Genetic selection for pig faecal enterotypes affects host upper gut microbiota and immune traits

F Blanc[1], C Larzul[2], G Lemonnier[1], N Bruneau[1], C Niort[3], MN Rossignol[1], C Rogel-Gaillard[1], J Estellé[1]

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[3] INRAE, GenESI, Surgères, France

Jordi.Estelle@inrae.fr

Background

- **Intestinal microbiota**
  - **Associated with phenotypes of interest for livestock production**:
    - Feed efficiency, health, robusness, growth, welfare, ...
  - Significant **impact of host genetics** on composition and diversity :
    - Heritability estimates & GWAS
    - Causal mutations !

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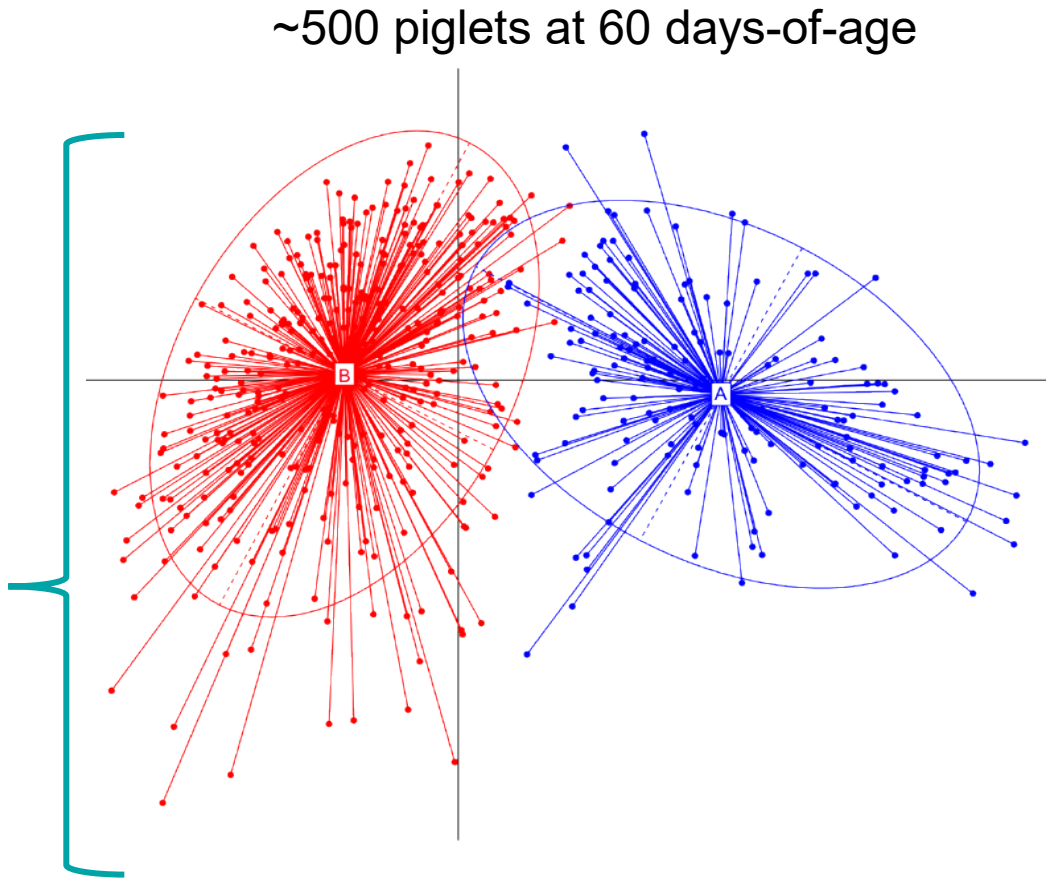
  - Significant **impact of host genetics** on composition and diversity :
    - Heritability estimates & GWAS
    - Causal mutations !
  - The **pig faecal microbial ecosystem** is organised into **two major enterotypes**
    - **Enterotype PM :** characterised by *Prevotella* & *Mitsuokella* abundance
    - **Enterotype RT** : characterised by *Ruminococcus* & *Treponema* abundance



Ramayo-Caldas et al. 2016. ISME Journal

Enterowhat?

- Ecotype = a group of organisms that is adapted to a specific environment.

Ecotype A

Ecotype B

Our research question :

It is possible to use host genetic selection to influence faecal microbiota composition?

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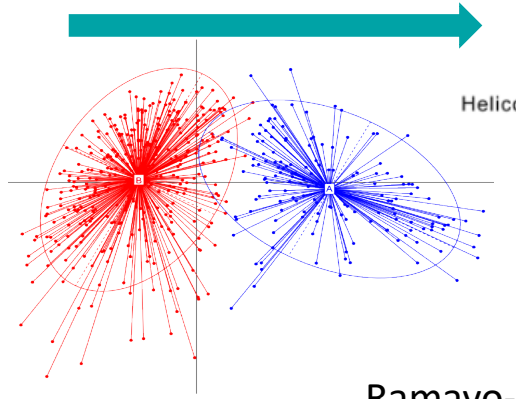
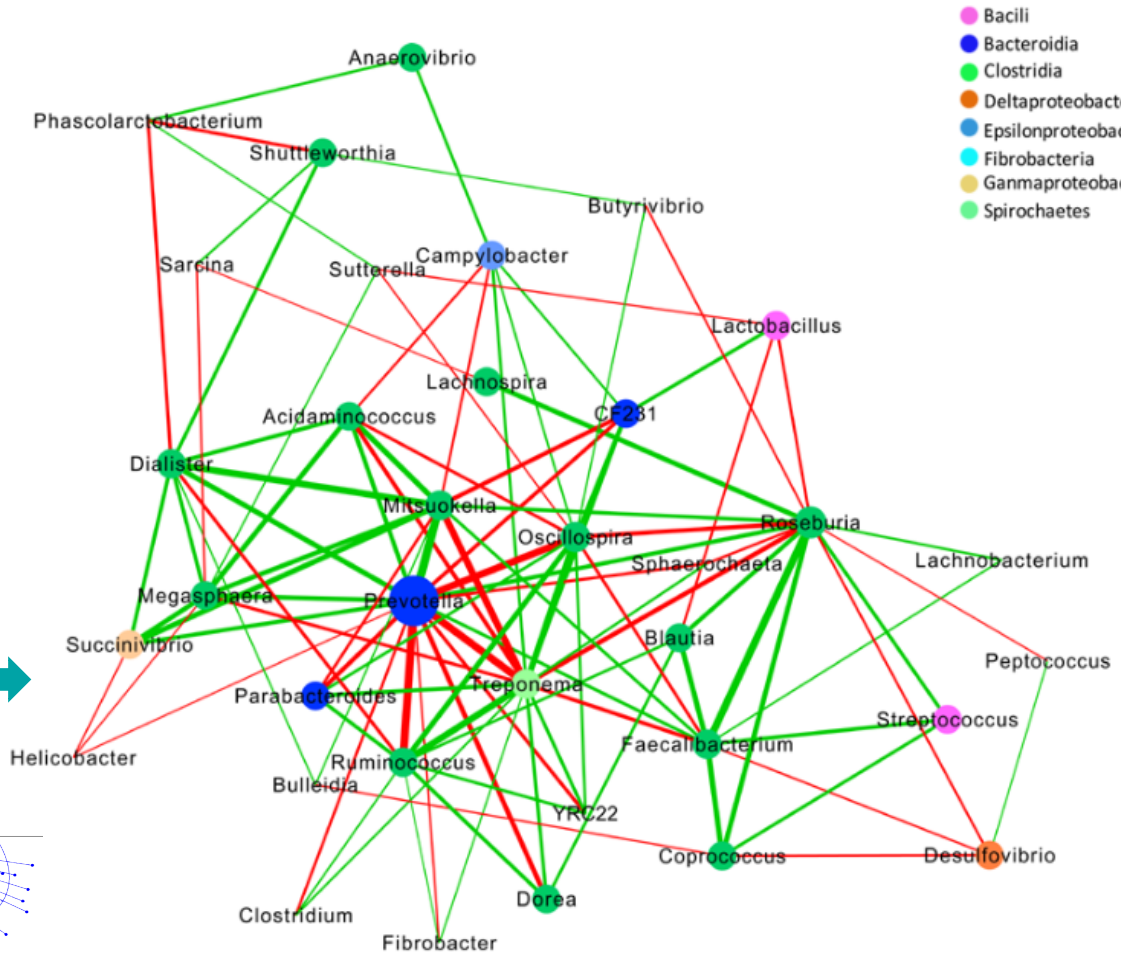
Key driving taxa from network interactions?





