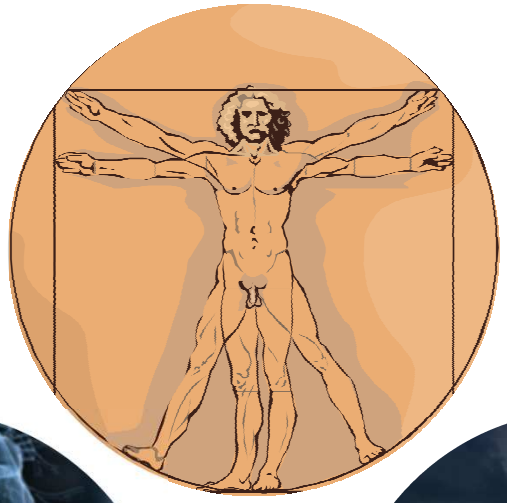
Microbiologie als Impuls voor Gezonde Teelt

Hauke Smidt

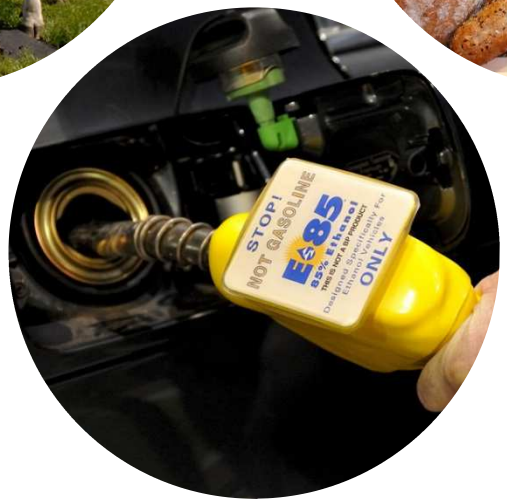
CTBG Relatiedag, Ede, 14 juni 2018

WAGENINGEN
UNIVERSITY & RESEARCH

Microbial Ecosystems are Key to our Existence



Microbial Ecosystems are Key to our Society



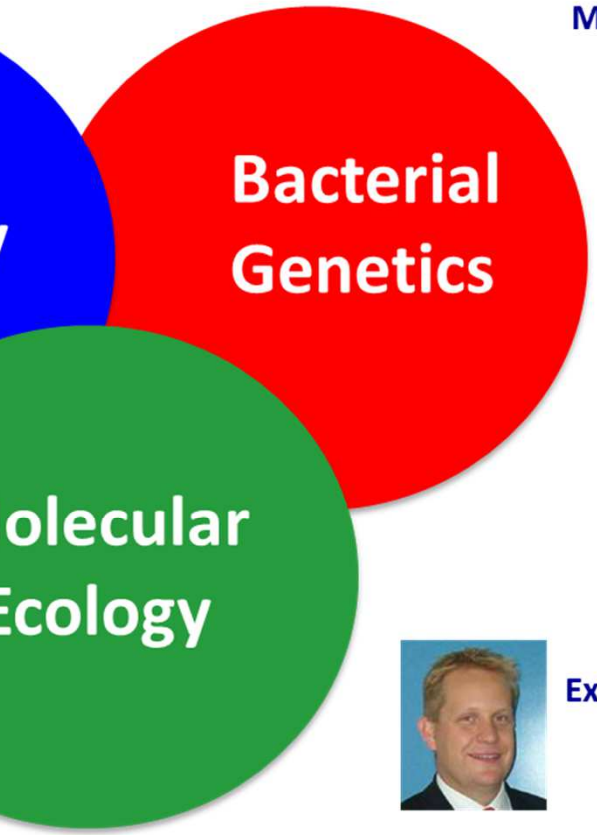
Laboratory of Microbiology – Our Mission

- Cultivation & molecular-driven, genomics-based and systems biology-inspired research & education
- Focus on microbial interactions, biotransformations and their control
- Covering a wide expertise in bacteria, archaea, (anaerobic) fungi and viruses

Laboratory of Microbiology

- Head: Willem M.de Vos ± 100 co-workers in 3 groups

Dr. Diana Sousa



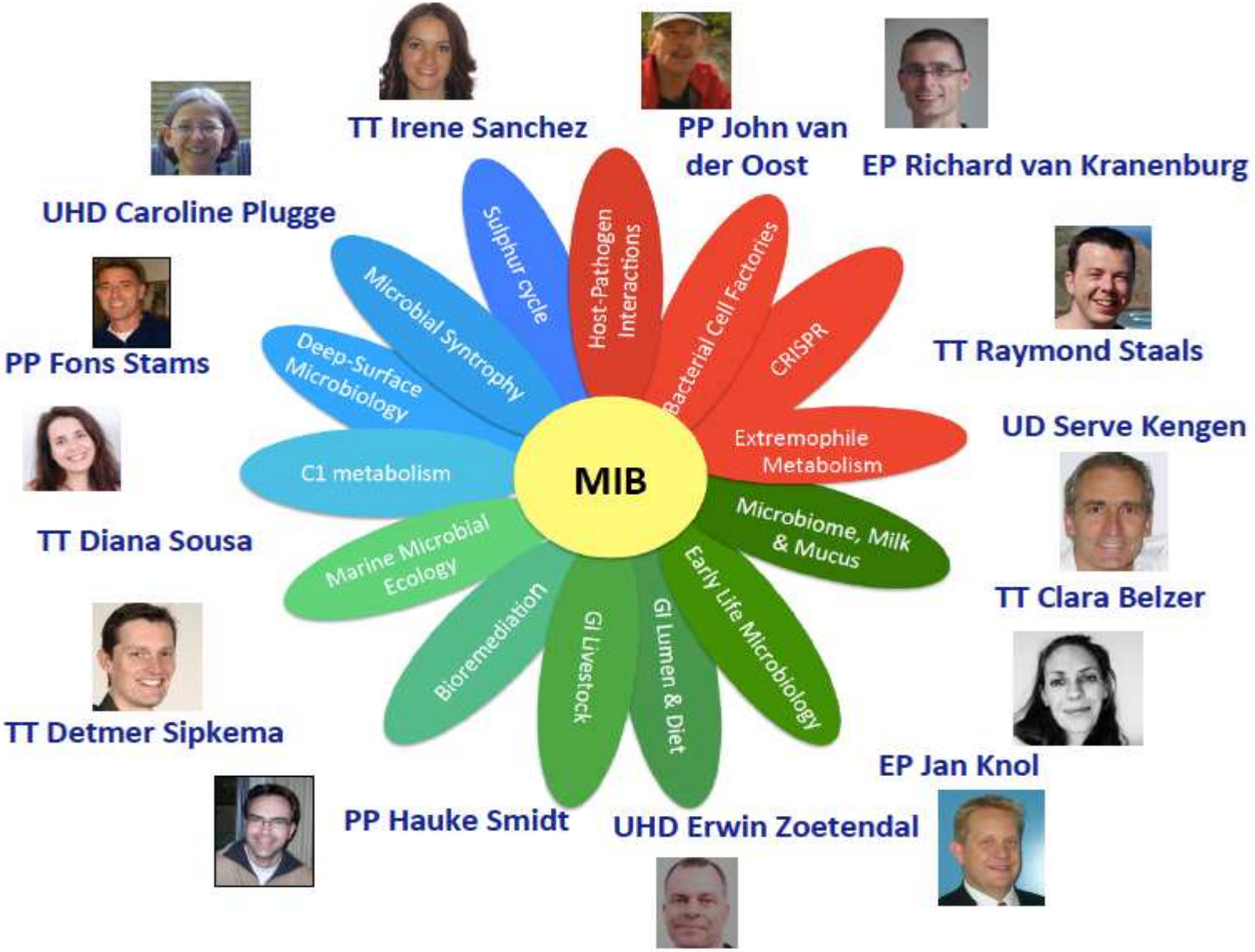
Prof John van der Oost
Microbiology & Biochemistry

Extraordinary Prof - Corbion
Bacterial Cell Factories
Richard van Kranenburg

Prof Hauke Smidt
Complex Ecosystems

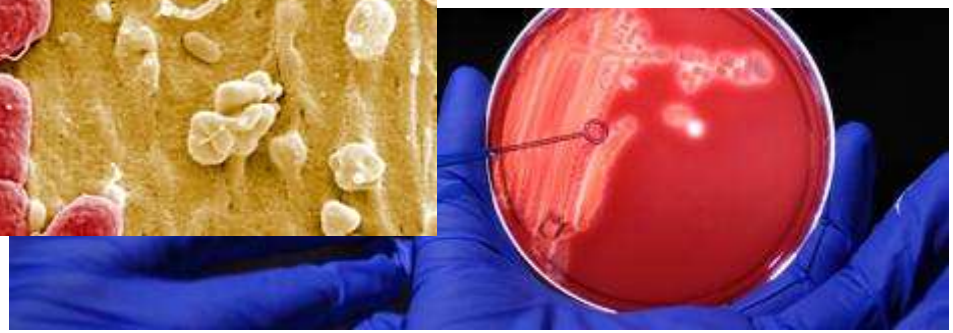
Extraordinary Prof – Danone
Early Life Microbiology
Jan Knol

Laboratory of Microbiology



The world inside us – the intestinal ecosystem

- Intestinal pathogens are front-page news



- Worries about increasing spread of antibiotic resistance in bacteria in humans & farm animals

The world inside – the intestinal ecosystem

More than just bad bugs....

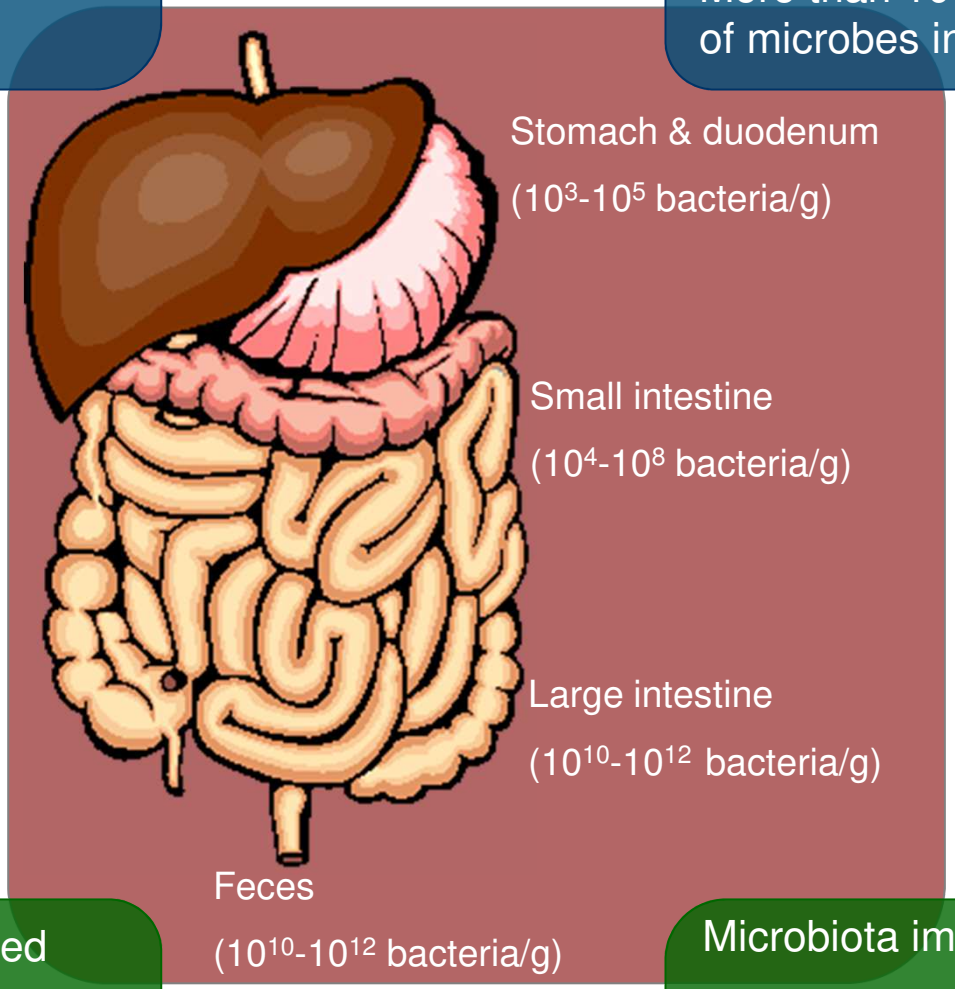
microbial world impressions of an artist & pioneer microbial ecologist

