

# Darmgezondheid: Gezondheid zit in de darmen

9:15 De darm binnenstebuiten

Prof. Ger Rijkers  
*University College Roosevelt*

# Darmgezondheid: Gezondheid zit in de darmen

WHO definition of Health

**Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity.**



*Preamble to the Constitution of the World Health Organization as adopted by the International Health Conference, New York, 19-22 June, 1946; signed on 22 July 1946 by the representatives of 61 States (Official Records of the World Health Organization, no. 2, p. 100) and entered into force on 7 April 1948.*

This Definition has not been amended since 1948.

## ANALYSIS

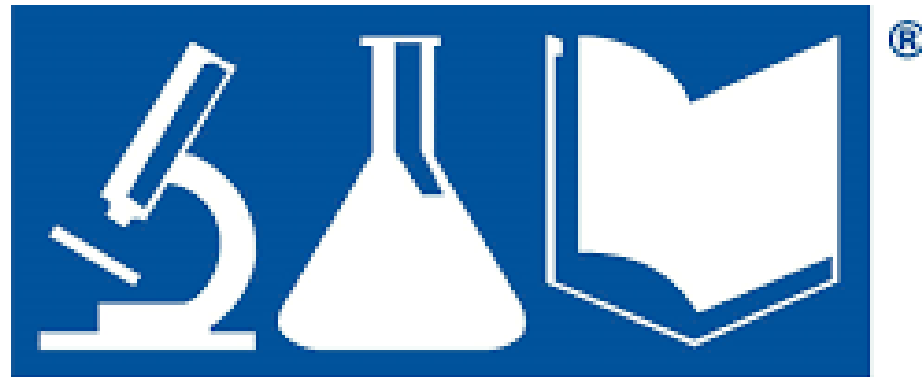
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### How should we define health?

The WHO definition of health as complete wellbeing is no longer fit for purpose given the rise of chronic disease. **Machteld Huber and colleagues** propose changing the emphasis towards the ability to adapt and self manage in the face of social, physical, and emotional challenges

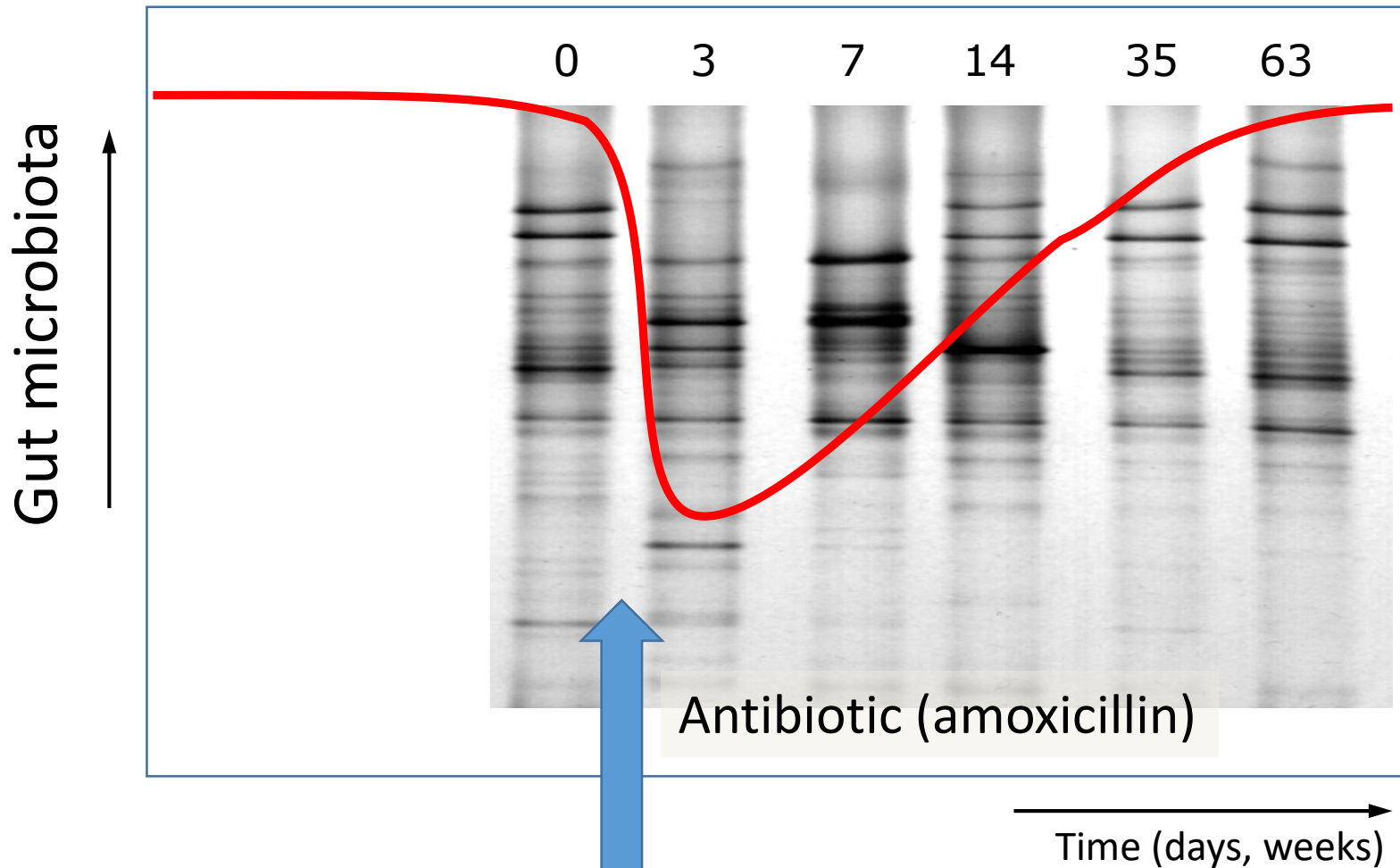
Machteld Huber *senior researcher*<sup>1</sup>, J André Knottnerus *president, Scientific Council for Government Policy*<sup>2</sup>, Lawrence Green *editor in chief, Oxford Bibliographies Online—public health*<sup>3</sup>, Henriëtte van der Horst *head*<sup>4</sup>, Alejandro R Jadad *professor*<sup>5</sup>, Daan Kromhout *vice president, Health Council of the Netherlands*<sup>6</sup>, Brian Leonard *professor*<sup>7</sup>, Kate Lorig *professor*<sup>8</sup>, Maria Isabel Loureiro *coordinator for health promotion and protection*<sup>9</sup>, Jos W M van der Meer *professor*<sup>10</sup>, Paul Schnabel *director*<sup>11</sup>, Richard Smith *director*<sup>12</sup>, Chris van Weel *head*<sup>13</sup>, Henk Smid *director*<sup>14</sup>

the ability to adapt and to self manage.



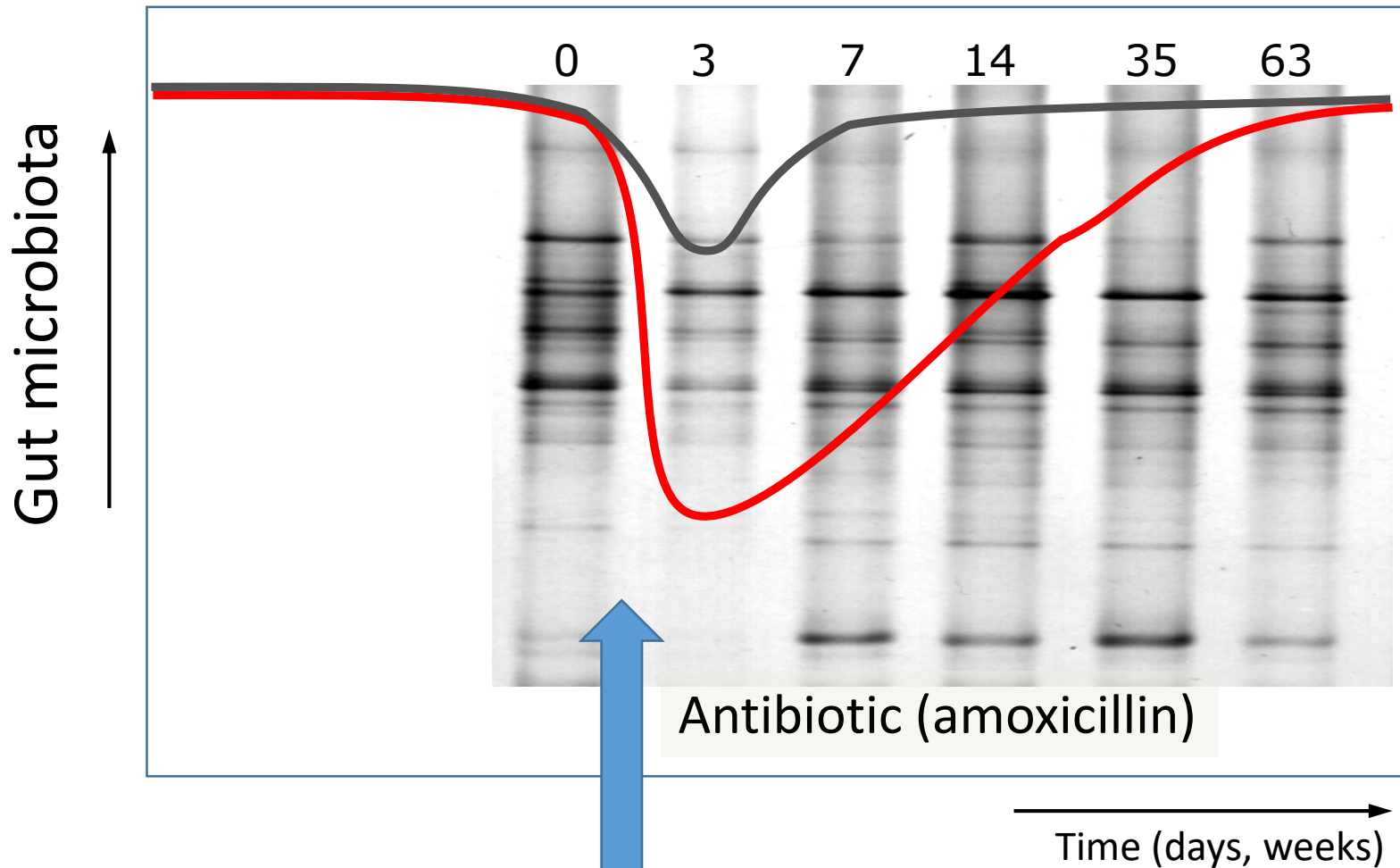
**ADAPT**  
INTERNATIONAL

# Maintaining Health Readjust (homeostasis)



# Maintaining Health Readjust (homeostasis)

\*Probiotics: *B. bifidum*, *B. lactis*, *B. longum*, *E. faecium*, *L. rhamnosus*, *L. paracasei*,  
*L. plantarum* (2x), *L. acidophilus* (2x)



