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

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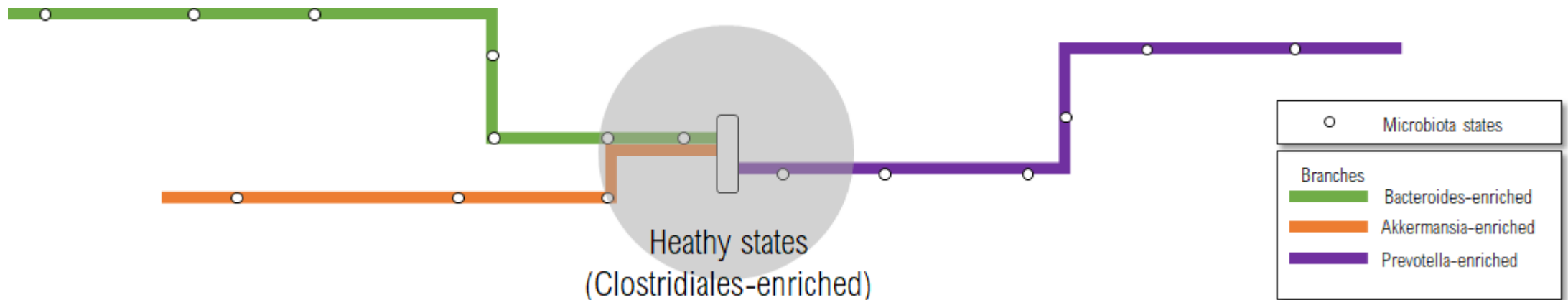
> Branches and ecological states of the gut microbiome:

Mapping for future personalized nutritional and therapeutic interventions

Julien Tap

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Journées Polepharma de Microbiomique- Rouen 2023

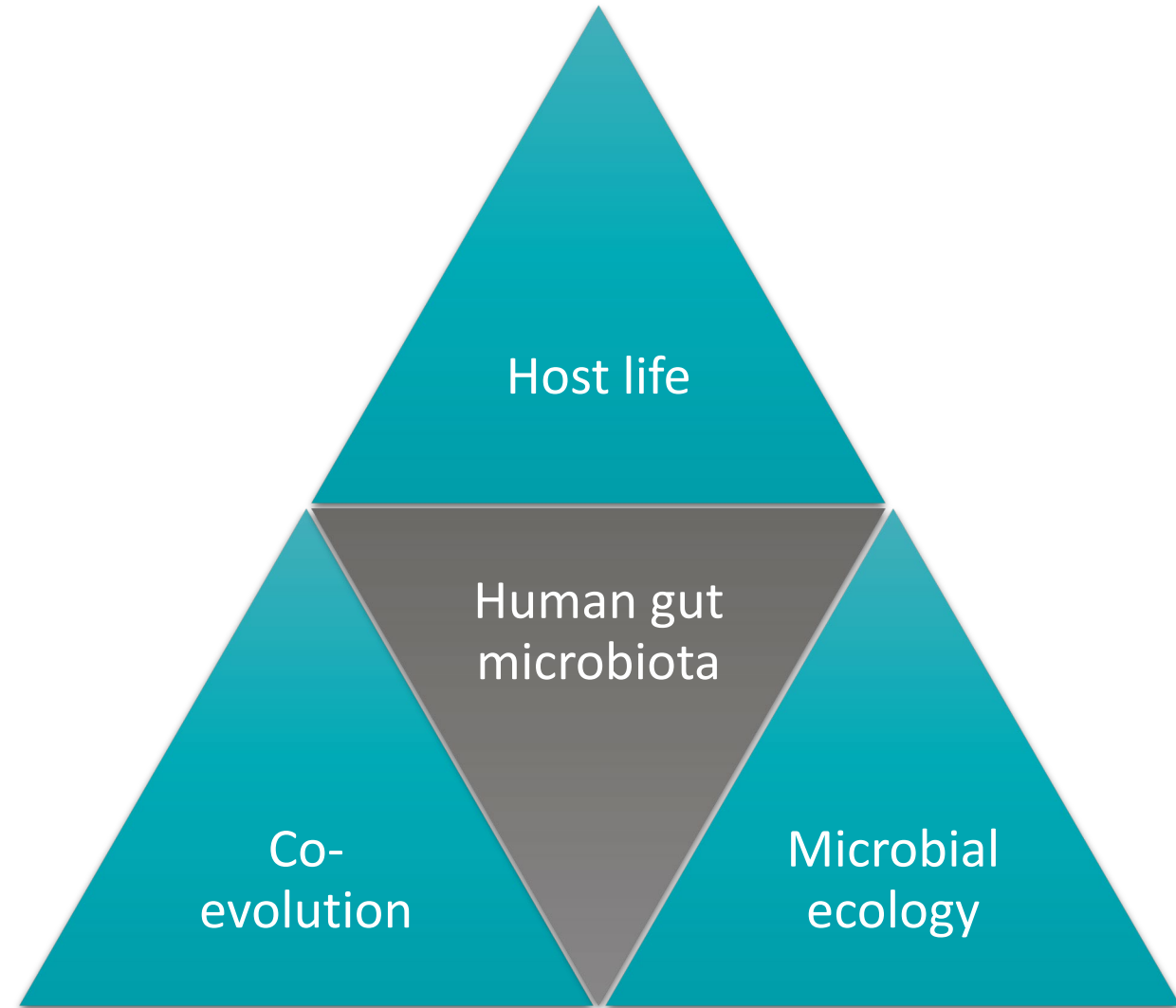
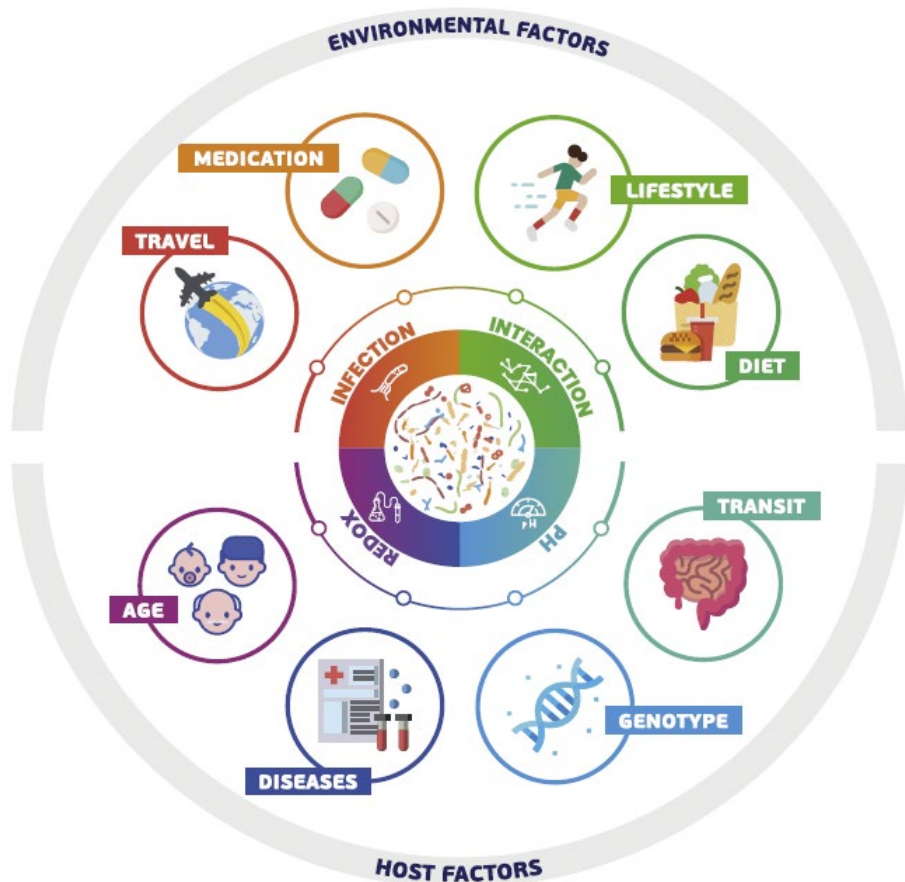


