Sélection animale et microbiote intestinal

Claire Rogel-Gaillard

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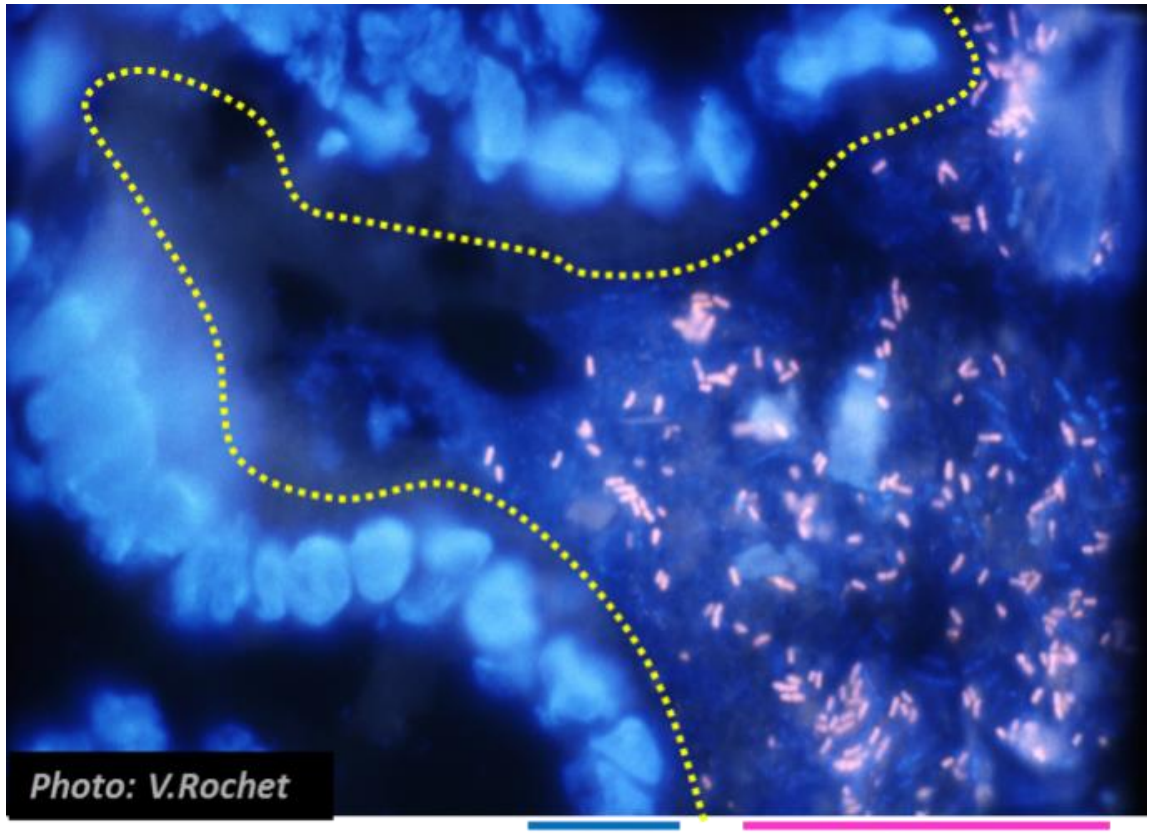
LE MICROBIOTE INTESTINAL : DE QUOI PARLE-T-ON ?



Epithélium intestinal
(animal - hôte)

⇔

Microbiote intestinal
(écosystème microbien symbiotique)

Un dialogue permanent

- Ensemble des communautés microbiennes qui résident et se multiplient dans le tube digestif de leur hôte : bactéries (en majorité), archées (méthanogènes), virus + protozoaires, champignons, helminthes
- Environ 50 000 milliards de microbes (~ nb de cellules dans le corps humain)
- Quelques centaines d'espèces bactériennes par individu
- Environ 600 000 gènes microbiens vs 23 000 gènes dans le génome d'un mammifère hôte (25:1)
- Transfert horizontal de gènes bactériens

LE MICROBIOTE INTESTINAL : QUEL INTÉRÊT EN ÉLEVAGE ?

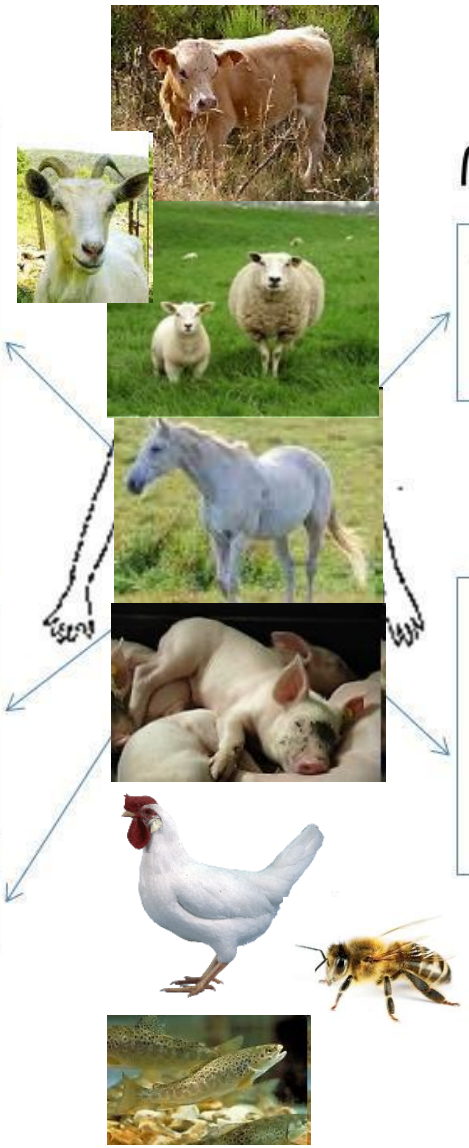
Emissions de méthane

Efficacité alimentaire

Fonctions trophiques et métaboliques
- Modulation de la dépense énergétique
- Accessibilité des nutriments
- Production d'acides gras à chaînes courtes
- Régulation de l'adiposité
- Production de vitamines
- Dégradation des fibres alimentaires

Fonction intestinale
- Régénération épithéliale
- Motilité de l'intestin
- Limitation de la perméabilité de l'intestin

