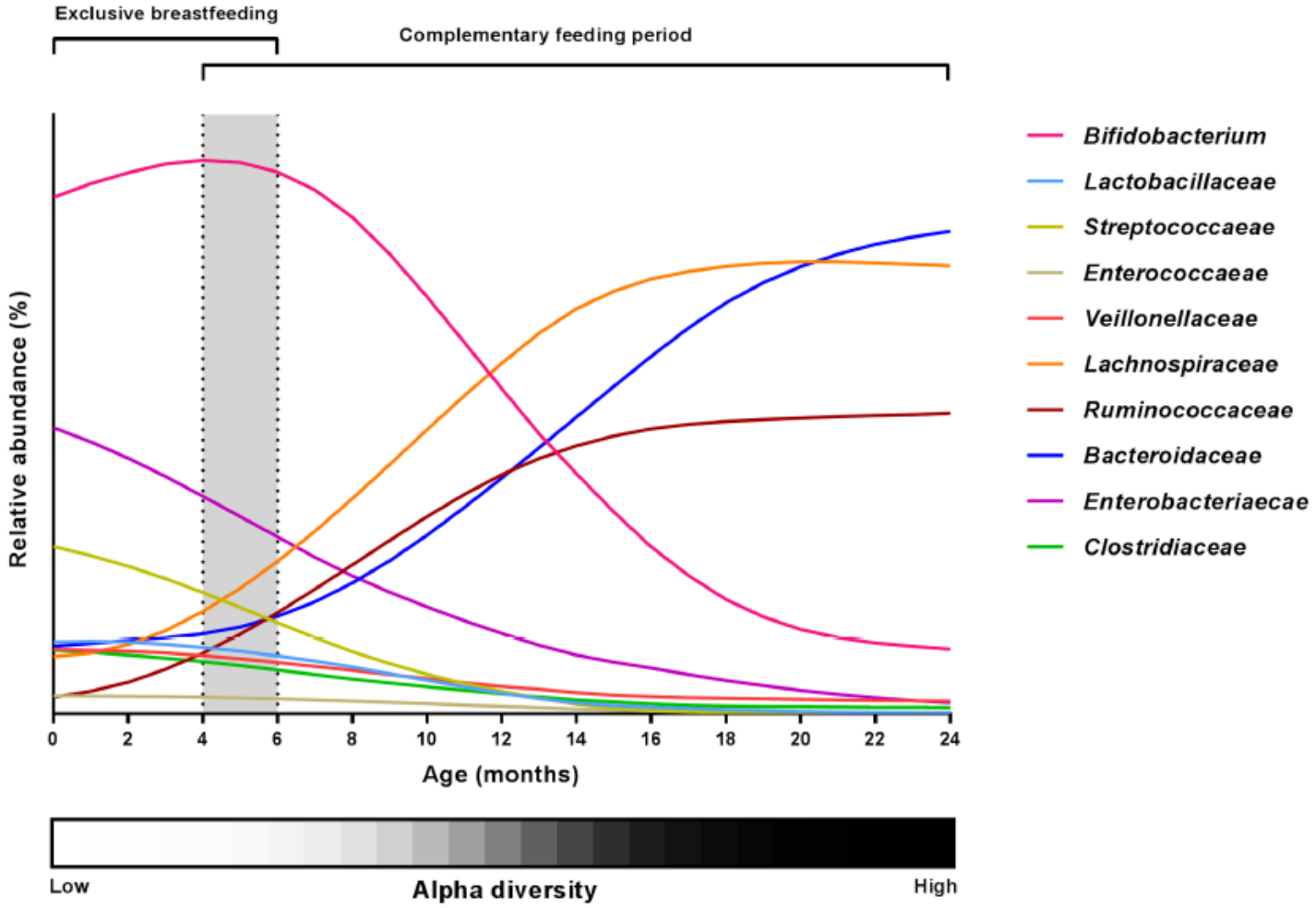
Infant health – order of bacterial appearence seems to matter



Laursen et al. 2017, Front Microbiol, 8, 356

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Main drivers of the **microbial colonization** of the infant intestine

Mode of delivery
Vaginally born vs Cesarean section

Gestational age at birth
Preterm

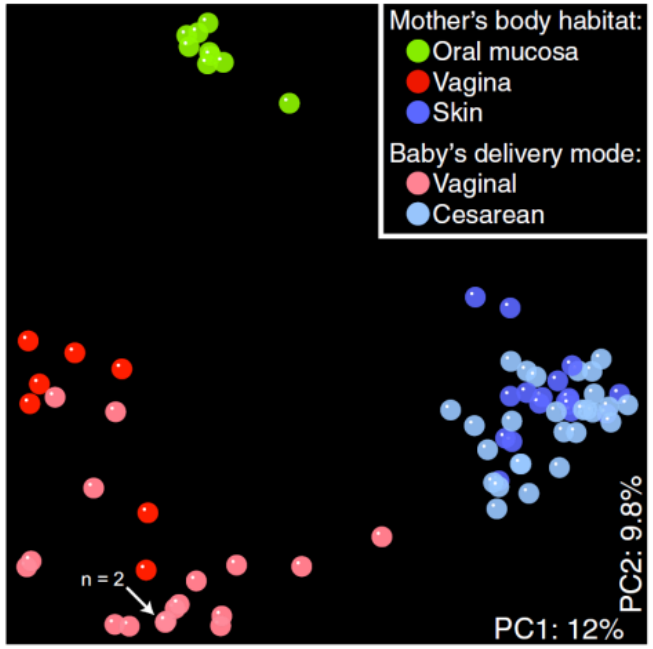
Infant feeding mode
Breast-feeding (Ig, HMO) vs Formula-feeding