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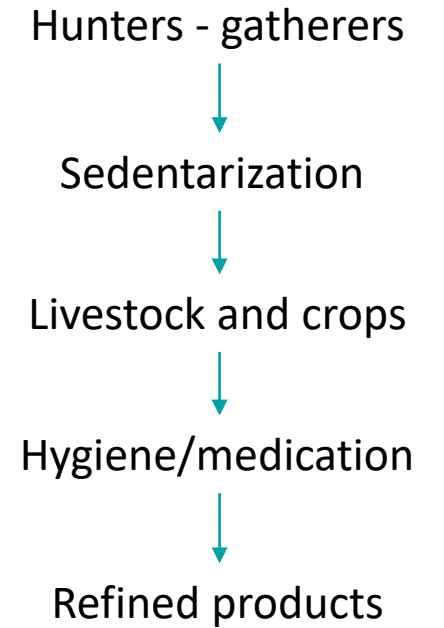
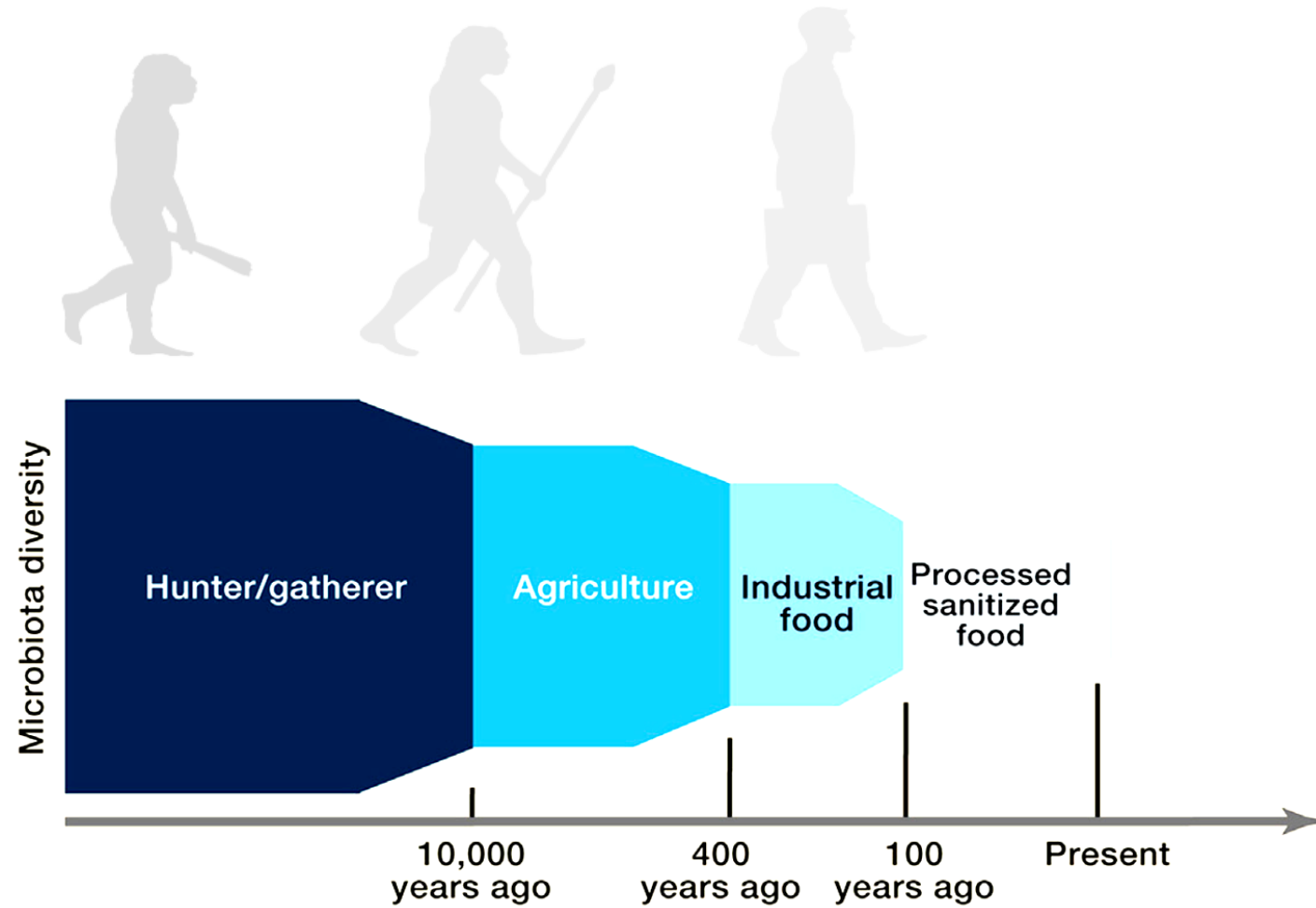
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➤ Different factors shapes the human gut microbiome

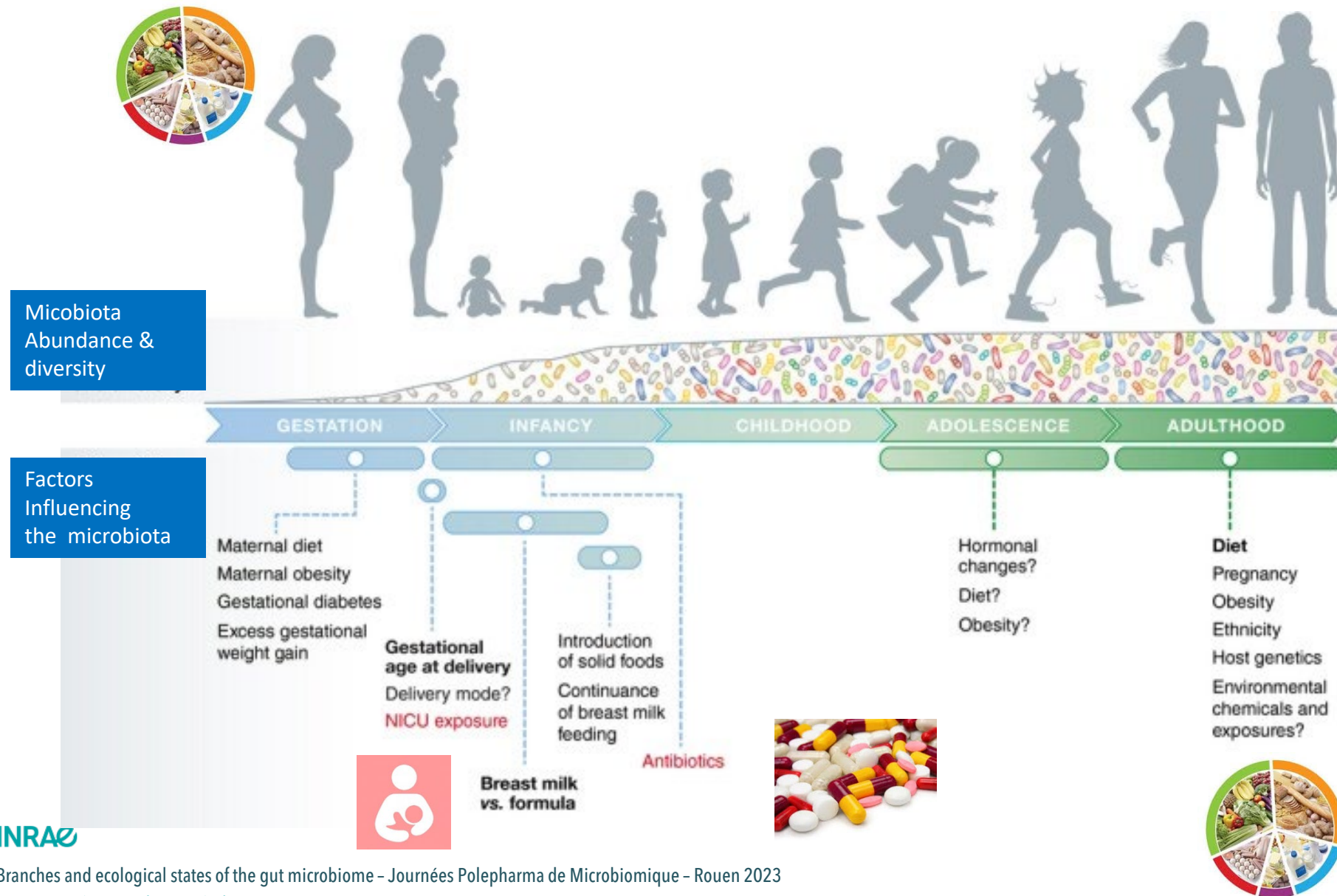


> Diet and lifestyle effect host microbiome symbiosis

Are we uncoupling our metagenome and our genome?



> Gut microbiome throughout life span



➤ Microbiome states resilience as key factor



Healthy state



Resistance



Recovery

Resilience

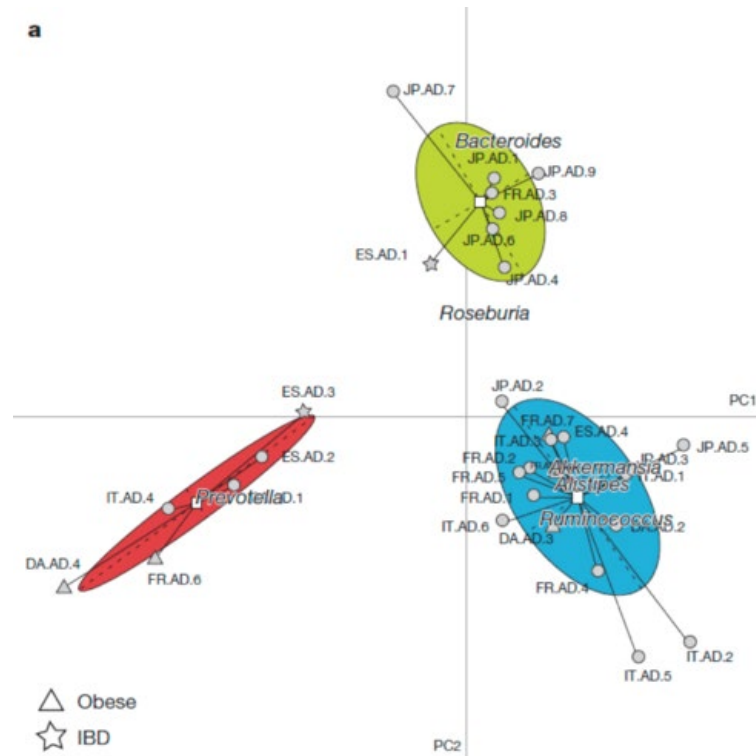
Healthy state



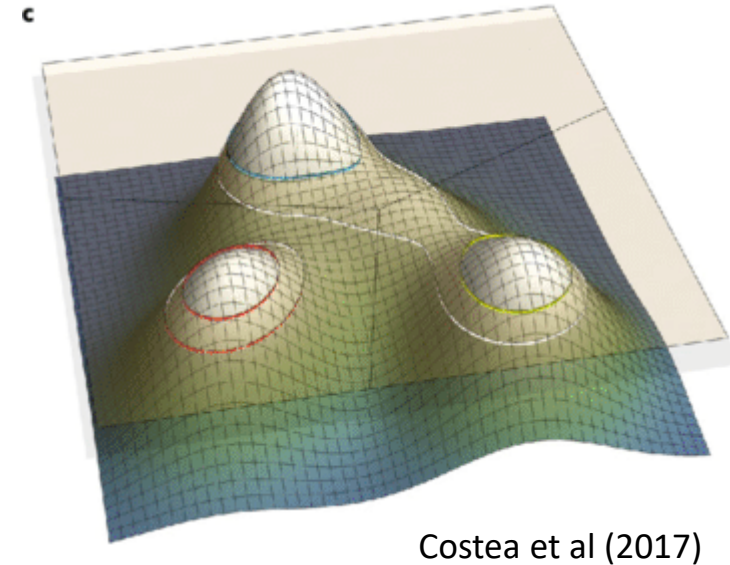
Degraded state



➤ Several attempts to decipher the microbiome structure



Arumugam, Raes et al (2010)



Costea et al (2017)

