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# Branches and ecological states of the gut microbiome: Mapping for future personalized nutritional and therapeutic interventions

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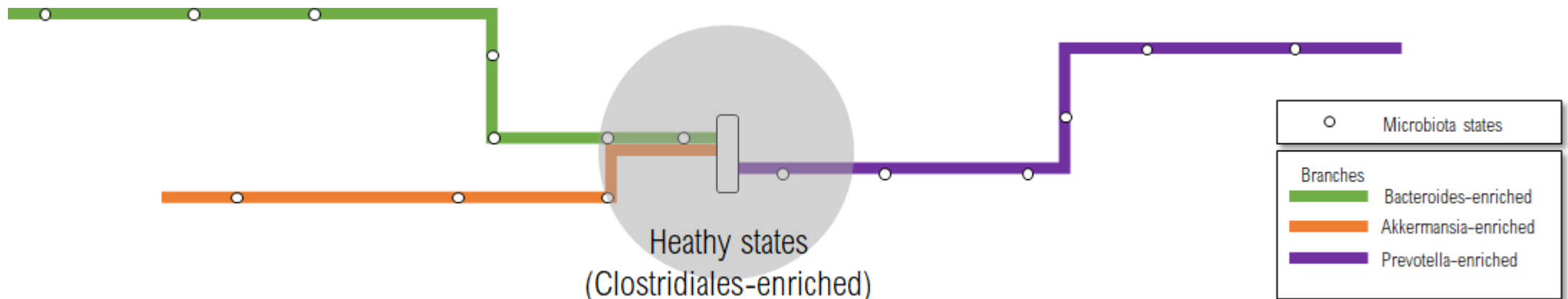
# > Branches and ecological states of the gut microbiome:

## Mapping for future personalized nutritional and therapeutic interventions

Julien Tap

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Journées Polepharma de Microbiomique- Rouen 2023

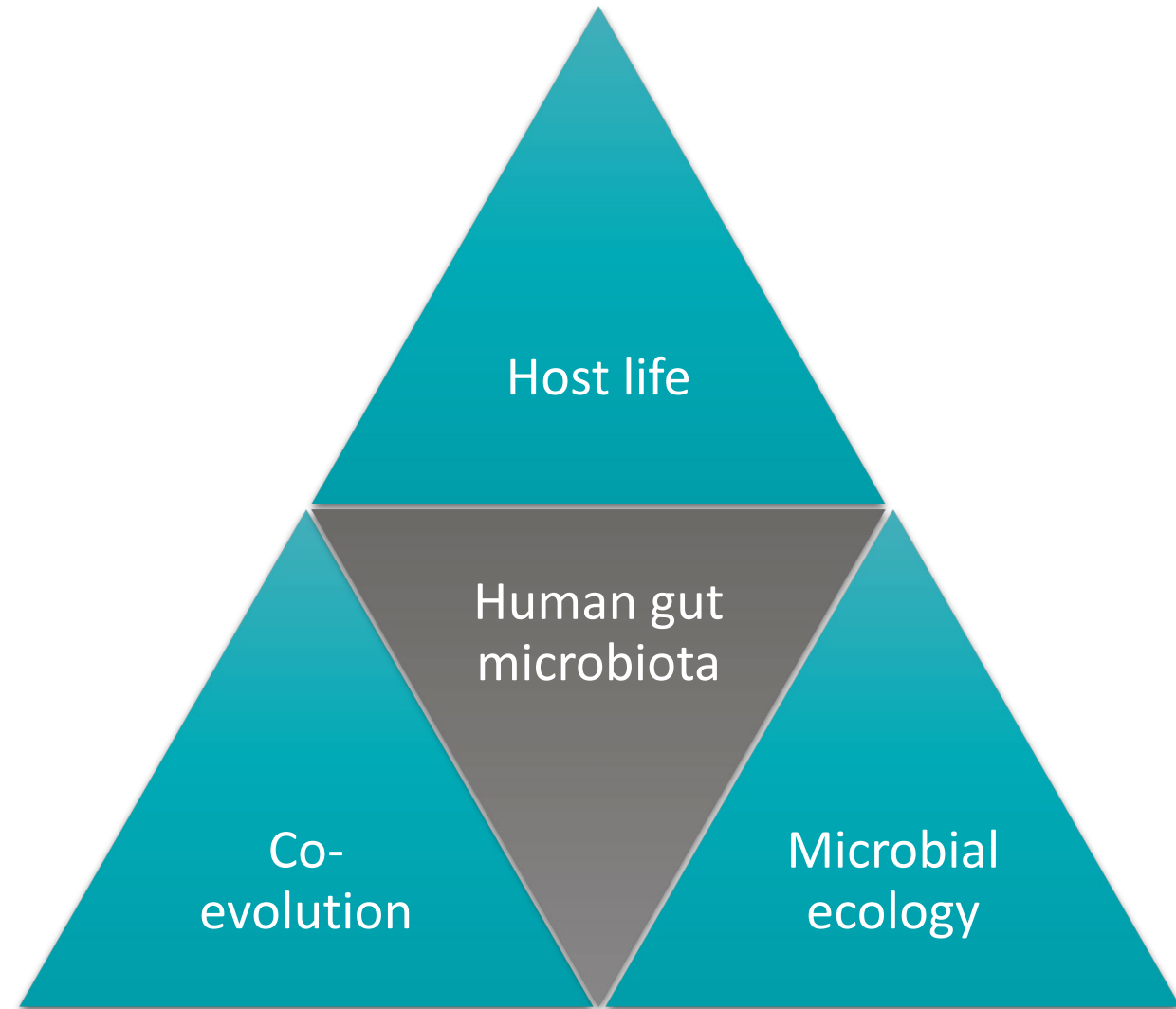
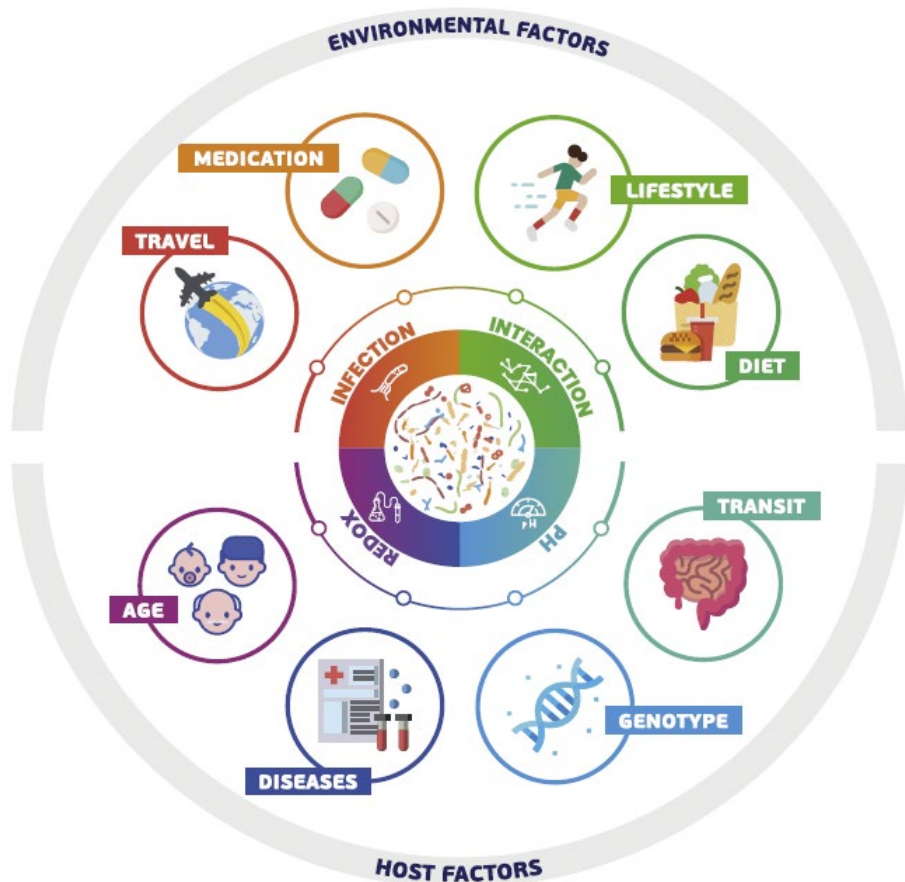


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Branches and ecological states of the gut microbiome - Journées Polepharma de Microbiomique - Rouen 2023