Angiogénèse intestinale



Bien-être, comportement

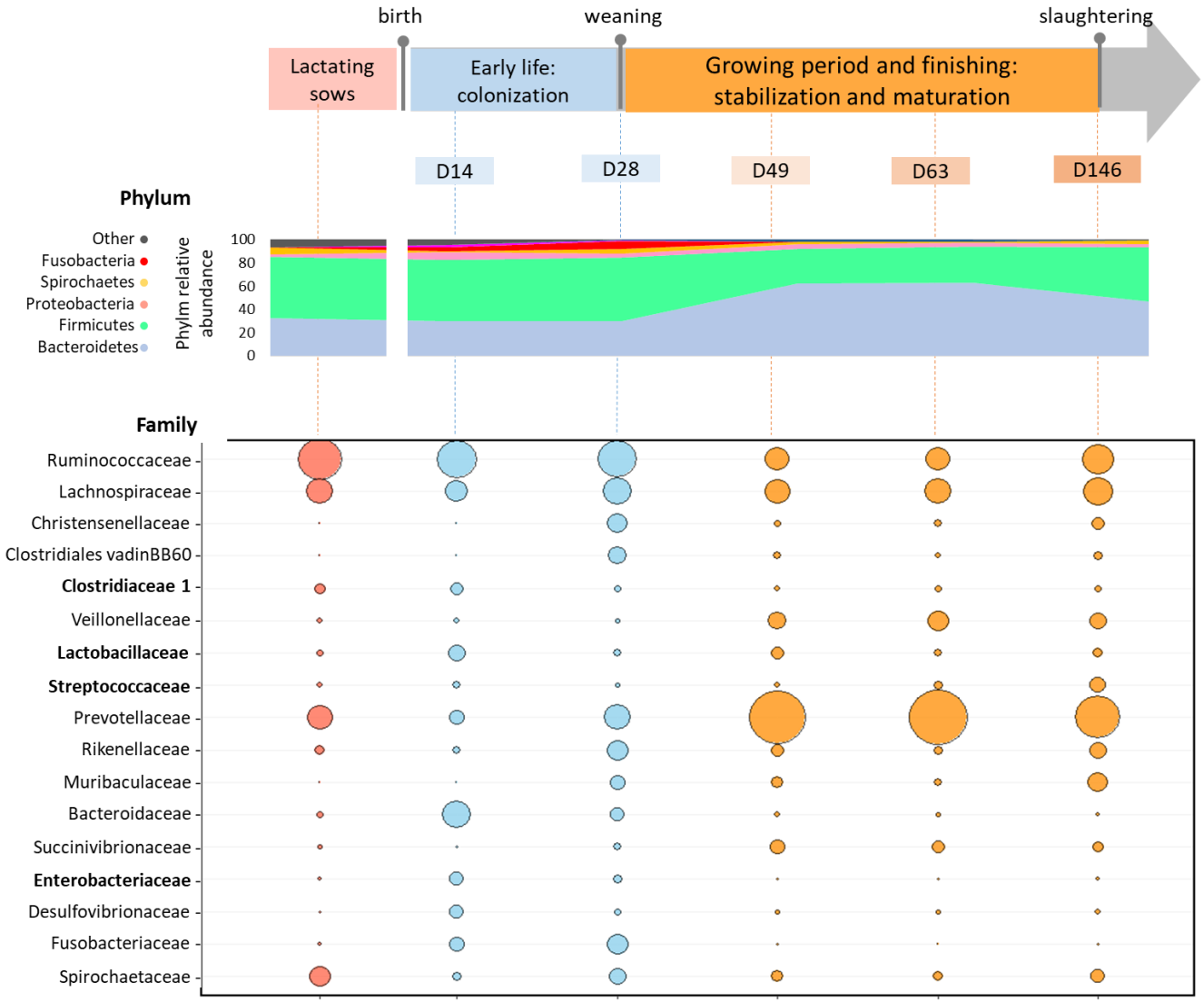
Axe microbiote-intestin-cerveau
- Anxiété
- Perception de la douleur
- Comportement

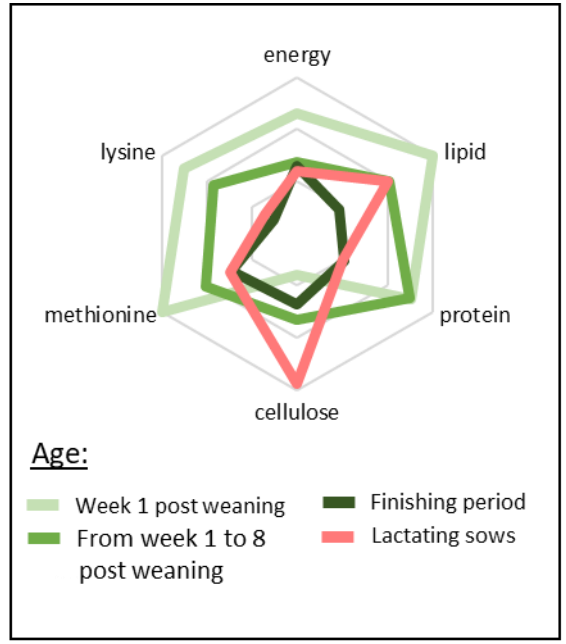
Fonction immunitaire et protection contre les pathogènes
- Maturation des tissus lymphoïdes associés
- Immunité des muqueuses et systémique
- Homéostasie immunitaire

Capacité immune, Résistance aux maladies

Adapté de Estelle et al., 2016. JRP 48, 267-272

LE MICROBIOTE INTESTINAL :
UN ÉCOSYSTÈME DYNAMIQUE AU COURS DE LA VIE DE SON HÔTE





Abondance relative des familles

- > 0.1%
- > 2%
- > 10%
- > 25%
- > 50%

Borey et al., 2022, Understanding the development of the gut microbiome in pigs: an overview. ebook, Burleigh Dodds editor