Antoon Akkermans

The world inside us – the intestinal ecosystem

Microbial cells outnumber host cells by ~~10~~ 2-fold

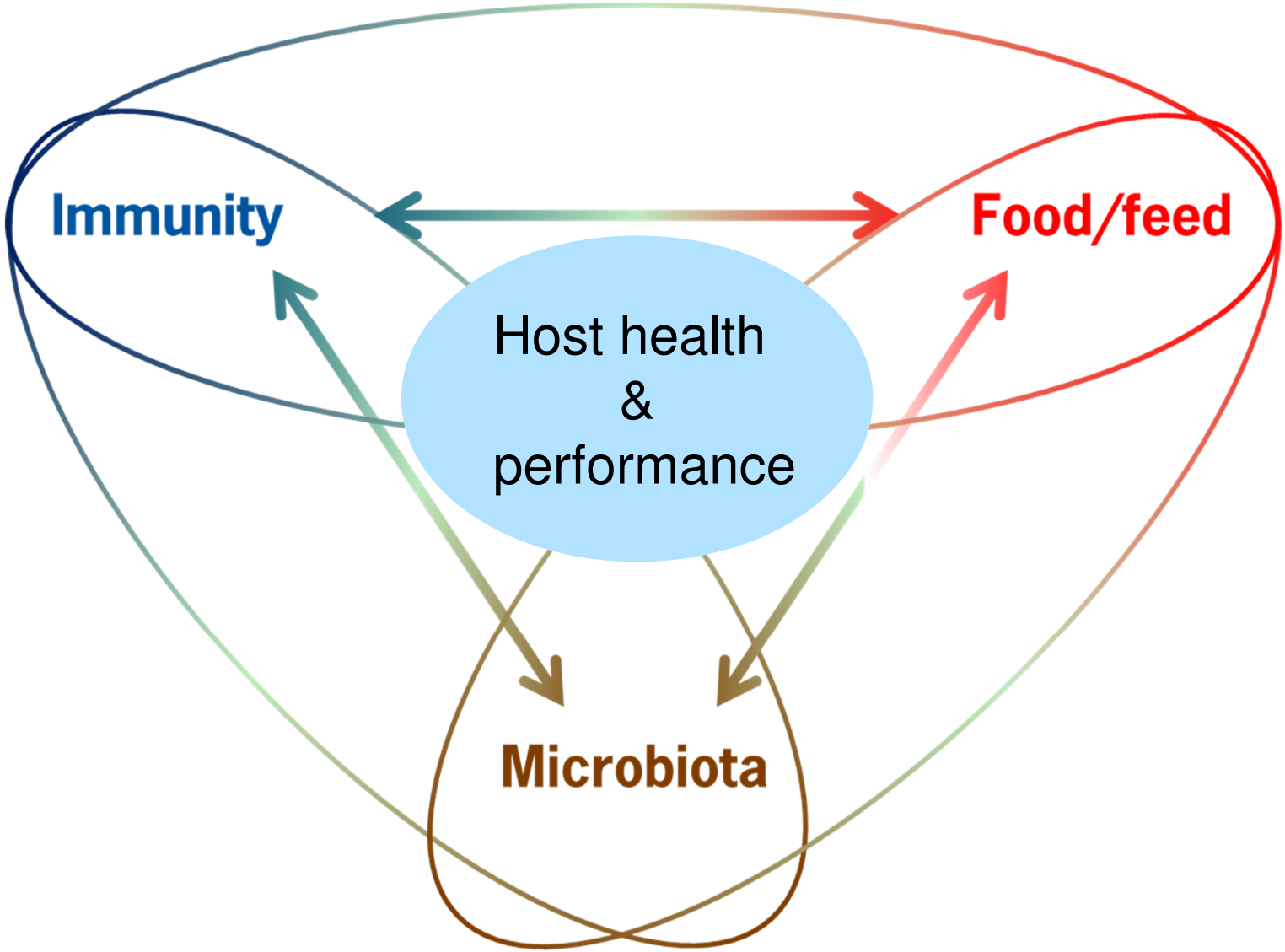
More than 1000 different species of microbes in the intestine



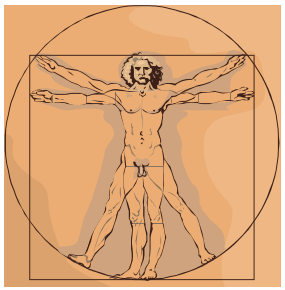
Diet/microbiota related diseases are increasing

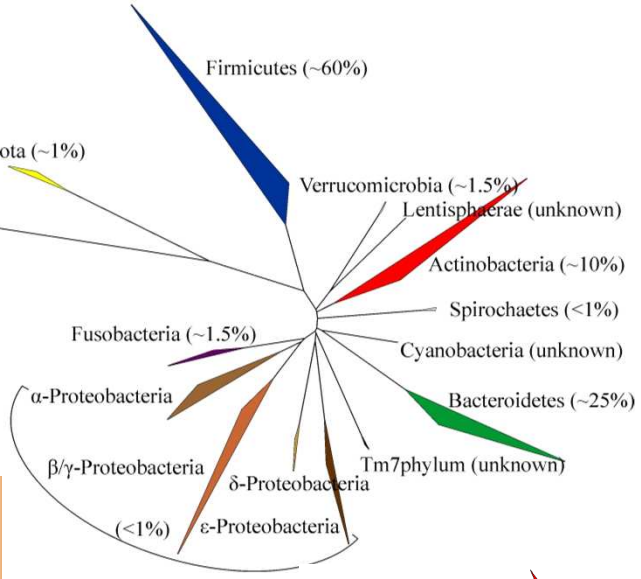
Microbiota impact on health: IBD, allergy, obesity…

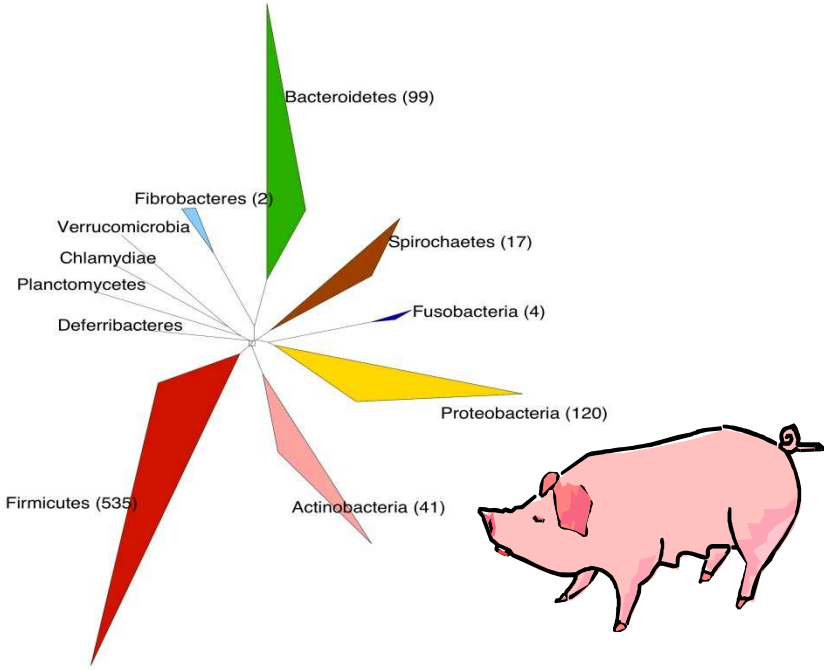
The “Golden Triangle” of intestinal interactions

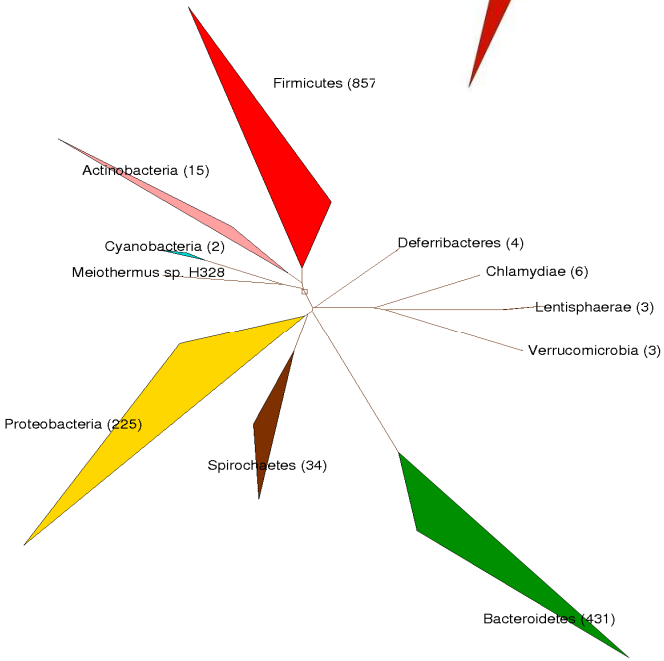


Which microbes can be found in the intestine?