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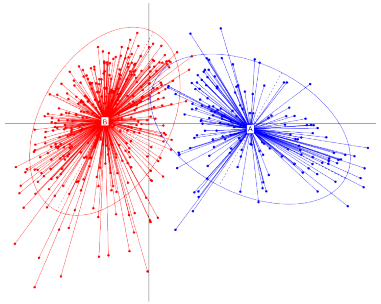
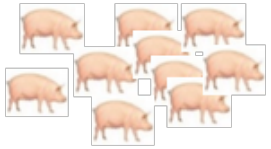
A divergent selection experiment for pig enterotypes

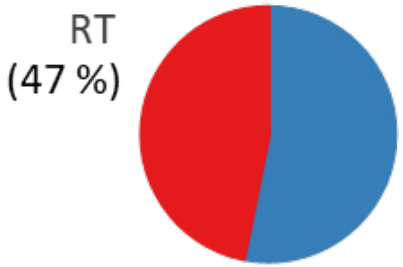


♂ x ♀ ⇨ **Generation G0**

N = 30 N = 30



316 piglets from 30 litters



Line HPM
direct selection on *Prevotella* and *Mitsuokella* at D60

Pigs with enterotype PM

♂ x ♀

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Pigs with enterotype RT

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HPM vs HRT lines

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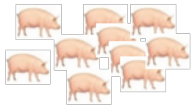

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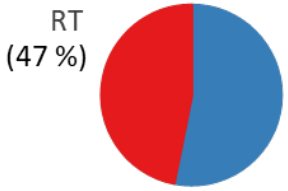

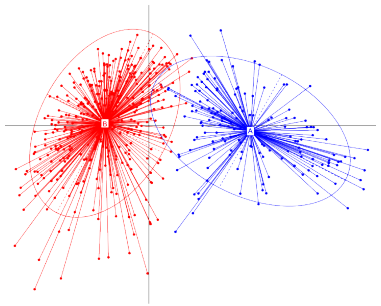

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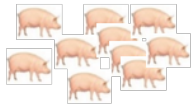
HPM-G1



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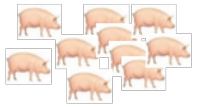
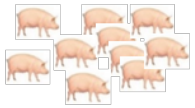


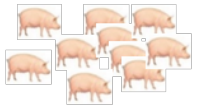
N = 139

HRT-G1

HPM-G2



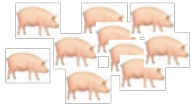
N = 114



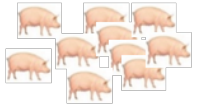
N = 114

HRT-G2

HPM-G3



N = 126



N = 125

HRT-G3

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HPM vs HRT

- **Four taxa, but global impact on microbiota ecosystem !**

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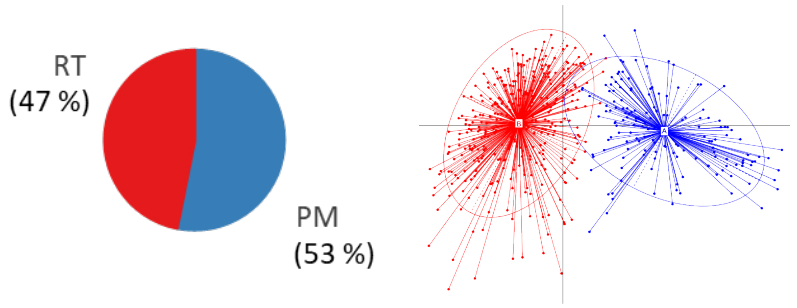

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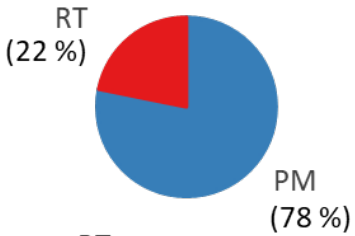

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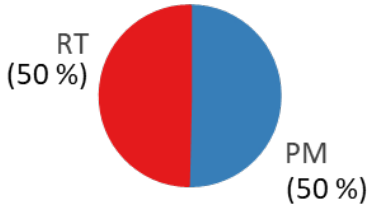
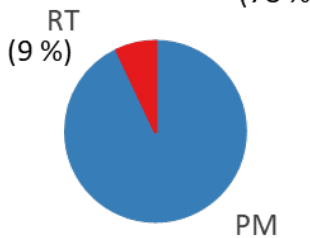
HRT-G1