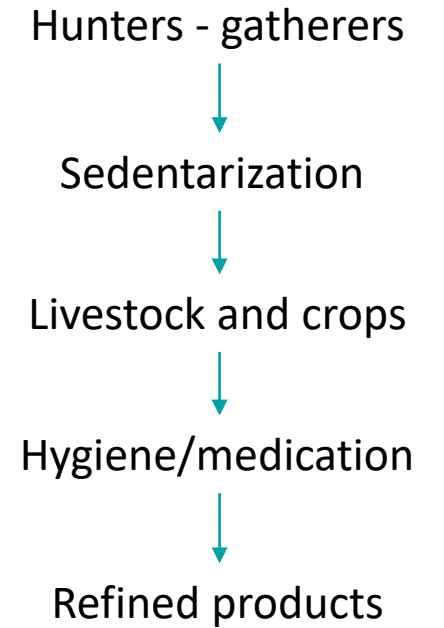
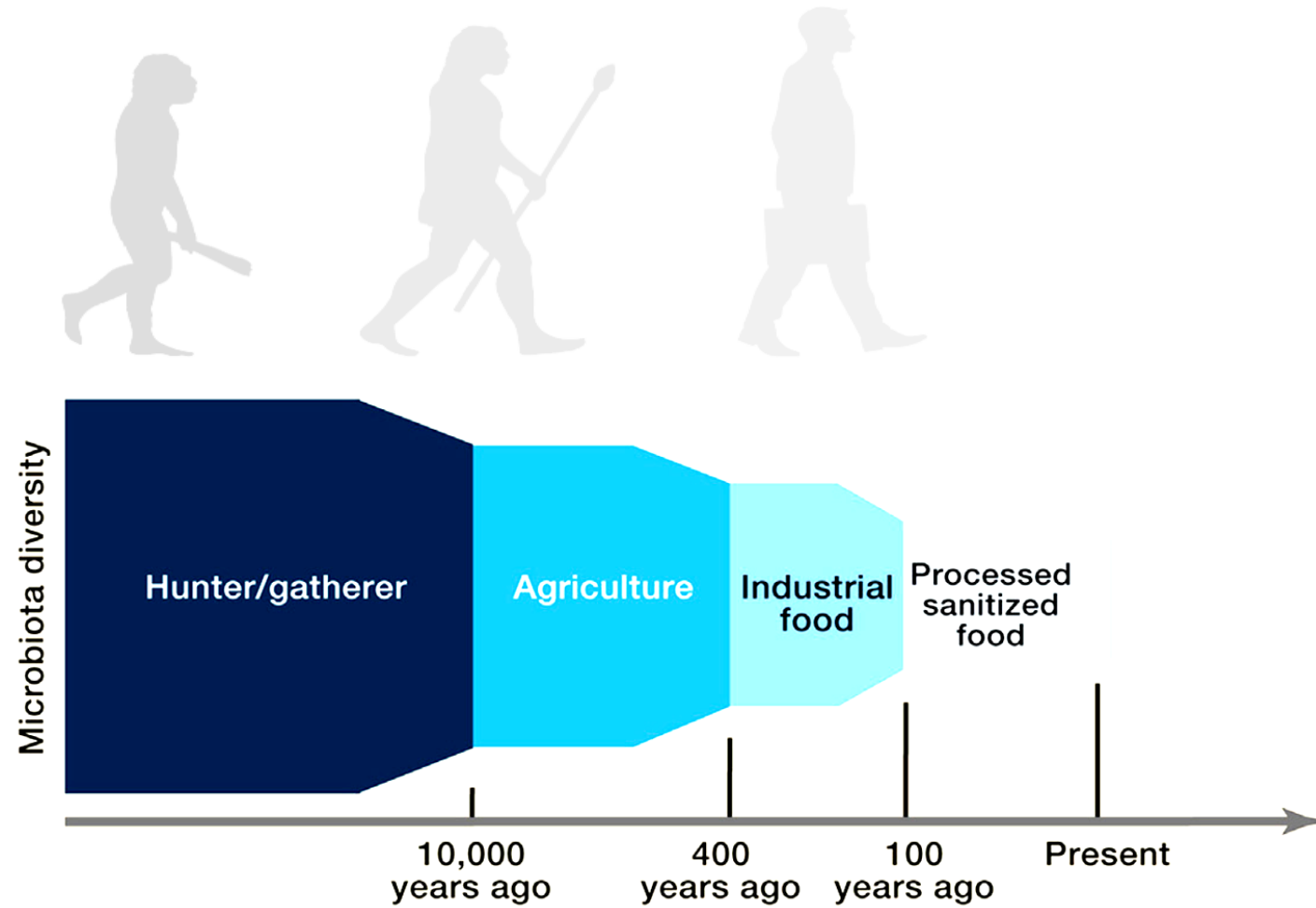
22.11.23 / Julien Tap / fme.micalis.fr

# ➤ Different factors shapes the human gut microbiome

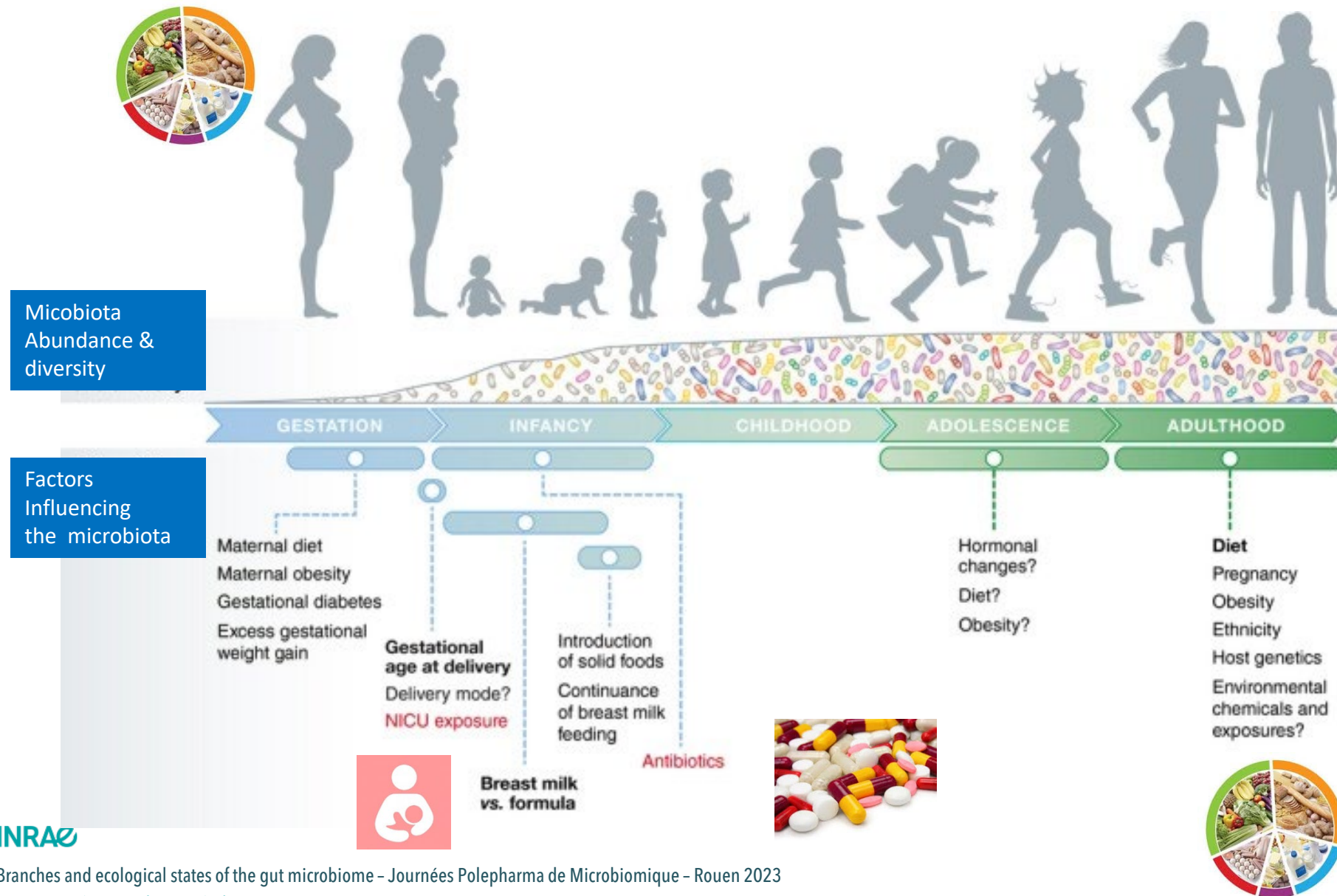


# > Diet and lifestyle effect host microbiome symbiosis

Are we uncoupling our metagenome and our genome?



# > Gut microbiome throughout life span



# ➤ Microbiome states resilience as key factor



Healthy state



Resistance



Recovery

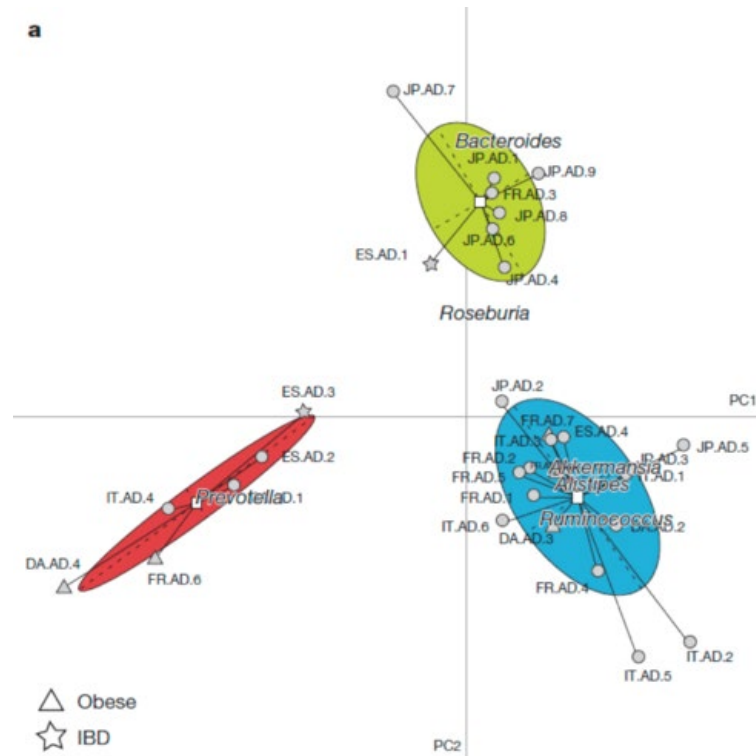
Resilience

Healthy state

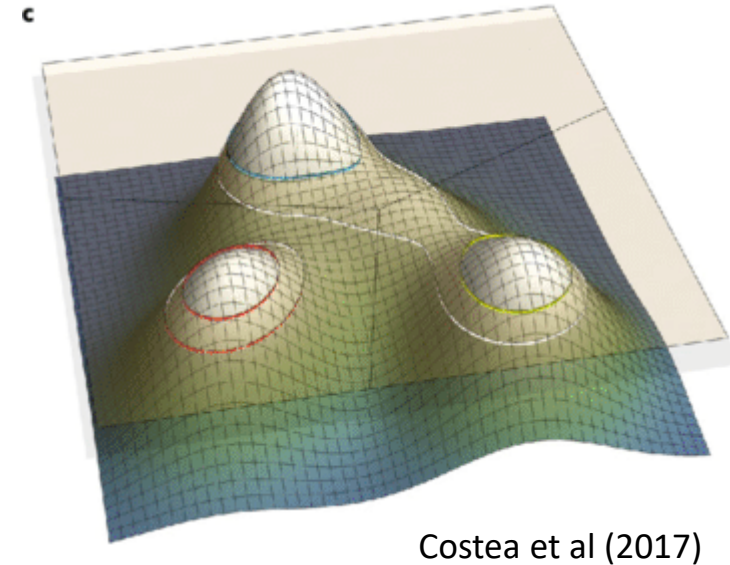


Degraded state

## ➤ Several attempts to decipher the microbiome structure



Arumugam, Raes et al (2010)



Costea et al (2017)