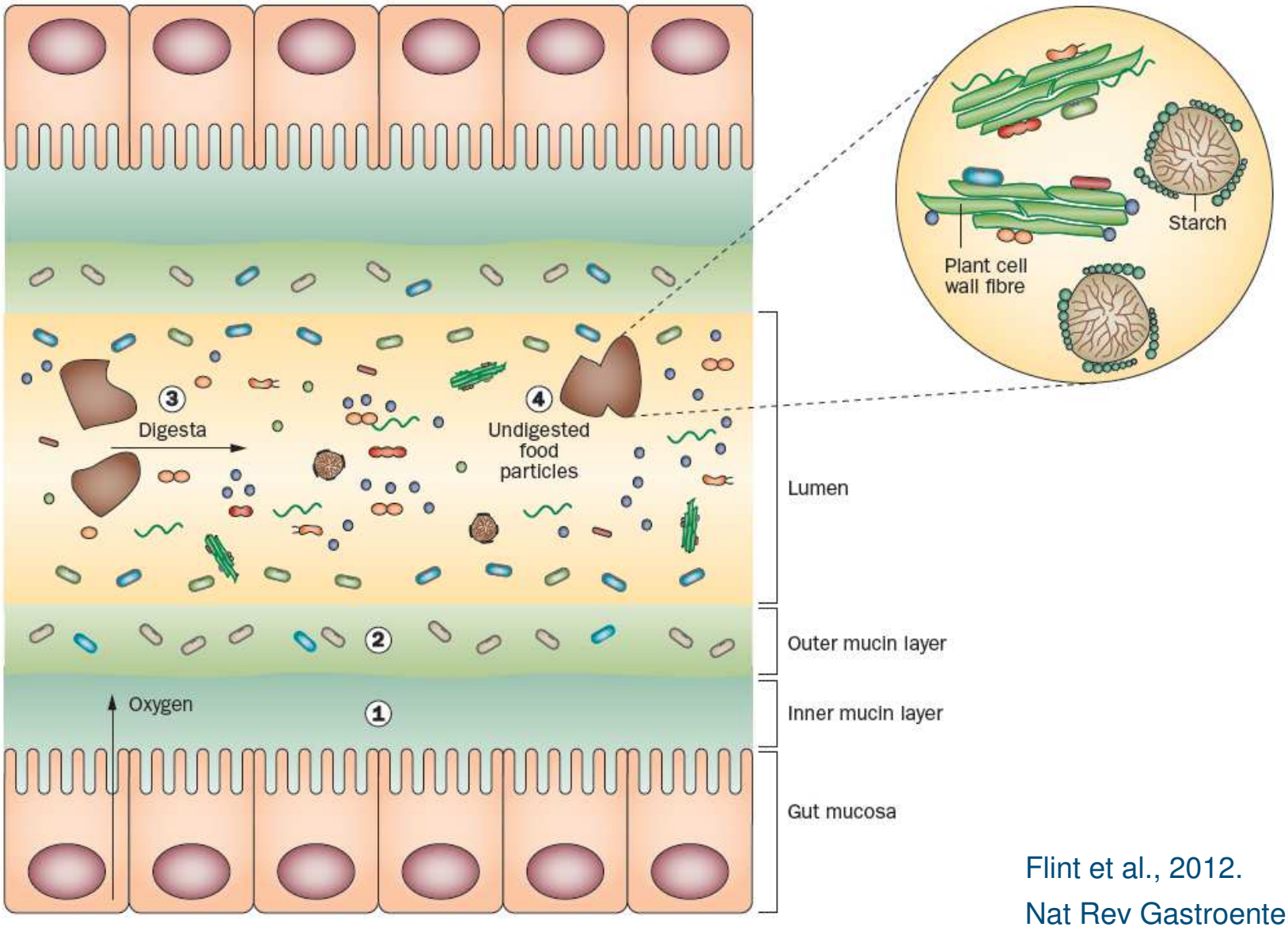






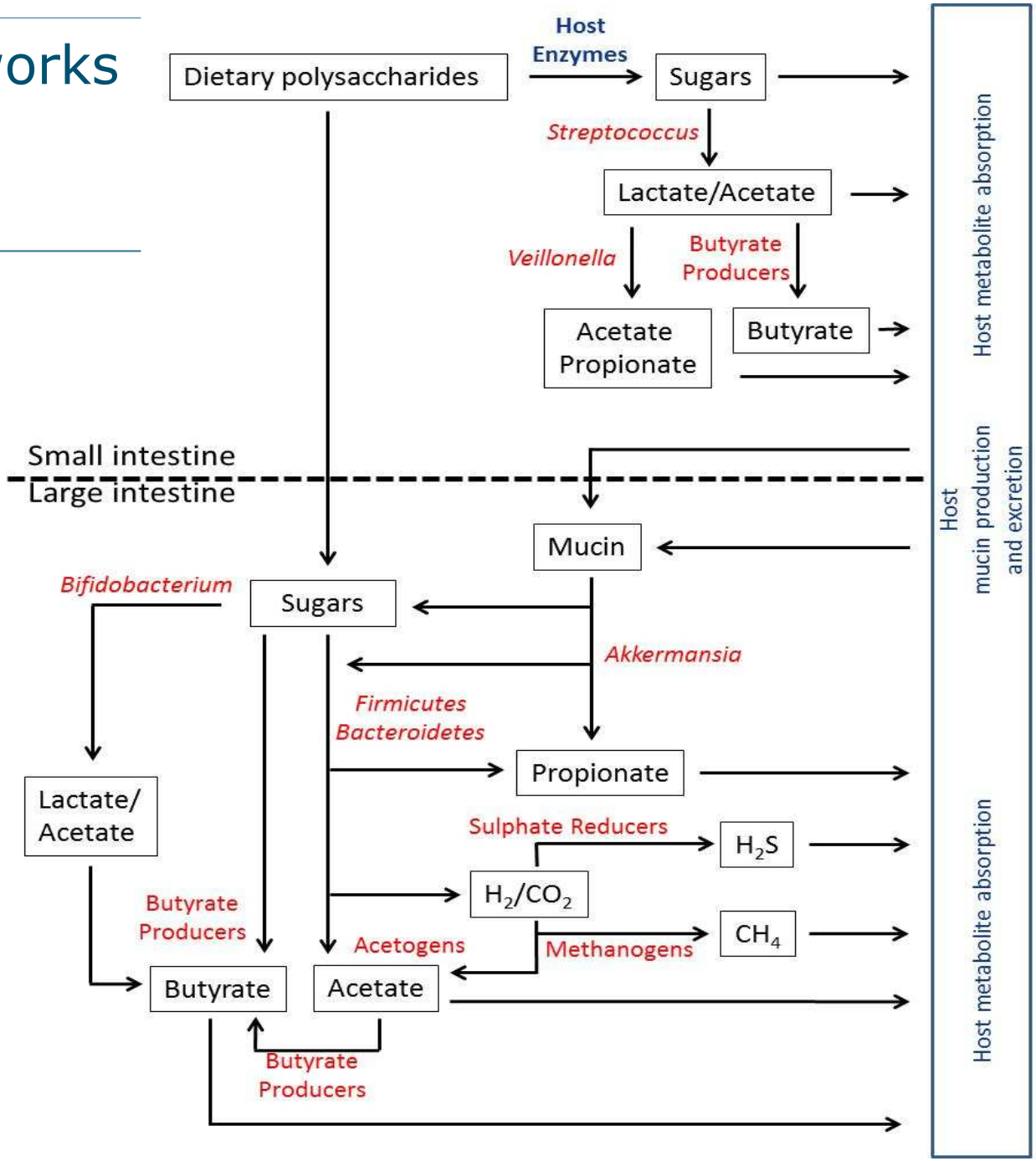


Where in the intestine do we find them?



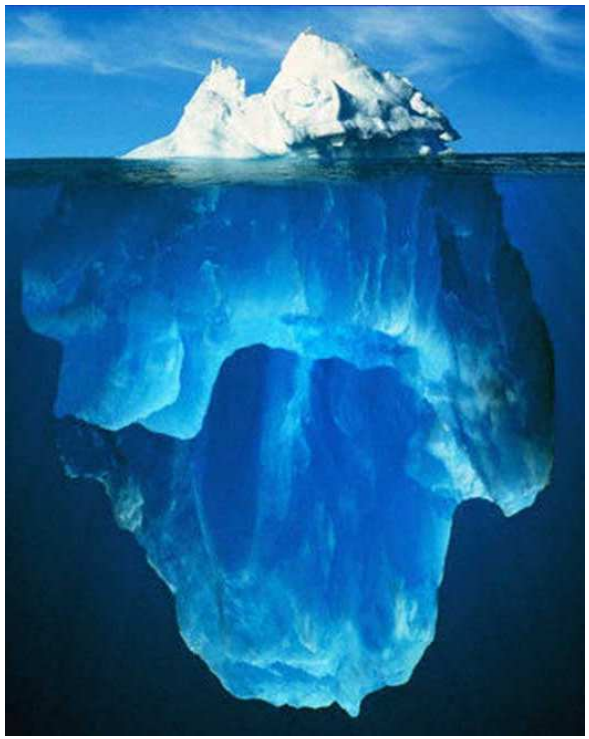
Flint et al., 2012.
Nat Rev Gastroenterol Hepatol.

Interactive networks of microbes – ~~Complementary~~ roles in carbohydrate fermentation



Zoetendal & de Vos. 2014

Most micro-organisms have not been cultured



- Cultured fraction
  - Intestine 10-50%
  - Activated sludge 1-15%
  - Soils <1%
  - Seawater <0.1%
- Incomplete picture of microbial diversity and function