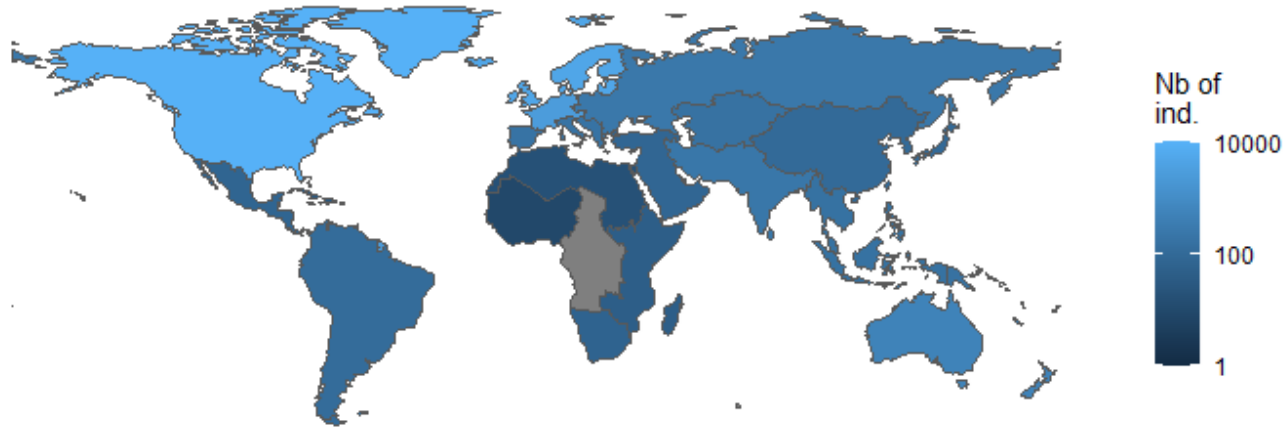
Dirichlet Multinomial Mixture (DMM) modeling

Limits:

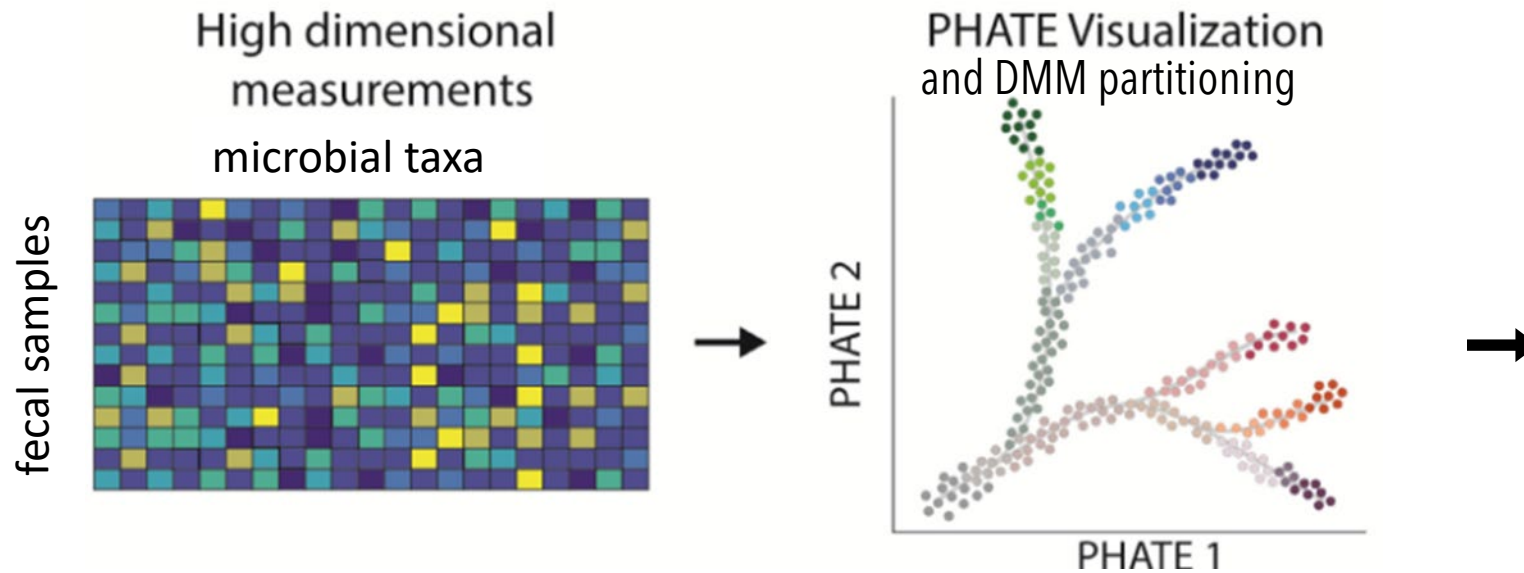
Few association with diet

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

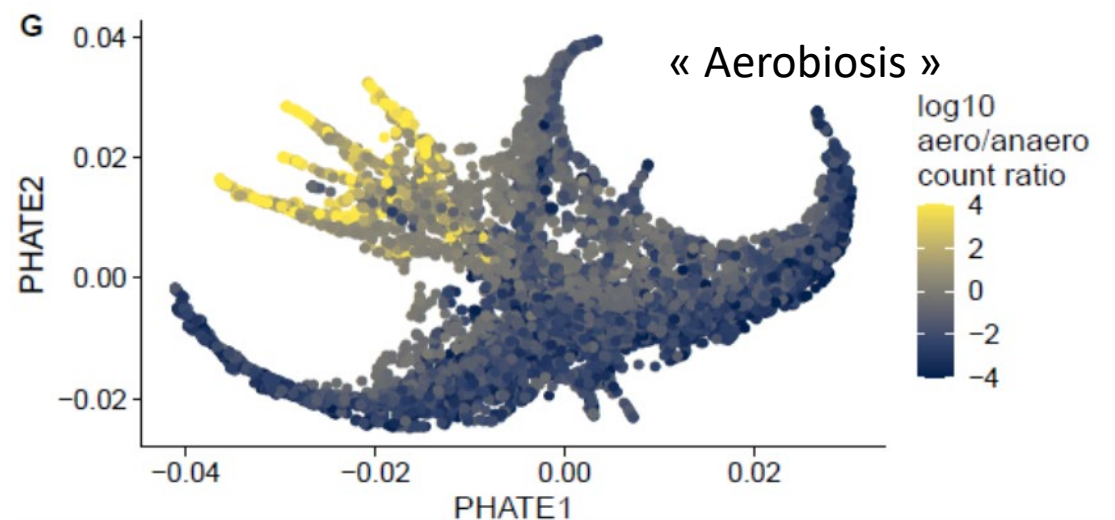
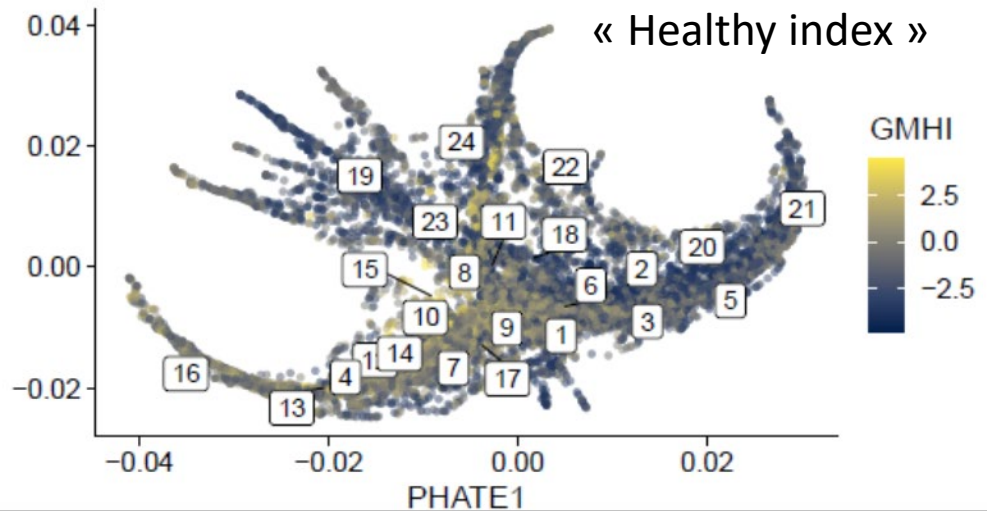
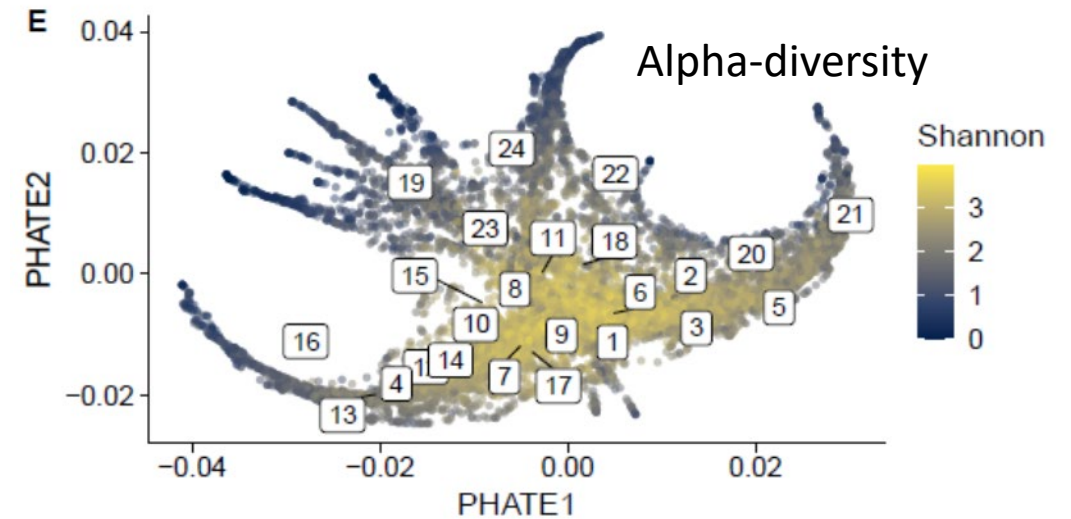
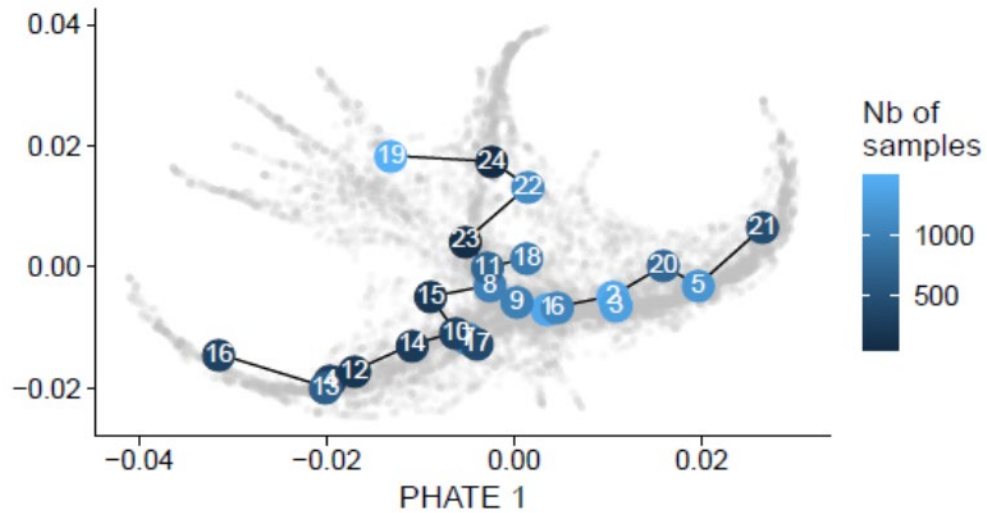