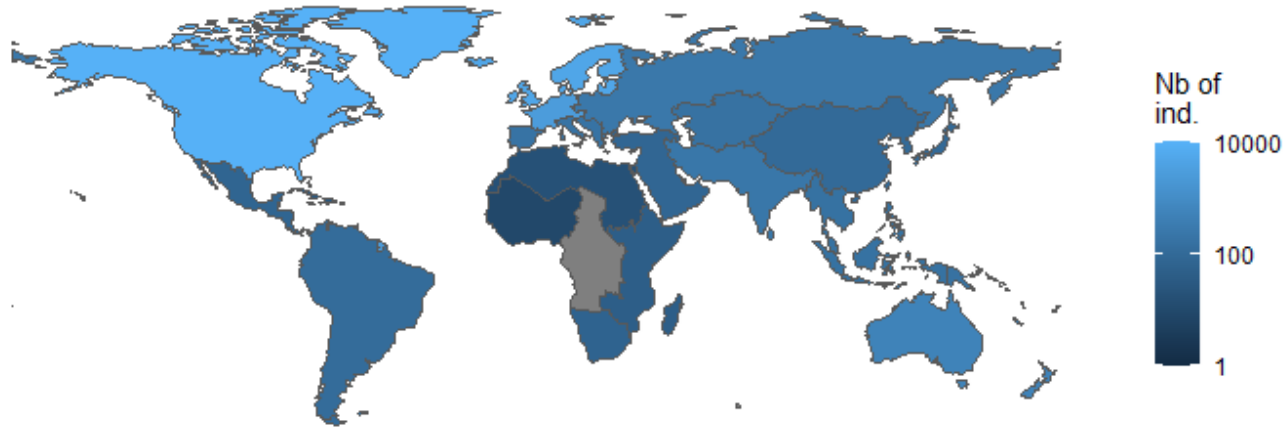
Dirichlet Multinomial Mixture (DMM) modeling

Limits:

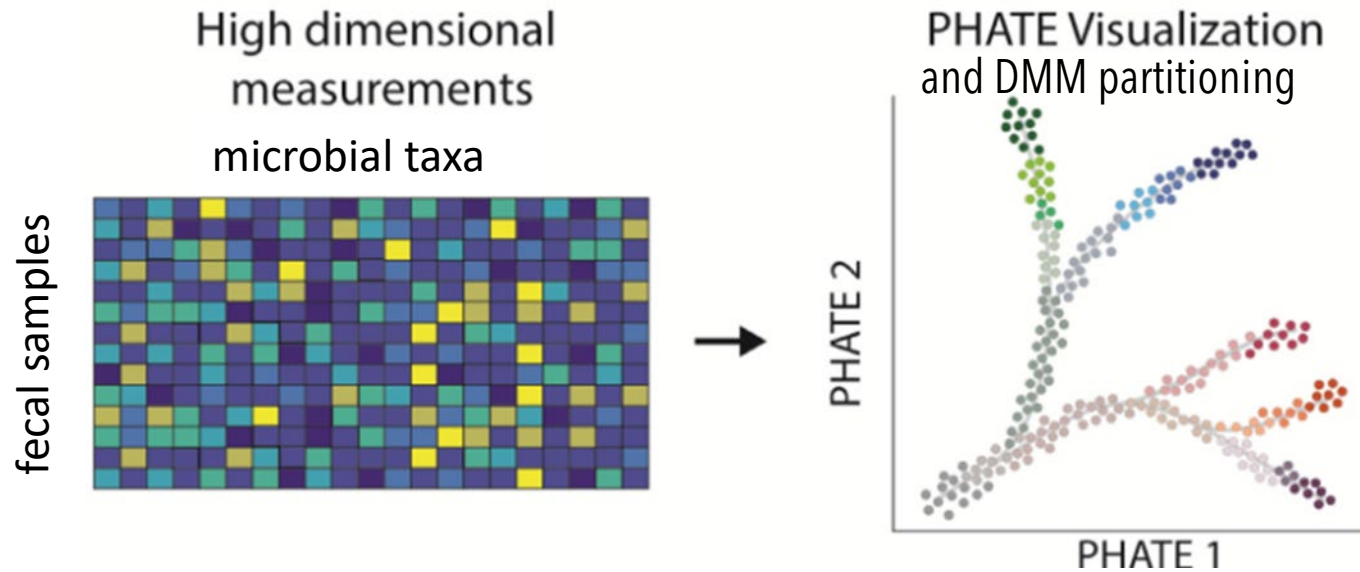
Few association with diet

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

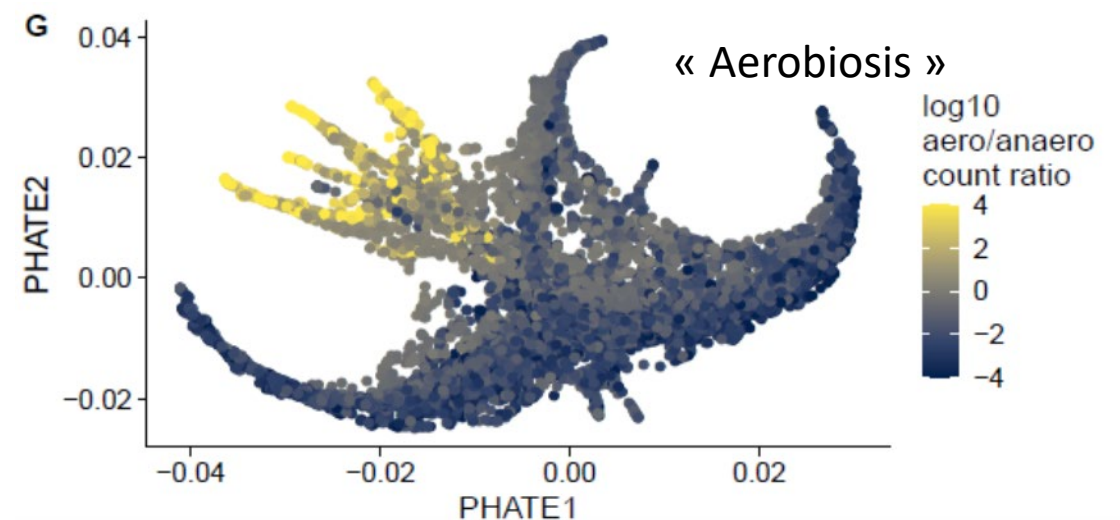
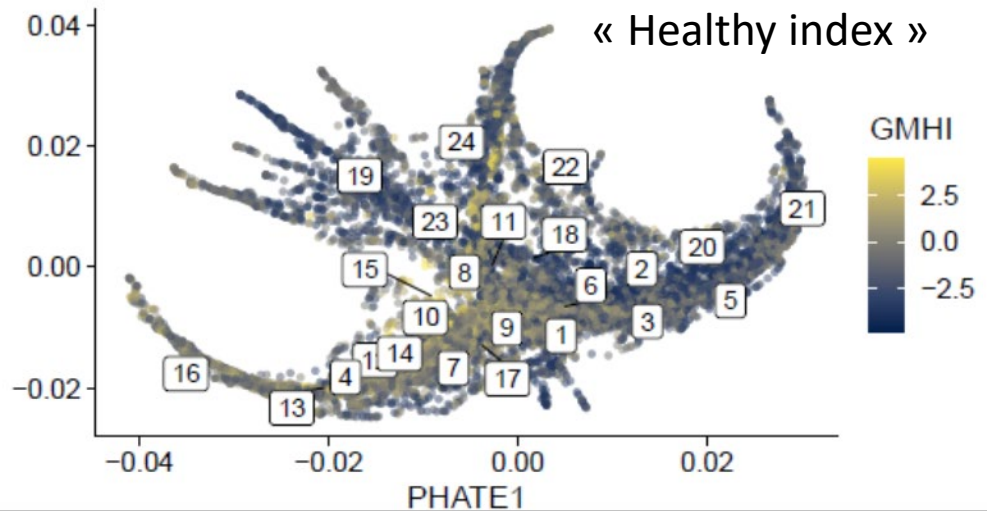
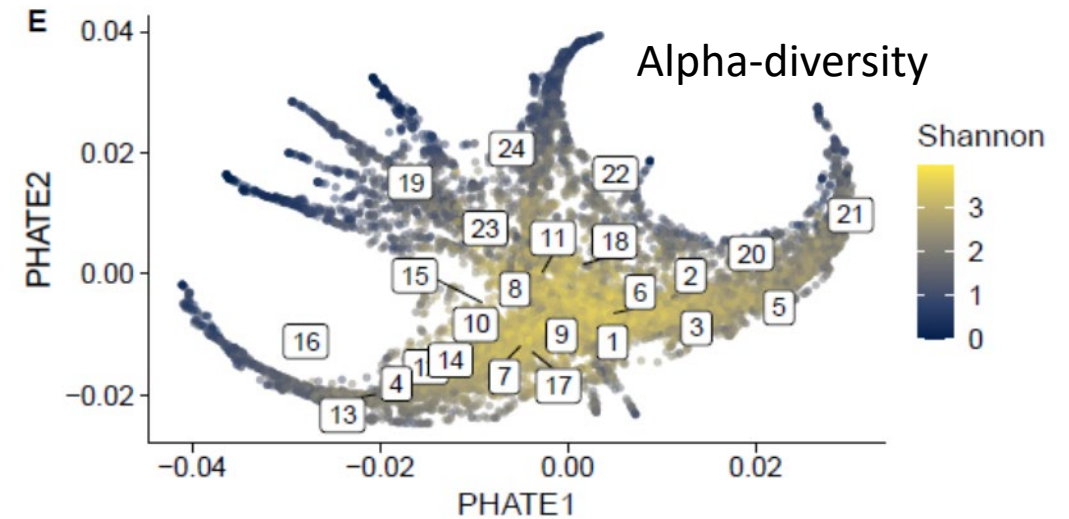
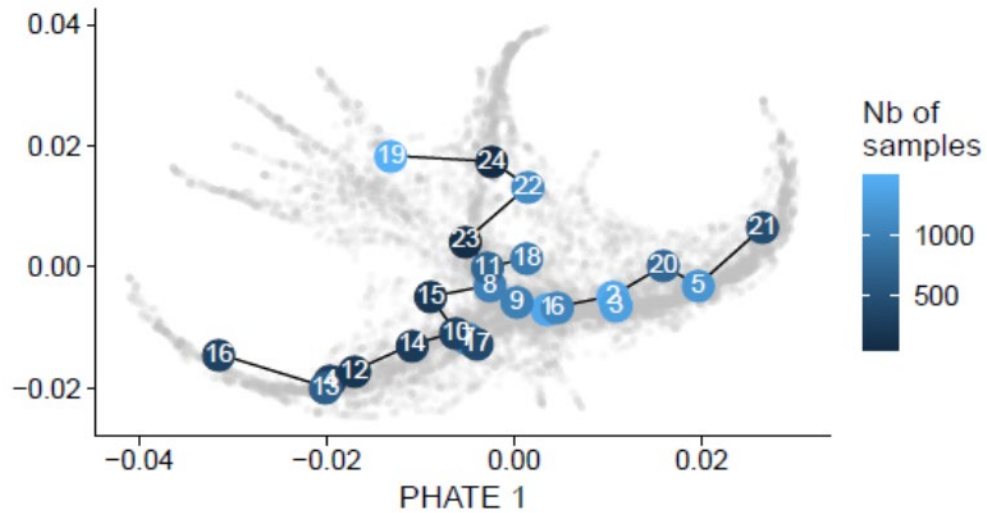