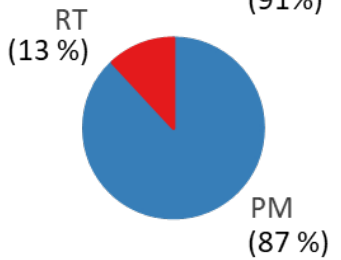


HPM-G2

N = 114

N = 114

HRT-G2



HPM-G3

N = 126

N = 125

HRT-G3

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HPM vs HRT

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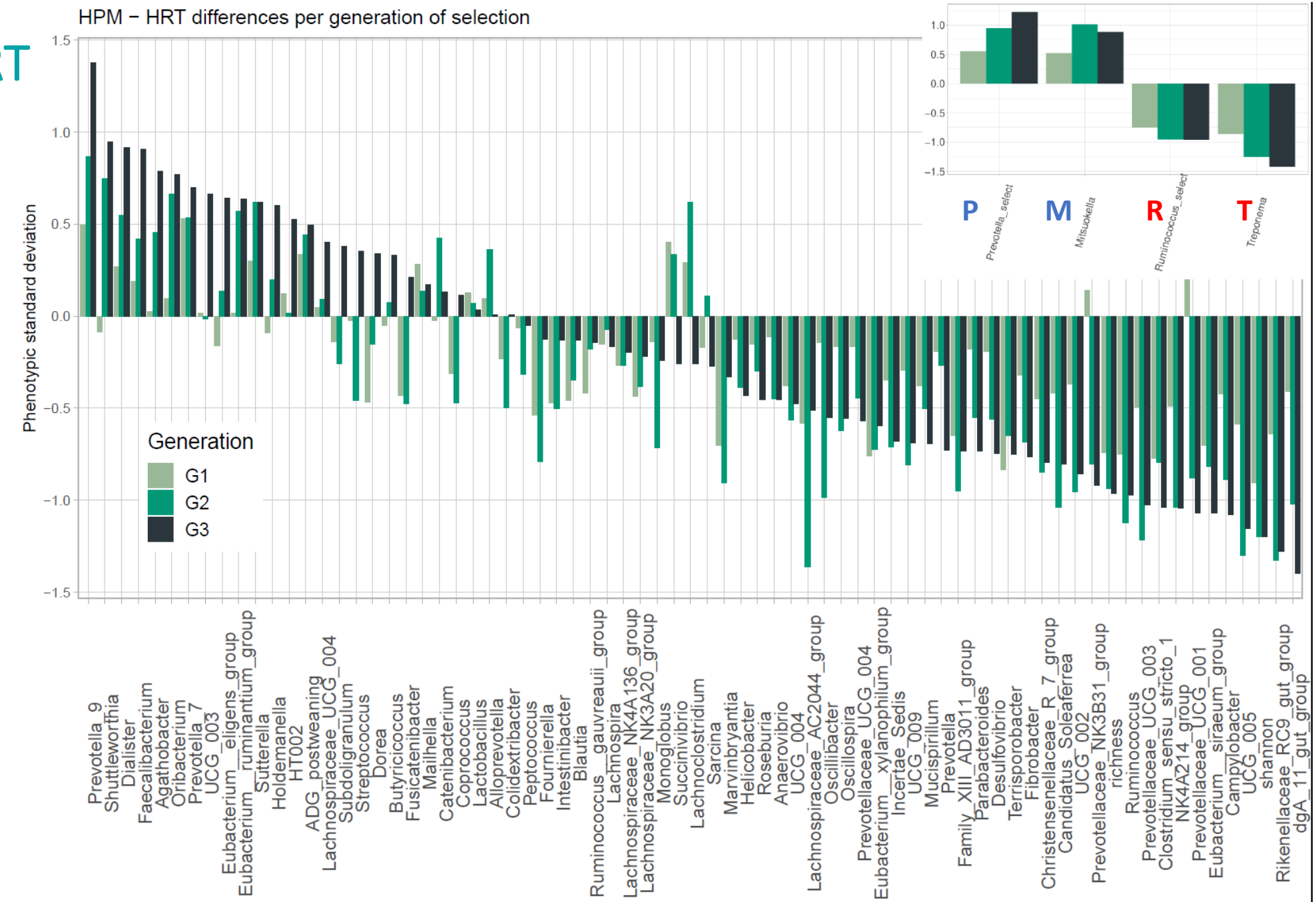

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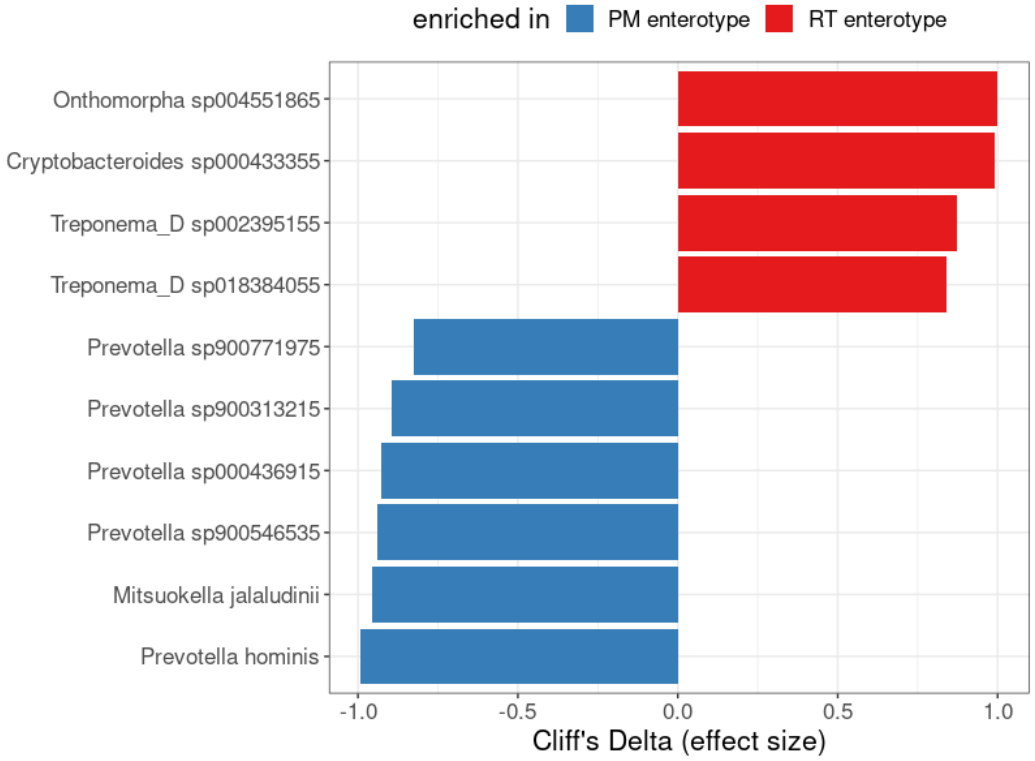
HPM vs HRT lines

- Whole metagenome sequencing on G0 (n= 15 *vs.* 15) : who are they and what are they doing ?

Metagenomic species :



KEGG Ortologs :

	PM enterotype	RT enterotype
KOs	starch degradation	general nucleoside transport
	polysaccharide metabolism	peptide/nickel transport system
Pathways (Top-4)	Biosynthesis of amino acids	ABC transporters
	Phenylalanine, tyrosine and tryptophan biosynthesis	Carbon metabolism
	2-Oxocarboxylic acid metabolism	Methane metabolism
	Valine, leucine and isoleucine biosynthesis	Valine, leucine and isoleucine degradation

HPM animals have better growth (ADG) at 60 days of age !

