

5<sup>e</sup> Journée Cap de Rouen  
« La vitamine D au cœur de tous les systèmes »

# Microbiote intestinal et vitamine D : une relation en pleine lumière

**Dr Julie Rodriguez**

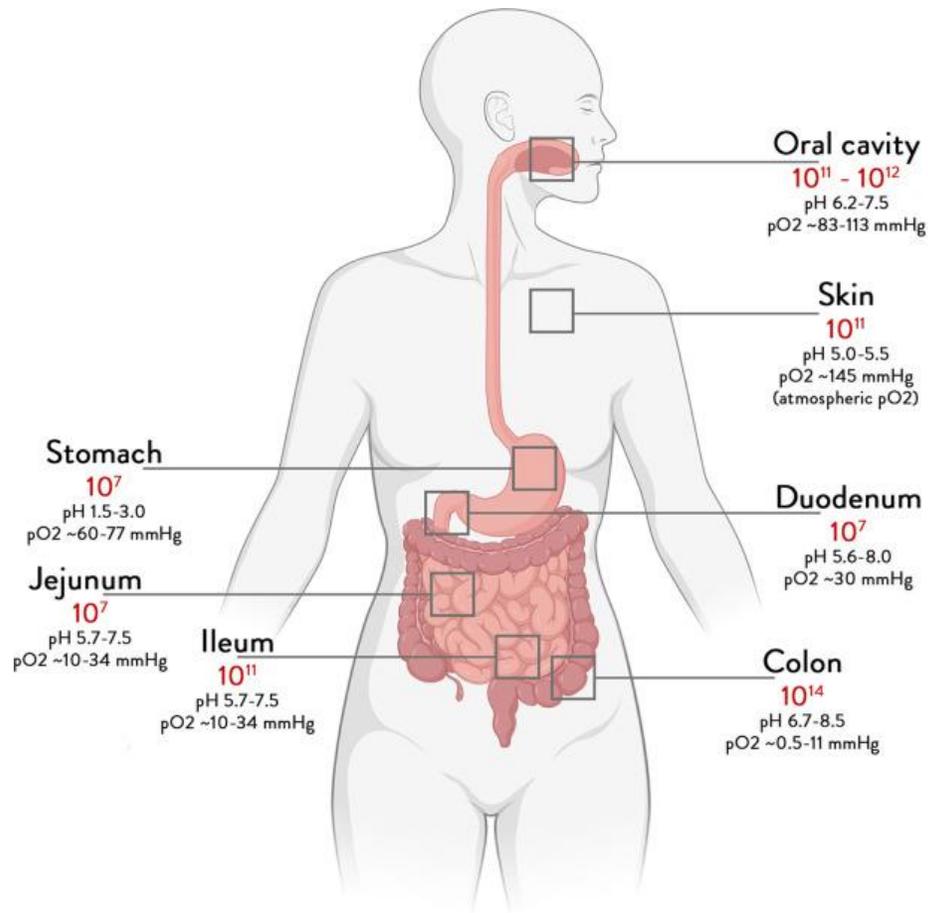
Chargée de projet sur le Microbiome



Candidate CRCN Inserm CSS3 2025

Equipe « Micronutriments et Maladies Métaboliques »

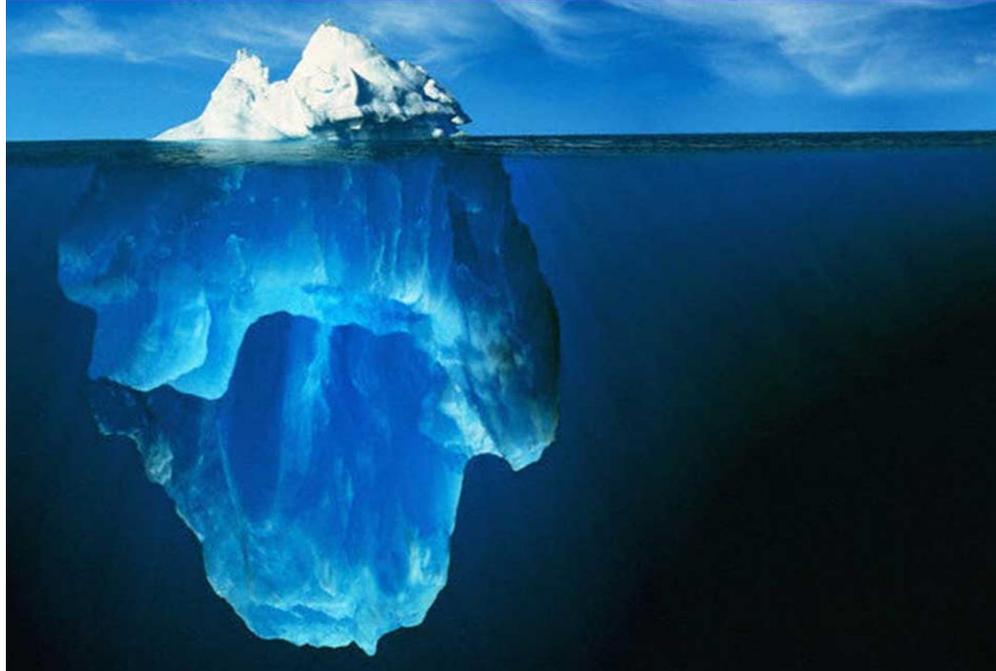
# Le Microbiome intestinal: un intérêt croissant pour la santé humaine



