Intestinal Microbiota and Probiotics

Seppo Salminen
Functional Foods Forum
Faculty of Medicine
University of Turku
Turku, Finland

Bacteriome – Microbiome?

- Gut **microbiome** is a vast ecosystem of organisms (bacteria, yeasts, fungi, viruses and protozoa) in our digestive tract, which collectively weigh up to 2kg

- While bacterial composition of the microbiome is called **bacteriome**, the virome refers to the viral fraction comprising viruses

Probiotic?

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

- Hill et al 2014

Consensus Panel on scope and appropriate use of the term ‘probiotic’

functional foods forum

CONSENSUS STATEMENTS

OPEN

EXPERT CONSENSUS DOCUMENT

The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic

100 MOST IMPORTANT SPECIES FOR HUMAN EVOLUTION (Friends)

functional foods forum

Lactobacillus (5th most important)!

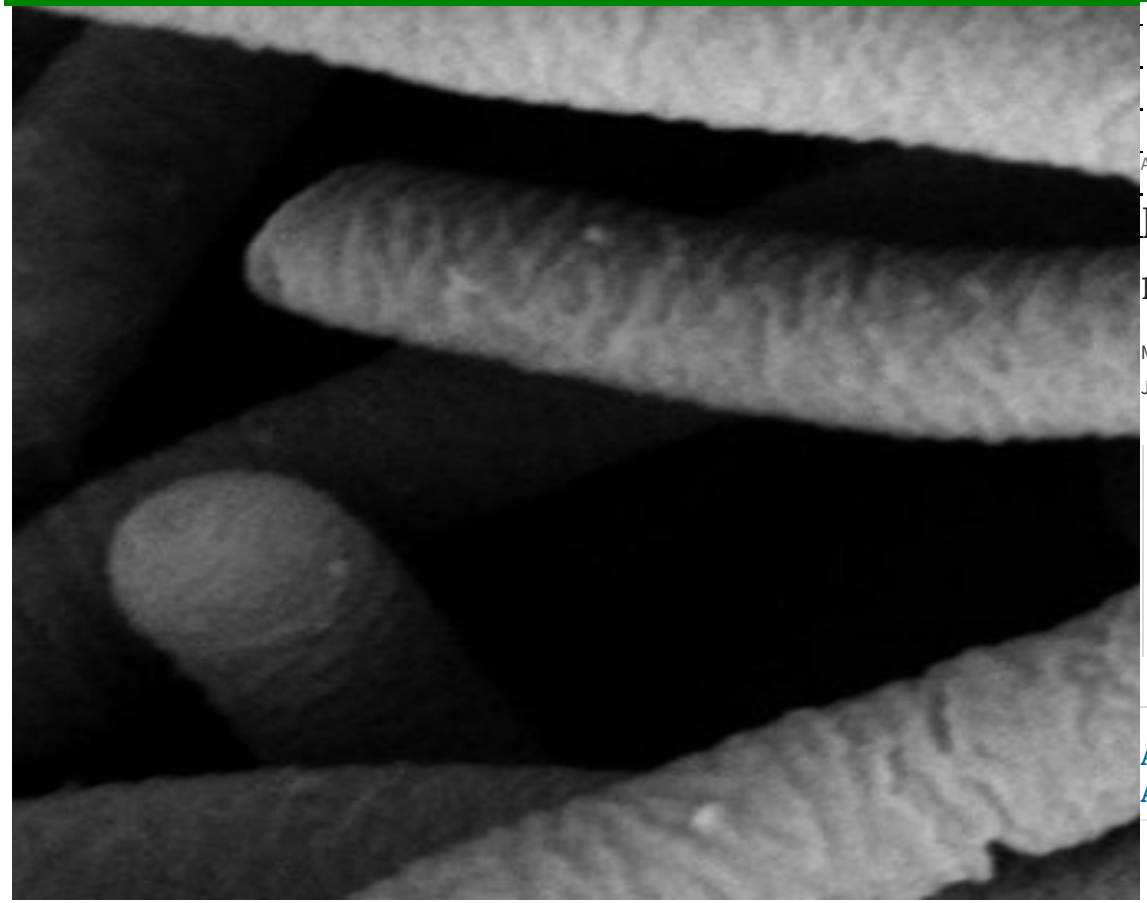
Food preservation by fermentation (nutrition, shelf-life, metabolites)

Preserving intestinal integrity,

barrier against harmful microbes (bacterial cells, metabolites)

Seppo Salminen

Gut Bacteria Impact Intestinal Integrity



Seppo Salminen

Article

Nutritional preferences of human gut bacteria reveal their metabolic idiosyncrasies

Melanie Tramontano, Sergej Andrejev, Mihaela Pruteanu, Martina Klünemann, Michael Kuhn, Marco Galardini, Paula Jouhten, Aleksej Zelezniak, Georg Zeller, Peer Bork, Athanasios Typas & Kiran Raosaheb Patil

Nature Microbiology **3**, 514–522 (2018)
doi:10.1038/s41564-018-0123-9

Bacterial physiology
Bacterial techniques and applications
Microbiology techniques
Microbiome

Received: 17 March 2017
Accepted: 07 February 2018
Published online: 19 March 2018

Abstract

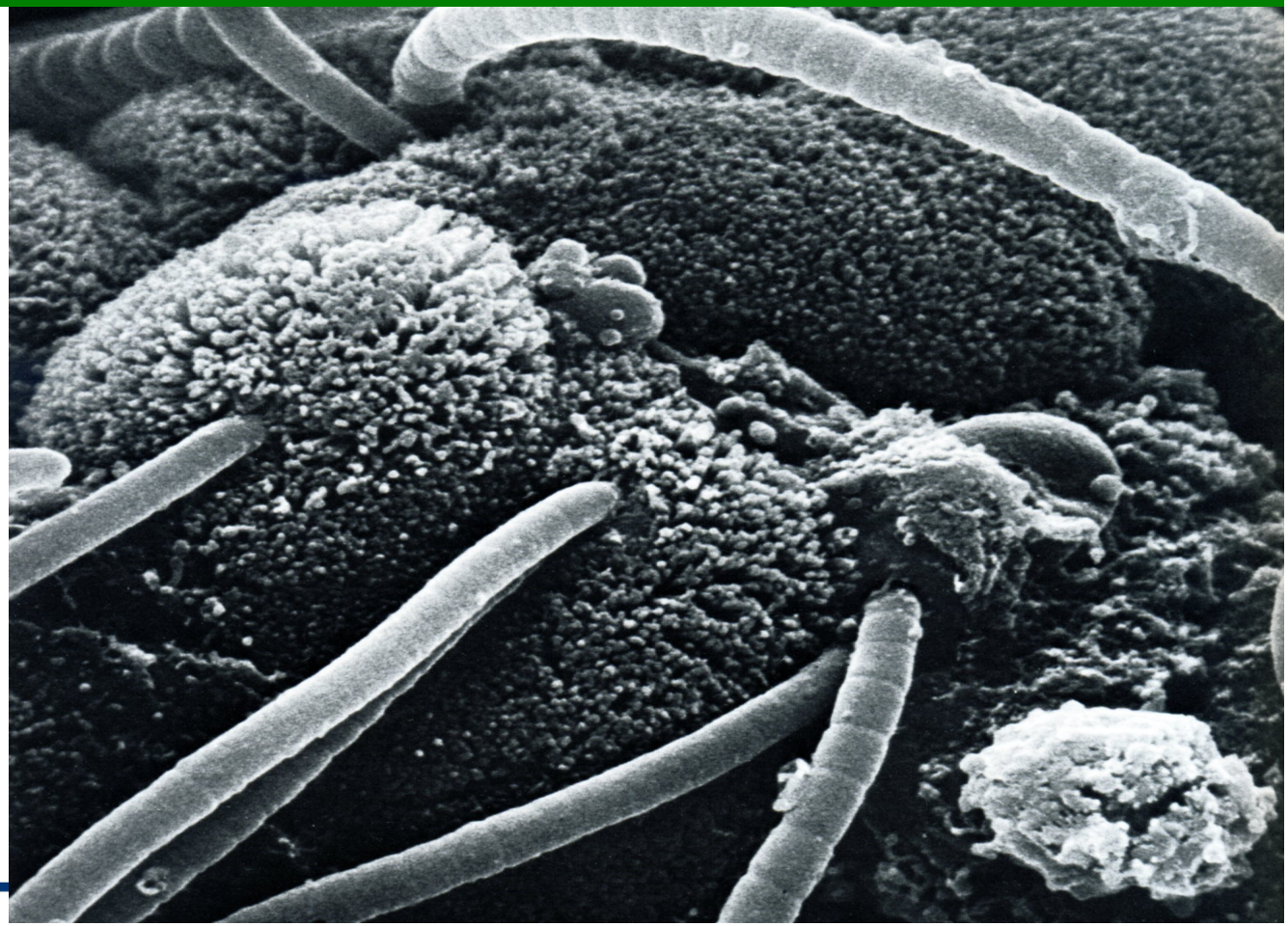
Abstract

Bacterial metabolism plays a fundamental role in gut microbiota ecology and host–