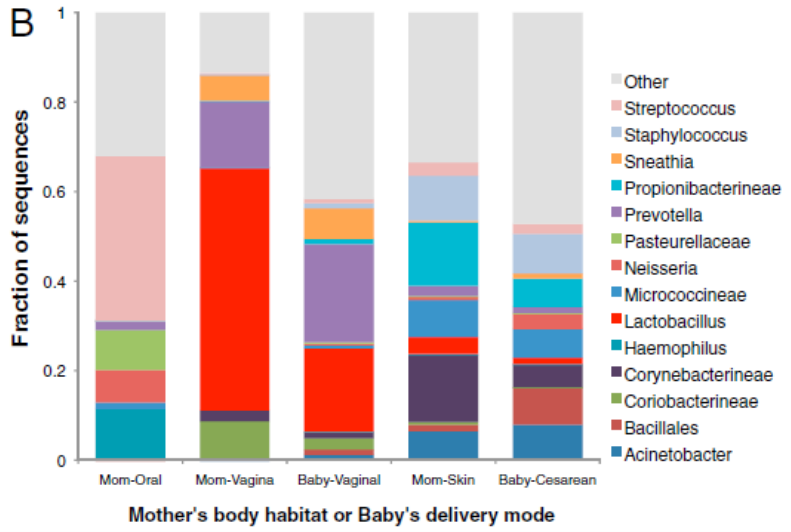
Maternal diet

Environment
Family lifestyle and Geographical location

Host genetics

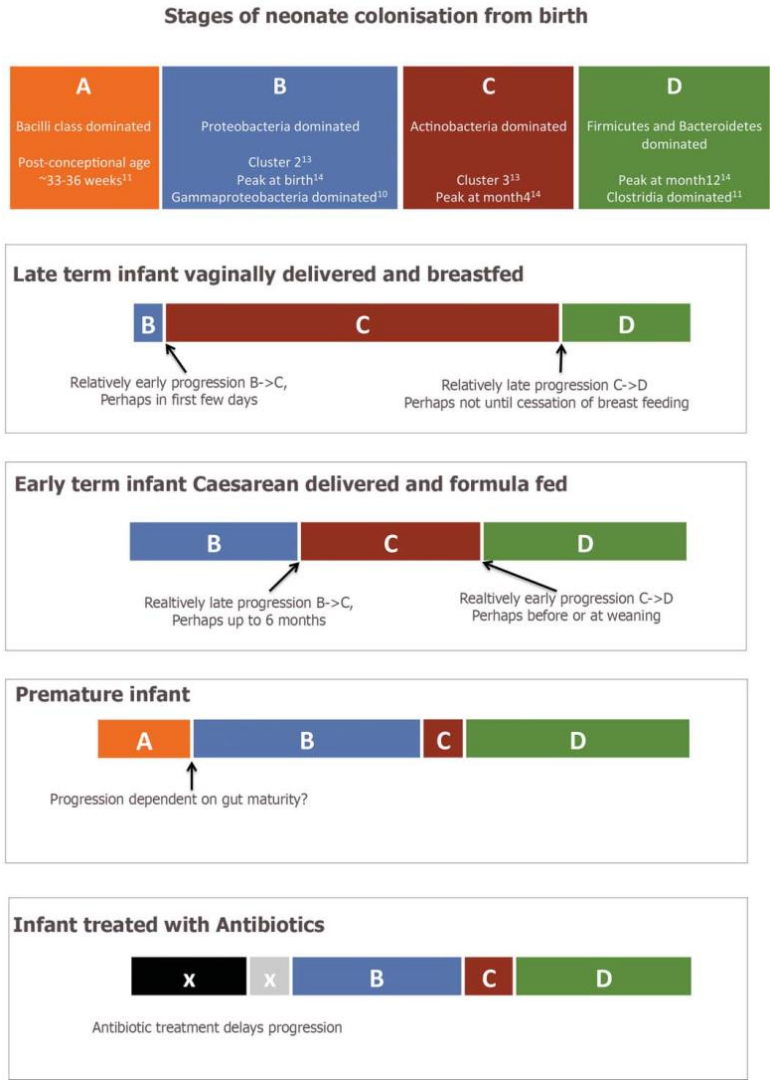
10 newborns < 24h
4 Vaginally delivered
6 C-section