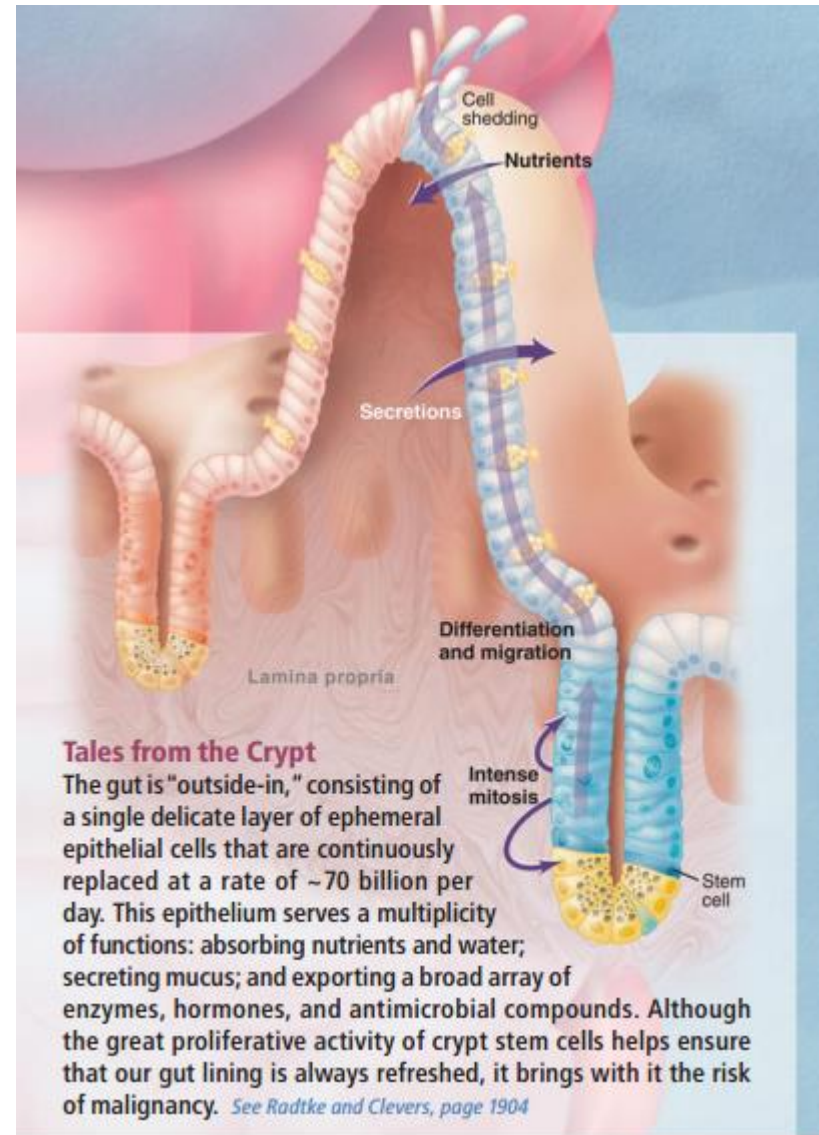
25 March 2005

# Science

Vol. 307 No. 5717  
Pages 1421-2016 \$10

The Gut  
**INNER  
TUBE  
OF LIFE**

# Inner Tube of Life



## Tales from the Crypt

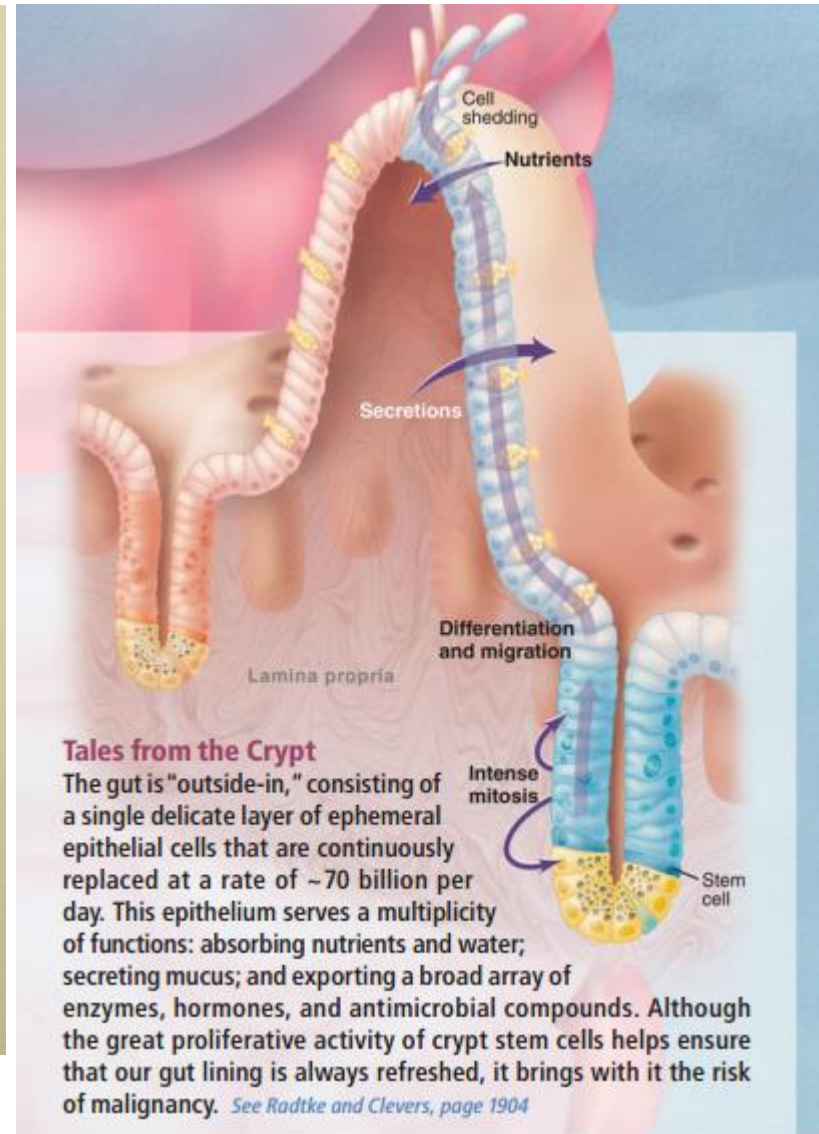
The gut is "outside-in," consisting of a single delicate layer of ephemeral epithelial cells that are continuously replaced at a rate of ~70 billion per day. This epithelium serves a multiplicity of functions: absorbing nutrients and water; secreting mucus; and exporting a broad array of enzymes, hormones, and antimicrobial compounds. Although the great proliferative activity of crypt stem cells helps ensure that our gut lining is always refreshed, it brings with it the risk of malignancy. *See Radtke and Clevers, page 1904*



# Inside Out

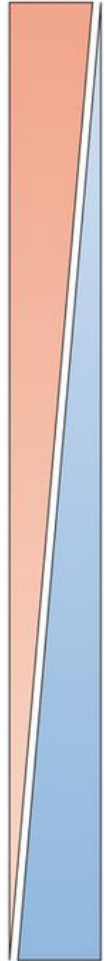


The beauty of art is to show something that is not really possible. Sjaak Sinnige



### Metabolites

Vitamin A and AHR ligands

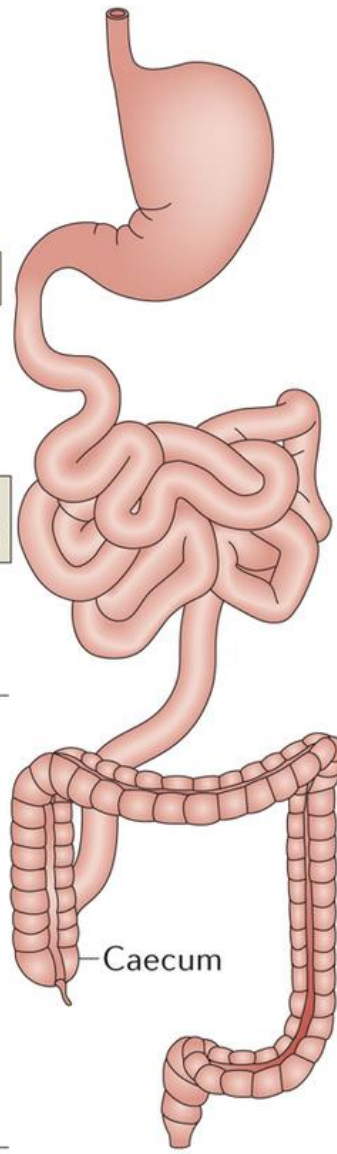


SCFAs

Lactobacilli

- Lactobacilli
- Streptococci

- Clostridia
- Enterobacteria
- Enterococcus
- *E. faecalis*
- Bacteroides
- Bifidobacteria
- Fusobacteria
- Lactobacilli
- Peptococci
- Peptostreptococci
- Prevotellaceae
- Roseburia
- Ruminococci
- Verrucomicrobia



Stomach

Microbial load per ml

$10^2$  to  $10^3$

Duodenum

$<10^5$

Jejunum

Ileum

$10^3$  to  $10^7$

Colon with caecum and appendix

$10^9$  to  $10^{12}$

A vibrant yellow background is filled with a dense, colorful collage of various microscopic organisms, including bacteria, viruses, and cells, creating a complex and dynamic visual texture. The organisms are rendered in shades of blue, green, purple, and brown, with some appearing as elongated rods, others as spherical cells, and some as thin, filamentous structures.

# SCIENTIFIC AMERICAN

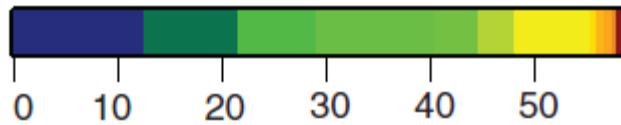
June 2012

ScientificAmerican.com

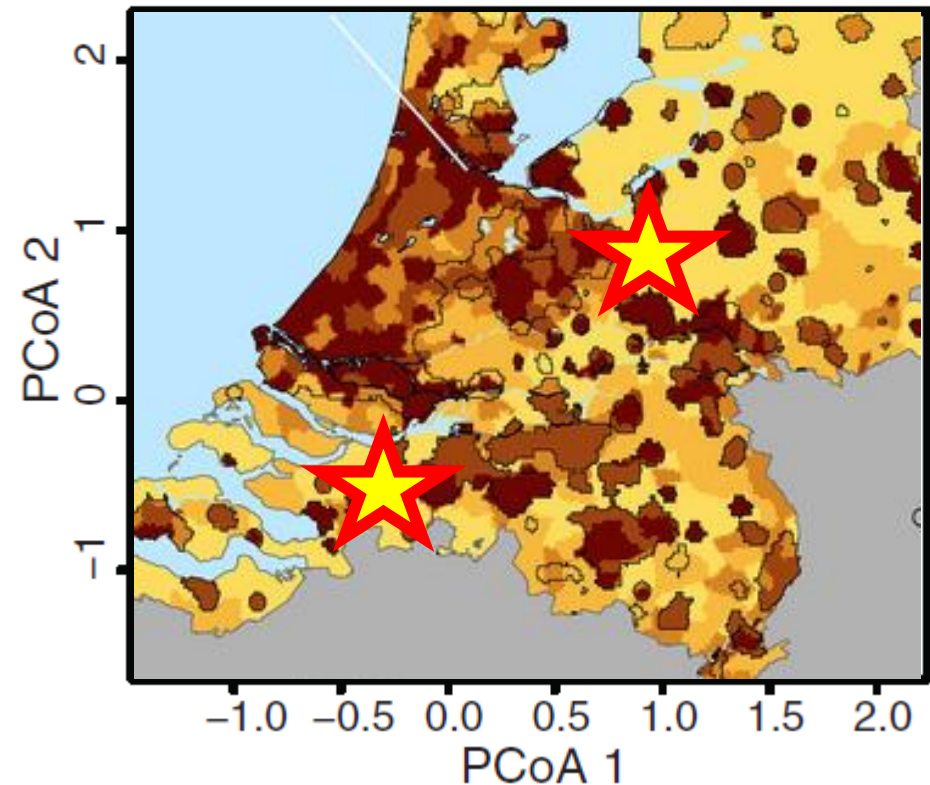
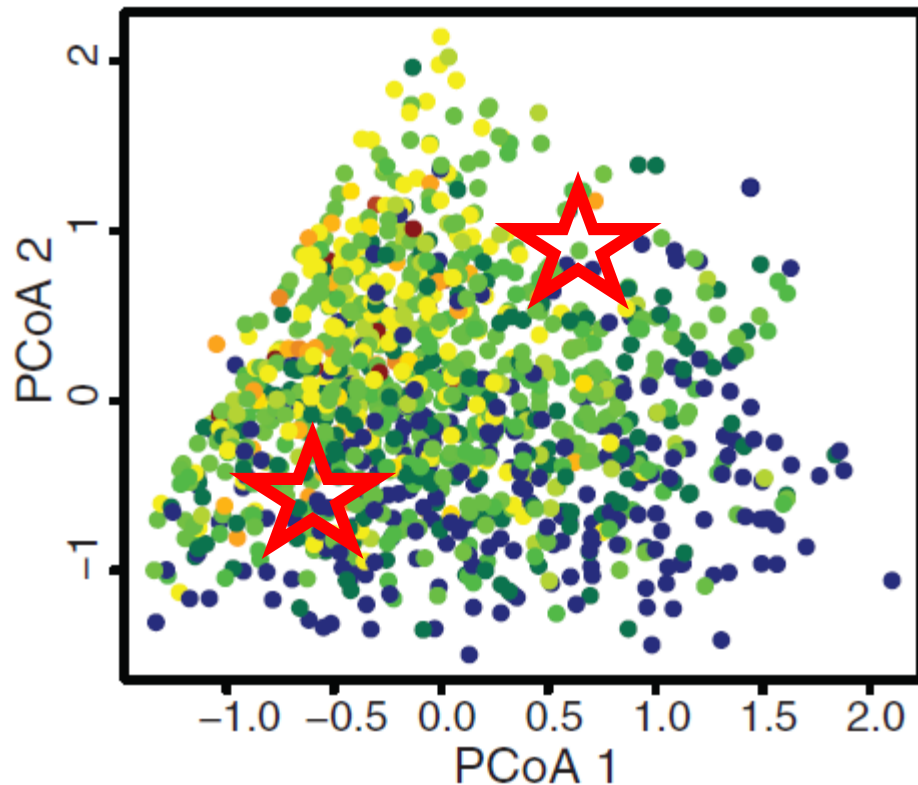
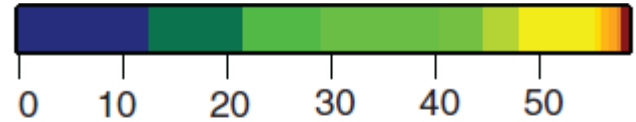
# Your Inner Ecosystem