Time-series analysis to detect microbiome states

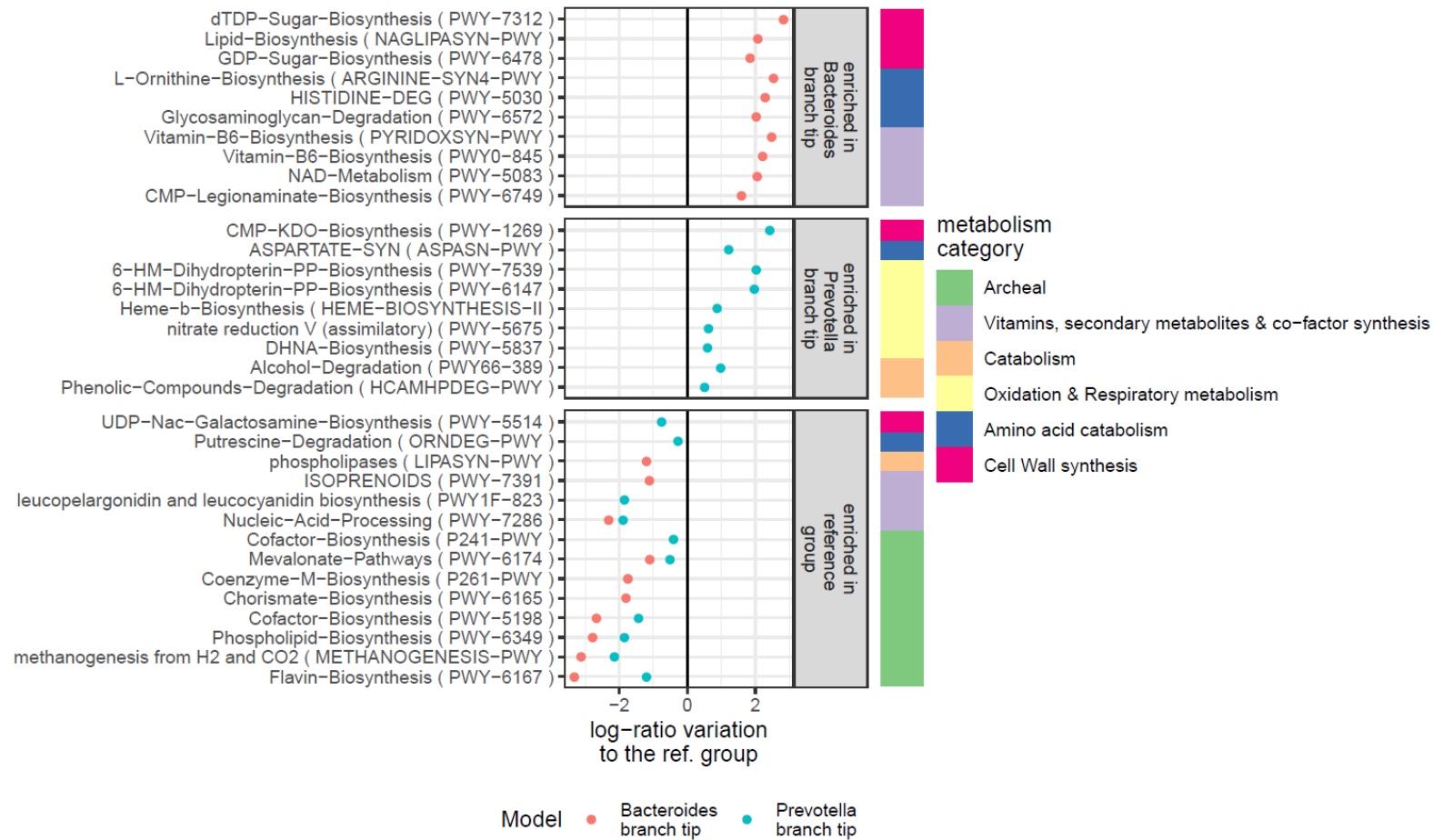
Region of birth, Lifestyle, diet, and health modelization



➤ Human Gut microbiome structured as branches



➤ Low-diversity tips of branches display functional shifts



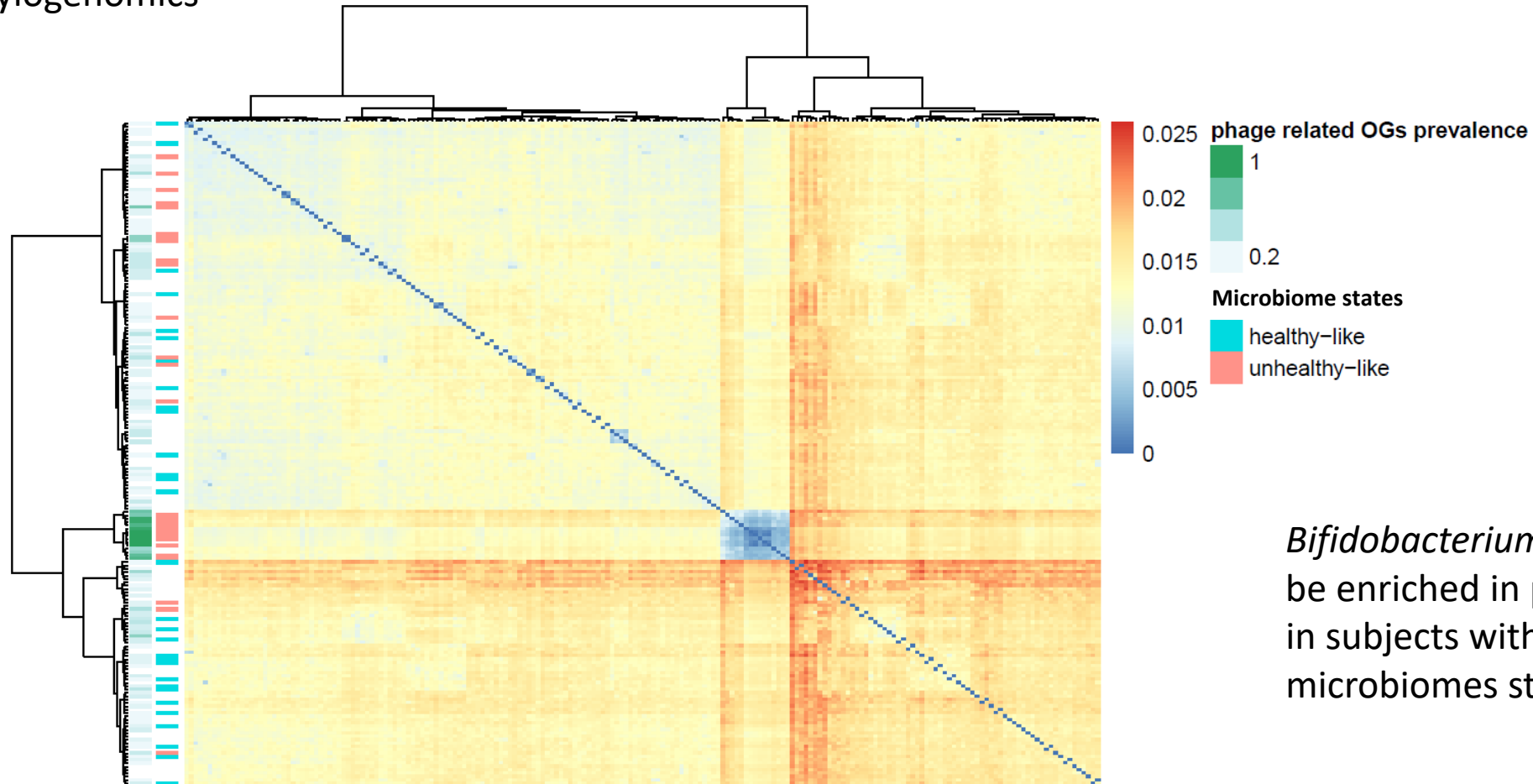
amino acid catabolism increase in *Bacteroides* branch tip