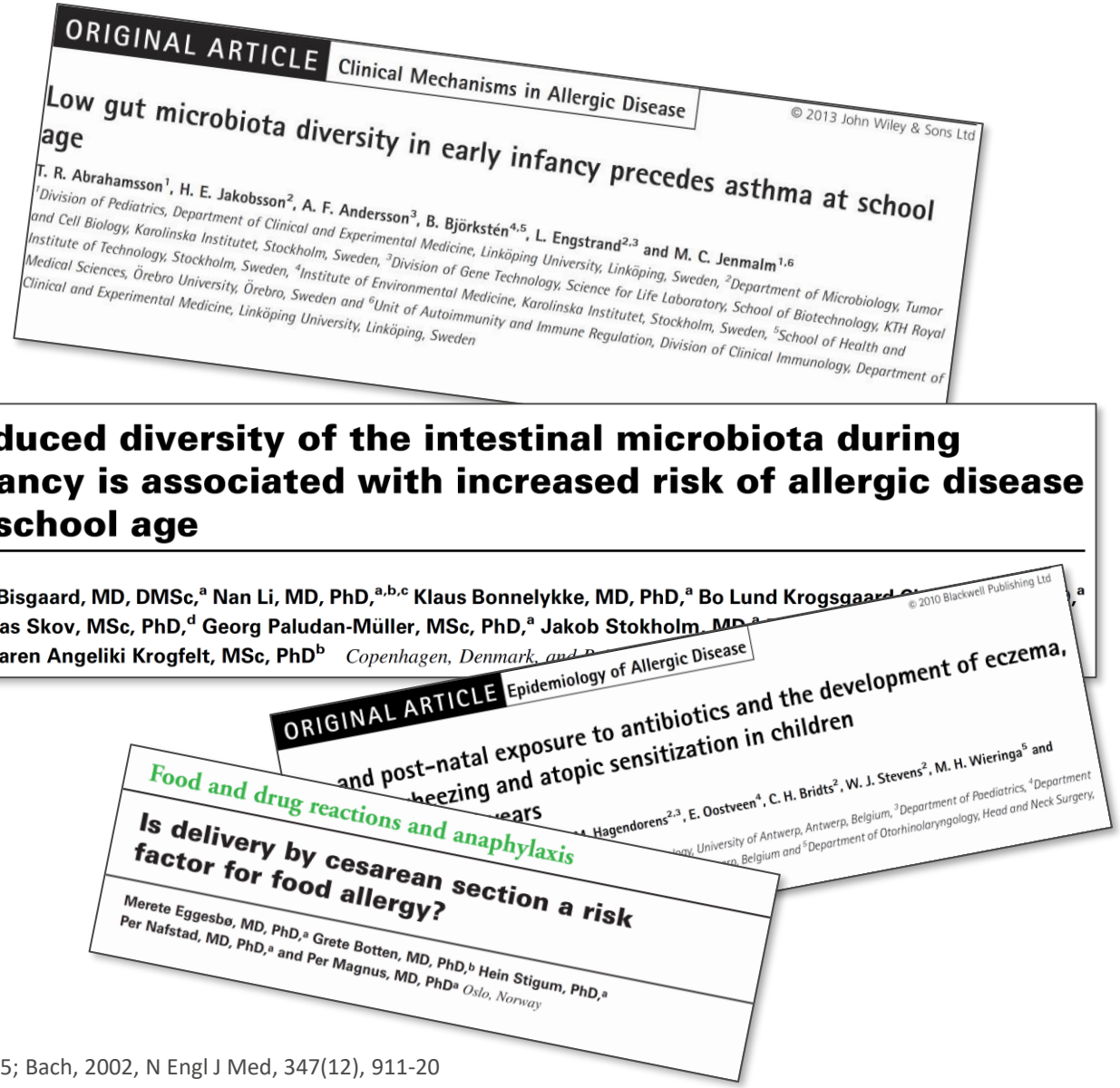




Mulligan & Friedman, 2017, J Endocrinol, 235,1; Dominguez-Bello et al. 2010, PNAS, 107(26), 11981-11975

Balancing the microbiota composition **during infancy**





ORIGINAL ARTICLE Clinical Mechanisms in Allergic Disease

© 2013 John Wiley & Sons Ltd

Low gut microbiota diversity in early infancy precedes asthma at school age

T. R. Abrahamsson[1], H. E. Jakobsson[2], A. F. Andersson[3], B. Björkstén[4,5], L. Engstrand[2,3] and M. C. Jenmalm[1,6]

[1]Division of Pediatrics, Department of Clinical and Experimental Medicine, Linköping University, Linköping, Sweden, [2]Department of Microbiology, Tumor and Cell Biology, Karolinska Institutet, Stockholm, Sweden, [3]Division of Gene Technology, Science for Life Laboratory, School of Biotechnology, KTH Royal Institute of Technology, Stockholm, Sweden, [4]Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden, [5]School of Health and Medical Sciences, Örebro University, Örebro, Sweden and [6]Unit of Autoimmunity and Immune Regulation, Division of Clinical Immunology, Department of Clinical and Experimental Medicine, Linköping University, Linköping, Sweden

Reduced diversity of the intestinal microbiota during infancy is associated with increased risk of allergic disease at school age

Hans Bisgaard, MD, DMSc,[a] Nan Li, MD, PhD,[a,b,c] Klaus Bonnelykke, MD, PhD,[a] Bo Lund Krogsgaard [illegible],[a] Thomas Skov, MSc, PhD,[d] Georg Paludan-Müller, MSc, PhD,[a] Jakob Stokholm, MD,[a] and Karen Angeliki Krogfelt, MSc, PhD[b] *Copenhagen, Denmark, and [illegible]*

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ORIGINAL ARTICLE Epidemiology of Allergic Disease

[illegible] and post-natal exposure to antibiotics and the development of eczema, [illegible]heezing and atopic sensitization in children

[illegible]ears

[illegible] Hagendorens[2,3], E. Oostveen[4], C. H. Bridts[2], W. J. Stevens[2], M. H. Wieringa[5] and [illegible]

[illegible]logy, University of Antwerp, Antwerp, Belgium, [3]Department of Paediatrics, [4]Department [illegible], Belgium and [5]Department of Otorhinolaryngology, Head and Neck Surgery,

Food and drug reactions and anaphylaxis

Is delivery by cesarean section a risk factor for food allergy?

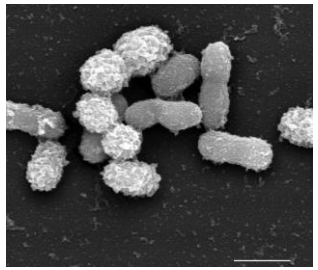
Merete Eggesbø, MD, PhD,[a] Grete Botten, MD, PhD,[b] Hein Stigum, PhD,[a] Per Nafstad, MD, PhD,[a] and Per Magnus, MD, PhD[a] *Oslo, Norway*

Dogra et al., 2015, Gut Microbes, 6(5), 321-325; Bach, 2002, N Engl J Med, 347(12), 911-20

Areas of research where **microbial composition** seems crucial

Metabolic health

- *Akkermansia municiphila*



Derrien et al. 2017, Microb pathog, 106, 171-181

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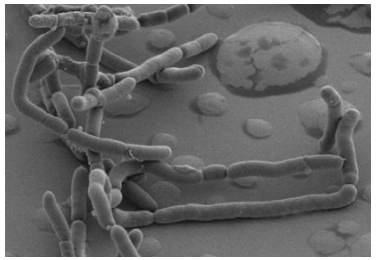

https://presse.inserm.fr/en/treating-intestinal-pain-with-bacteria/22063/

Necrotizing EnteroColitis

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Necrotizing EnteroColitis (NEC)

Pathology

Inflammatory disease of the intestines

Severe NEC affects 5-7% of very preterm infants

Surgical intervention is often needed

NEC-related mortality 15-20%

Associated morbidities include

- intestinal strictures
- short gut syndrome
- neurodevelopmental disorders

Probiotics reduce NEC and death

Probiotic bacteria colonize the intestines

Administration of probiotics is extensively studied in very preterm infants

Cochrane-review includes >5000 infants

- NEC risk reduction 57%
- Overall mortality risk reduction 35%

Intervention in preterm NEC infants with Chr Hansen strains

Bifidobacterium infantis (BB-02 3.0x10E^8 CFU)
Streptococcus thermophilus (TH-4 3.5x10E^8 CFU)
Bifidobacterium lactis (BB-12 3.5x10E^8 CFU)

