



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

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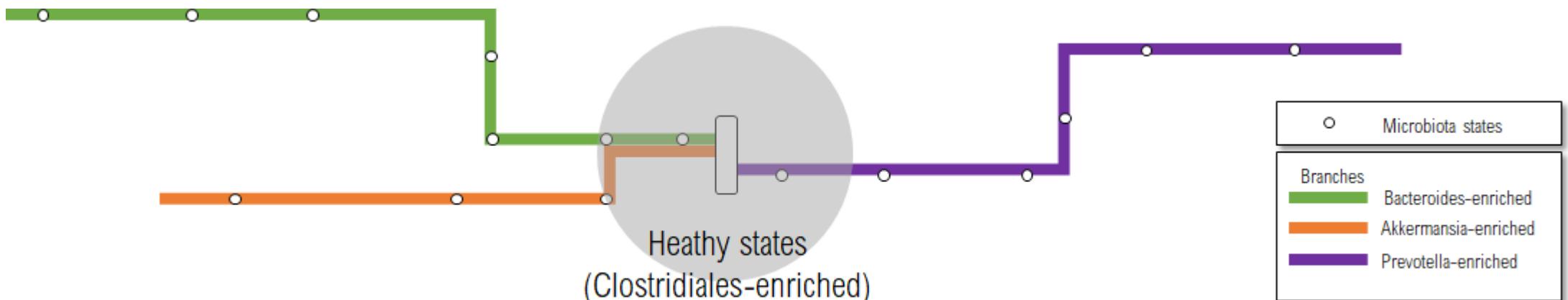
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# > Branches and ecological states of the gut microbiome: Mapping for future personalized nutritional and therapeutic interventions

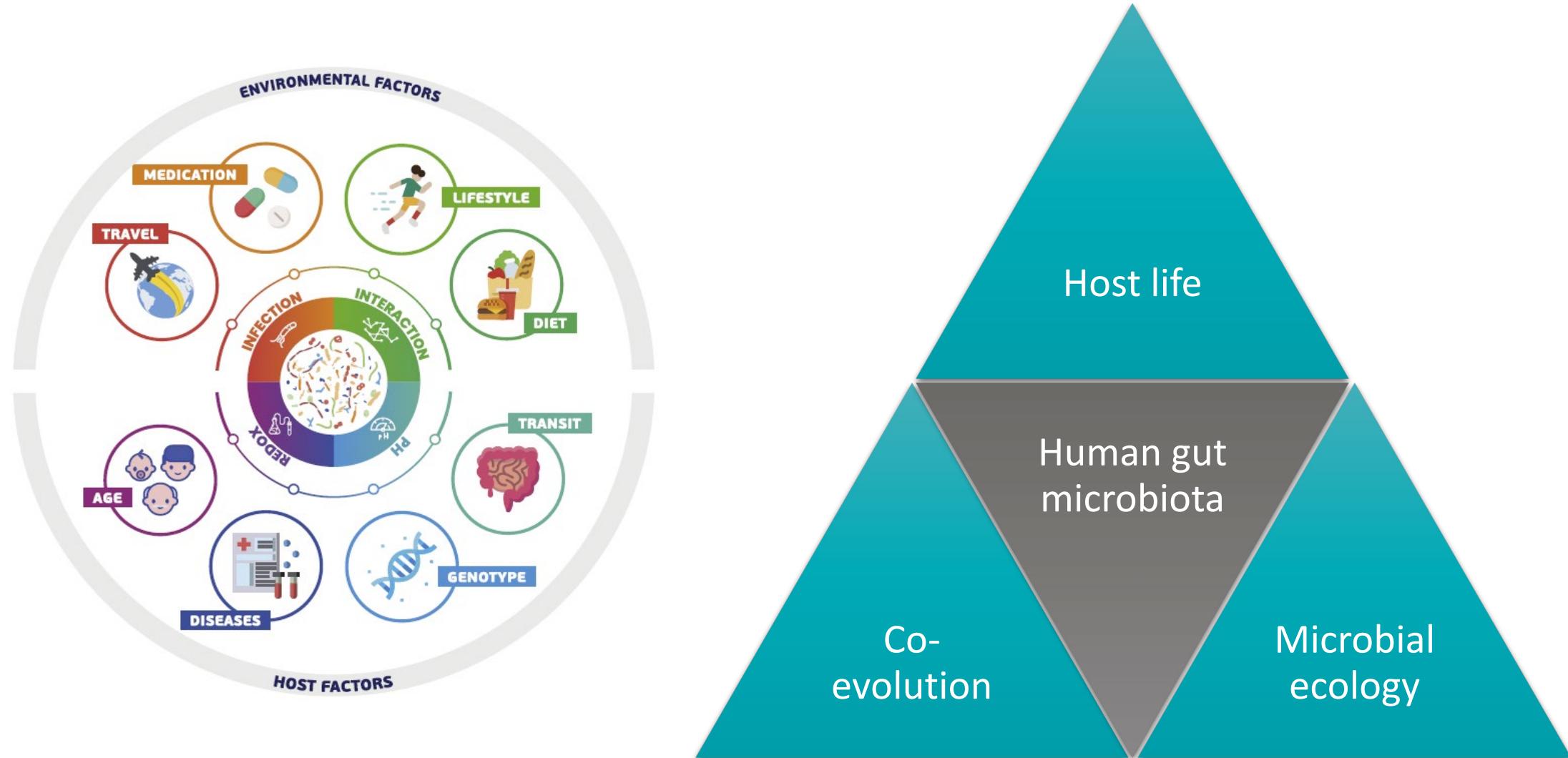
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Journées Polepharma de Microbiomique- Rouen 2023