# we're all different

Abundance of Bacteroidetes



Abundance of Homo sapiens



# HOW DO WE GET OUR MICROBIOME?

## BIRTH:

A newborn gets its microbes from:

- ▲ its mother's birth canal
- ▲ skin of its mother and other caregivers



## BREAST MILK:

Breast milk has been fine-tuned over millions of years to provide:

- ▲ nutrients, vitamins, and antibodies
- ▲ diverse microbes to populate the baby's gut



## ENVIRONMENT:

For the rest of the baby's life, it will continuously encounter new microbes from:

- ▲ soil and water
- ▲ people, pets, plants
- ▲ new and diverse foods



▲ skin of its mother and other caregivers



# SCIENTIFIC REPORTS



OPEN

## Intestinal colonisation patterns in breastfed and formula-fed infants during the first 12 weeks of life reveal sequential microbiota signatures

Received: 8 March 2017

Accepted: 6 July 2017

Published online: 16 August 2017

Harro M. Timmerman<sup>1</sup>, Nicole B. M. M. Rutten<sup>2</sup>, Jos Boekhorst<sup>1</sup>, Delphine M. Saulnier<sup>1,7</sup>, Guus A. M. Kortman<sup>1</sup>, Nikhat Contractor<sup>3,8</sup>, Martin Kullen<sup>3,9</sup>, Esther Floris<sup>1</sup>, Hermie J. M. Harmsen<sup>5</sup>, Arine M. Vlieger<sup>2</sup>, Michiel Kleerebezem<sup>1,6</sup> & Ger T. Rijkers<sup>2,4</sup>



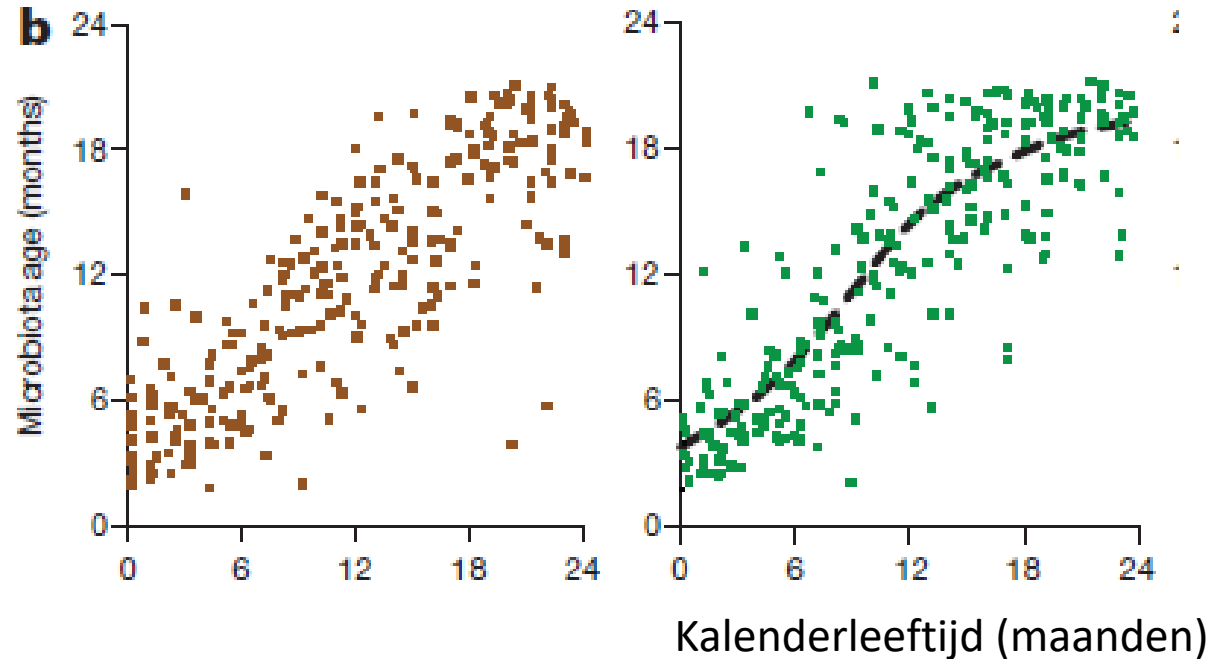
# Normal development gutmicrobiota

**a**

Rank	OTU ID	Taxonomic annotation
1	326792	<i>Faecalibacterium prausnitzii</i>
2	189827	<i>Ruminococcus</i> sp. 5 1 39BFAA
3	470663	<i>Lactobacillus ruminis</i>
4	191687	<i>Dorea longicatena</i>
5	72820	<i>Bifidobacterium longum</i>
6	194745	<i>Ruminococcus</i> sp. 5 1 39BFAA
7	15141	<i>Lactobacillus mucosae</i>
8	561483	<i>Bifidobacterium</i> sp.
9	217996	<i>Staphylococcus</i> sp.
10	364234	<i>Ruminococcus</i> sp. 5 1 39BFAA
11	287510	<i>Catenibacterium mitsuokai</i>
12	261912	<i>Dorea formicigenerans</i>
13	361809	<i>Ruminococcus torques</i>
14	108747	<i>Streptococcus thermophilus</i>
15	533785	<i>Bifidobacterium</i> sp.
16	9514	<i>Haemophilus parainfluenzae</i>
17	561636	<i>Streptococcus</i> sp.
18	312461	<i>Clostridium</i> sp.
19	470139	<i>Clostridium ramosum</i>
20	181834	<i>Clostridium</i> sp.
21	148099	<i>Weissella cibaria</i>
22	469873	<i>Bifidobacterium</i> sp.
23	185951	<i>Clostridiales</i> sp.
24	212619	<i>Ruminococcaceae</i> sp.

Increasing importance in accuracy of model

**b**





The whole world is reading  
pirated papers pp. 497 & 508

Neurochemistry of sleeping  
and waking pp. 517 & 550

Halogenated olefins  
via the *E* train p. 569

# Science

\$15  
29 APRIL 2016  
sciencemag.org

AAAS



**SPECIAL ISSUE**  
**MICROBIOTA**  
**AT WORK**

## Figure 1. Some Functions of the Gut Microbiota and Disease Associations.

### Influences

Immune maturation  
and homeostasis  
Host cell proliferation  
Vascularization  
Neurologic signaling  
Pathogen burden  
Intestinal endocrine  
functions  
Bacterial diversity  
Energy biogenesis

### Biosynthesis

Vitamins  
Steroid hormones  
Neurotransmitters

### Metabolism

Branched-chain and  
aromatic amino acids  
Dietary components  
Bile salts  
Drugs  
Xenobiotics



obesity

# American style diet



**Figure 1. Some Functions of the Gut Microbiota and Disease Associations.**

Neurologic  
Psychiatric  
Respiratory  
Cardiovascular  
Gastrointestinal  
Hepatic  
Autoimmune  
Metabolic  
Oncologic

Ellen Blaak

Luc Colemont

# Gut/brain axis and the microbiota

## Brain–Gut–Bone Marrow Axis

Implications for Hypertension and Related Therapeutics

### Microbiota-gut-brain axis and the central nervous system

Acne vulgaris, probiotics and the gut-brain-skin axis - back to the future?

Emerging pathogenic links between microbiota and the gut–lung axis

**Gut-liver axis: gut microbiota in shaping hepatic innate immunity**

Comparative effects of intraduodenal fat and glucose on the gut-incretin axis

**The gut–kidney axis in IgA nephropathy: role of microbiota and diet on genetic predisposition**

**KEYWORDS:** Athletic performance; Gut-muscle-axis; Probiotics; Protein utilization; Sports nutrition

PubMed ▾

"gut immune axis" |



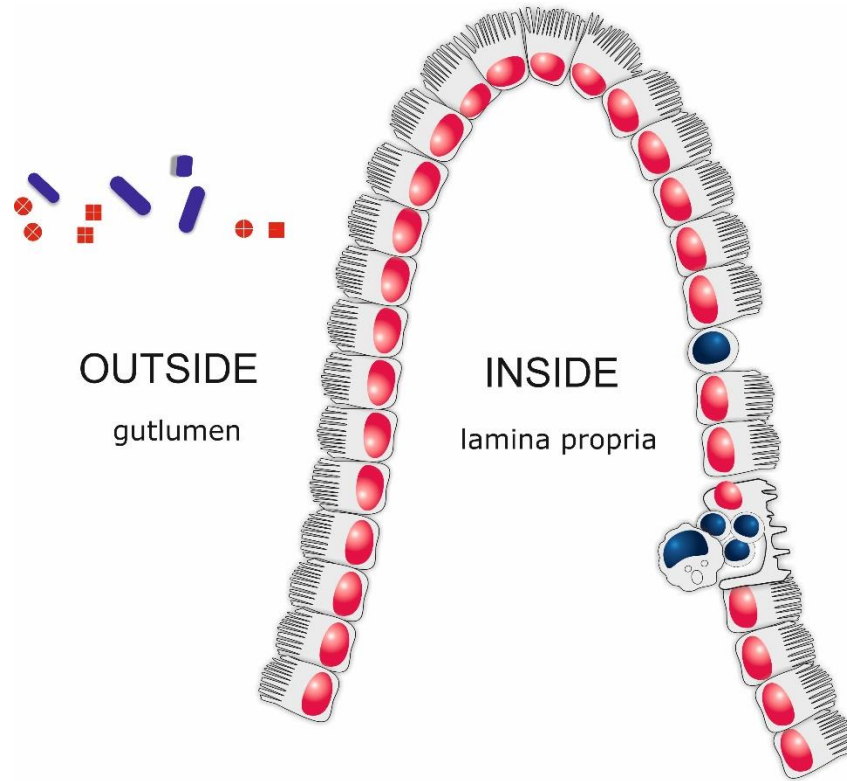
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# Mucosal dilemmas