Our research questions :

It is possible to use host genetic selection to influence faecal microbiota compositio

Larzul *et al. Microbiome* (2024) 12:116
https://doi.org/10.1186/s40168-024-01827-8

Microbiome

RESEARCH Open Access

Driving gut microbiota enterotypes through host genetics

Catherine Larzul[1*†], Jordi Estellé[2*†], Marion Borey[2], Fany Blanc[2], Gaëtan Lemonnier[2], Yvon Billon[3], Mamadou Gabou Thiam[4], Benoît Quinquis[4], Nathalie Galleron[4], Deborah Jardet[2], Jérôme Lecardonnel[2], Florian Plaza Oñate[4] and Claire Rogel-Gaillard[2*]

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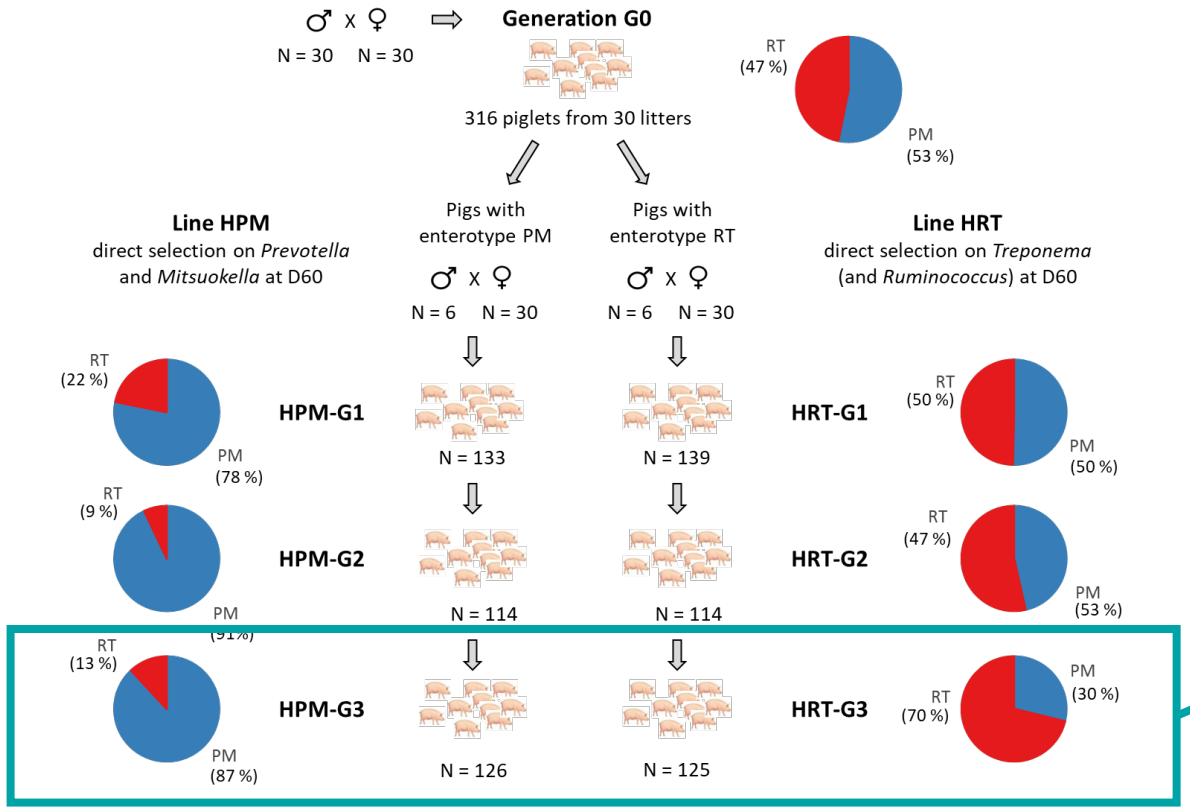
→ **ADG** → 

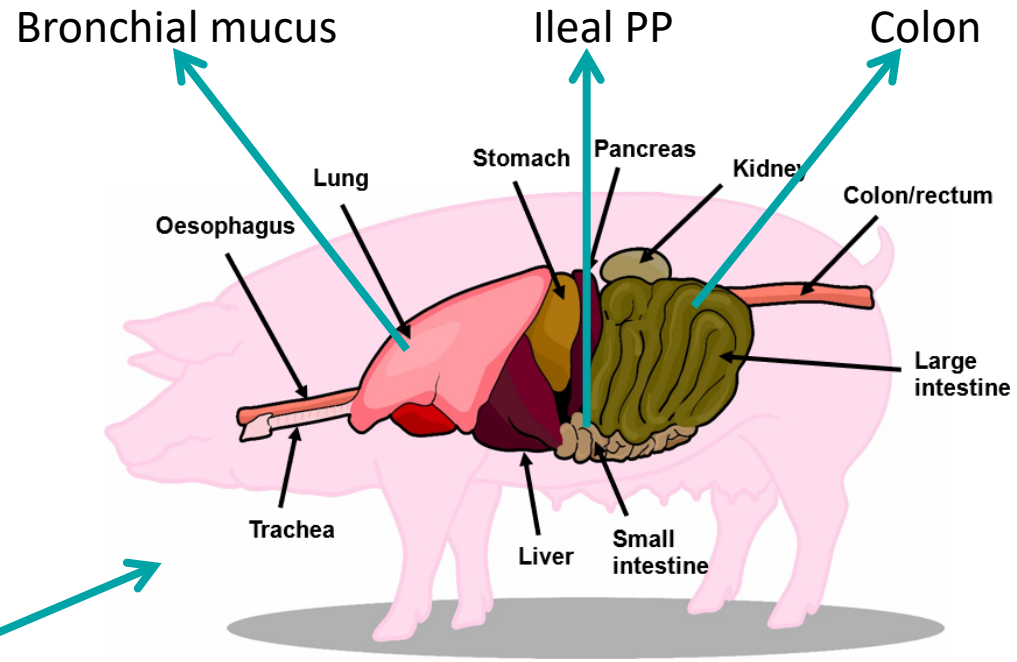
Other microbiota?

Other traits?

At G3 : differences in gut and respiratory microbiota ?