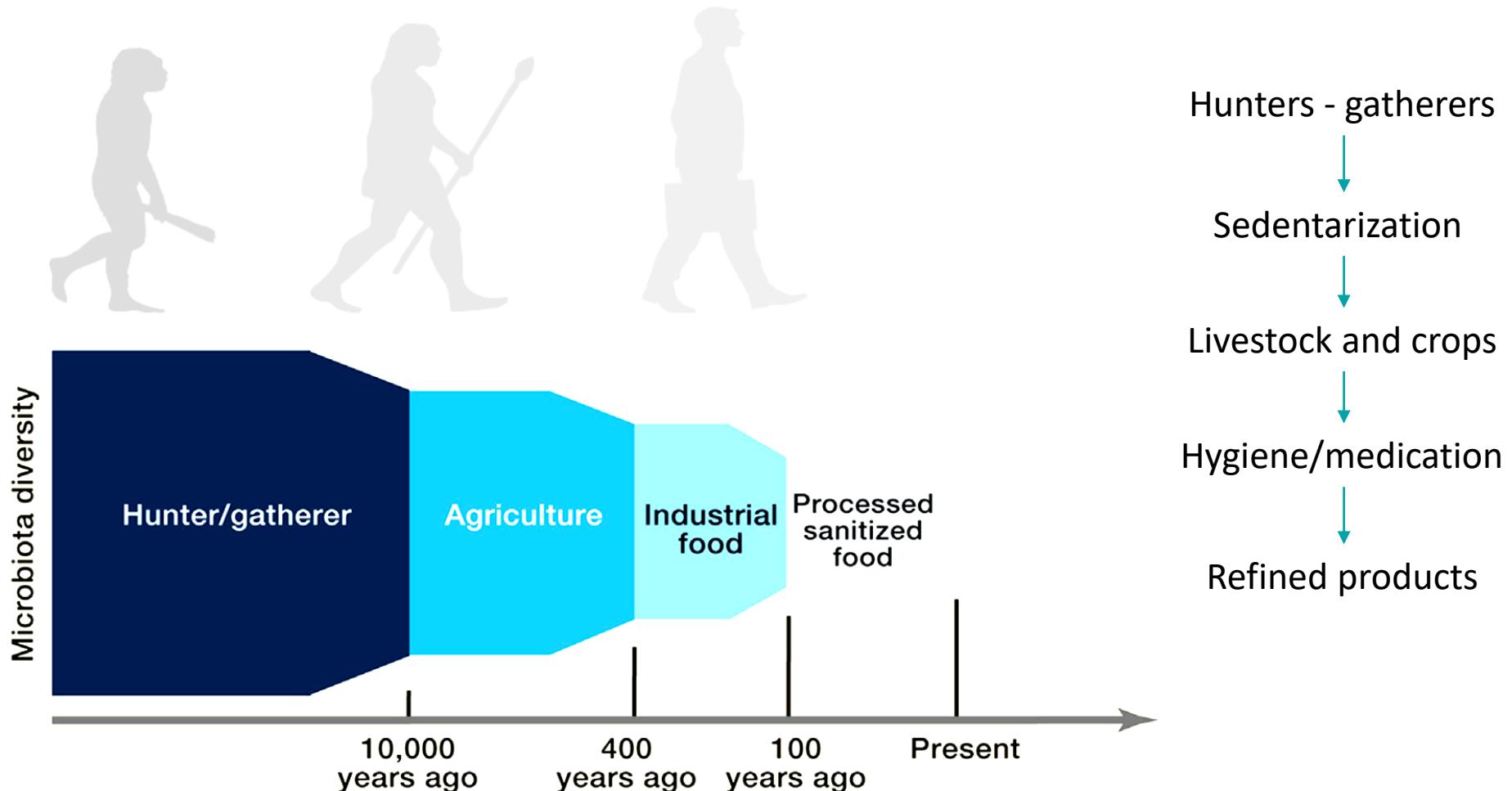


## > Different factors shapes the human gut microbiome



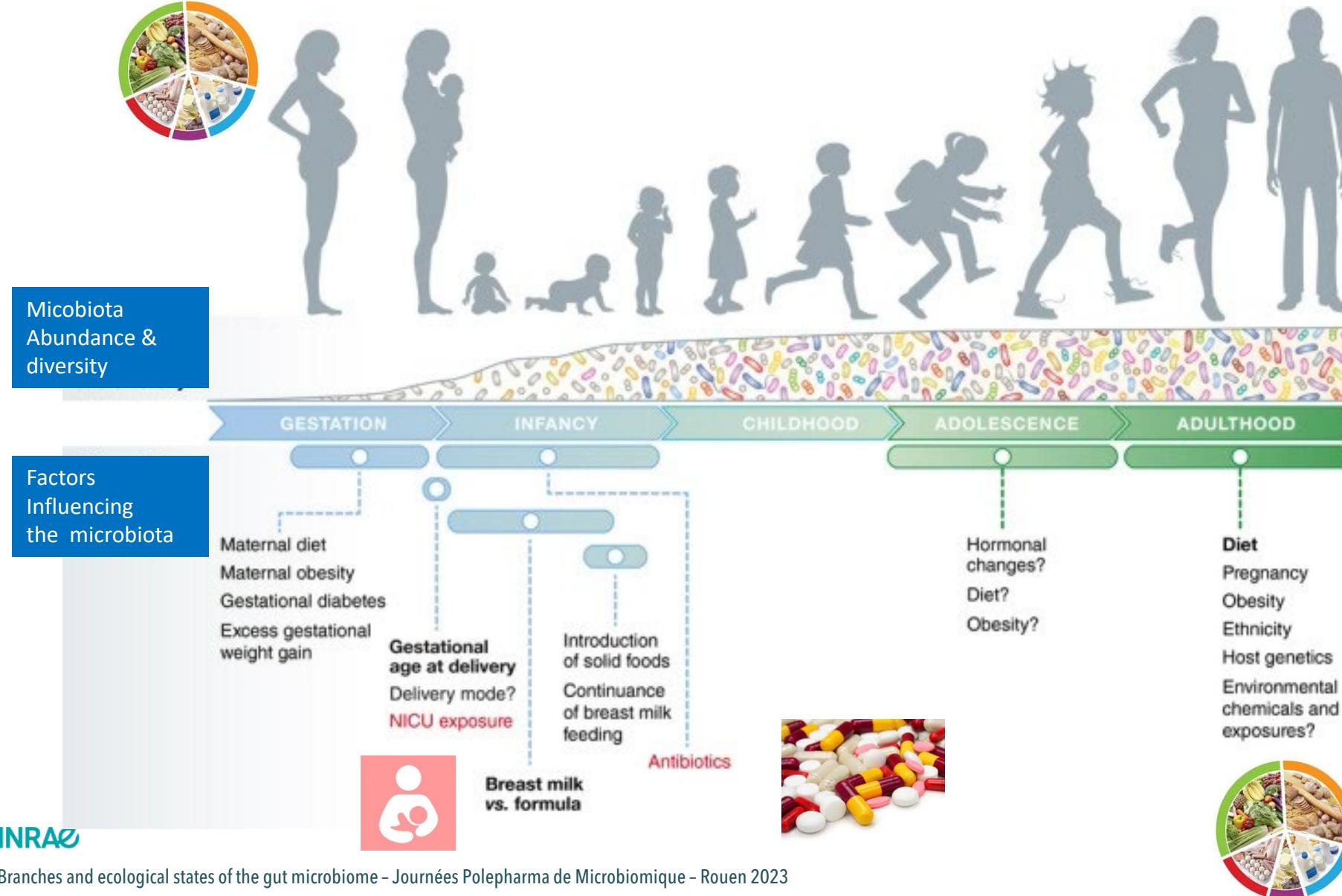
# > Diet and lifestyle effect host microbiome symbiosis

Are we uncoupling our metagenome and our genome?



# > Gut microbiome throughout life span

4



# > Microbiome states resilience as key factor



Healthy state



Resistance



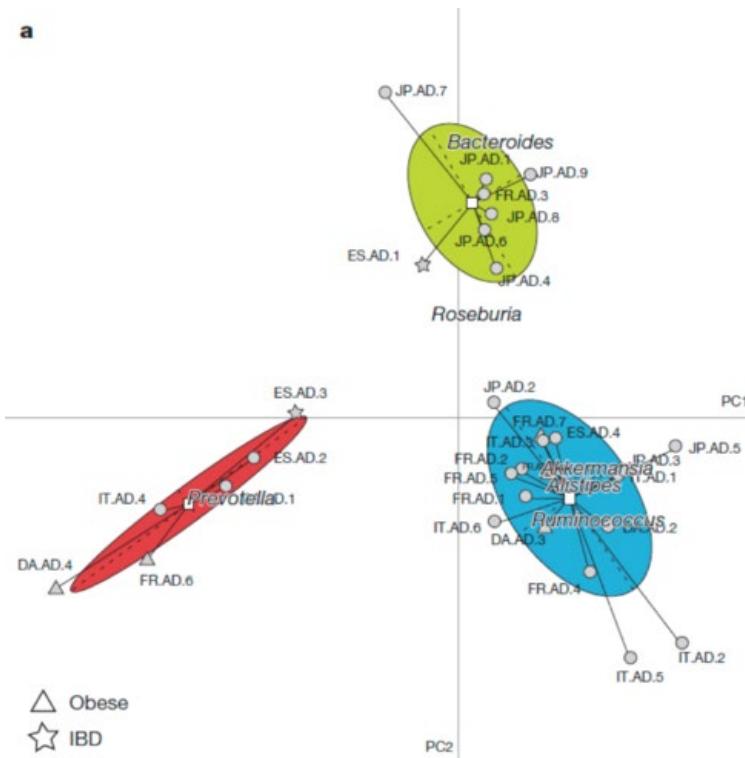
Recovery

Resilience

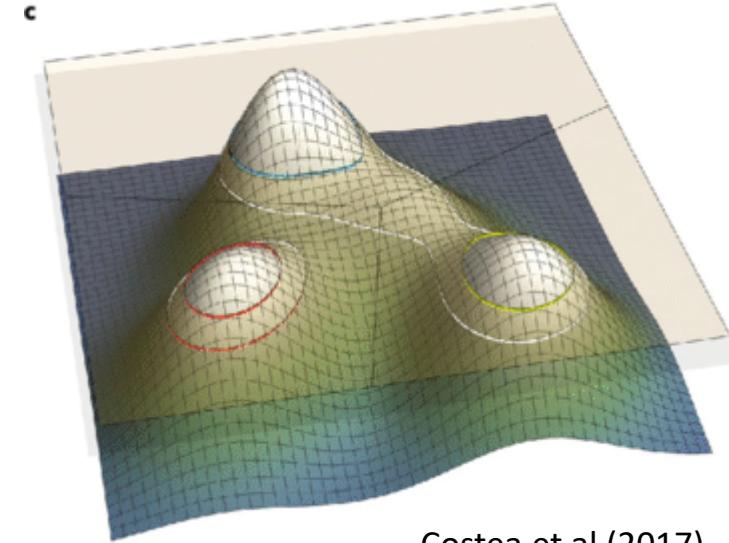


Degraded state

## > Several attempts to decipher the microbiome structure



Arumugam, Raes et al (2010)



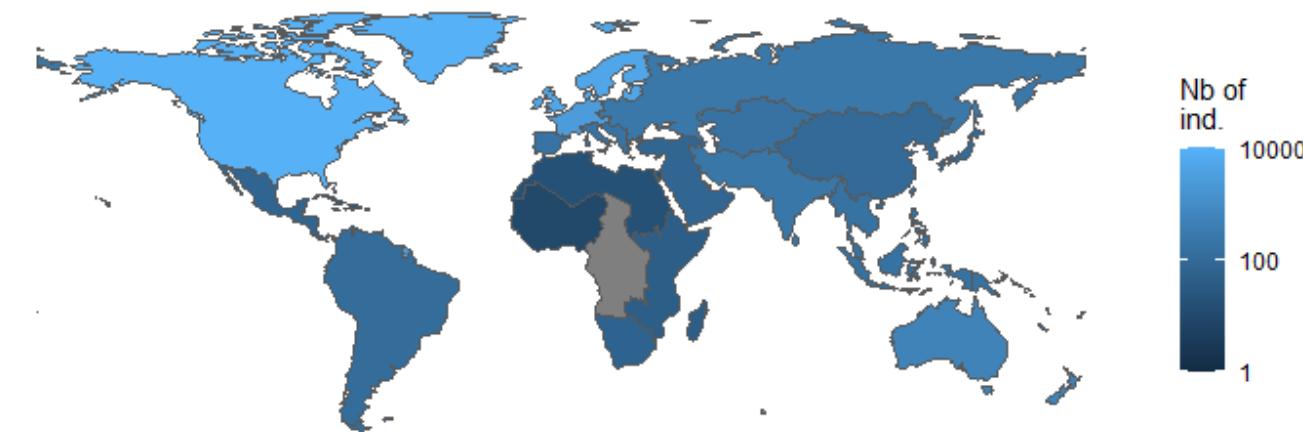
Dirichlet Multinomial Mixture (DMM) modeling

Limits:

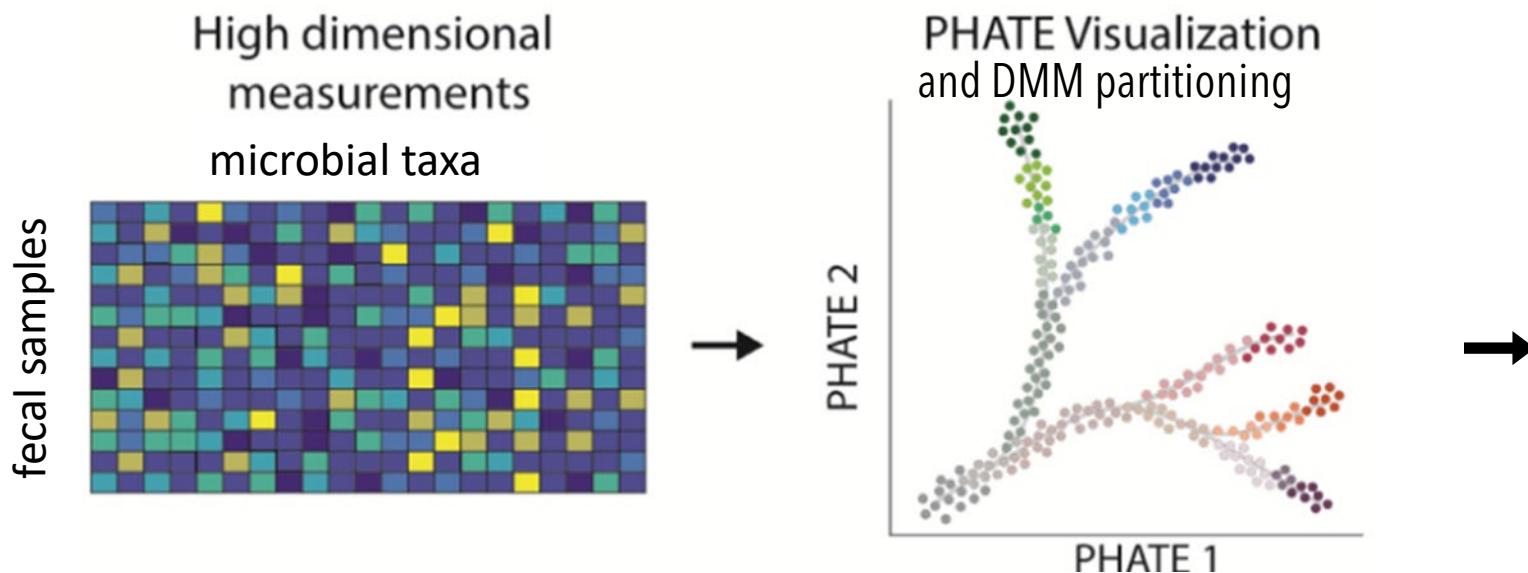
Few association with diet

Few stability assessment (e.g. with time-series)

