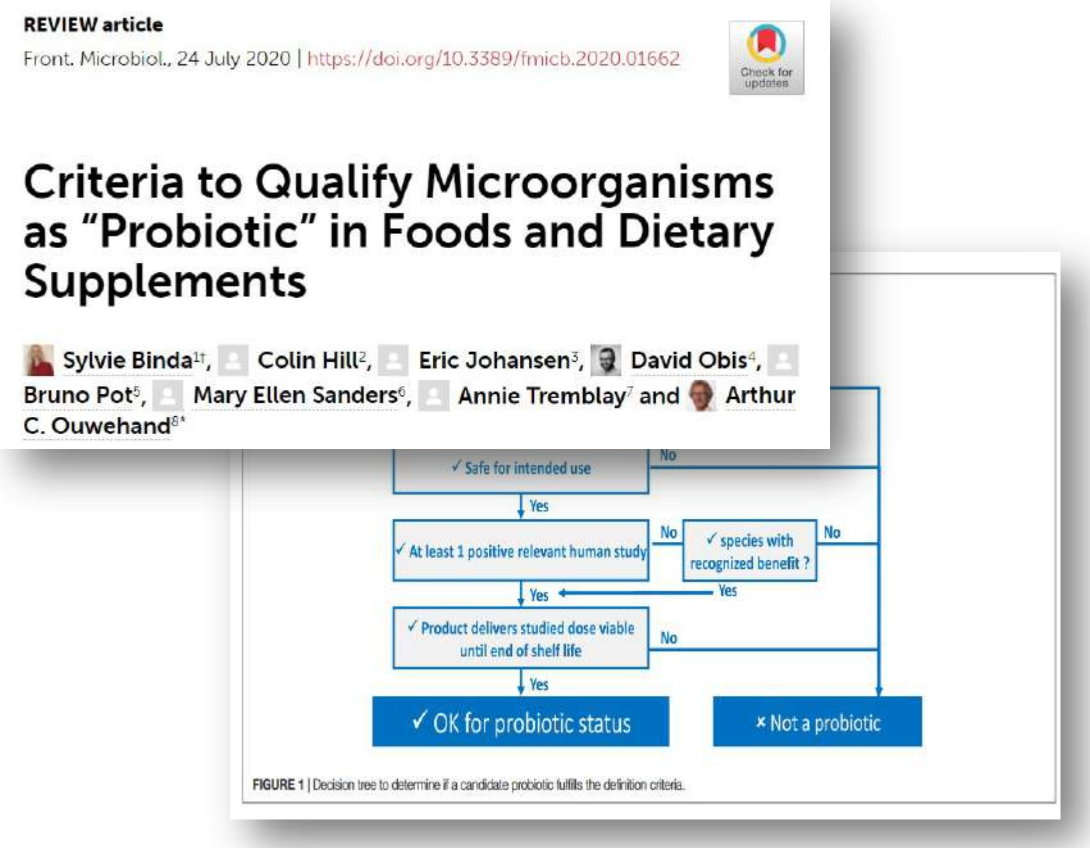
IPA EUROPE : Sylvie Binda
Scientific Committee ChairWoman

ipa
EUROPE
INTERNATIONAL
PROBIOTICS ASSOCIATION

IPA EU Scientific Workgroup: A need for a scientific conversation & collective thinking in order to develop science & scientific argumentation for the promotion of probiotics



REVIEW article

Front. Microbiol., 24 July 2020 | https://doi.org/10.3389/fmicb.2020.01662

Check for updates

Criteria to Qualify Microorganisms as "Probiotic" in Foods and Dietary Supplements

Sylvie Binda[1†], Colin Hill[2], Eric Johansen[3], David Obis[4], Bruno Pot[5], Mary Ellen Sanders[6], Annie Tremblay[7] and Arthur C. Ouwehand[8*]

FIGURE 1 | Decision tree to determine if a candidate probiotic fulfils the definition criteria.

Probiotic criteria publication with ISAPP

Webinars in Collaboration with the International 11th Congress Probiotics, Prebiotics and new Foods

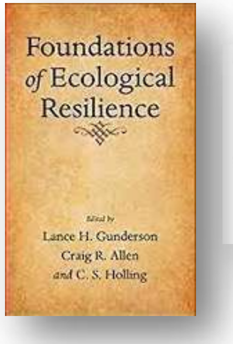
IPA EU Microbiome resilience project

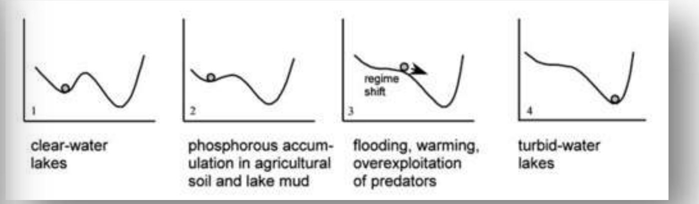
Born in 2016 in IPA EU scientific working group

- **Initial purpose : evaluate the scientific consensus behind diet and microbiota and especially the effect of diet enriched with probiotics (living microbes)**
- **Identify & build a « state of the art » towards a possible submission to authorities**

Ecological concepts application to microbiome and human health: Historical perspective

1958 First emergence of discussions on ecosystem stability and resilience. (Elton, 1958)





2011 Introduction of the ecological view of the gut microbiota with precursors as Relman & Deflethsen

2004 Definitions are established & ecological concepts are defined

In the 1960s the ecological definitions of "stability" varied depending on individuals and context

1973 Initiation of in-depth discussions on the meaning of ecosystem resilience

"Traditional conservation ecology is based on assessments of ecosystem resilience in the face of landscape disturbance. Resilience depends in turn on growth rates of community members, interactions between members, and nutrient availability ("ecosystem-level factors")."

Holling C. Resilience and stability of ecological systems. Annual review of ecology and systematics. **1973**;4:1–23.)

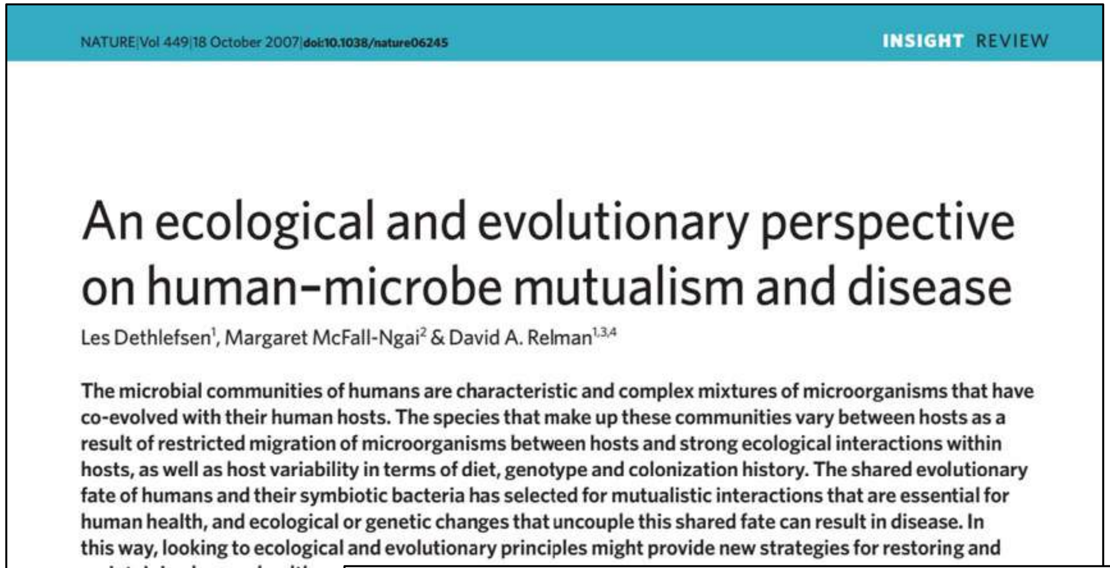
"capacity of a system to absorb disturbance and reorganize while undergoing change so as to still retain essentially the same function, structure, identity, and feedbacks".

Walker B, **Holling CS**, Carpenter SR, Kinzig A. Resilience, adaptability and transformability in social-ecological systems. Ecol Soc. **2004** Dec;9(2):5.)

(Folke C, Carpenter S, Walker B, Scheffer M, Elmqvist T, Gunderson L, Holling CS. Regime shifts, resilience, and biodiversity in ecosystem management. Annu. Rev. Ecol. Evol. Syst.. **2004** Dec 15;35:557-81.)

https://www.resalliance.org/key-concepts

How an ecological concept can be translated to a living ecosystem : the microbiome



NATURE|Vol 449|18 October 2007|doi:10.1038/nature06245

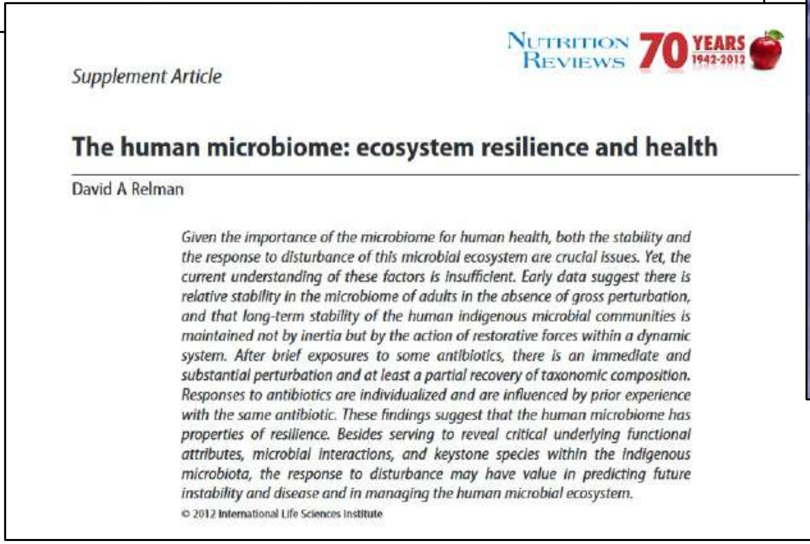
INSIGHT REVIEW

An ecological and evolutionary perspective on human–microbe mutualism and disease

Les Dethlefsen[1], Margaret McFall-Ngai[2] & David A. Relman[1,3,4]

The microbial communities of humans are characteristic and complex mixtures of microorganisms that have co-evolved with their human hosts. The species that make up these communities vary between hosts as a result of restricted migration of microorganisms between hosts and strong ecological interactions within hosts, as well as host variability in terms of diet, genotype and colonization history. The shared evolutionary fate of humans and their symbiotic bacteria has selected for mutualistic interactions that are essential for human health, and ecological or genetic changes that uncouple this shared fate can result in disease. In this way, looking to ecological and evolutionary principles might provide new strategies for restoring and maintaining human health.