Time-series analysis to detect microbiome states

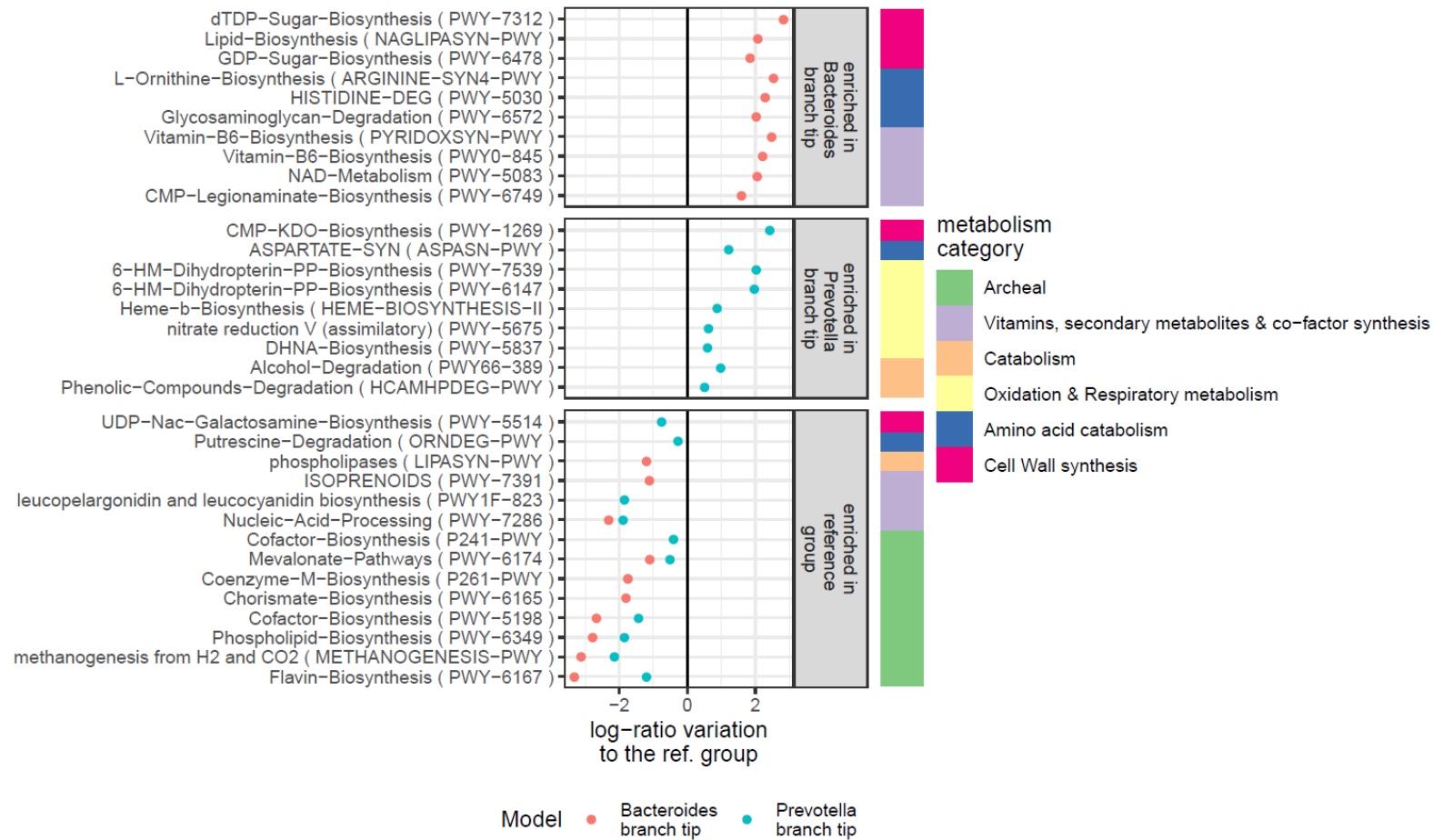
Region of birth, Lifestyle, diet, and health modelization



