Next-Gen Fermented Food: Harnessing Gut Microbiome Diversity and Functions

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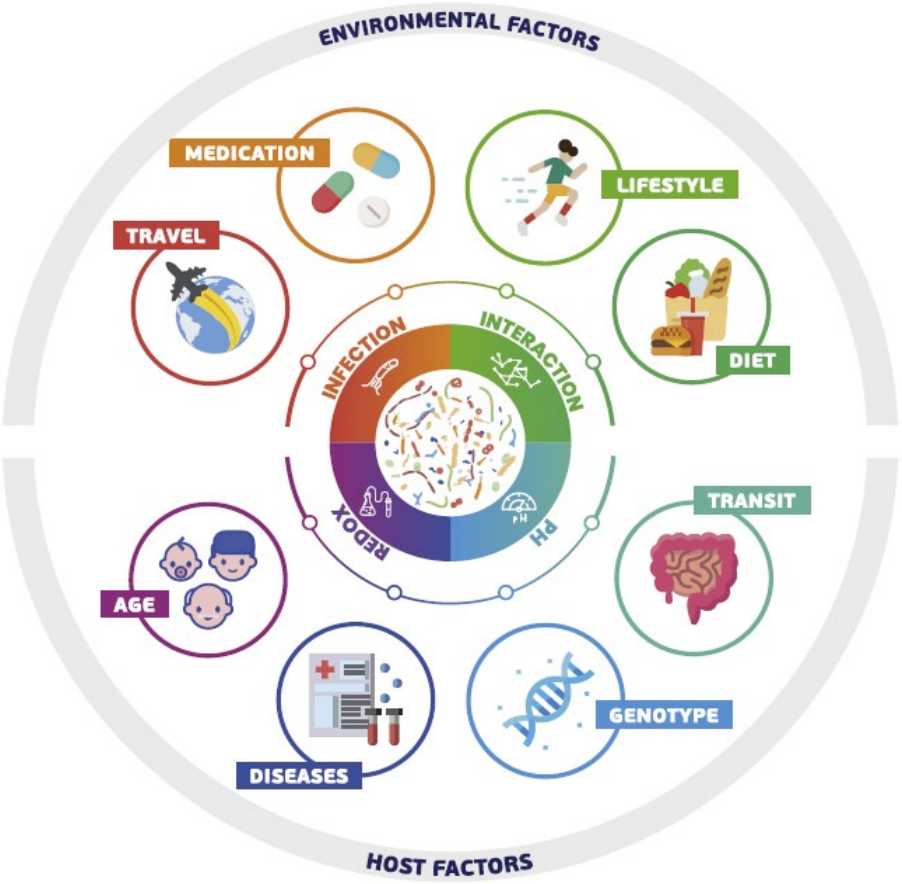
Julien Tap
INRAE MICALIS
LAB Symposium 2023 - Egmond aan Zee

Different factors shapes the human gut microbiome



Host life

Human gut microbiota

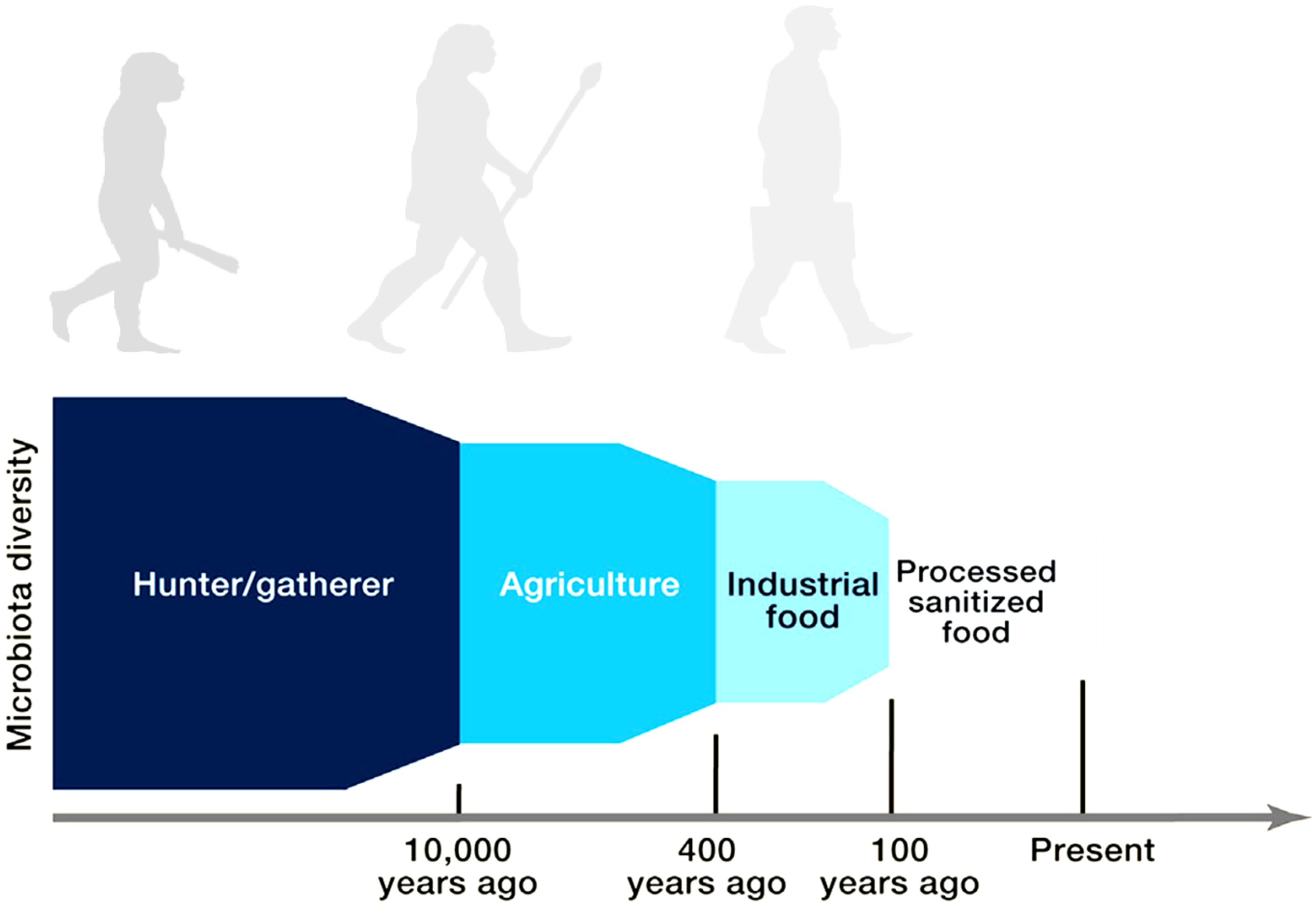
Co-evolution

Microbial ecology

Tap et al., 2022

Diet and lifestyle effect host microbiome symbiosis

Are we uncoupling our metagenome and our genome?

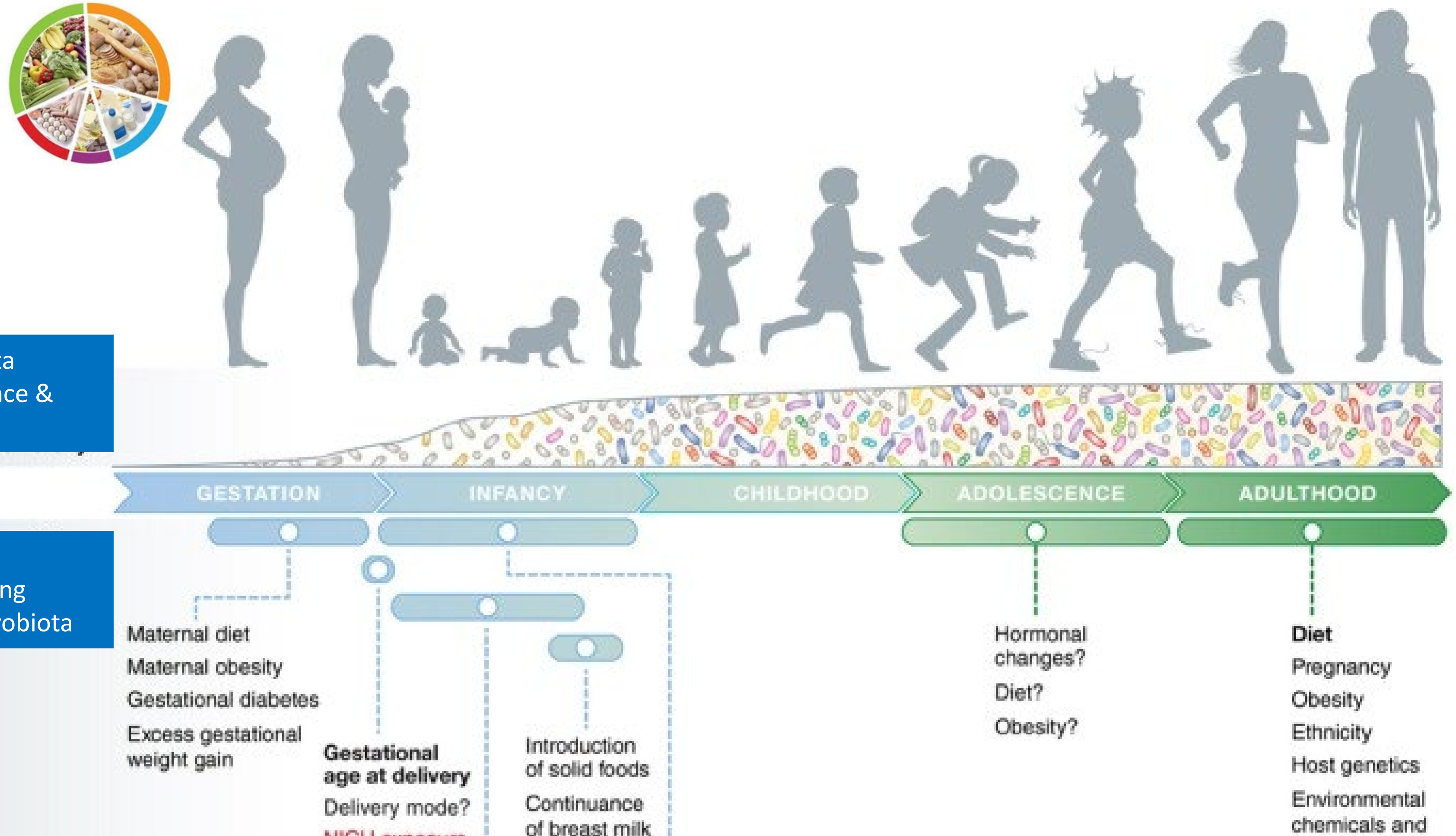


Hunters - gatherers
↓
Sedentarization
↓
Livestock and crops
↓
Hygiene/medication
↓
Refined products

Gut microbiome throughout life span

Micobiota Abundance & diversity

Factors Influencing the microbiota



Maternal diet
Maternal obesity
Gestational diabetes
Excess gestational weight gain