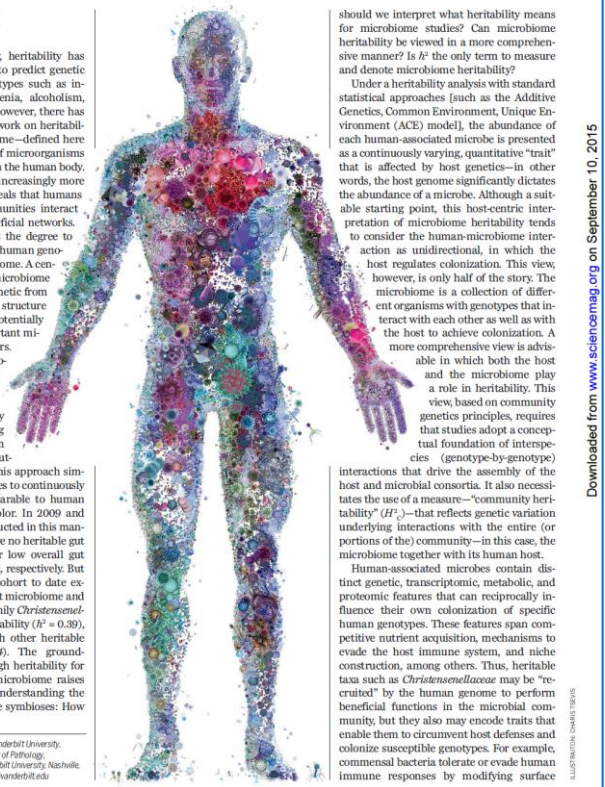
QUI FAIT QUOI ET QUAND ?

MICROBIOME

Rethinking heritability of the microbiome

How should microbiome heritability be measured and interpreted?

By Edward J. van Opstal[1] and Seth R. Bordenstein[1,2]



For almost a century, heritability has been routinely used to predict genetic influences on phenotypes such as intelligence, schizophrenia, alcoholism, and depression (*1*). However, there has been relatively little work on heritability of the human microbiome—defined here as the number and types of microorganisms and viruses present in or on the human body. This question has become increasingly more interesting as research reveals that humans and their microbial communities interact in complex and often beneficial networks. An underlying question is the degree to which environment versus human genotype influences the microbiome. A central goal of quantifying microbiome heritability is to discern genetic from environmental factors that structure the microbiome and to potentially identify functionally important microbial community members.

Twin-based studies provide one method for quantifying heritability (h^2) of microbial taxa. In such analyses, heritability is measured by comparing variation in microbial taxon abundances that is attributable to human genetics. This approach simplifies microbial abundances to continuously varying phenotypes, comparable to human height, weight, and eye color. In 2009 and 2012, studies of twins conducted in this manner concluded that there are no heritable gut microbial members (*2*), or low overall gut microbiome heritability (*3*), respectively. But in 2014, the largest twin cohort to date examined members of the gut microbiome and found that the bacterial family *Christensenellaceae* has the highest heritability (h^2 = 0.39), and associates closely with other heritable gut bacterial families (*4*). The groundbreaking discovery of a high heritability for members of the human microbiome raises specific questions about understanding the genetics of human-microbe symbioses: How should we interpret what heritability means for microbiome studies? Can microbiome heritability be viewed in a more comprehensive manner? Is h^2 the only term to measure and denote microbiome heritability?

Under a heritability analysis with standard statistical approaches [such as the Additive Genetics, Common Environment, Unique Environment (ACE) model], the abundance of each human-associated microbe is presented as a continuously varying, quantitative "trait" that is affected by host genetics—in other words, the host genome significantly dictates the abundance of a microbe. Although a suitable starting point, this host-centric interpretation of microbiome heritability tends to consider the human-microbiome interaction as unidirectional, in which the host regulates colonization. This view, however, is only half of the story. The microbiome is a collection of different organisms with genotypes that interact with each other as well as with the host to achieve colonization. A more comprehensive view is advisable in which both the host and the microbiome play a role in heritability. This view, based on community genetics principles, requires that studies adopt a conceptual foundation of interspecies (genotype-by-genotype) interactions that drive the assembly of the host and microbial consortia. It also necessitates the use of a measure—"community heritability" (H^2_c)—that reflects genetic variation underlying interactions with the entire (or portions of the) community—in this case, the microbiome together with its human host.

Human-associated microbes contain distinct genetic, transcriptomic, metabolic, and proteomic features that can reciprocally influence their own colonization of specific human genotypes. These features span competitive nutrient acquisition, mechanisms to evade the host immune system, and niche construction, among others. Thus, heritable taxa such as *Christensenellaceae* may be "recruited" by the human genome to perform beneficial functions in the microbial community, but they also may encode traits that enable them to circumvent host defenses and colonize susceptible genotypes. For example, commensal bacteria tolerate or evade human immune responses by modifying surface

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Science, 2015

Human Genetics Shape the Gut Microbiome

Cell, 2014

Julia K. Goodrich,[1,2] Jillian L. Waters,[1,2] Angela C. Poole,[1,2] Jessica L. Sutter,[1,2] Omry Koren,[1,2,7] Ran Blekhman,[1,8] Michelle Beaumont,[3] William Van Treuren,[4] Rob Knight,[4,5,6] Jordana T. Bell,[3] Timothy D. Spector,[3] Andrew G. Clark,[1] and Ruth E. Ley[1,2,*]

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*Correspondence: rel222@cornell.edu
http://dx.doi.org/10.1016/j.cell.2014.09.053