oxidative stress response increase in *Prevotella* branch tip



➤ Altered states showed functional differences within species

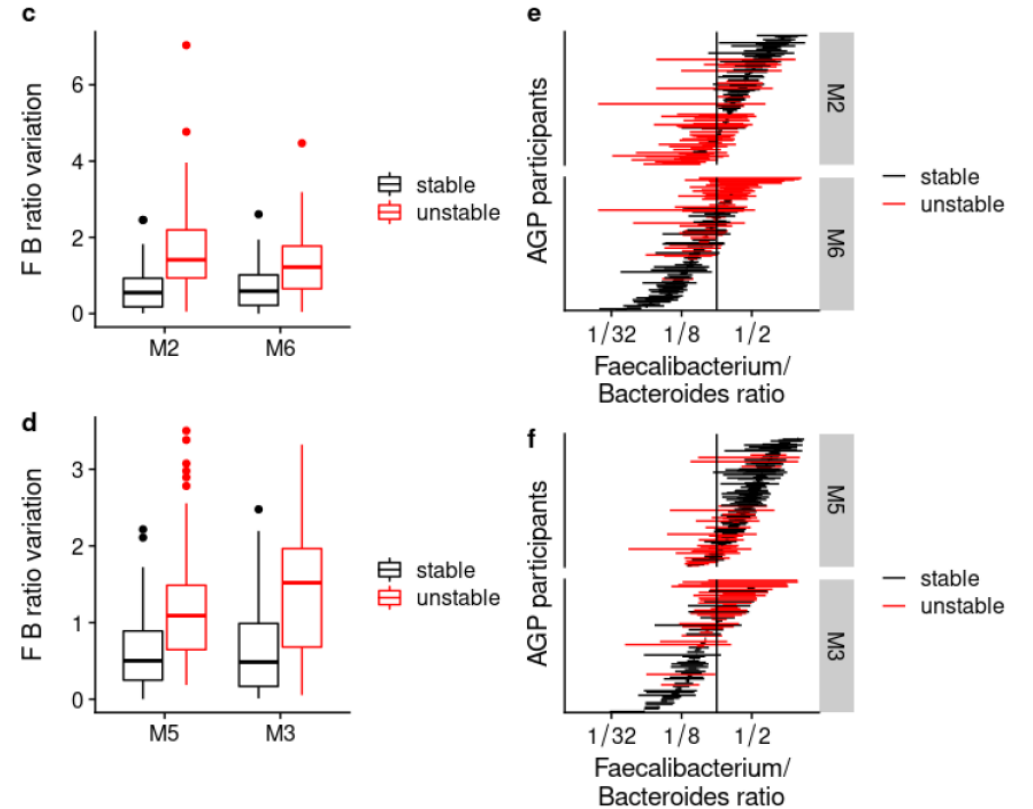
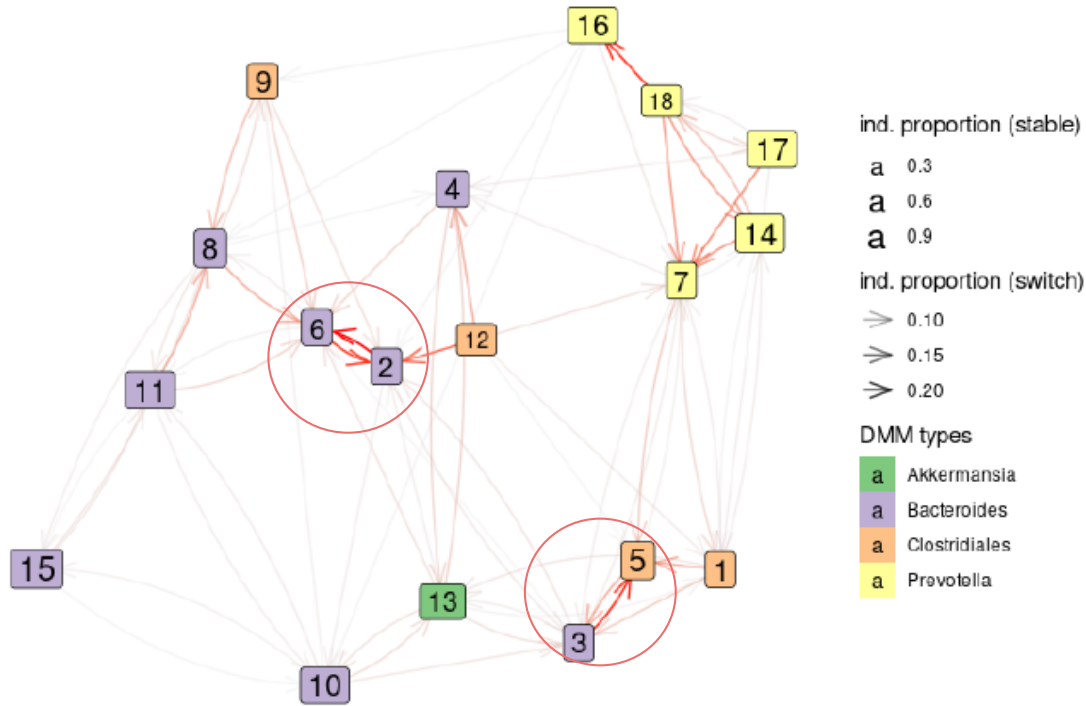
400 *B. bifidum* MAGS
phylogenomics



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

➤ Dynamics between partitions are associated to branches

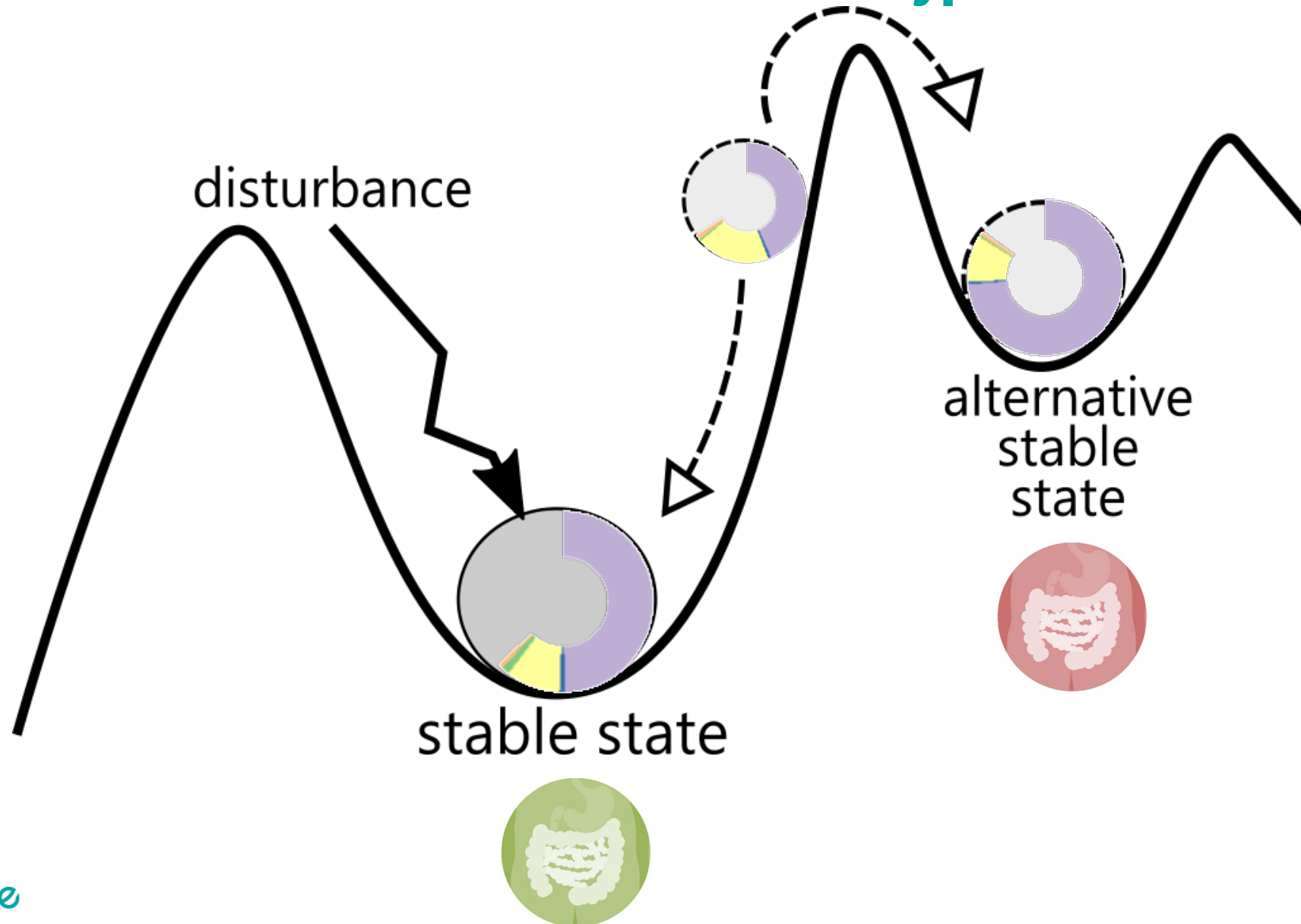
827 participants 2,998 samples 2,171 time-pairs



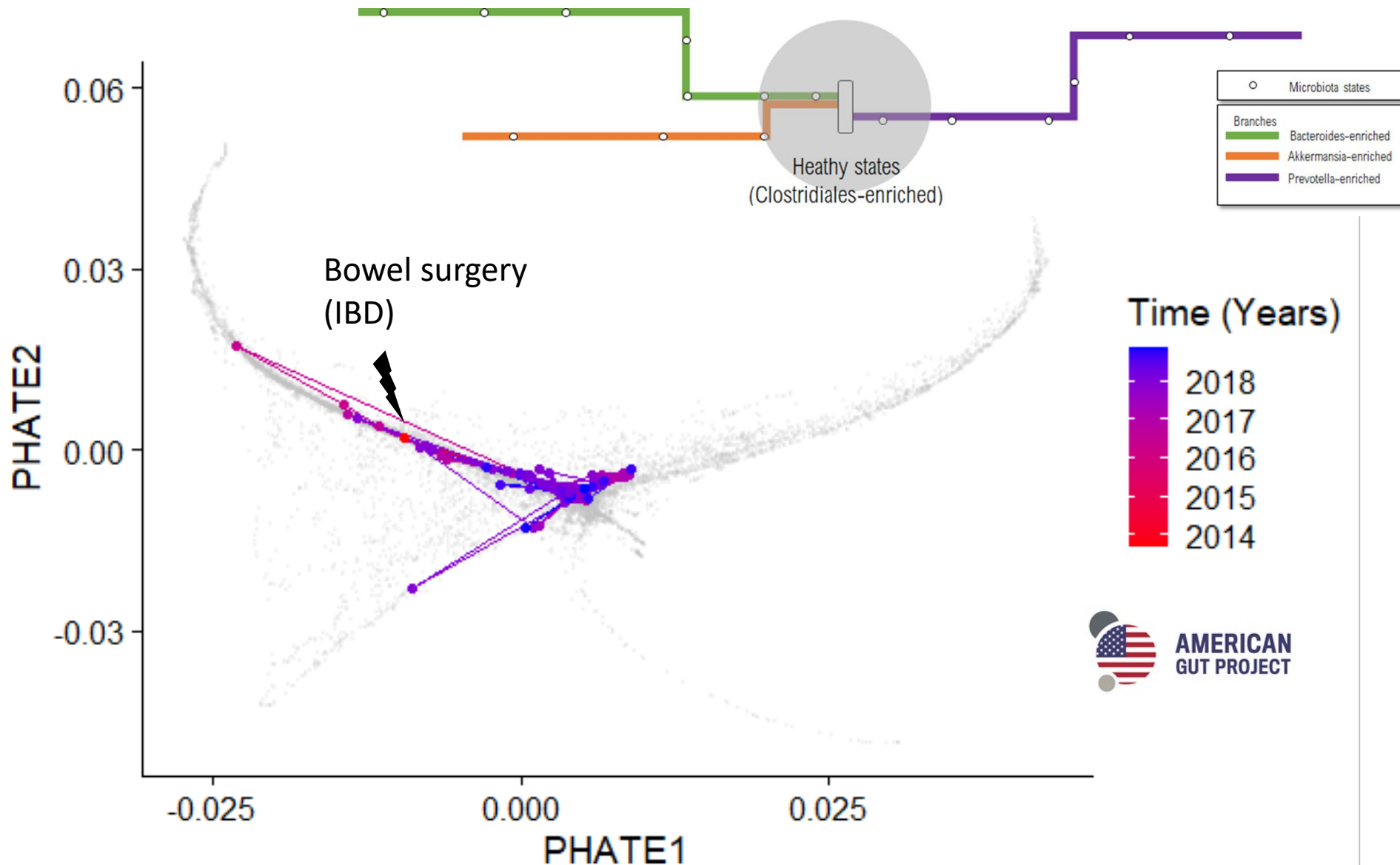
Faecalibacterium/Bacteroides as a tipping element explaining the switch between some states