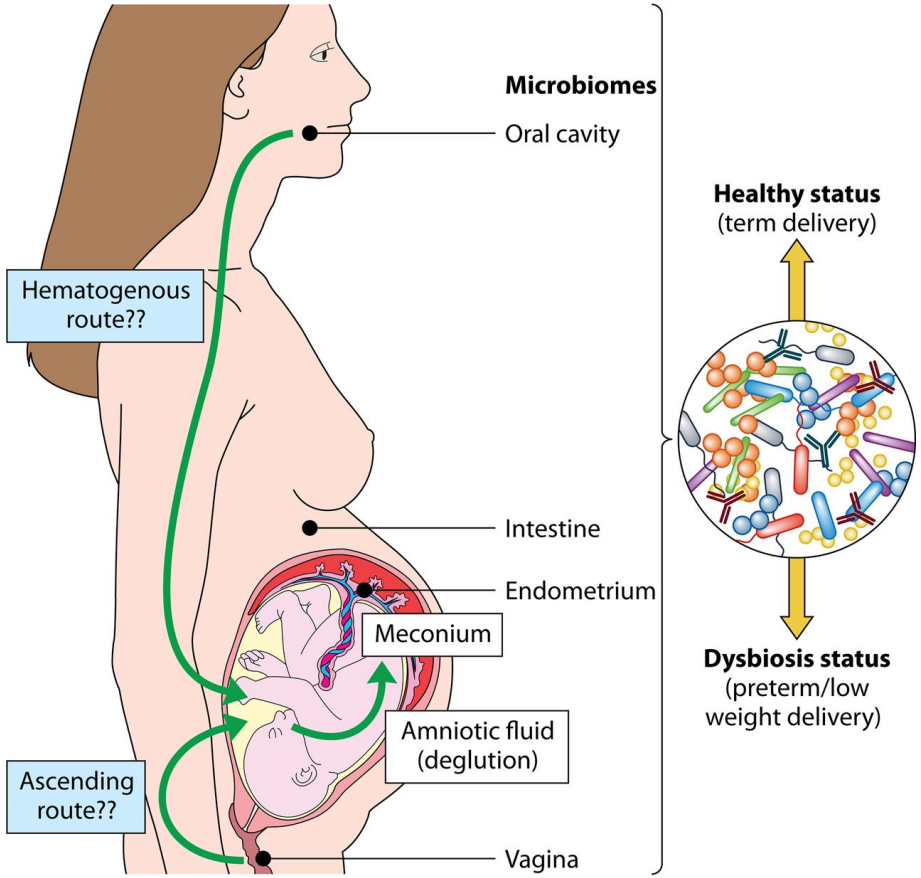
Lactobacilli/Bifidobacteria protect against pathogens and chemicals

Microbiota & intestinal integrity – one of the first demonstrations with lactobacilli