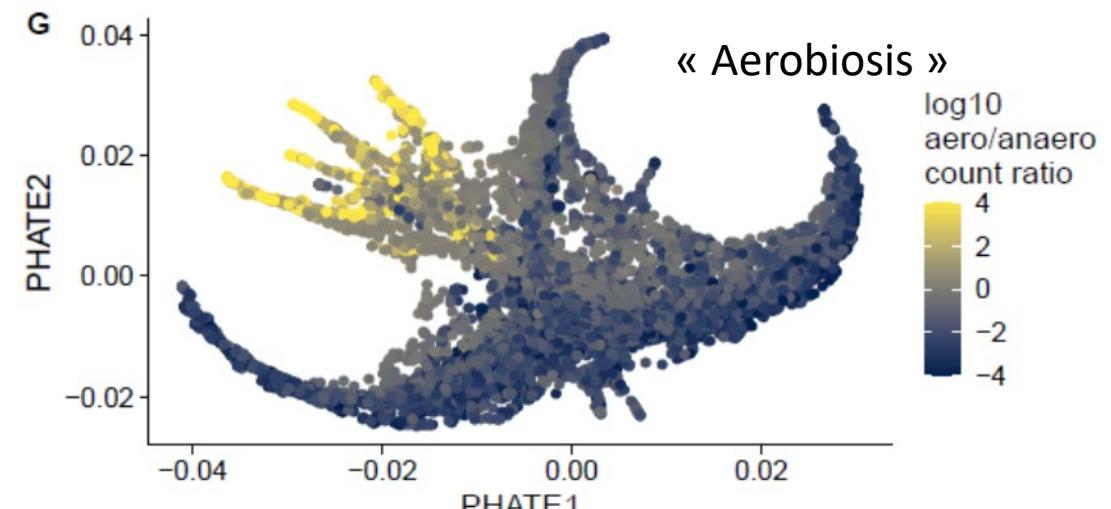
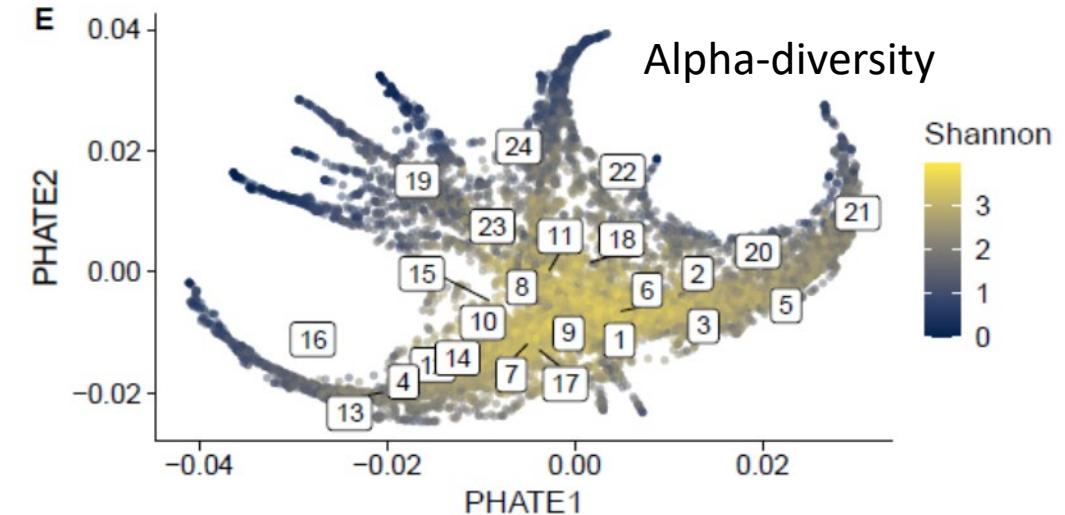
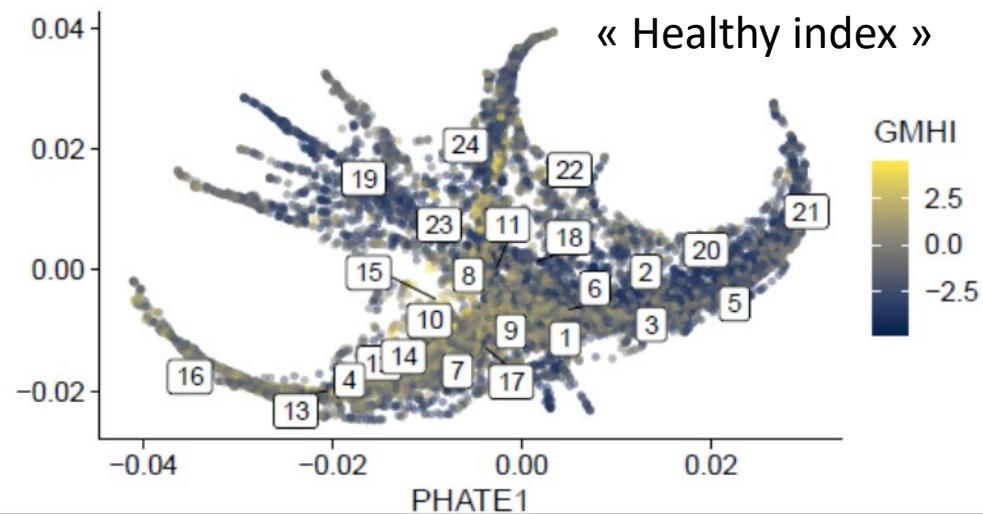
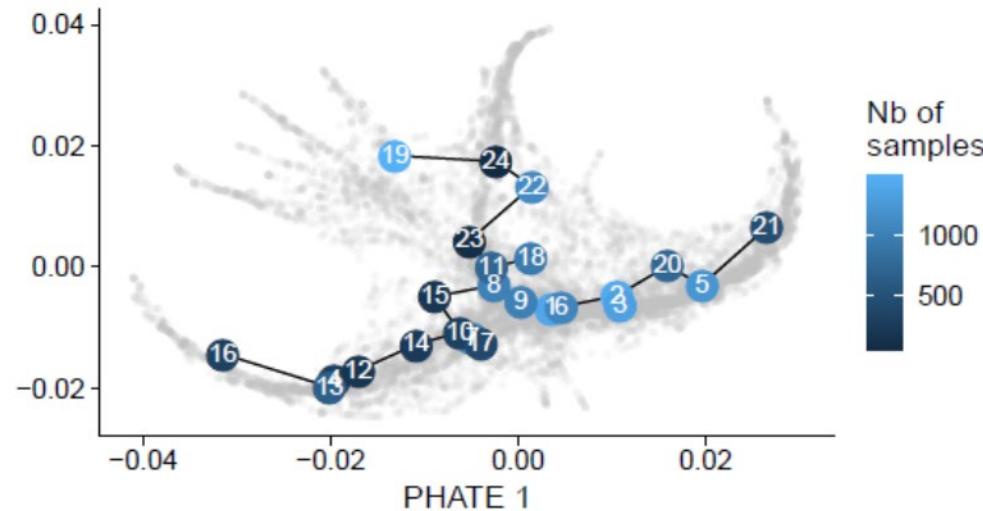
# > 35,000 human gut microbiome samples analyzed



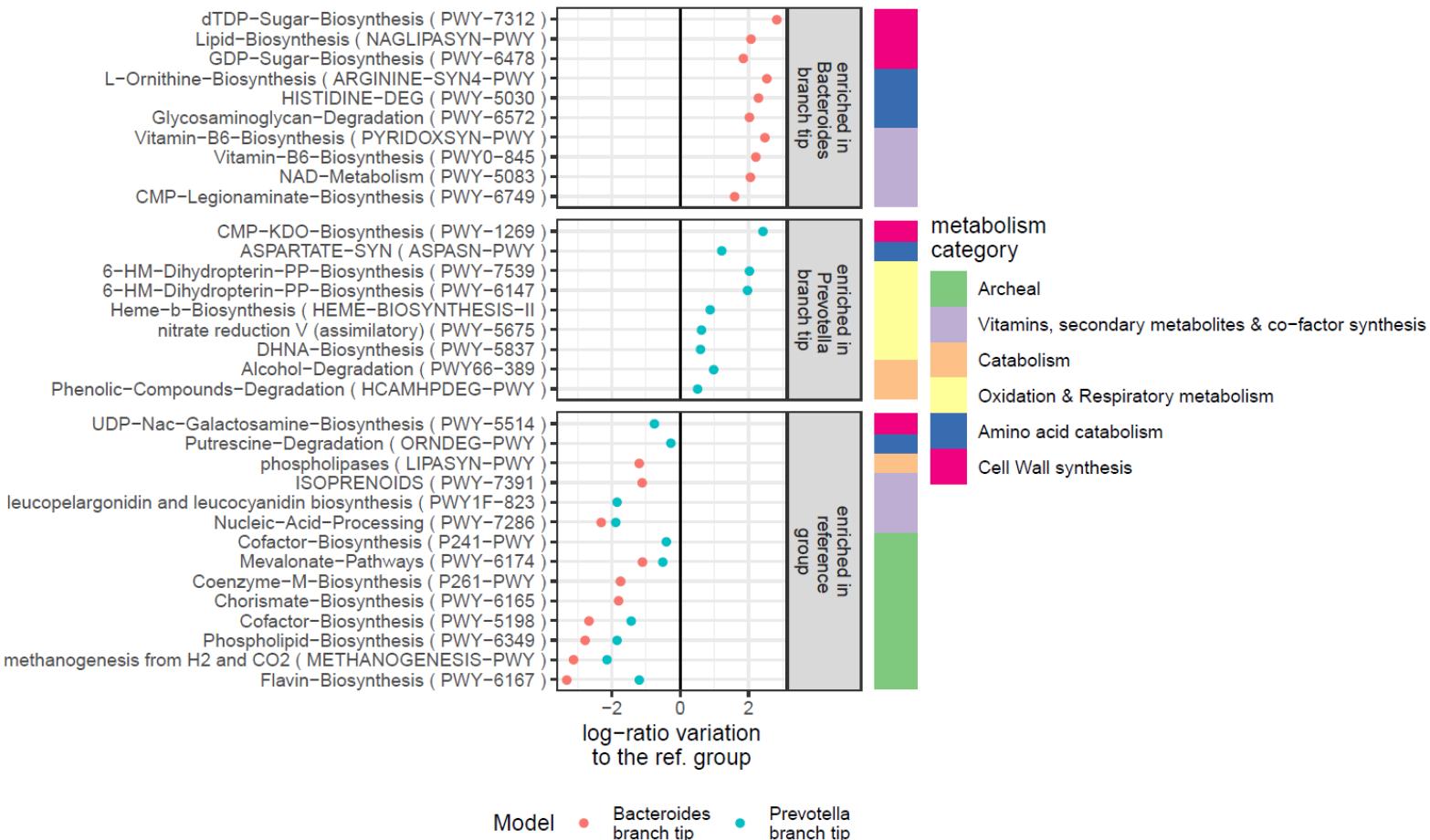
New computational method that help observe **global and local structure** at the same time