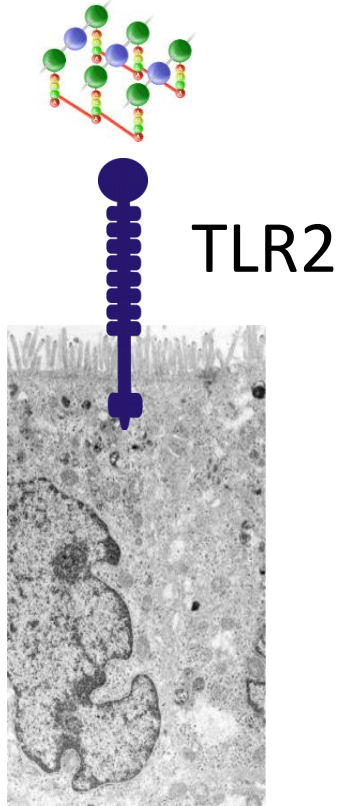
recognize and attack: response

recognize and do not attack: tolerance

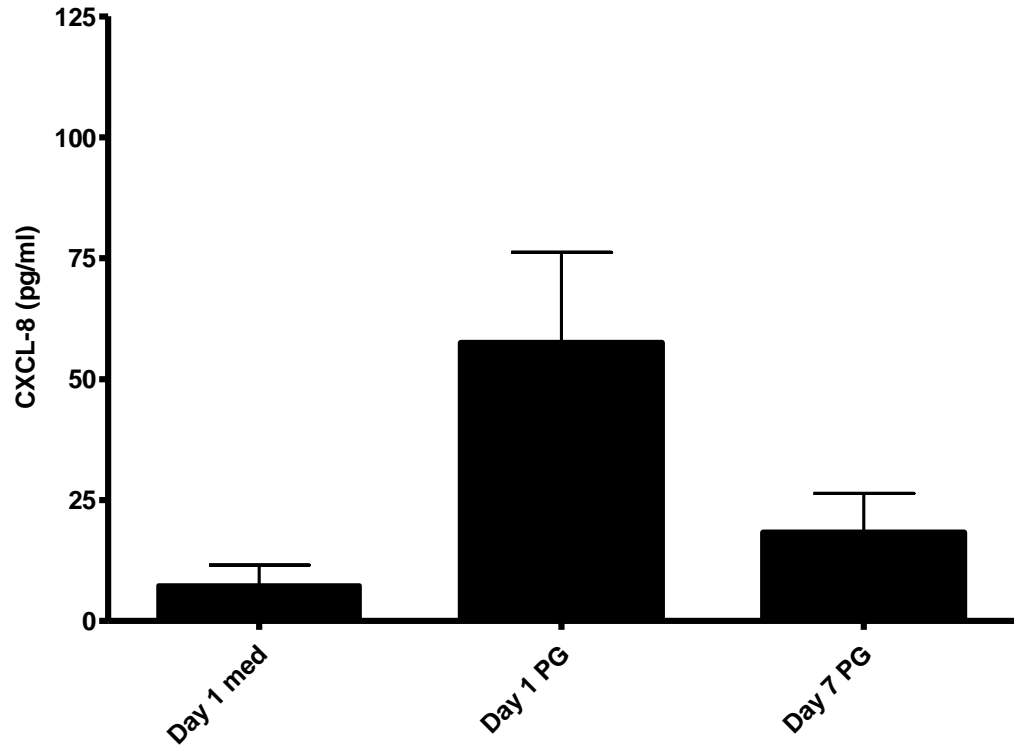


# Neonatal tolerance

Peptidoglycan

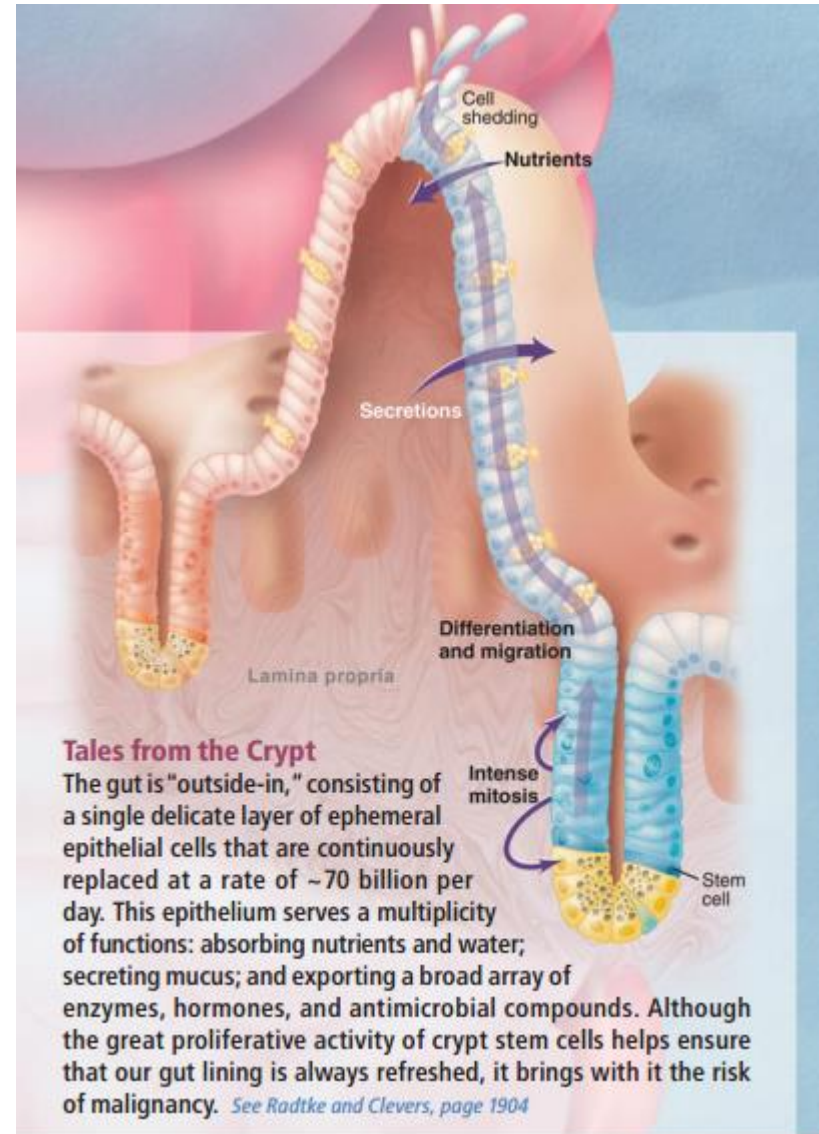


↓  
CXCL8  
IL-8

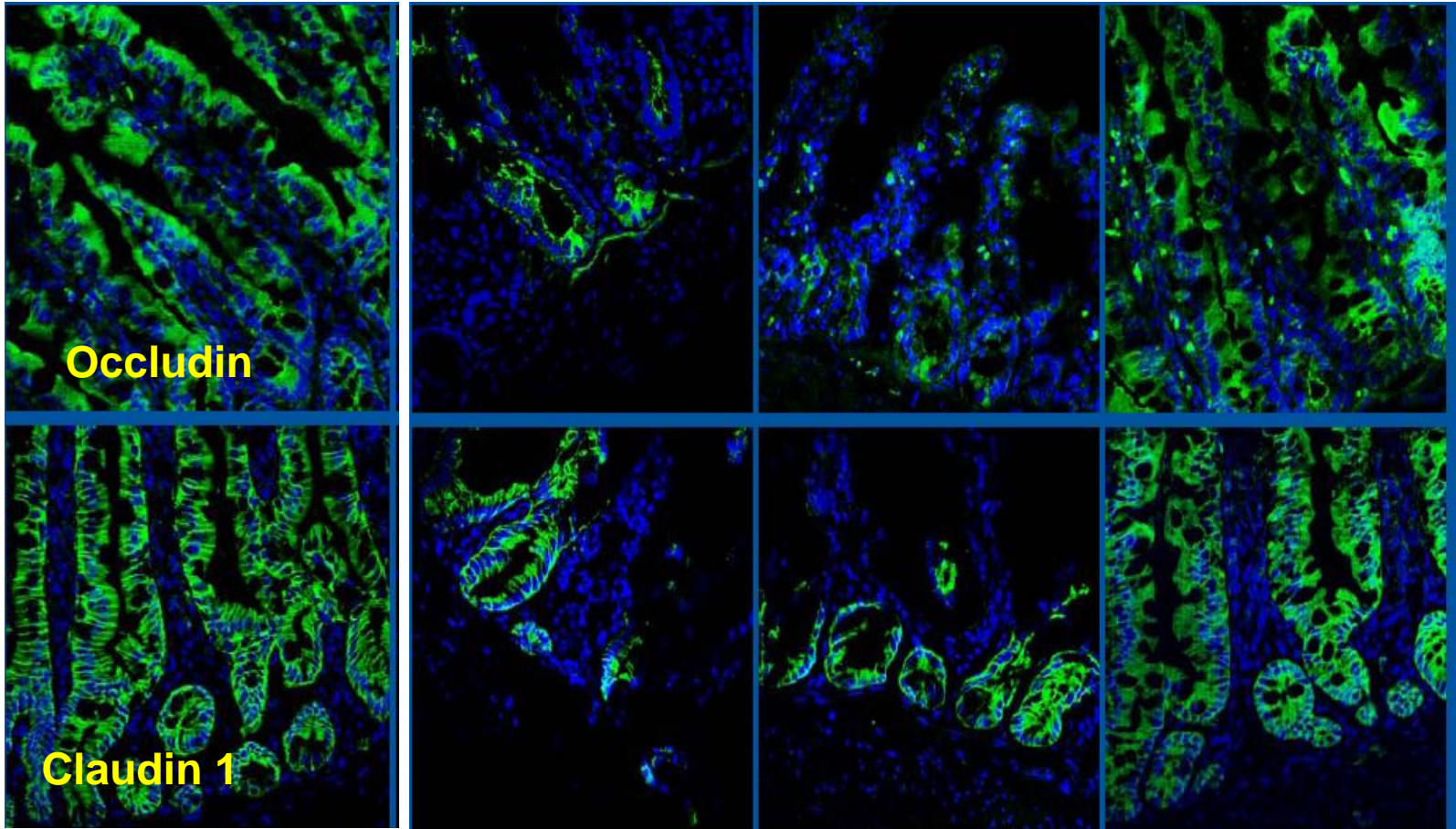


*Data Edward Nieuwenhuis*

# Inner Tube of Life



# maintenance of gut barrier integrity



Occludin

Claudin 1

Coldwater stress	-	+	+	+
Multispecies probiotics	-	-	placebo	+

# inflammatoire darmziekten

**Aanvallen**

buiten

voeding

bacterien