Gestational age at delivery
Delivery mode?
NICU exposure

Introduction of solid foods
Continuance of breast milk feeding

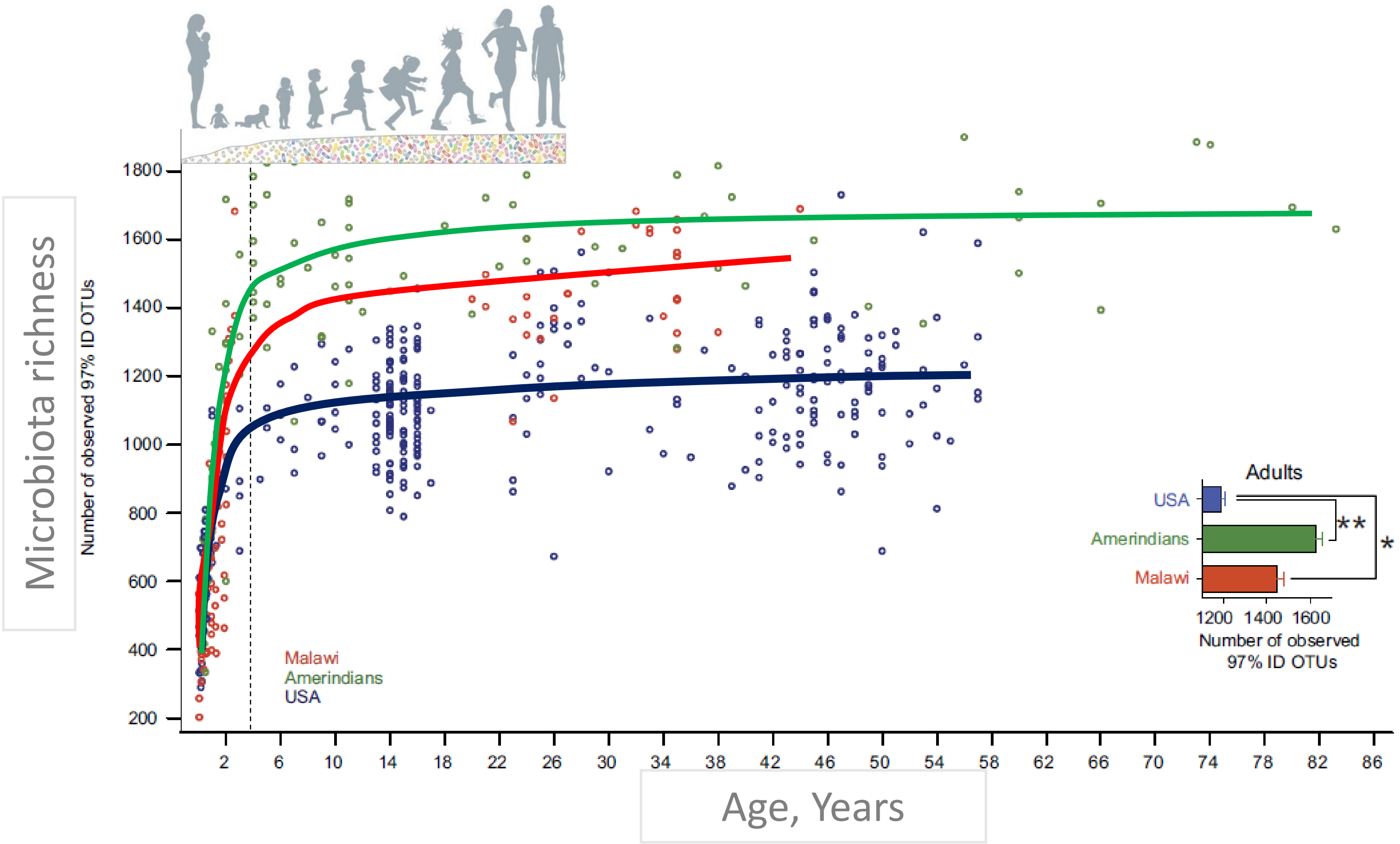
Antibiotics

Breast milk vs. formula

Hormonal changes?
Diet?
Obesity?

Diet
Pregnancy
Obesity
Ethnicity
Host genetics
Environmental chemicals and exposures?

Gut Microbiome diversity associated with the region of birth during the lifespan



Microbiome states resilience as key factor


Healthy state


Resistance

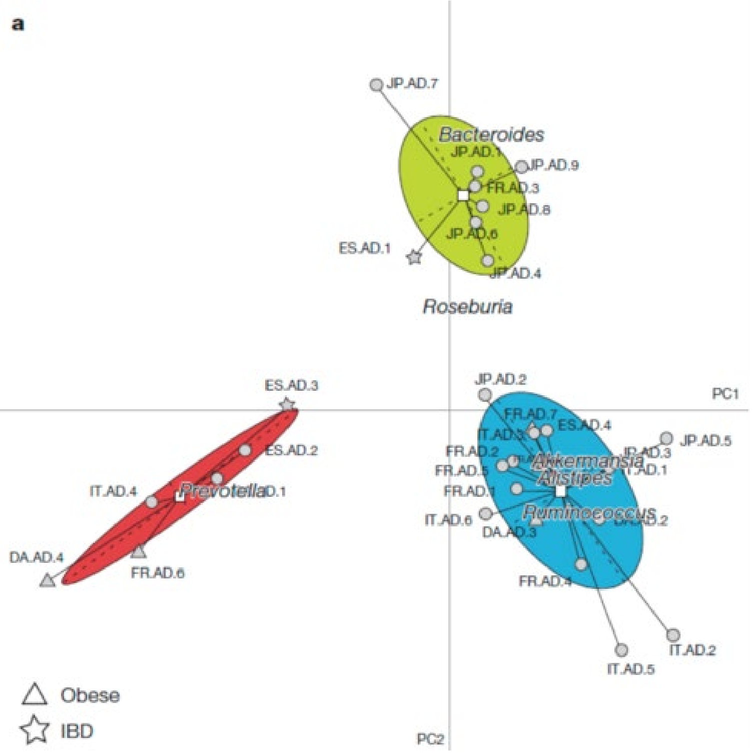

Recovery

Resilience

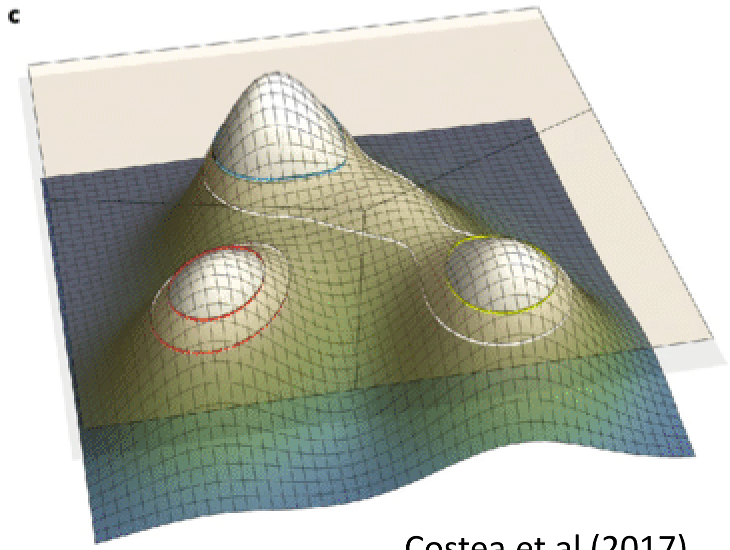
Healthy state


Degraded state

Several attempts to decipher the microbiome structure



Arumugam, Raes et al (2010)

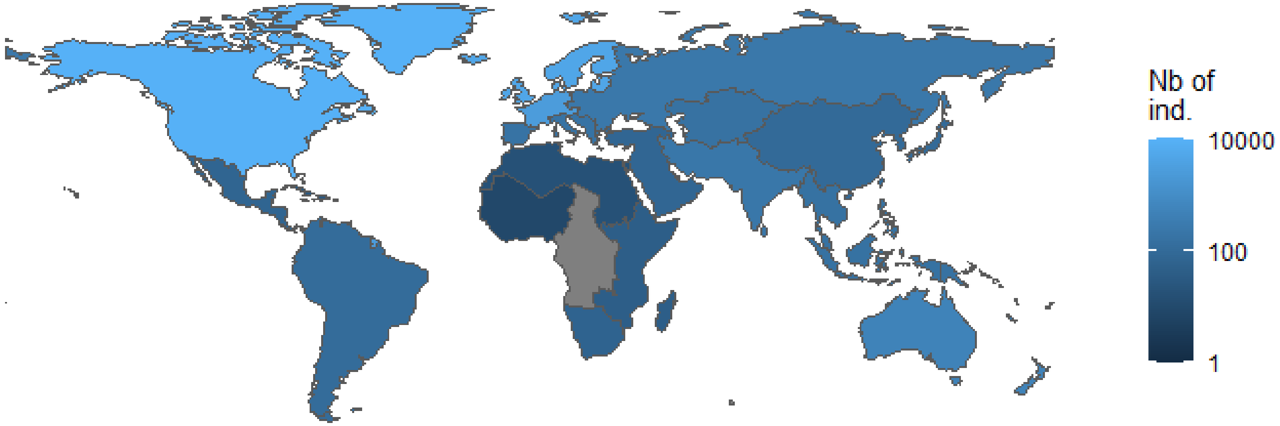


Costea et al (2017)

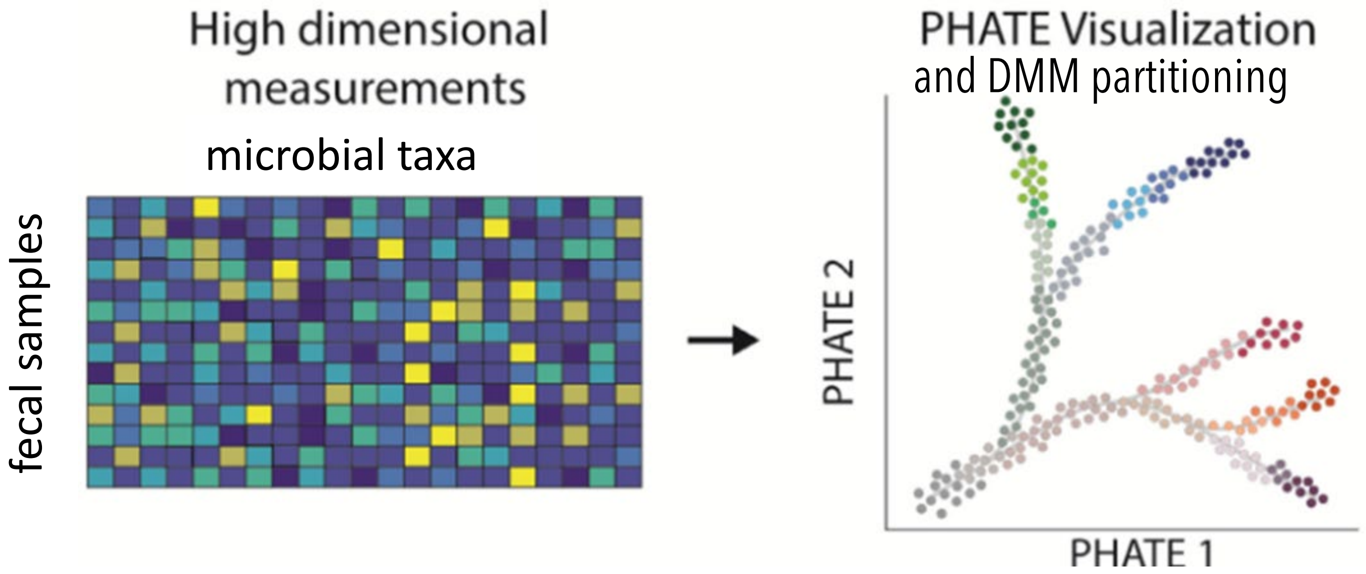
Dirichlet Multinomial Mixture (DMM) modeling

Limits:
Few association with diet
Few stability assessment (e.g. with time-series)