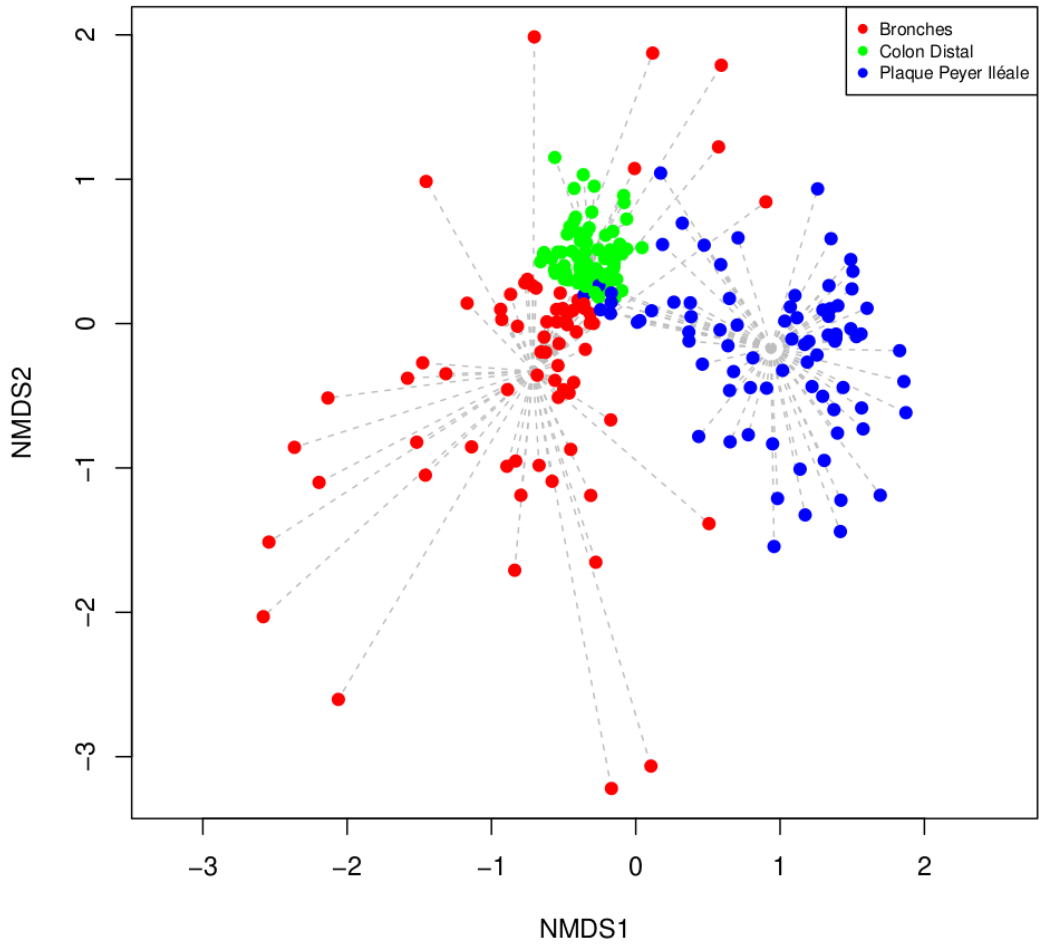


16S microbiota analysis on :



N = 40 HPM vs. 40 HRT

At G3 : differences in gut and respiratory microbiota ?



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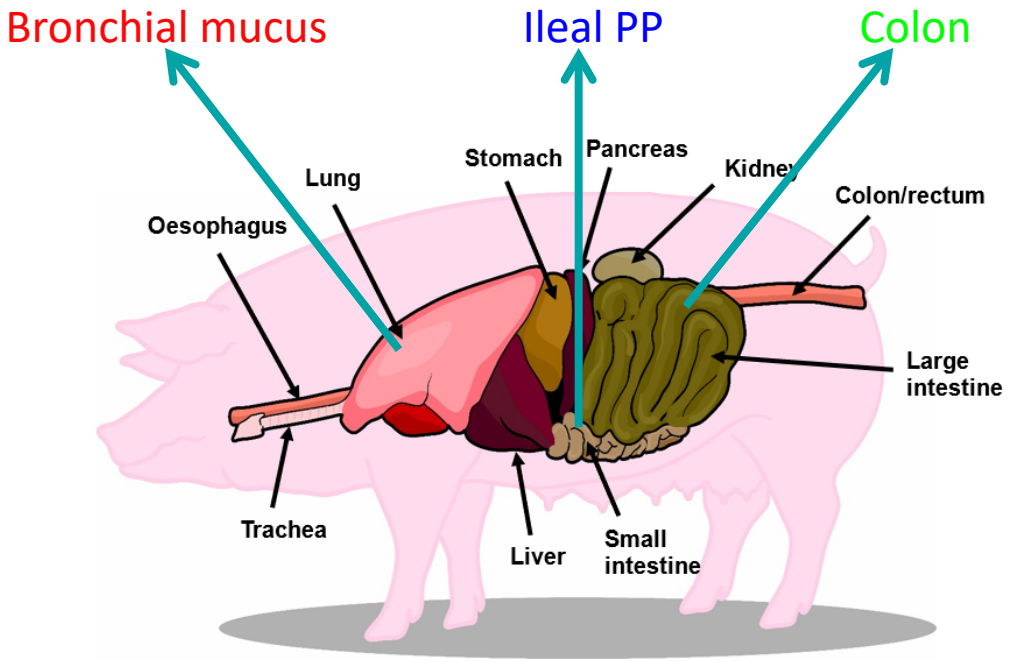

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16S sequencing
DADA2 + SILVA
Vegan NMDS

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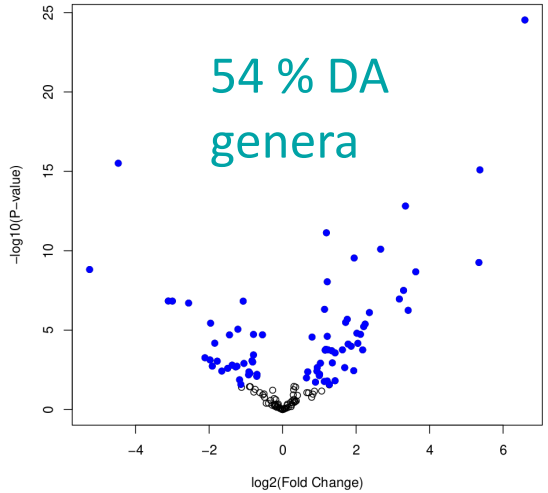
At G3 : differences HPM vs. HRT in gut and respiratory microbiota ?



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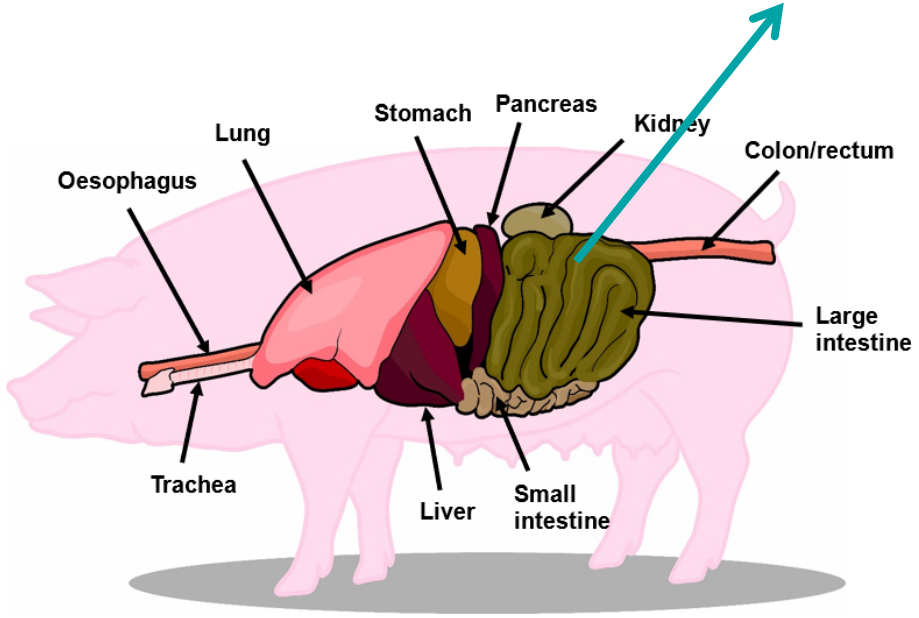

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- Strong microbiota differences between lines at colon
  - Differences in the expected direction as HPM vs. HRT

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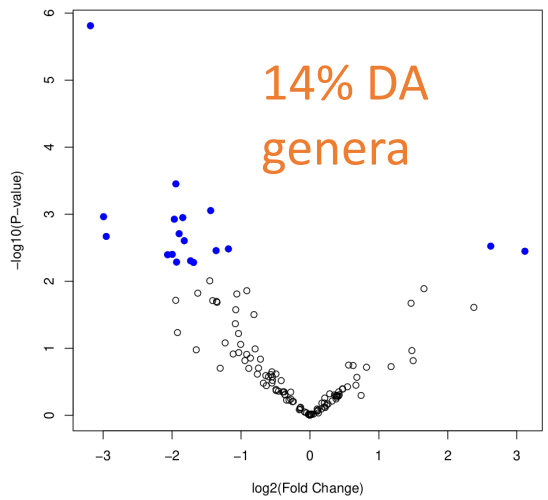