# > Human Gut microbiome structured as branches



# > Low-diversity tips of branches display functional shifts

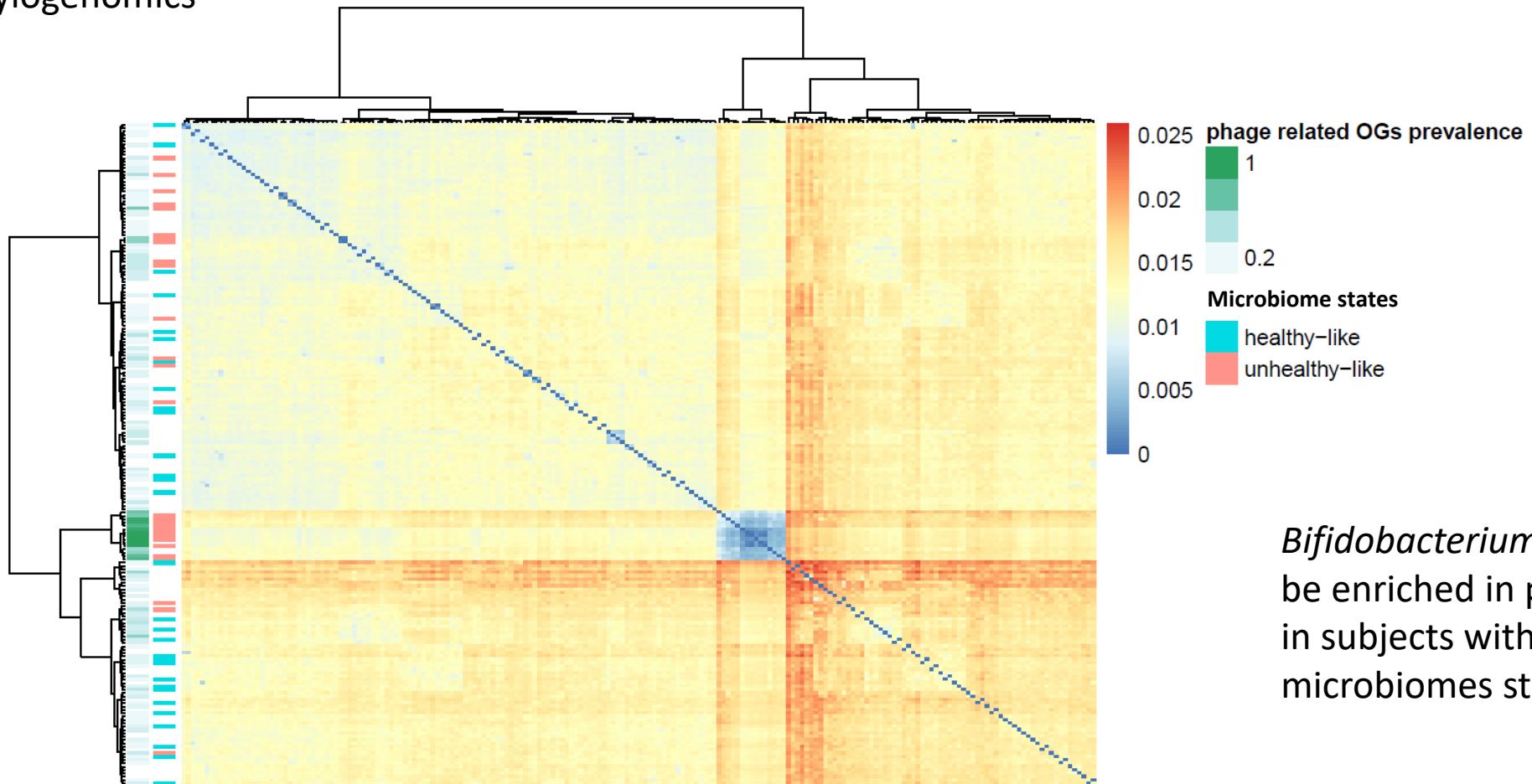


amino acid catabolism increase  
in *Bacteroides* branch tip

oxidative stress response increase  
in *Prevotella* branch tip

# > Altered states showed functional differences within species

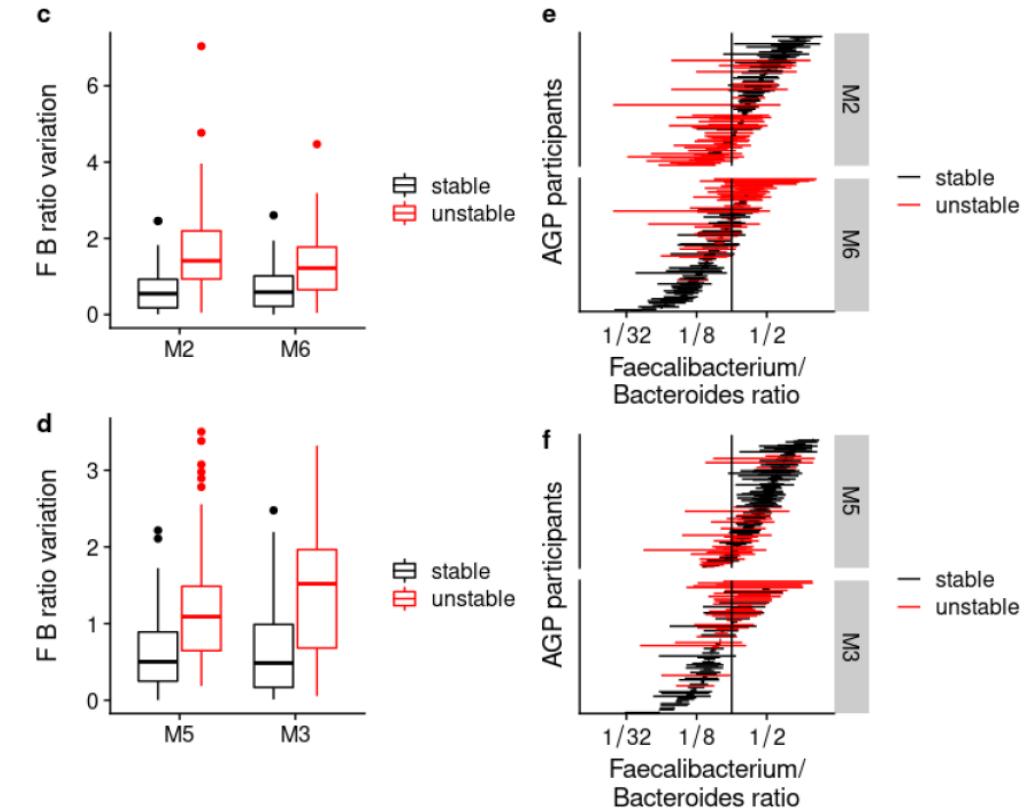
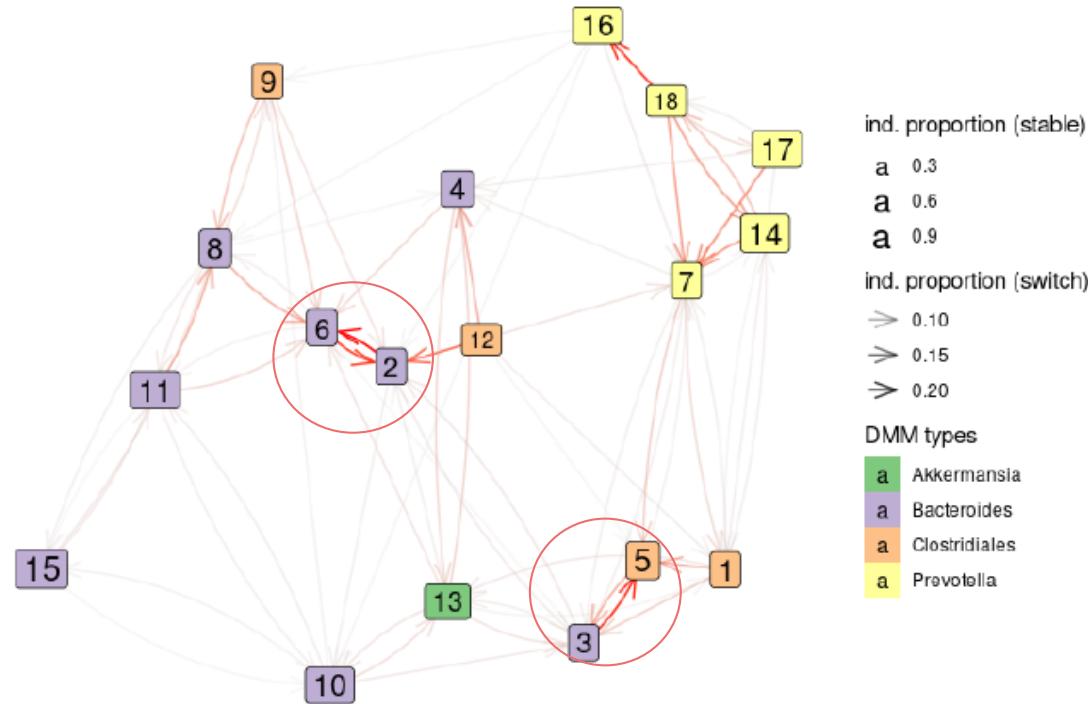
400 *B. bifidum* MAGS  
phylogenomics