2007



NUTRITION REVIEWS 70 YEARS 1942-2012

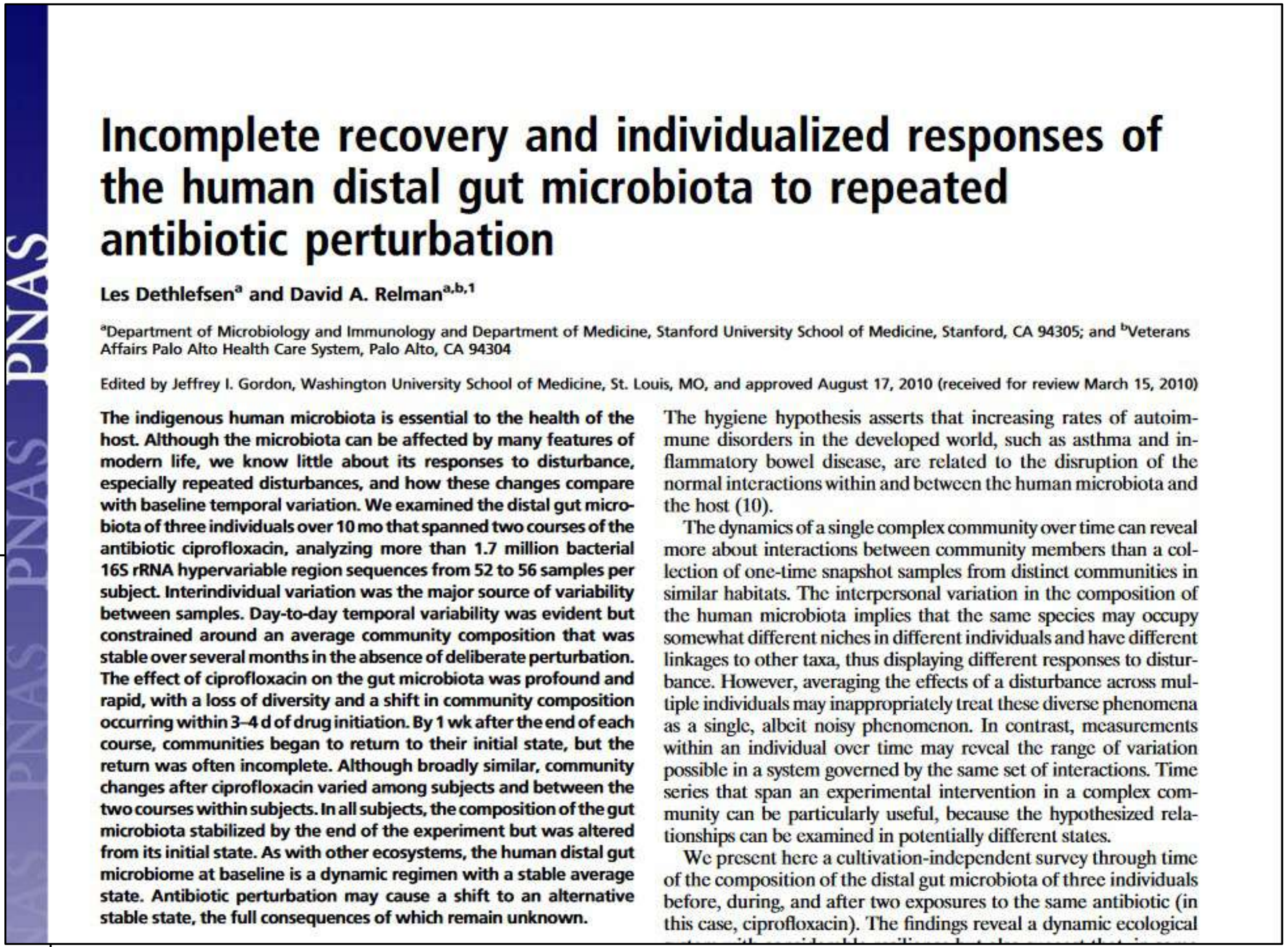
Supplement Article

The human microbiome: ecosystem resilience and health

David A Relman

Given the importance of the microbiome for human health, both the stability and the response to disturbance of this microbial ecosystem are crucial issues. Yet, the current understanding of these factors is insufficient. Early data suggest there is relative stability in the microbiome of adults in the absence of gross perturbation, and that long-term stability of the human indigenous microbial communities is maintained not by inertia but by the action of restorative forces within a dynamic system. After brief exposures to some antibiotics, there is an immediate and substantial perturbation and at least a partial recovery of taxonomic composition. Responses to antibiotics are individualized and are influenced by prior experience with the same antibiotic. These findings suggest that the human microbiome has properties of resilience. Besides serving to reveal critical underlying functional attributes, microbial interactions, and keystone species within the indigenous microbiota, the response to disturbance may have value in predicting future instability and disease and in managing the human microbial ecosystem.

2012



PNAS PNAS PNAS PNAS

Incomplete recovery and individualized responses of the human distal gut microbiota to repeated antibiotic perturbation

Les Dethlefsen[a] and David A. Relman[a,b,1]

[a]Department of Microbiology and Immunology and Department of Medicine, Stanford University School of Medicine, Stanford, CA 94305; and [b]Veterans Affairs Palo Alto Health Care System, Palo Alto, CA 94304

Edited by Jeffrey I. Gordon, Washington University School of Medicine, St. Louis, MO, and approved August 17, 2010 (received for review March 15, 2010)

The indigenous human microbiota is essential to the health of the host. Although the microbiota can be affected by many features of modern life, we know little about its responses to disturbance, especially repeated disturbances, and how these changes compare with baseline temporal variation. We examined the distal gut microbiota of three individuals over 10 mo that spanned two courses of the antibiotic ciprofloxacin, analyzing more than 1.7 million bacterial 16S rRNA hypervariable region sequences from 52 to 56 samples per subject. Interindividual variation was the major source of variability between samples. Day-to-day temporal variability was evident but constrained around an average community composition that was stable over several months in the absence of deliberate perturbation. The effect of ciprofloxacin on the gut microbiota was profound and rapid, with a loss of diversity and a shift in community composition occurring within 3–4 d of drug initiation. By 1 wk after the end of each course, communities began to return to their initial state, but the return was often incomplete. Although broadly similar, community changes after ciprofloxacin varied among subjects and between the two courses within subjects. In all subjects, the composition of the gut microbiota stabilized by the end of the experiment but was altered from its initial state. As with other ecosystems, the human distal gut microbiome at baseline is a dynamic regimen with a stable average state. Antibiotic perturbation may cause a shift to an alternative stable state, the full consequences of which remain unknown.

The hygiene hypothesis asserts that increasing rates of autoimmune disorders in the developed world, such as asthma and inflammatory bowel disease, are related to the disruption of the normal interactions within and between the human microbiota and the host (10).

The dynamics of a single complex community over time can reveal more about interactions between community members than a collection of one-time snapshot samples from distinct communities in similar habitats. The interpersonal variation in the composition of the human microbiota implies that the same species may occupy somewhat different niches in different individuals and have different linkages to other taxa, thus displaying different responses to disturbance. However, averaging the effects of a disturbance across multiple individuals may inappropriately treat these diverse phenomena as a single, albeit noisy phenomenon. In contrast, measurements within an individual over time may reveal the range of variation possible in a system governed by the same set of interactions. Time series that span an experimental intervention in a complex community can be particularly useful, because the hypothesized relationships can be examined in potentially different states.

We present here a cultivation-independent survey through time of the composition of the distal gut microbiota of three individuals before, during, and after two exposures to the same antibiotic (in this case, ciprofloxacin). The findings reveal a dynamic ecological

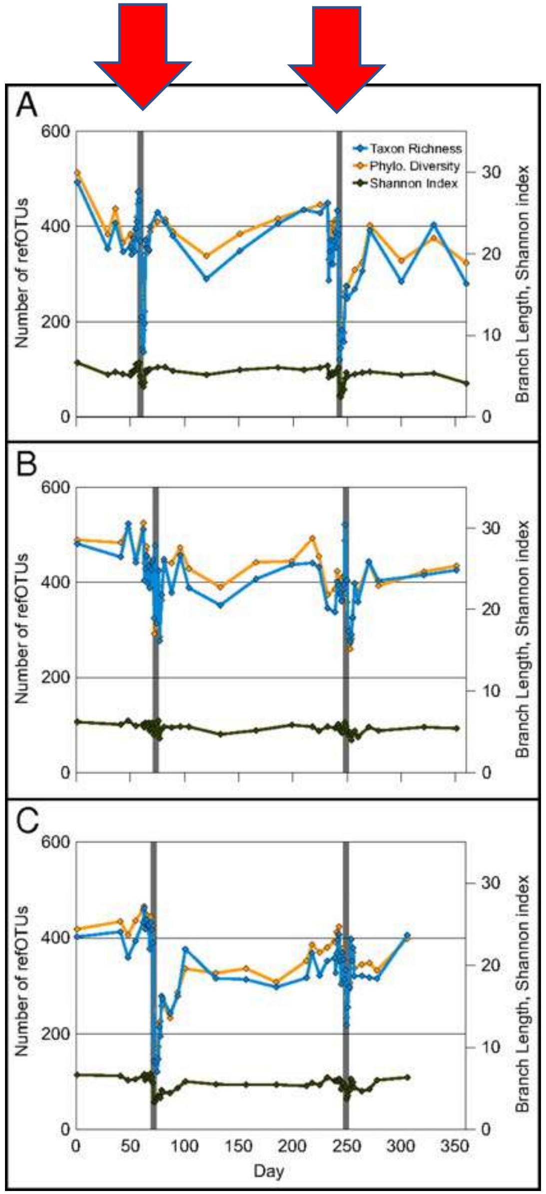
2011

The human microbiome : Ecosystem resilience & health

⇒ **The first to translate ecological concept to the human microbiome : he developped a "perturbation" model by antibiotics in order to**
  - ⇒ **Demonstrate the applicability of the ecological view of the microbiome**
  - ⇒ **See the relevance of the observation of the early degradations of the stability landscape ,**
  - ⇒ **ATB treatments can lead to temporary microbiota dysbiosis**
  - ⇒ **repeated ATB treatments can affect the resilience of the microbiota. Identify the components of the "catastrophic regime shift"**

> *"because we have only a limited understanding of the ecosystem services provided to us by our resident microbiota, caution and additional research are warranted."*
>
> David A. Relman, 2012

Perturbation (Ciprofloxacin 5 days)