35,000 human gut microbiome samples analyzed



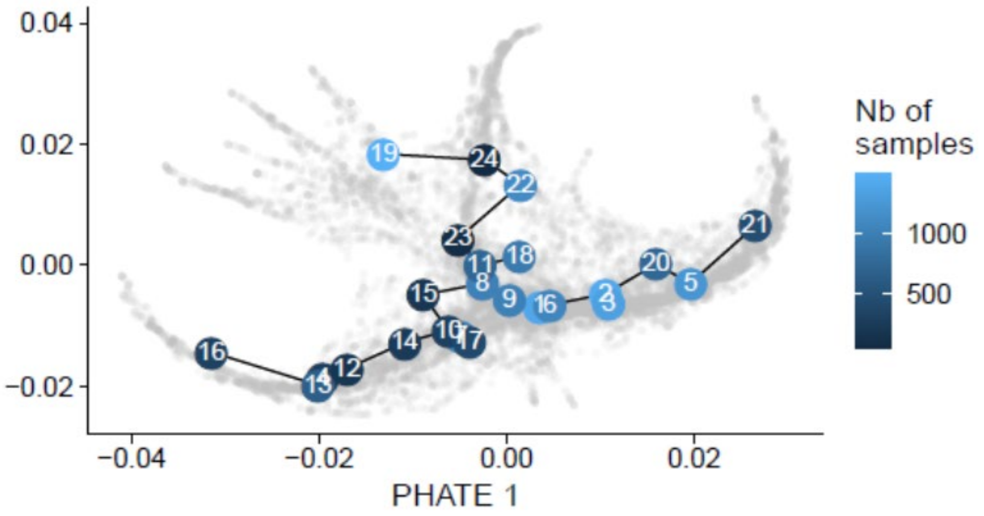
New computational method that help observe **global and local structure** at the same time

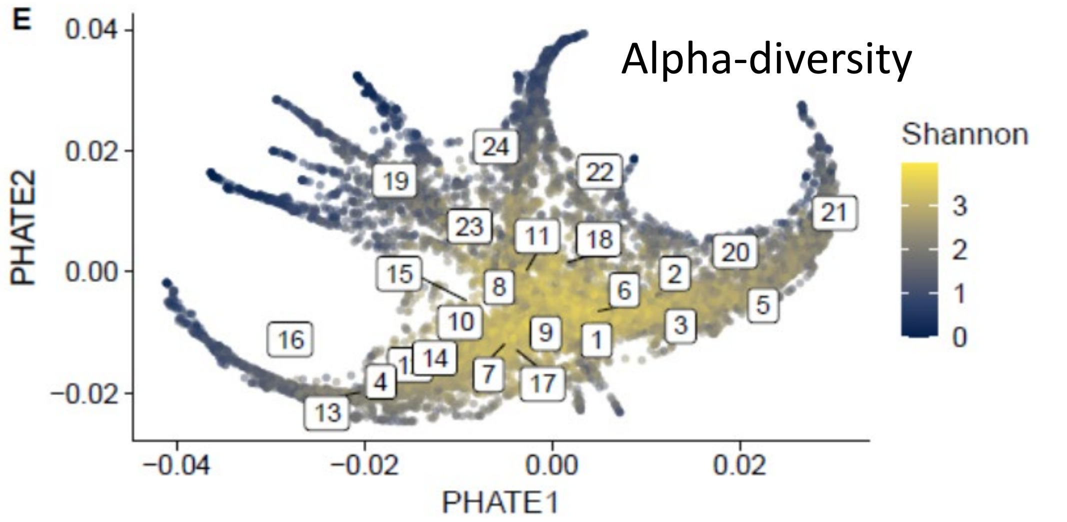


Time-series analysis to detect microbiome states

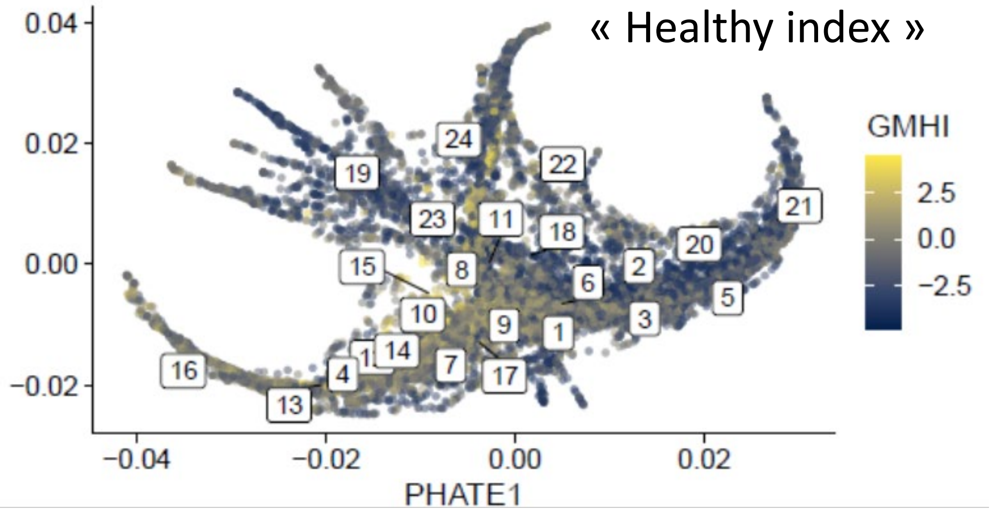
Region of birth, Lifestyle, diet, and health modelization

Human Gut microbiome structured as branches

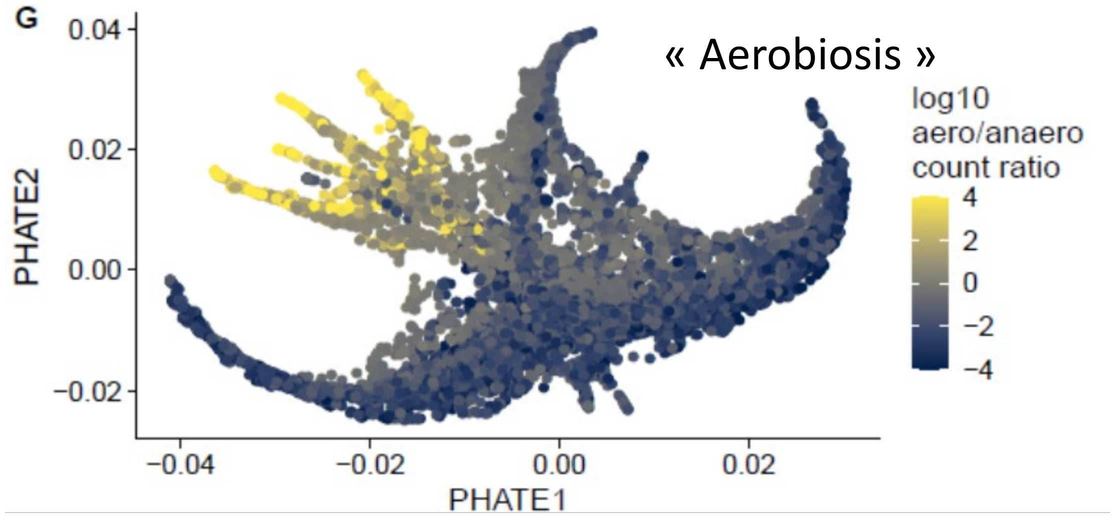




Alpha-diversity

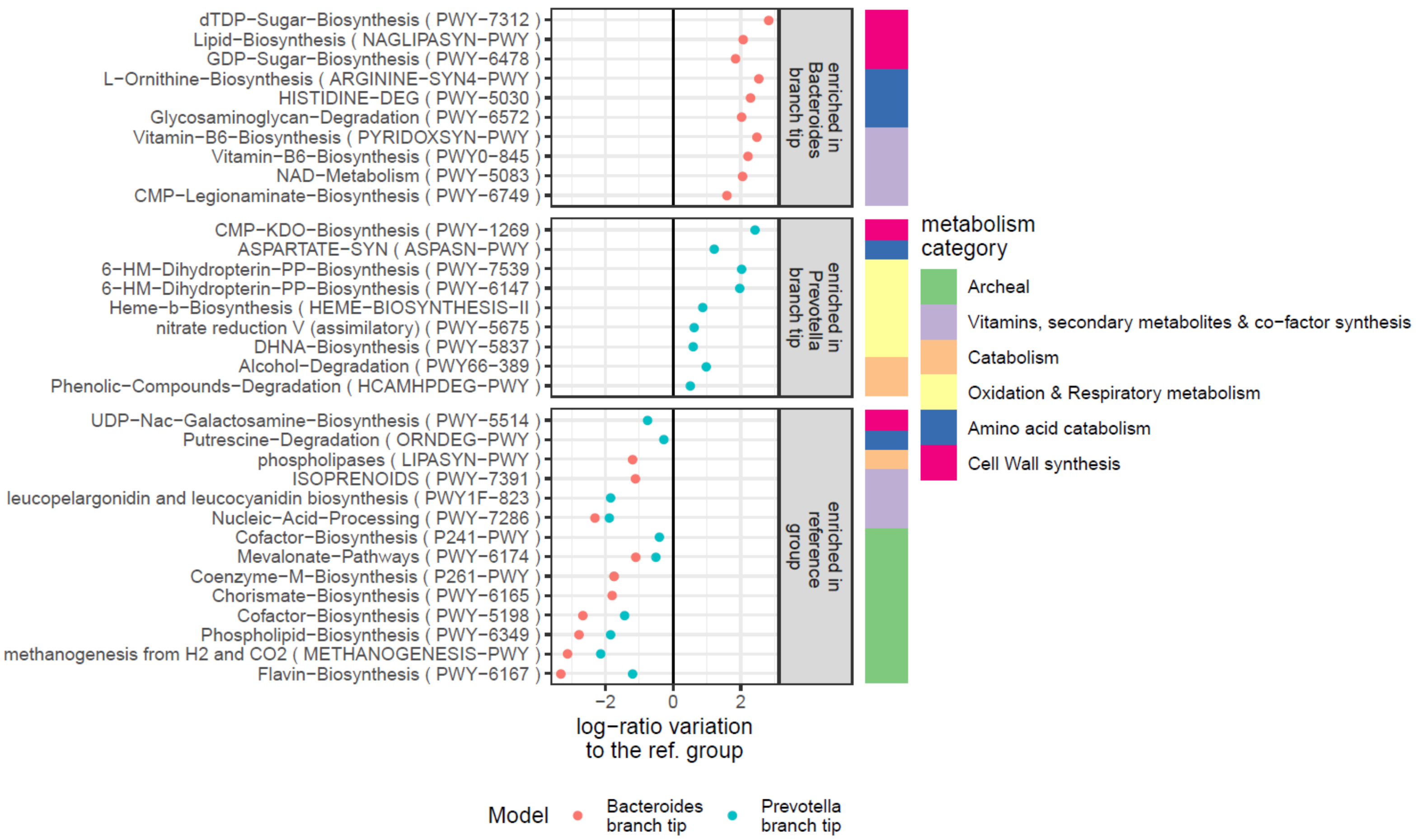


« Healthy index »



« Aerobiosis »