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

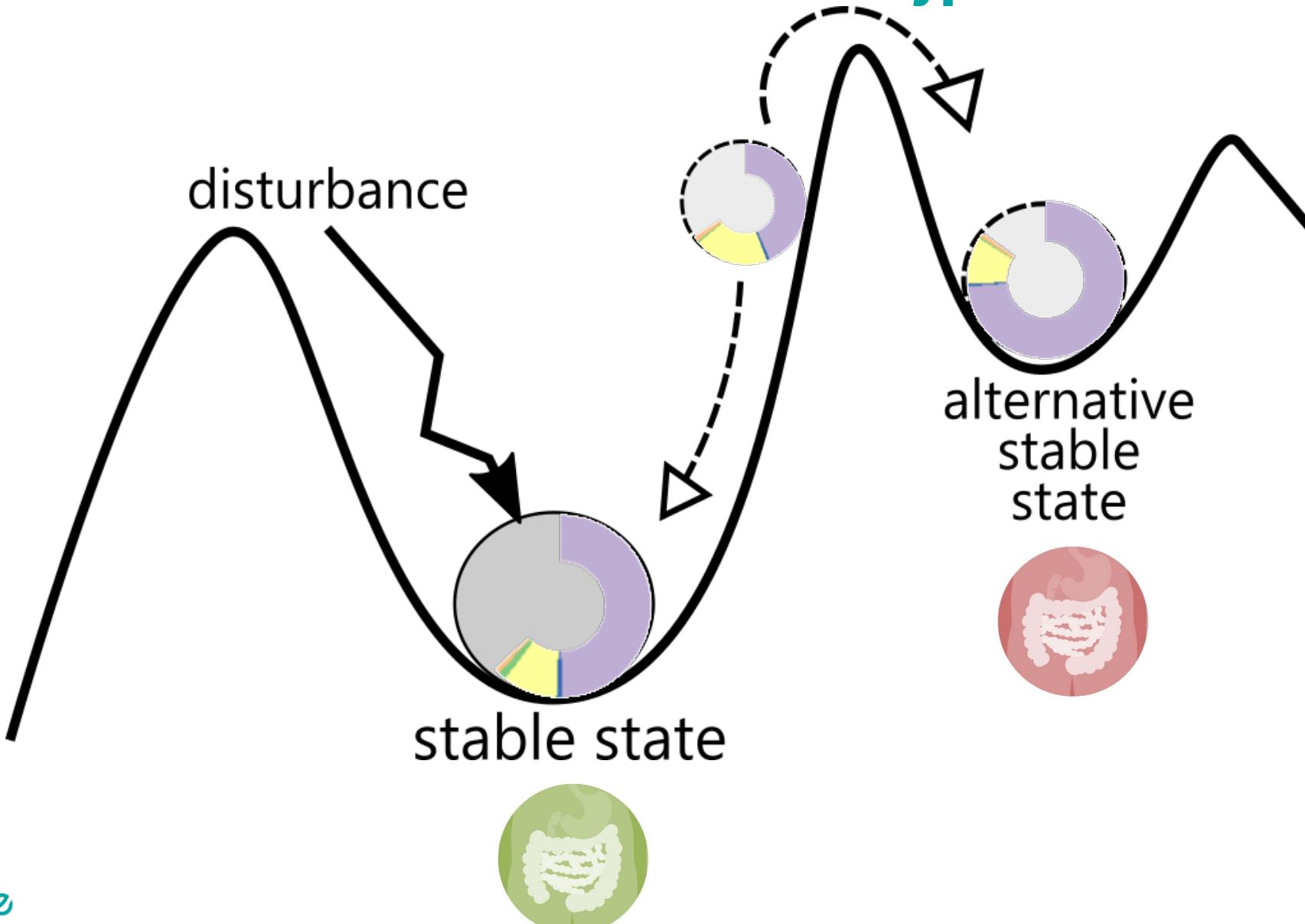
# > Dynamics between partitions are associated to branches

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

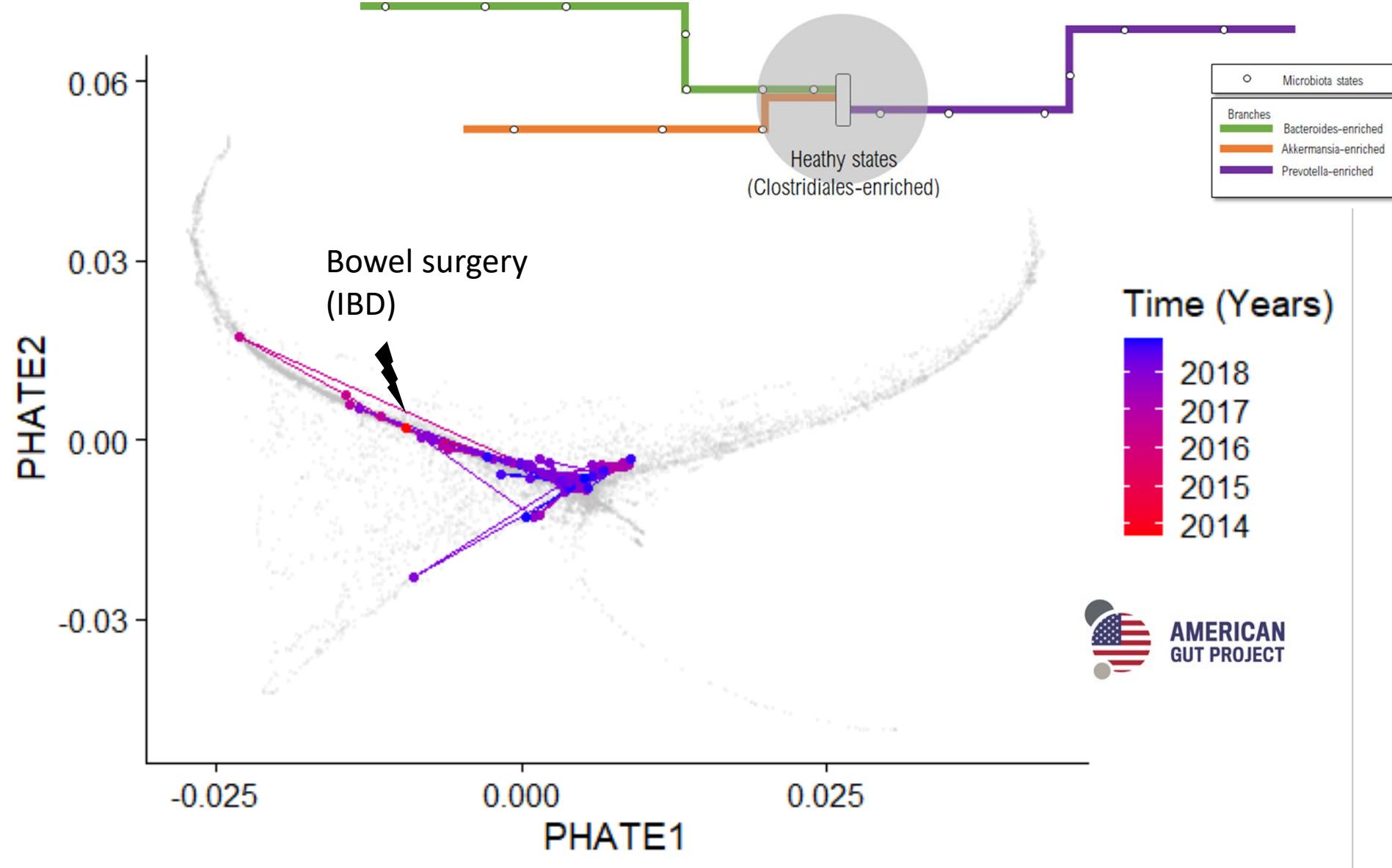


*Feecalibacterium/Bacteroides* as a tipping element  
explaining the switch between some states

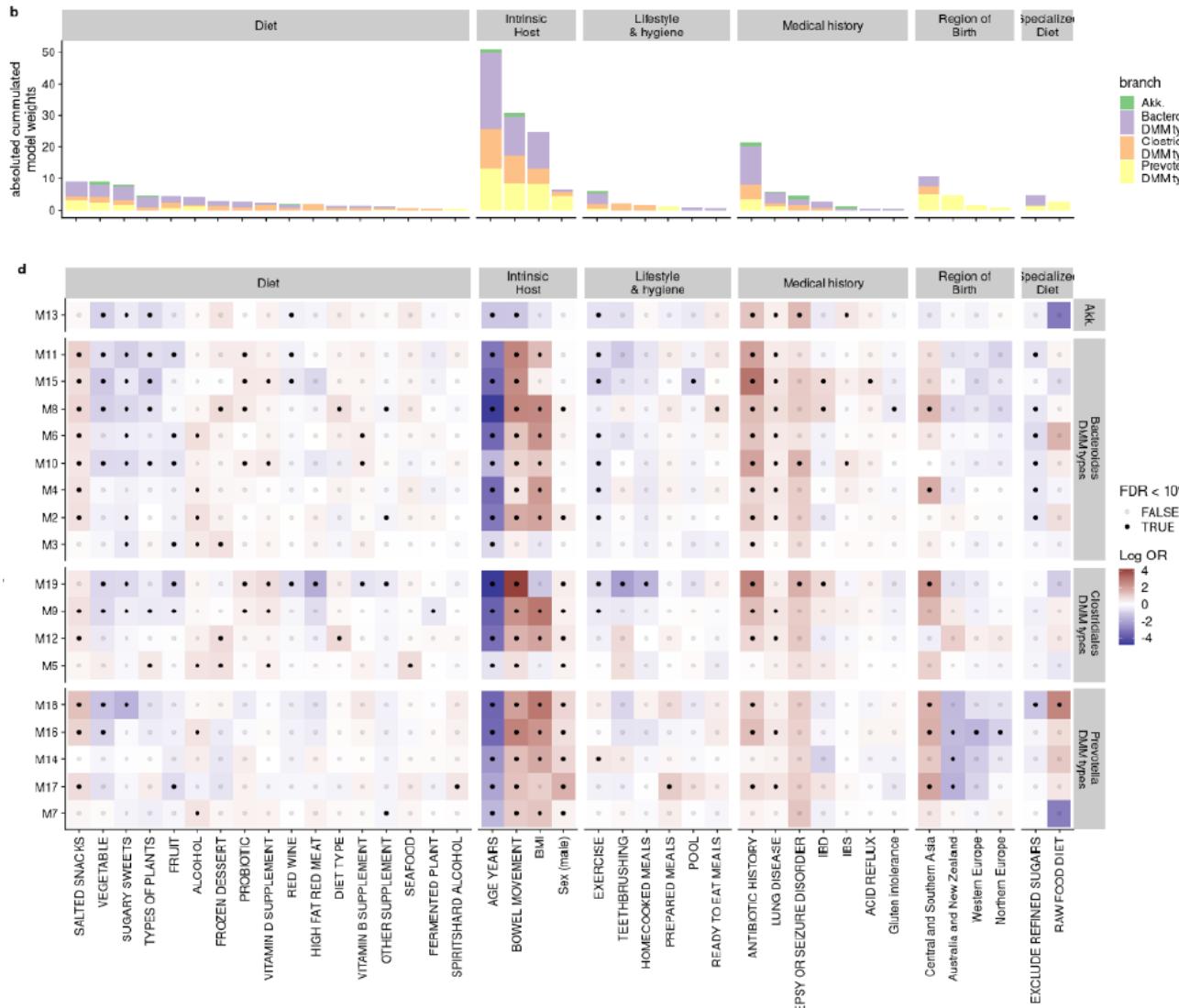
## > Gut microbiome alternative stable states hypothesis