Environment dominates over host genetics in shaping human gut microbiota

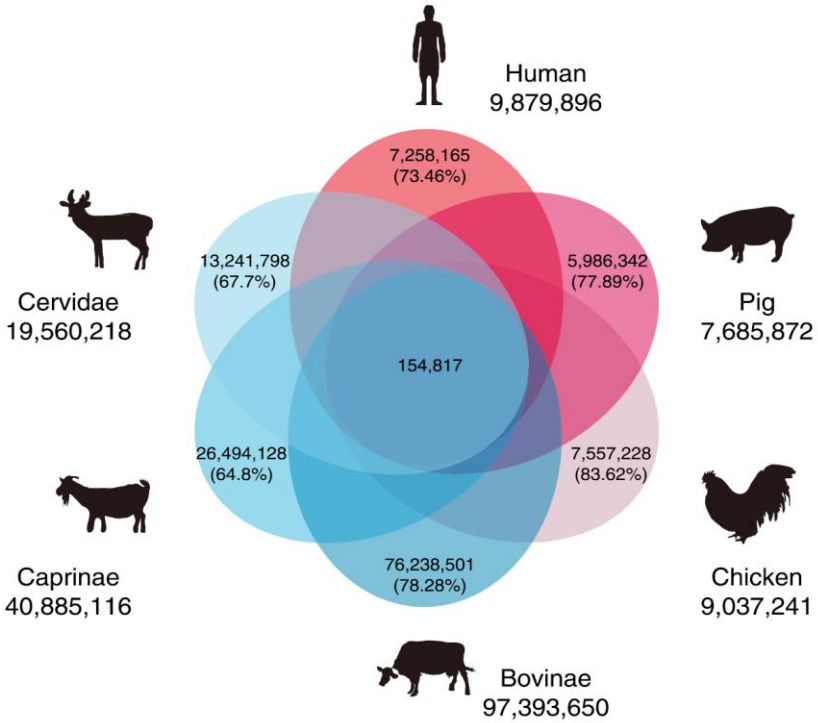
Nature, 2018

Daphna Rothschild[1,2]*, Omer Weissbrod[1,2]*, Elad Barkan[1,2]*, Alexander Kurilshikov[3], Tal Korem[1,2], David Zeevi[1,2], Paul I. Costea[1,2], Anastasia Godneva[1,2], Iris N. Kalka[1,2], Noam Bar[1,2], Smadar Shilo[1,2], Dar Lador[1,2], Arnau Vich Vila[3,4], Niv Zmora[5,6,7], Meirav Pevsner-Fischer[5], David Israeli[8], Noa Kosower[1,2], Gal Malka[1,2], Bat Chen Wolf[1,2], Tali Avnit-Sagi[1,2], Maya Lotan-Pompan[1,2], Adina Weinberger[1,2], Zamir Halpern[7,9], Shai Carmi[10], Jingyuan Fu[3,11], Cisca Wijmenga[3,12], Alexandra Zhernakova[3], Eran Elinav[5]§ & Eran Segal[1,2]§

DIVERSITÉ DU MICROBIOTE : INTER ET INTRA ESPÈCES ANIMALES

Comparaison des catalogues de gènes du microbiote intestinal entre espèces :

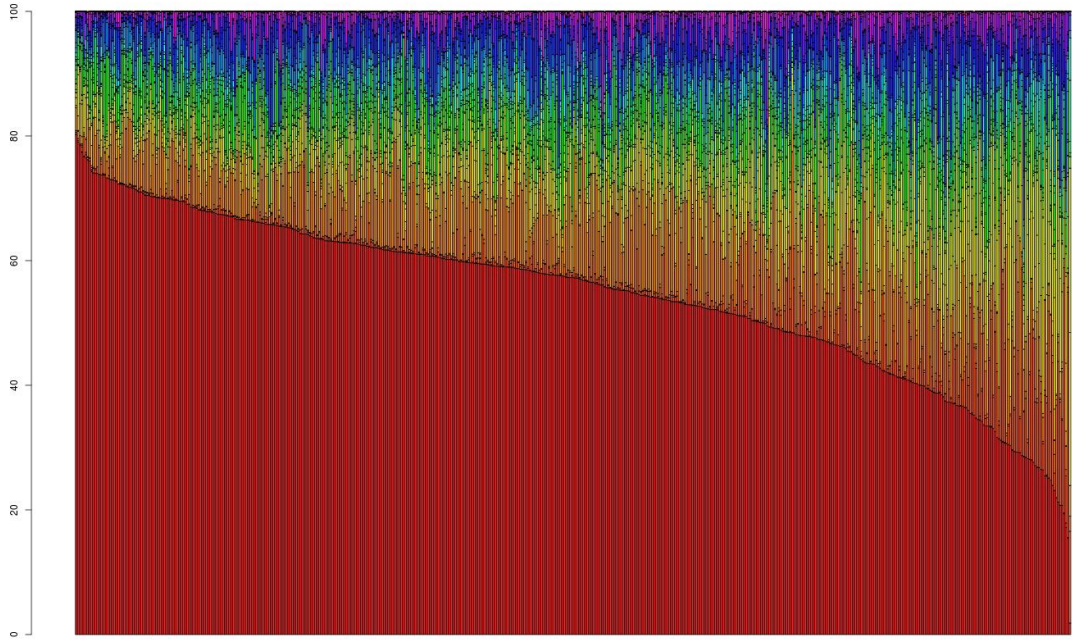
- peu de gènes en commun
- co-évolution hôte-microbiote
- Influence de la génétique de l'hôte

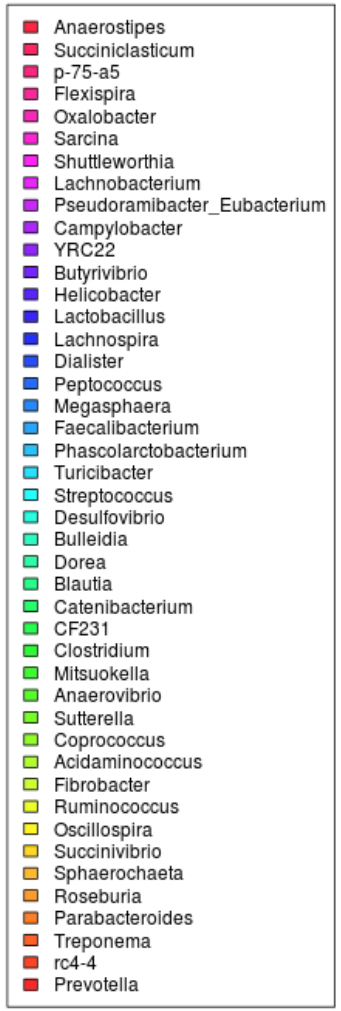


Xie et al., Microbiome, 2021

Variabilité inter-individuelle du microbiote intestinal

- Quel déterminisme ?
- Liens avec des caractères d'intérêt en élevage ?
- Quel usage ?