Both viable, dormant & non-viable lactobacilli adhere to mucosa

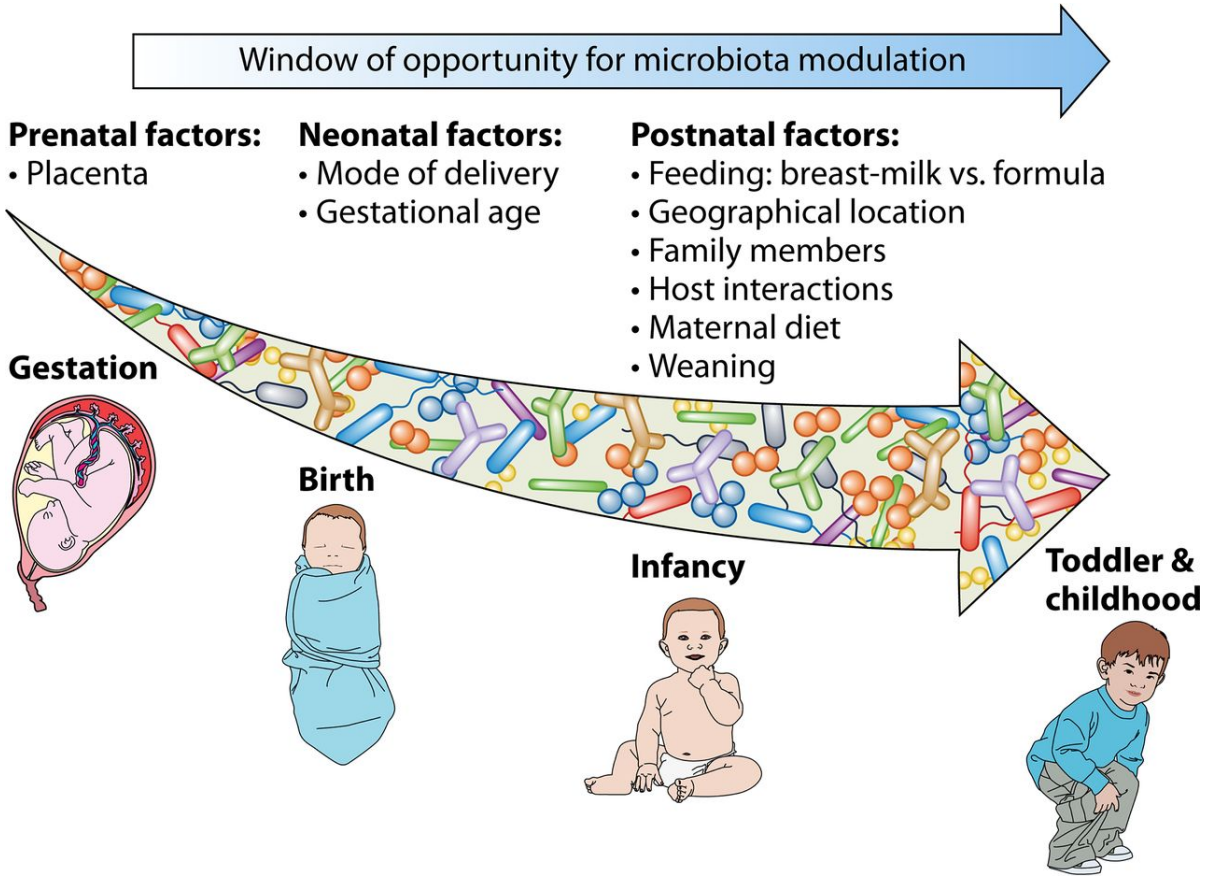


Colonization routes of maternal microbes to infant

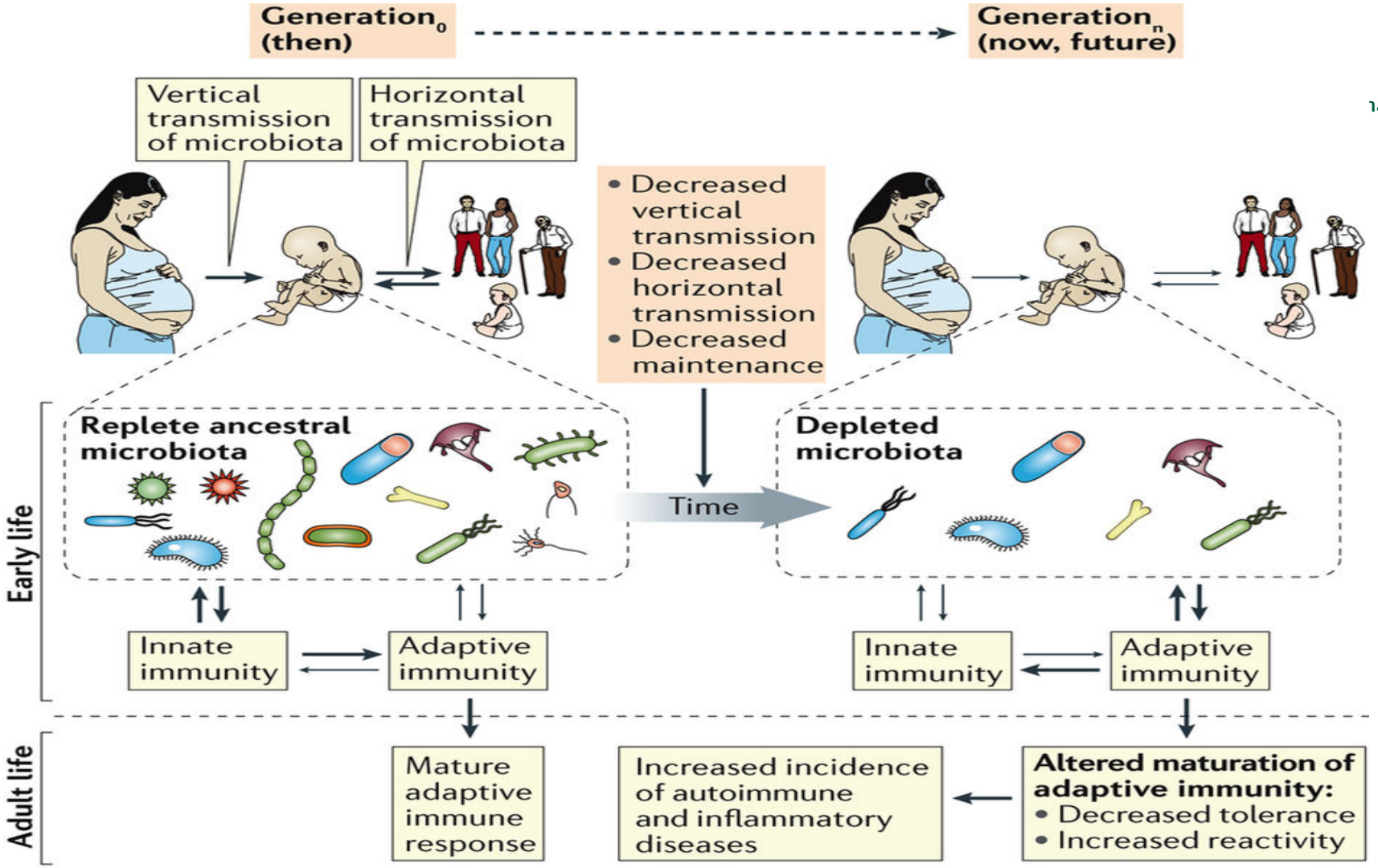


Christian Milani et al. Microbiol. Mol. Biol. Rev. 2017;81:e00036-17

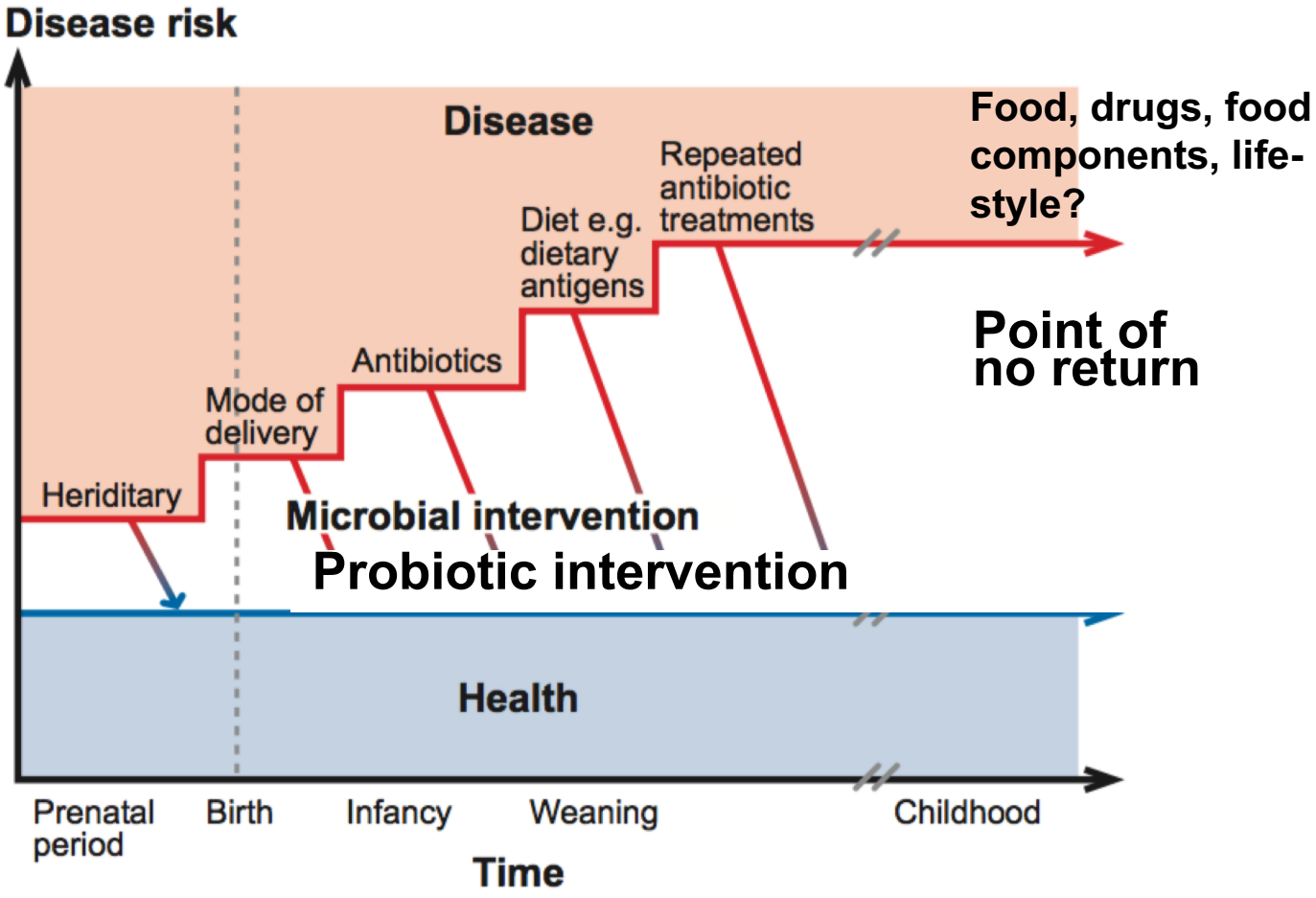
Windows of Opportunity to Modulate



Christian Milani et al. Microbiol. Mol. Biol. Rev. 2017;81:e00036-17


Generation$_0$ (then)
Generation$_n$ (now, future)
Vertical transmission of microbiota
Horizontal transmission of microbiota
• Decreased vertical transmission
• Decreased horizontal transmission
• Decreased maintenance
Replete ancestral microbiota
Depleted microbiota
Time
Early life
Innate immunity
Adaptive immunity
Innate immunity
Adaptive immunity
Adult life
Mature adaptive immune response
Increased incidence of autoimmune and inflammatory diseases
Altered maturation of adaptive immunity:
• Decreased tolerance
• Increased reactivity

Factors Deviating Gut Microbiota?



Many drugs influence microbiota: foods may influence microbiota?