Amann et al., 1995. Microbiol. Rev. 59:143-169

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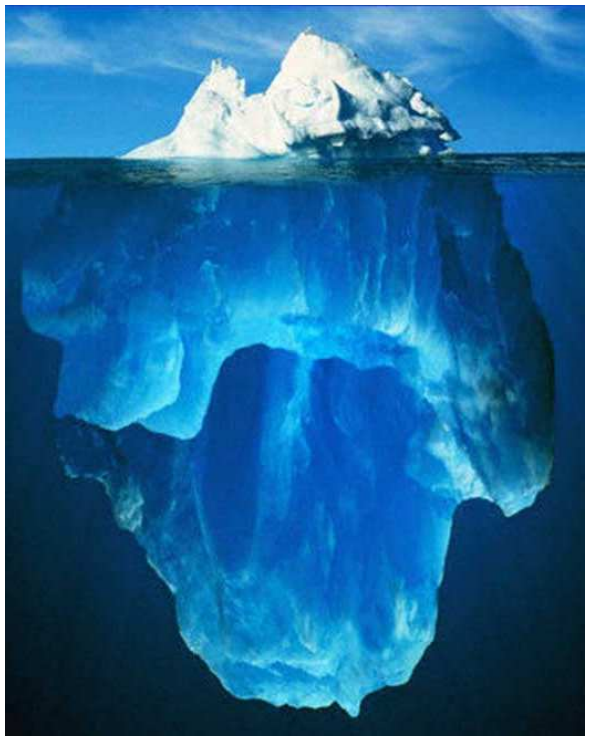
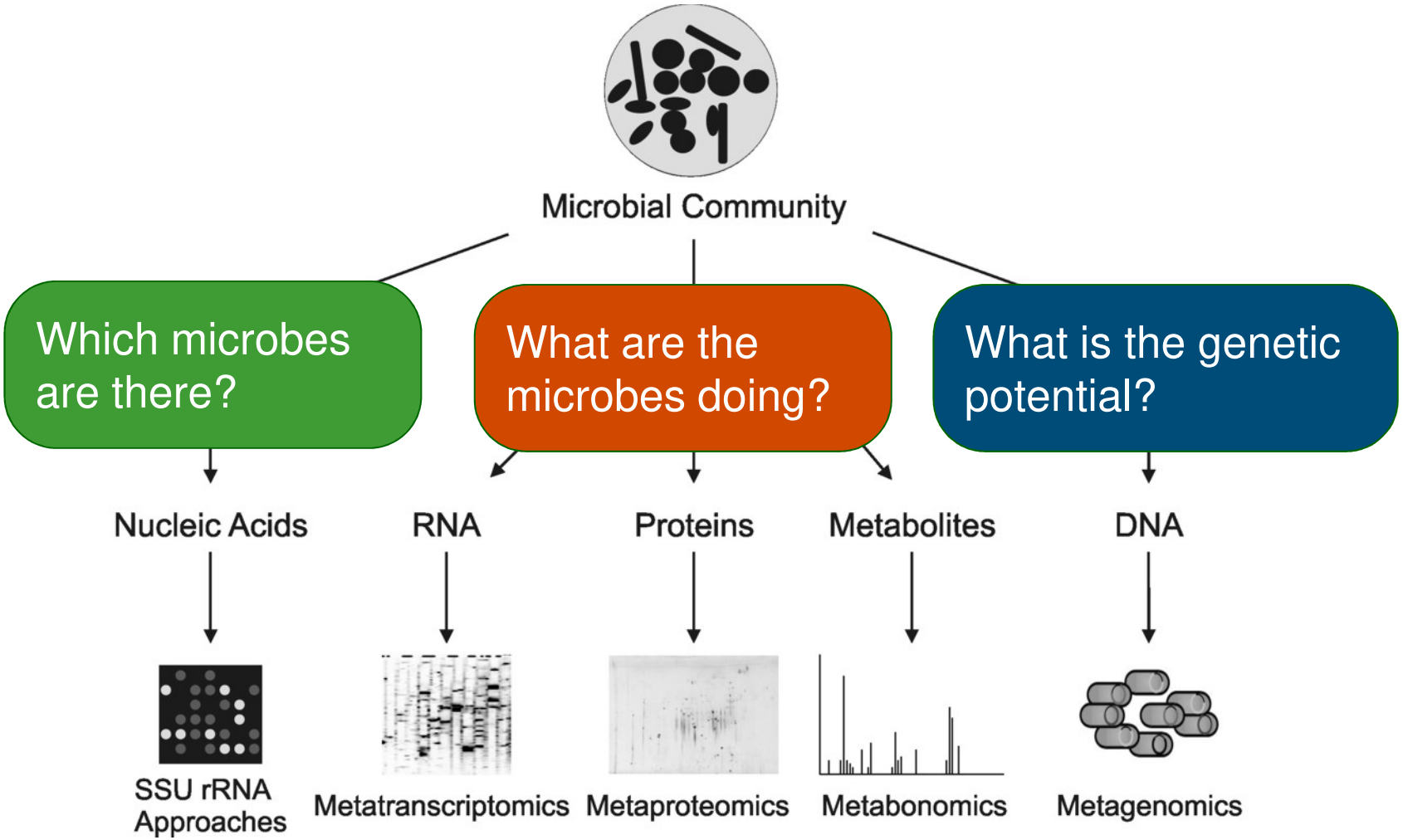


- Molecular genomics-based approaches needed

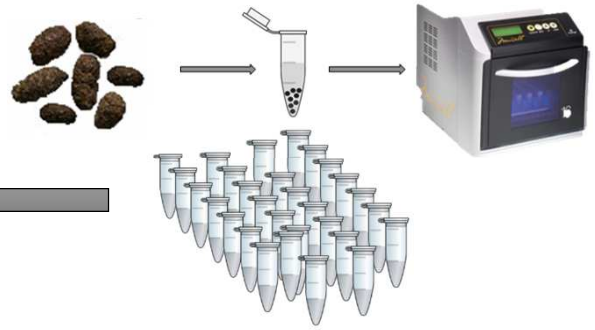
Discerning Composition & Function



Microbial biomarkers for health & disease

I. Amplicon sequencing

DNA extraction



16S rRNA gene PCR
& library preparation

NG-tax

pipeline for raw data processing

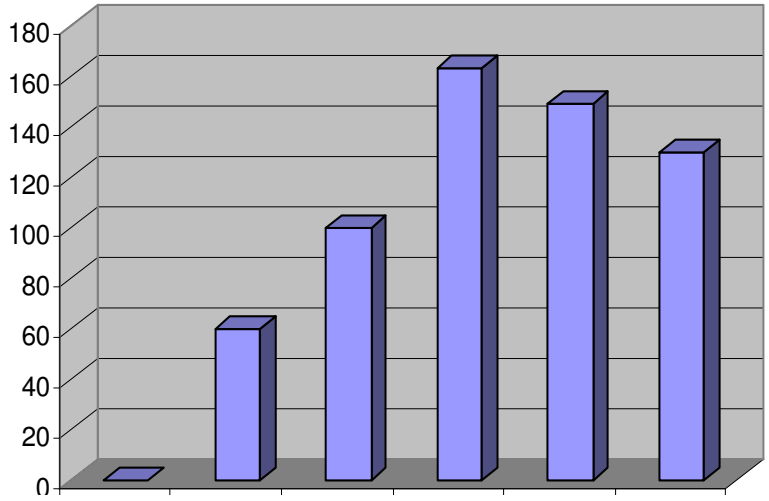
- Microbial composition
- Homogeneity of the microbiota:
  - Within a species group
  - Within a location group

Prediction of Function based on available reference genomes

PICRUSt

Phylogenetic Investigation of Communities by Reconstruction of Unobserved STates

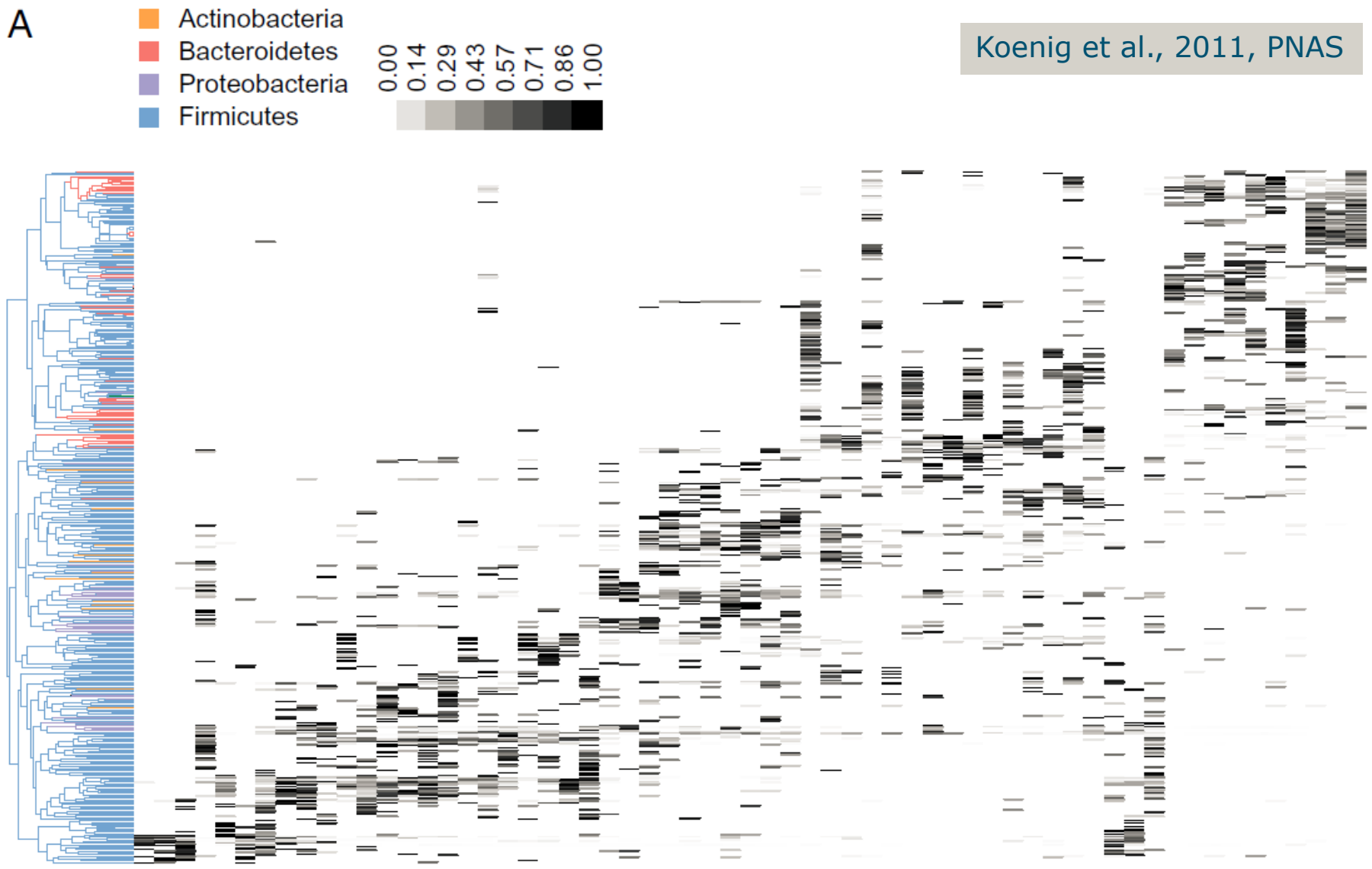
Changes in Microbial Diversity during Life