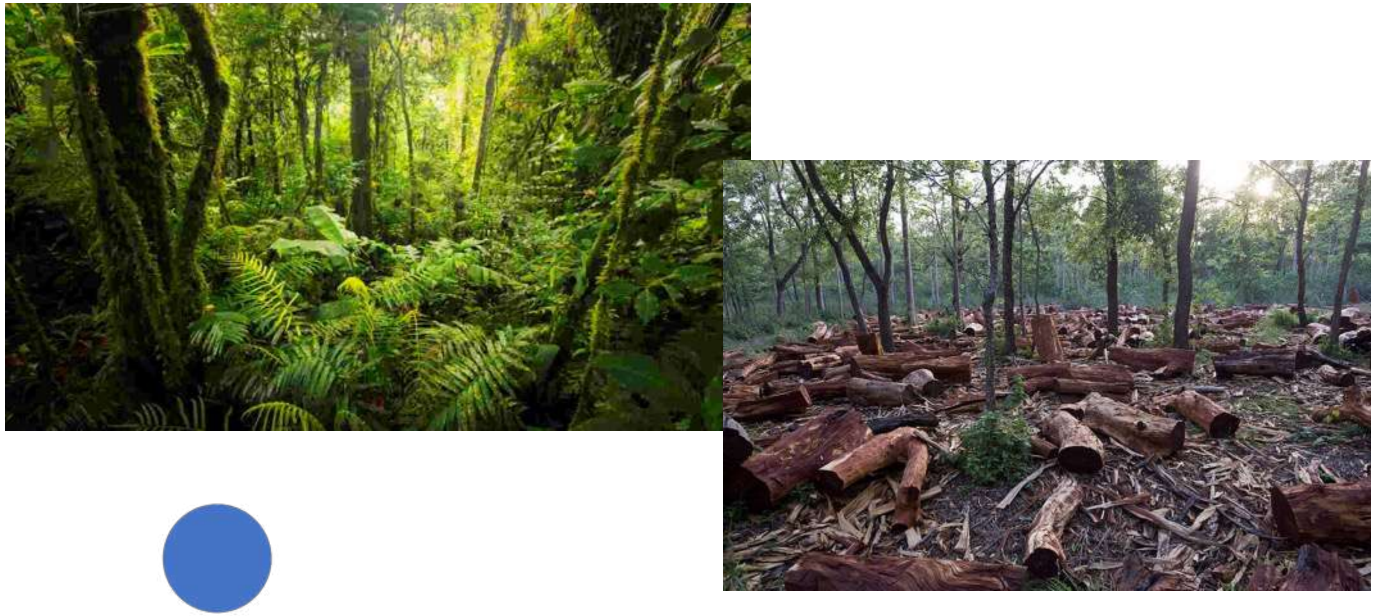
Subject 1

Subject 2

Subject 3

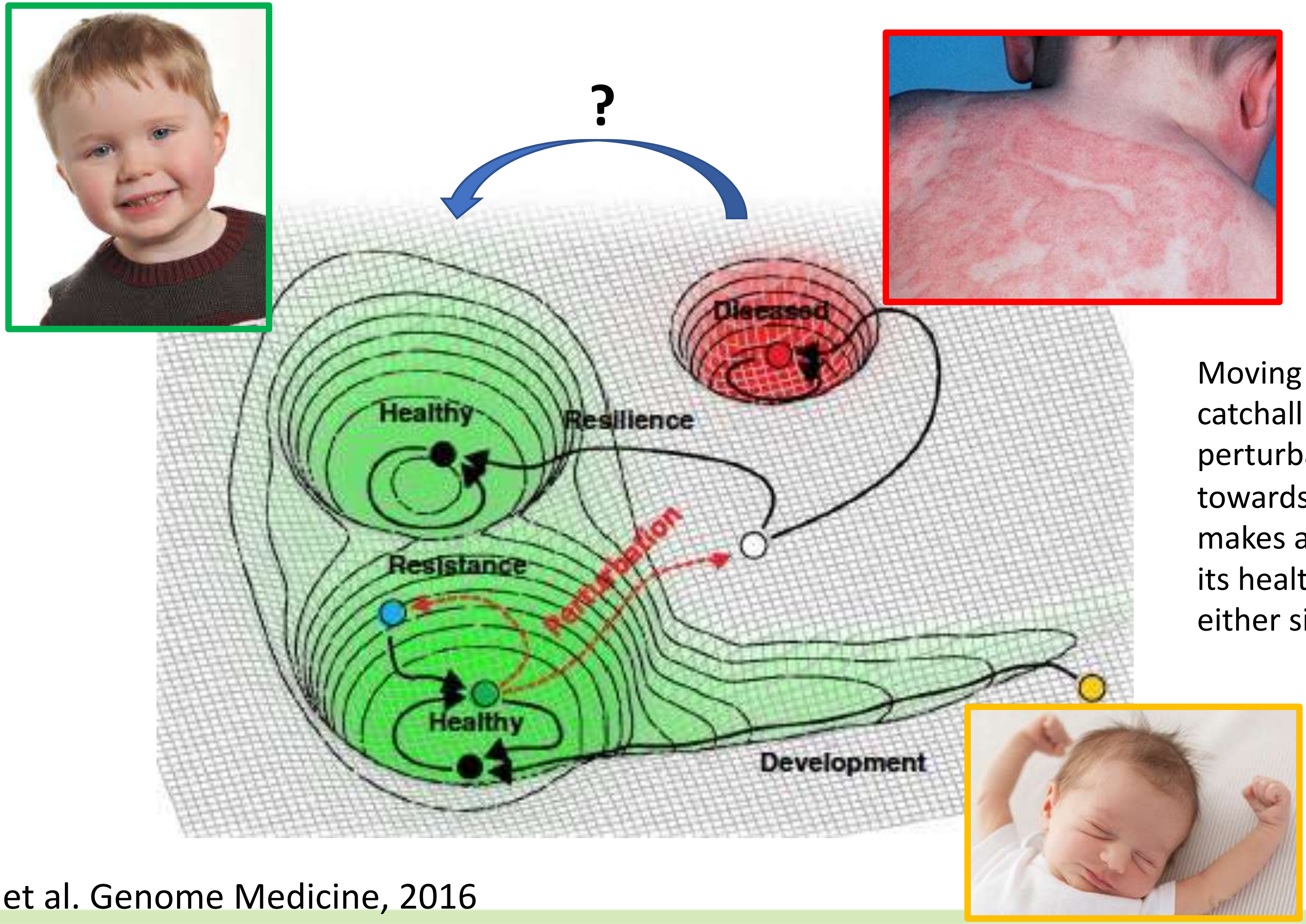
A living ecosystem

≠



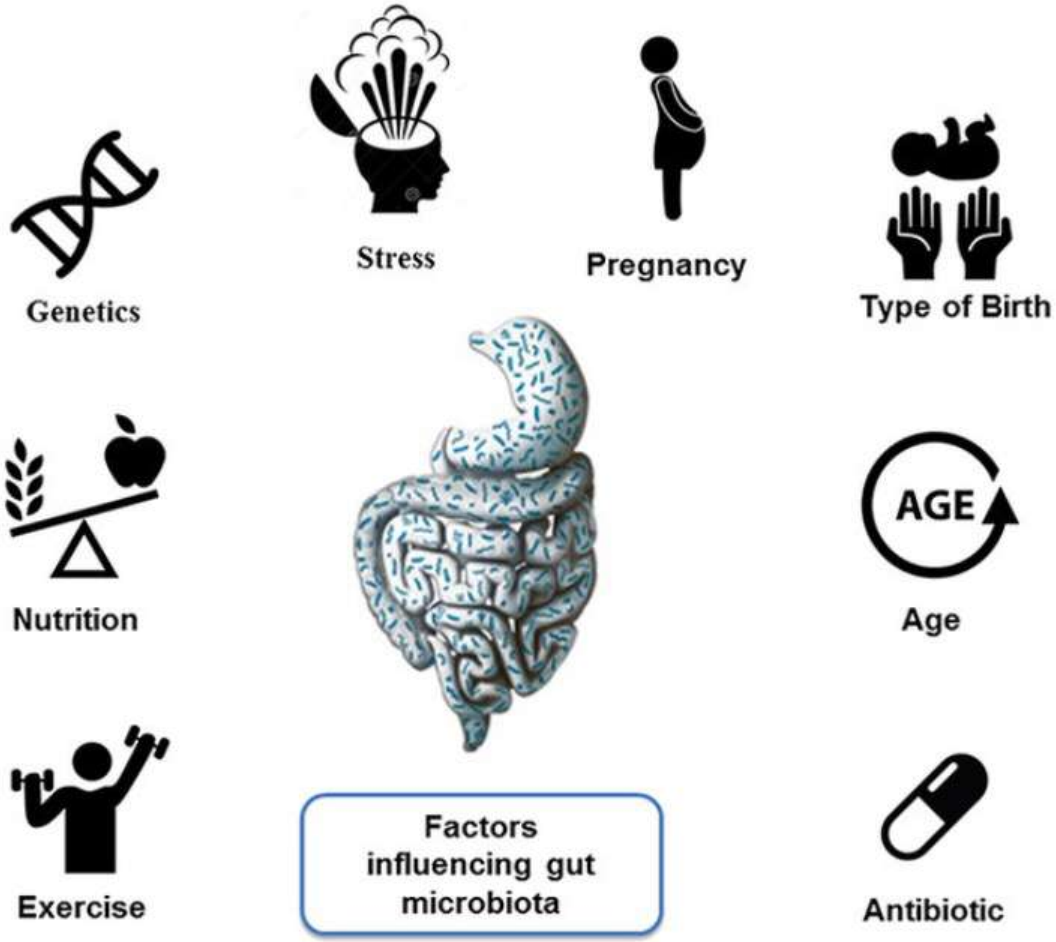
≠

Intestinal microbiota : stable states & trajectories



Moving away from “dysbiosis” as a catchall concept for both transient perturbations and diseased state towards understanding what makes a microbiota bounce back to its healthy “steady-state” from either situations.

Lloyd-Price et al. Genome Medicine, 2016



Cerda, 2016

Dietary challenges (temporary changes)

- Different source of protein or fats (e.g. plant *vs* animal)
- FODMAPs
- Lactose/dairy or other food intolerance (inducing diarrhea)

Antibiotics

- Number of prescriptions
- Nature

Sampling procedures

- *i.e.* enemas undertaken before colonoscopy (medical procedure)

Impact of Diet on microbiota

From Power *et al*, BJN, 2014
Include publications from 2009 to 2012

Temporary

change

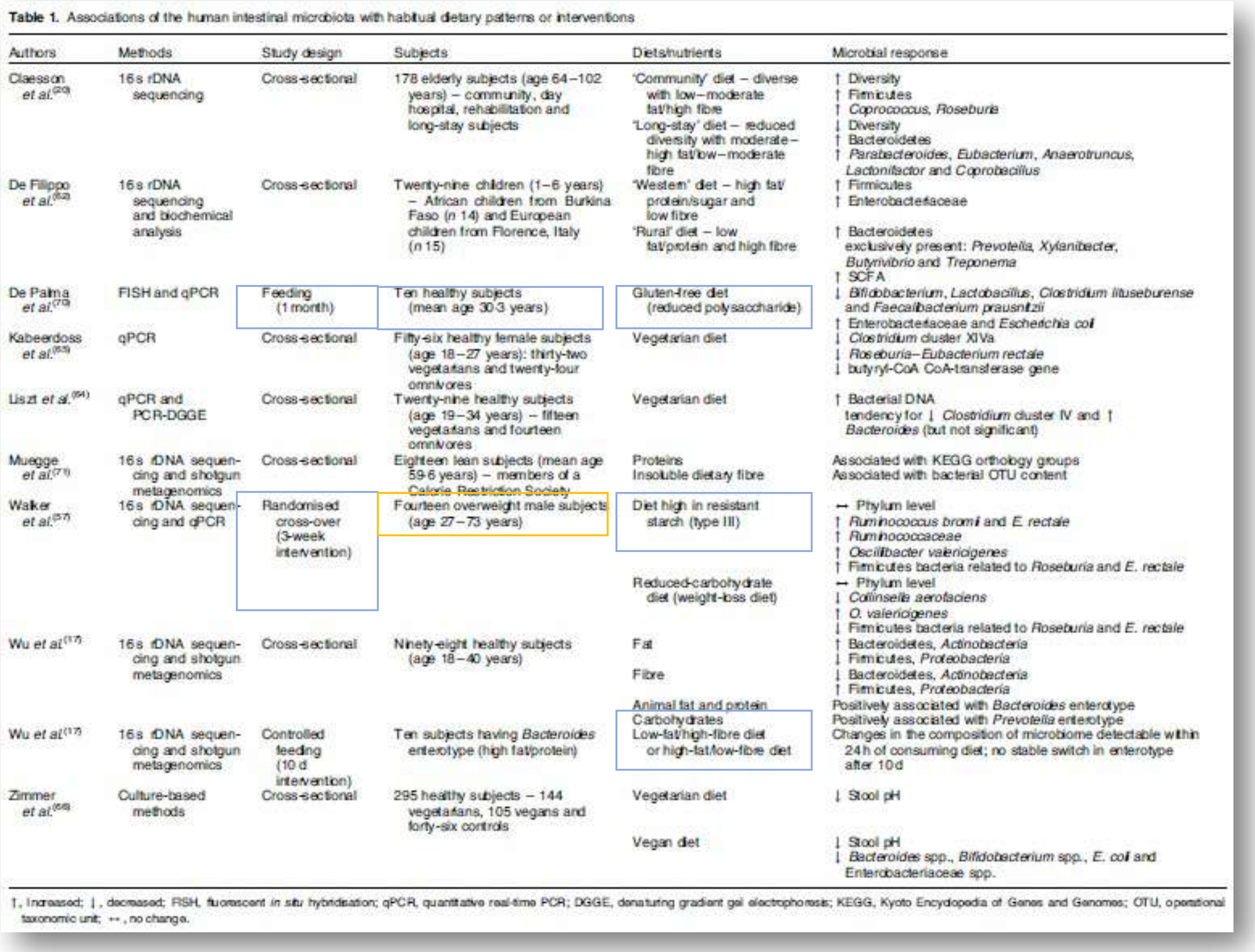


Table 1. Associations of the human intestinal microbiota with habitual dietary patterns or interventions