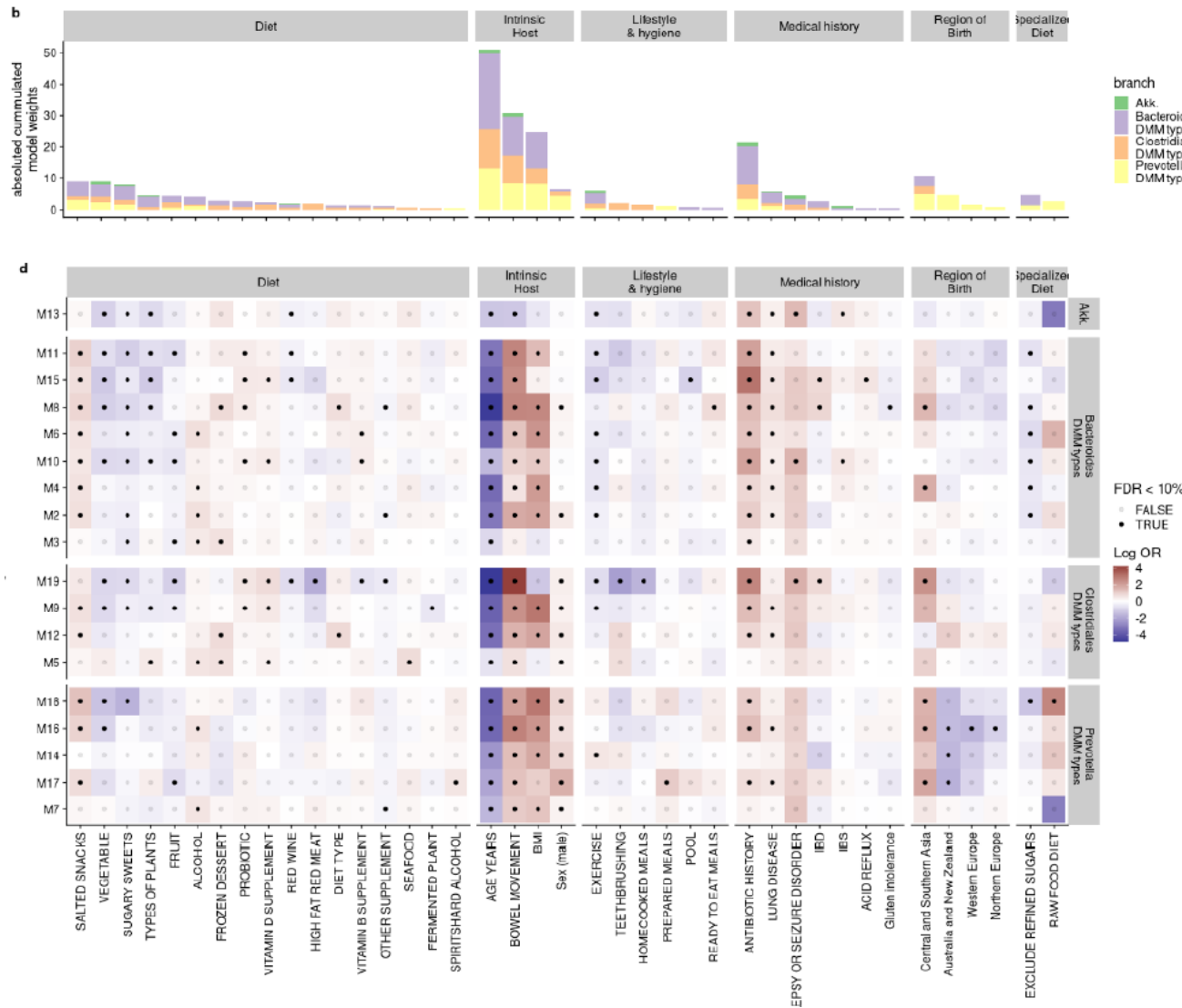
> Gut microbiome alternative stable states hypothesis



> Branches help to monitor gut microbiome recovery



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

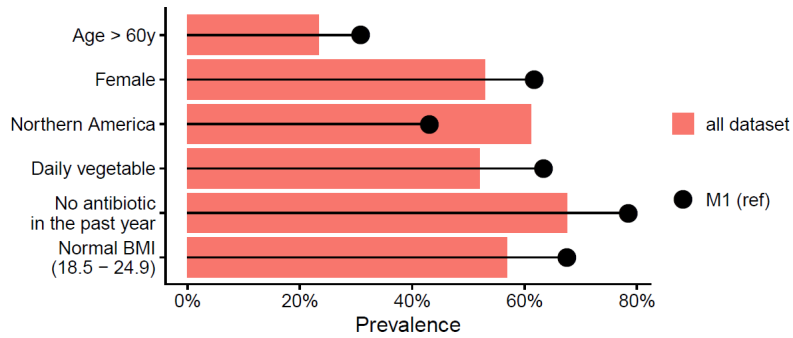


Sex, exercises frequency and **region of birth** associated differentially between branches

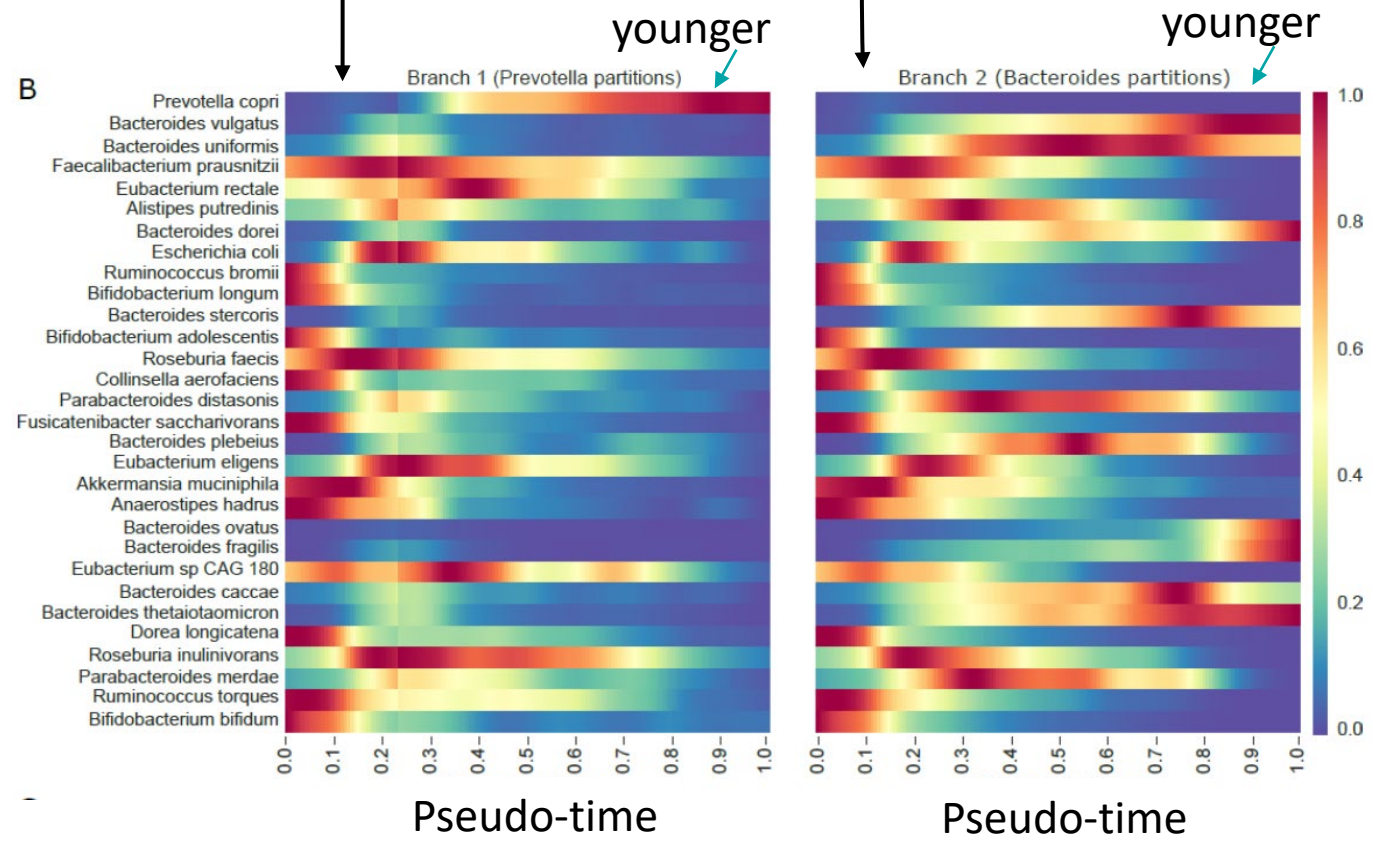
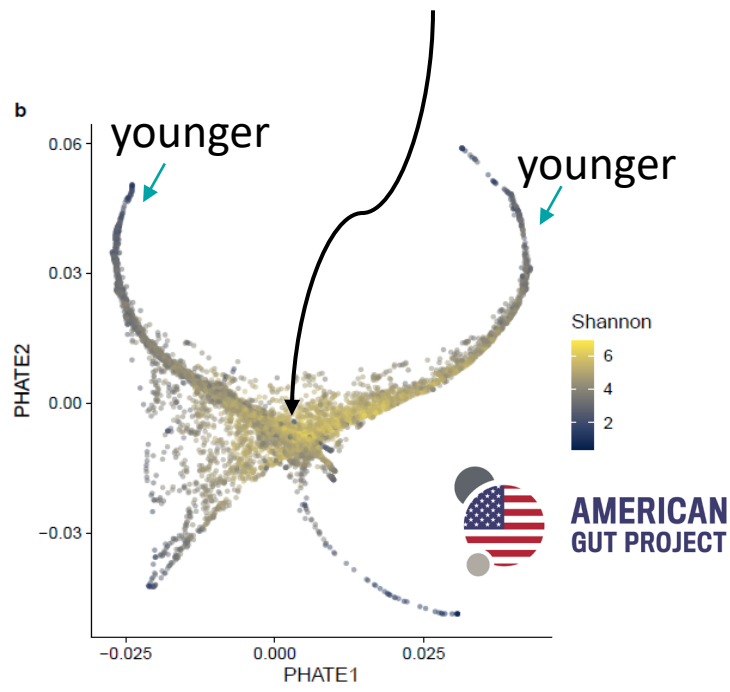
Lifestyle and hygiene associated with altered state within *Bacteroides* branch