- ❖ Poids total ~1,5 kg
  - ❖ Ratio bactéries/ cellules eucaryotes = 1,3
  - ❖ Nombre de gènes dans le microbiome > nombre de gènes dans le génome humain
- 
- ❖ Plus de 1000 espèces bactériennes différentes
  - ❖ Des milliers de métabolites produits, peu sont décrits
  - ❖ Certains composants peuvent être délétères pour la santé de l'hôte (LPS)

# Le Microbiome intestinal: un intérêt croissant pour la santé humaine

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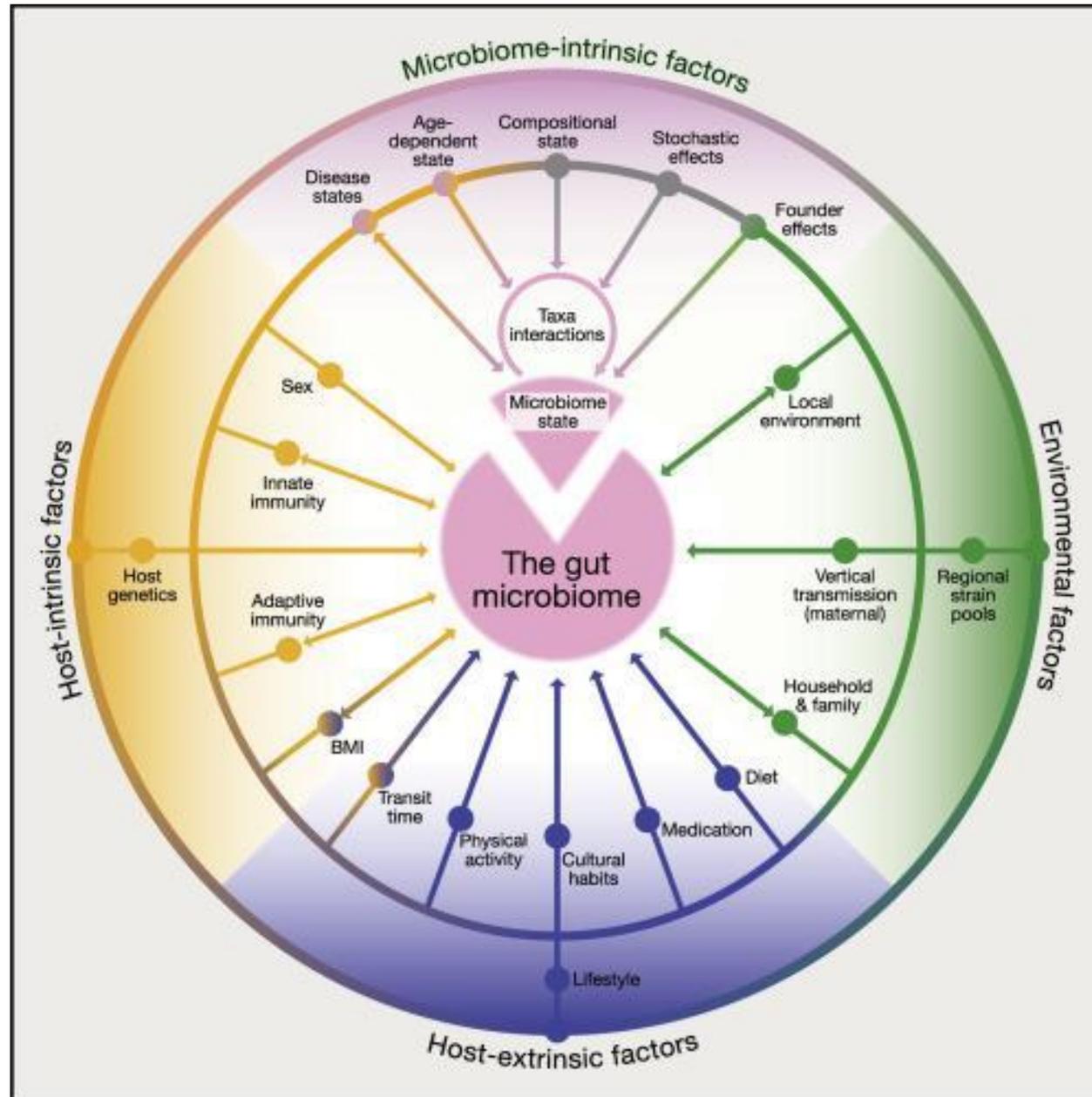