518 porcelets de race Large White à 60 jours d'âge, dans un environnement contrôlé et partagé

Ramayo-Caldas et al., 2016, ISME J

LA "MICROBIABILITÉ" = m^2

m^2 : % de la variance phénotypique expliquée par la variabilité du microbiote

OPEN ACCESS Freely available online

PLOS ONE

Metagenomic Predictions: From Microbiome to Complex Health and Environmental Phenotypes in Humans and Cattle

PLOSOne, 2013

Elizabeth M. Ross[1,2,3]*, Peter J. Moate[4], Leah C. Marett[4], Ben G. Cocks[1,2,3], Ben J. Hayes[1,2,3]

Predicting Growth and Carcass Traits in Swine Using Microbiome Data and Machine Learning Algorithms

Sci Reports, 2019

Christian Maltecca[1], Duc Lu[1], Constantino Schillebeeckx[2], Nathan P. McNulty[2], Clint Schwab[3], Caleb Shull[3] & Francesco Tiezzi[1]

Genetics, 2017

Host Genome Influence on Gut Microbial Composition and Microbial Prediction of Complex Traits in Pigs

Amelia Camarinha-Silva,*,[1] Maria Maushammer,*,[1] Robin Wellmann,* Marius Vital,[†] Siegfried Preuss,* and Jörn Bennewitz*,[2]

*Institute of Animal Science, University of Hohenheim, 70599 Stuttgart, Germany and [†]Microbial Interactions and Processes Research Group, Helmholtz Centre for Infection Research, 38124 Braunschweig, Germany

207 truies Piétrain (Allemagne)

Table 2 Estimated microbiability (m^2) and heritability (h^2) with SE and *P*-values for DG, FC, and feed intake

Trait	m^2	SE	*P*-value	h^2	SE	*P*-value
DG	0.28	0.13	0.01	0.42	0.14	<0.01
FC	0.21	0.14	0.01	0.19	0.13	0.08
FI	0.16	0.10	0.03	0.11	0.11	0.22

$m^2 = \sigma^2_m/\sigma^2_p$, as defined by Difford *et al.* (2016).

DG: daily gain, FC: feed conversion, FI: feed intake

INFLUENCE DE LA GÉNÉTIQUE DE L'HÔTE SUR SON MICROBIOTE

Genetics, 2017

Host Genome Influence on Gut Microbial Composition and Microbial Prediction of Complex Traits in Pigs

Amelia Camarinha-Silva,*,[1] Maria Maushammer,*,[1] Robin Wellmann,* Marius Vital,[†] Siegfried Preuss,* and Jörn Bennewitz*,[2]
*Institute of Animal Science, University of Hohenheim, 70599 Stuttgart, Germany and [†]Microbial Interactions and Processes Research Group, Helmholtz Centre for Infection Research, 38124 Braunschweig, Germany

207 truies de race Piétrain (Allemagne)

Table 1 Estimated heritability (h^2) and *P*-value for the relative abundances of bacterial genera

Bacteria	h^2	SE	*P*-value[a]
Alloprevotella	0.34	0.16	0.01
Blautia	0.33	0.14	<0.01
Catenibacterium	0.39	0.16	0.01
Lactobacillus	0.34	0.16	0.02
Uncultured *Spirochaetales*	0.52	0.15	<0.01
Uncultured *Spirochaetes*	0.32	0.17	0.01
Uncultured *Succinivibrionaceae*	0.57	0.14	<0.01
Uncultured *Veillonellaceae*	0.33	0.15	0.01

[a] All *p*-values showed a FDR < 0.12.

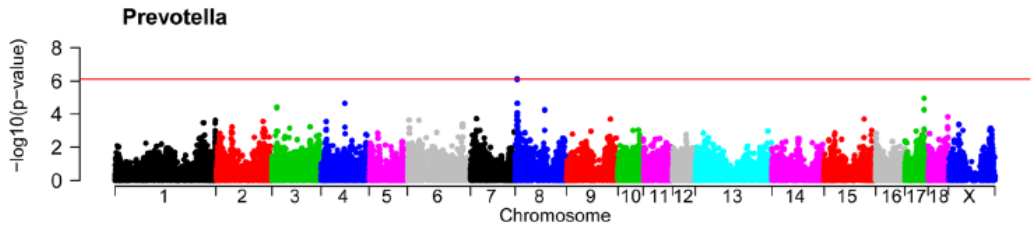
Association between the pig genome and its gut microbiota composition

Sci Report, 2019

Daniel Crespo-Piazuelo[1,2], Lourdes Migura-Garcia[3], Jordi Estellé[4], Lourdes Criado-Mesas[1], Manuel Revilla[1,2], Anna Castelló[1,2], María Muñoz[5,6], Juan M. García-Casco[5,6], Ana I. Fernández[5], Maria Ballester[3] & Josep M. Folch[1,2]

285 porcs croisés F1 (Duroc x Ibérique)
GWAS (45K SNP chip)