Authors	Methods	Study design	Subjects	Diets/nutrients	Microbial response
Claesson *et al.*(20)	16s rDNA sequencing	Cross-sectional	178 elderly subjects (age 64–102 years) – community, day hospital, rehabilitation and long-stay subjects	'Community' diet – diverse with low–moderate fat/high fibre	↑ Diversity ↑ Firmicutes ↑ *Coprococcus*, *Roseburia*
				'Long-stay' diet – reduced diversity with moderate–high fat/low–moderate fibre	↓ Diversity ↑ Bacteroidetes ↑ *Parabacteroides*, *Eubacterium*, *Anaerotruncus*, *Lactonifactor* and *Coprobacillus*
De Filippo *et al.*(52)	16s rDNA sequencing and biochemical analysis	Cross-sectional	Twenty-nine children (1–6 years) – African children from Burkina Faso (*n* 14) and European children from Florence, Italy (*n* 15)	'Western' diet – high fat/protein/sugar and low fibre	↑ Firmicutes ↑ Enterobacteriaceae
				'Rural' diet – low fat/protein and high fibre	↑ Bacteroidetes exclusively present: *Prevotella*, *Xylanibacter*, *Butyrivibrio* and *Treponema* ↑ SCFA
De Palma *et al.*(70)	FISH and qPCR	Feeding (1 month)	Ten healthy subjects (mean age 30·3 years)	Gluten-free diet (reduced polysaccharide)	↓ *Bifidobacterium*, *Lactobacillus*, *Clostridium lituseburense* and *Faecalibacterium prausnitzii* ↑ Enterobacteriaceae and *Escherichia coli*
Kabeerdoss *et al.*(53)	qPCR	Cross-sectional	Fifty-six healthy female subjects (age 18–27 years): thirty-two vegetarians and twenty-four omnivores	Vegetarian diet	↓ *Clostridium* cluster XIVa ↓ *Roseburia*–*Eubacterium rectale* ↓ butyryl-CoA CoA-transferase gene
Liszt *et al.*(54)	qPCR and PCR-DGGE	Cross-sectional	Twenty-nine healthy subjects (age 19–34 years) – fifteen vegetarians and fourteen omnivores	Vegetarian diet	↑ Bacterial DNA tendency for ↓ *Clostridium* cluster IV and ↑ *Bacteroides* (but not significant)
Muegge *et al.*(71)	16s rDNA sequencing and shotgun metagenomics	Cross-sectional	Eighteen lean subjects (mean age 59·6 years) – members of a Calorie Restriction Society	Proteins Insoluble dietary fibre	Associated with KEGG orthology groups Associated with bacterial OTU content
Walker *et al.*(57)	16s rDNA sequencing and qPCR	Randomised cross-over (3-week intervention)	Fourteen overweight male subjects (age 27–73 years)	Diet high in resistant starch (type III)	↔ Phylum level ↑ *Ruminococcus bromii* and *E. rectale* ↑ *Ruminococcaceae* ↑ *Oscillibacter valericigenes* ↑ Firmicutes bacteria related to *Roseburia* and *E. rectale*
				Reduced-carbohydrate diet (weight-loss diet)	↔ Phylum level ↓ *Collinsella aerofaciens* ↑ *O. valericigenes* ↓ Firmicutes bacteria related to *Roseburia* and *E. rectale*
Wu *et al.*(17)	16s rDNA sequencing and shotgun metagenomics	Cross-sectional	Ninety-eight healthy subjects (age 18–40 years)	Fat	↑ Bacteroidetes, *Actinobacteria* ↓ Firmicutes, *Proteobacteria*
				Fibre	↓ Bacteroidetes, *Actinobacteria* ↑ Firmicutes, *Proteobacteria*
				Animal fat and protein	Positively associated with *Bacteroides* enterotype
				Carbohydrates	Positively associated with *Prevotella* enterotype
Wu *et al.*(17)	16s rDNA sequencing and shotgun metagenomics	Controlled feeding (10 d intervention)	Ten subjects having *Bacteroides* enterotype (high fat/protein)	Low-fat/high-fibre diet or high-fat/low-fibre diet	Changes in the composition of microbiome detectable within 24 h of consuming diet; no stable switch in enterotype after 10 d
Zimmer *et al.*(56)	Culture-based methods	Cross-sectional	295 healthy subjects – 144 vegetarians, 105 vegans and forty-six controls	Vegetarian diet	↓ Stool pH
				Vegan diet	↓ Stool pH ↓ *Bacteroides* spp., *Bifidobacterium* spp., *E. coli* and Enterobacteriaceae spp.

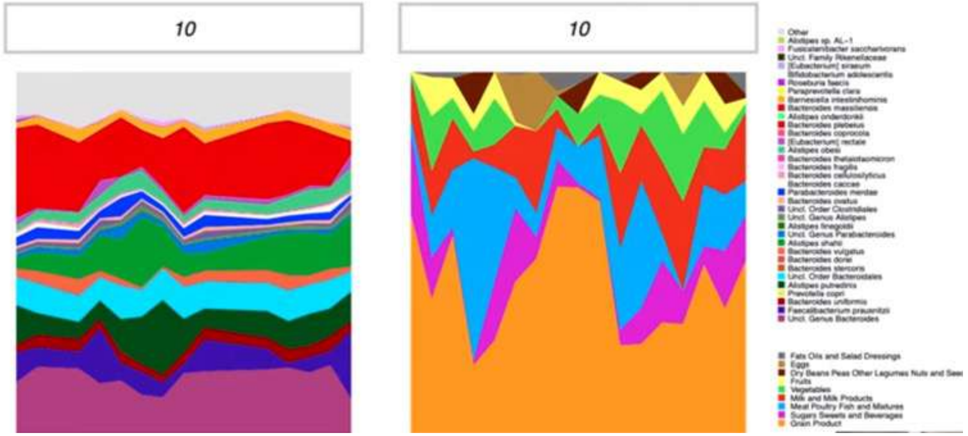
↑, Increased; ↓, decreased; FISH, fluorescent *in situ* hybridisation; qPCR, quantitative real-time PCR; DGGE, denaturing gradient gel electrophoresis; KEGG, Kyoto Encyclopedia of Genes and Genomes; OTU, operational taxonomic unit; ↔, no change.

What’s a perturbation for microbiota ?

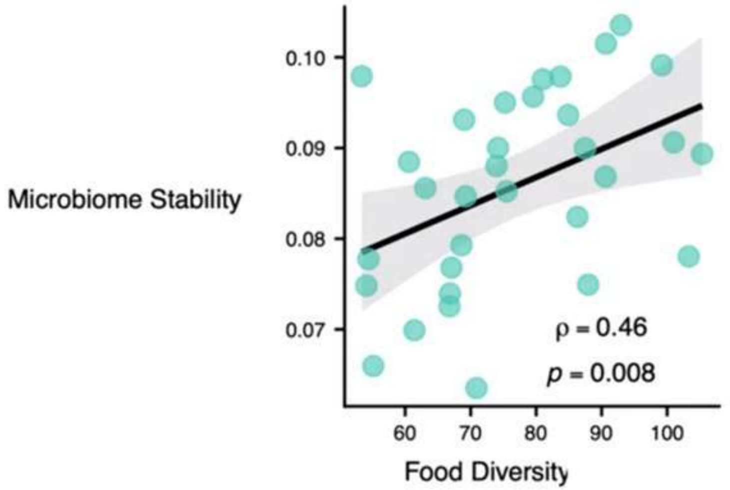
Longitudinal sampling and daily dietary records to model microbiome changes in response to diet

24-h food records and fecal shotgun metagenomes from 34 healthy human subjects collected daily over 17 days

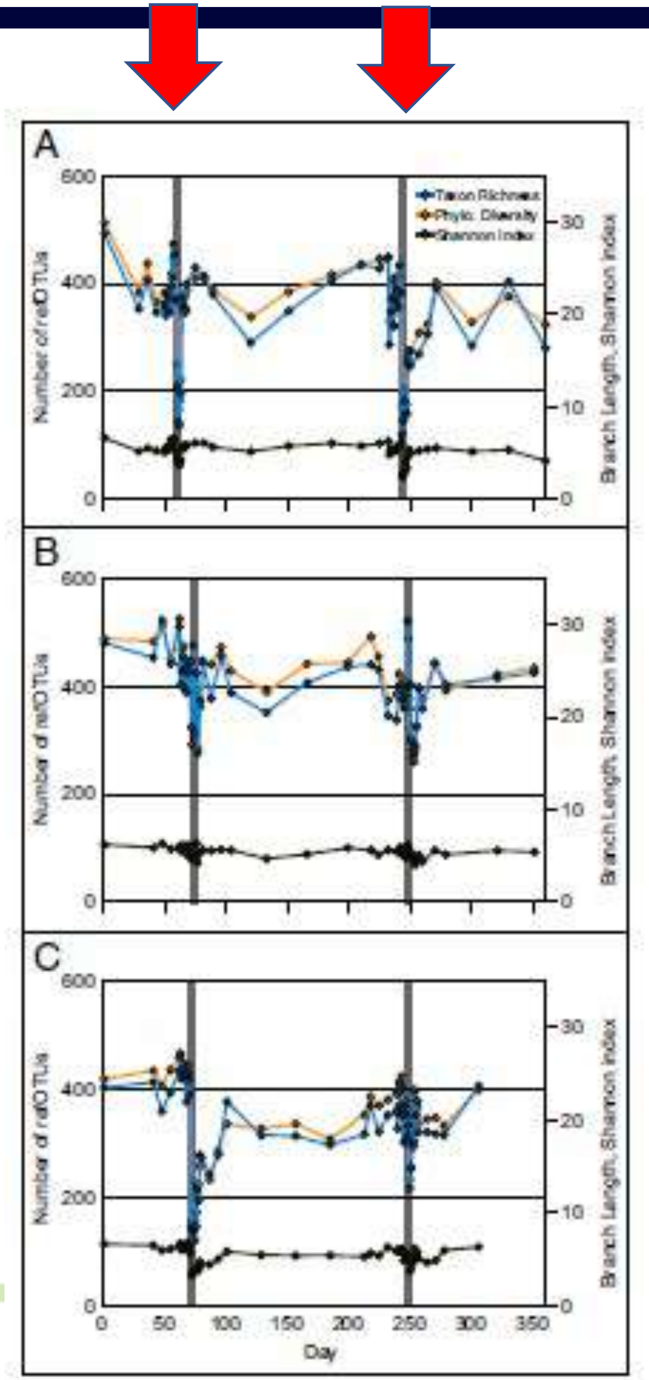
Stable microbiome despite variable dietary intake



Dietary diversity correlates with microbiome stability



Abigail Johnson Integrating Microbiome and Dietary Data
Johnson et al., 2019, Cell Host & Microbe 25, 789−802



Incomplete recovery and individualized responses of the human distal gut microbiota to repeated antibiotic perturbation

PNAS

Dethlefsen and Relman, 2011

⇒ ATB treatment can lead to temporary microbiota dysbiosis

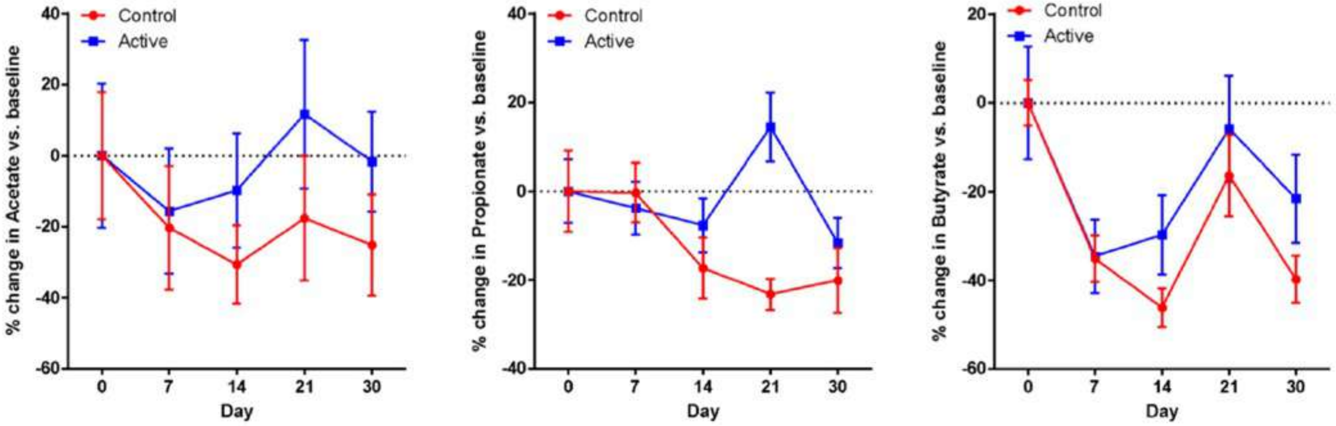
⇒ Repeted ATB treatments can affect the resilience of the microbiota