# ➤ Human Gut microbiome structured as branches



# ➤ Low-diversity tips of branches display functional shifts

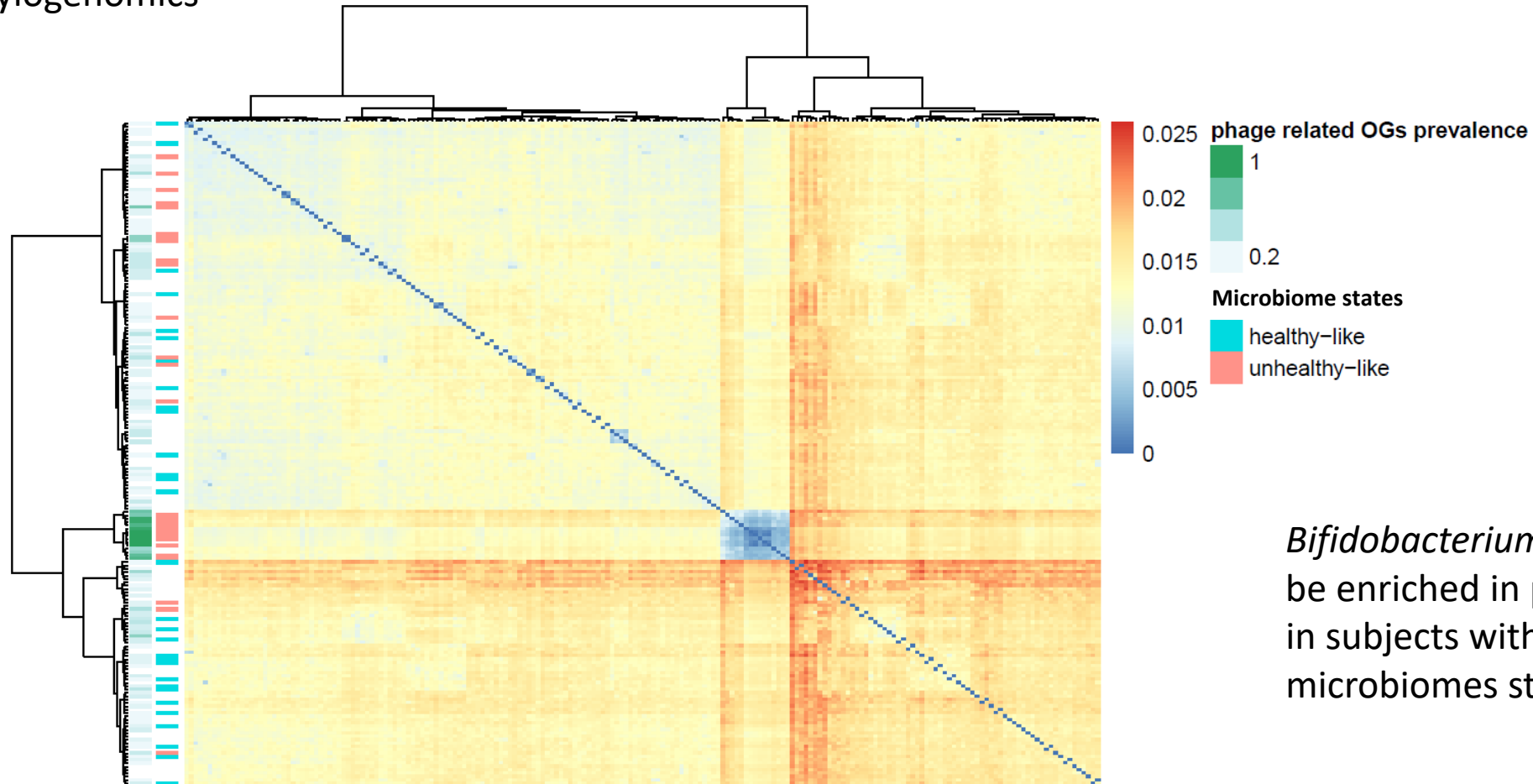


amino acid catabolism increase  
in *Bacteroides* branch tip

oxidative stress response increase  
in *Prevotella* branch tip

# ➤ Altered states showed functional differences within species

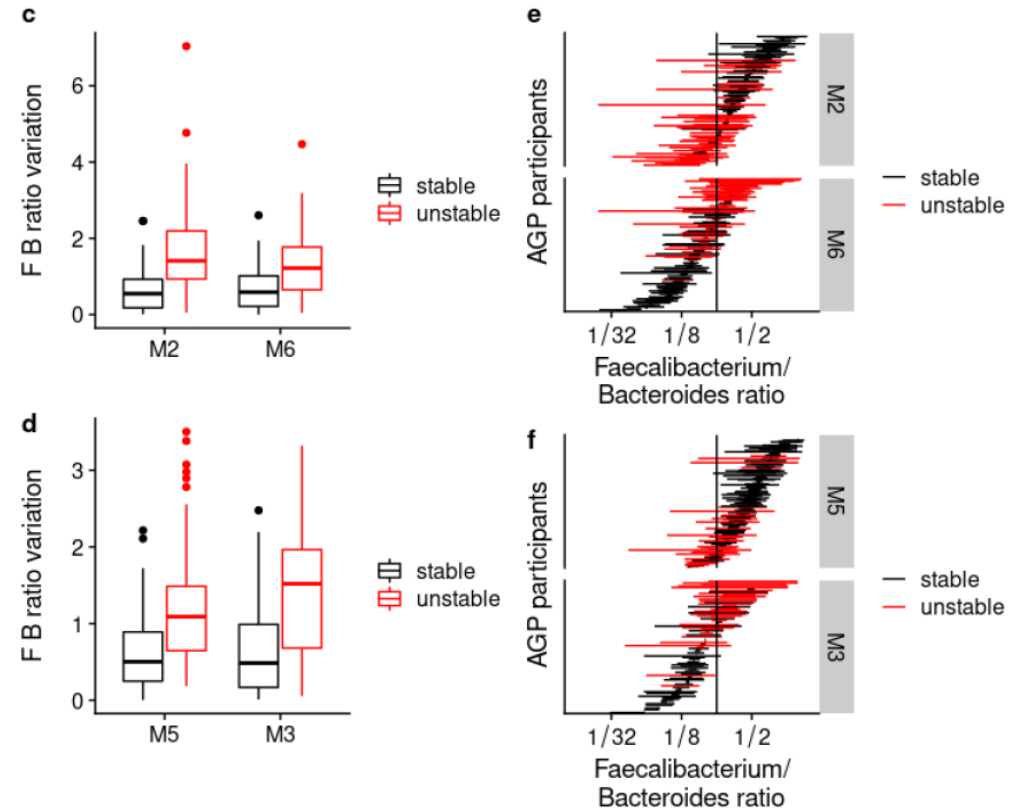
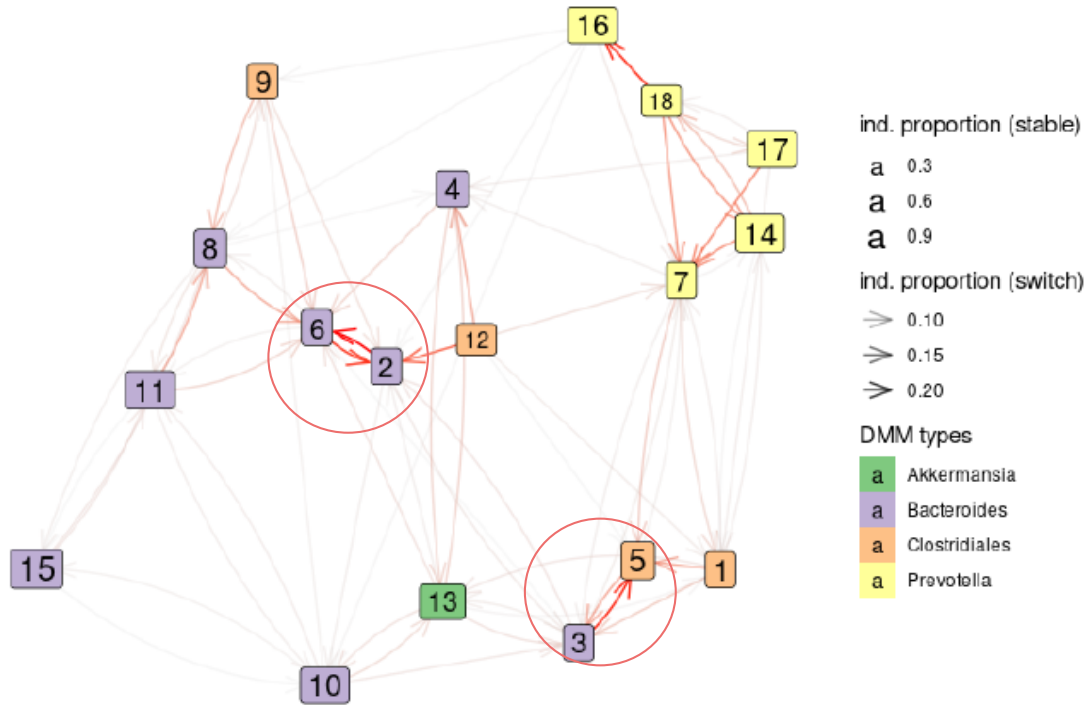
400 *B. bifidum* MAGS  
phylogenomics



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

# ➤ Dynamics between partitions are associated to branches

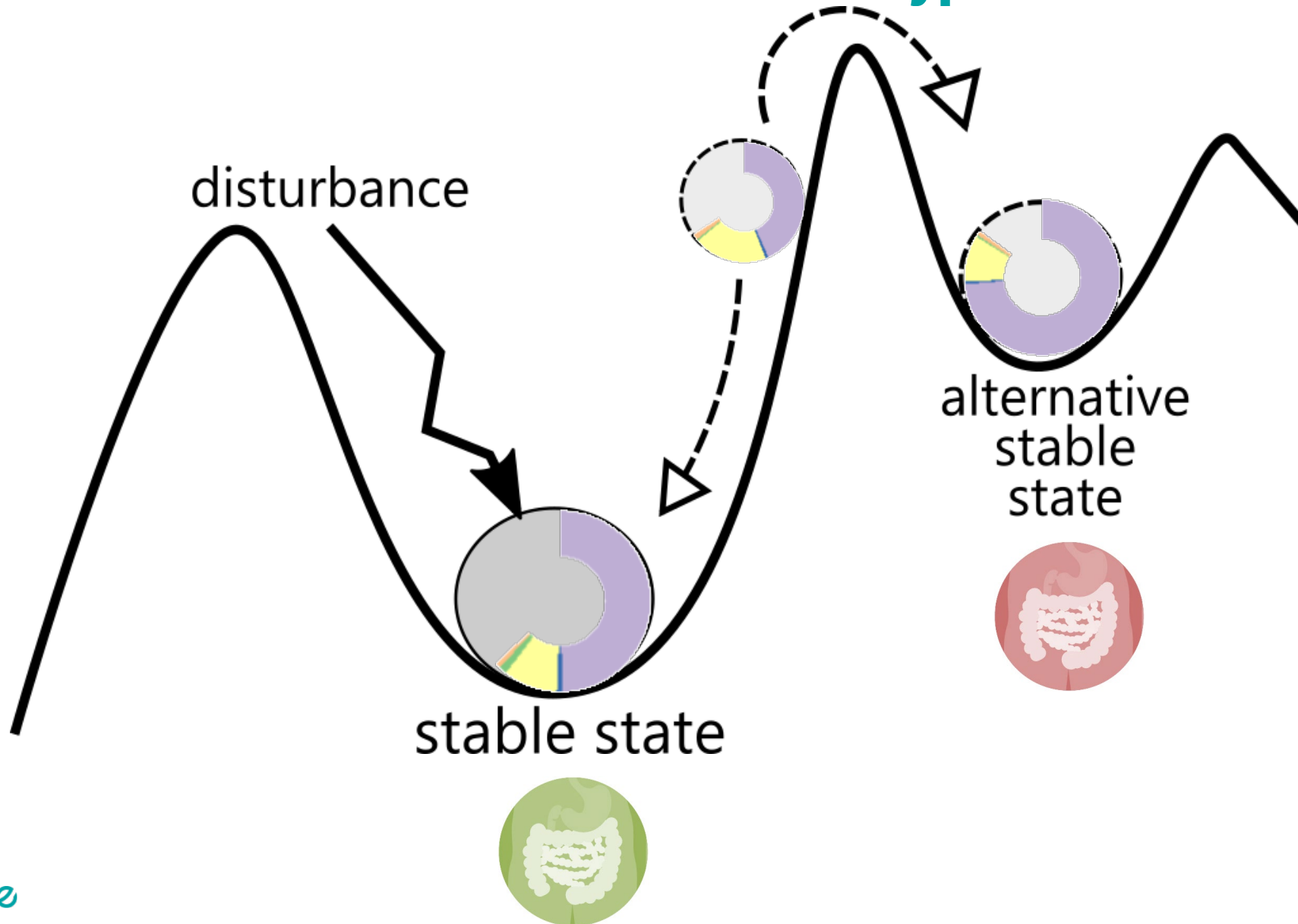
827 participants    2,998 samples    2,171 time-pairs



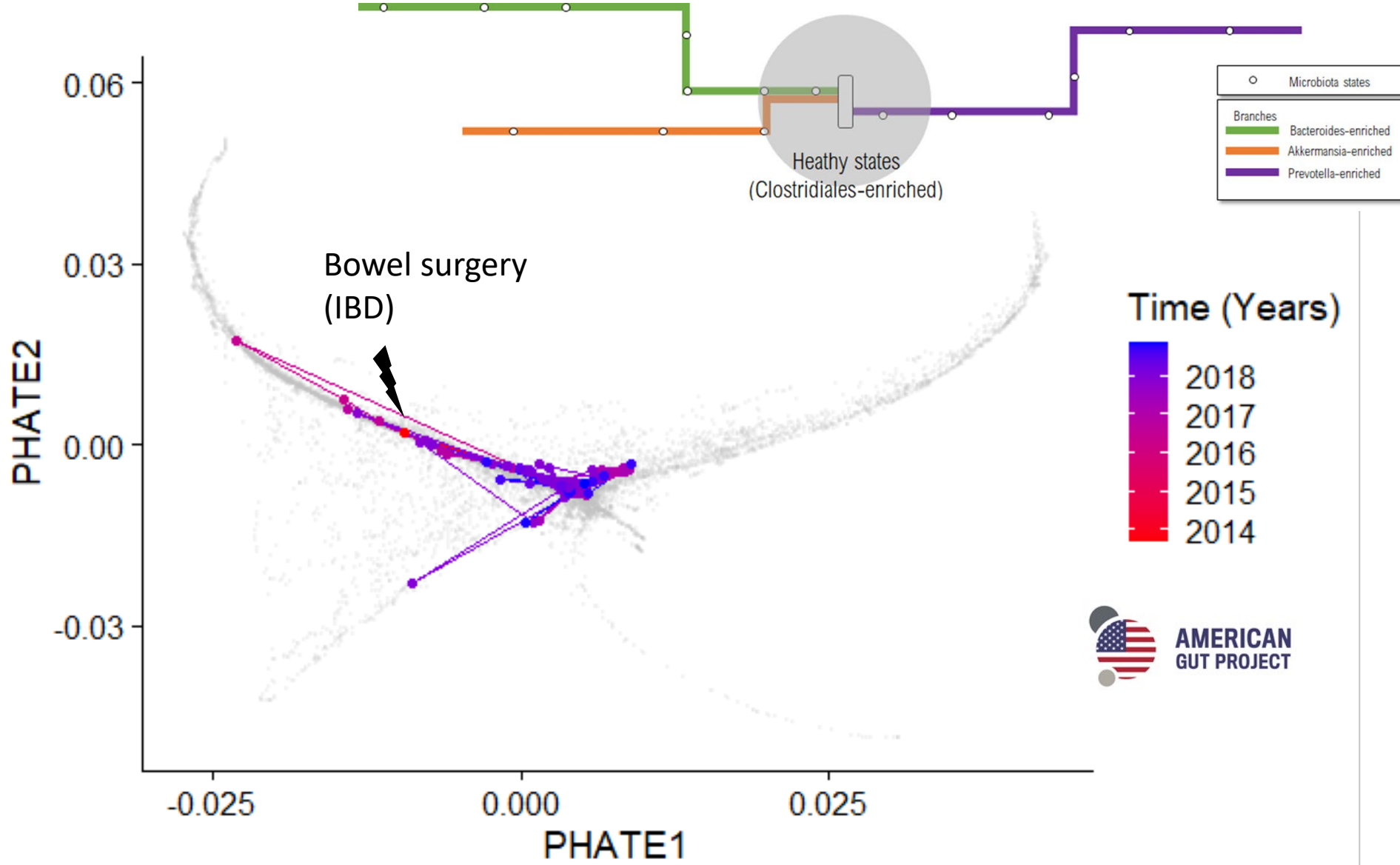
*Faecalibacterium/Bacteroides* as a tipping element explaining the switch between some states