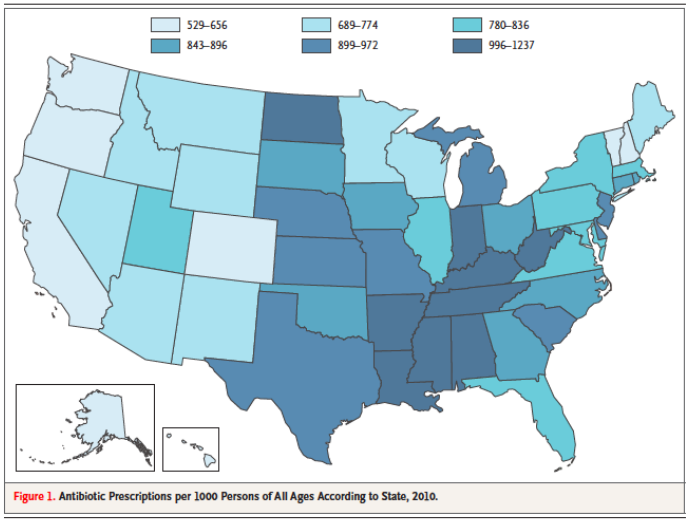
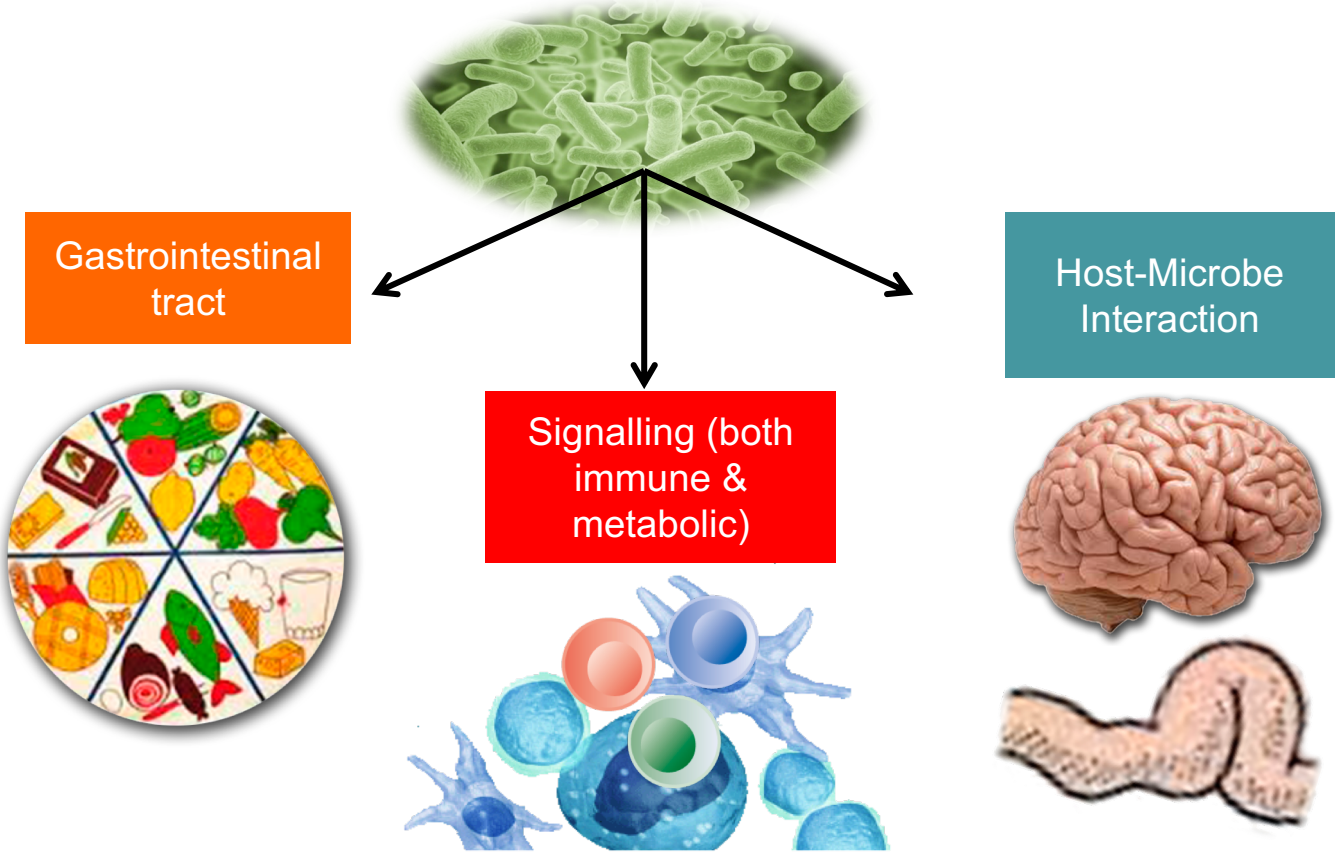


Figure 1. Antibiotic Prescriptions per 1000 Persons of All Ages According to State, 2010.

For example
NSAID, Proton pump regulators, antipsychotics…

Microbiota in human health

functional foods forum



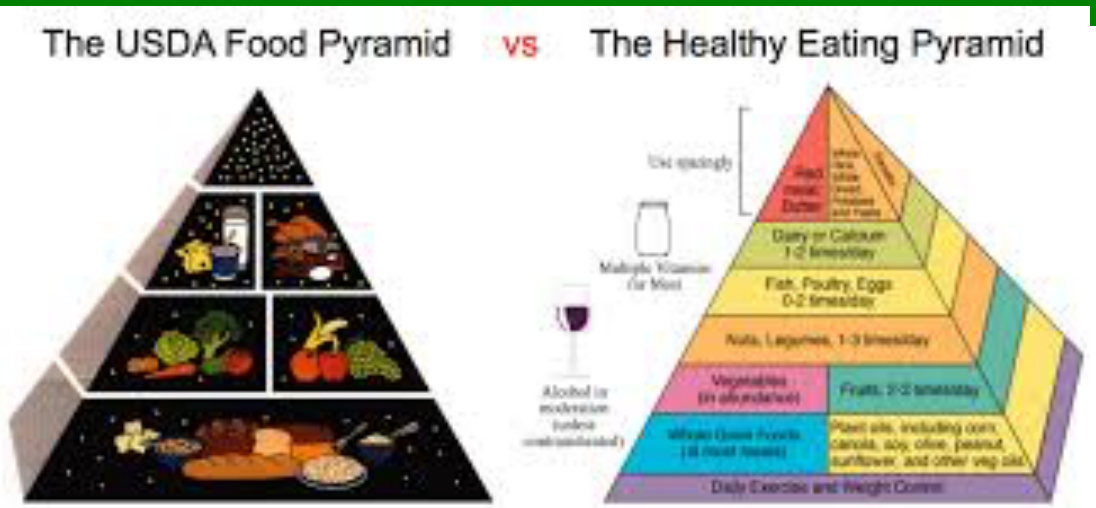
THE MICROBES WE EAT?

Tradition of fermented foods – stability and exposure to microbes?

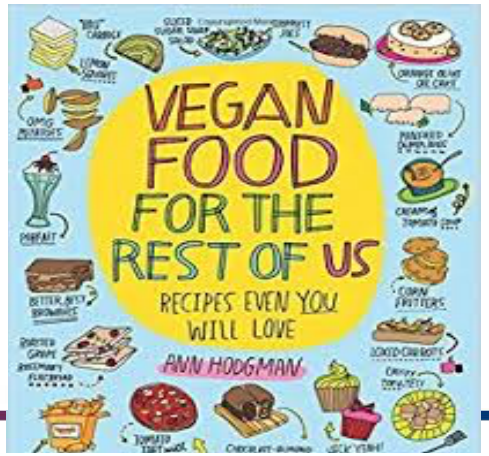
Now ”sterilization” of foods

Live bacteria missing from our diet, and the products of microbial metabolism in foods?

THE MICROBES WE EAT (United States)?



<70%



THE MICROBES WE EAT?

- Abundance & taxonomy of microbes consumed in a day's meals for 3 diet types

- **(1) the Average American (AMERICAN): focused on convenience foods**

- **(2) USDA recommended (USDA): emphasizing fruits and vegetables, lean meat, dairy, and whole grains**

- **(3) Vegan (VEGAN): excluding all animal products.**

LANG ET AL PEER
JOURNAL 2014

THE MICROBES WE EAT?

- Based on plate counts
- USDA meal plan had the highest total amount of microbes at 1.3×10^9 CFU per day
- the VEGAN meal plan 6×10^6 CFU per day
- **The AMERICAN meal plan 1.4×10^6 CFU per day**

LANG ET AL PEER
JOURNAL 2014

al foods forum

What is the role of fermented foods in health?

Live bacteria, not necessarily probiotics?