Low-diversity tips of branches display functional shifts

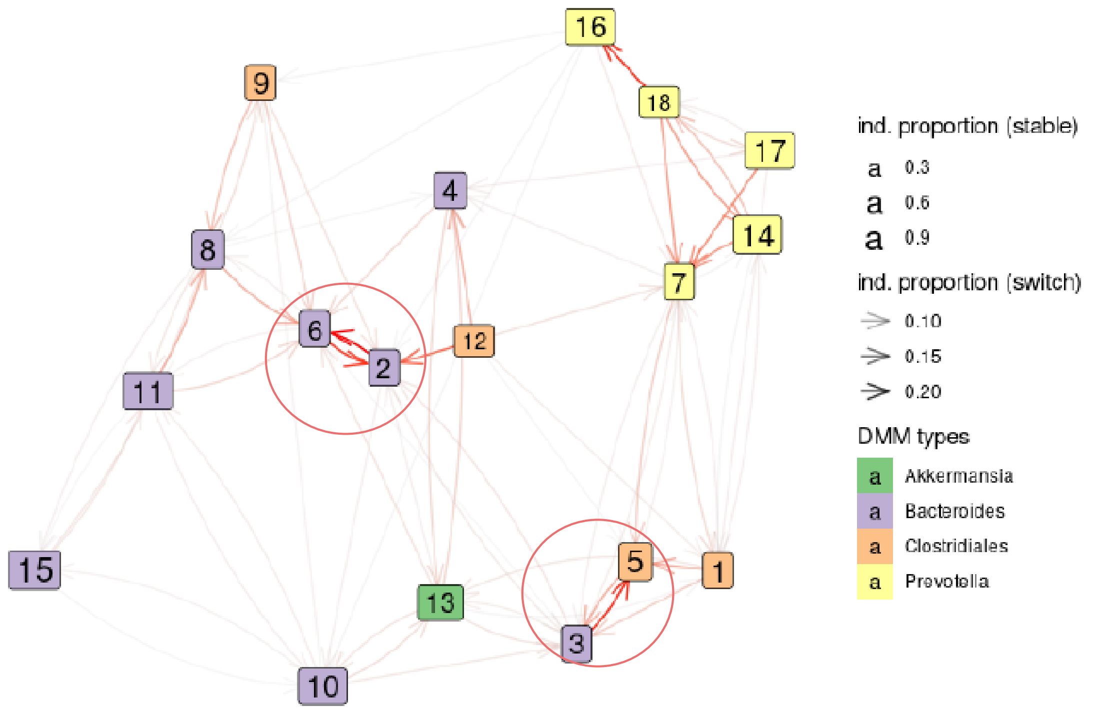


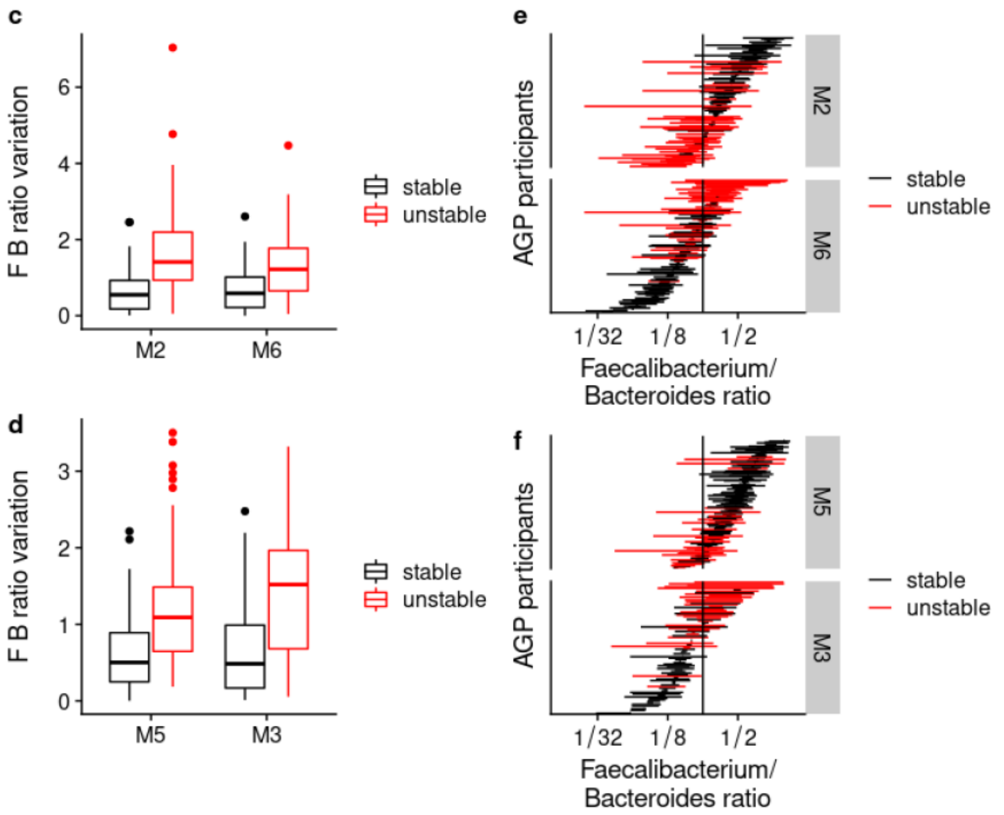
amino acid catabolism increase in *Bacteroides* branch tip

oxidative stress response increase in *Prevotella* branch tip

Dynamics between partitions are associated to branches

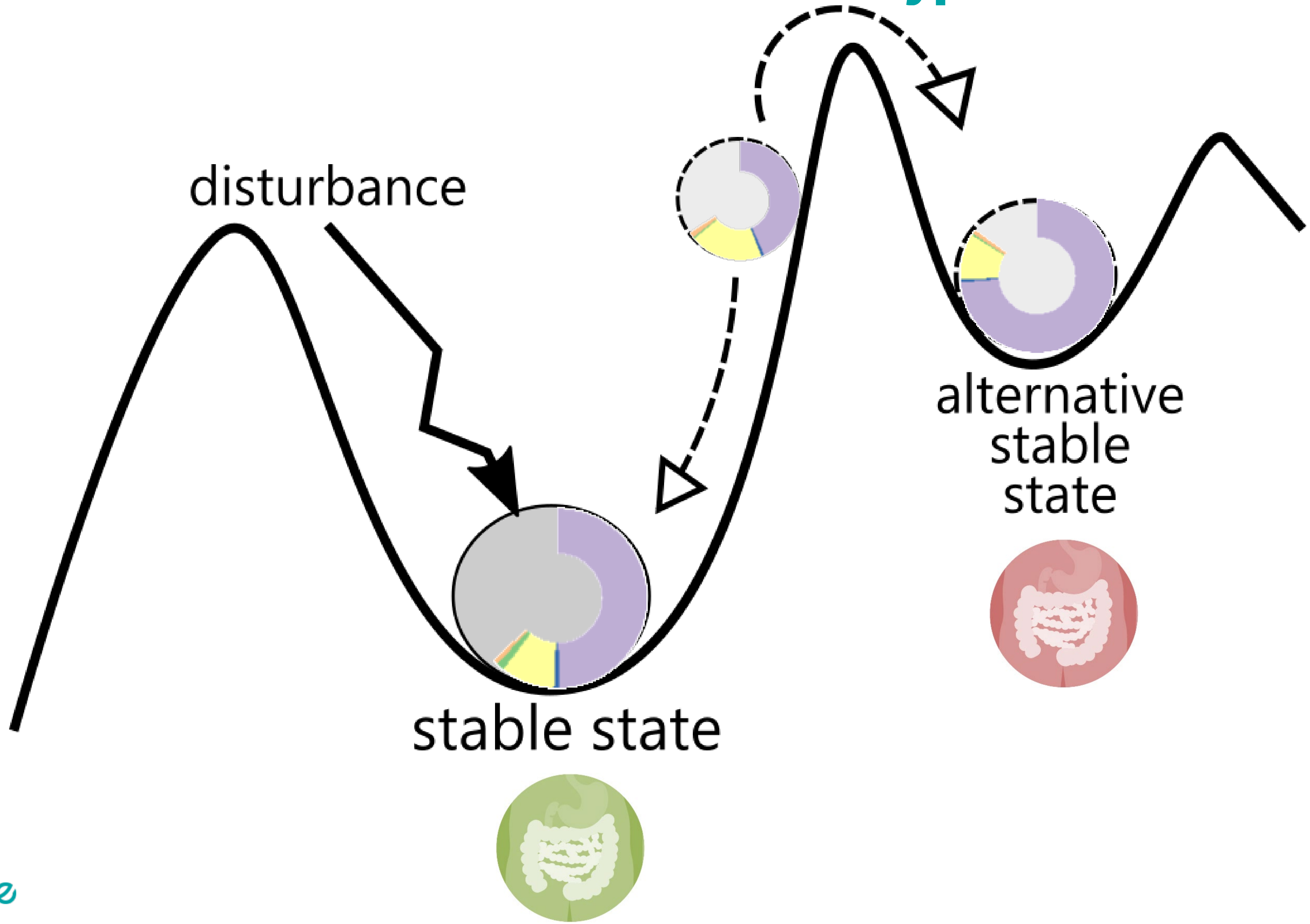
827 participants 2,998 samples 2,171 time-pairs



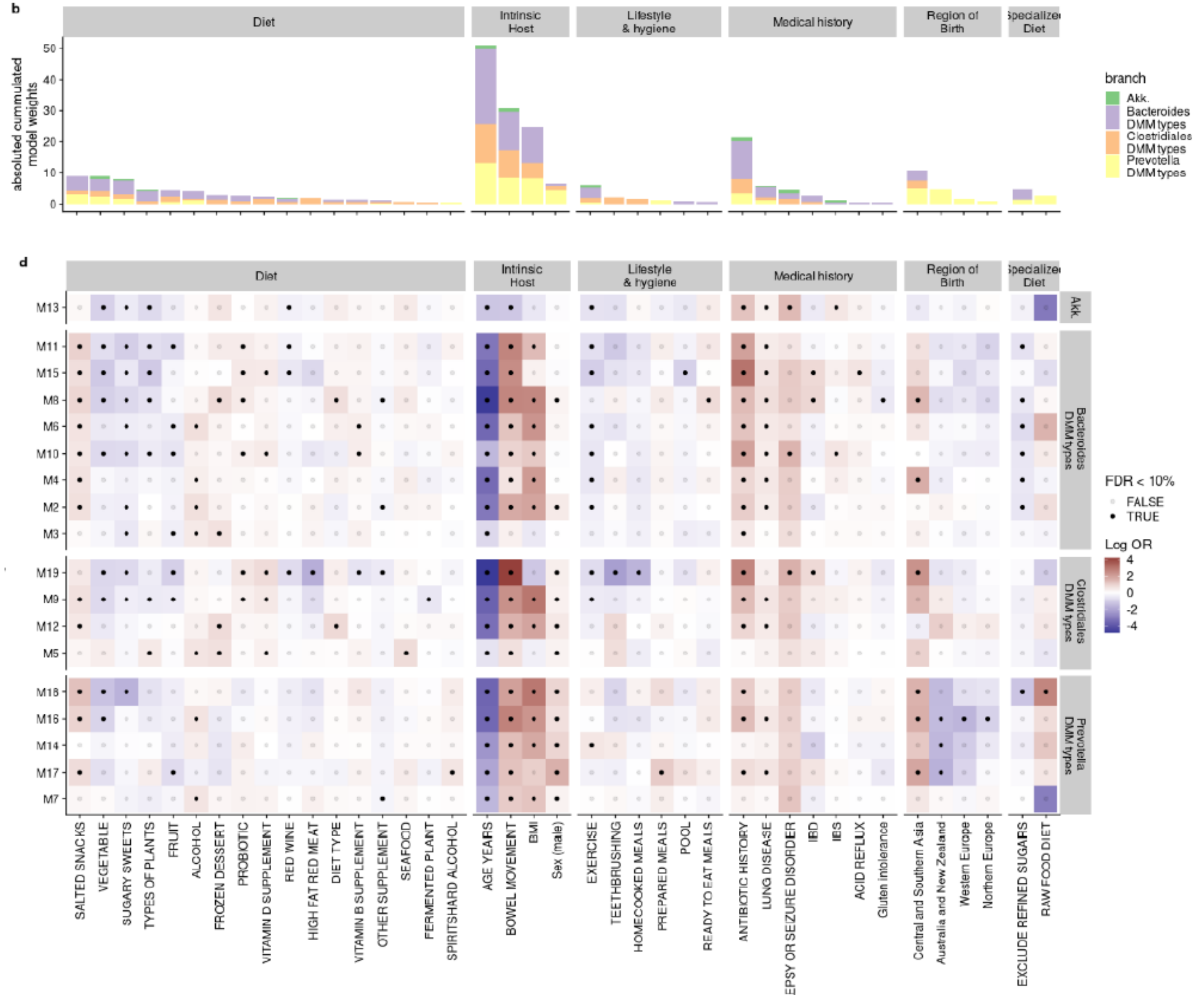


Feacalibacterium/Bacteroides as a tipping element explaining the switch between some states

Gut microbiome alternative stable states hypothesis



Gut microbiome states are differentially associated with host and env factors

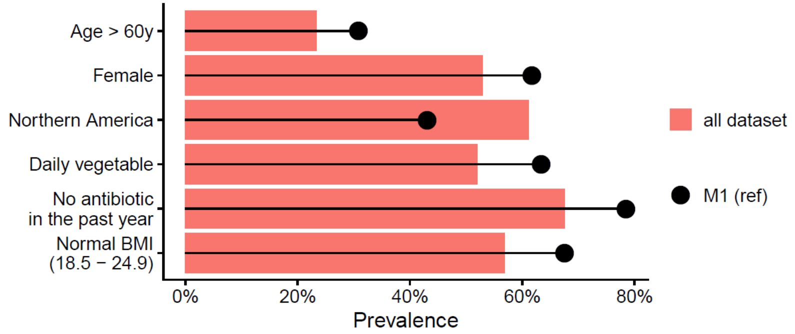


Sex, exercises frequency and **region of birth** associated differentially between branches

Lifestyle and hygiene associated with altered state within *Bacteroides* branch

Specialized diet associated with altered state within *Prevotella* branch

Do we already observe a intergenerationally mass extinction ?