La métagénomique a donné un nouvel élan à la recherche sur le microbiome.

L'impact du microbiome sur notre santé est de plus en plus décrit, à travers sa participation sur la régulation de:

- L'immunité
- Le métabolisme
- La barrière intestinale
- Les fonctions digestives et l'absorption des nutriments
- Les fonctions neurologiques
- La synthèse de certains micronutriments et de métabolites bioactifs

# De nombreux facteurs modulent la composition et/ou la fonction du MI



# Nutrition & microbiome : prédominance des études sur les macronutriments

Les interactions entre micronutriments et microbiome intestinal sont encore peu documentées.

nature reviews microbiology

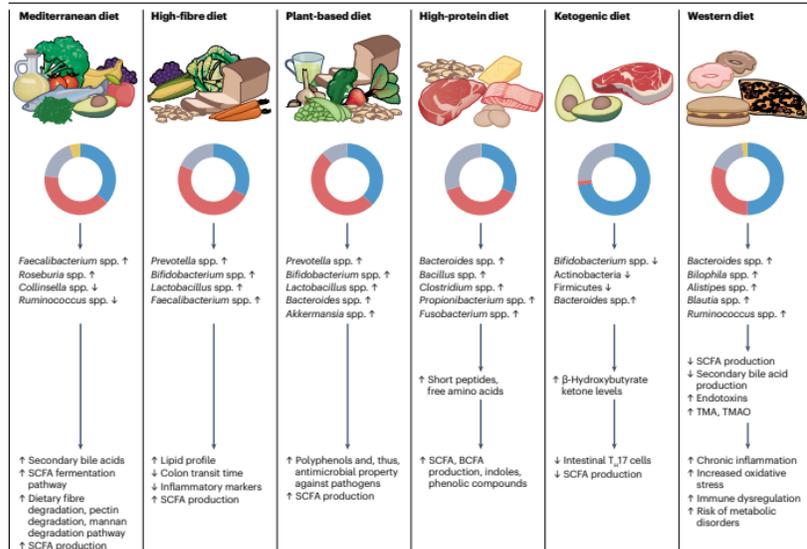
<https://doi.org/10.1038/s41579-024-01068-4>

Review article

Check for updates

## The interplay between diet and the gut microbiome: implications for health and disease

Review article



### The role of diet in shaping human gut microbiota

Emanuele Rinninella<sup>a,b,1</sup>, Ege Tohumcu<sup>b,c,1</sup>, Pauline Raoul<sup>a,b</sup>, Marcello Fiorani<sup>b,c</sup>, Marco Cintoni<sup>a,b</sup>, Maria Cristina Mele<sup>a,b</sup>, Giovanni Cammarota<sup>b,c</sup>, Antonio Gasbarrini<sup>b,c,2</sup>, Gianluca Ianiro<sup>b,c,\*,2</sup>

GUT MICROBES  
2024, VOL. 16, NO. 1, 2350785  
<https://doi.org/10.1080/19490976.2024.2350785>