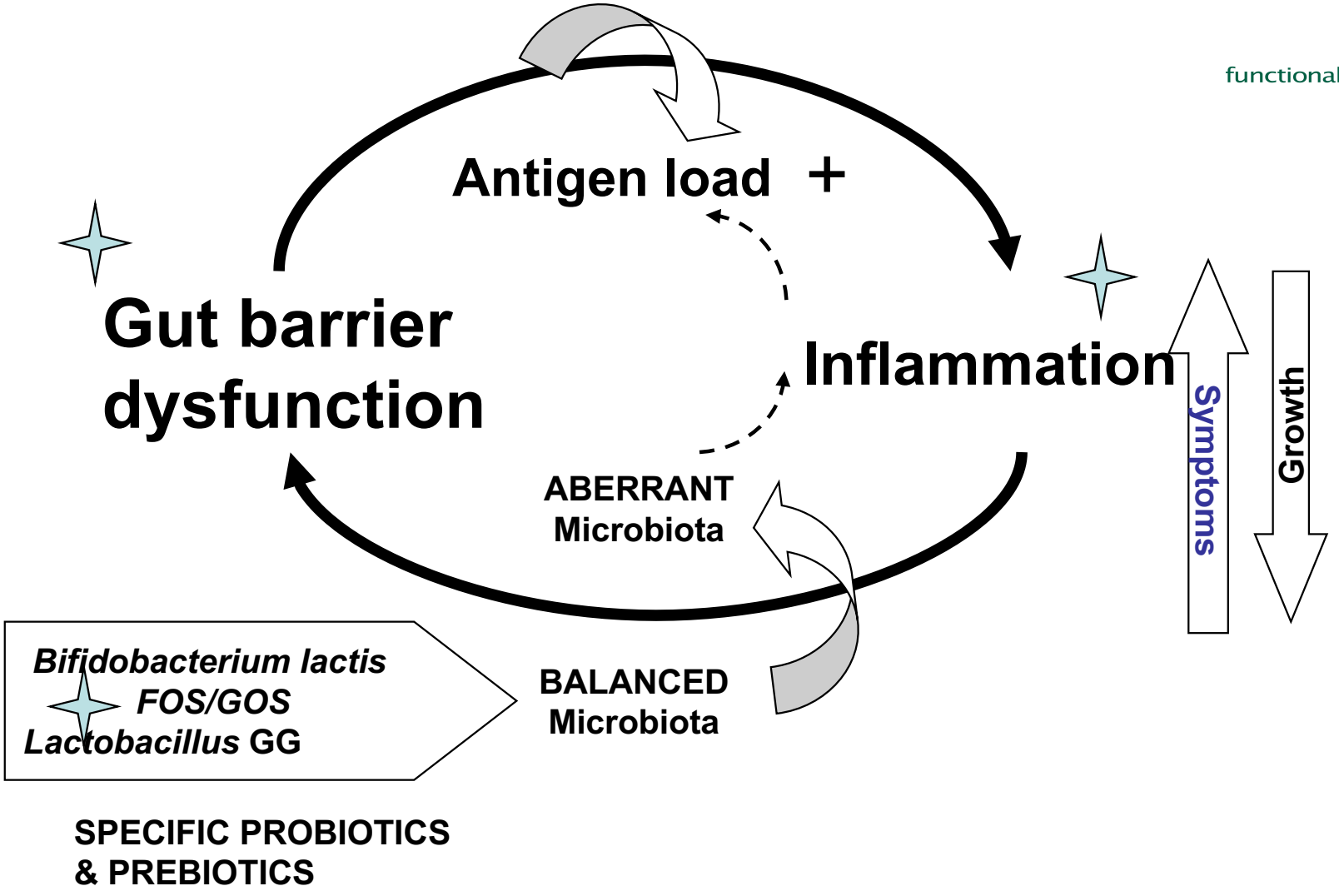
Bacterial metabolites and by-products?

functional foods forum

Can we reverse microbiota programming?

TURUN YLIOPISTO
UNIVERSITY OF TURKU

functional foods forum



Prevention of atopic eczema: specific probiotic

(Kalliomäki *et al* Lancet -2001, 2003; Laitinen K *et al*, Br J Nutr 2005, Lundelin et al 2017)