52 SNPs
17 régions génomiques(6 genera)
39 gènes candidats



GENÈSE DU PROJET ENTEROTYPIG : SÉLECTION DIRECTE SUR LE MICROBIOTE

1

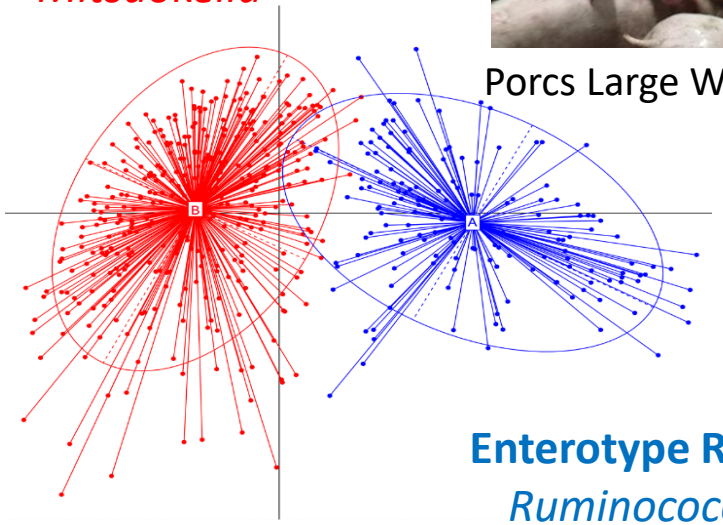
2 entérotypes chez les porcelets de 60j

Enterotype PM

Prevotella

Mitsuokella

Porcs Large White



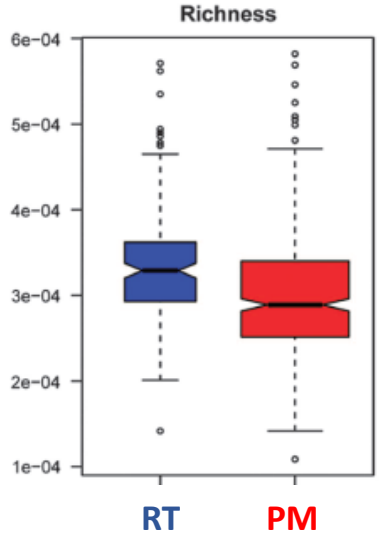
Enterotype RT

Ruminococcus

Treponema

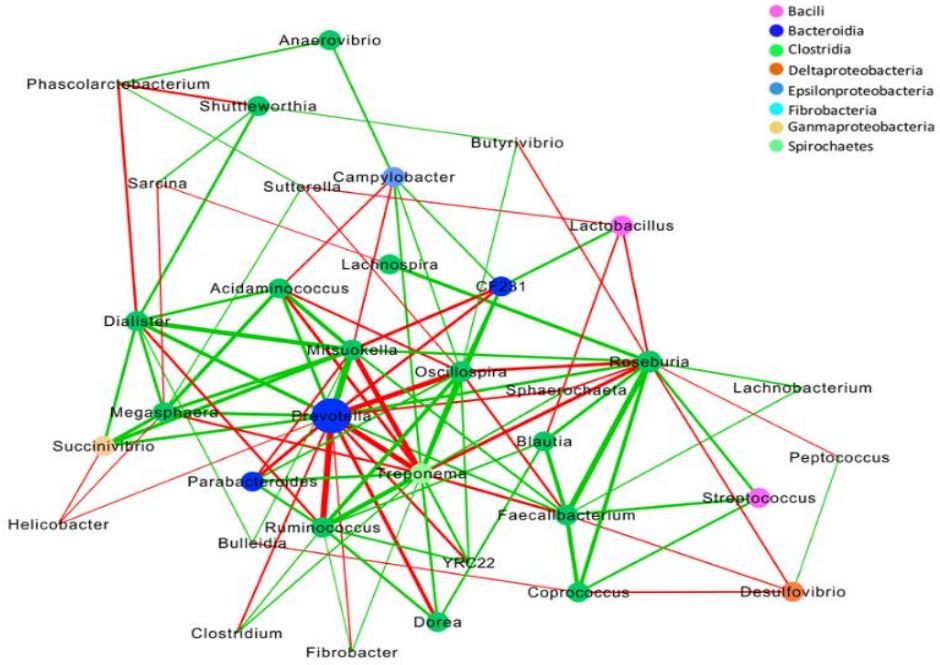
2

RT plus diversifié que PM



3

Les entérotypes sont des écosystèmes fonctionnels



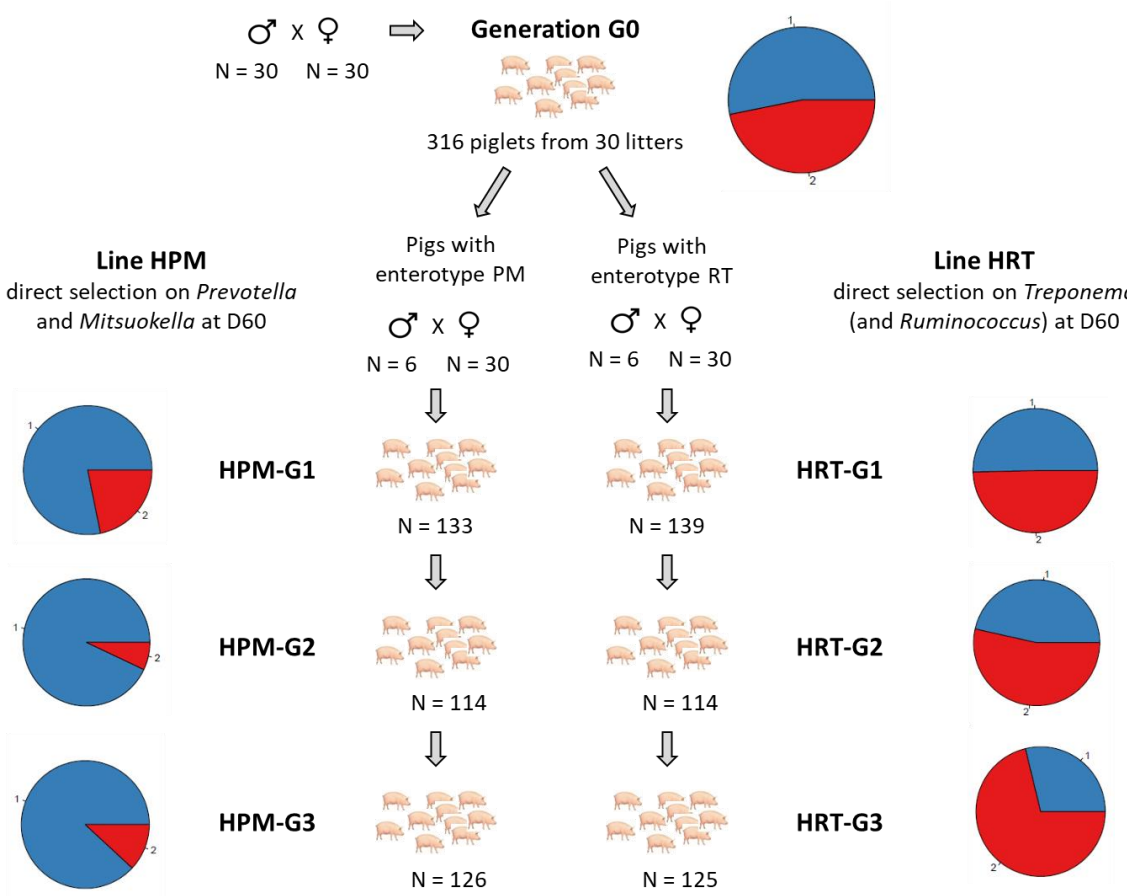
4

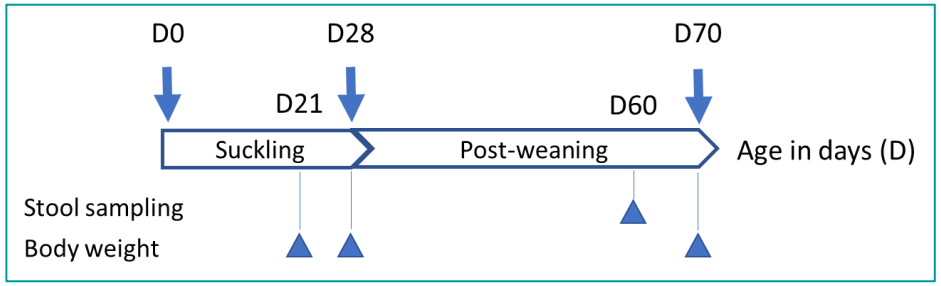
h^2 significative de l'abondance relative des genres bactériens du microbiote fécal à 60 jours