**Inflammatie**

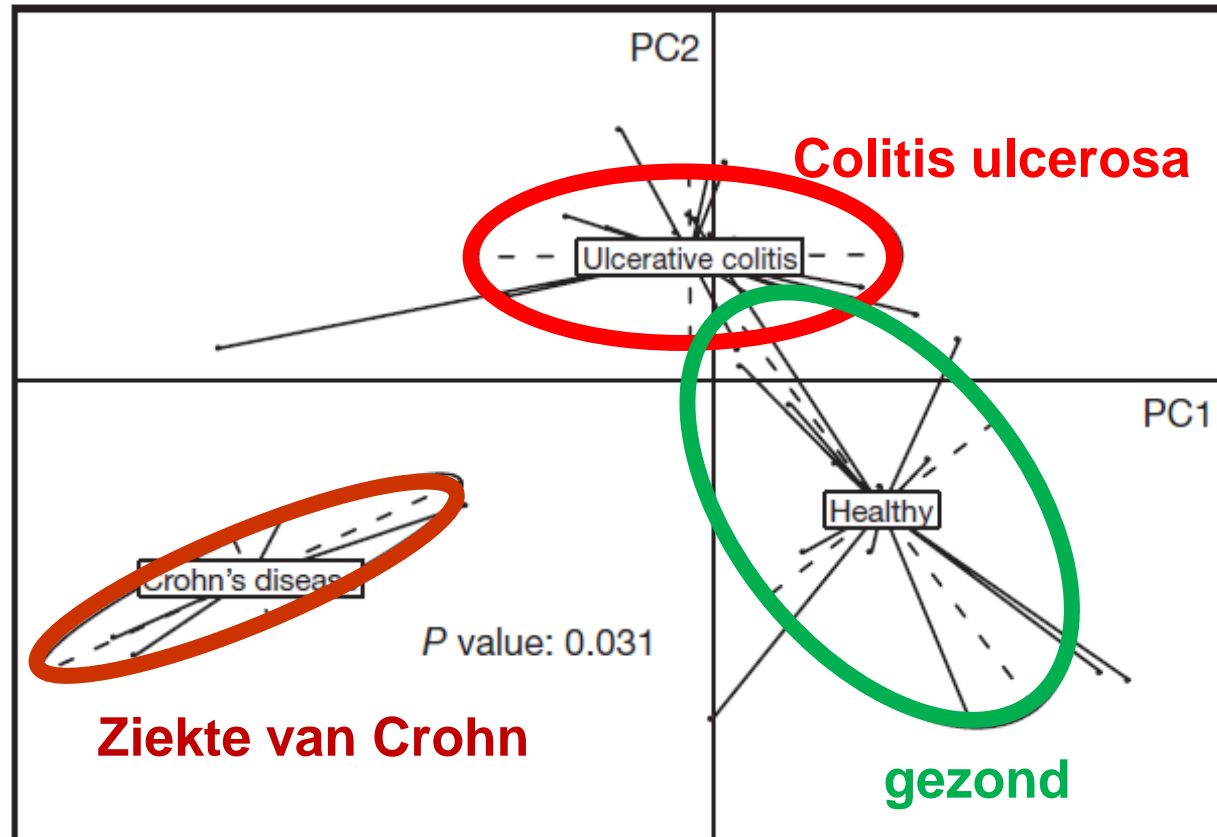


binnen

**Verdedigen**

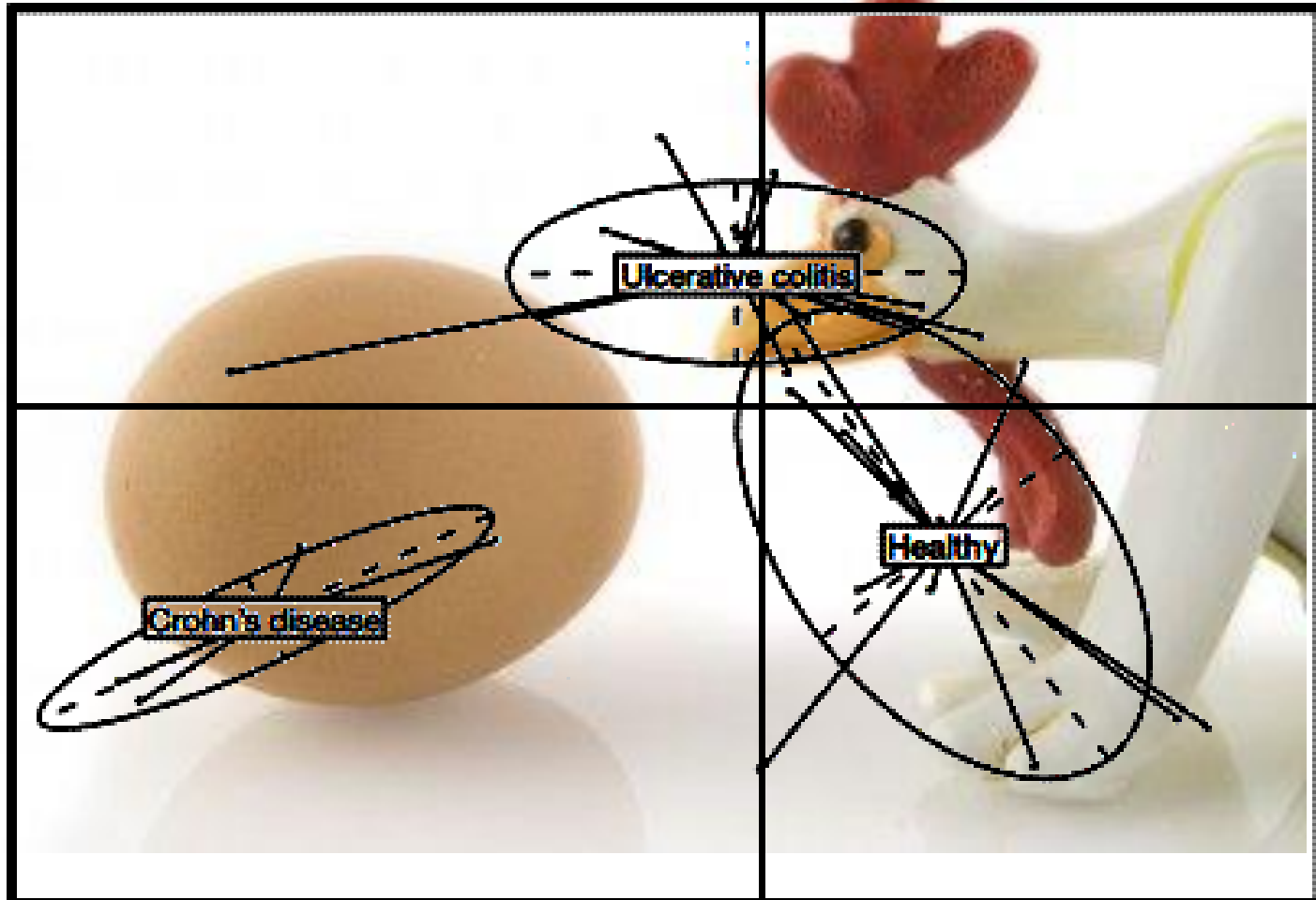
Mucosaal immuunsysteem

# inflammatoire darmziekten

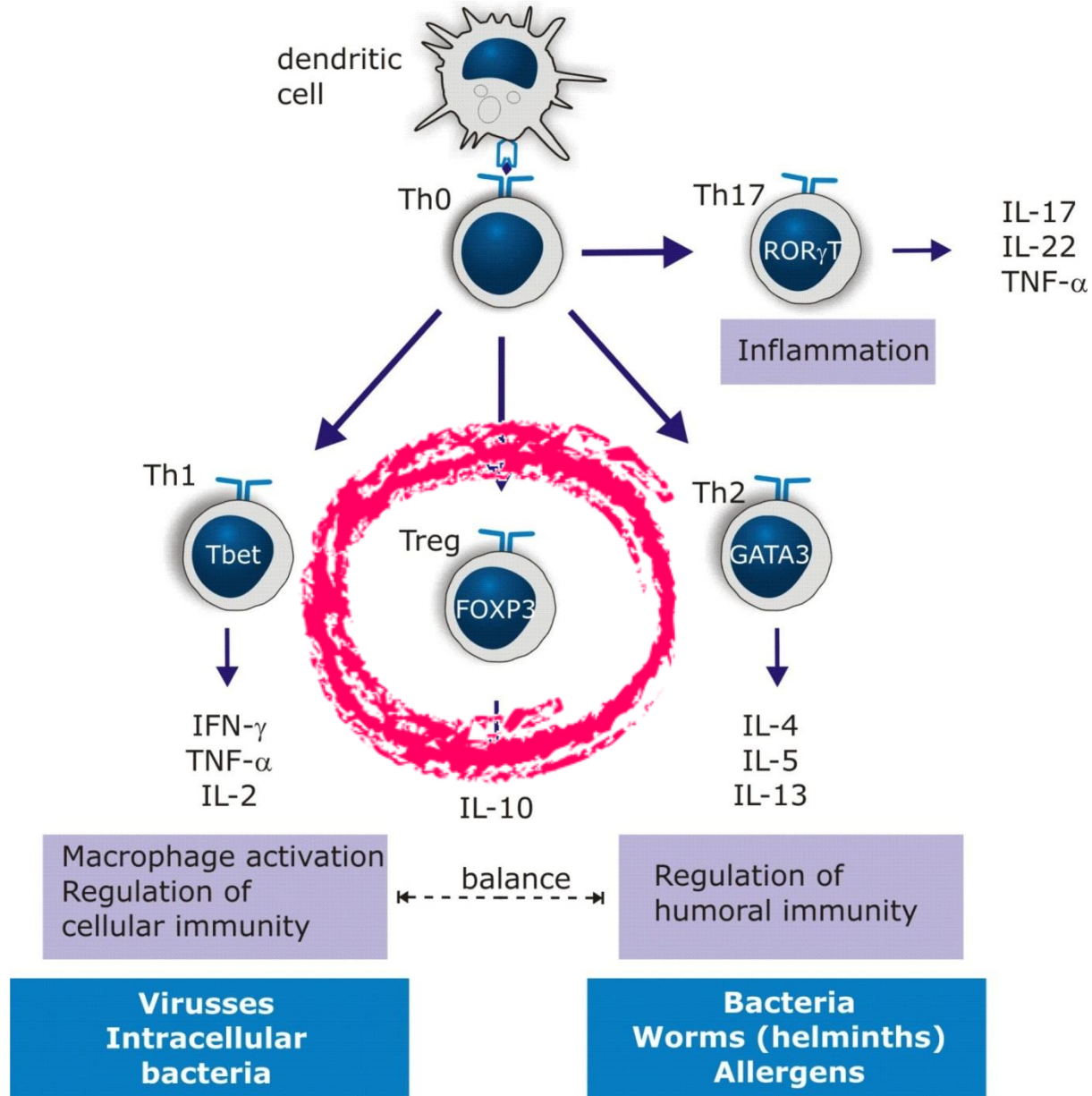


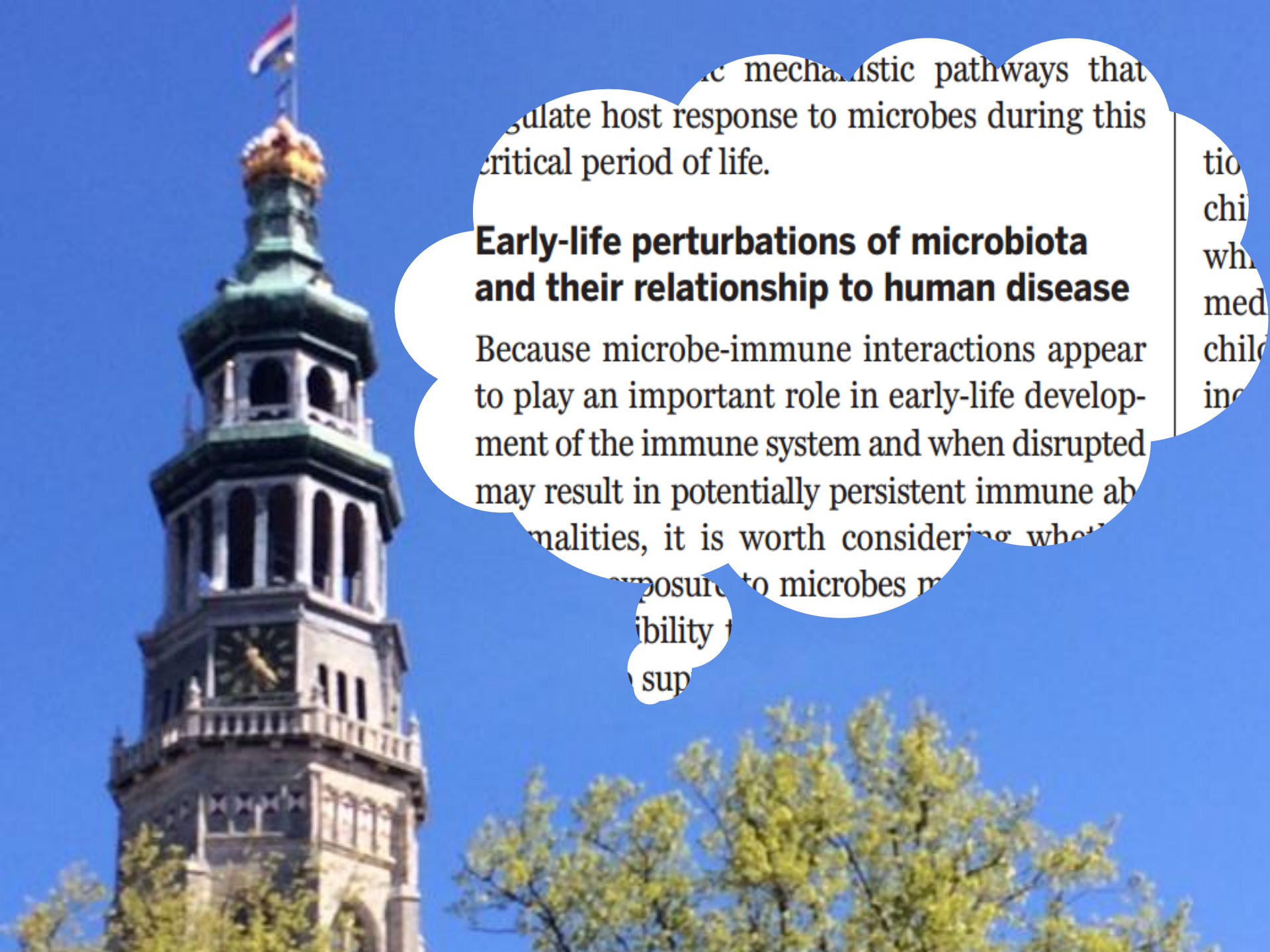
**Figure 4 | Bacterial species abundance differentiates IBD patients and healthy individuals.** Principal component analysis with health status as

# inflammatoire darmsziekten



# Mucosale immuunsysteem in de darm





...mechanistic pathways that regulate host response to microbes during this critical period of life.