Positive on NEC reduction as a secondary endpoint

	Probiotic Group, *n* = 548	Control Group, *n* = 551	RR (95% CI)	*P* Value
NEC				
NEC (Bell stage 2 or more), *n* (%)	11 (2.0)	24 (4.4)	0.46 (0.23 to 0.93)	.03
Subgroup analyses:				
Gestational age				[a]
<28 wk, *n* (%)	11 (5.0)	17 (7.2)	0.69	
≥28 wk, *n* (%)	0	7 (2.2)		
Birth weight				.08[b]
<1000 g, *n* (%)	10 (4.3)	14 (5.9)	0.73	
≥1000 g, *n* (%)	1 (0.3)	10 (3.2)	0.10	
Age at NEC (Bell stage 2 or more), d, median (IQR)	20.5 (15.5–34.5)	21 (17.0–30.5)		.99

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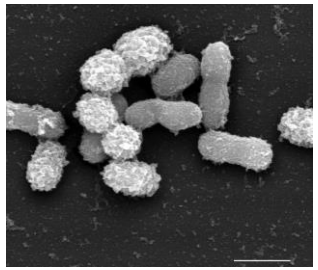
- *Akkermansia municiphila*



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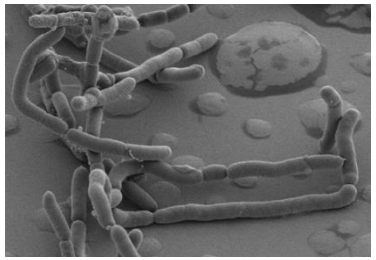

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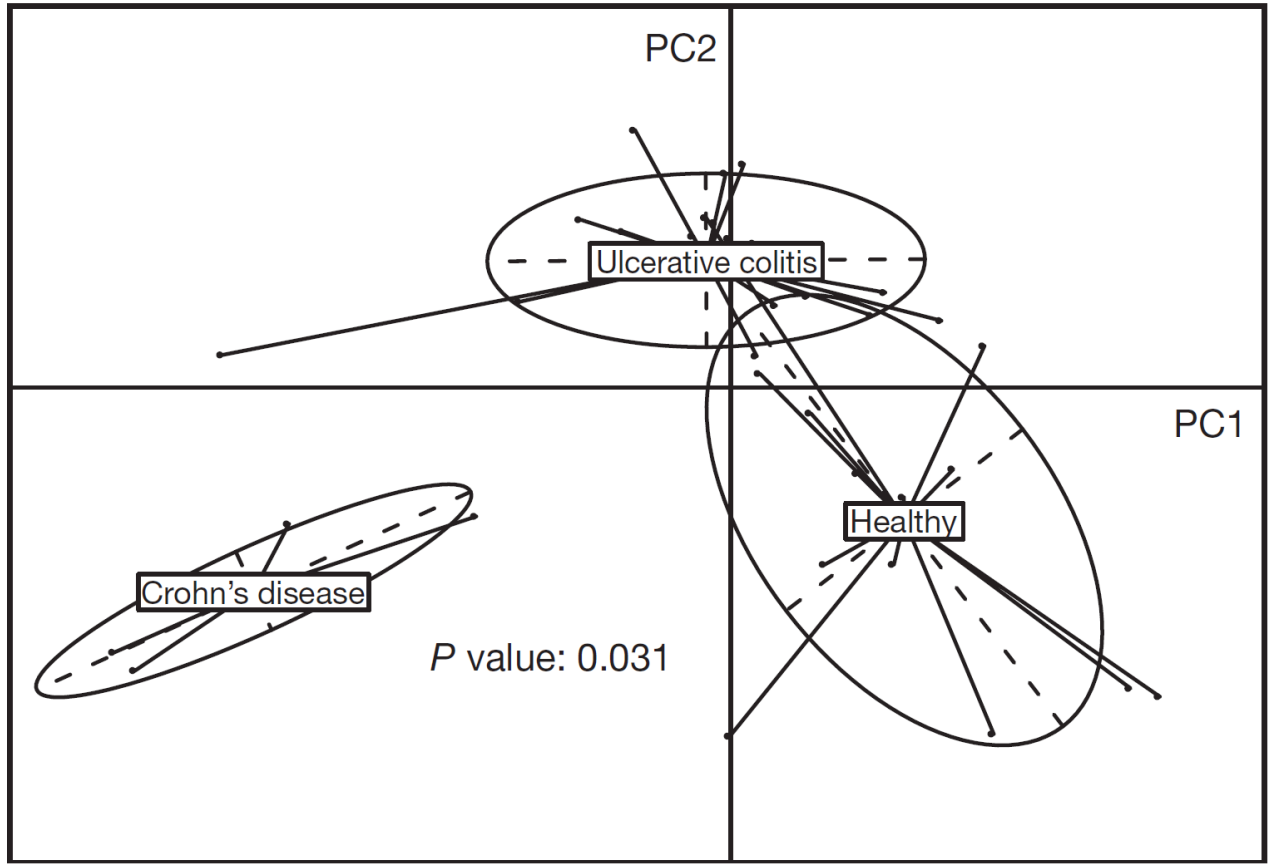
Bacterial species abundance differentiates IBD patients and healthy individuals