Born Sterile - Less Diversity at Older Age

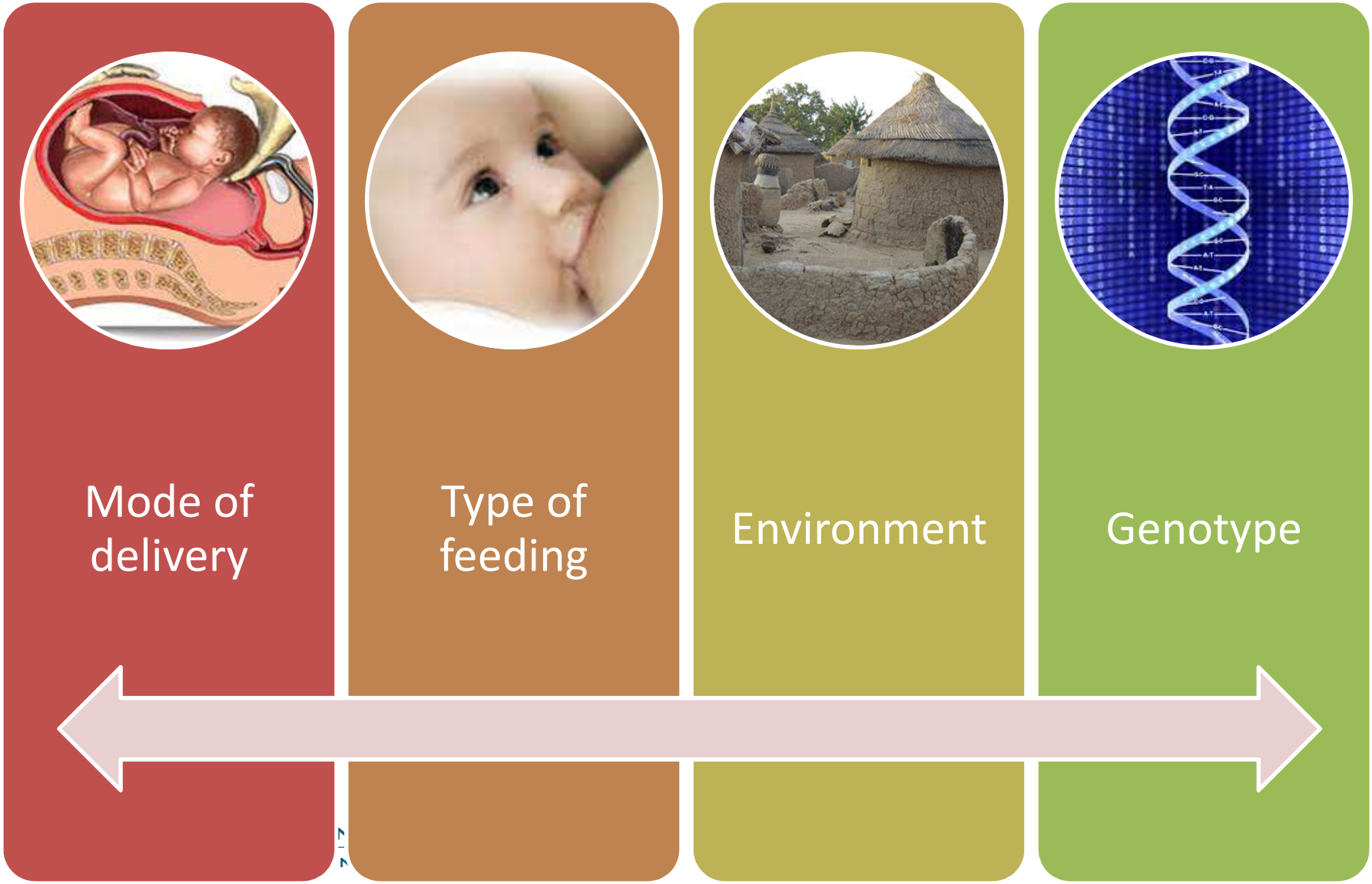
Biagi E, Nylund L, Candela M, Ostan R, Bucci L, Pini E, Nikkïla J, Monti D, Satokari R, Franceschi C, Brigidi P, De Vos WM (2010) PLoS One 17: e10667.

Microbial succession in newborns



Koenig et al., 2011, PNAS

Many factors can affect microbiota

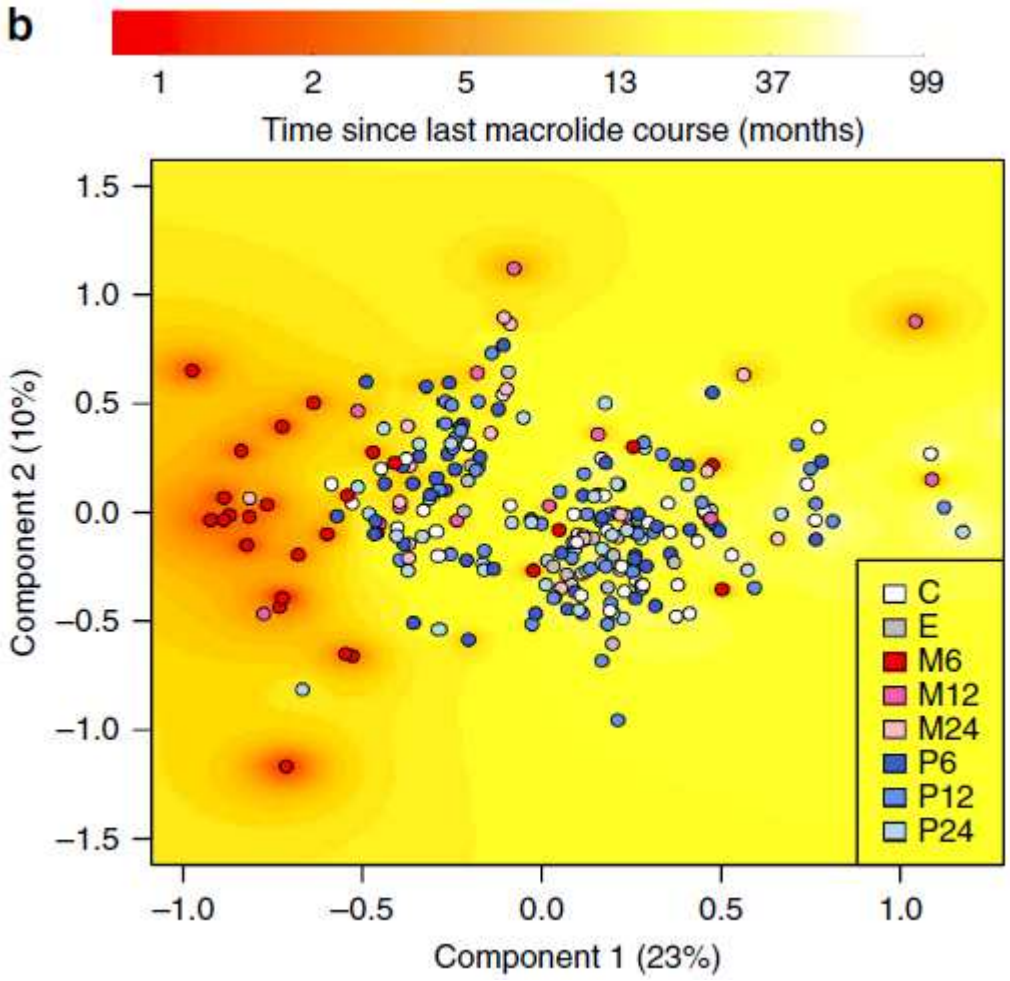


Growing up in a microbial world

- The ‘pioneer’ species received from the mother seem to be important
- Transmission of bacteria from the maternal vaginal flora, and lower intestinal tract
- Infants born by Caesarean section are predisposed to development of allergies and asthma later in life
- Pre-mature born infants are more susceptible to infections and have insufficient energy uptake

Antibiotic use affects microbiome composition & function in pre-school children

Korpela et al., 2016, Nat.Comm.



- Study in 142 2–7 year-old Finnish children (sampled at two time points)

- Macrolides leave stronger & longer-lasting mark than penicillins

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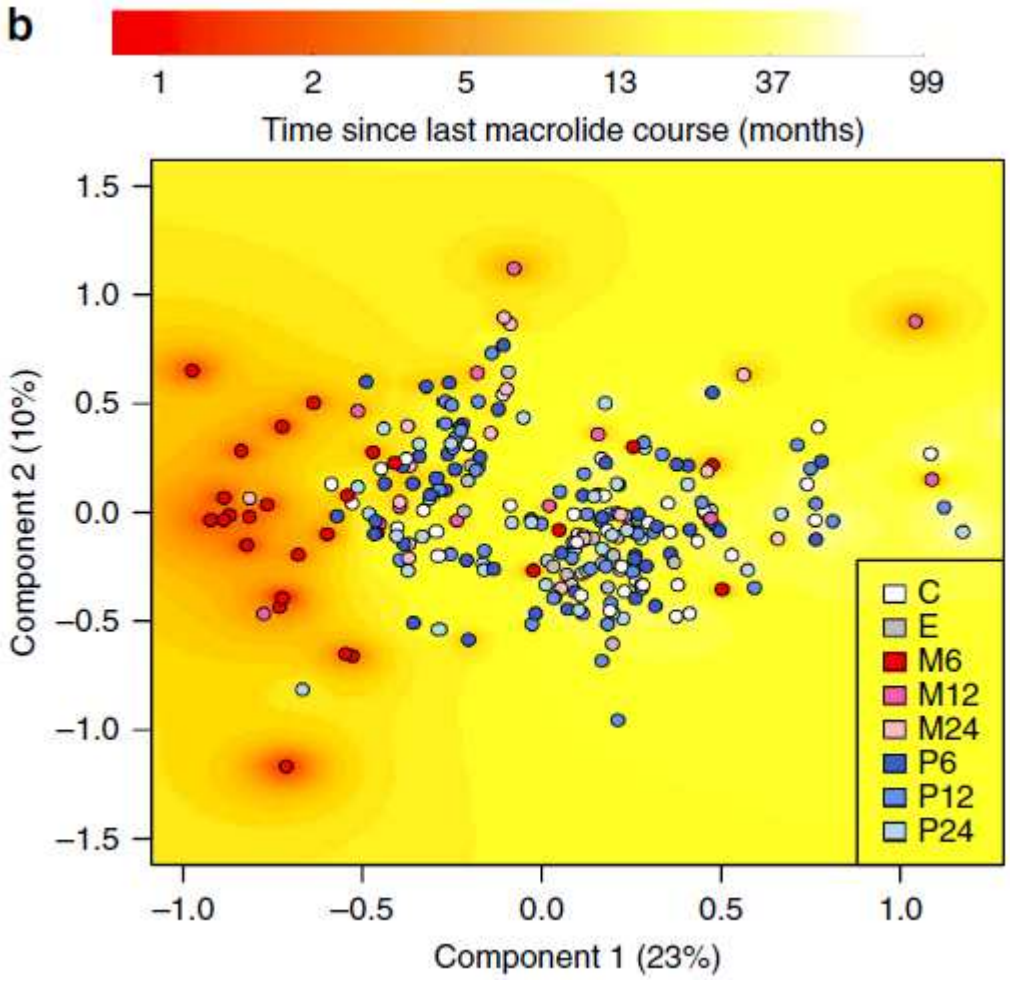
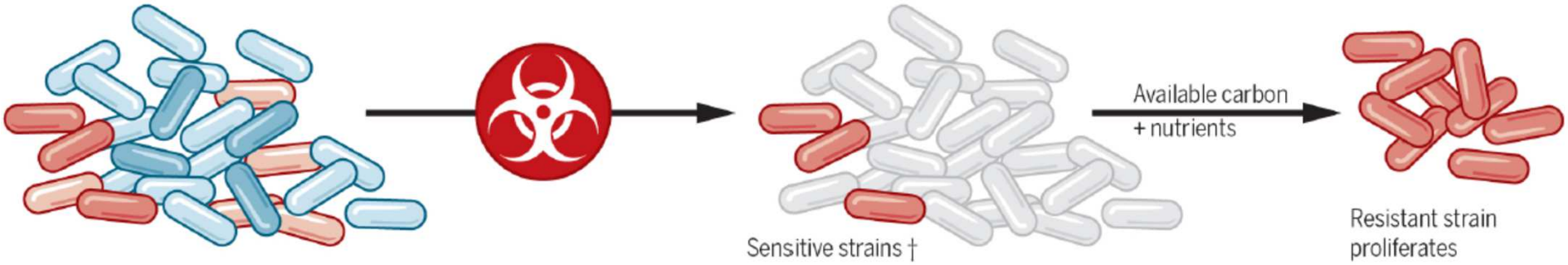
Korpela et al., 2016, Nat.Comm.