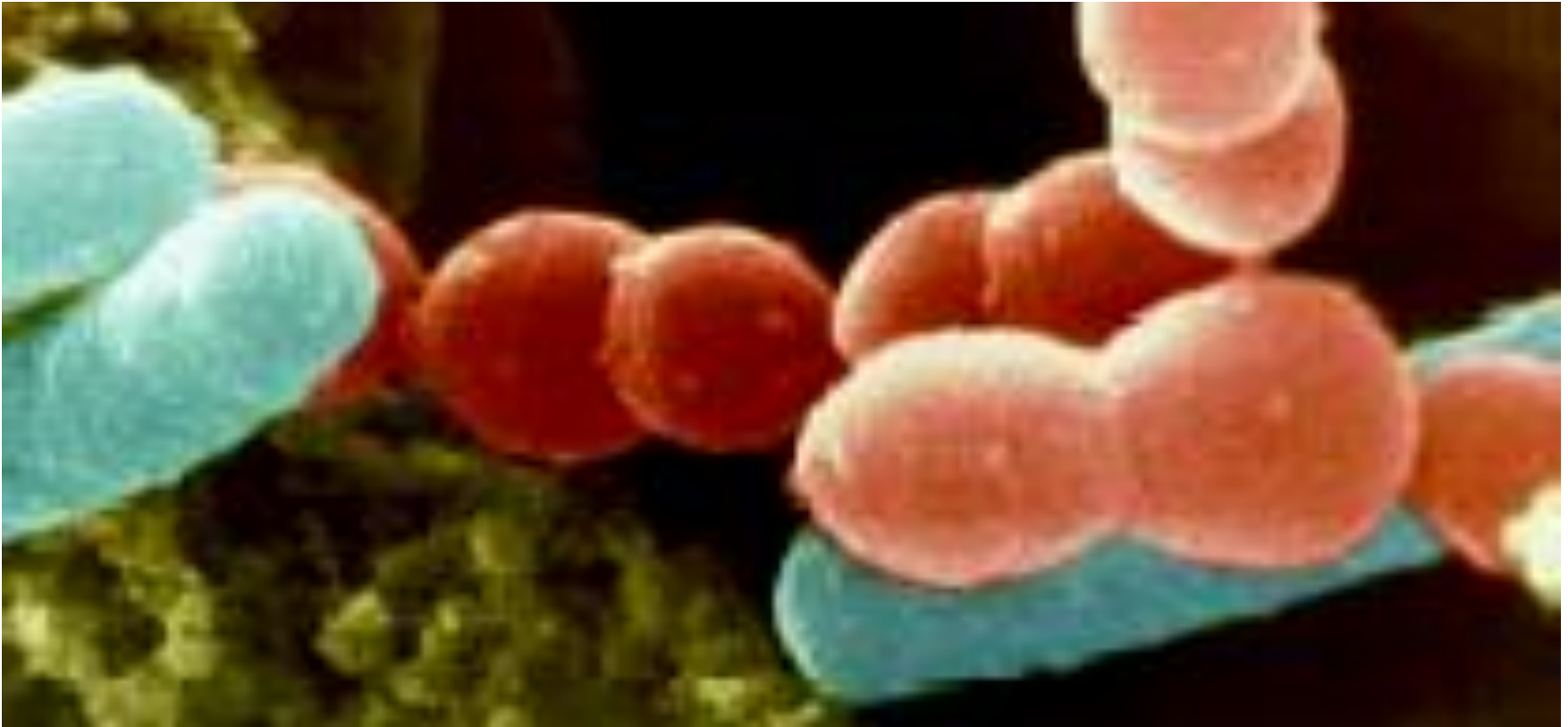
### **Early-life perturbations of microbiota and their relationship to human disease**

Because microbe-immune interactions appear to play an important role in early-life development of the immune system and when disrupted may result in potentially persistent immune abnormalities, it is worth considering whether exposure to microbes may influence the ability to suppress

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child  
wh  
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child  
inc



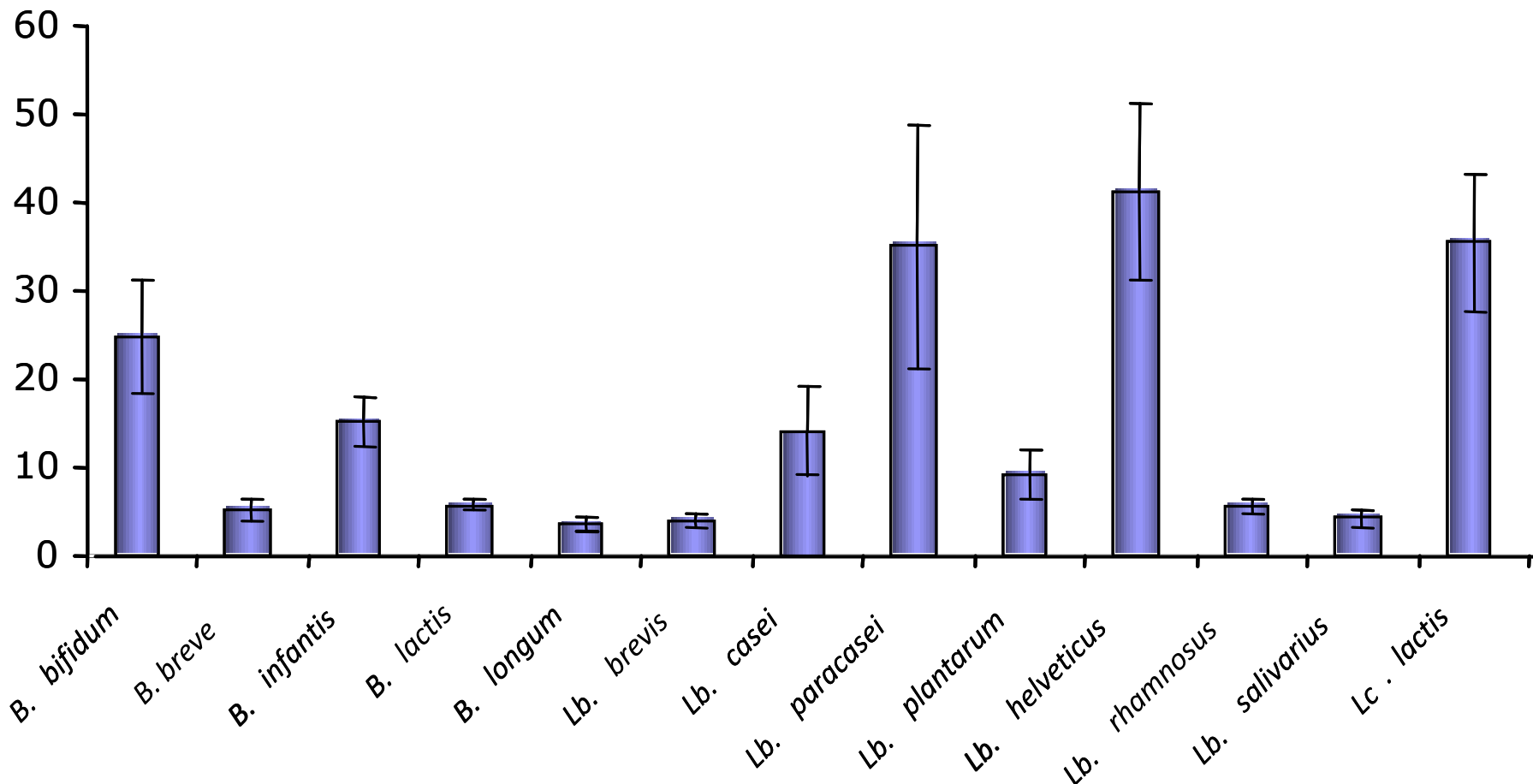
# Probiotics



“live microorganisms that, when administered in adequate amounts, confer a health benefit on the host”

Hill, C. *et al. Nat. Rev. Gastroenterol. Hepatol.* advance online publication 10 June 2014;

# Induction of regulatory T cells by probiotics

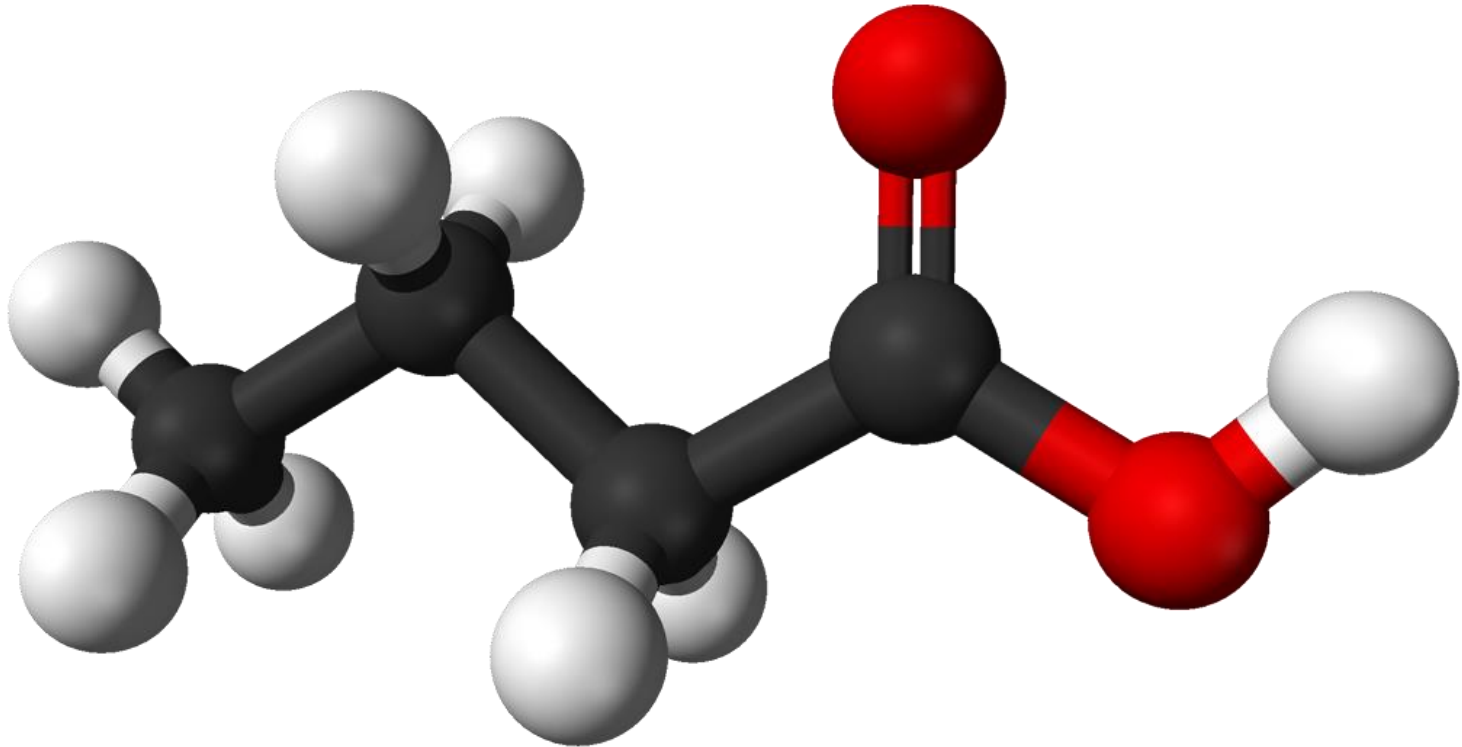


*Clin Exp Allergy*. 2010 Jan;40(1):103-10.