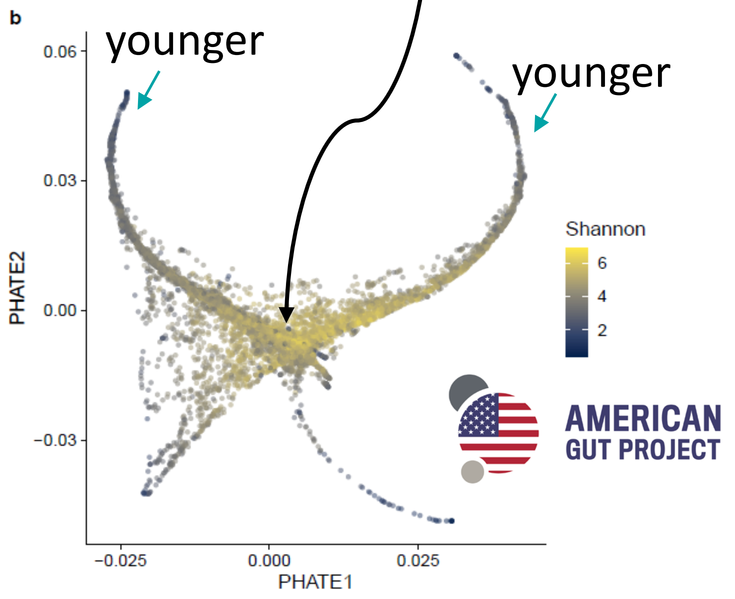
Older and healthy diet and lifestyle

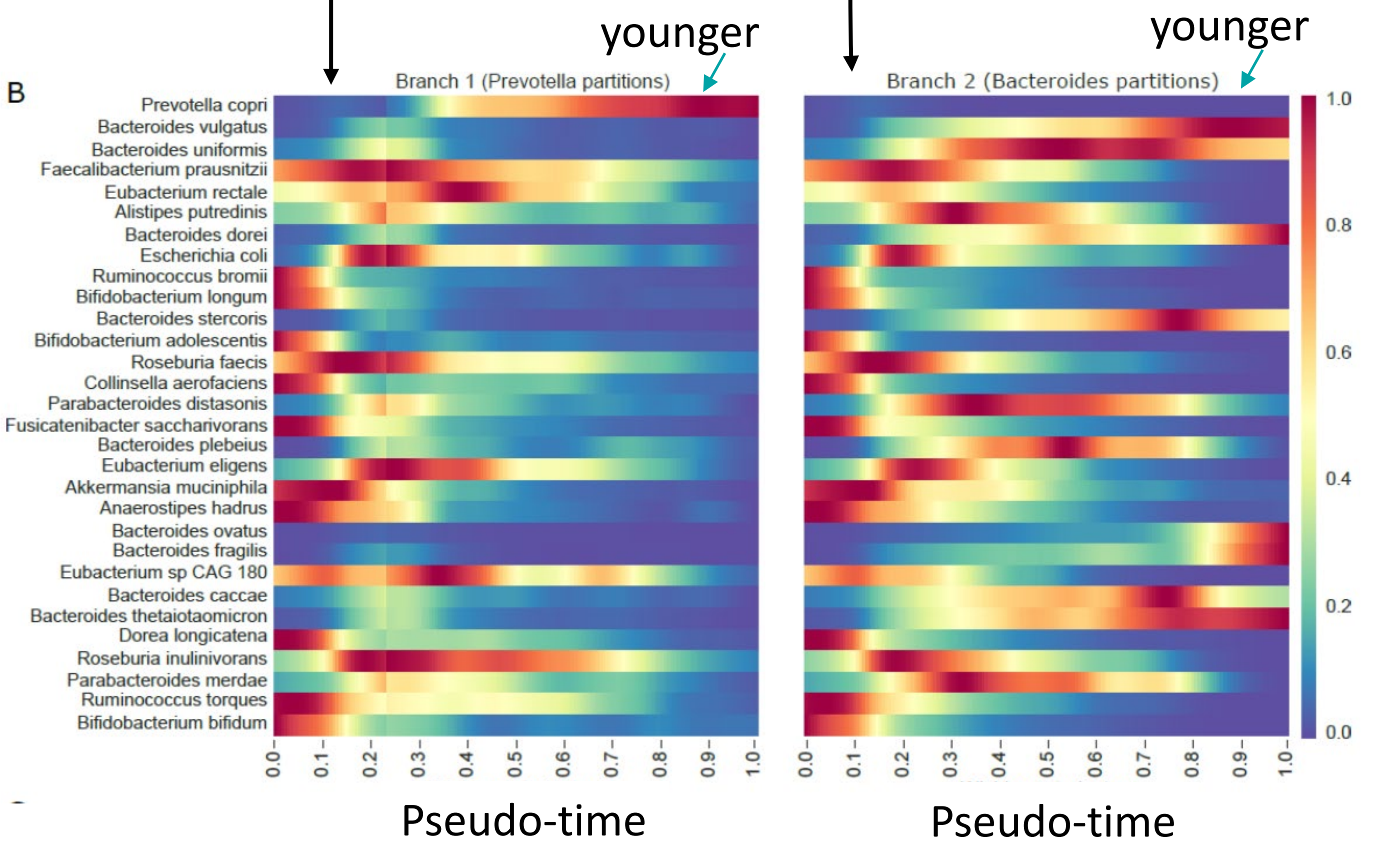
≡ WIRED

SABRINA WEISS SCIENCE 04.01.2023 12:00 PM

A Mass Extinction Is Taking Place in the Human Gut

To preserve humankind's diverse bacteria, scientists are harvesting, freezing, and storing poop from around the world.

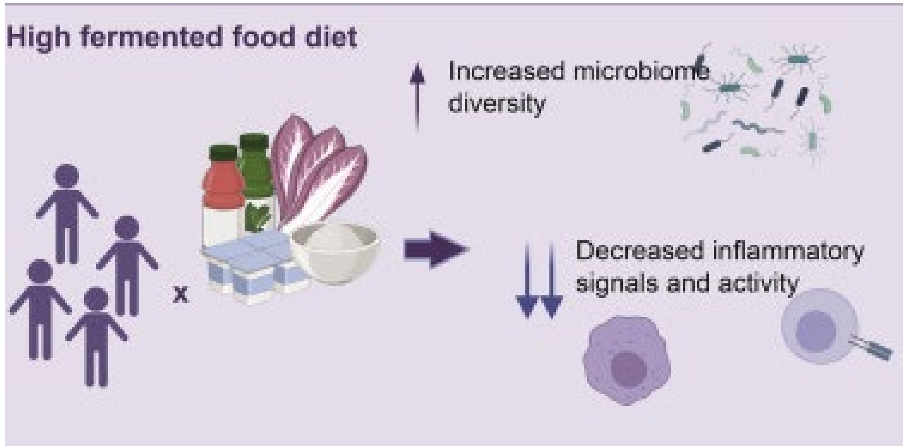


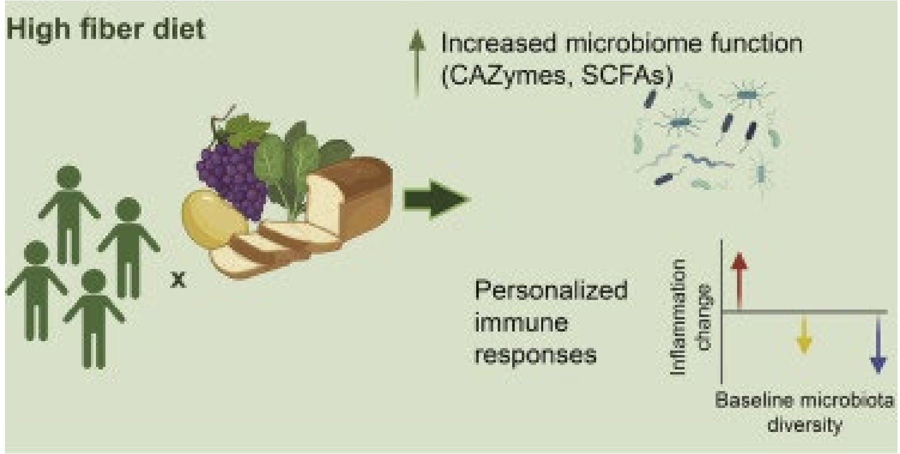


Tap et al., Nature Comm. 2023

Harnessing the microbial potential of fermented foods to avoid the point of no return

How fermented foods can fit precision nutrition for health?