functional foods forum

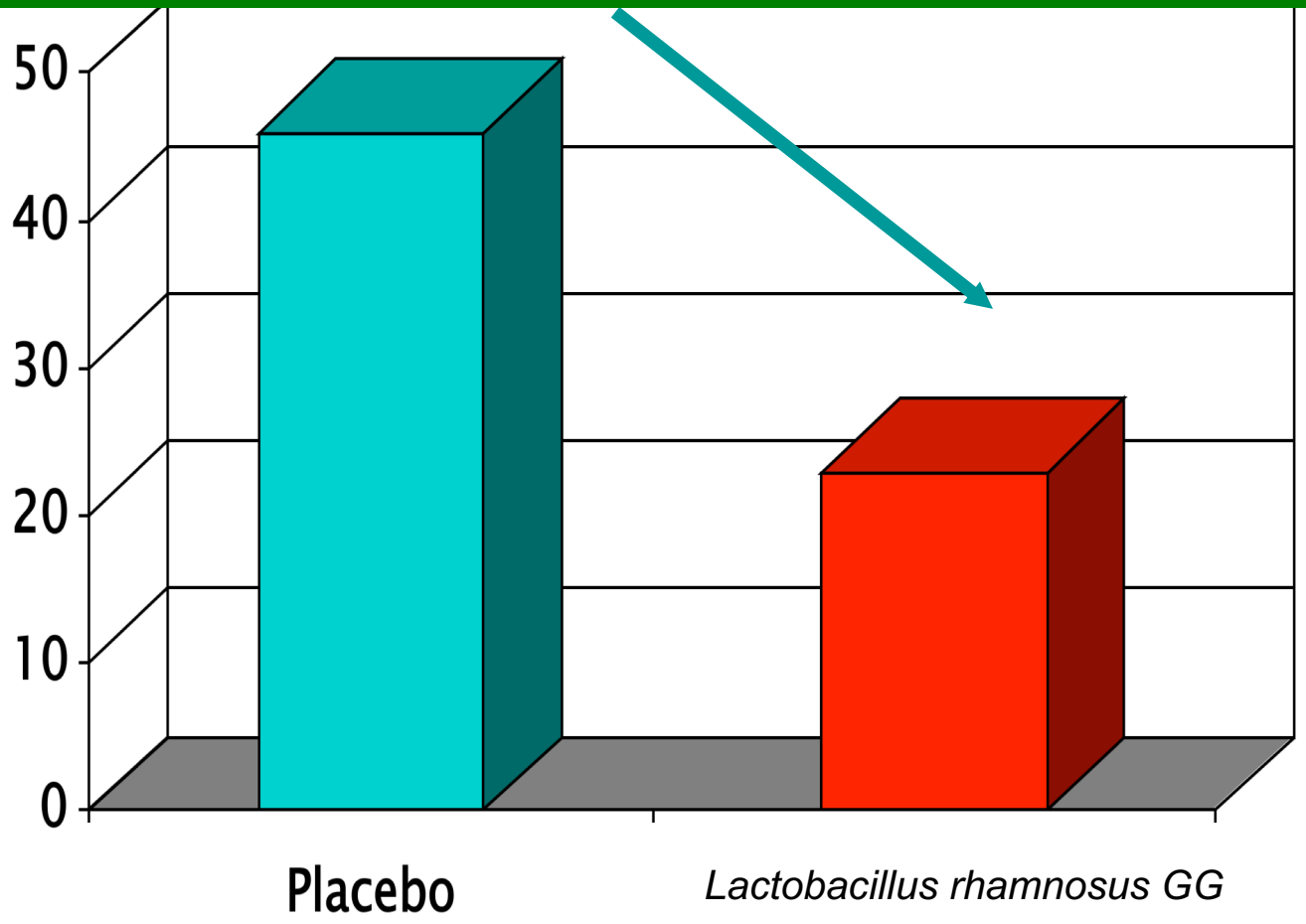
Mother

(*n* = 159) with family history of allergic disease

Infants

Perinatally: probiotics (LGG) vs. placebo

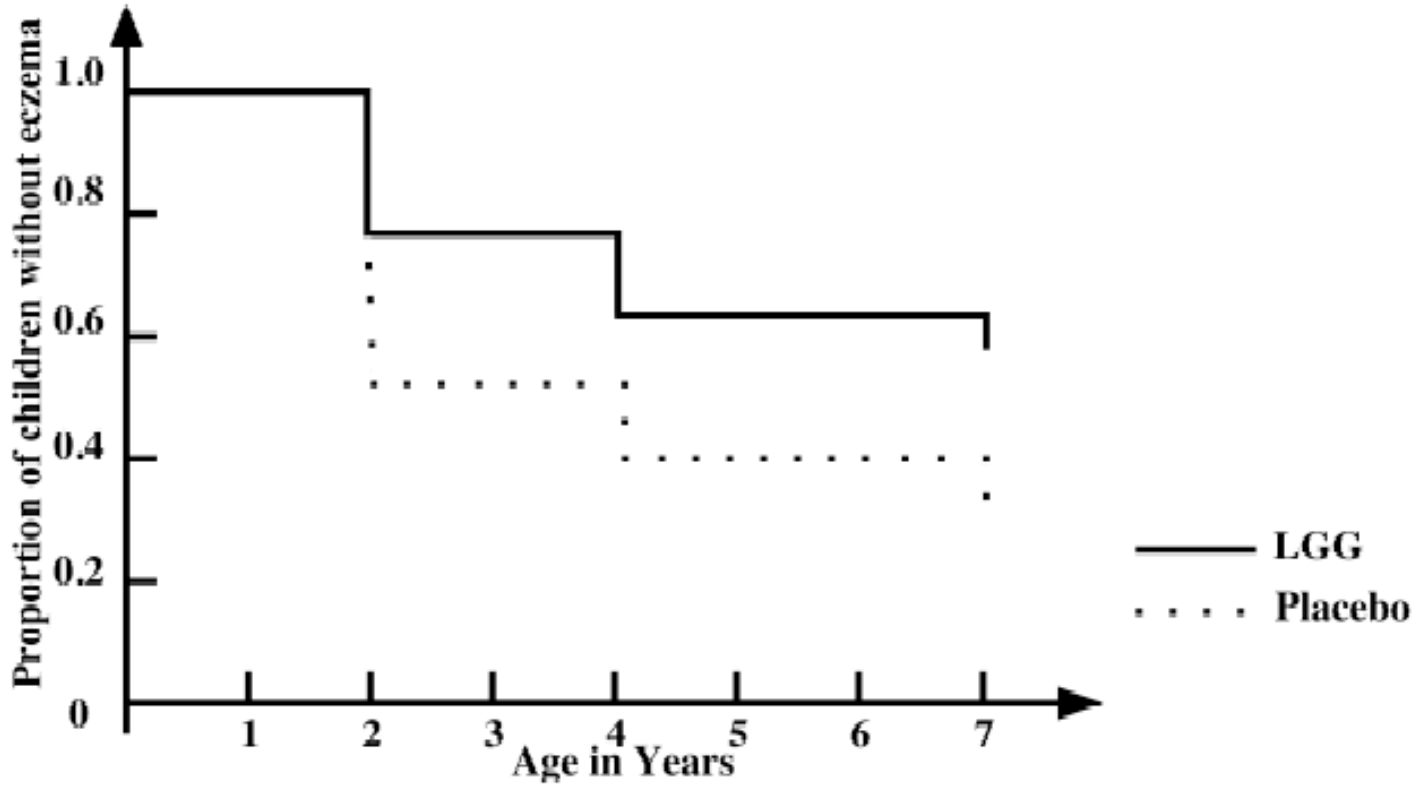
Perinatal LGG & Eczema?



5

–15.6)

Cumulative incidence of eczema (7 years) now 15- year follow-up



Norway?

onal foods forum

Probiotic milk consumption in pregnancy and infancy and subsequent childhood allergic diseases

Randi J. Bertelsen, PhD,[a,b] Anne Lise Brantsæter, PhD,[c] Maria C. Magnus, MPH,[b,d] Margaretha Haugen, PhD,[c] Ronny Myhre, PhD,[e] Bo Jacobsson, MD, PhD,[e,f] Matthew P. Longnecker, MD, ScD,[b] Helle M. Meltzer, PhD,[c] and Stephanie J. London, MD, DrPH[b] *Oslo, Norway, Research Triangle Park, NC, and Gothenburg, Sweden*

Conclusions: In this population-based cohort consumption of probiotic milk products was related to a reduced incidence of atopic eczema and rhinoconjunctivitis, but no association was seen for incidence of asthma by 36 months of age. (J Allergy Clin Immunol 2014;133:165-71.)

74000 mothers questionned on probiotic consumption during
2 and 3rd trimester of pregnancy and one year following delivery

Bertelsen et al JACI 2014

Conclusions: Norway

functional foods forum

Clinical implications: These results provide support for the hypothesis that probiotics in pregnancy might help prevent eczema and rhinoconjunctivitis in early childhood for the general population; continued probiotic intake after birth might also contribute.

WAO RECOMMENDATIONS: probiotics?

onal foods forum

Fiocchi *et al. World Allergy Organization Journal* (2015) 8:4
DOI 10.1186/s40413-015-0055-2

WAO journal
WORLD ALLERGY ORGANIZATION

POSITION ARTICLE AND GUIDELINES Open Access

World Allergy Organization-McMaster University Guidelines for Allergic Disease Prevention (GLAD-P): Probiotics

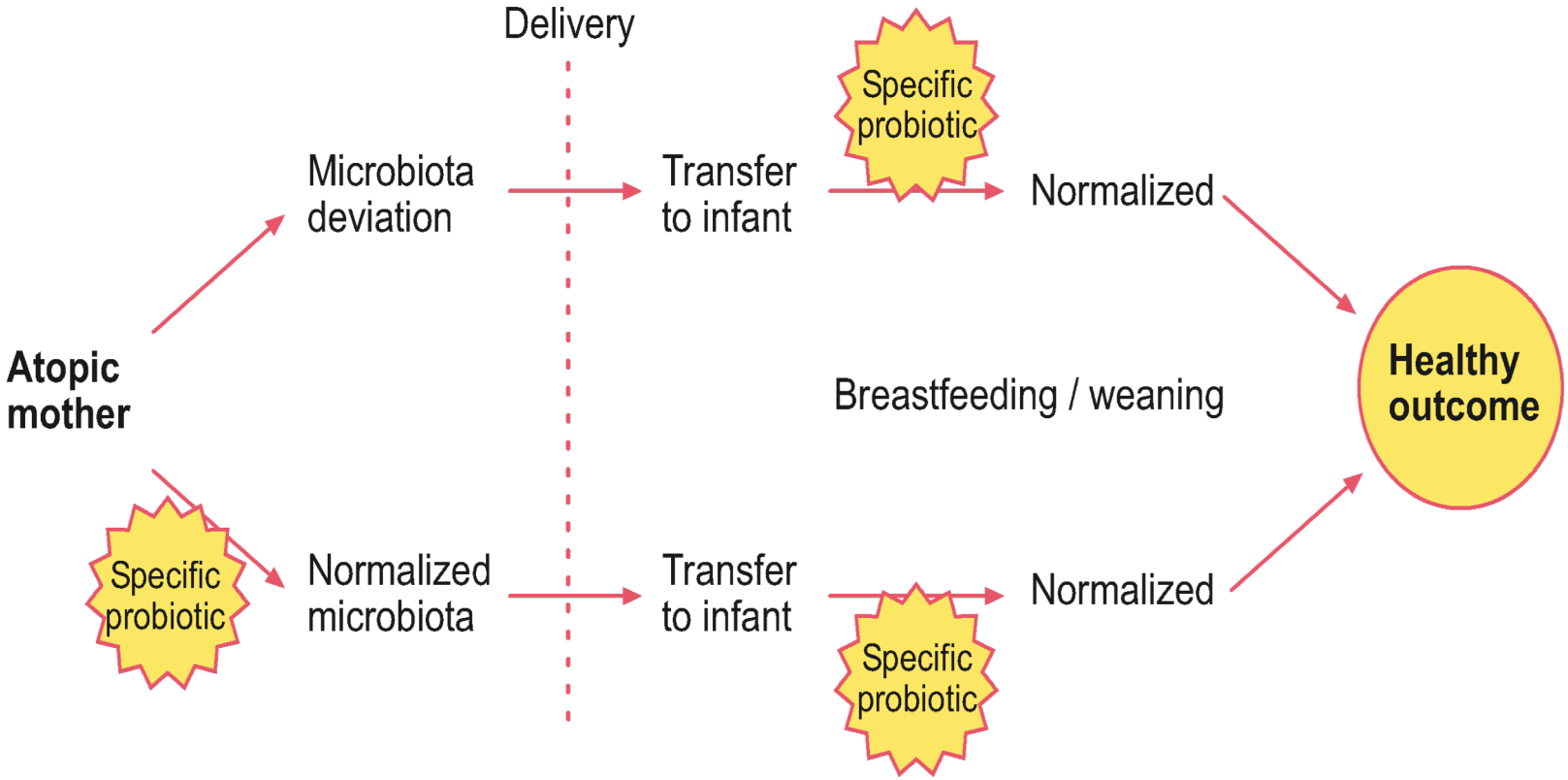
Results: Currently available evidence does not indicate that probiotic supplementation reduces the risk of developing allergy in children. However, considering all critical outcomes in this context, the WAO guideline panel determined that there is a likely net benefit from using probiotics resulting primarily from prevention of eczema. The WAO guideline panel suggests: a) using probiotics in pregnant women at high risk for having an allergic child; b) using probiotics in women who breastfeed infants at high risk of developing allergy; and c) using probiotics in infants at high risk of developing allergy. All recommendations are conditional and supported by very low quality evidence.