*Lactic acid bacteria differ in their ability to induce functional regulatory T cells in humans.*

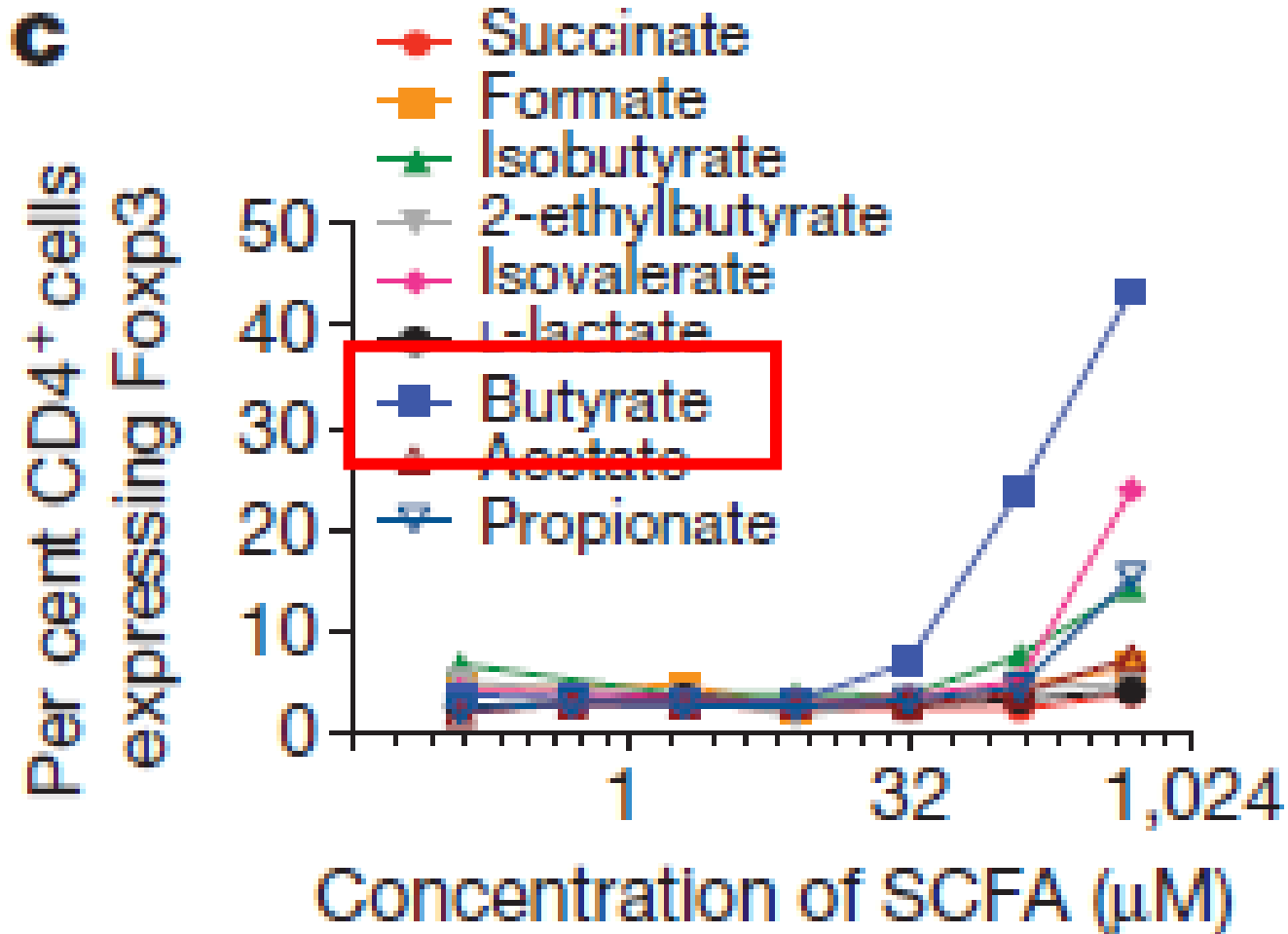
[de Roock S](#), [van Elk M](#), [van Dijk ME](#), [Timmerman HM](#), [Rijkers GT](#), [Prakken BJ](#), [Hoekstra MO](#), [de Klier IM](#).

# Microbiota



**Mucosal immune system**

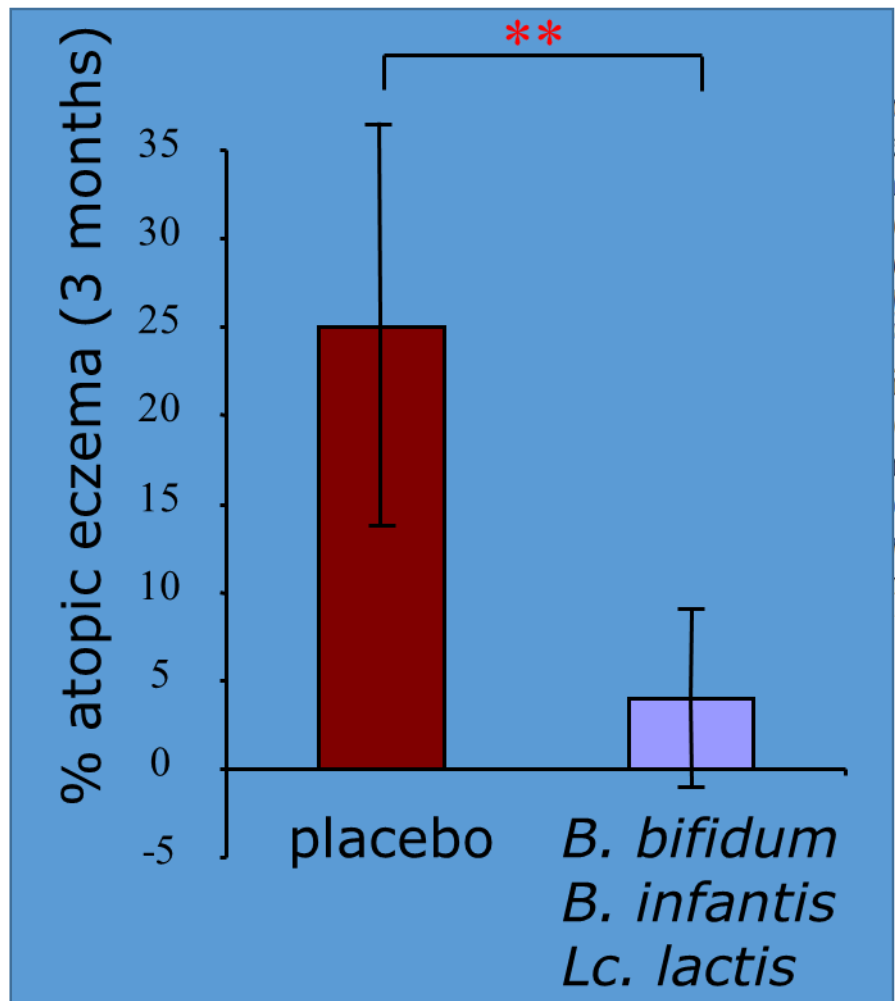
# SCFA induce Treg





# Original article

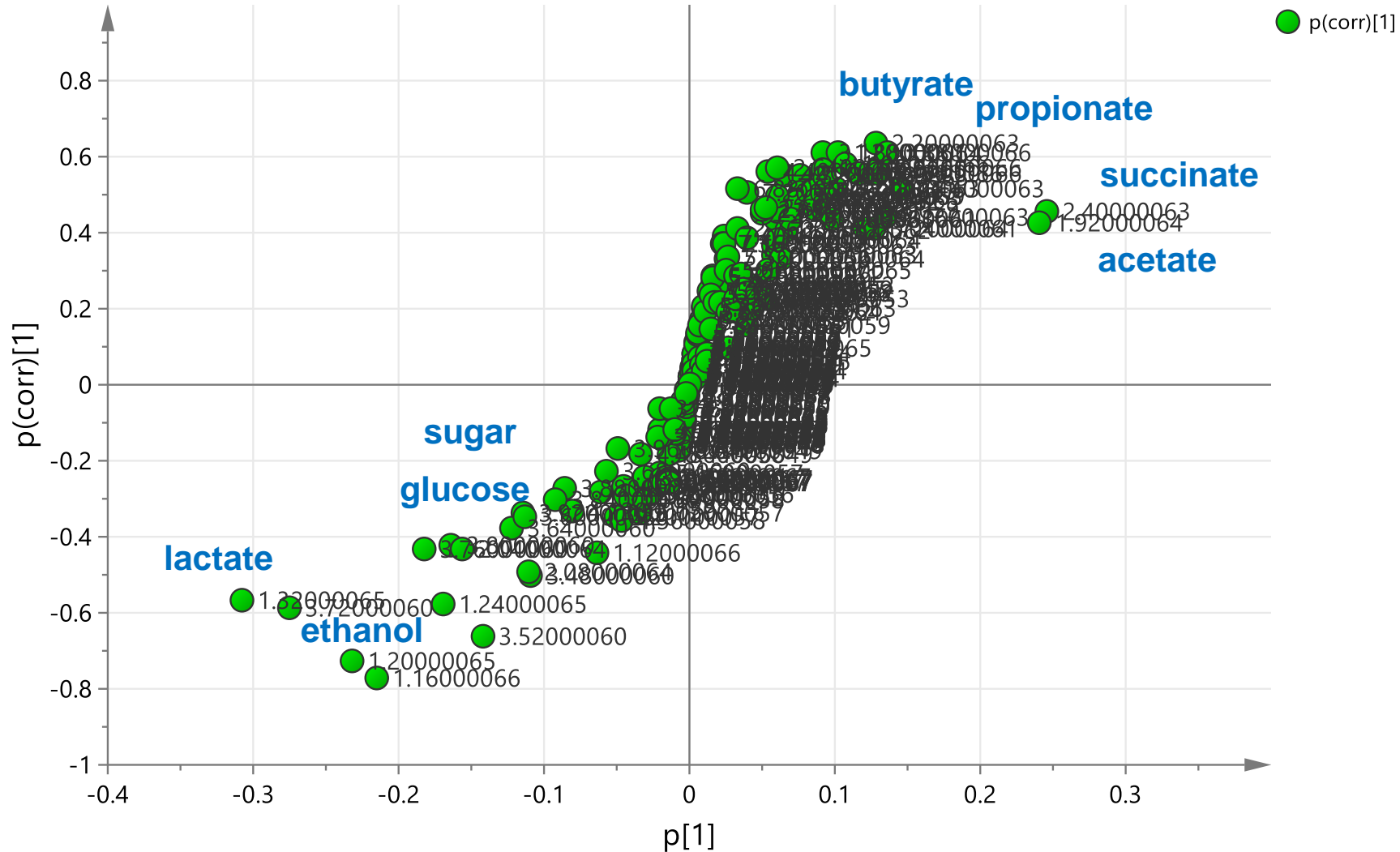
## The effects of selected probiotic strains on the development of eczema (the Panda study)