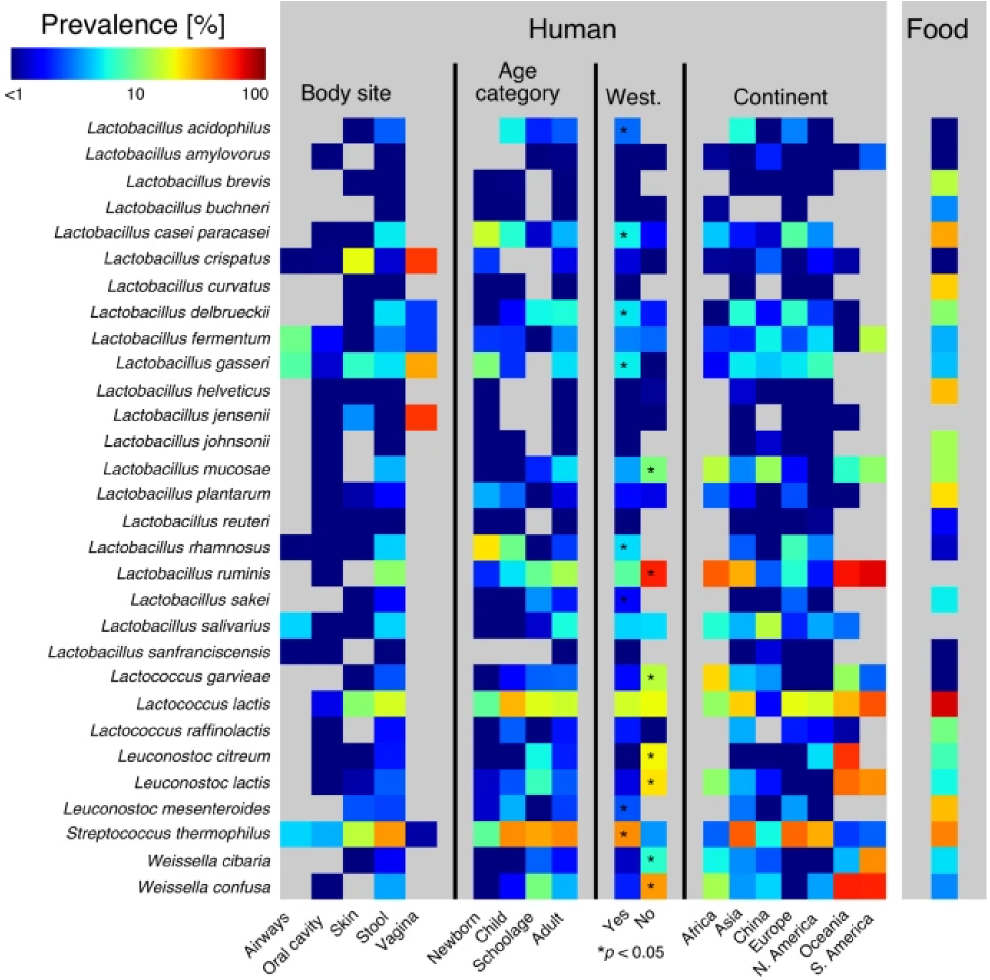


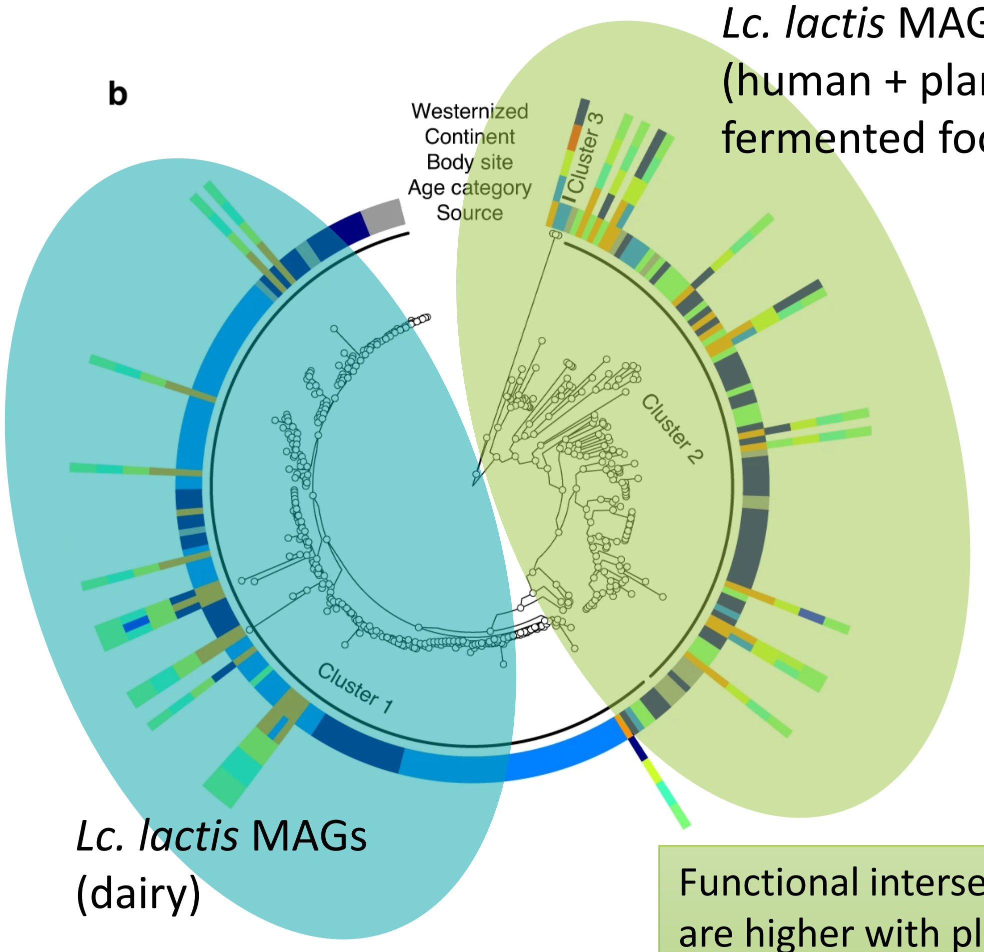
Fermented foods valuable solution in countering the decreased microbiome diversity

Personalized immune as function of gut microbiota baseline

Wastyk et al., 2021

Large intersection between food and human microbial species but subtype matters





Lc. lactis MAGs (human + plant-based fermented food)

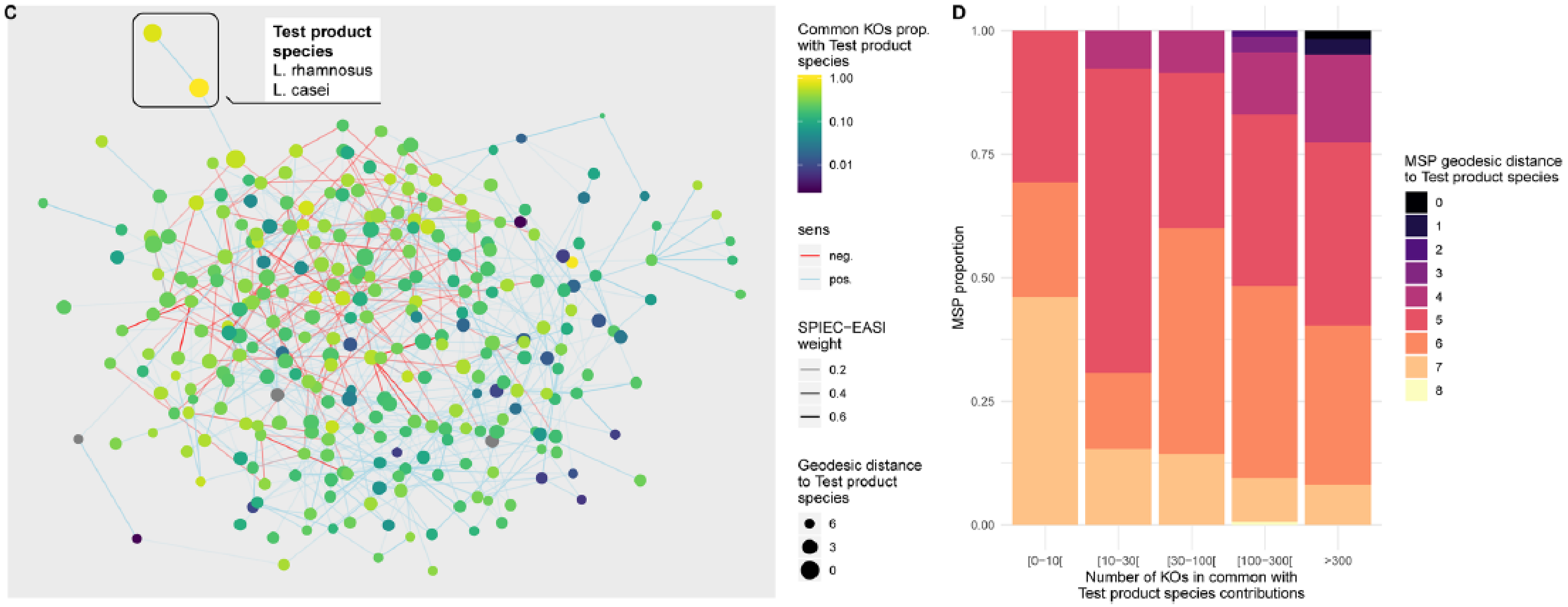
Lc. lactis MAGs (dairy)