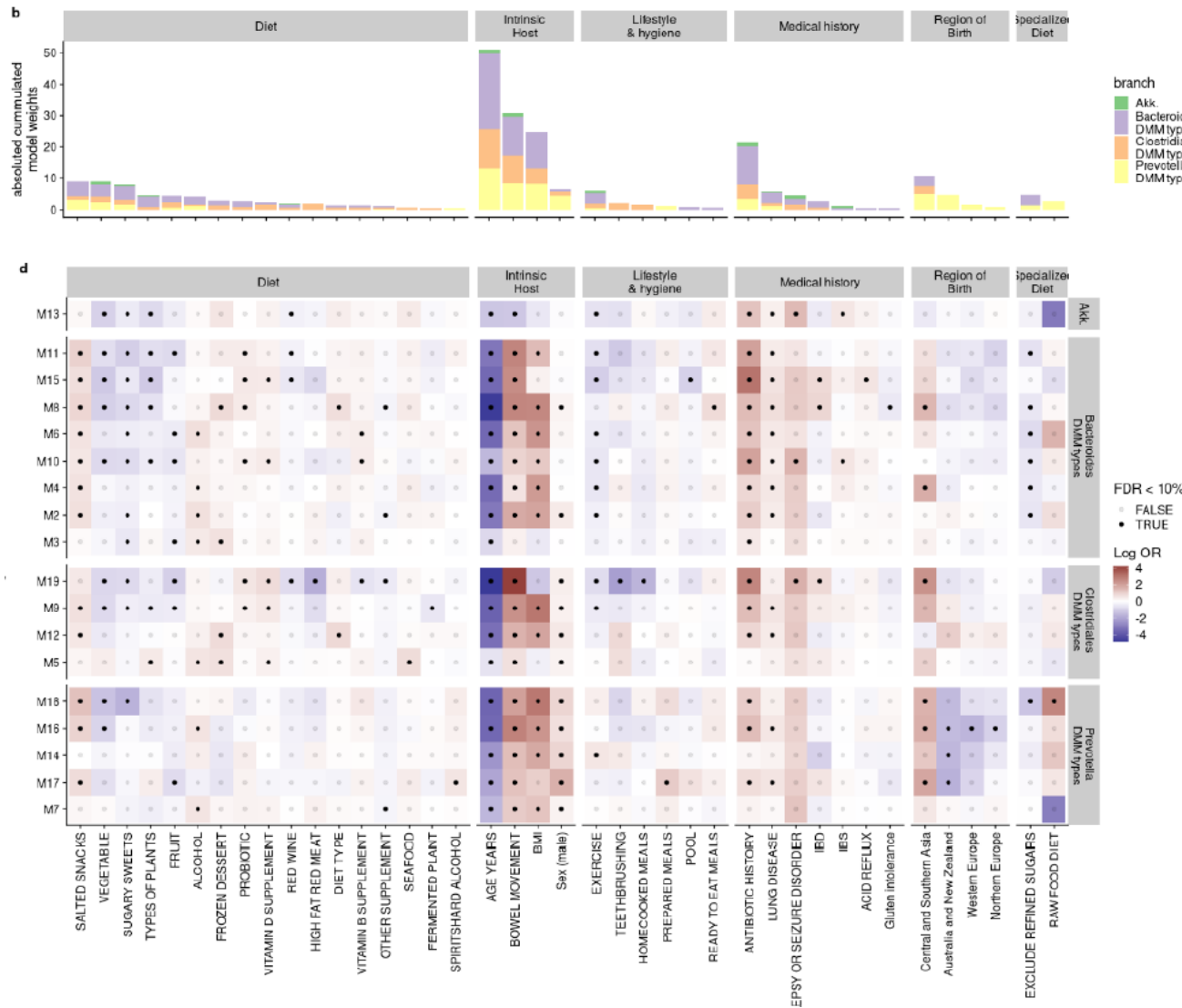
# > Gut microbiome alternative stable states hypothesis



# > Branches help to monitor gut microbiome recovery



# ➤ Gut microbiome states are differentially associated with host and env factors

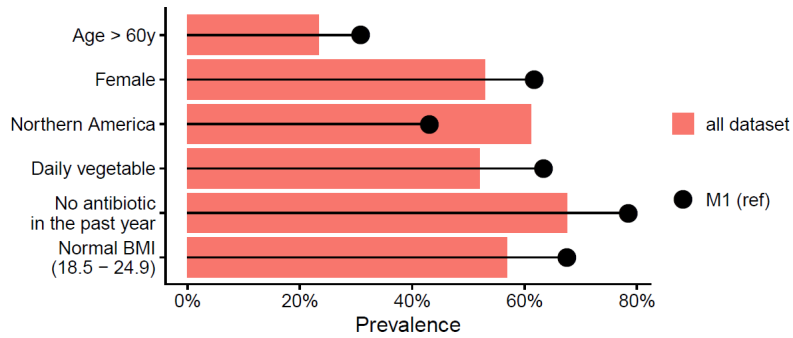


Sex, exercises frequency and **region of birth** associated differentially between branches

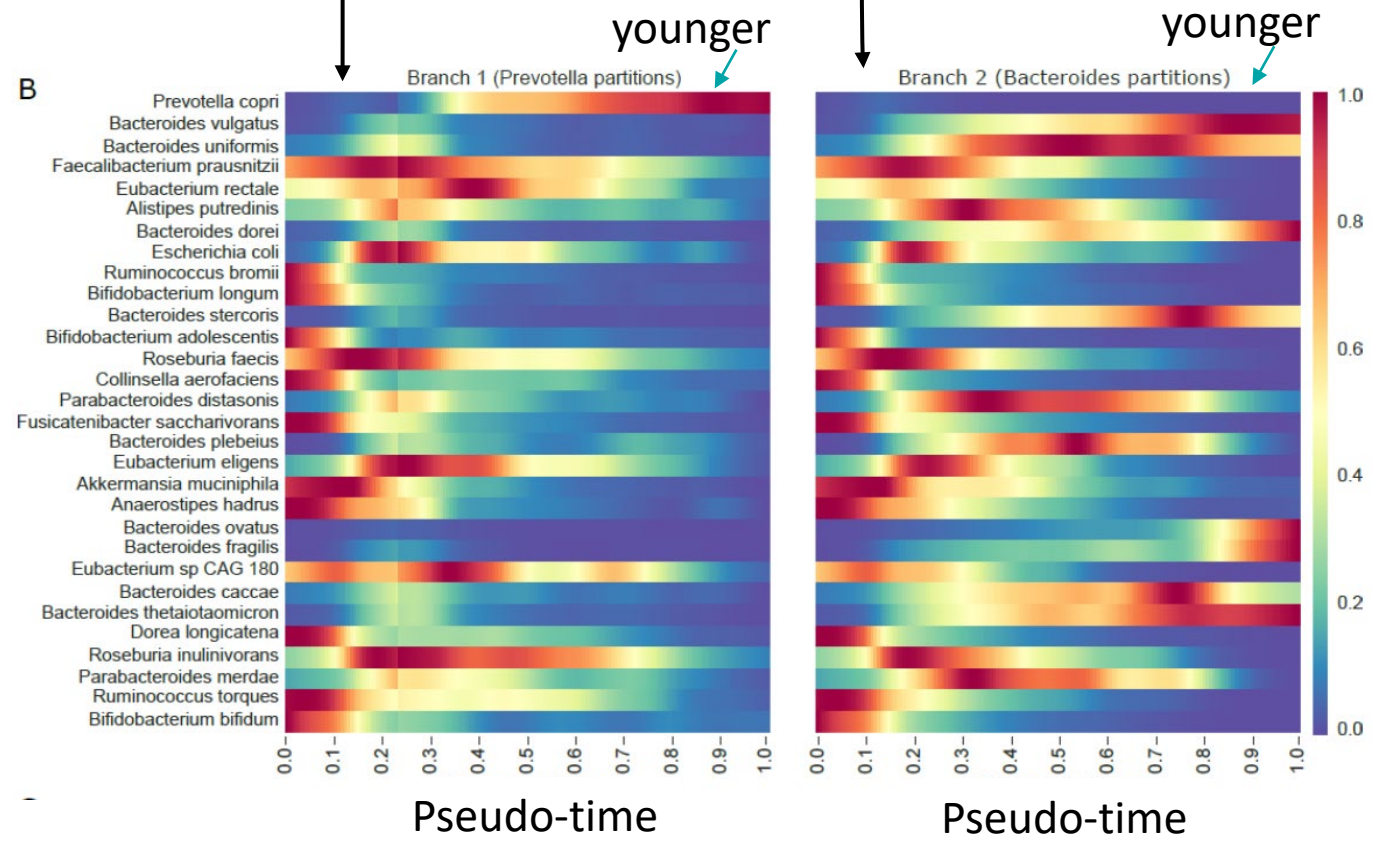
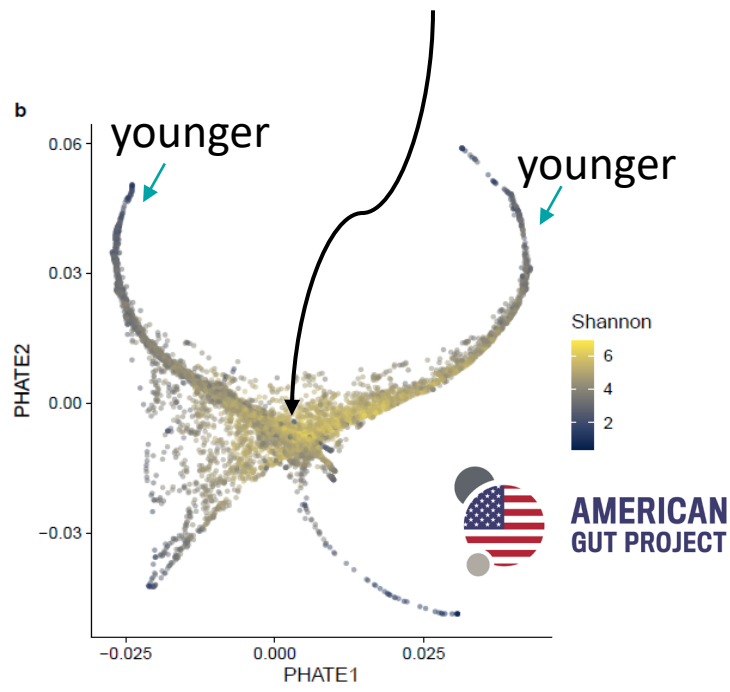
Lifestyle and hygiene associated with altered state within *Bacteroides* branch