Fig: Measure of biological diversity for samples from 3 subjects (A,B,C) before, during after ciprofloxacin treatment

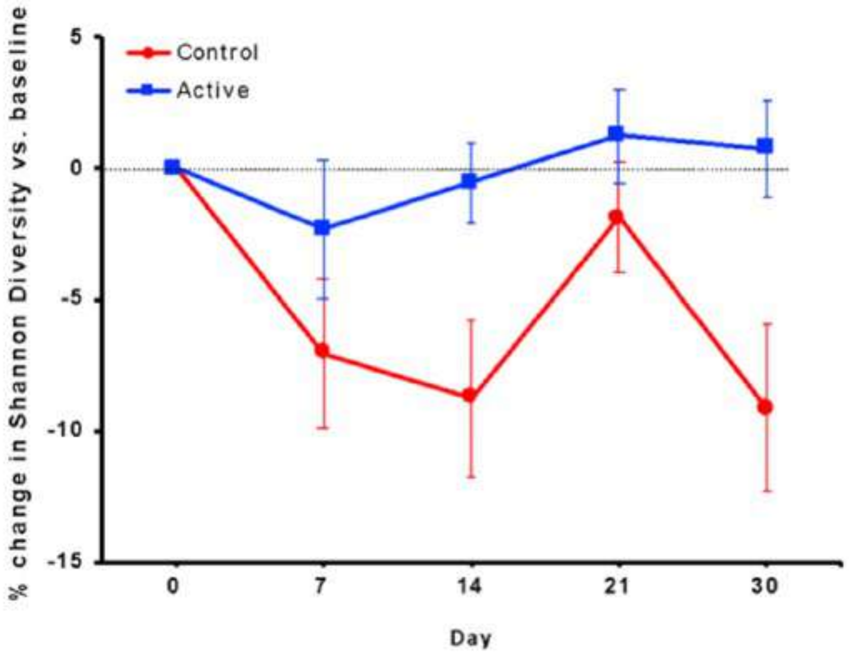
More recent results on probiotics and microbiota recovery after an antibiotic challenge

Concurrent administration of amoxicillin/clavulanate and BB-12 yogurt to healthy subjects

significantly smaller decrease in the fecal SCFA levels

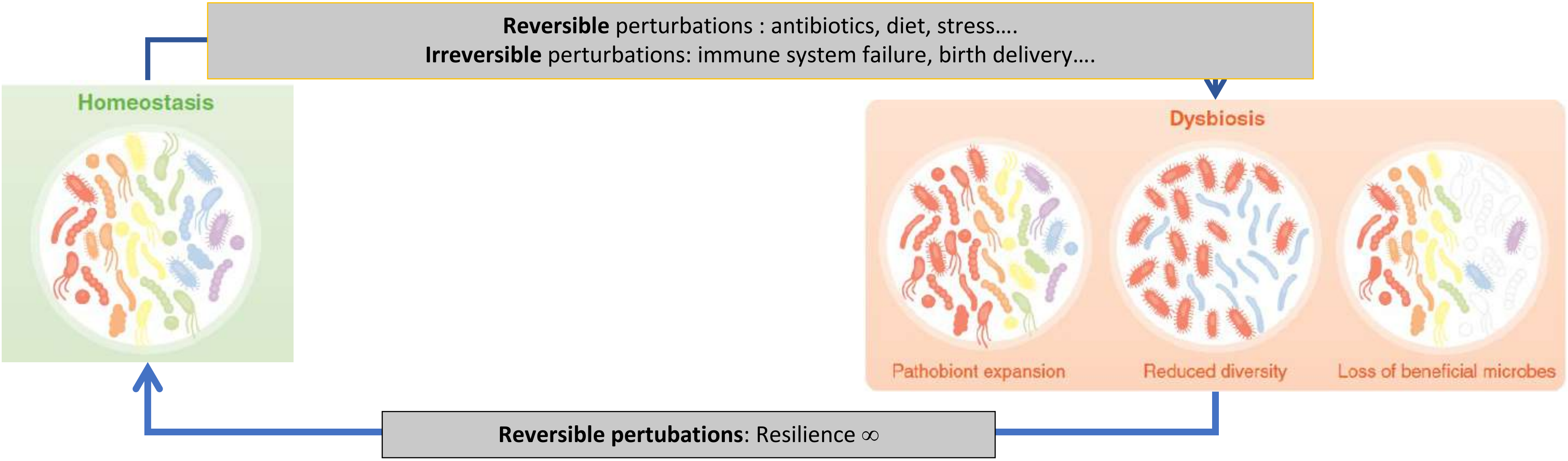


more stable taxonomic profile of the microbiota over time than the control group



Merenstein et aL. Nutrients **2021**, 13, 2814.

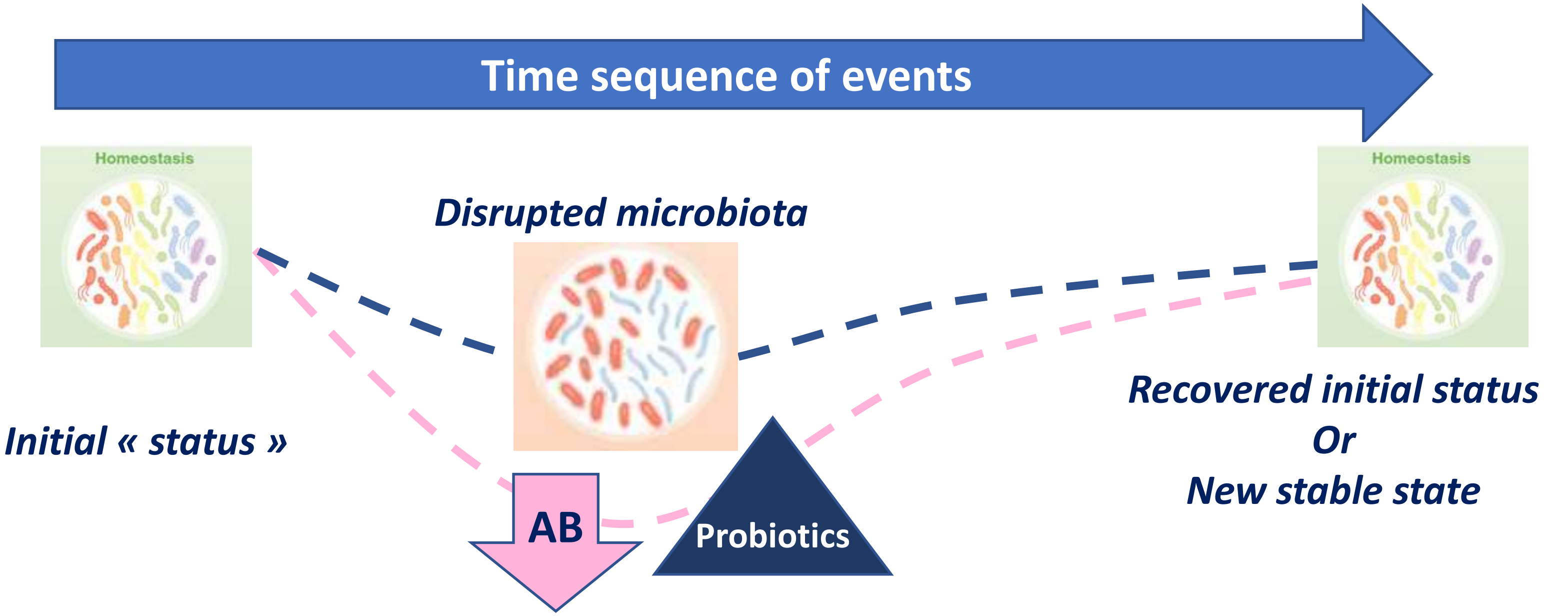
In 2016, SCIENCE STARTS TO MATURE on a CONSENSUAL VIEW ON UNBALANCED MICROBIOTA (not really on « normal » microbiota)



Reversible perturbations : antibiotics, diet, stress….
Irreversible perturbations: immune system failure, birth delivery….

Reversible pertubations: Resilience ∞

Use of clinical evidence: Validation of the model of clinical demonstration :



Time sequence of events

Disrupted microbiota

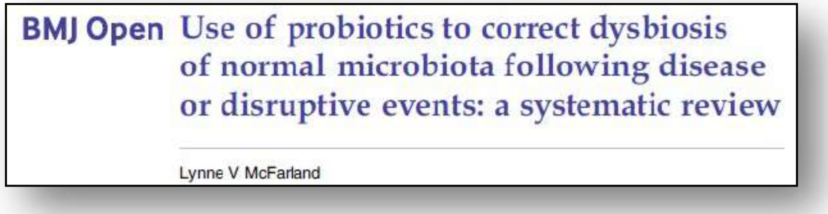
Initial « status »

Recovered initial status
Or
New stable state

AB

Probiotics

- AB challenge model
- General population
- Adult mainly
- Evaluate different probiotics & different doses
- Follow of disruption period & time for recovery



BMJ Open Use of probiotics to correct dysbiosis of normal microbiota following disease or disruptive events: a systematic review

Lynne V McFarland

Summary of the « state of the art » work conducted

- **Publications between 1991 – 2016**
- **Controlled trials**
- **Antibiotic treatment**
- **Microbiota assessment**
- **Healthy subjectsc above 3 years of age (mean age)**
  - Diseased subjects included only when receiving antibiotics for respiratory infections, tonsillitis, gastroenteritis or presence of H. pylori