WAO RECOMMENDATIONS

al foods forum

- WAO guideline panel determined that there is a likely net benefit from using probiotics and suggests:
- Using probiotics in pregnant women at high risk for having an allergic child
- Using probiotics in women who breastfeed infants at high risk of developing allergy
- Using probiotics in infants at high risk of developing allergy

Allergy prevention and probiotics?



functional foods forum

Can a probiotic influence microbiota in obesity?

A challenge to Nutrition Couselling and Food & Drug Development!

Seppo Salminen

TURUN YLIOPISTO
UNIVERSITY OF TURKU

Human History

- Hunter-gatherers
  - Food supply not safe
  - Important to build reserves
  - Food scarce
  - No overweight problem
- Regulation of barrier against pathogens & energy intake towards storage

Microbiota and Obesity?

- Industrial society
- Alterations in eating behaviour?
- Food always available, safer food
- Mechanisms of storage remain while barrier is not challenged
- Other factors in overweight
  - Noncaloric factors such as reduced sleeping time, decreased calcium intake, eating behaviour

Microbiota and Obesity?

- Microbiota development
  - Millions of years of history
- Protection by barrier and rapid recovery and utilization of energy in food by microbes –tendency to storage of energy
- Microbiota is different and has different functions in GI tract

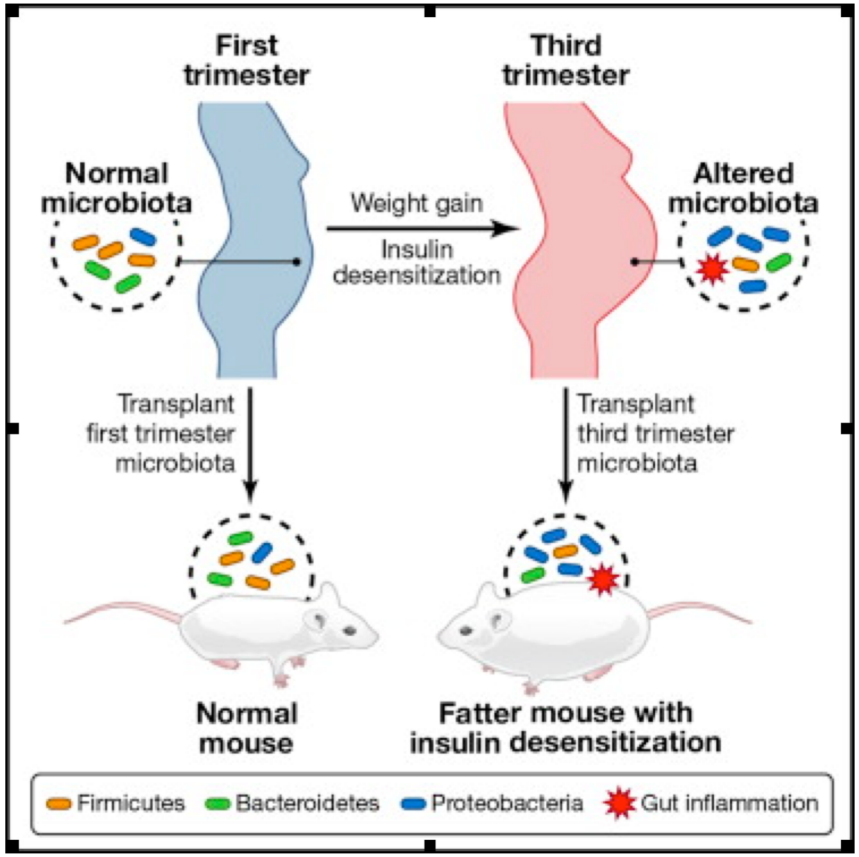
Small Intestine Microbiota and Fat Absorption

- Small bowel microbiota regulate host dietary fat digestion and absorption
- Gut microbes and their mediators drive lipid absorption through multiple mechanisms
- High-fat diet-induced jejunal microbiota directly increase gut lipid absorption

Large Intestine Microbiota and Fibre?

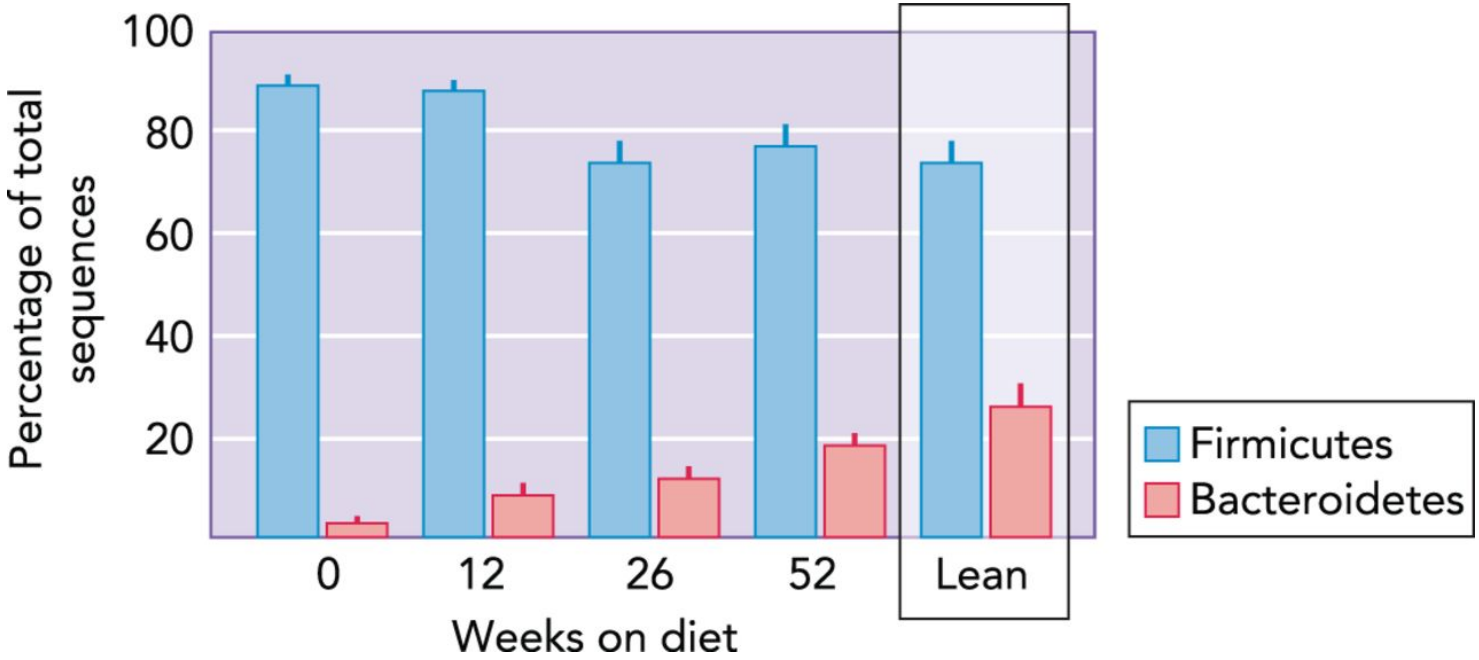
- Large bowel microbiota regulate dietary carbohydrate digestion and absorption
- High-carbohydrate/fibre diet influences energy uptake and storage from fibre

MICROBIOTA & WEIGHT GAIN DURING PREGNANCY?



Koren et al 2012 Cell

Human Gut Microbes - associated with obesity?