Specialized diet associated with altered state within *Prevotella* branch

# > Do we already observe a intergenerationally mass extinction ?



Older and healthy diet and lifestyle

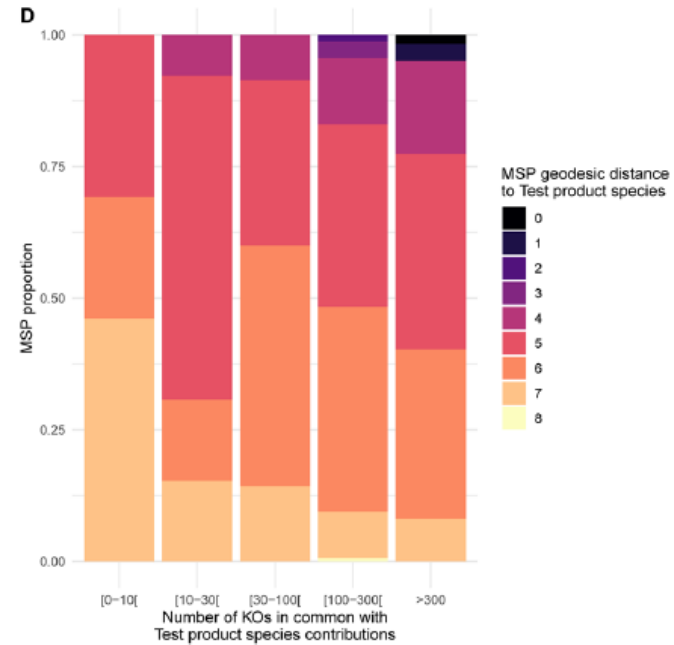
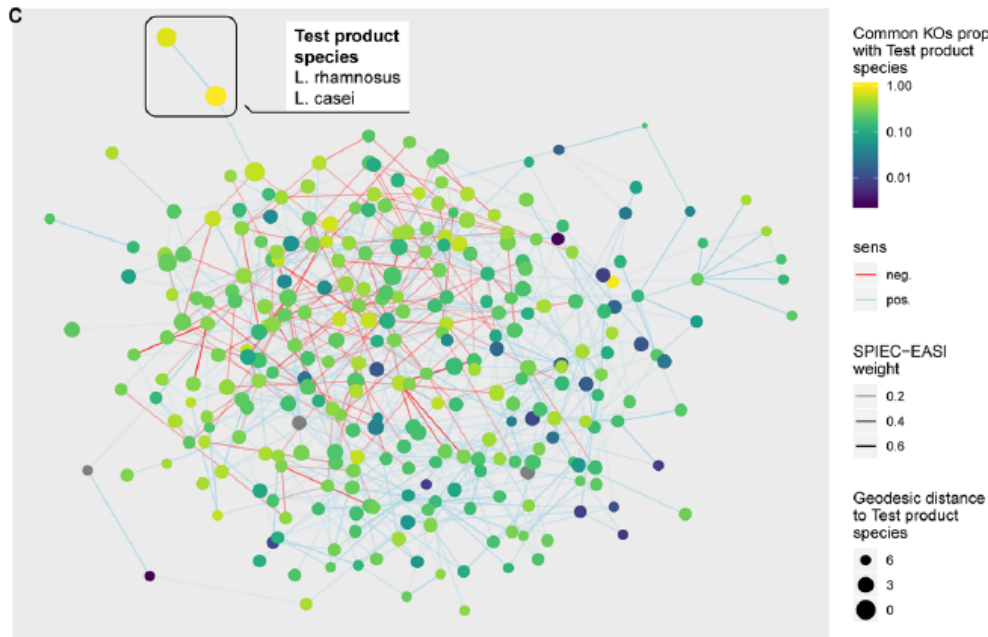


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# ➤ Probiotics engraftment are gut microbiome baseline dependent

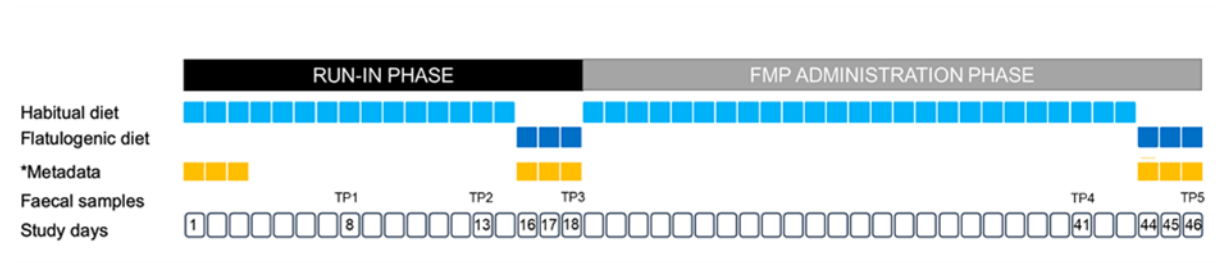
Modular coalescence between gut and biotics species



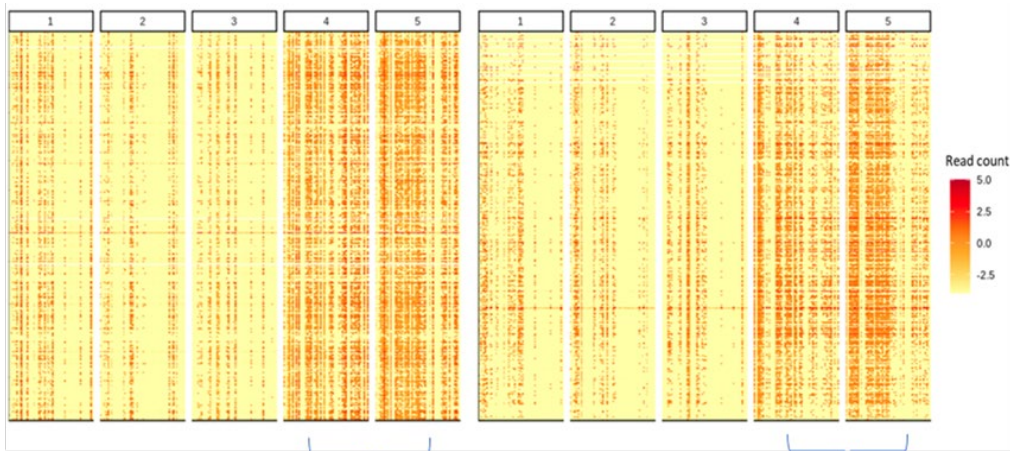
“Engraftment” as function of existing niche and metabolic pathway



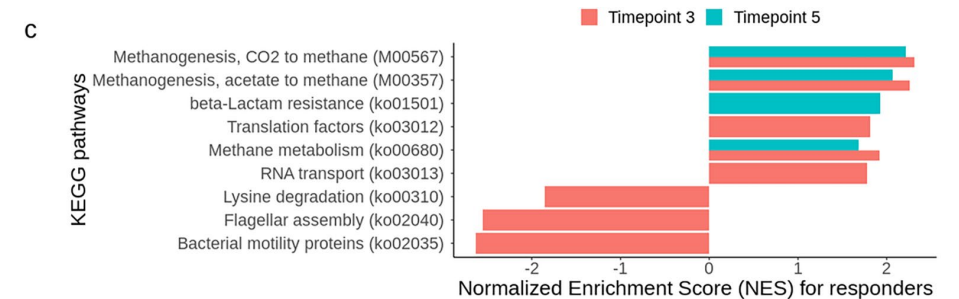
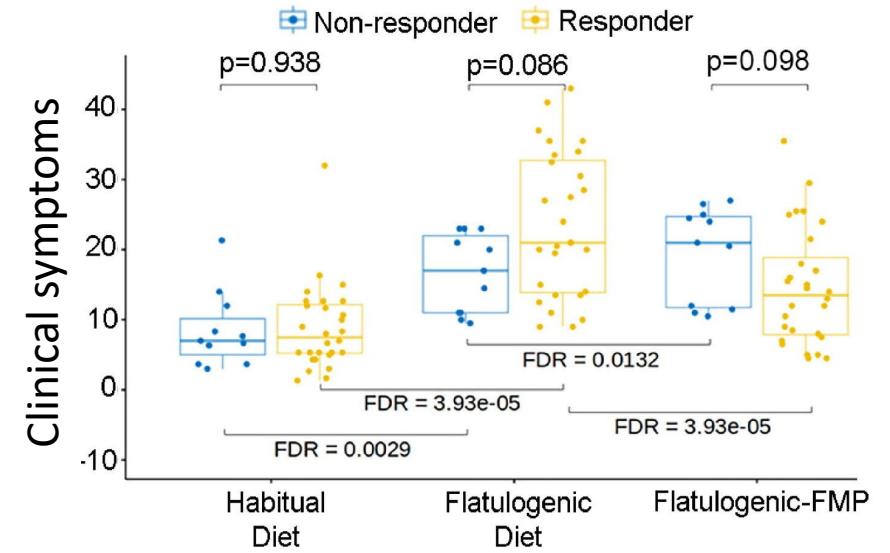
# ➤ Probiotics clinical effect is gut microbiome baseline dependent