- **21 studies**
- **19 strains**
- **6 taxa**

B. animalis subsp. lactis

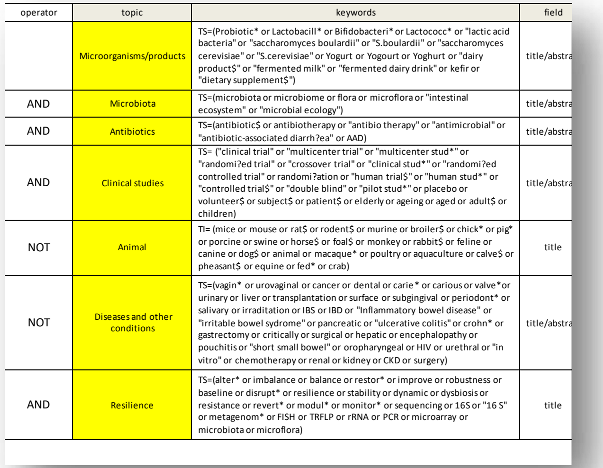
B. bifidum

L.acidophilus

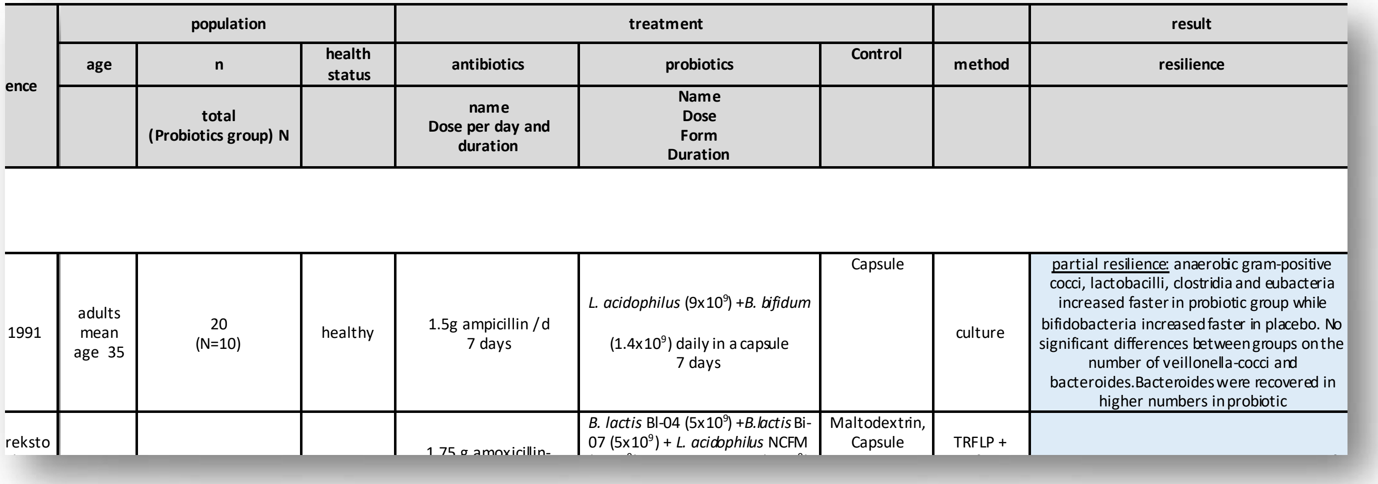
L casei/paracasei

L. rhamnosus

S. boulardii



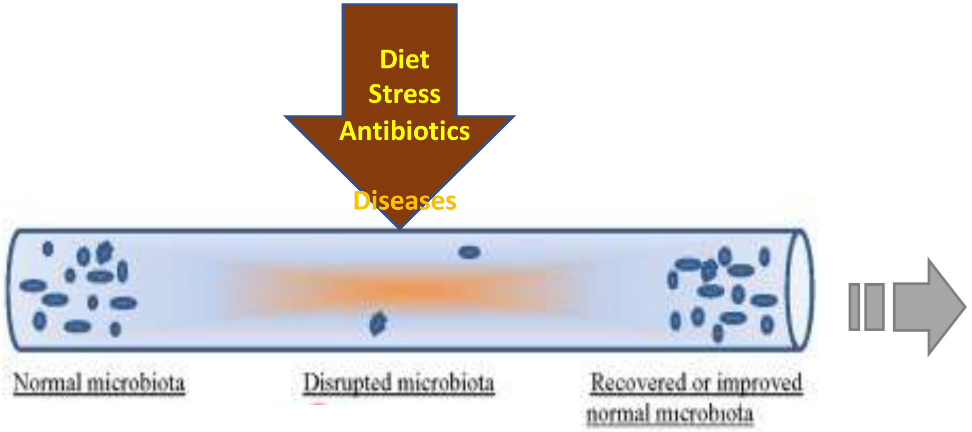
operator	topic	keywords	field
	Microorganisms/products	TS=(Probiotic* or Lactobacill* or Bifidobacteri* or Lactococc* or "lactic acid bacteria" or "saccharomyces boulardii" or "S.boulardii" or "saccharomyces cerevisiae" or "S.cerevisiae" or Yogurt or Yogourt or Yoghurt or "dairy product$" or "fermented milk" or "fermented dairy drink" or kefir or "dietary supplement$")	title/abstra
AND	Microbiota	TS=(microbiota or microbiome or flora or microflora or "intestinal ecosystem" or "microbial ecology")	title/abstra
AND	Antibiotics	TS=(antibiotic$ or antibiotherapy or "antibio therapy" or "antimicrobial" or "antibiotic-associated diarrh?ea" or AAD)	title/abstra
AND	Clinical studies	TS= ("clinical trial" or "multicenter trial" or "multicenter stud*" or "randomi?ed trial" or "crossover trial" or "clinical stud*" or "randomi?ed controlled trial" or randomi?ation or "human trial$" or "human stud*" or "controlled trial$" or "double blind" or "pilot stud*" or placebo or volunteer$ or subject$ or patient$ or elderly or ageing or aged or adult$ or children)	title/abstra
NOT	Animal	TI= (mice or mouse or rat$ or rodent$ or murine or broiler$ or chick* or pig* or porcine or swine or horse$ or foal$ or monkey or rabbit$ or feline or canine or dog$ or animal or macaque* or poultry or aquaculture or calve$ or pheasant$ or equine or fed* or crab)	title
NOT	Diseases and other conditions	TS=(vagin* or urovaginal or cancer or dental or carie* or carious or valve*or urinary or liver or transplantation or surface or subgingival or periodont* or salivary or irraditation or IBS or IBD or "Inflammatory bowel disease" or "irritable bowel sydrome" or pancreatic or "ulcerative colitis" or crohn* or gastrectomy or critically or surgical or hepatic or encephalopathy or pouchitis or "short small bowel" or oropharyngeal or HIV or urethral or "in vitro" or chemotherapy or renal or kidney or CKD or surgery)	title/abstra
AND	Resilience	TS=(alter* or imbalance or balance or restor* or improve or robustness or baseline or disrupt* or resilience or stability or dynamic or dysbiosis or resistance or revert* or modul* or monitor* or sequencing or 16S or "16 S" or metagenom* or FISH or TRFLP or rRNA or PCR or microarray or microbiota or microflora)	title



	population			treatment				result
ence	age	n	health status	antibiotics	probiotics	Control	method	resilience
		total (Probiotics group) N		name Dose per day and duration	Name Dose Form Duration			
1991	adults mean age 35	20 (N=10)	healthy	1.5g ampicillin / d 7 days	*L. acidophilus* (9x10^9) +*B. bifidum* (1.4x10^9) daily in a capsule 7 days	Capsule	culture	partial resilience: anaerobic gram-positive cocci, lactobacilli, clostridia and eubacteria increased faster in probiotic group while bifidobacteria increased faster in placebo. No significant differences between groups on the number of veillonella-cocci and bacteroides.Bacteroides were recovered in higher numbers in probiotic
reksto				1.75 g amoxicillin-	*B. lactis* Bl-04 (5x10^9) +*B.lactis* Bi-07 (5x10^9) + *L. acidophilus* NCFM	Maltodextrin, Capsule	TRFLP +	

Microbiota resilience

Its ability to recover after a « challenge »



Health impact of challenges and impairement of recovery

Short term

- Risk of Pathogen growth and GI infection
- Risk of AAD

Long term

- Recurrent perturbations lead to a decrease in resilience capacity of the microbiota.
- Shifts in the bacterial composition and diversity of the microbiota can lead to intestinal dysfunctions
- Risk of IBD, obesity, diabete, allergy, …

Ex of proposed claims

- Help recovery of individual microbiota
- Help for better recovery of individual microbiota under/after challenge condition (such as ATB treatment/in subjects receiving antibiotic treatment)
- contribute to maintaining individual intestinal microbiota in subjects receiving antibiotic treatment

ISAPP

2018:

Dissemination activities

Mary Ellen Sanders PhD, Sylvie Binda PhD, Seppo Salminen PhD and Karen Scott PhD

Explores the concept of ‘resilience’ in the context of human physiology, i.e. the ability to remain healthy even when exposed to a stress, or to recover from a stress faster

ISAPP Science Blog

JANUARY 16, 2018 RESILIENCE AS A MEASURE OF HEALTH: IMPLICATIONS FOR HEALTH CLAIMS FOR FOODS

Posted at 8:15 am in featured, ISAPP Blogs by ISAPP
0 Likes
Share

January 16, 2018. By Mary Ellen Sanders PhD, Sylvie Binda PhD, Seppo Salminen PhD, Karen Scott PhD

Demonstrating health benefits for healthy people is a challenge faced by those attempting to communicate claims on a health promoting food. Foods, in many global regulatory frameworks, are intended for the general population. Therefore, any benefits ascribed to them, the logic goes, must be demonstrated in the generally healthy population.

An old concept has new-found notoriety in the context of offering an approach for establishing health benefits for healthy people. It is the concept of resilience. In an ecological sense, resilience refers to the ability of an ecosystem to withstand perturbation and continue normal function, i.e. maintain homeostasis. In the context of human physiology, resilience enables a host to remain healthy even when exposed to a stress, or to recover from a stress faster. A variety of external challenges such as drugs, pathogens, emotional stress, poor diet among others, may perturb normal physiological function or disrupt the gut ecosystem. Individuals more able to maintain stability of physiological functions when exposed to such challenges would be healthier than those who cannot maintain stability. Thus, a food would be considered to have a beneficial effect if it could increase the resilience of the consumer to a challenge.

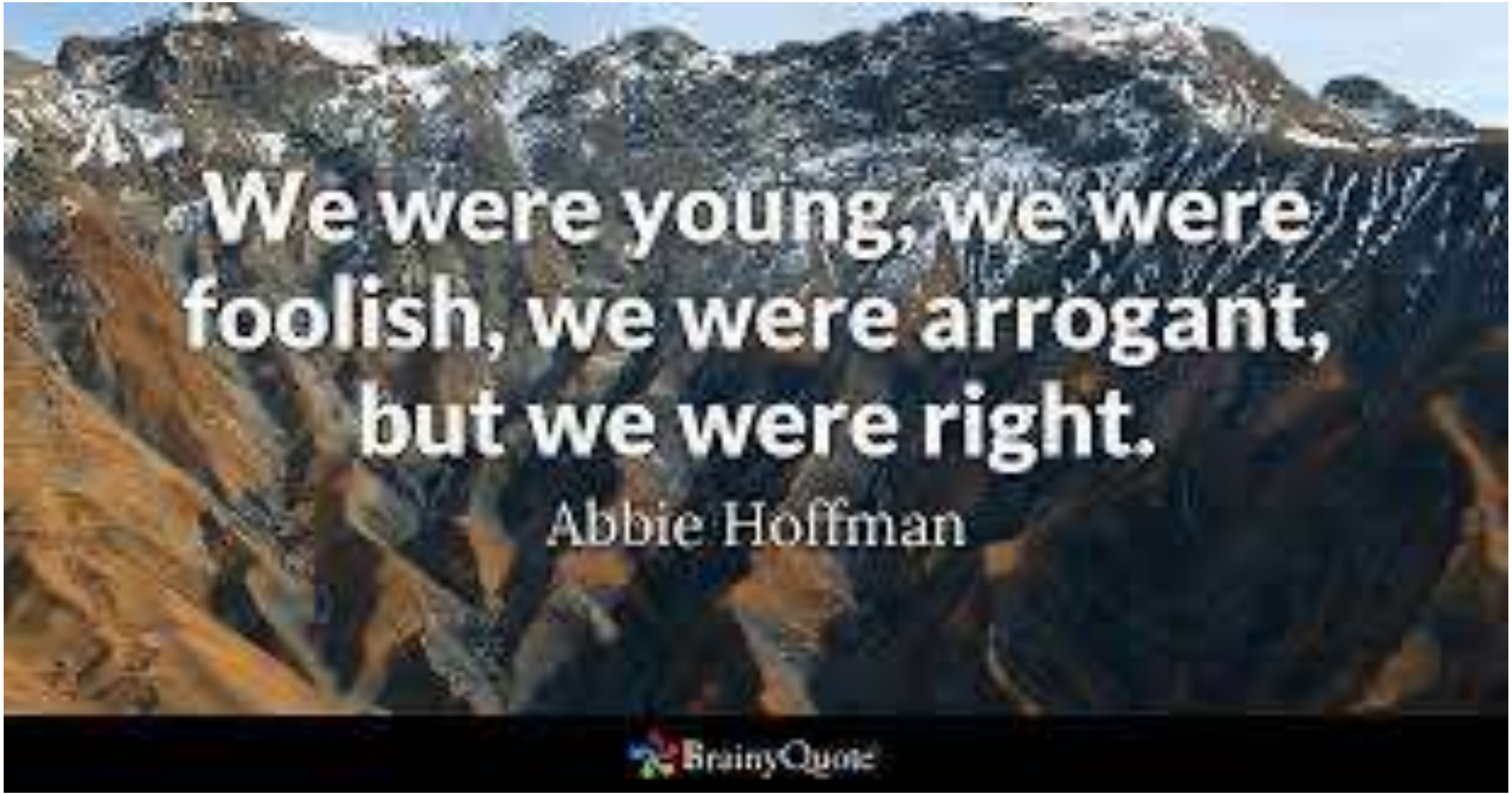
This concept was described in an EFSA guidance document on biological relevance of data in scientific assessments:

"When subject to a disturbance, a biological system enters in a transient state: a process variable has been changed and the system has not yet reached steady state. Some systems, including humans, have the capacity to regulate their internal environment and to maintain a stable, relatively constant condition of properties; it is called 'homeostatic

In 2019:

We had a 70-pages Scientific Monograph covering old & recent findings

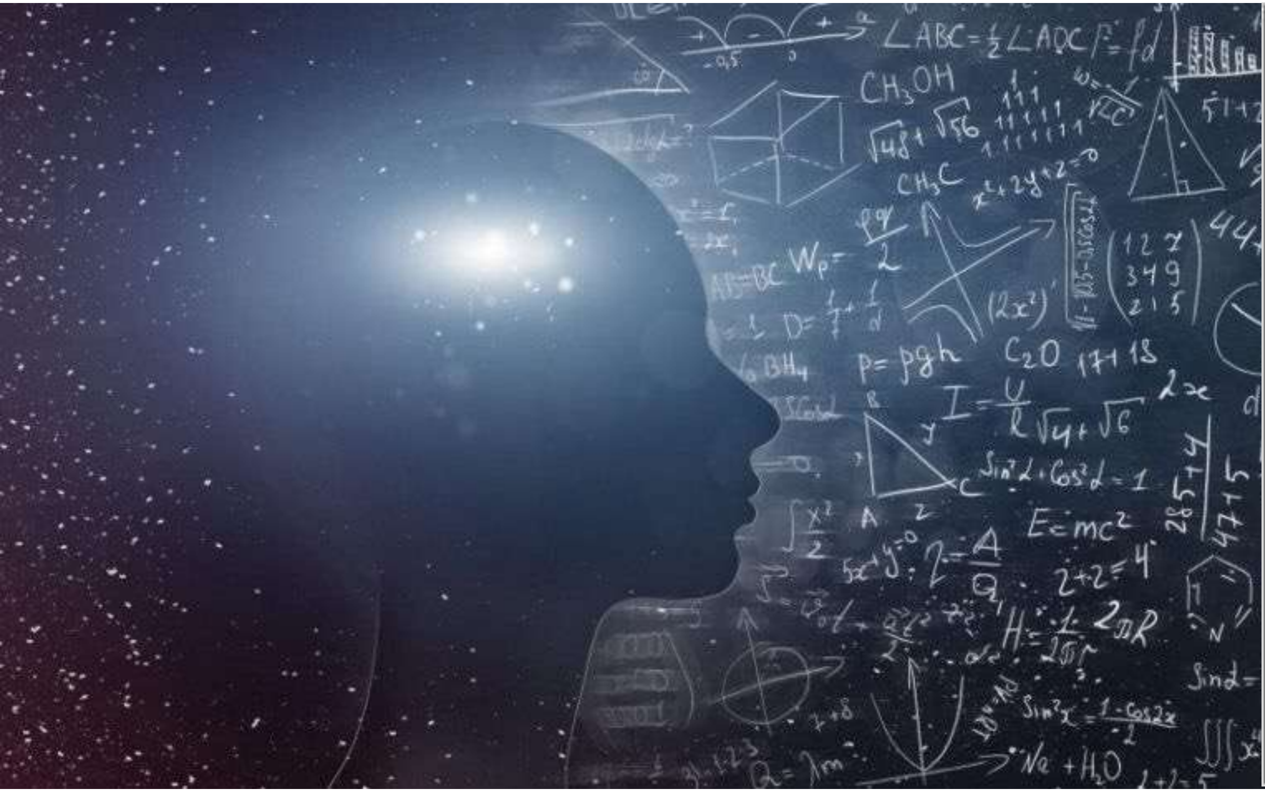
The decision was taken to not submit this as a « dossier »

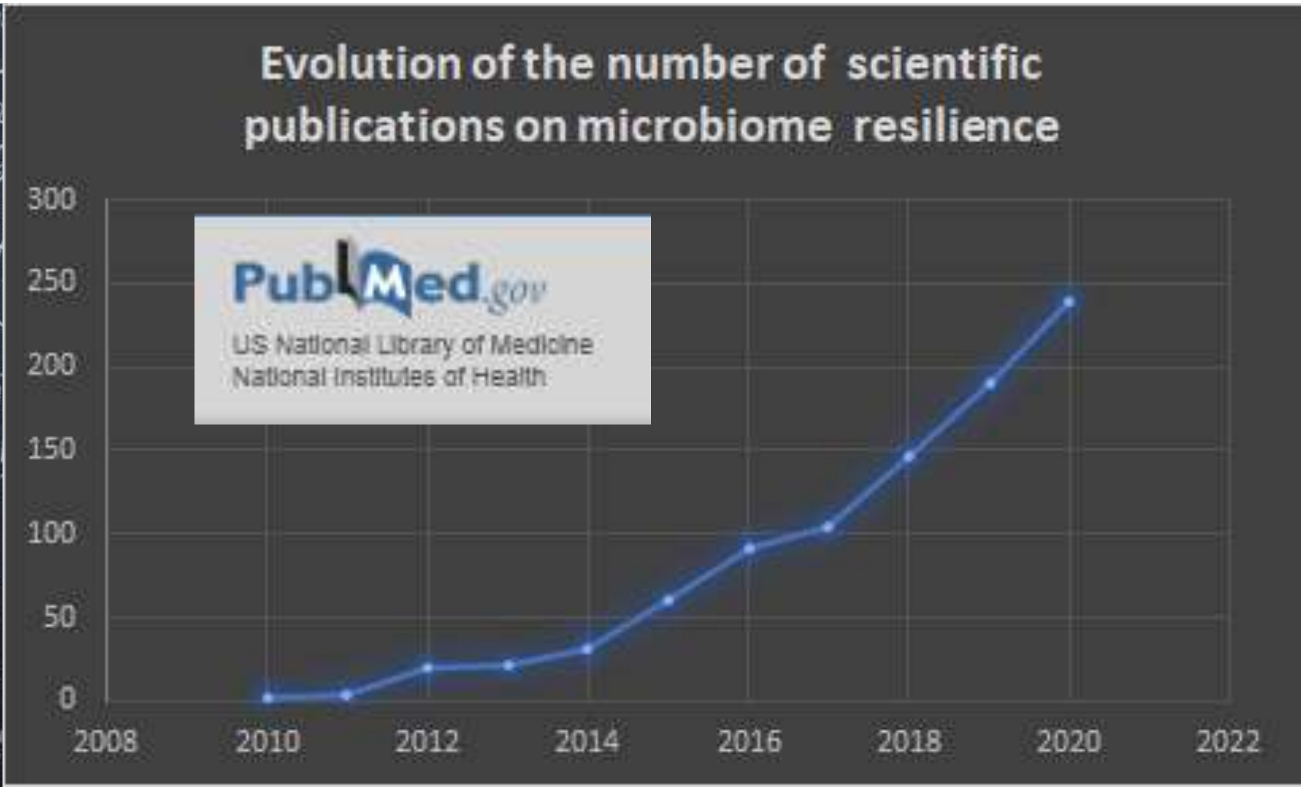


We were young, we were foolish, we were arrogant, but we were right.

Abbie Hoffman

Microbiota resilience: a topic more than ever attractive within the scientific community




Evolution of the number of scientific publications on microbiome resilience

Overview of Existing claims with microbiota & « resilience » concepts

« Probiotics that naturally forms part of the gut flora »
« Provide live microorganisms that naturally form part of the gut flora »
« Probiotic that contributes to healthy gut flora »
« Provides live microorganisms that contribute to healthy gut flora » - Canada

”helps to maintain healhy gastrointestinal bacteria population » - South Koera

« supports the balance of the intestinal flora” - Italy

« Proper diet and regular consumption of food with probiotics, can help to (…) regenenerate the intestinal flora » - Columbia

« helps to maintain a desirable balance of beneficial bacteria in the digestive system » - Singapore

« enhancement of intestinal ecology ” - Phlipinnes

« the daily consumption of milk or dairy products which countains live bacteria helps to maintain the intestinal floral » - Chile

Non defined health claim

Non defined health claims:

- “Intestinal microbiota”
- “Balanced microbiota”
- “Beneficial/healthy microbiota”

Non beneficial physiological effects:

- Increasing numbers of bifidobacteria or lactobacilli.
- • Decreasing numbers of commensal microorganisms (e.g.
- enterobacteria, clostridia, bacteroides, etc.)
- Changes in gut microbiome composition
- Changes in SCFAs

In august 17, EFSA in its guidance document on biological relevance of data in scientific assesments defines :

“Resilience represents the amount of disturbance that can be absorbed by a system before the system changes or loses its normal function, or the time taken to return to a stable state, within the normal operation range following the disturbance (Gunderson, 2000). [Reducing] homeostatic capacity … might be detrimental, whereas increasing the capacity could be beneficial.”

Editorial: Exploring the need to include microbiomes into EFSA’s scientific assessments

Caroline Merten, Reinhilde Schoonjans, Diana Di Gioia, Carmen Peláez, Yolanda Sanz, Daniela Maurici and Tobin Robinson

In June 2020, EFSA discussed the interest to embark on a thematic area of microbiomes

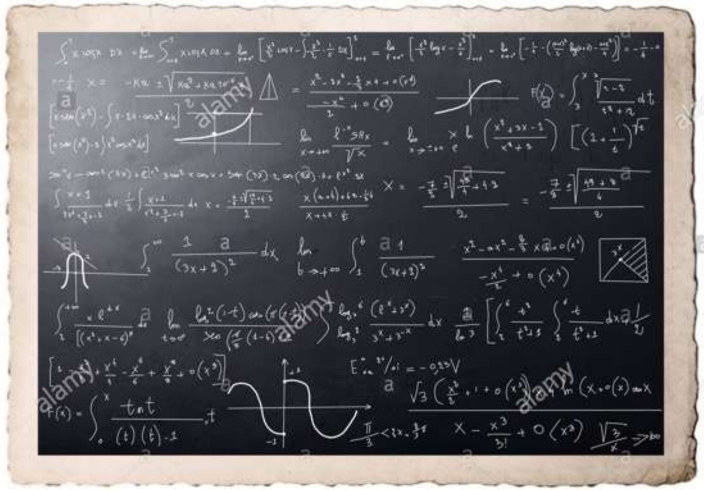
“How to evaluate the impact on microbiomes by various substances under EFSA assessment?”

“How to evaluate the impact of microbiomes on human, animal and plant health?”

“Extreme and sustained adverse exposure can lead to profound ecological disruptions and a breakdown in the host–microbiome partnership, contributing to adverse health outcomes”

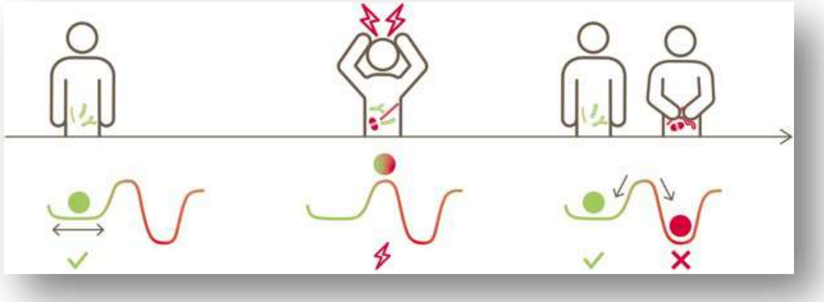
How to define and calculate a resilience index ?