Specialized diet associated with altered state within *Prevotella* branch

> Do we already observe a intergenerationally mass extinction ?

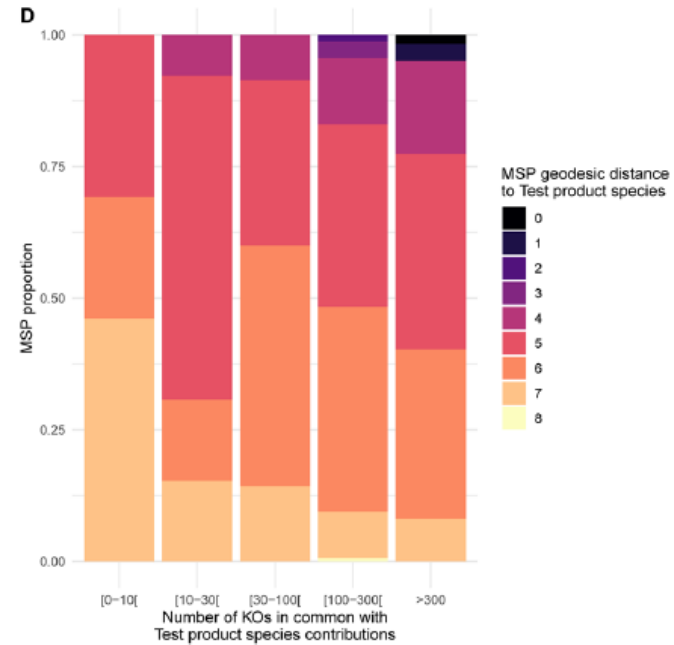
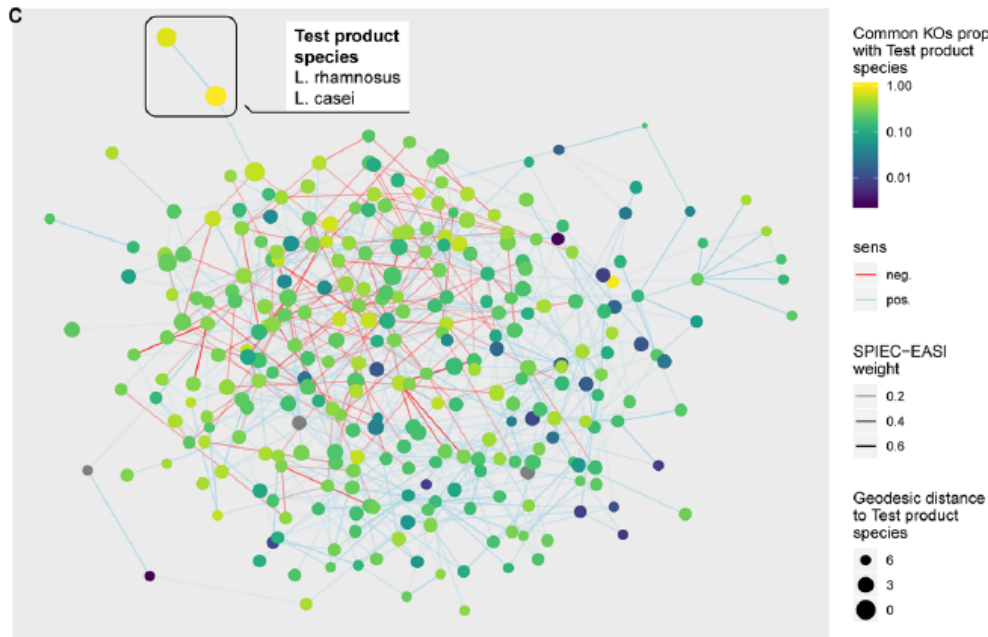


Older and healthy diet and lifestyle



➤ Probiotics engraftment are gut microbiome baseline dependent

Modular coalescence between gut and biotics species



“Engraftment” as function of existing niche and metabolic pathway

Alvarez et al., 2020

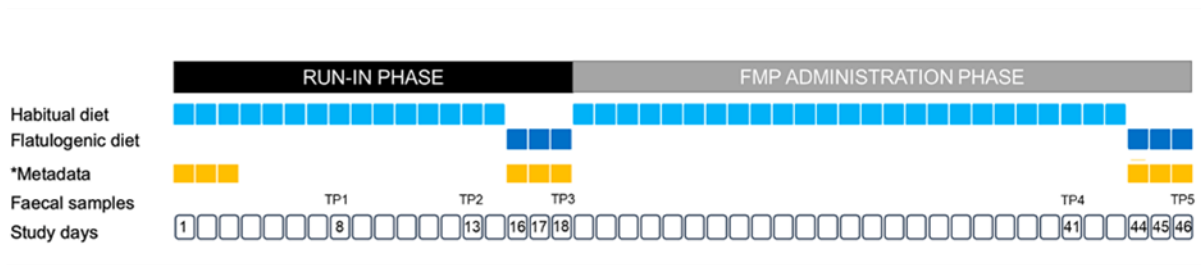


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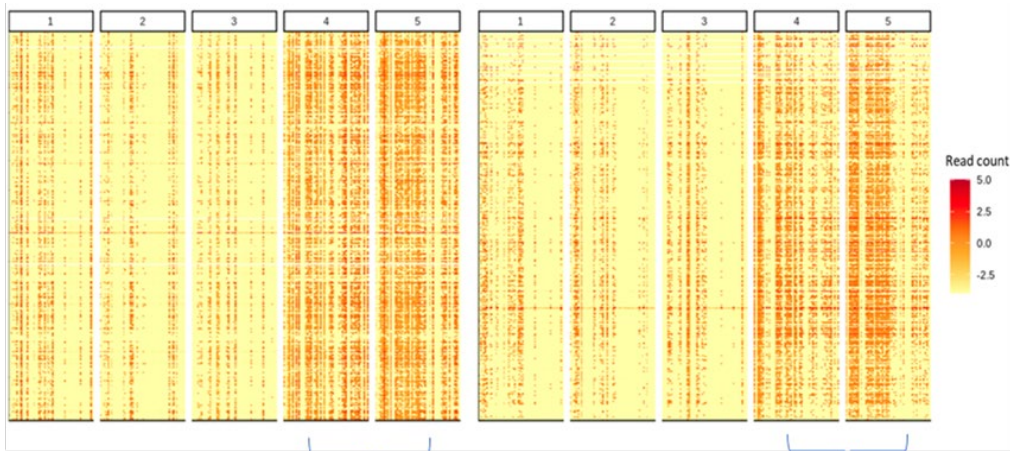
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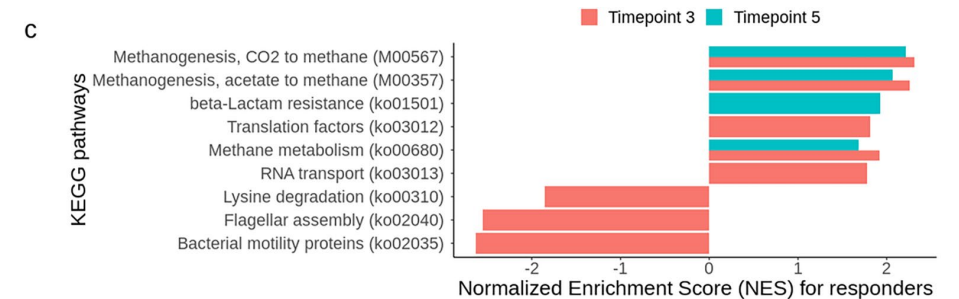
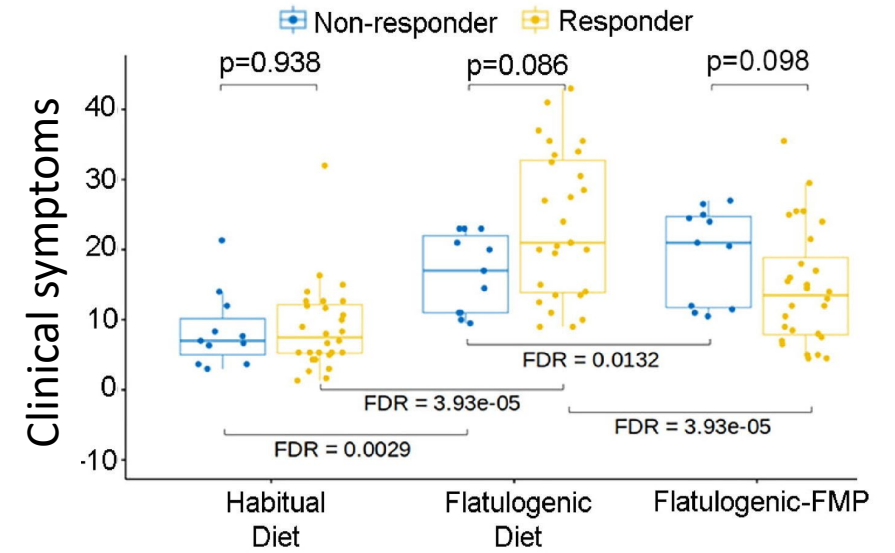
➤ Probiotics clinical effect is gut microbiome baseline dependent