5

Meilleure croissance des porcs avec l'entérotype PM jusqu'au post-sevrage

ENTEROTYPIG : RÉPONSE À LA SÉLECTION SUR LE MICROBIOTE FÉCAL





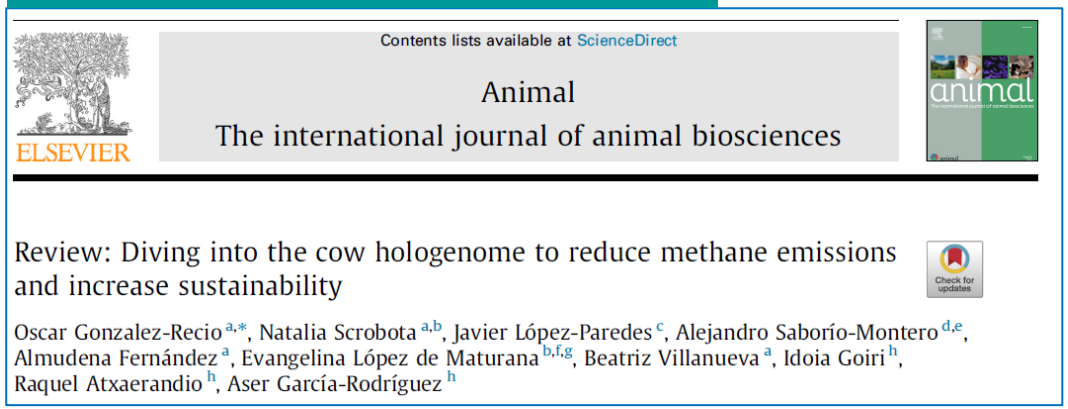
- Augmentation de la prévalence des entérotypes à chaque génération pour chacune des lignées
  - Sélection directe sur les genres qui qualifient les entérotypes
  - Sélection à l'échelle de l'écosystème
- Héritabilités significatives de l'abondance des genres bactériens
- Effet faible de la portée
- Corrélations génétiques : entérotype PM plus favorable à la croissance jusqu'au post-sevrage (70j)

Démonstration expérimentale que le microbiote fécal peut être modifié par une sélection génétique directionnelle avec des niveaux de réponse en accord avec les prédictions

Larzul et al., 2023, https://doi.org/10.21203/rs.3.rs-3081627/v2 (preprint)

DES PRIORITÉS EN ÉLEVAGE QUI STIMULENT LES RECHERCHES SUR LES MICROBIOTES

Réduire les émissions de méthane


Contents lists available at ScienceDirect

Animal

The international journal of animal biosciences

ELSEVIER

Review: Diving into the cow hologenome to reduce methane emissions and increase sustainability

Oscar Gonzalez-Recio [a,*], Natalia Scrobota [a,b], Javier López-Paredes [c], Alejandro Saborío-Montero [d,e], Almudena Fernández [a], Evangelina López de Maturana [b,f,g], Beatriz Villanueva [a], Idoia Goiri [h], Raquel Atxaerandio [h], Aser García-Rodríguez [h]

Améliorer la santé et le bien-être


Beldowska et al.
Journal of Animal Science and Biotechnology (2023) 14:37
https://doi.org/10.1186/s40104-023-00853-0

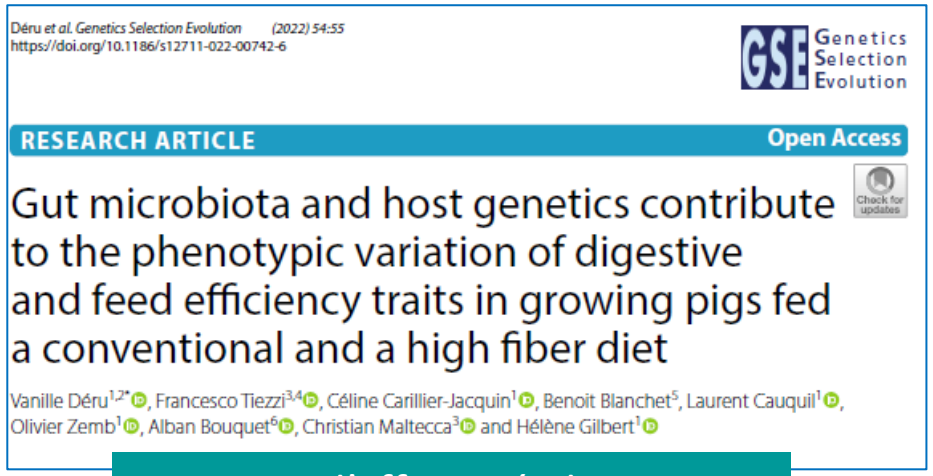
Journal of Animal Science and Biotechnology

REVIEW Open Access

State of the art in research on the gut-liver and gut-brain axis in poultry

Aleksandra Beldowska[1], Marcin Barszcz[2] and Aleksandra Dunislawska[1*]

COMPROMIS FONCTIONNELS


Déru et al. Genetics Selection Evolution (2022) 54:55
https://doi.org/10.1186/s12711-022-00742-6