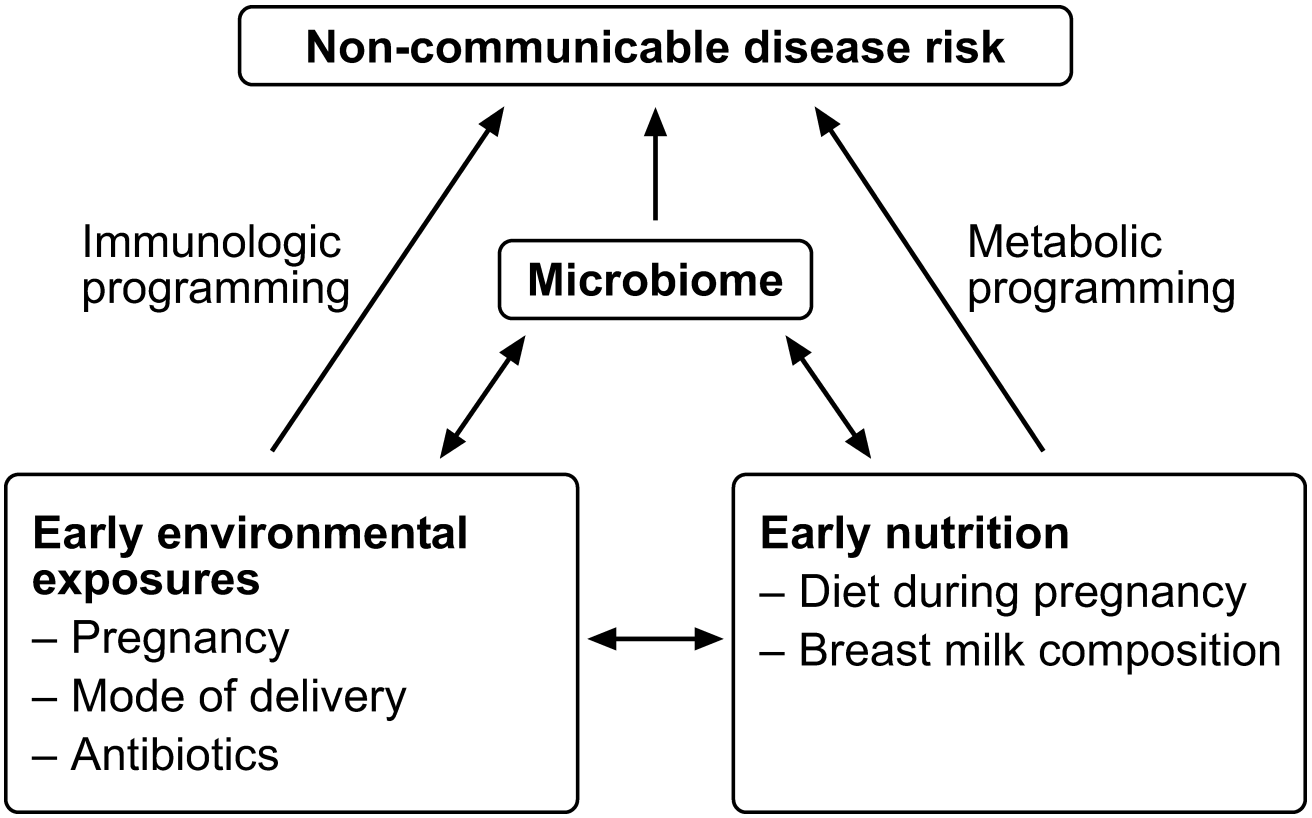
Bacteroidetes and Firmicutes in obese individuals before diet, obese individuals had fewer Bacteroidetes and more Firmicutes phyla.

Ley et al 2006; Youngji Cho, and Stephanie A. Shore Physiology 2016;31:108-116

Probiotics and Obesity?

- Several probiotic trials ongoing
- Preliminary results promise impact on overweight and obesity risk reduction
- Nutrition counseling effective during pregnancy – with specific probiotics even more effective
- Waist circumpherence reduced

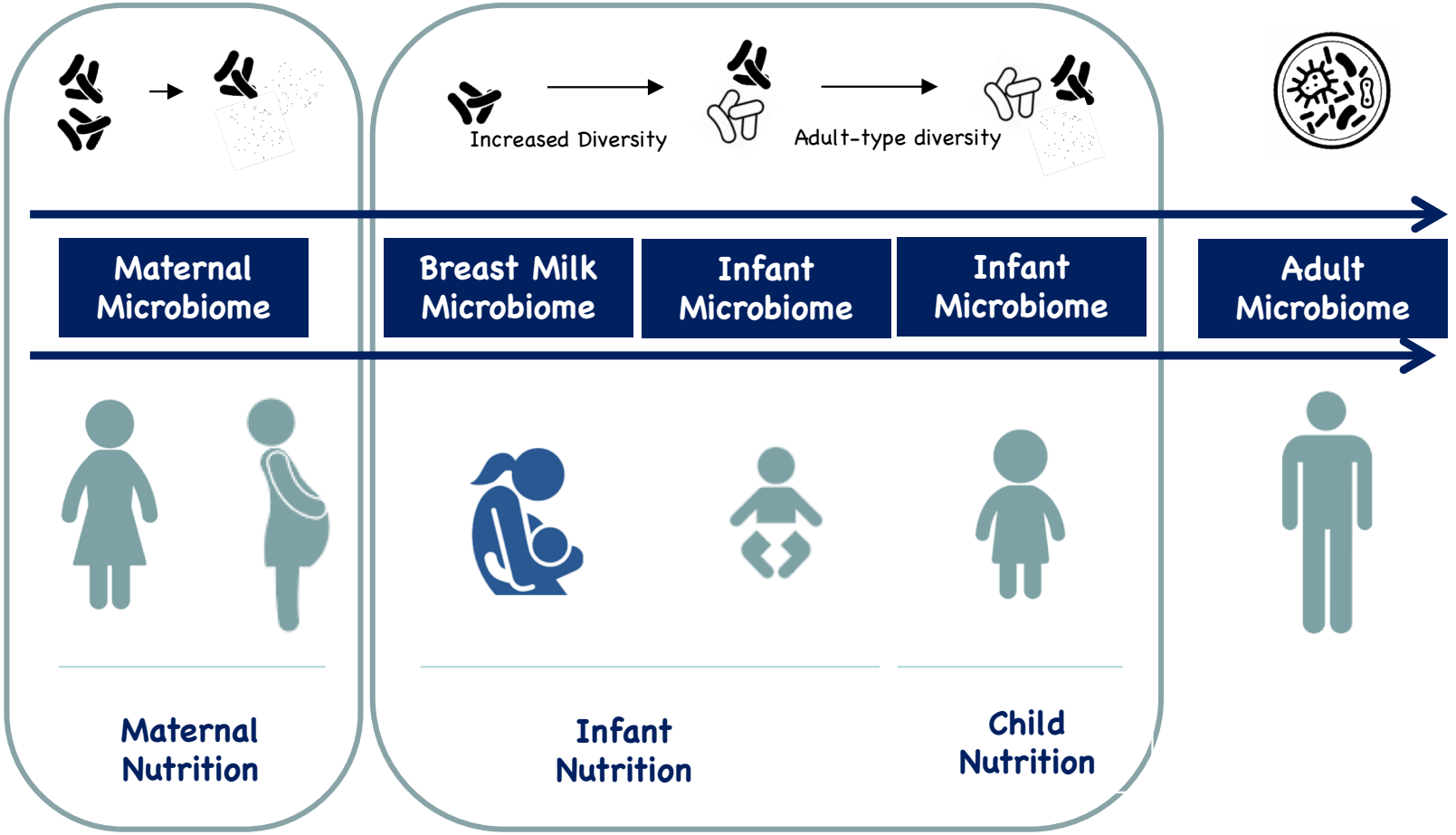
Non-communicable disease risk?



Homeostatic Capacity - Resilience of Microbiota?

- Resilience disturbance that can be absorbed by a system before the system loses its normal function
- Time to return to a stable state following the disturbance

Probiotics Do Influence Outcomes



IN SEARCH OF NOVEL MODULATORS…

- Examples:
  - *Clostridium butyricum**
  - *Bacteroides xylanisolvens**
  - *Akkermansia muciniphila*
  - *Bacillus cereus*
  - *Enterobacterium halleii*
  - *Faecalibacterium prausnizii*
  - Fructophilic lactic acid bacteria
  - *Butyricicoccus pullicaecorum*

TURUN YLIOPISTO
UNIVERSITY OF TURKU

*

RAPID TOOLS FOR MICROBIOTA?

functional foods forum

TURUN YLIOPISTO
UNIVERSITY OF TURKU