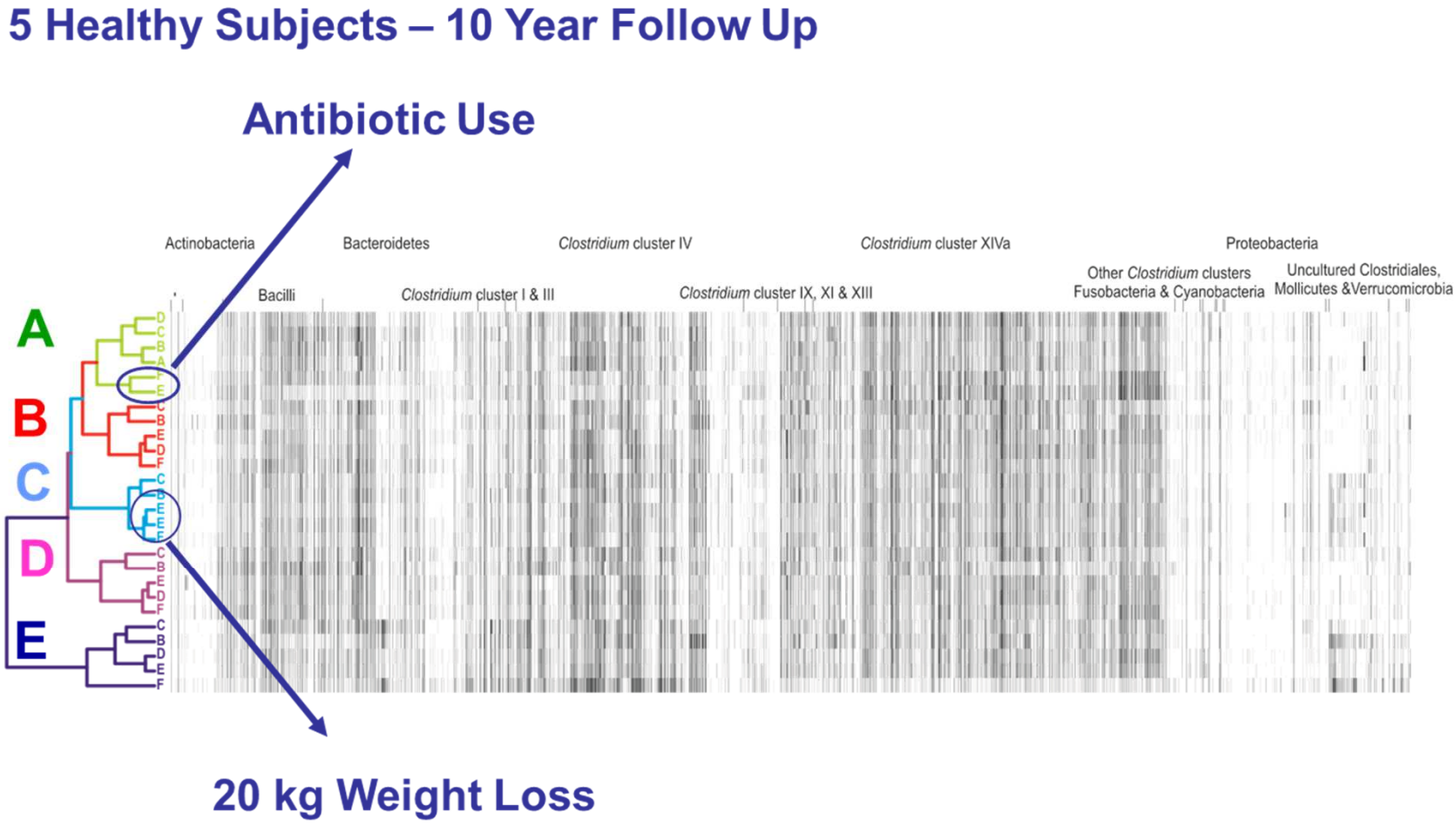
- Study in 142 2–7 year-old Finnish children (sampled at two time points)
- Macrolides leave stronger & longer-lasting mark than penicillins
- Increased macrolide resistance
- Increased risk of asthma
- Predisposition to antibiotic-associated weight gain

What happens upon exposure to “toxic” compounds?

Atashgai et al., 2018, Science



The Healthy Microbiome Is Stable & Personalized – A Decade Study

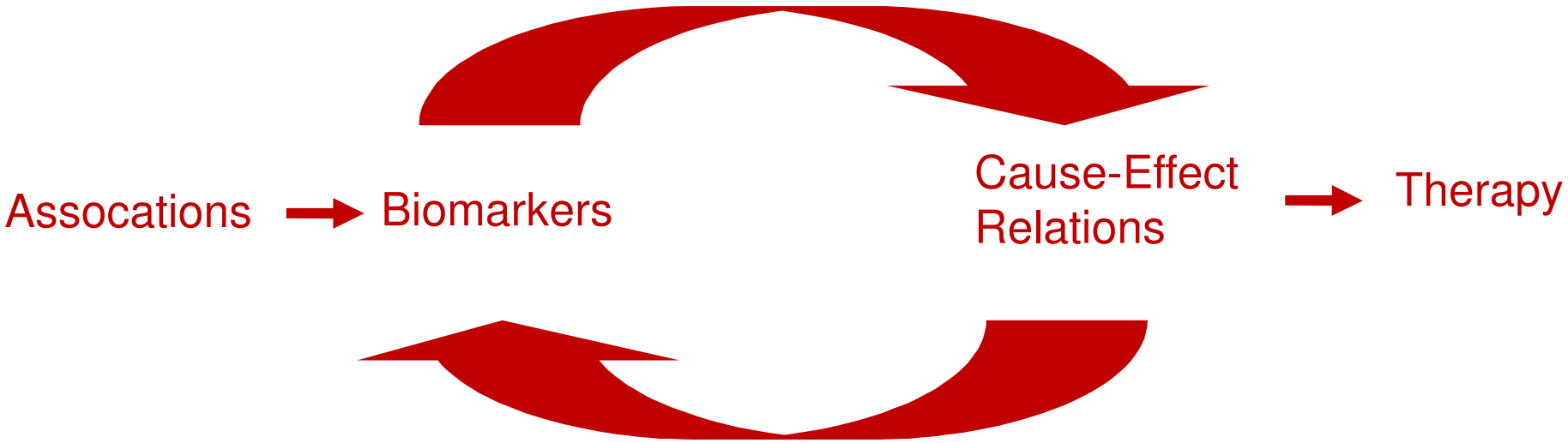


M Rajilić-Stojanović M, H Heilig, S Tims, EG Zoetendal & WM de Vos (2012) Long-term monitoring of the human intestinal microbiota composition. Env Microbiol

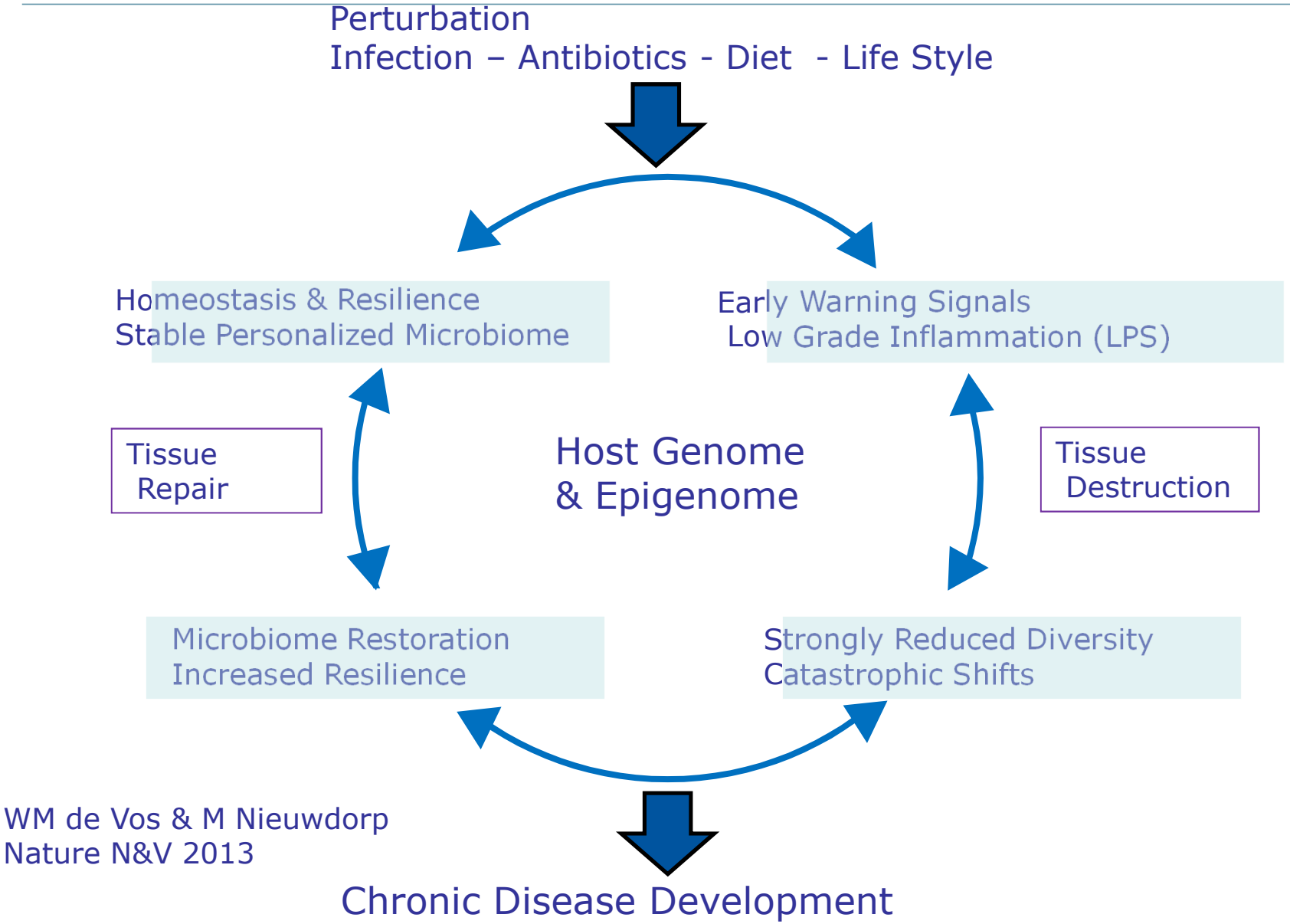
Intestinal Microbiome & Predisposition to Disease