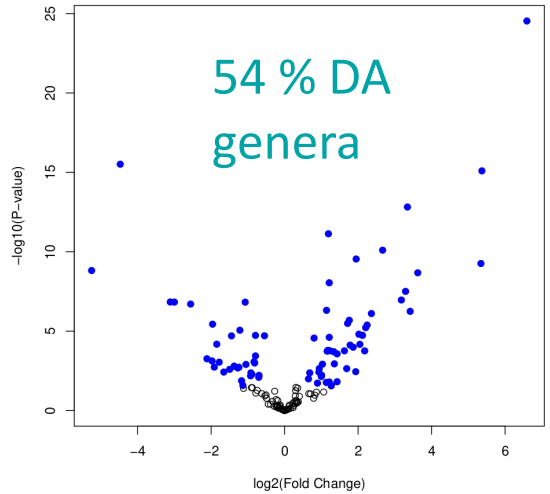

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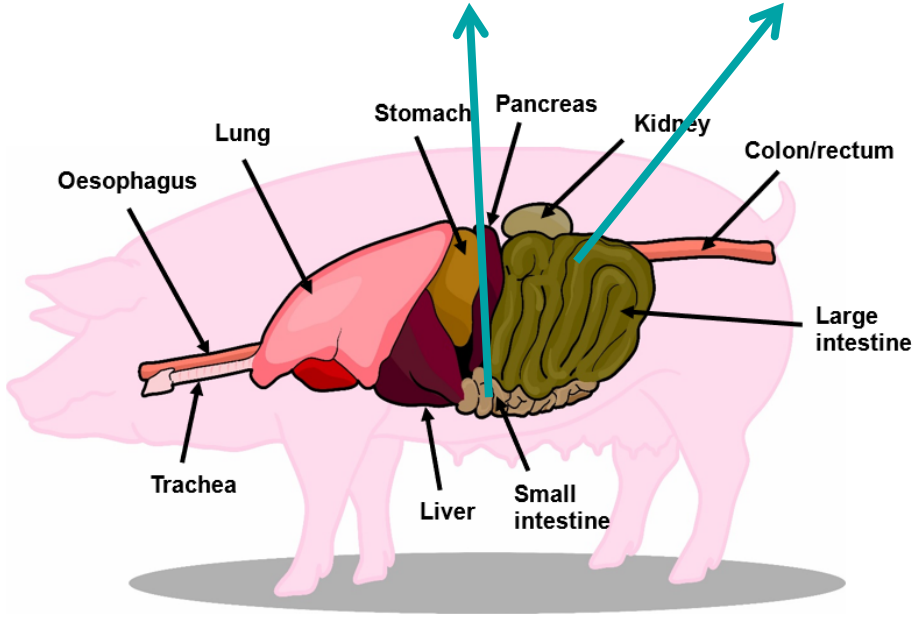

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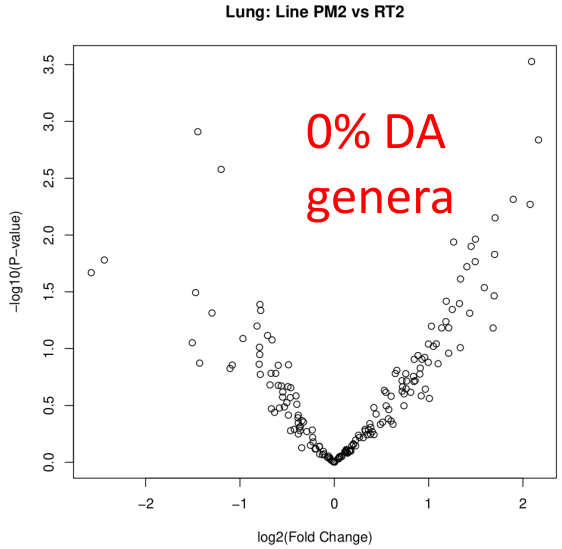

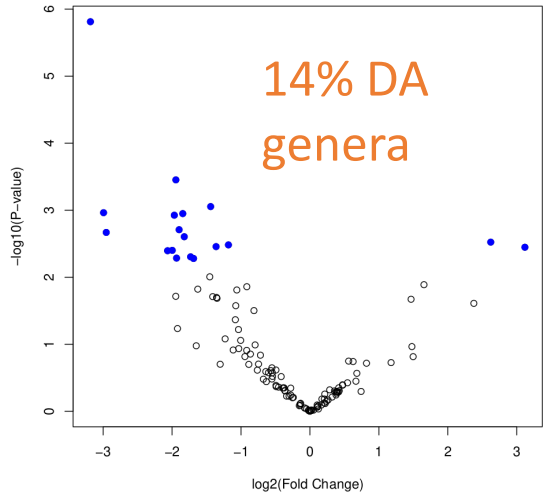

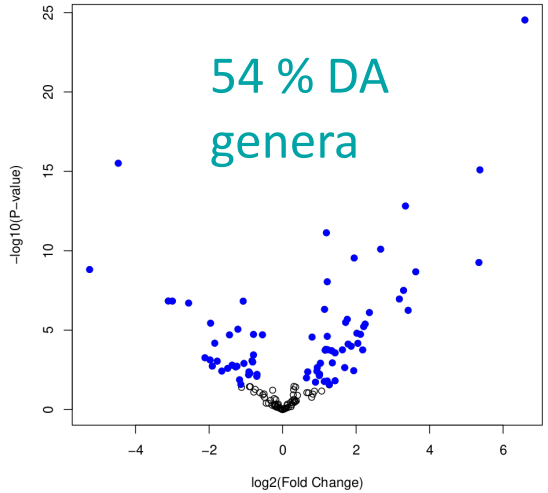

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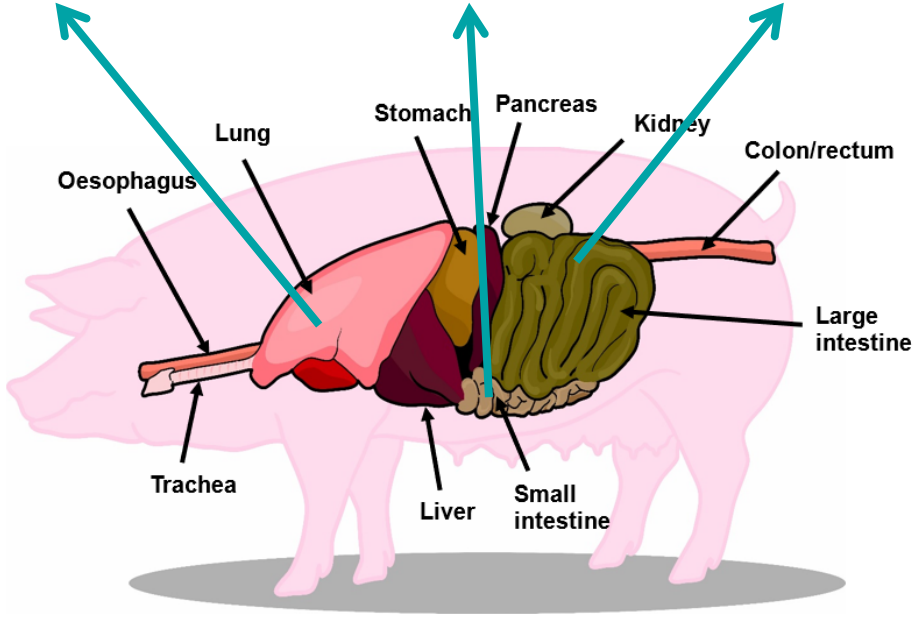

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- No differences found in respiratory microbiota!