## > Branches help to monitor gut microbiome recovery



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

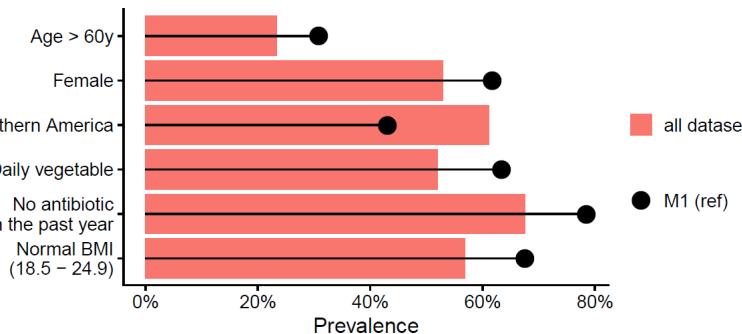


Sex, exercises frequency and **region of birth** associated differentially between branches

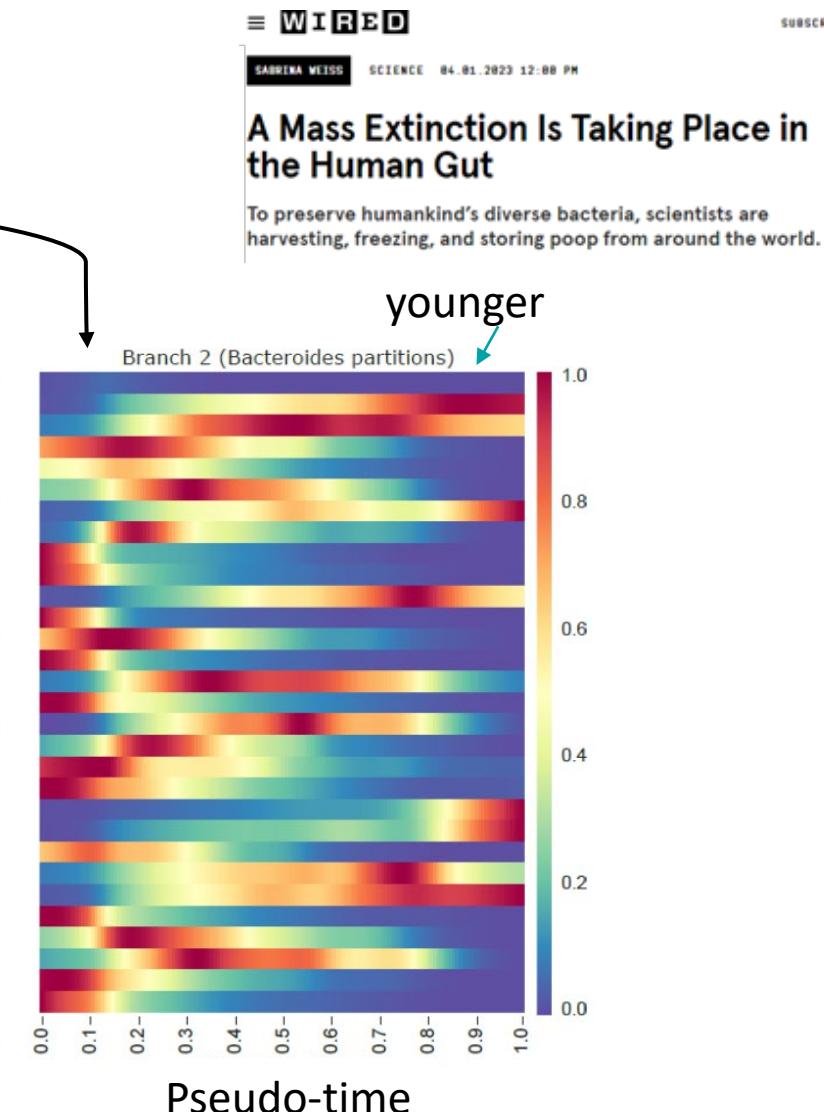
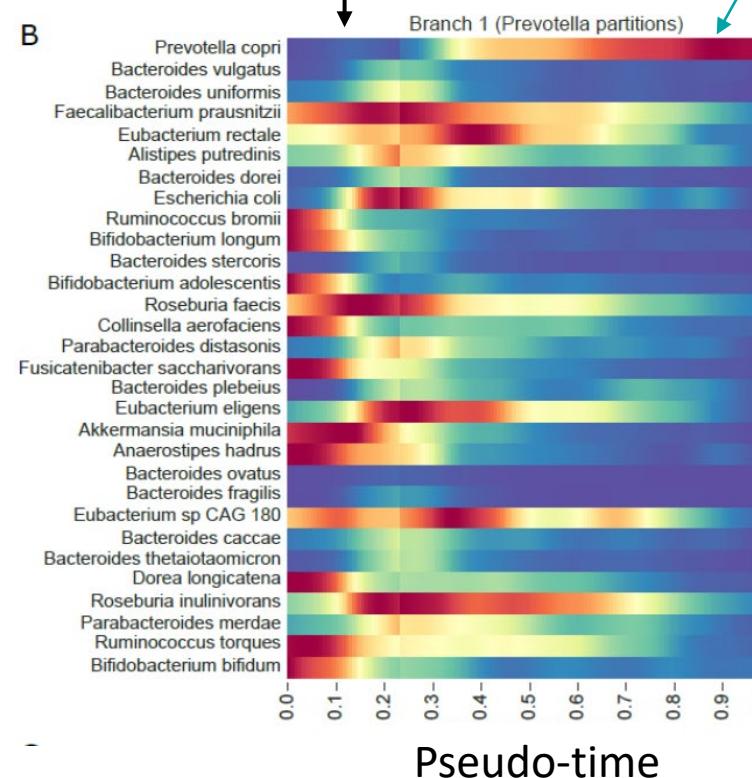
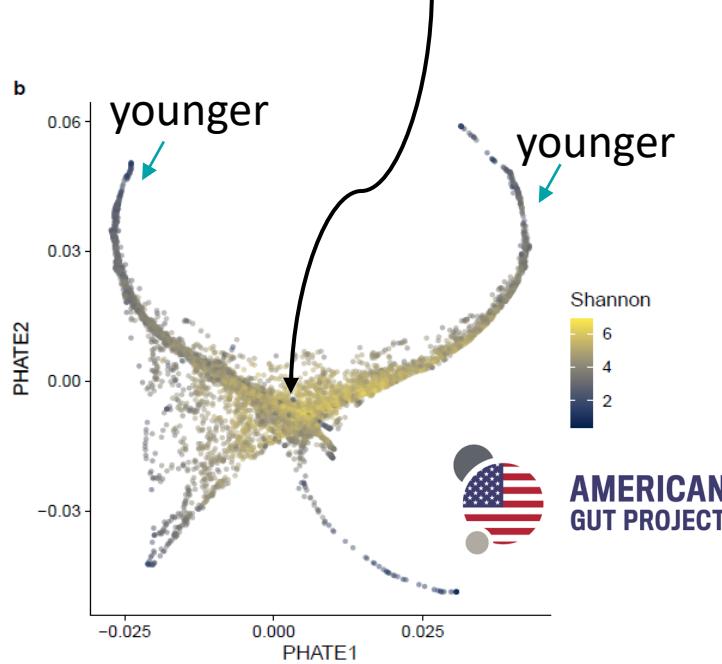
Lifestyle and hygiene associated with altered state within *Bacteroides* branch