“A quantitative measure of how much the microbiota has deviated [from baseline] and how quickly and fully it has recovered”



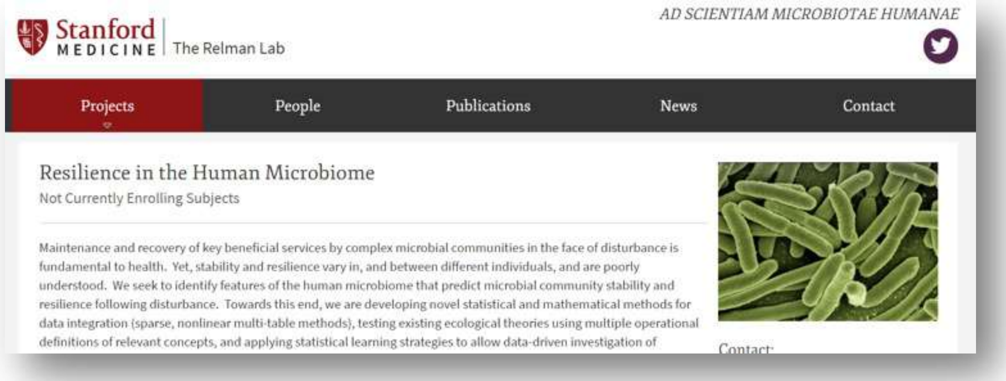
Strong interest in the simplicity of an index integrating the interindividual and complexity

Are we there yet?



Source: Dogra et al. Frontiers in Microbiology, 2020;11:572921.
https://www.frontiersin.org/articles/10.3389/fmicb.2020.572921/full

Outputs of recent initiatives



Stanford MEDICINE | The Relman Lab

AD SCIENTIAM MICROBIOTAE HUMANAE

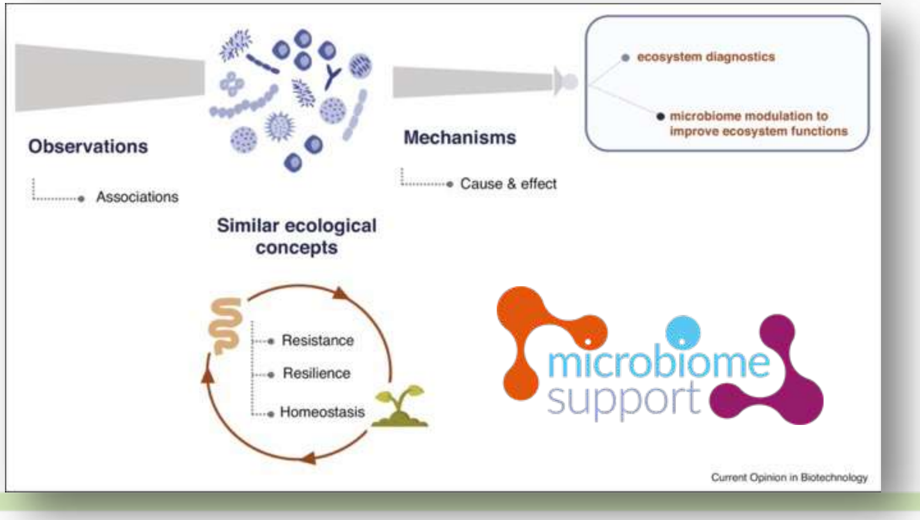
Resilience in the Human Microbiome

Not Currently Enrolling Subjects

Maintenance and recovery of key beneficial services by complex microbial communities in the face of disturbance is fundamental to health. Yet, stability and resilience vary in, and between different individuals, and are poorly understood. We seek to identify features of the human microbiome that predict microbial community stability and resilience following disturbance. Towards this end, we are developing novel statistical and mathematical methods for data integration (sparse, nonlinear multi-table methods), testing existing ecological theories using multiple operational definitions of relevant concepts, and applying statistical learning strategies to allow data-driven investigation of

Contact:

See interesting website (Stanford University) for key current gaps and an ongoing study from the Relman lab
https://med.stanford.edu/relmanlab/projects/resilience-in-the-human-microbiome.html
https://humanmicrobiota.weebly.com/about-our-study.html



Meisner et al 2022, Current Opinion in Biotechnology. DOI:10.1016/j.copbio.2021.08.003

ITALIAN MICROBIOME INITIATIVE FOR IMPROVED HUMAN HEALTH AND AGRI-FOOD PRODUCTION

Presidenza del Consiglio dei Ministri
Comitato Nazionale per la Biosicurezza, le Biotecnologie e le Scienze della Vita
CNBBSV

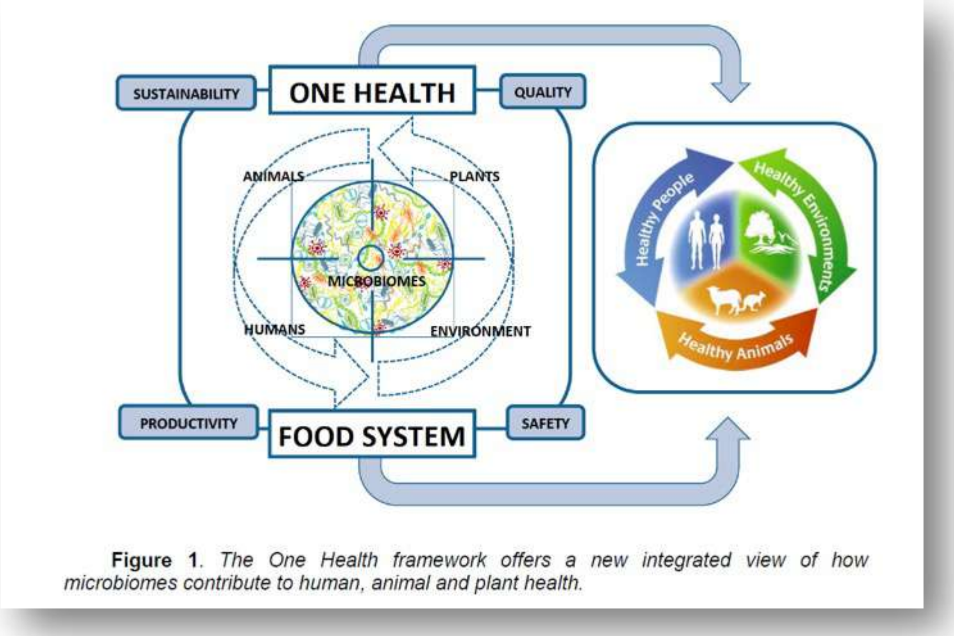
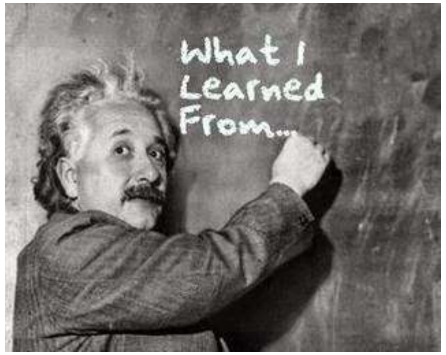


Figure 1. *The One Health framework offers a new integrated view of how microbiomes contribute to human, animal and plant health.*

Additional Gaps, needs & challenges

- Controlling trials for most common microbiome stressors (known vs unknown confounders?)
- Dietary Strategies for maintenance and restoration of functions, resilience
- What shapes stability and resilience of the microbiome (are all stressors equal for everyone?)
- What are the appropriate scales, durations or other dimensions to describe the microbiome and its response to environmental factors

Take-Home messages & call for action



The study of the microbiome stability is key to understand its relation to health maintenance

Probiotics could play a positive role to support microbiome resilience

(re)Design nutritional interventions in order to demonstrate the impact of diet enriched with live microbes

Join us to go on to elucidate & help contribute to build a consensus

A need for a scientific conversation & collective thinking in order to develop science & scientific argumentation for the promotion of probiotics

IPA EU Resilience Project Team

Sylvie Binda (Lallemand Health Solutions)

David Obis (Danone)

Artur Ouwehand (IFF)

Bruno Pot (Yakult)

Questions?

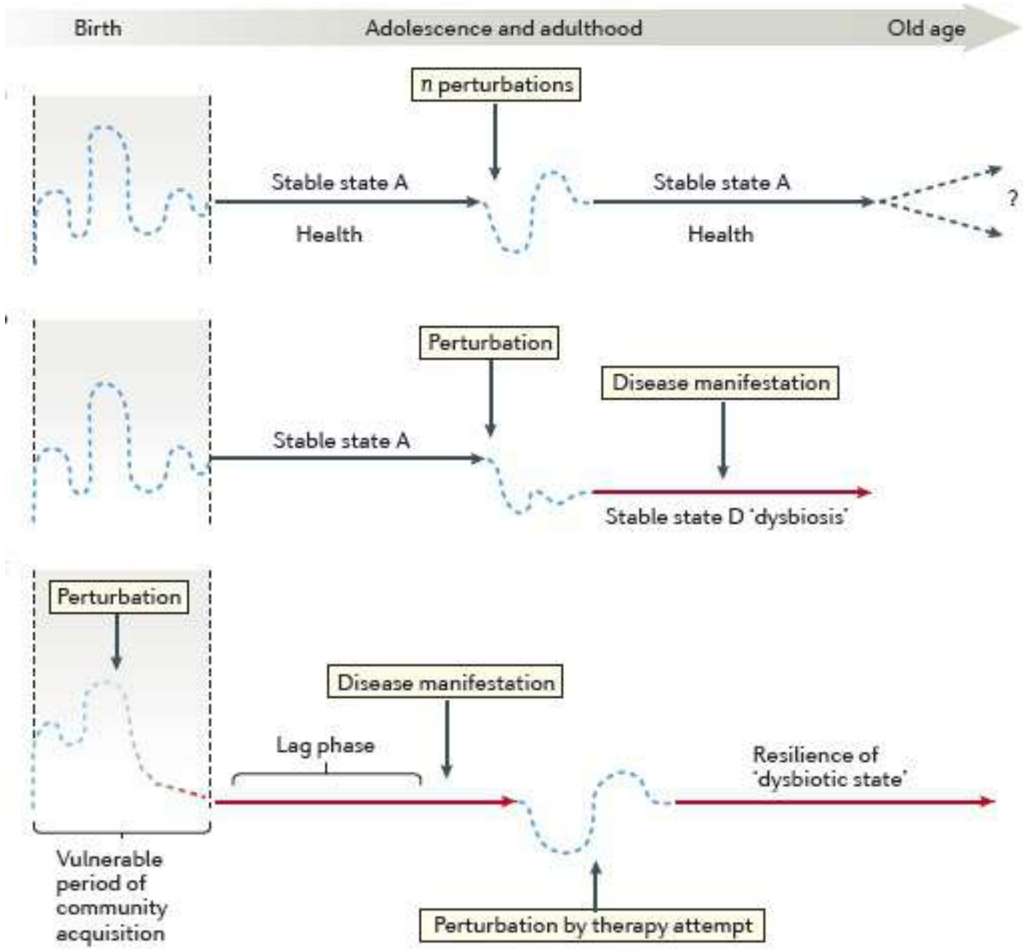
OPINION

The resilience of the intestinal microbiota influences health and disease

Felix Sommer, Jacqueline Moltzau Anderson, Richa Bharti, Jeroen Raes and Philip Rosenstiel

Schematic representation of resilience and health and disease

Review paper, terms, resilience has key role in health and disease. Concepts & mecanisms illustration. Understanding resilience is key.



The human microbiome : Ecosystem resilience & health

"Among the most important questions in need of attention, ***what are the features of microbial diversity most desired for states of health*** *in humans?* ***How are these features most effectively measured****?* ***What disturbance regimes are most desired,*** *and* ***what range of disturbance regimes is tolerated*** *during states of health? What are the microbial ecosystem services of greatest relevance to the wide variety of human states of health?* ***In humans at risk for disease linked to disrupted microbial communities, such as Crohn's disease, are flares of disease associated with (or due to) loss of microbial community resilience? Can we anticipate flares*** *by detecting* ***early degradation of the stability*** *landscape, or* ***predict treatment failures by identifying a 'catastrophic regime shift'?****"*

(**Relman DA**. The human microbiome: ecosystem resilience and health. *Nutr Rev*. **2012**;70 Suppl 1(Suppl 1):S2-S9.)

What are the possible means of interventions ?

Probiotics (included dietary microbes)

Fibers ?

....ability to adapt and self-manage in the face of social, physical and emotional challenges

BMJ

BMJ 2011;343:d4163 doi: 10.1136/bmj.d4163

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