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It is possible to use host genetic selection to influence faecal microbiota composition?

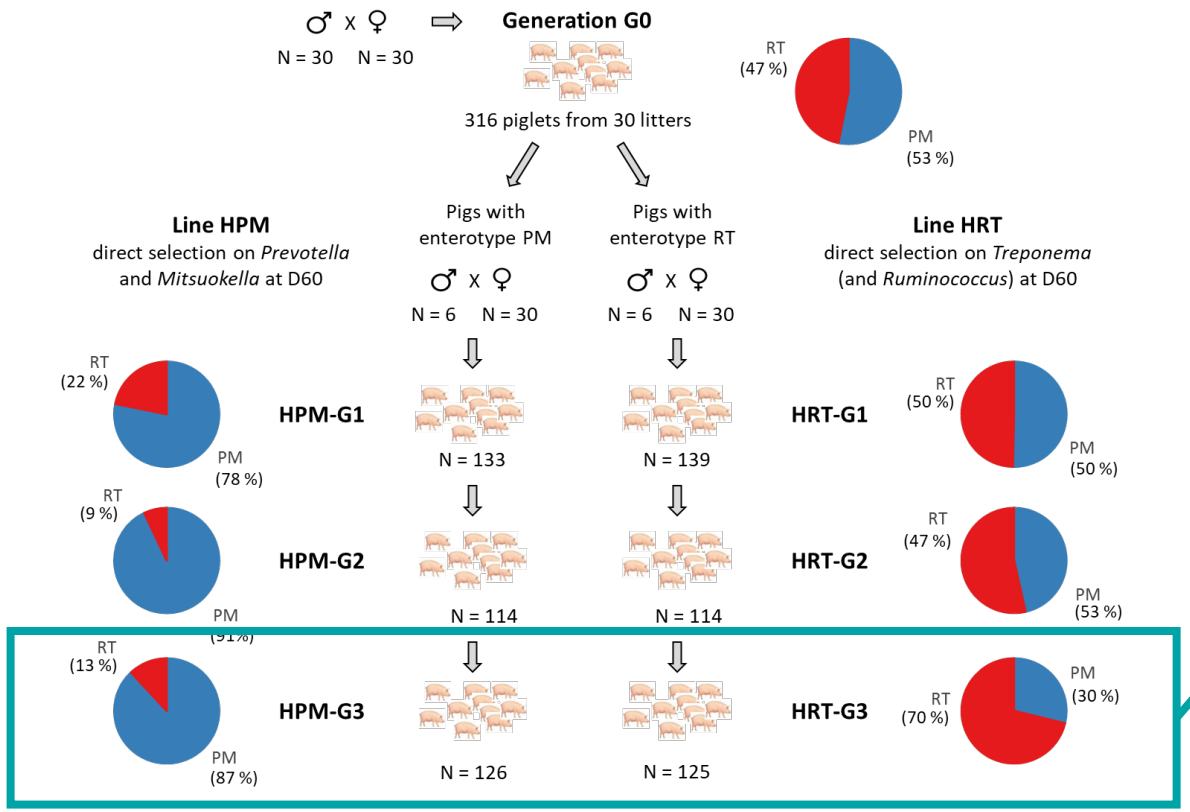
Would this selection have an impact on other ecosystems and also on host traits?

→ **ADG** → 

Other **digestive** microbiotas 

Other traits?

At G3 : differences in blood immune response traits ?



- Blood cell subpopulations by flow cytometry
- Plasma coloration
- Total IgG, IgA and IgM
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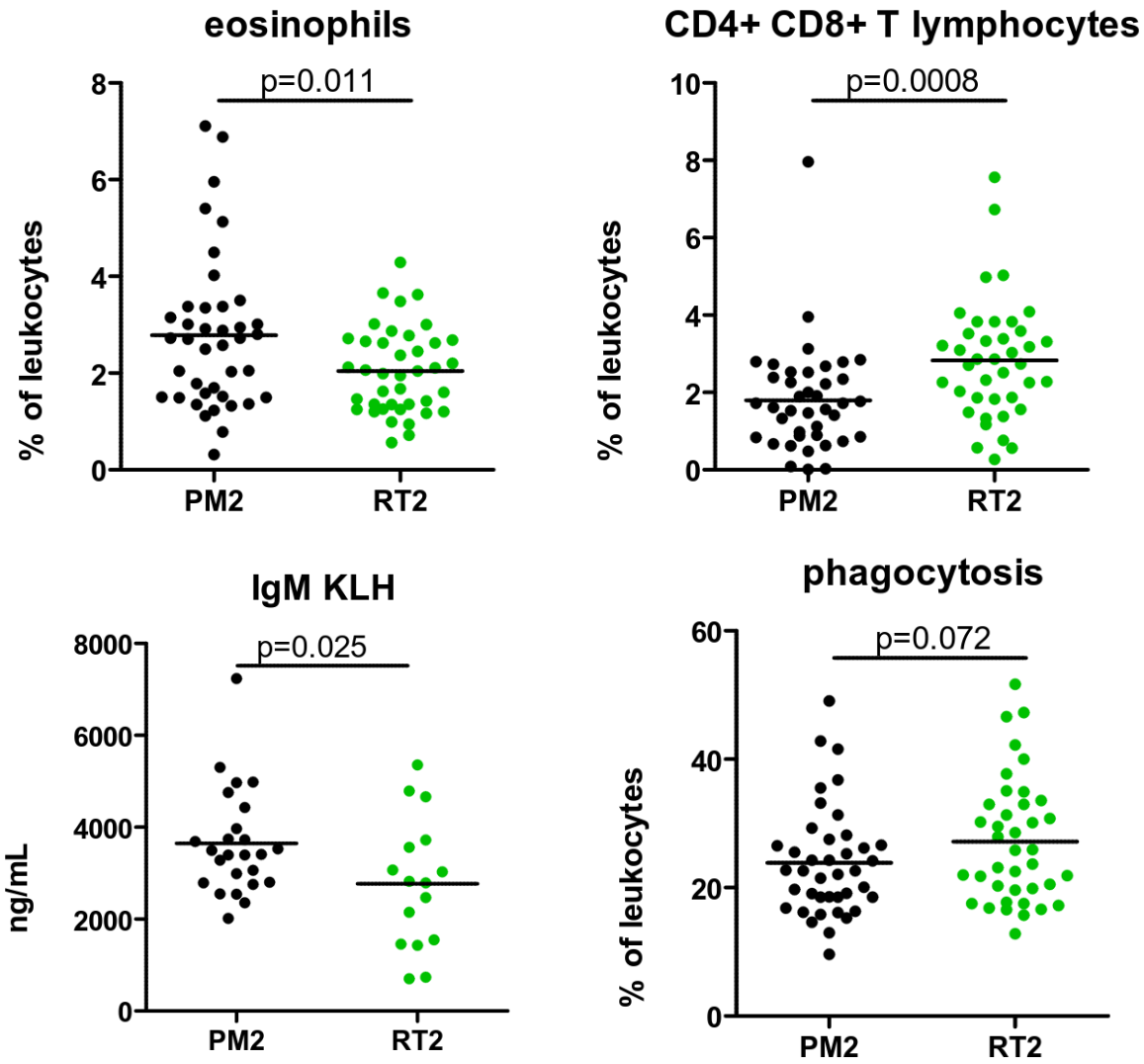