GSE Genetics Selection Evolution

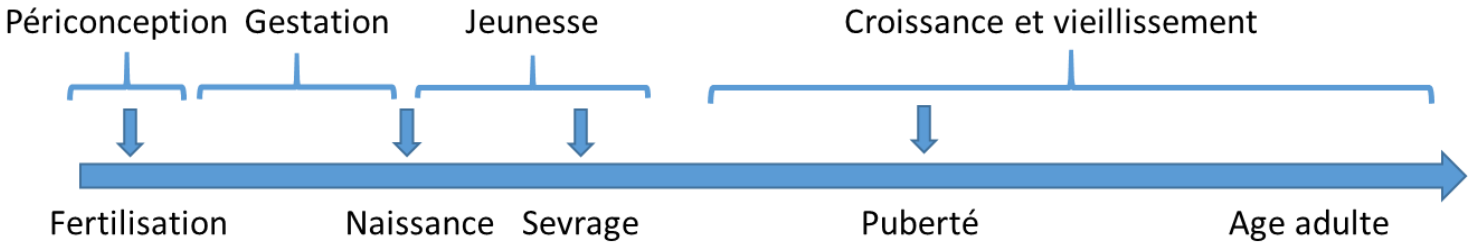
RESEARCH ARTICLE Open Access

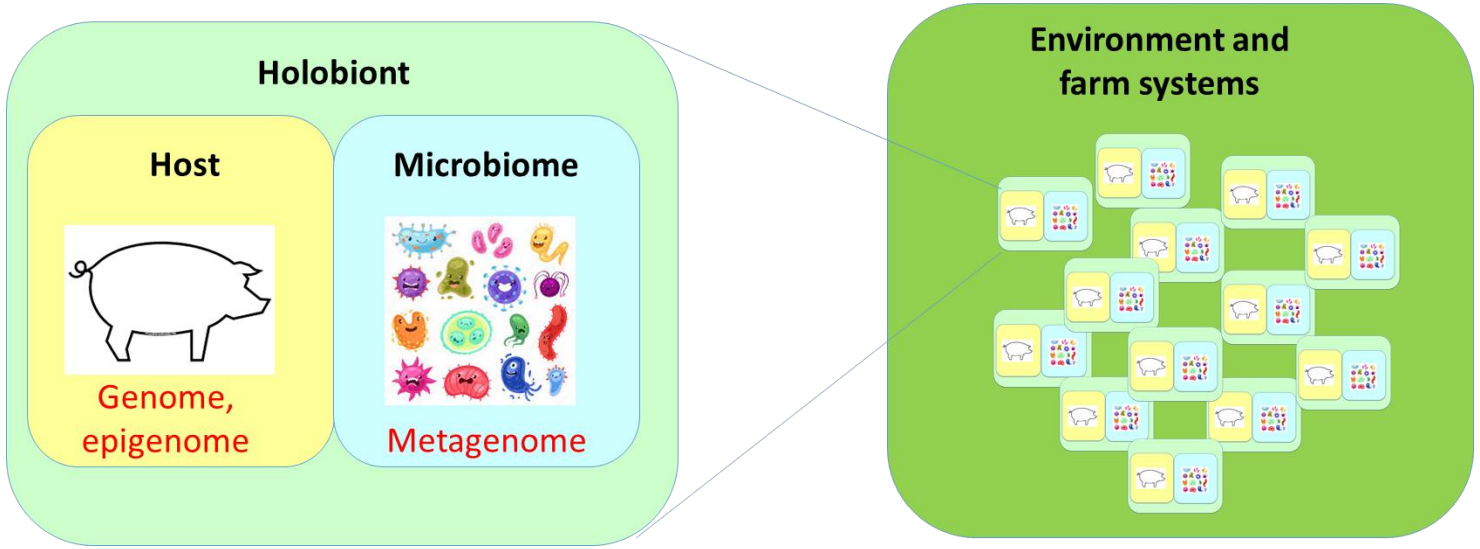
Gut microbiota and host genetics contribute to the phenotypic variation of digestive and feed efficiency traits in growing pigs fed a conventional and a high fiber diet

Vanille Déru[1,2*], Francesco Tiezzi[3,4], Céline Carillier-Jacquin[1], Benoit Blanchet[5], Laurent Cauquil[1], Olivier Zemb[1], Alban Bouquet[6], Christian Maltecca[3] and Hélène Gilbert[1]

Optimiser l'efficacité alimentaire

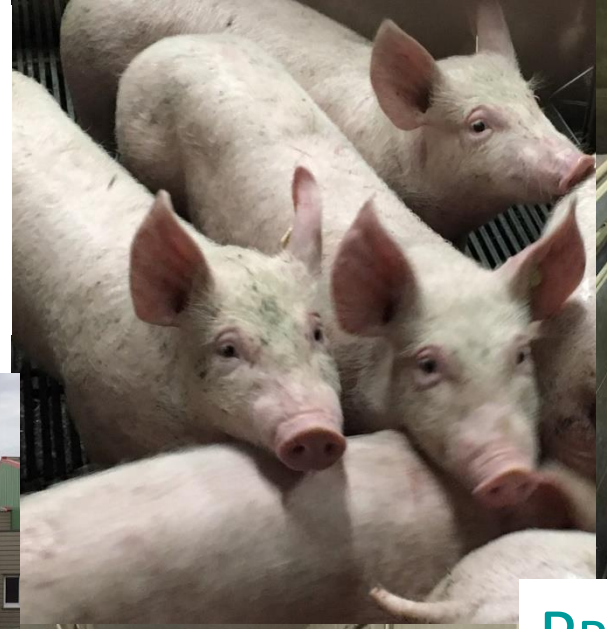
EN GUISE DE CONCLUSION





- Fenêtres temporelles d'intervention pour moduler efficacement les microbiomes
- Les microbiotes : biodiversité (invisible) à préserver en tant que ressources génétiques
- Holobionte : un nouveau paradigme pour étudier la construction et la plasticité du phénotype animal (liens entre phénotype et génotype)
- Mise en œuvre d'approches hologénomiques : G+E+M

Des travaux en équipe, au labo et sur le terrain



Projet Enterotypig

GABI – équipe Génétique Microbiote, santé: J Estelle, G Lemonnier,
GABI – plateforme @BRIDGe: J Lecardonnel, D Jardet, MN Rossignol,
GenPhySE: C Larzul
GENESI: Y Billon, W Hébrard

Financements INRAE : département Génétique animale et métaprogramme HOLOFLUX