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



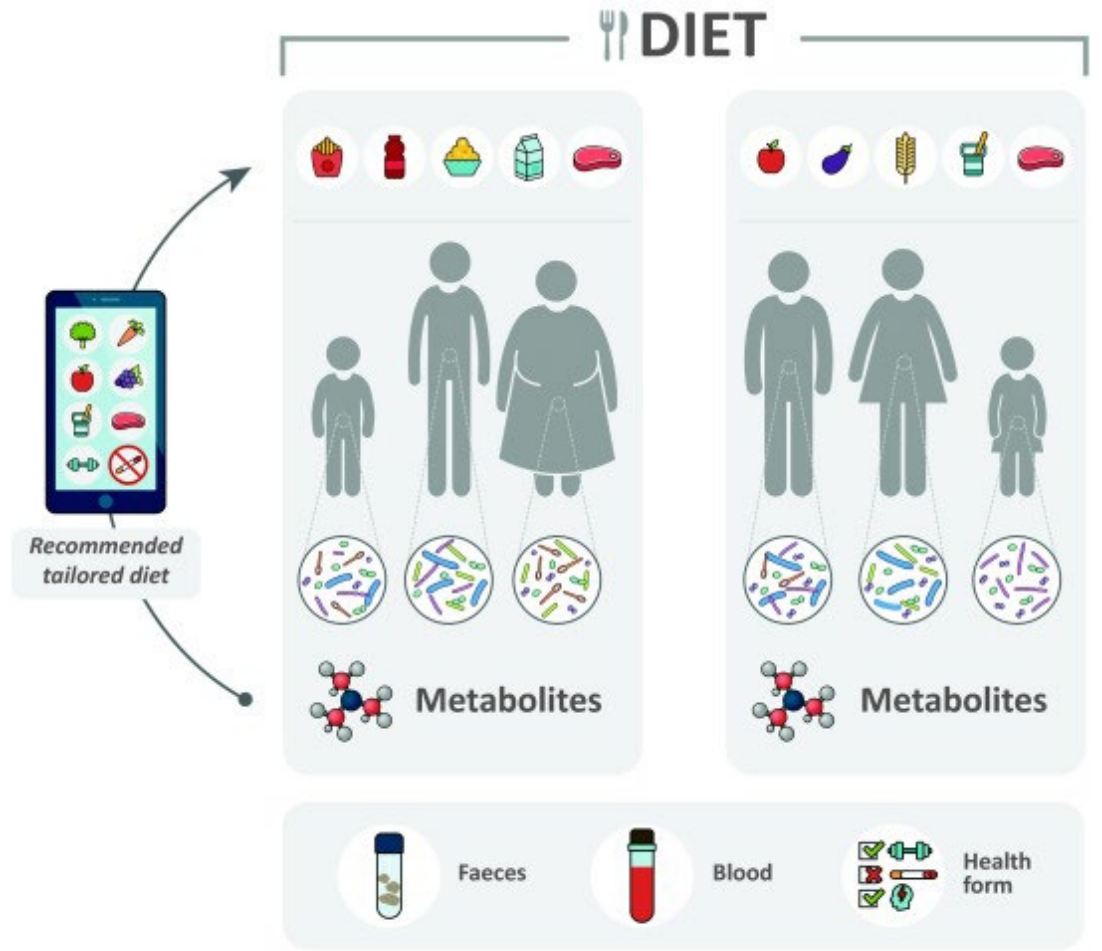
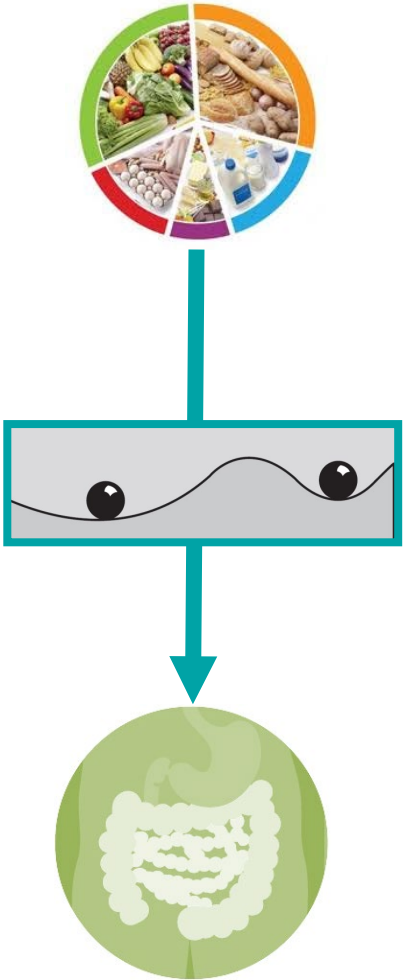
After FMP consumption, FMP active strains detected by metatranscriptomics



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



# > Endgame : From gut microbiome states to next-gen biotics



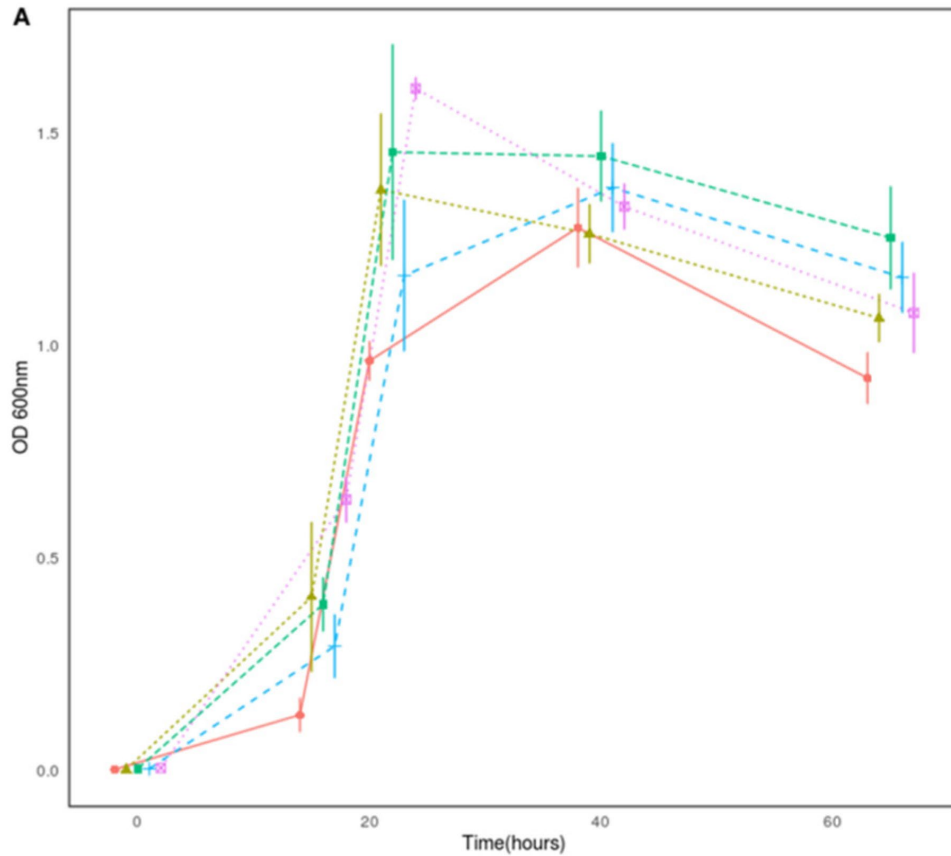
Trends in Microbiology

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



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



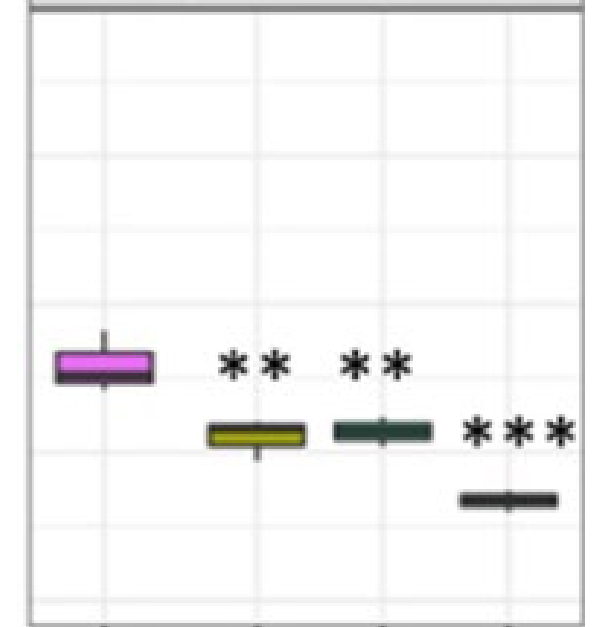
umax



F.prau

F.Prau  
+ LABs lysate

Decay slope



F.prau

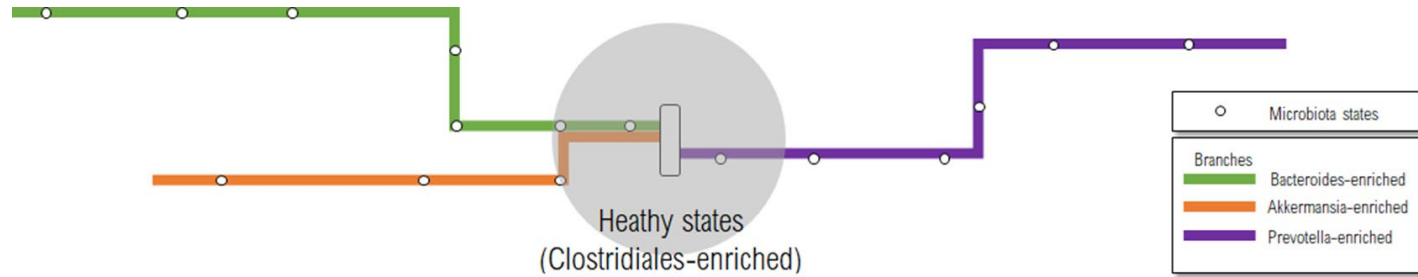
F.Prau  
+ LABs lysate

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

Lebas, Derrien and colleagues (2020)



## > Take home messages



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

## > Acknowledgments



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...



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