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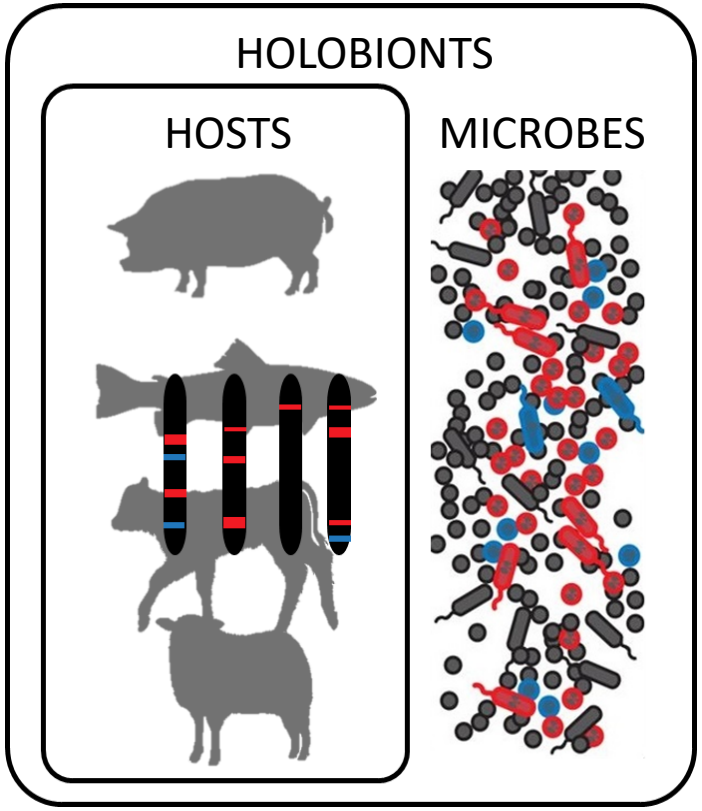
Conclusions & Perspectives

- Hosts or microbes? **Holobionts !**



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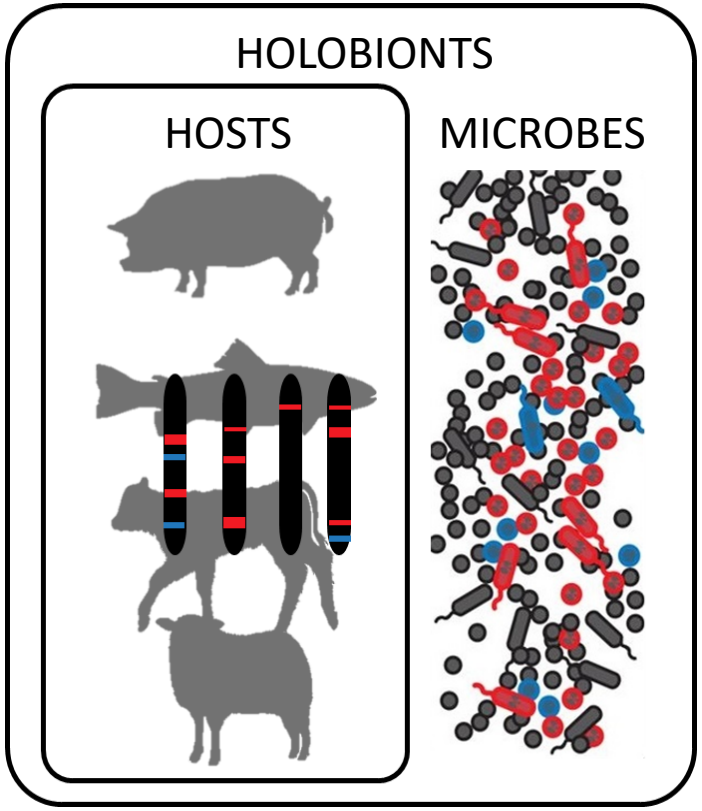

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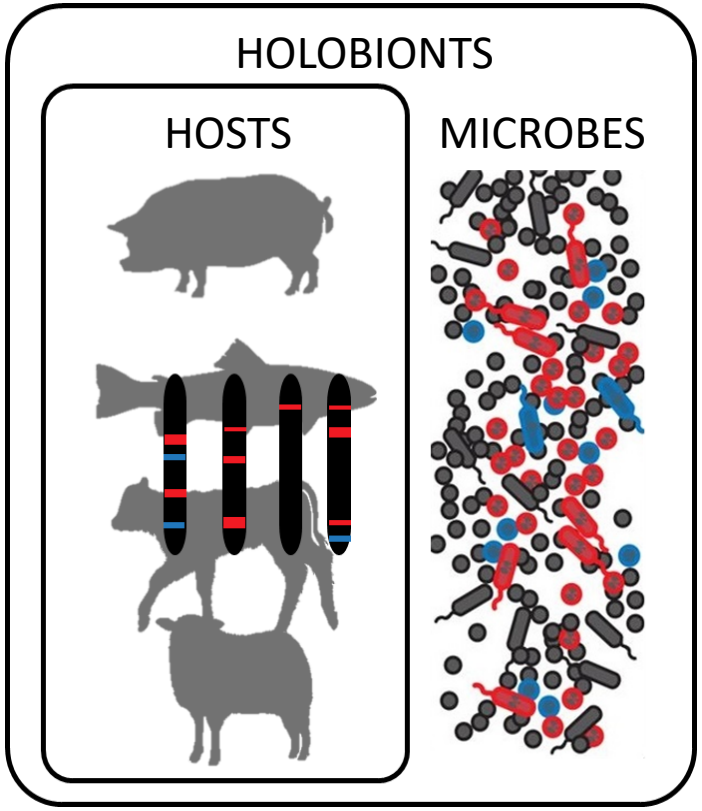

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- **Further steps :** selection on microbiota is possible but... **could it be useful for improving animal health in pig production?**

APP DGA
HOLOFLUX

HOLOBIONTS
(PEPR Agroécologie et Numérique)

SOA18 (007-A1)

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THANKS!

- GABI, équipe Génétique Microbiote Santé : J Estellé, G Lemonnier, M Borey, N Bruneau, F Blanc, C Rogel-Gaillard, **et al.**
- GABI, Plateforme @BRIDGe : D Jardet, B Houel, K Alexis-Alphonse, J Lecardonnel, MN Rossignol
- GenPhySE, équipe ModGen : C Larzul
- MGP, équipe InfoBIoStat : F Plaza-Onate et al.
- UE GenESI, équipe Porcs : C Niort, Y Billon, **et al.**