Specialized diet associated with altered state within *Prevotella* branch

# > Do we already observe a intergenerationally mass extinction?

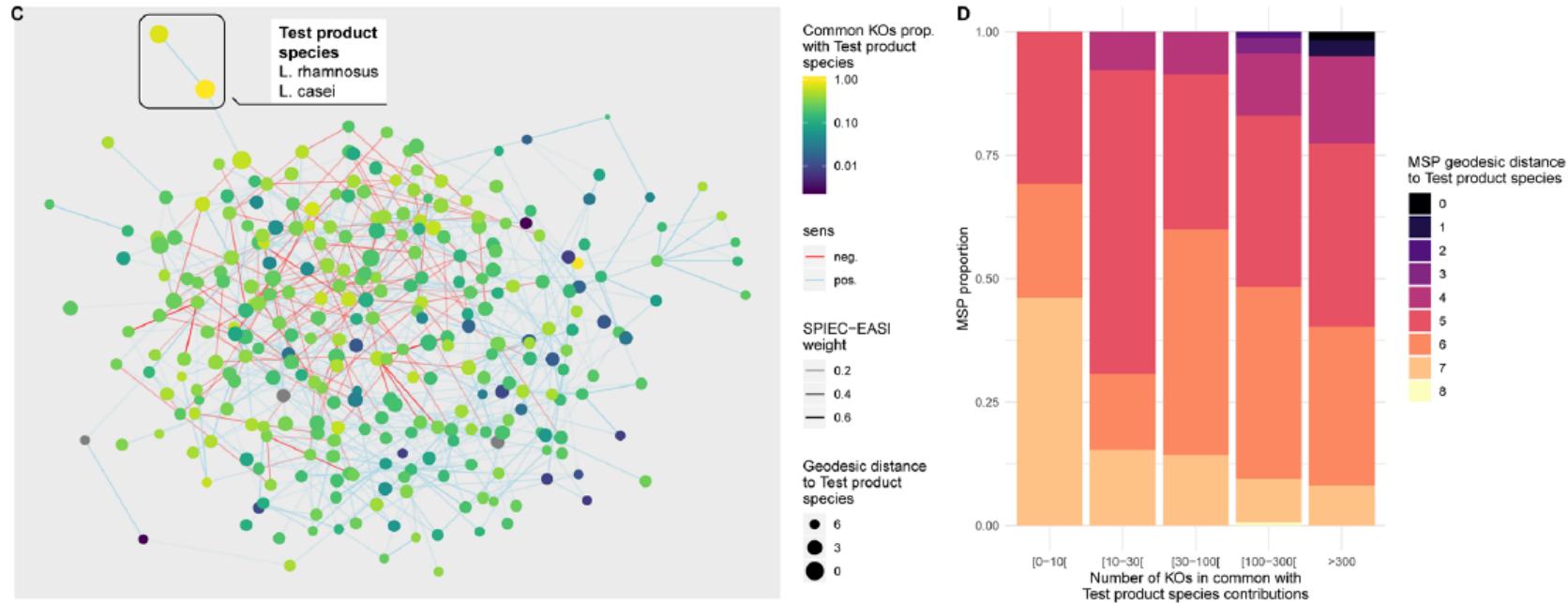


Older and healthy  
diet and lifestyle



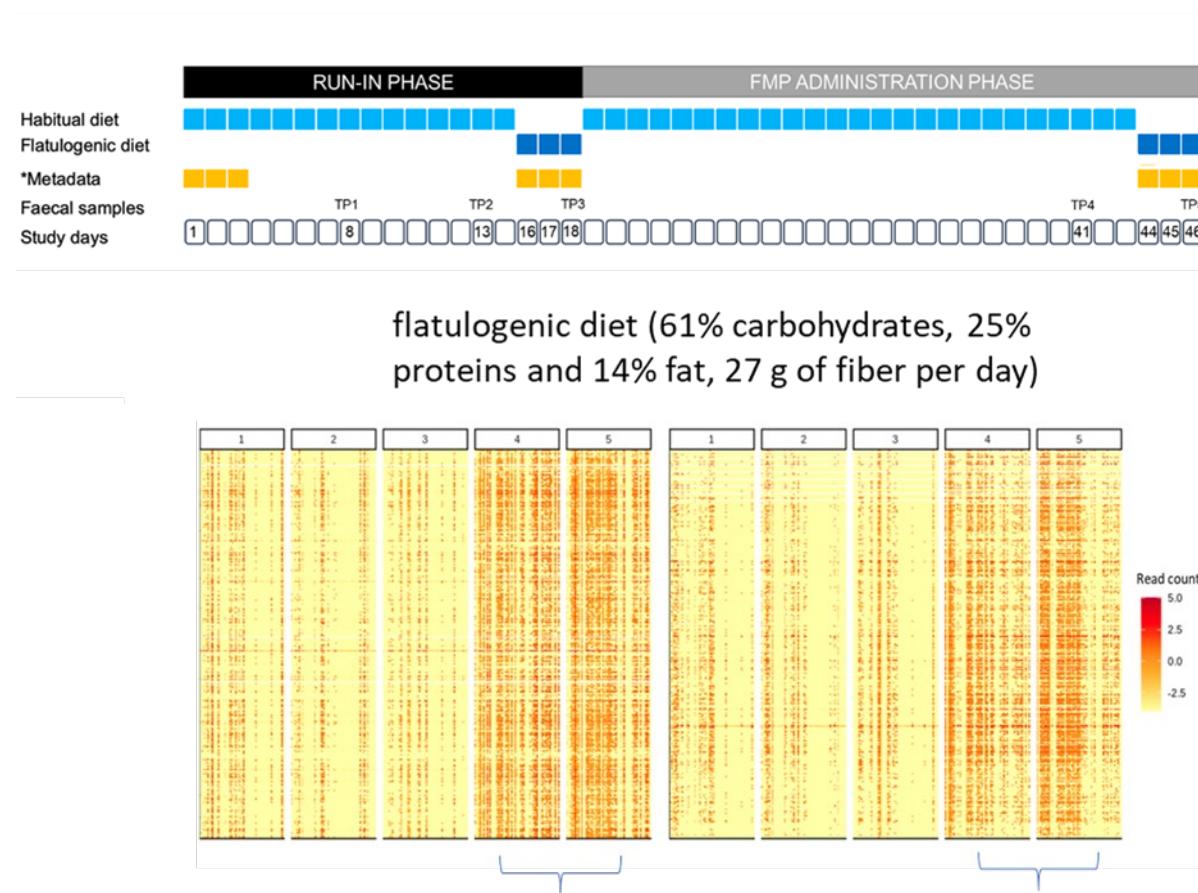
# Probiotics engraftment are gut microbiome baseline dependent

Modular coalescence between gut and biotics species

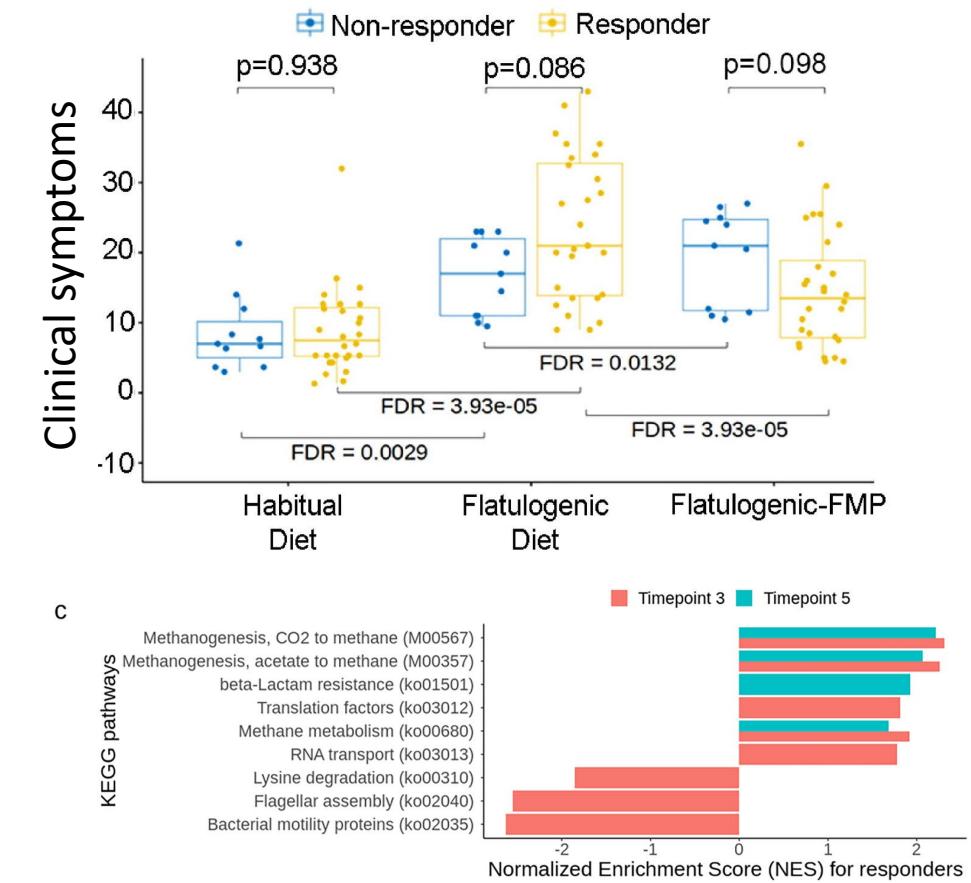


“Engraftment” as function of existing niche and metabolic pathway

# Probiotics clinical effect is gut microbiome baseline dependent

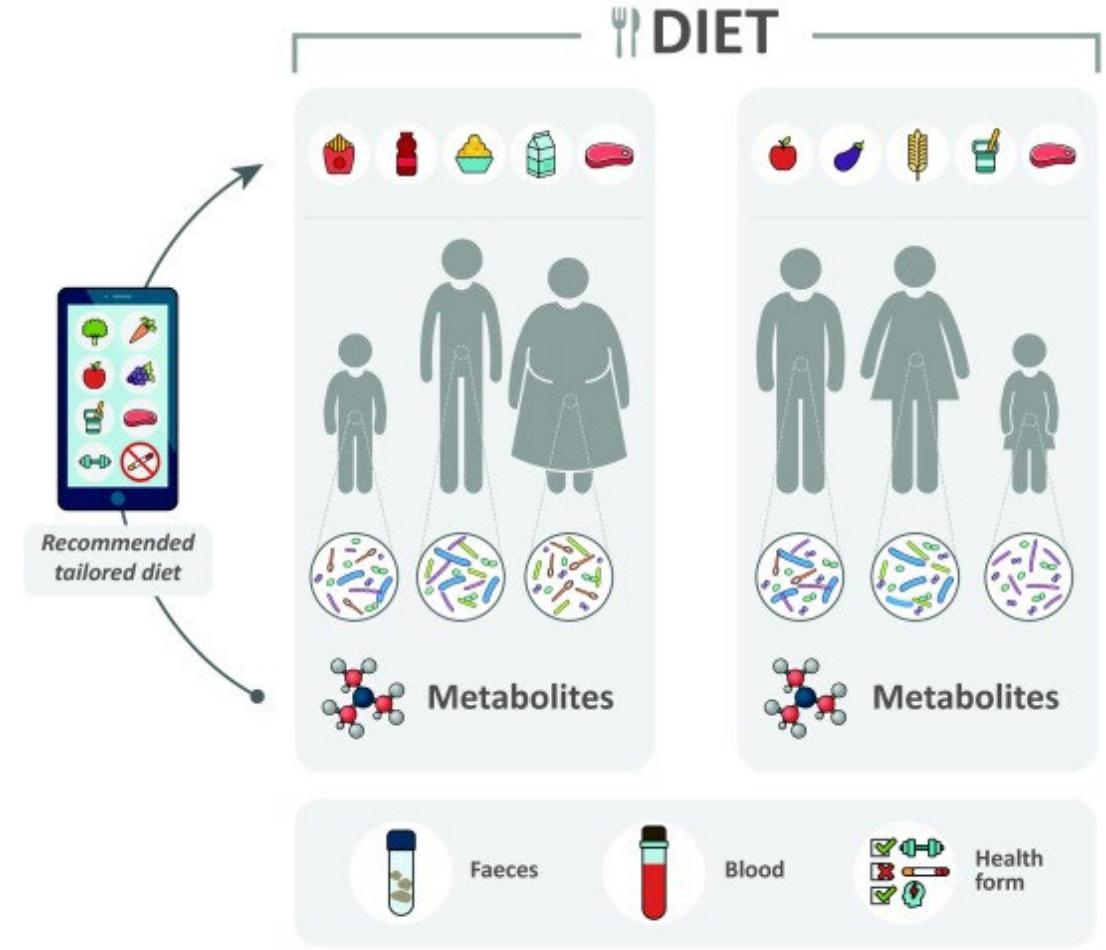
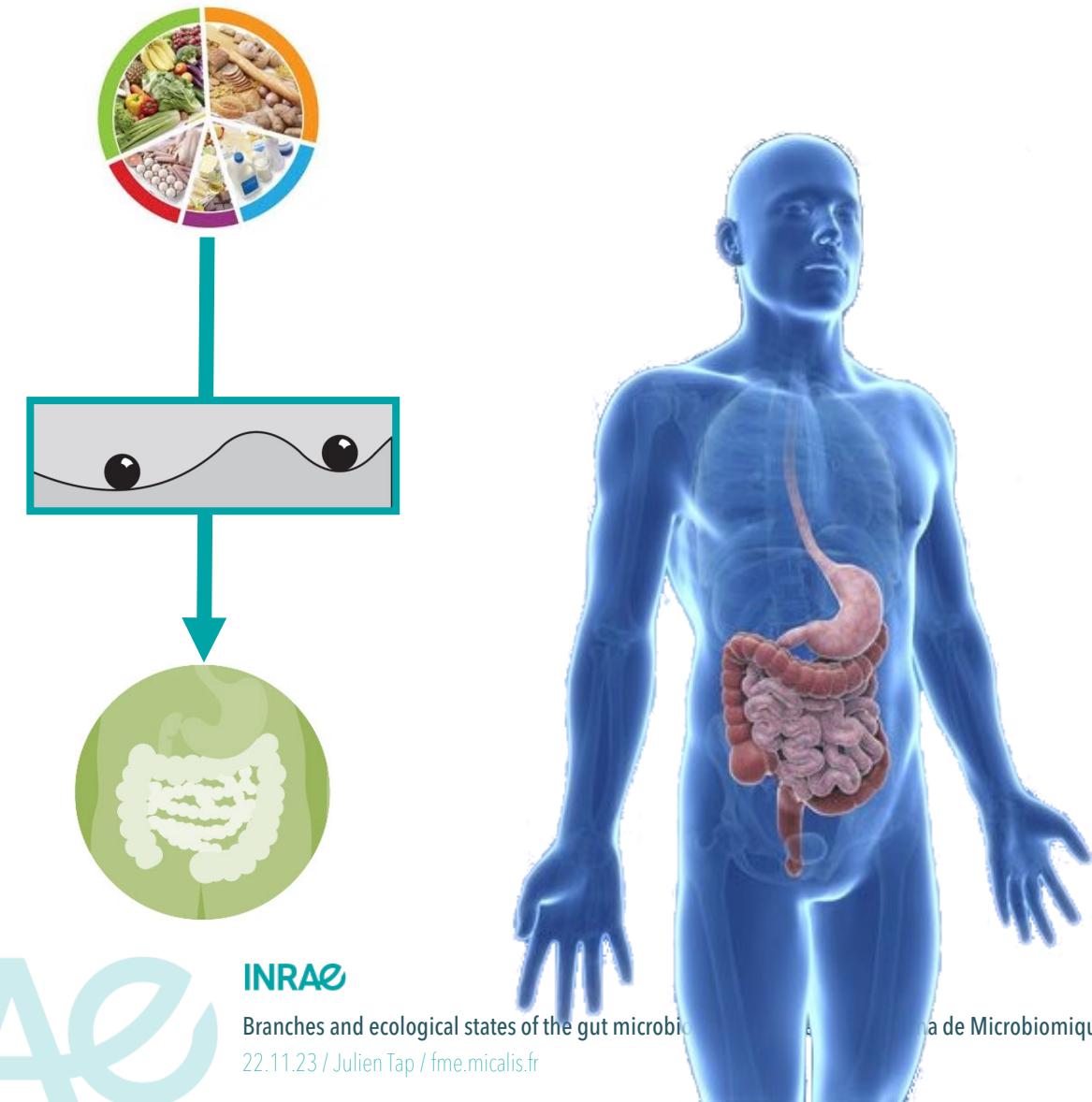