Functional intersections are higher with plant-based strains

Pasoli et al. 2020

Gut microbiome functional enrichment by fermented food is personalized

Modular coalescence between gut and food species

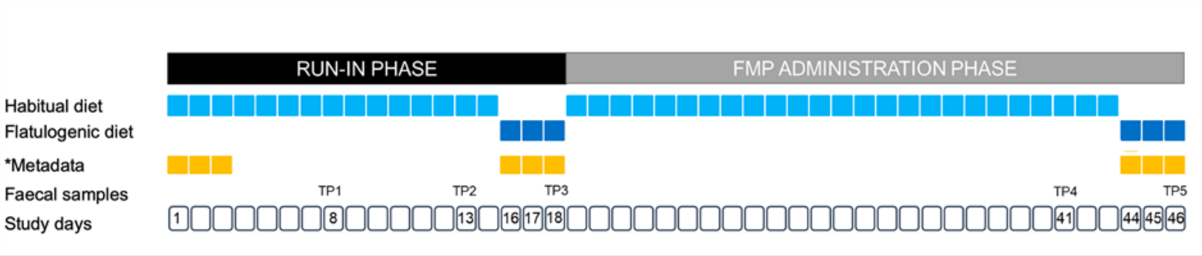


“Engraftment” as function of existing niche and metabolic pathway

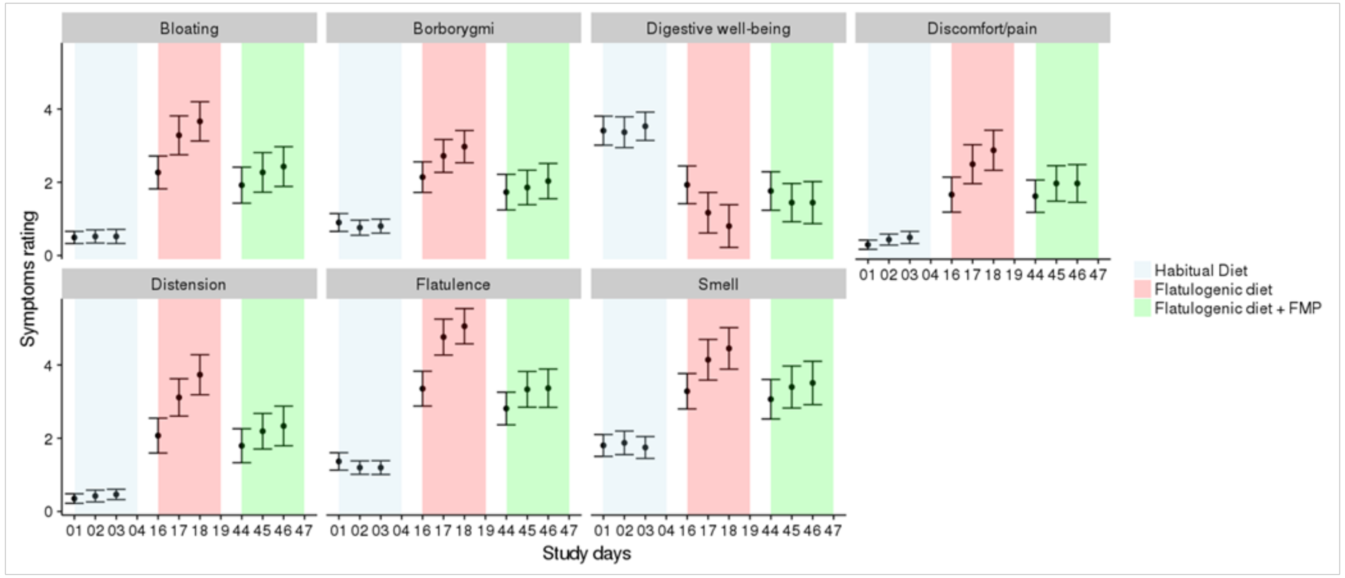
Alvarez et al., 2020

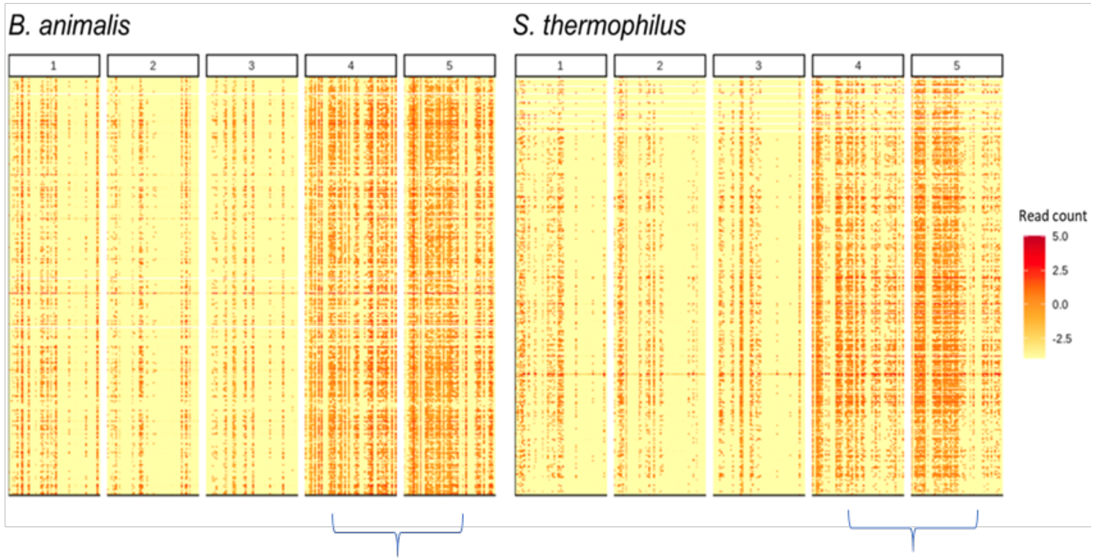
Fermented food strains are active in gut microbiome

FMP product
Streptococcus salivarius subsp. thermophilus strains (CNCM I-2773, CNCM I-2130, CNCM I-2272),
Lactobacillus delbrueckii subsp. bulgaricus (CNCM I-1519),
***Bifidobacterium animalis* subsp. *lactis* (CNCM I-2494)**
Lactococcus lactis subsp. *lactis* (CNCM I-1631).



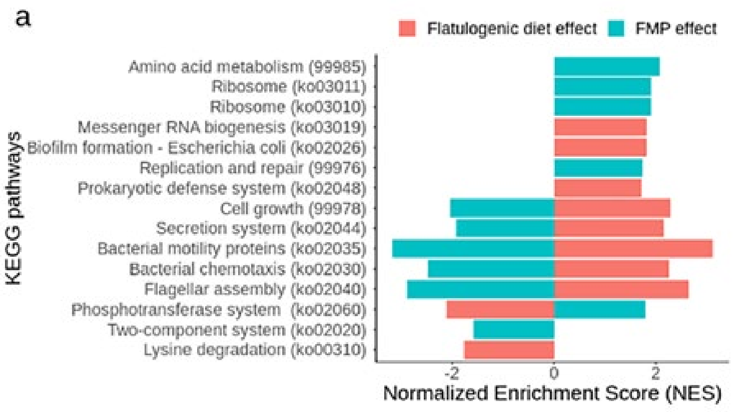
flatulogenic diet (61% carbohydrates, 25% proteins and 14% fat, 27 g of fiber per day)



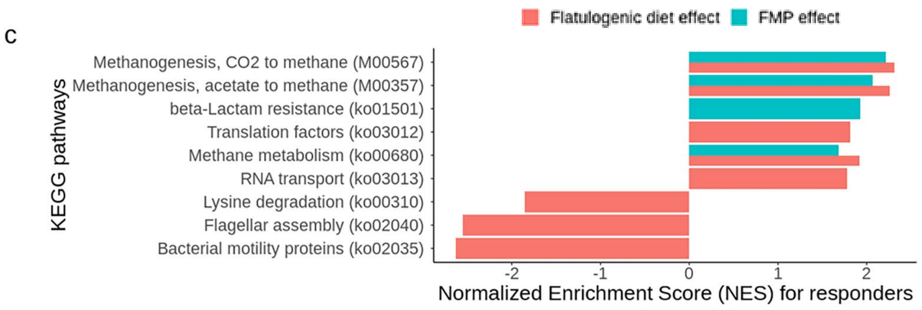


After FMP consumption, FMP active strains detected by metatranscriptomics

Fermented food consumption was associated with gut microbiota metabolic changes



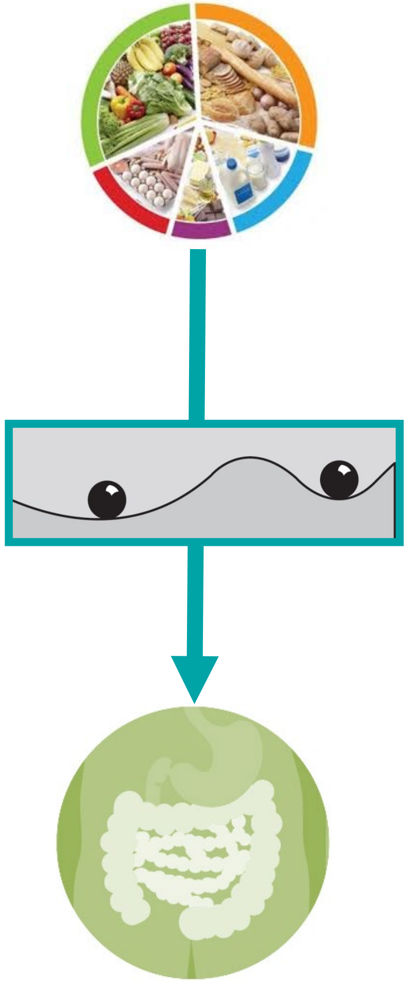
Flatulogenic diet might increase cell motility and cell growth whereas FMP consumption exhibited the opposite effect

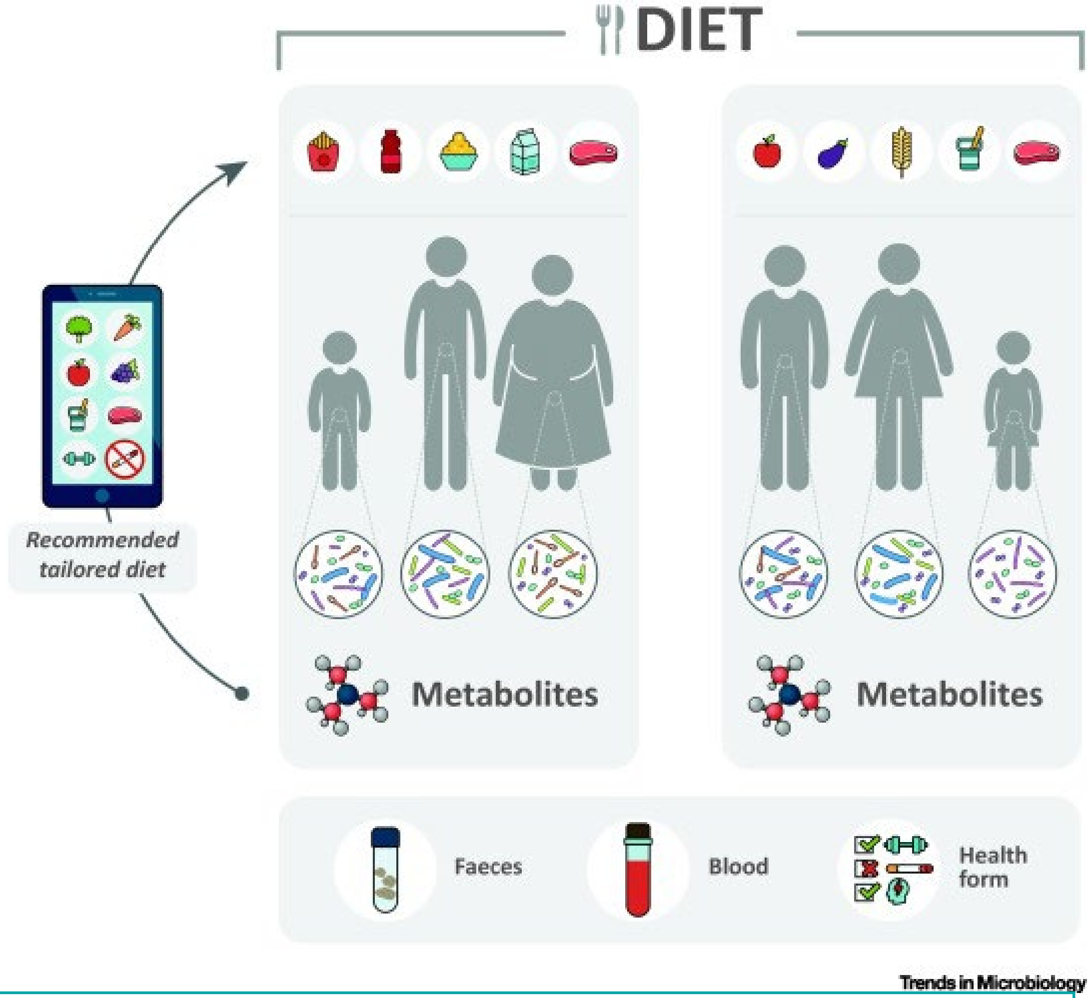


After FMP intake (TP5), higher responder group showed higher methanogenesis activity than low-responders

Oyarzun et al., 2022

Endgame : From gut microbiome states to next-gen fermented food



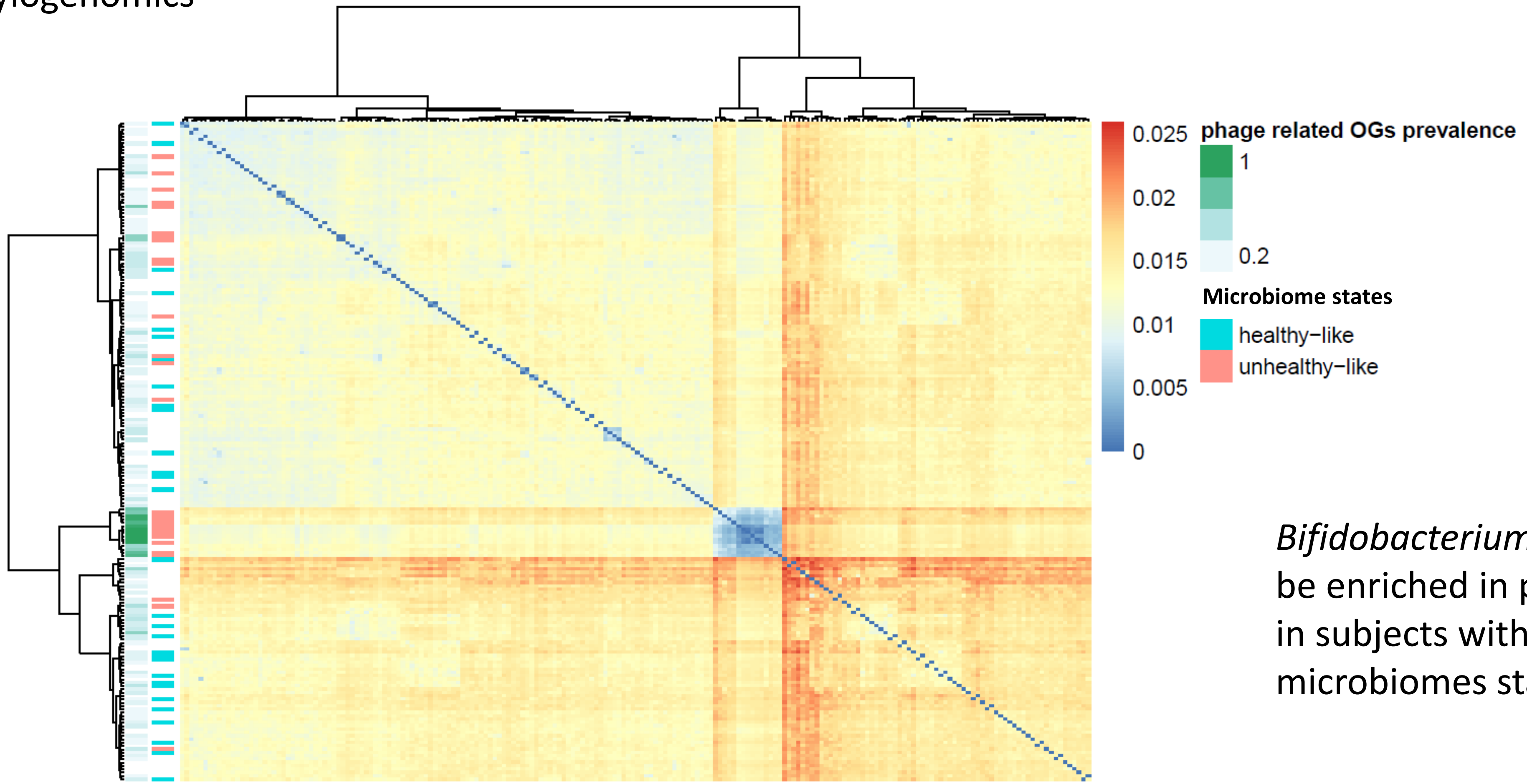


Trends in Microbiology

Prevent gut microbiome critical transition to strengthen its resilience using next-gen fermented food