Mainy Association Studies

Intestinal Microbiota Revolutions



Model for the Impact of Human Microbiome



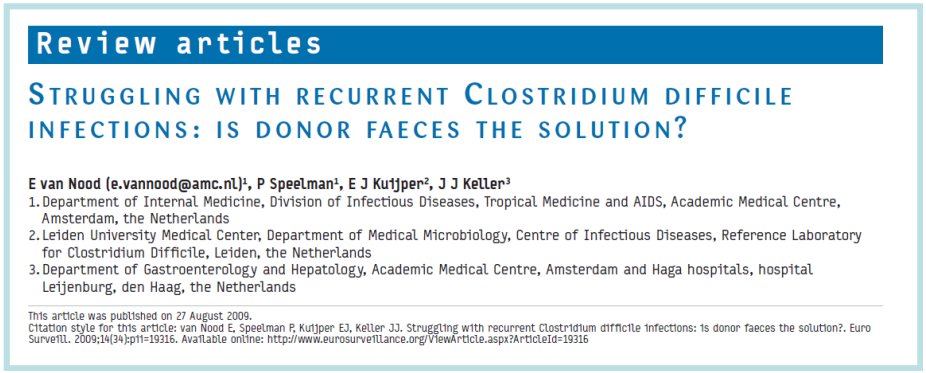
WM de Vos & M Nieuwdorp
Nature N&V 2013

Fecal Transplantations – Hundreds of Cases

Recurrent *C.difficile* Infections (CDI) Infections

Healthy Donors - Colonic or Duodenal Infusions

159 Mostly Single Cases Since 1958 - > 90 % Success

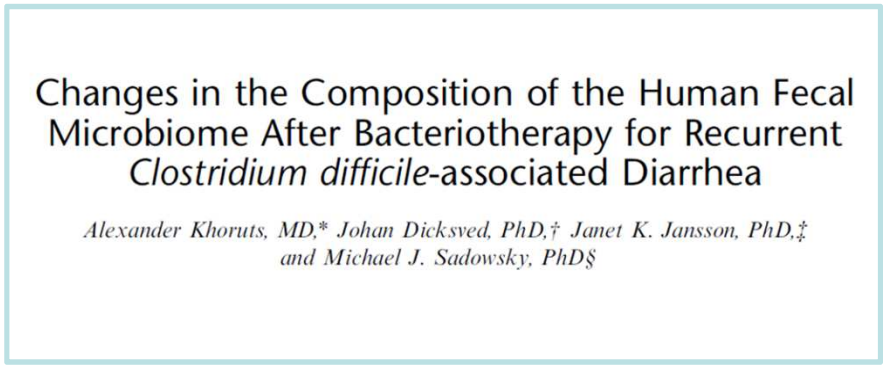


Review articles

STRUGGLING WITH RECURRENT CLOSTRIDIUM DIFFICILE INFECTIONS: IS DONOR FAECES THE SOLUTION?

E van Nood (e.vannood@amc.nl)[1], P Speelman[1], E J Kuijper[2], J J Keller[3]
1. Department of Internal Medicine, Division of Infectious Diseases, Tropical Medicine and AIDS, Academic Medical Centre, Amsterdam, the Netherlands
2. Leiden University Medical Center, Department of Medical Microbiology, Centre of Infectious Diseases, Reference Laboratory for Clostridium Difficile, Leiden, the Netherlands
3. Department of Gastroenterology and Hepatology, Academic Medical Centre, Amsterdam and Haga hospitals, hospital Leijenburg, den Haag, the Netherlands

This article was published on 27 August 2009.
Citation style for this article: van Nood E, Speelman P, Kuijper EJ, Keller JJ. Struggling with recurrent Clostridium difficile infections: is donor faeces the solution?. Euro Surveill. 2009;14(34):pii=19316. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19316



Changes in the Composition of the Human Fecal Microbiome After Bacteriotherapy for Recurrent *Clostridium difficile*-associated Diarrhea

Alexander Khoruts, MD, Johan Dicksved, PhD,† Janet K. Jansson, PhD,‡ and Michael J. Sadowsky, PhD§*

2011 Study – Placebo Controlled Study Microbiota of 13 Patients Followed Up

2010 Case Study – Microbiota of Single Patient Follow Up

Fecal Transplantation – it works

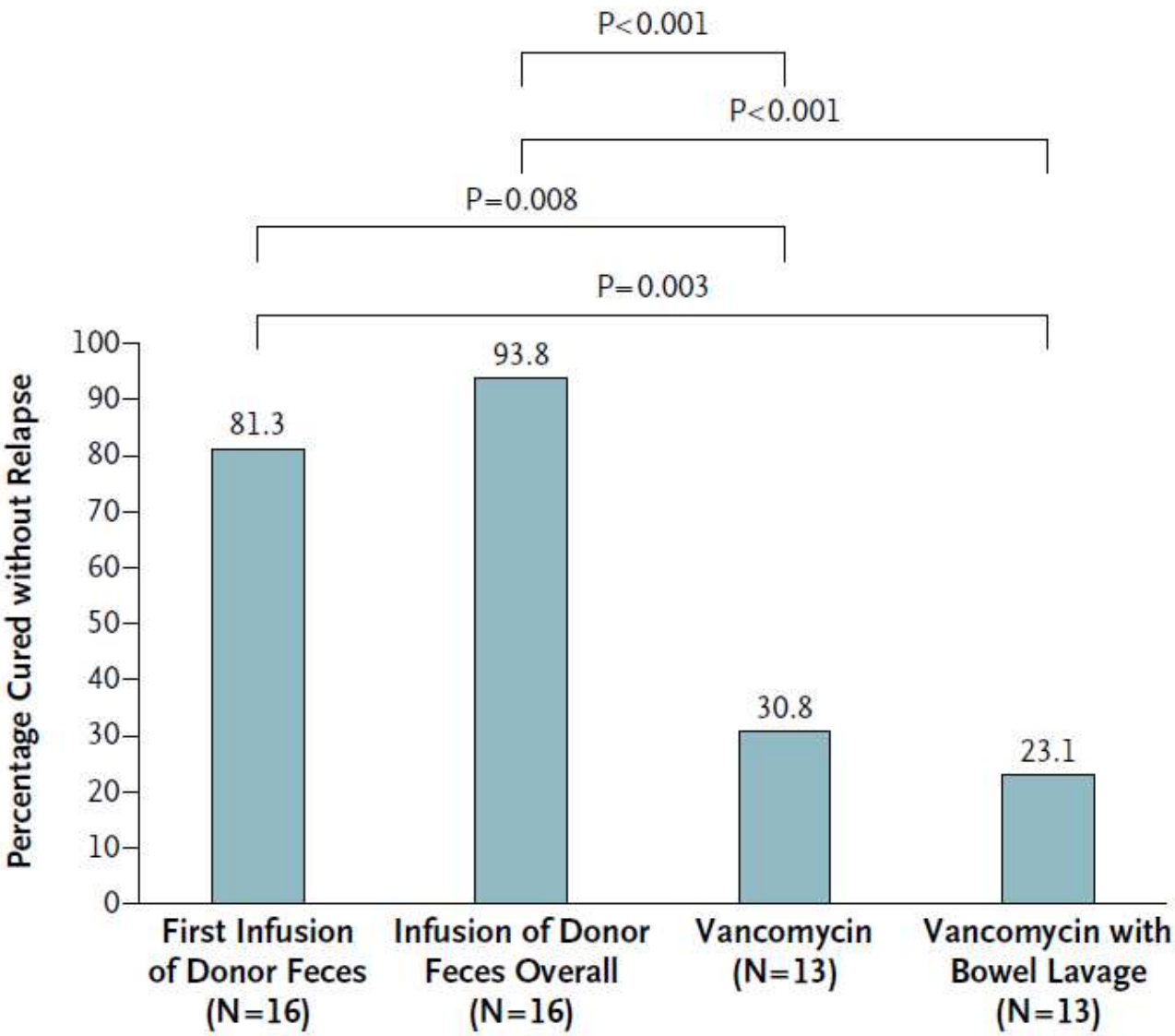
The NEW ENGLAND JOURNAL of MEDICINE 2013

ORIGINAL ARTICLE

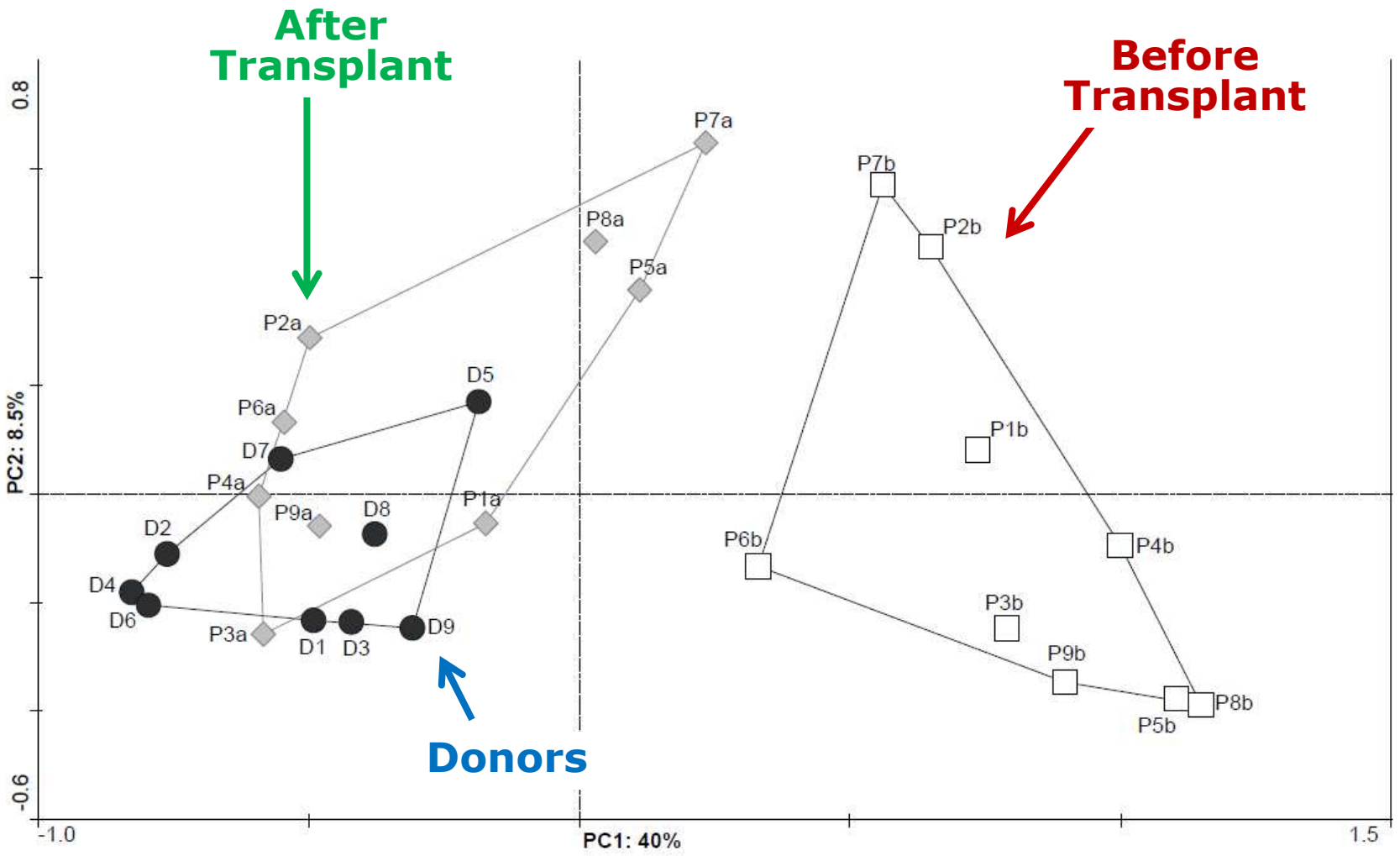
Duodenal Infusion of Donor Feces for Recurrent *Clostridium difficile*

Els van Nood, M.D., Anne Vrieze, M.D., Max Nieuwdorp, M.D., Ph.D., Susana Fuentes, Ph.D., Erwin G. Zoetendal, Ph.D., Willem M. de Vos, Ph.D., Caroline E. Visser, M.D., Ph.D., Ed J. Kuijper, M.D., Ph.D., Joep F.W.M. Bartelsman, M.D., Jan G.P. Tijssen, Ph.D., Peter Speelman, M.D., Ph.D., Marcel G.W. Dijkgraaf, Ph.D., and Josbert J. Keller, M.D., Ph.D.