Microbial alterations

- Decreased richness
- Altered taxonomic profiles
- Altered metabolic output

Qin et al. 2010, Nature, 464(7285), 59-65

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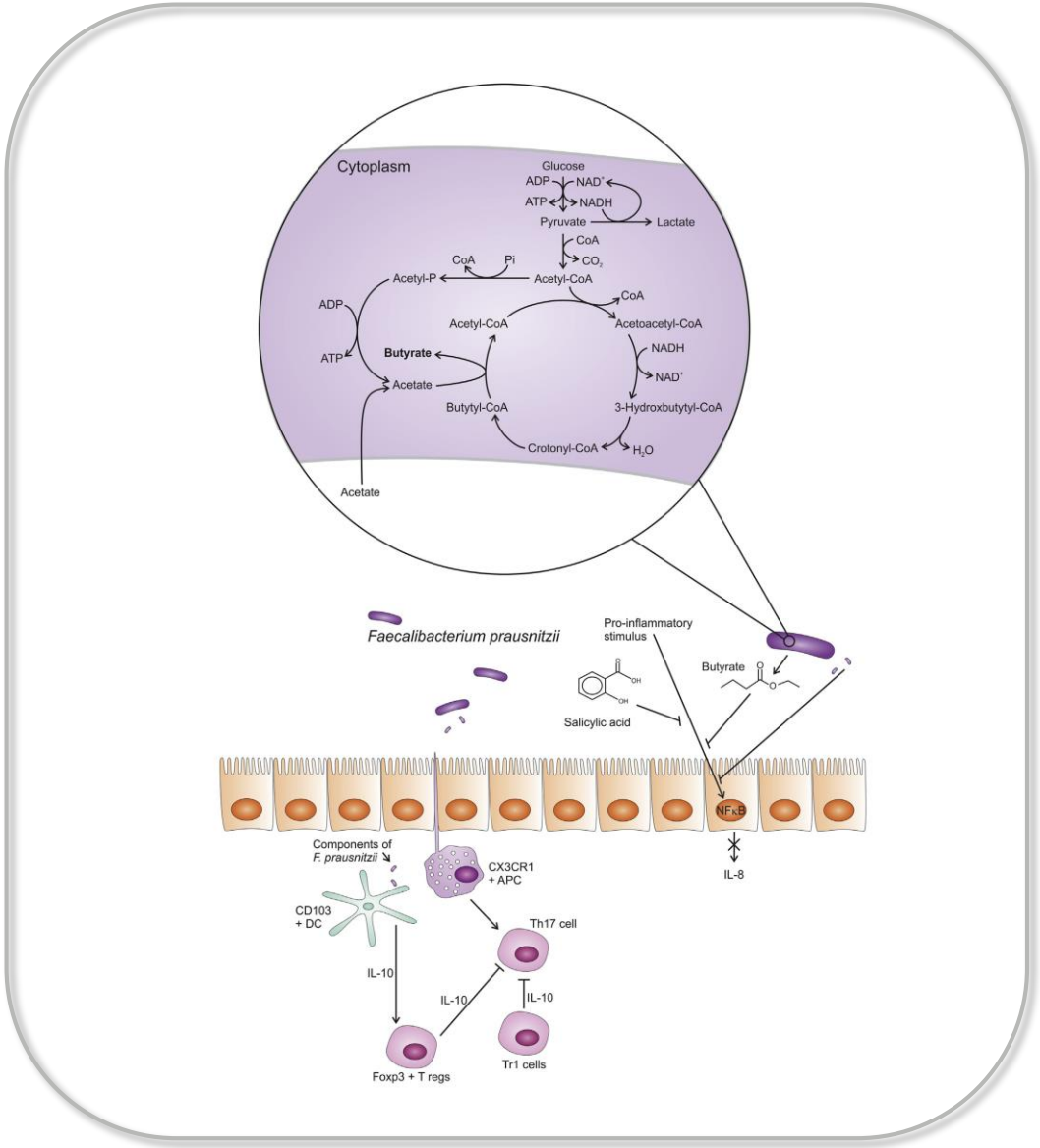
Anti-inflammatory activities by Faecalibacterium prausnitzii

- Represents around 5% of the total fecal microbiota in healthy adults
- Abundance decreased in IBD, IBS, colorectal cancer, obesity, celiac disease



- Extremely oxygen-sensitive
- Complicated to grow
- In animal studies *F.prausnitzii*
  - Inhibits symptoms in colitis models
  - Improve gut permeability
  - Decrease pain in restrained-stress model
- Mode of action
  - Active metabolites; Butyrate & Salicylic acid
  - Anti-inflammatory protein ”MAM”
  - Extracellular Polymeric Matrix, EPM

Ferreira-Halder et al. 2017, Best Pract & Res Clin Gastroenterol 31, 643; Martin et al. 2018, Front Microbiol, 9, 346

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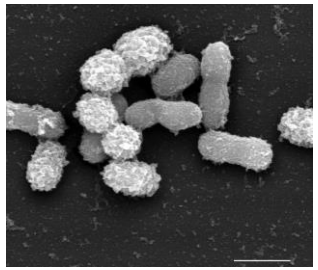

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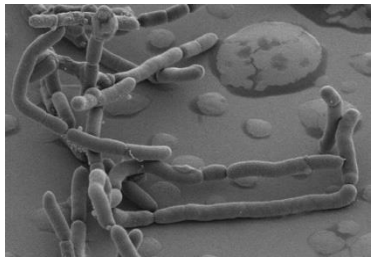