After FMP consumption, FMP active strains detected by metatranscriptomics



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

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



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

Trends in Microbiology

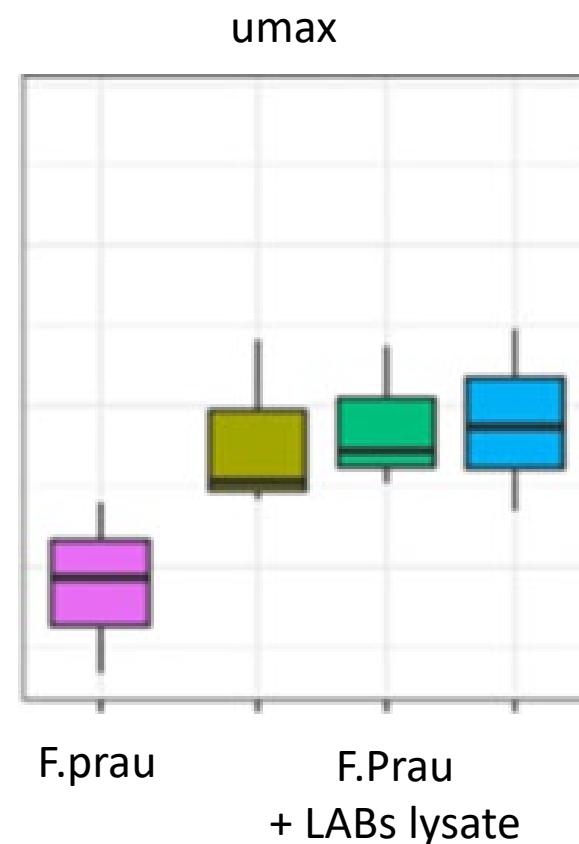
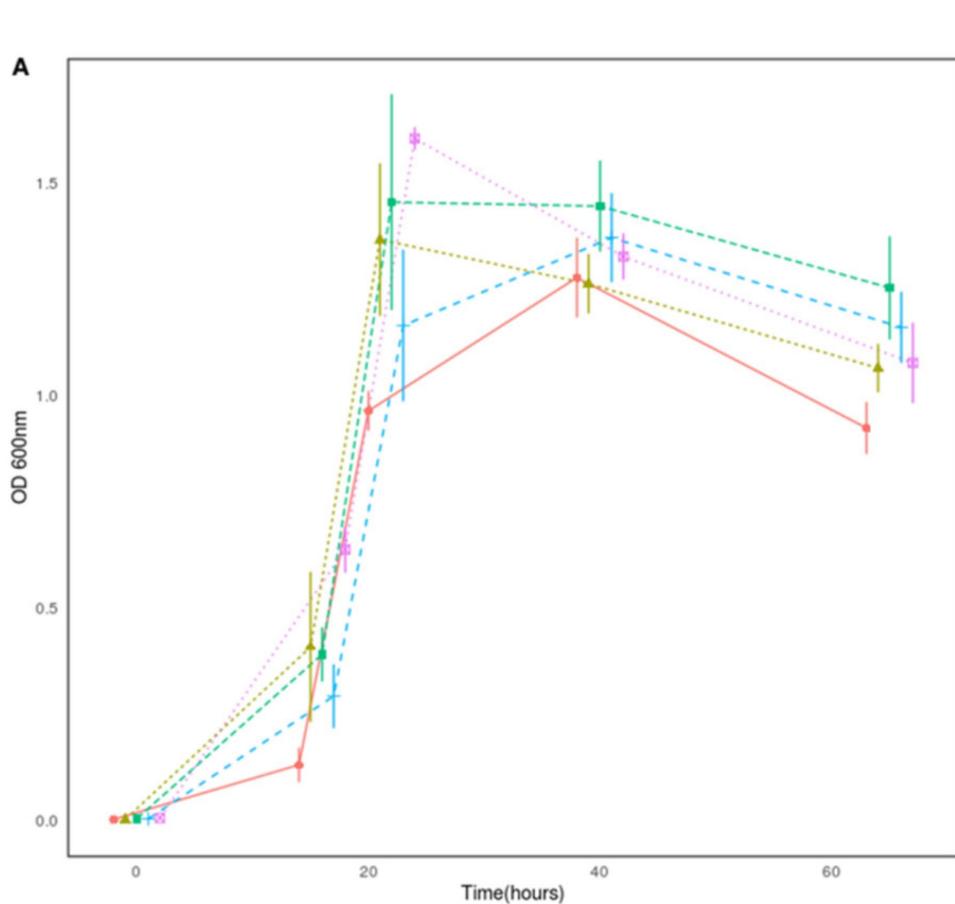
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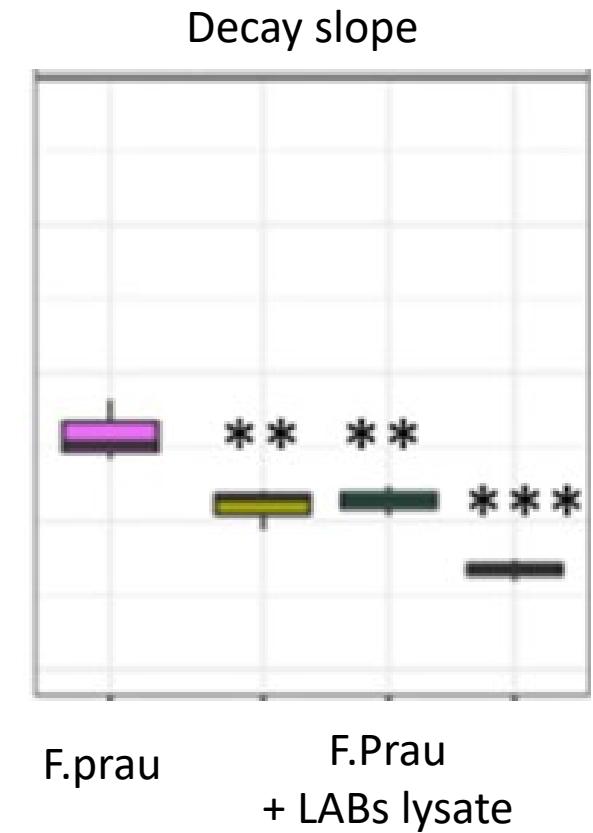
p. 18

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



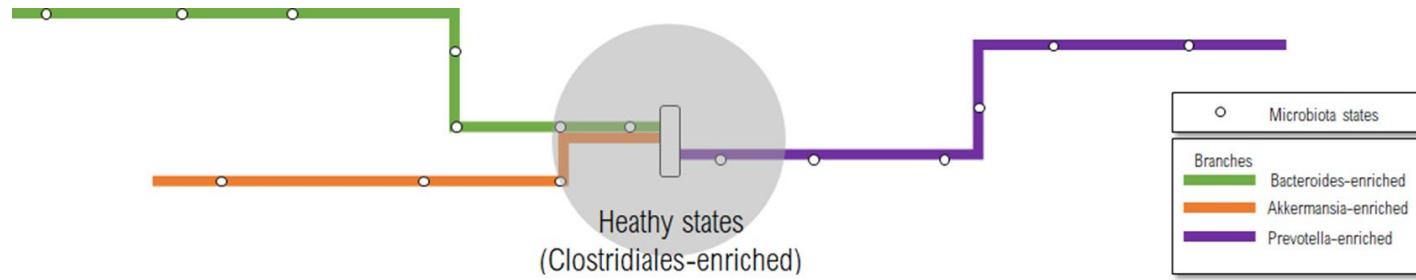
Increase of peptidoglycan levels for cell wall formation *F.prau*

Lebas, Derrien and colleagues (2020)



F.prau  
F.Prau + LABs lysate

## > 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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...

**Food Microbial Ecology lab**  
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