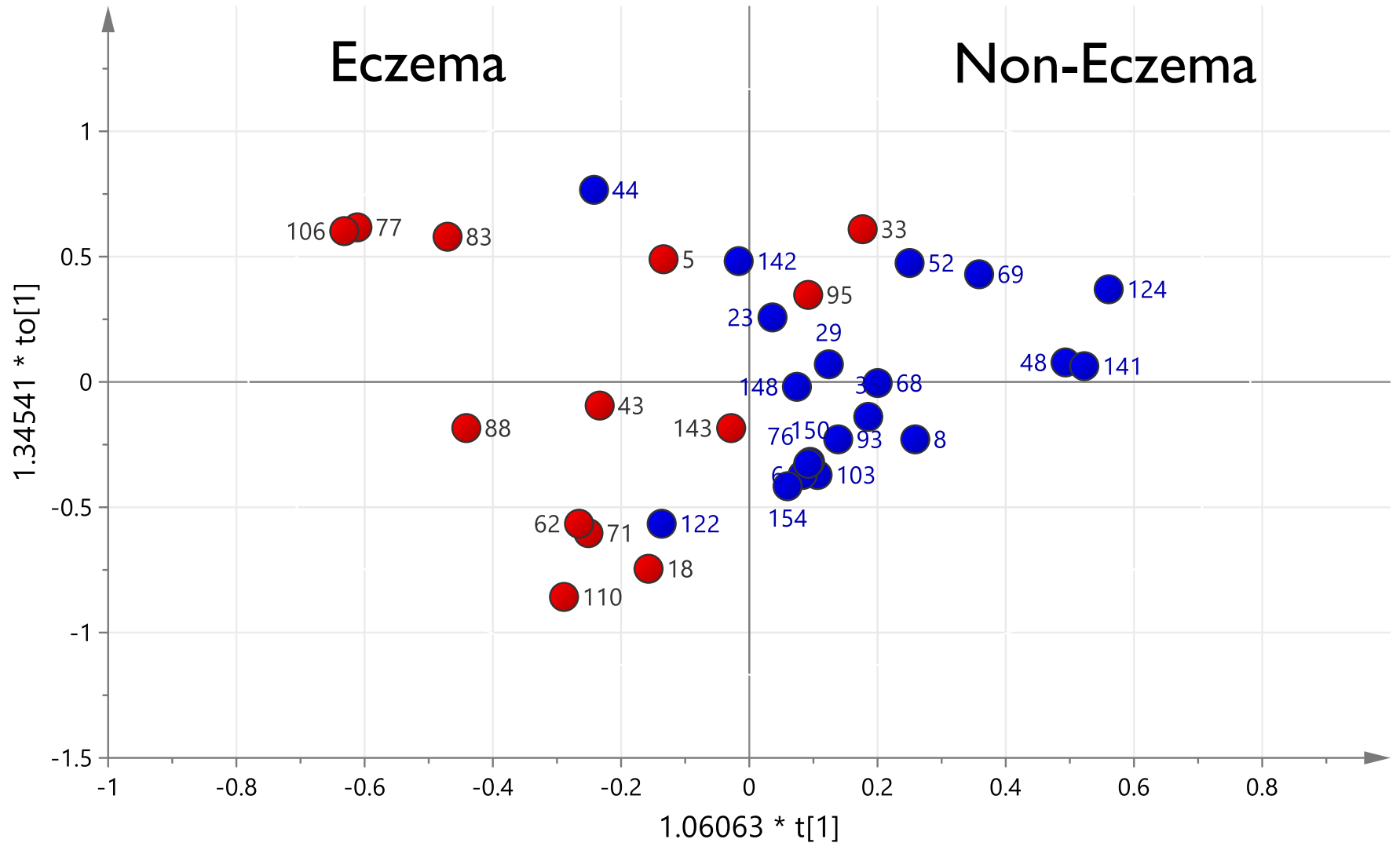
by administration of selected probiotic strains to high-risk children. In a randomized, controlled trial, a *Lactobacterium* (Panda) was given to children with a family history of eczema from the first 3 months of life. At 3 months of life, 6/50 children in the placebo group had eczema, which was similar to the 6/50 children in the probiotic group.

		3 M	1 Y	2 Y		
Placebo / eczema	1				1,3,4, van	
	2					
	3					
	4					
	5					ren's', the
	6					
	7					rsity
	8					again,
Probiotics/eczema	1					
	2					
	3					
	4					
	5					
	6					
	7					
	8					

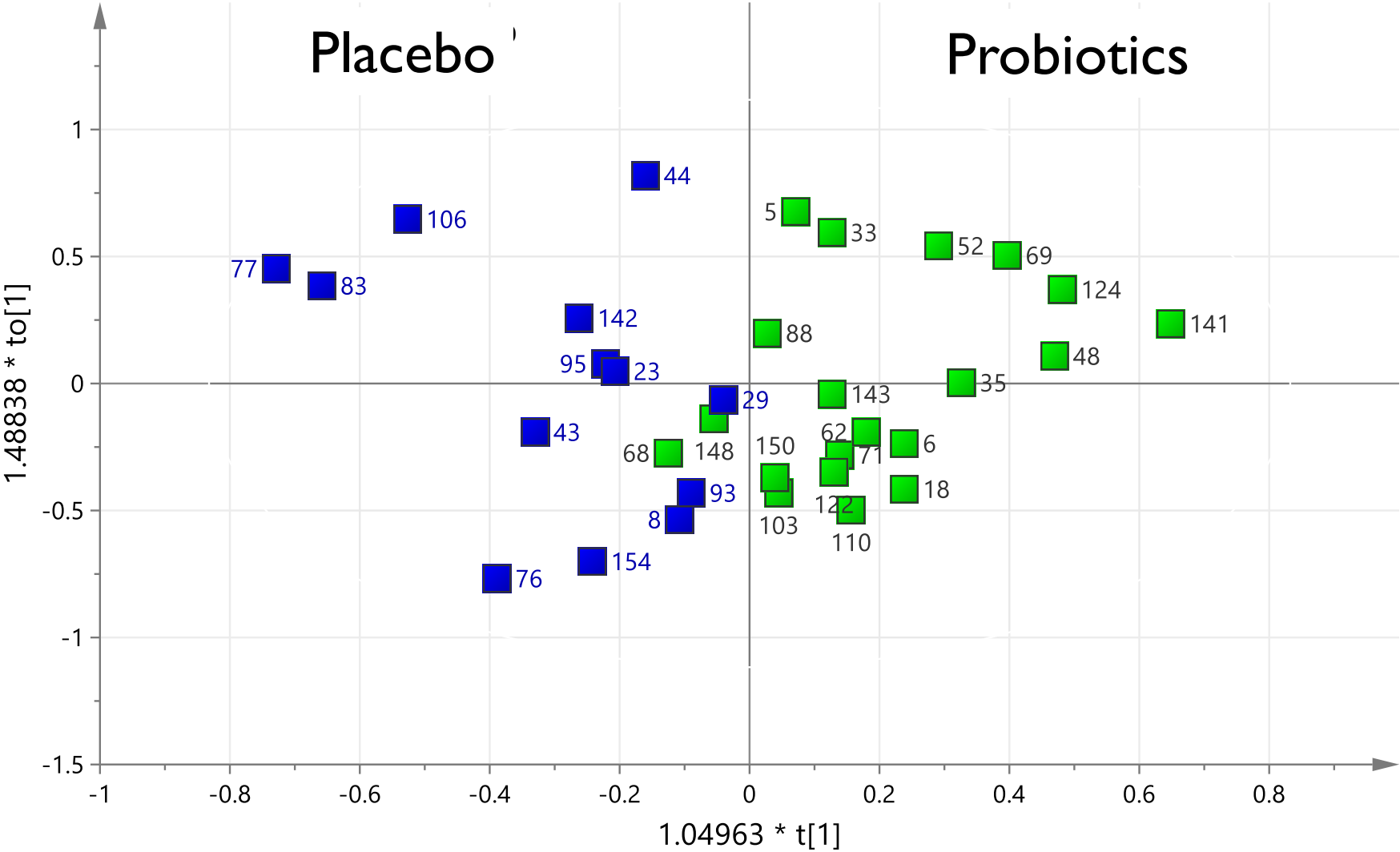
# Untargeted metabolomics: NMR



# Existing or future eczema: less butyrate

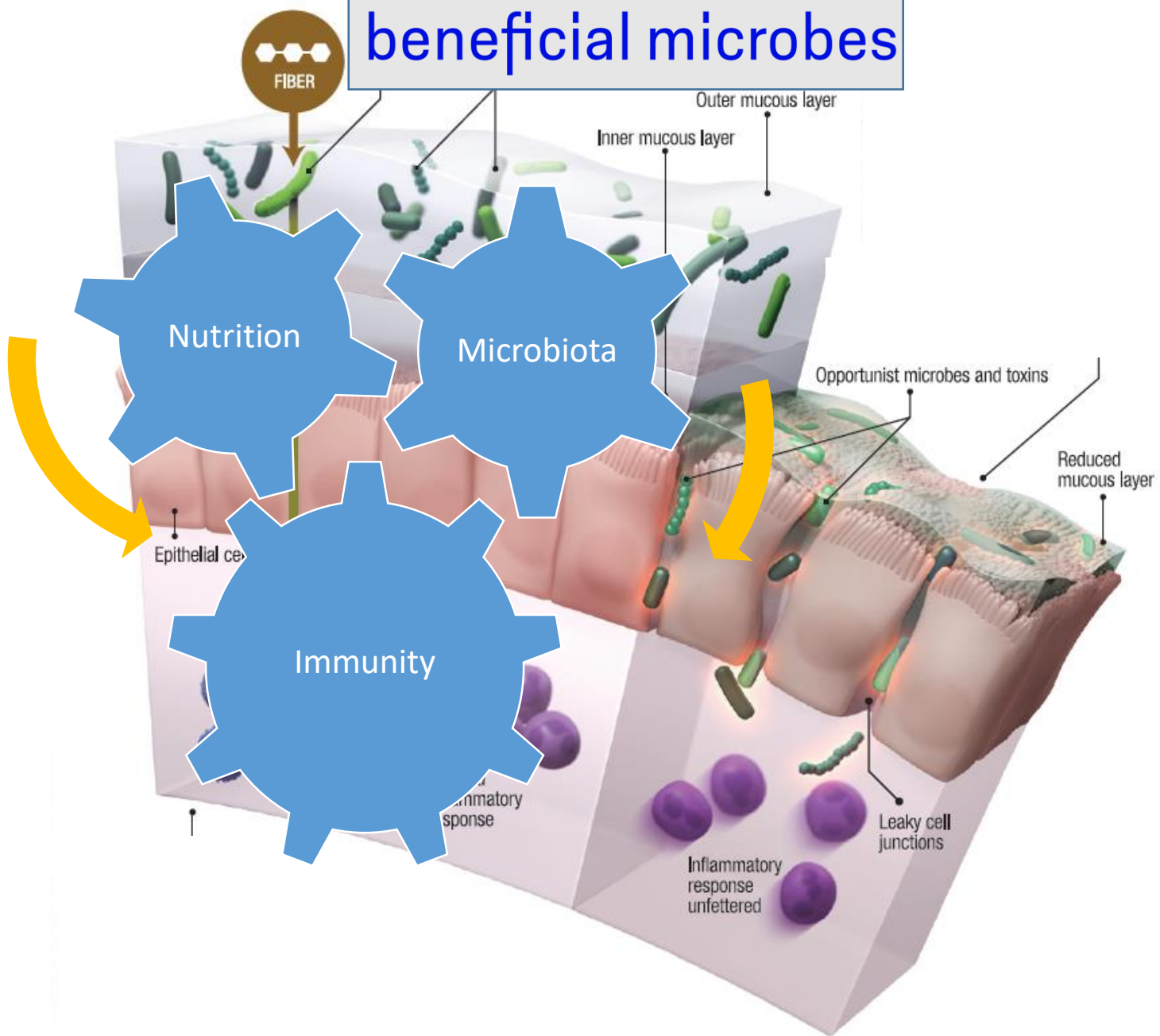


# Administration of probiotics: more butyrate





# beneficial microbes



**MICROBIOTA**

is  
the  
new

**BLACK**

WATCH THE  
**PARKING  
METERS**

*Parking Meters*

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