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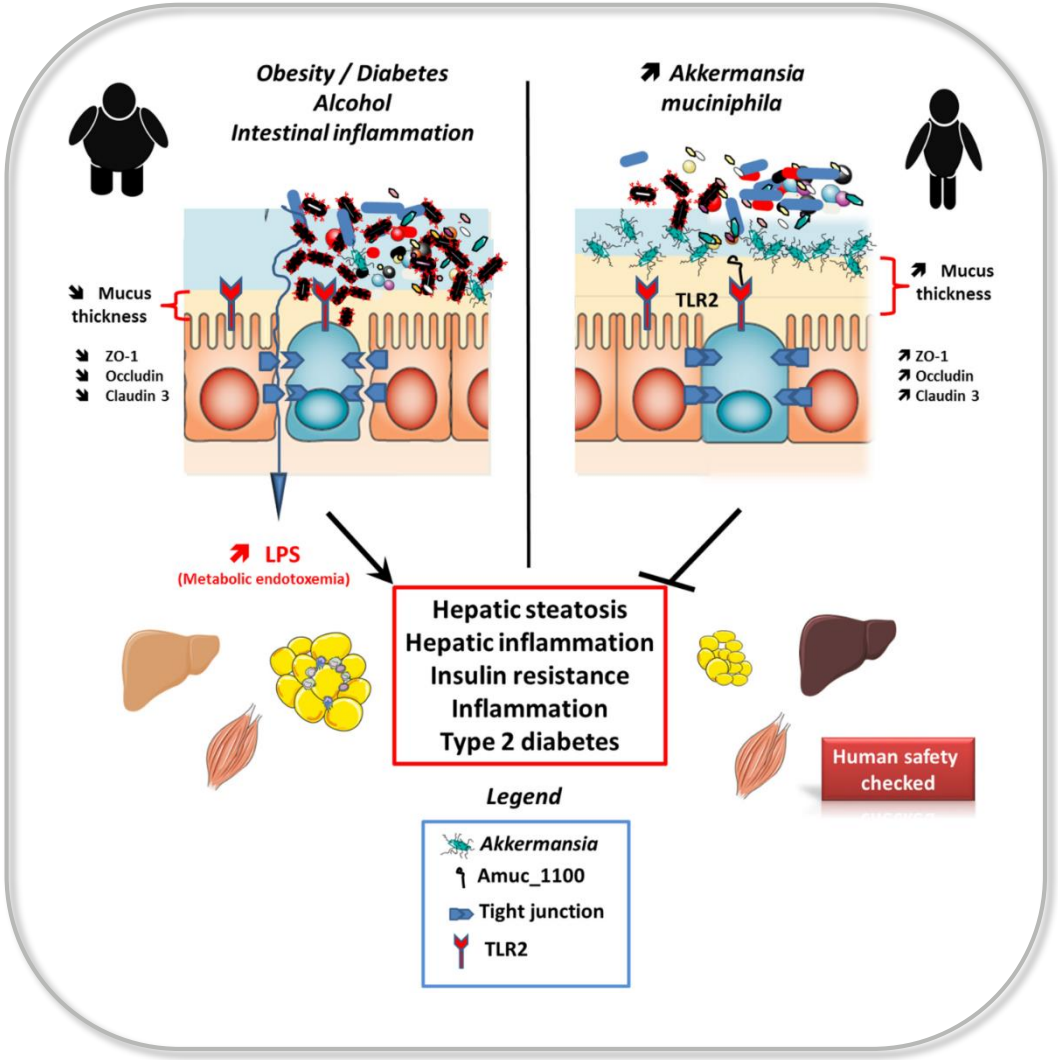
Metabolic health – *Akkermansia Municiphila*

- One of the most abundant single species in the human gut 0.5-5%
- Decreased abundance in obesity, T2D, IBD, hypertention, liver disease
- Antidiabetic medicine cause a significant increase in *A. municiphila* abundance



- Growth conditions complicated
  - Sensitive to O_2
  - Growth on mucin
- Daily administration of *A. municiphila* 2 x 10^8 bact/day partly protected against DIO in mice

Cani & de Vos, 2017, Frontiers in Microbiology, 8, 1765-

Next generation **probiotics**

Lactobacillus & bifidobacteria – still essential in many areas

- preterm babies
- infants
- vaginal health

Strict anaerobes

- Health related changes – cause or consequence???
- Often acknowledged due to decrease during disease conditions
- Not yet well characterized
- Stability is challenging
- Knowledge on survival through the GI tract is scarce
- Safety requirements (Generally Recognized As Safe, GRAS or Qualified Presumption of Safety, QPS)

FROM THE ANALYST'S COUCH

The human microbiome: opportunity or hype?

Pedro M. Valencia, Magali Richard, Jesse Brock and Elsy Boglioli

Nat Rev Drug Discov, (2017)12, 823-824


Keep it great!
with good bacteria in food
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Movie- *Bioprotection helps Keep food great !*


Bioprotection is a natural way to protect against spoilage and harmful contamination in food. This not only helps you to keep your products fresh and safe, it also helps you to build and protect your brand!
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Using nature’s good bacteria to ferment food is a traditional way to keep food fresh longer

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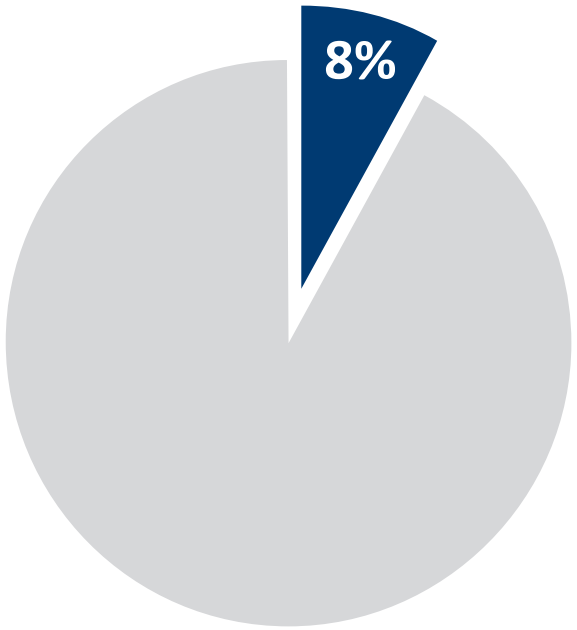
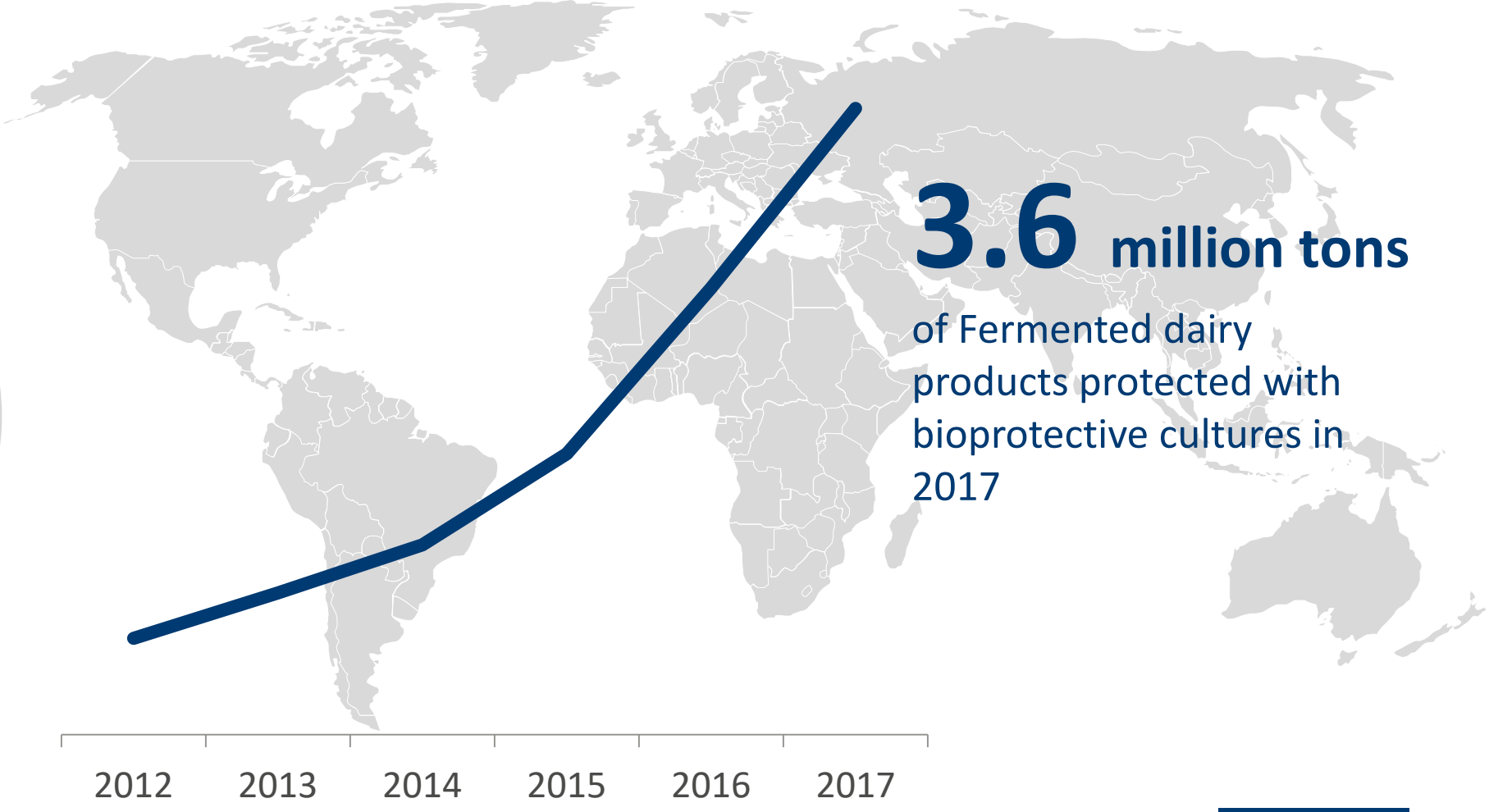
Use of bioprotective food cultures in dairy is growing rapidly worldwide