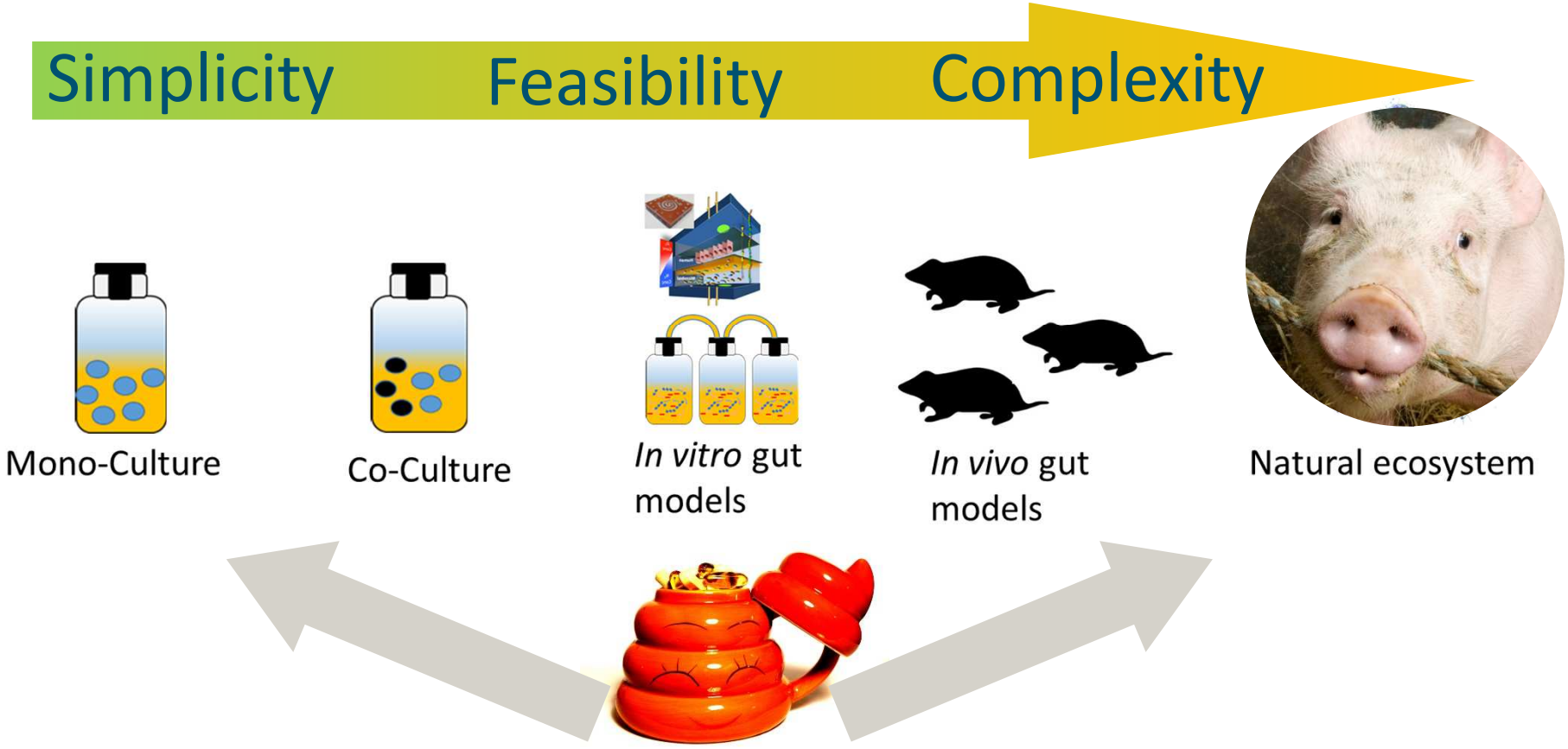
Fecal Transplantation – it works



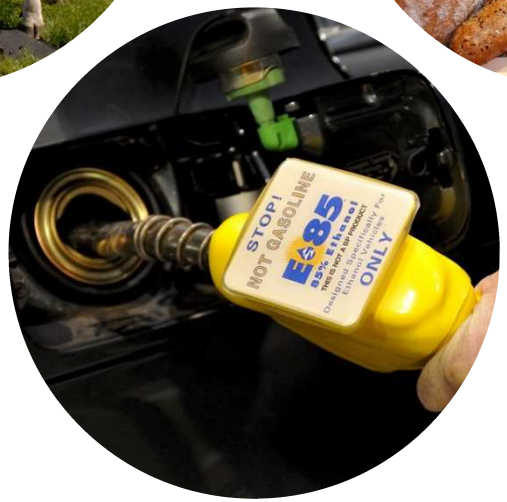
Microbiota reverts to healthy state after transplantation



Challenges ahead for microbiome therapeutics

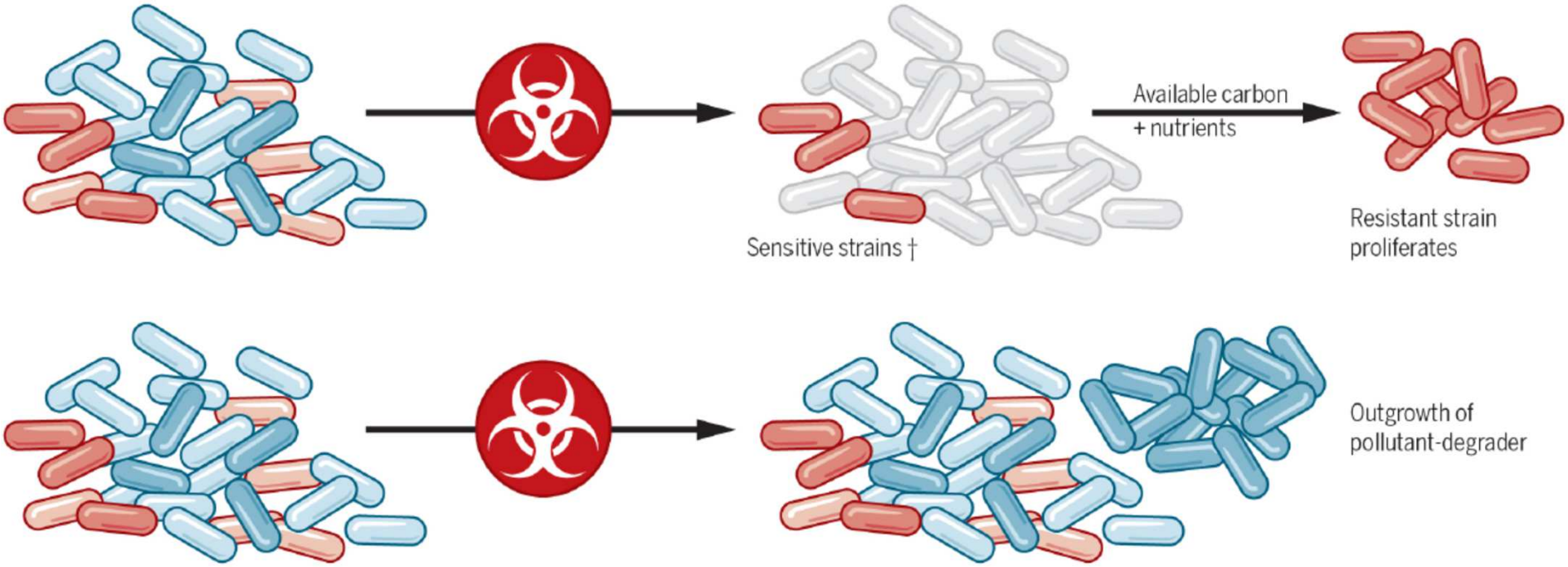


Microbiome Management – More than just Fecal Transplantation



What happens upon exposure to “toxic” compounds?

Atashgai et al., 2018, Science



REVIEW

Prospects for harnessing biocide resistance for bioremediation and detoxification

Bioaugmentation of aquifers contaminated with chlorinated solvents

Courtesy Hans Stroo (Stroo Consulting LLC) and Carol Aziz (Ramboll)

Where do we stand in terms of application?

- Tools to discern microbial composition & function
- Diagnostic biomarkers as “canaries in the coalmine” for ecosystem function
- Knowledge of microbial networks that support key “ecosystem services”
- Microbes & microbiomes as potential agents for microbiome management strategies

Microbiome Research

From

Stamp Collections

To

Correlations

To

Interactions

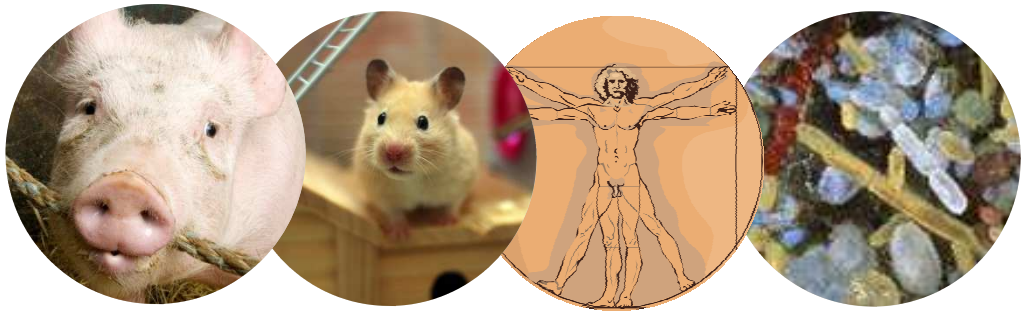
To

Novel Isolates & Consortium Engineering

To

Causality & Microbial Therapeutics

Take Home Messages



- High diversity intestinal microbiota; > 1000 phylotypes
- Need for functional genomics-based approaches for comprehensive characterization
- Microbiota is influenced by host (genetic background); age, environment & food
- Potential for pre- and probiotics, and more drastic means (transplantation) for steering microbiota
- Systems approaches towards knowledge-based microbiome management