Altered states showed functional differences within species

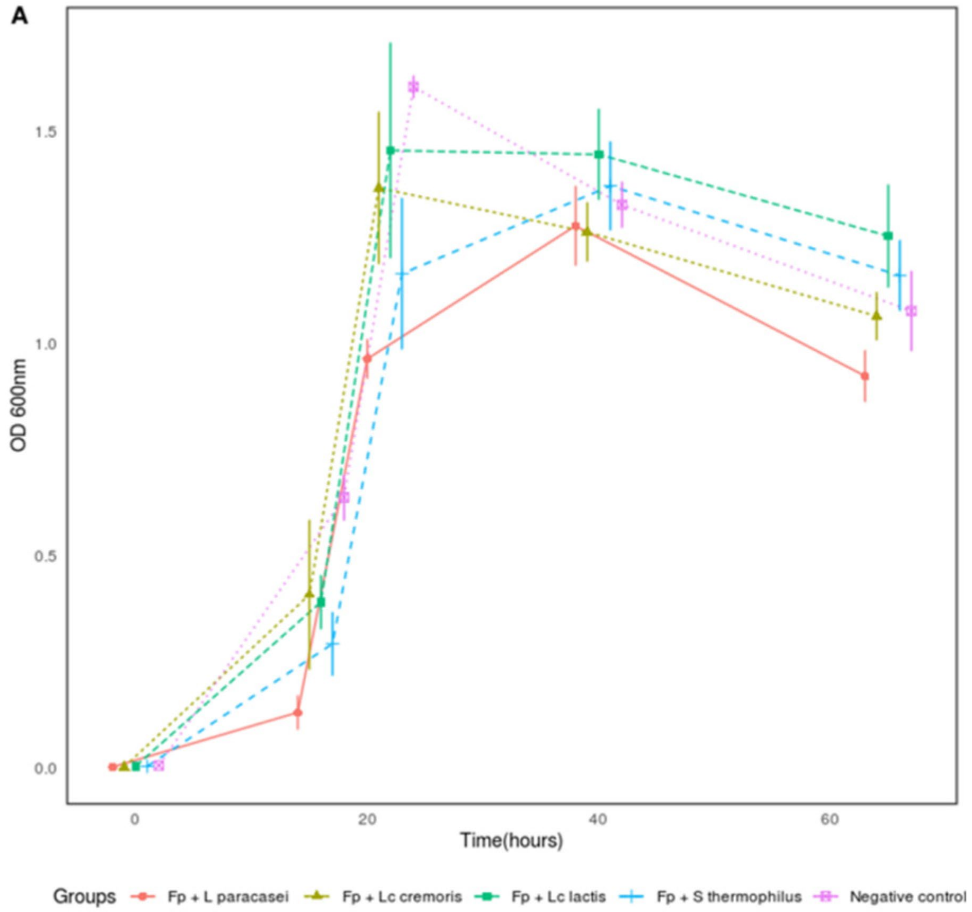
400 *B. bifidum* MAGS
phylogenomics

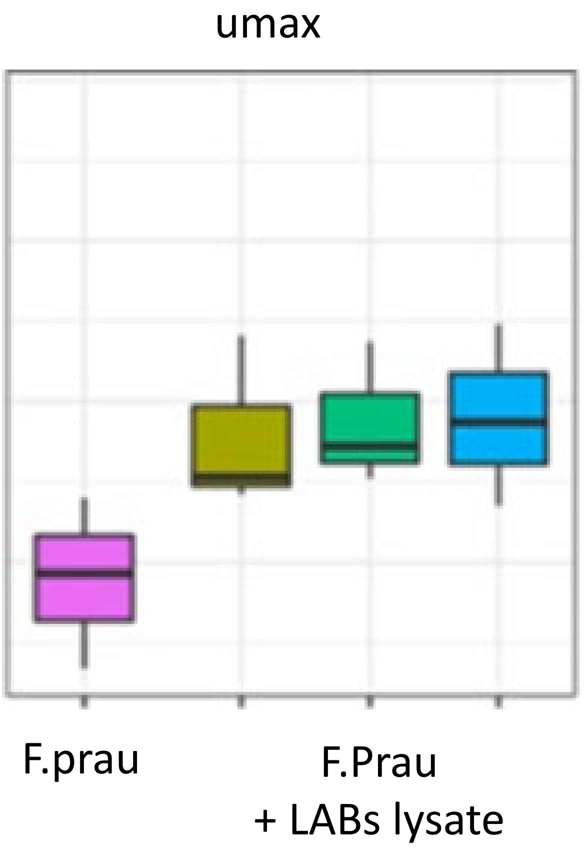


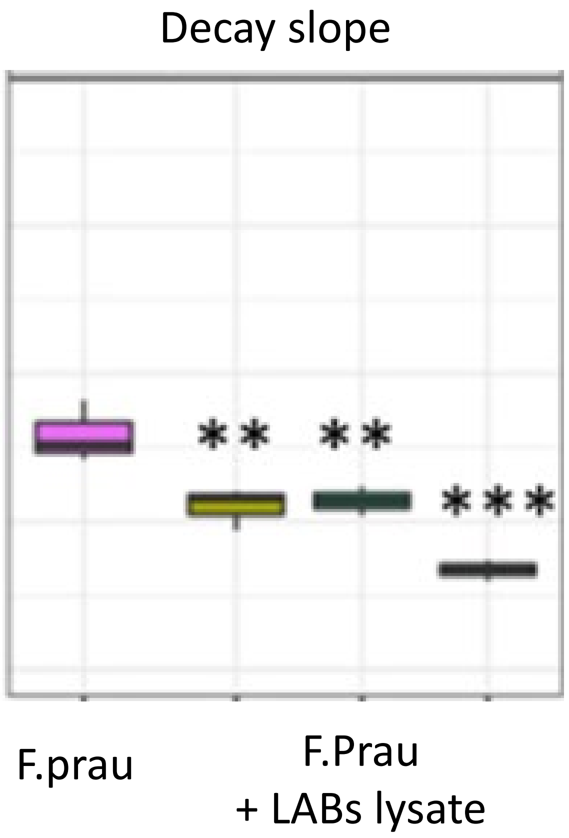
Bifidobacterium bifidum strains may be enriched in phage-related genes in subjects with altered gut microbiomes states

Ladeira *et al*, 2023

Towards selecting strains with abilities to prevent tipping point in gut microbiota





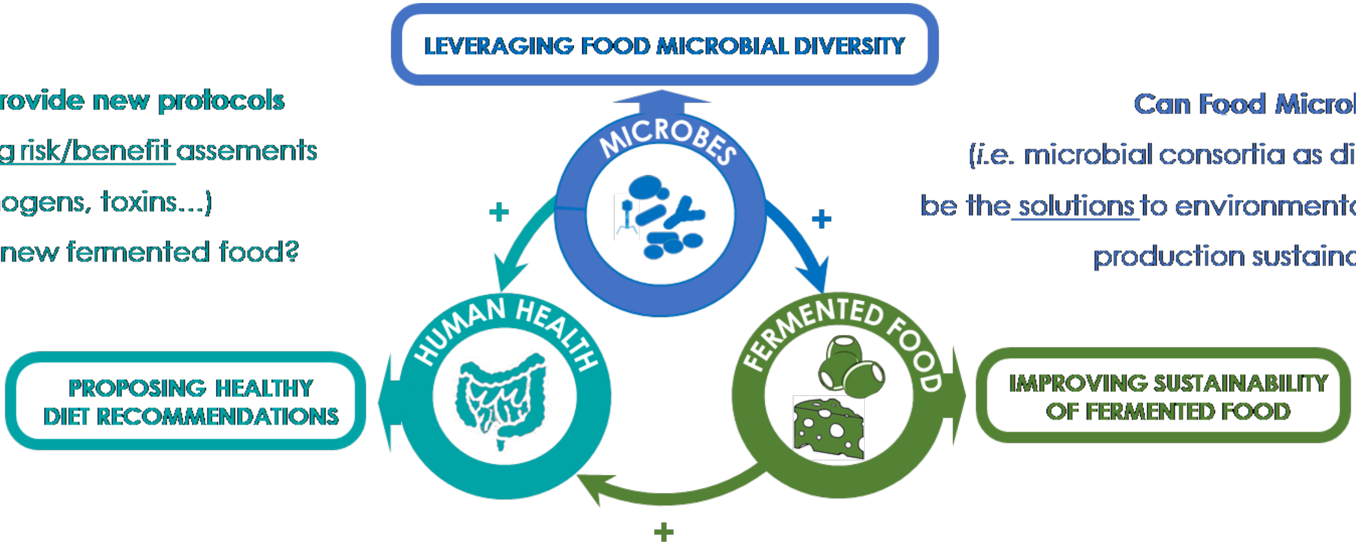


Increase of peptidoglycan levels for cell wall formation *F.prau*

Lebas, Derrien and colleagues (2020)

How to design next-gen and sustainable fermented food?

Can we provide new protocols
for improving risk/benefit assements
(pahogens, toxins…)
of old and new fermented food?



LEVERAGING FOOD MICROBIAL DIVERSITY

PROPOSING HEALTHY DIET RECOMMENDATIONS

IMPROVING SUSTAINABILITY OF FERMENTED FOOD

Can Food Microbes
(*i.e.* microbial consortia as dietary microbes)
be the solutions to environmental-friendly and food
production sustainability?

Can we demonstrate that fermented food consumption
improve human health and restore (maintain) human microbiome symbiotic relationship ?
What would be the impact
of transition from animal- to plant-based fermented food
(anti-nutritional factors, low availibility of certain nutrients…) ?

Stéphane Chaillou (Coord.)

DOMINO

Funded by
the European Union

Take home messages

- Gut microbiome ecological landscape is made of **local states** that are dynamically linked within "**branches**" where **critical transition** occurred
- Fermented foods and biotics can help but **effects may be personalized** thank to gut **microbiota states at baseline**
- Prototyping process of next gen fermented food should **include gut tipping elements** during screening for better **personalized and beneficial effects**.

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Food Microbial Ecology lab
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