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



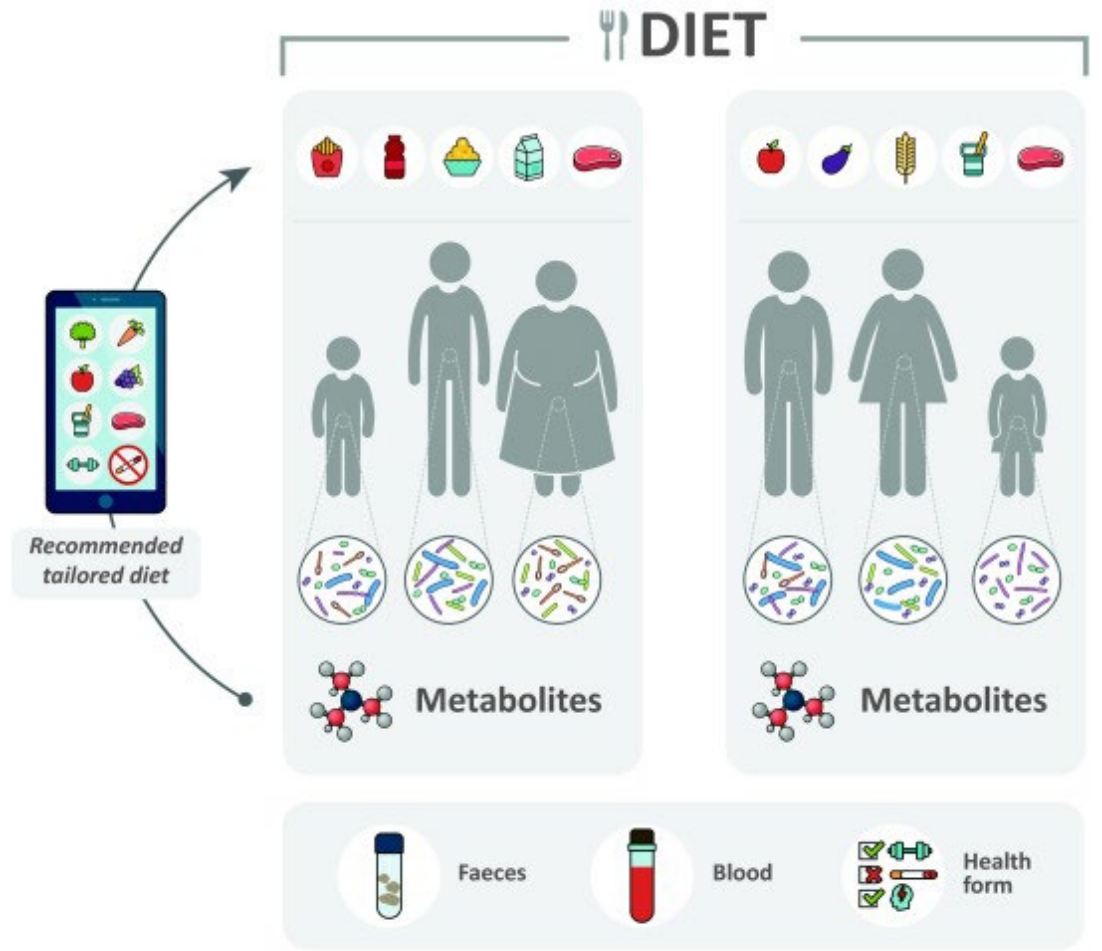
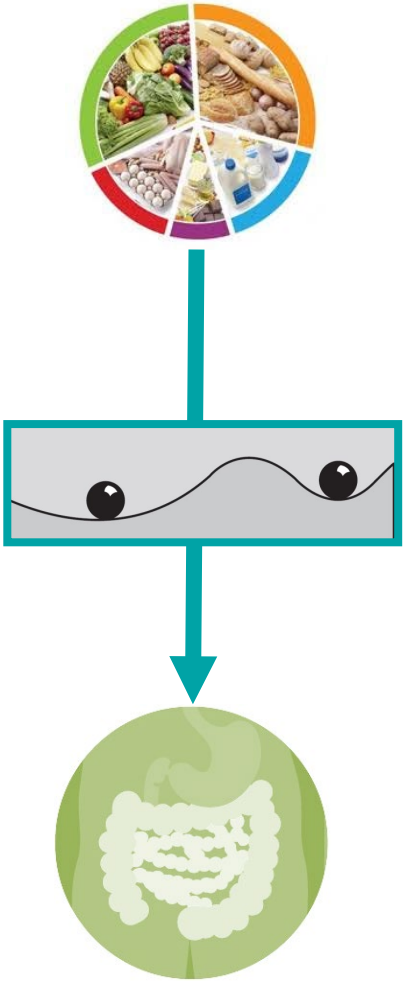
After FMP consumption, FMP active strains detected by metatranscriptomics



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

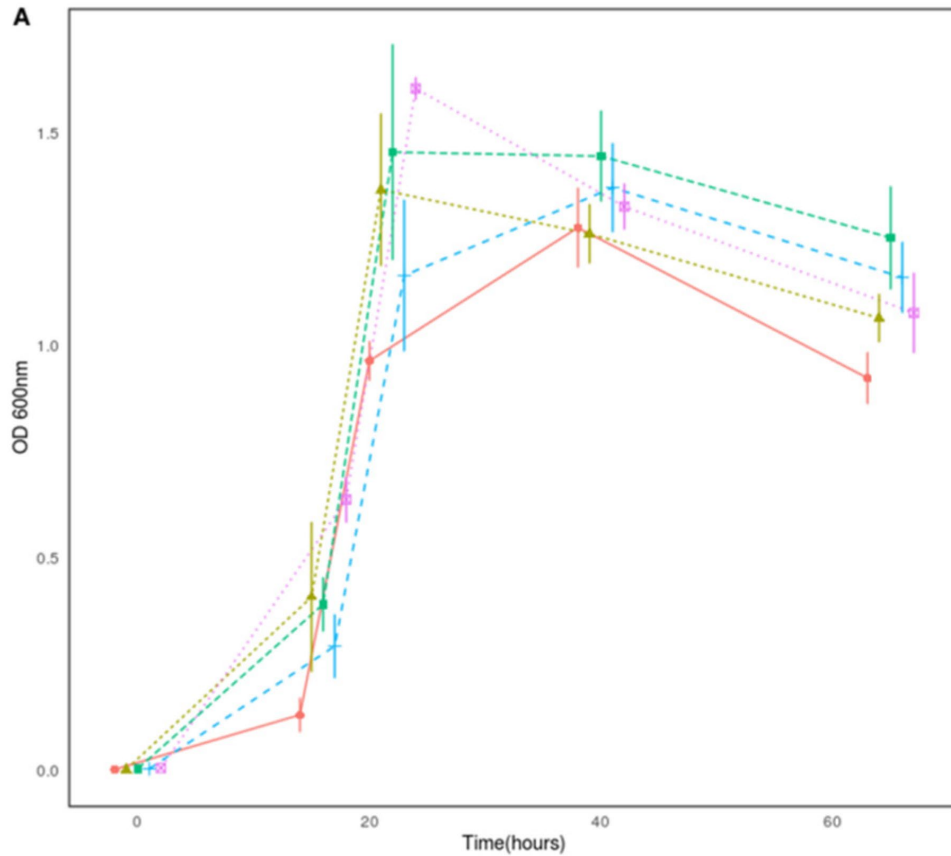
Prevent gut microbiome critical transition to strengthen its resilience using next-gen biotics



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



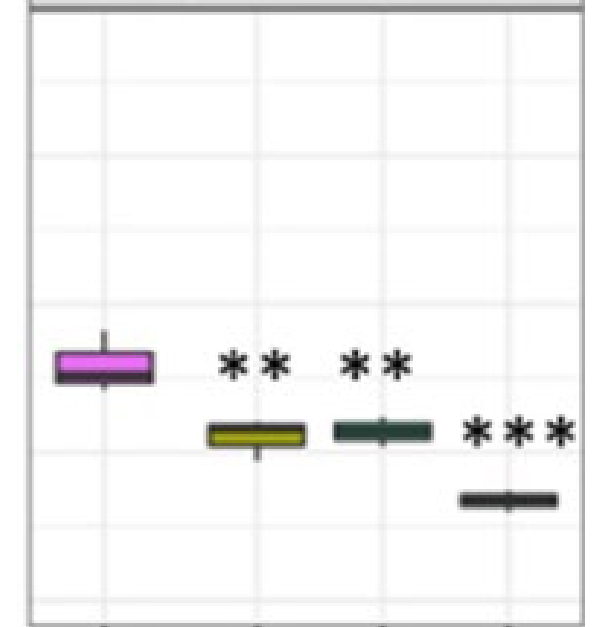
umax



F.prau

F.Prau
+ LABs lysate

Decay slope



F.prau

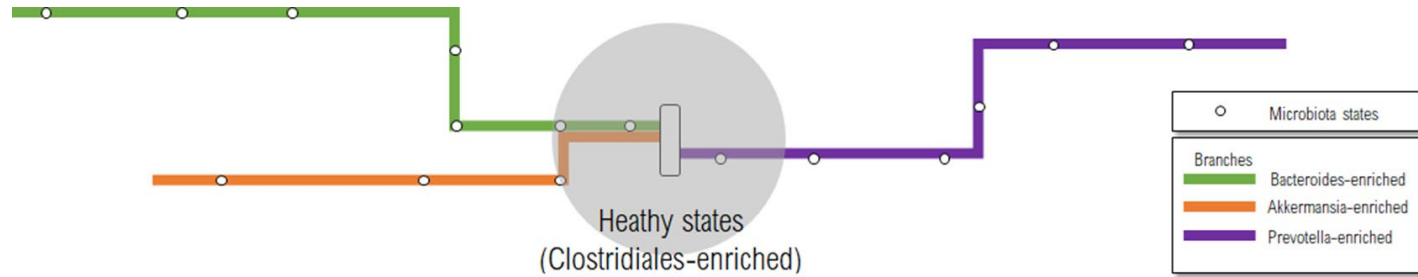
F.Prau
+ LABs lysate

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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