3.6 million tons

of Fermented dairy products protected with bioprotective cultures in 2017

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Keep it great!

Keep the label clean

If you improve quality and consistency the natural way. It adds to the appeal of the product. And help meet the consumer demand for products without artificial ingredients.

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Keep it great!

Keep it special

Bioprotective cultures help make sure consumers can enjoy the taste, goodness and quality of fermented dairy products, each and every time

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Keep it great! Make sure it stays the way you made it

A lot of things can happen after products leave the dairy. Bioprotective cultures can help secure quality throughout the value chain.

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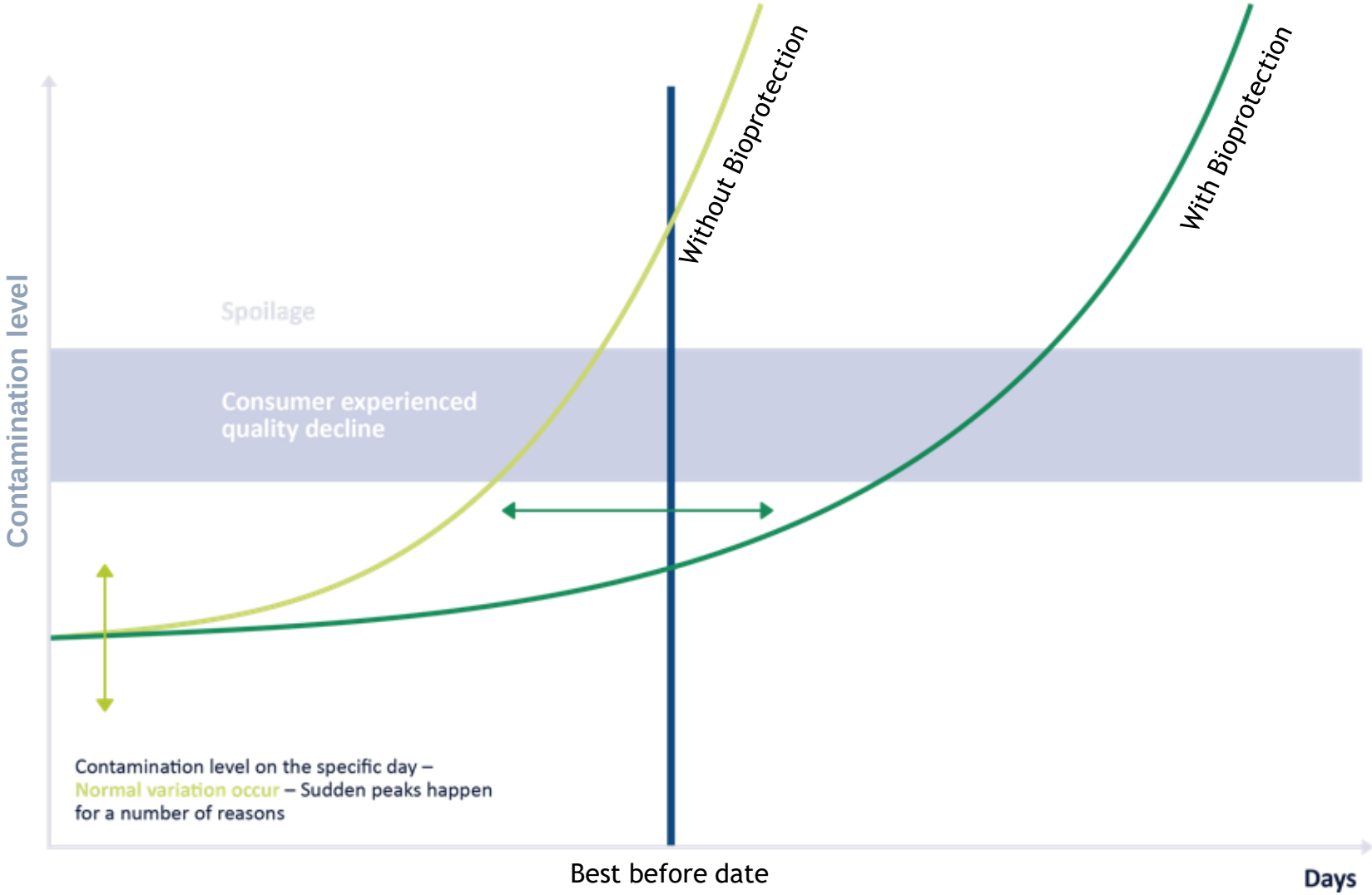
Food cultures can help enable **shelf life extension**



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Keep it great!
Reducing food waste in dairy with good bacteria
Wasted food is an economic and environmental burden. Use food cultures to keep products naturally fresh and safe throughout shelf life.
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The date is the biggest problem!

20%

of all dairy food is wasted globally

17% of all yogurt wasted in Europe

80%

Is due to date and shelf life related issues

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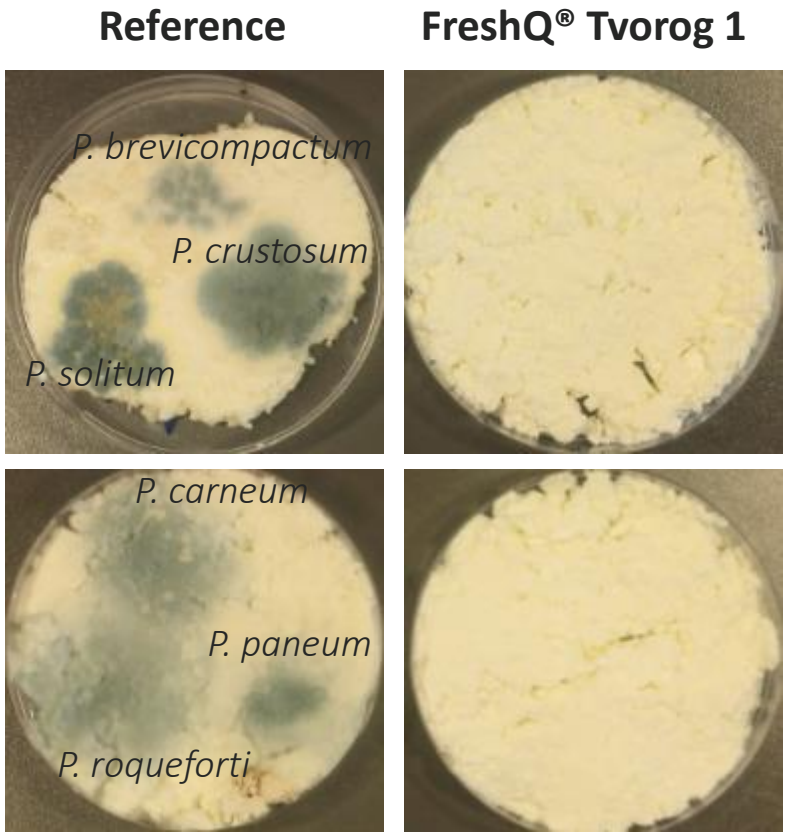
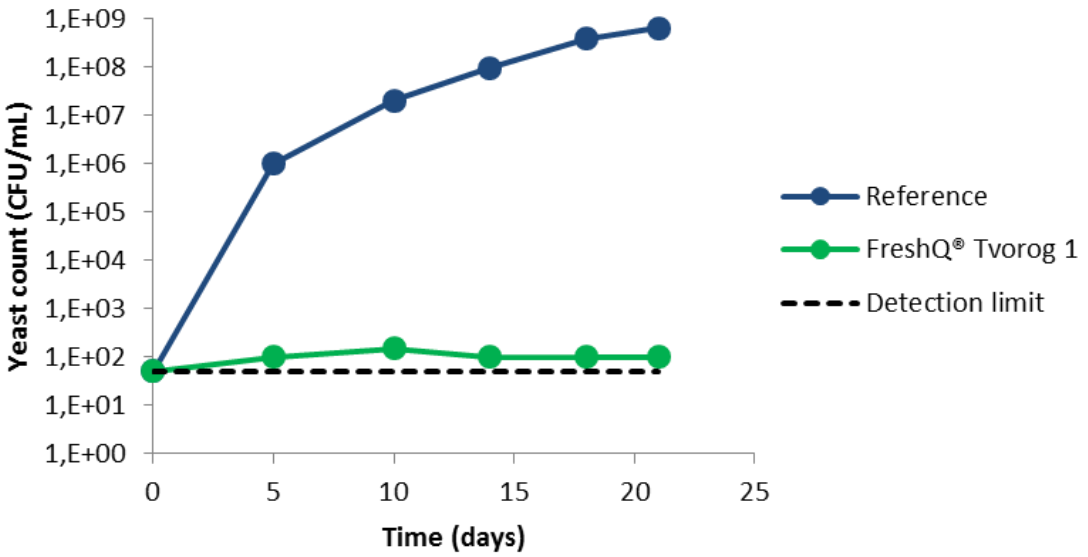
Bioprotective cultures delays outgrowth of molds and yeast in Tvorog



Example: Tvorog fermented with eXact® Fit 3 starter culture, with or without the addition of FreshQ®Tvorog 1 (50 U/T milk), added ***P. brevicompactum***, ***P. crustosum, P. solitum*** , ***P. carneum***, ***P. paneum*** and ***P. roqueforti*** (500 spores) and stored at 7˚C/45˚F for 28 days



Example: ***Debaryomyces hansenii*** (added at 50 cfu/g) in tvorog produced with eXact® Fit 3 starter culture, with and without addition of FreshQ® Tvorog 1 (50U/T milk) and stored at 7˚C/45˚F

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Thank you

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Everyday 1 billion people consume a Chr. Hansen product. Chr. Hansen develops and produces cultures, enzymes, probiotics, plant protection and natural colors for a rich variety of foods, confectionery, beverages, dietary supplements and even animal feed. We have done this since 1874 and have more than 2,800 dedicated innovative and technically skilled employees in over 30 countries.

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