Taylor & Francis  
Taylor & Francis Group

OPEN ACCESS Check for updates

### Diet-microbiota associations in gastrointestinal research: a systematic review

Kerith Duncanson<sup>a,b,c</sup>, Georgina Williams<sup>a,b,c</sup>, Emily C. Hoedt<sup>a,b,d</sup>, Clare E. Collins<sup>b,c</sup>, Simon Keely<sup>a,b,d</sup>, and Nicholas J. Talley<sup>a,b,c</sup>

nature communications

Article

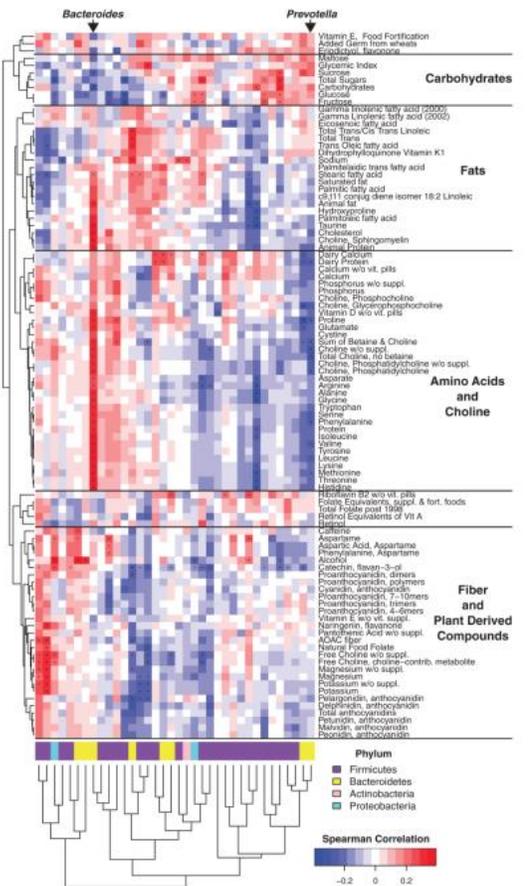
<https://doi.org/10.1038/s41467-023-38778-x>

## Host-diet-gut microbiome interactions influence human energy balance: a randomized clinical trial

NATIONAL INSTITUTES OF HEALTH  
NIH Public Access  
Author Manuscript  
Science. Author manuscript; available in PMC 2012 June 06.

Published in final edited form as:  
Science. 2011 October 7; 334(6052): 105–108. doi:10.1126/science.1208344.

### Linking Long-Term Dietary Patterns with Gut Microbial Enterotypes



## Les vitamines ne sont pas considérées comme des prébiotiques (selon la définition de *Gibson et al*)

*"Substrates that affect composition of the microbiota through mechanisms not involving selective utilization by host microorganisms are not prebiotics. These substrates would include antibiotics, minerals, vitamins and bacteriophages, which are not growth substrates, even though their intake might alter microbiota and metabolic composition."*

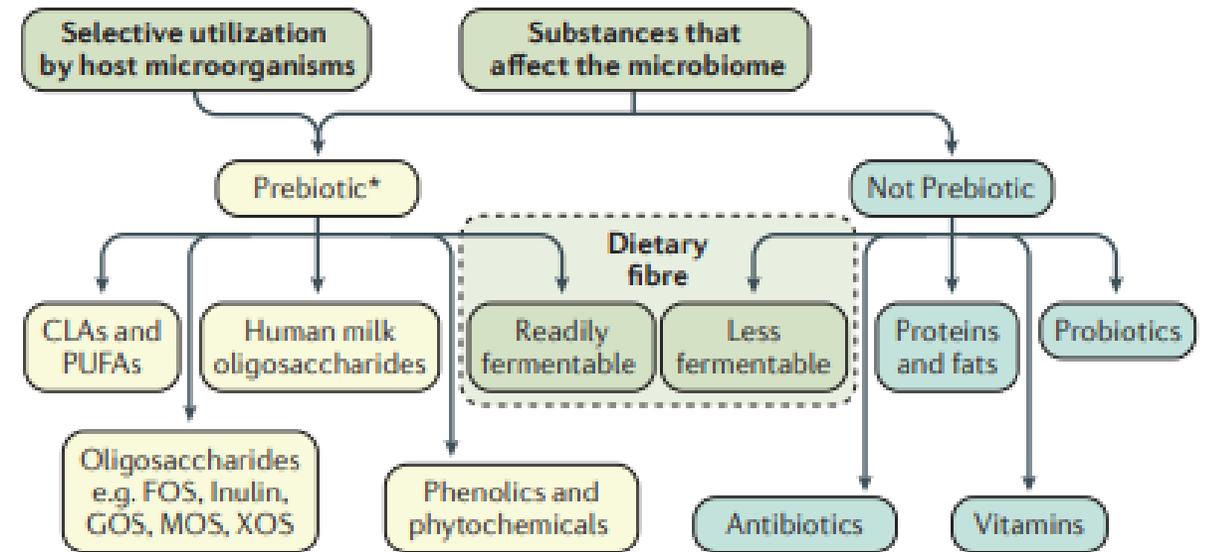
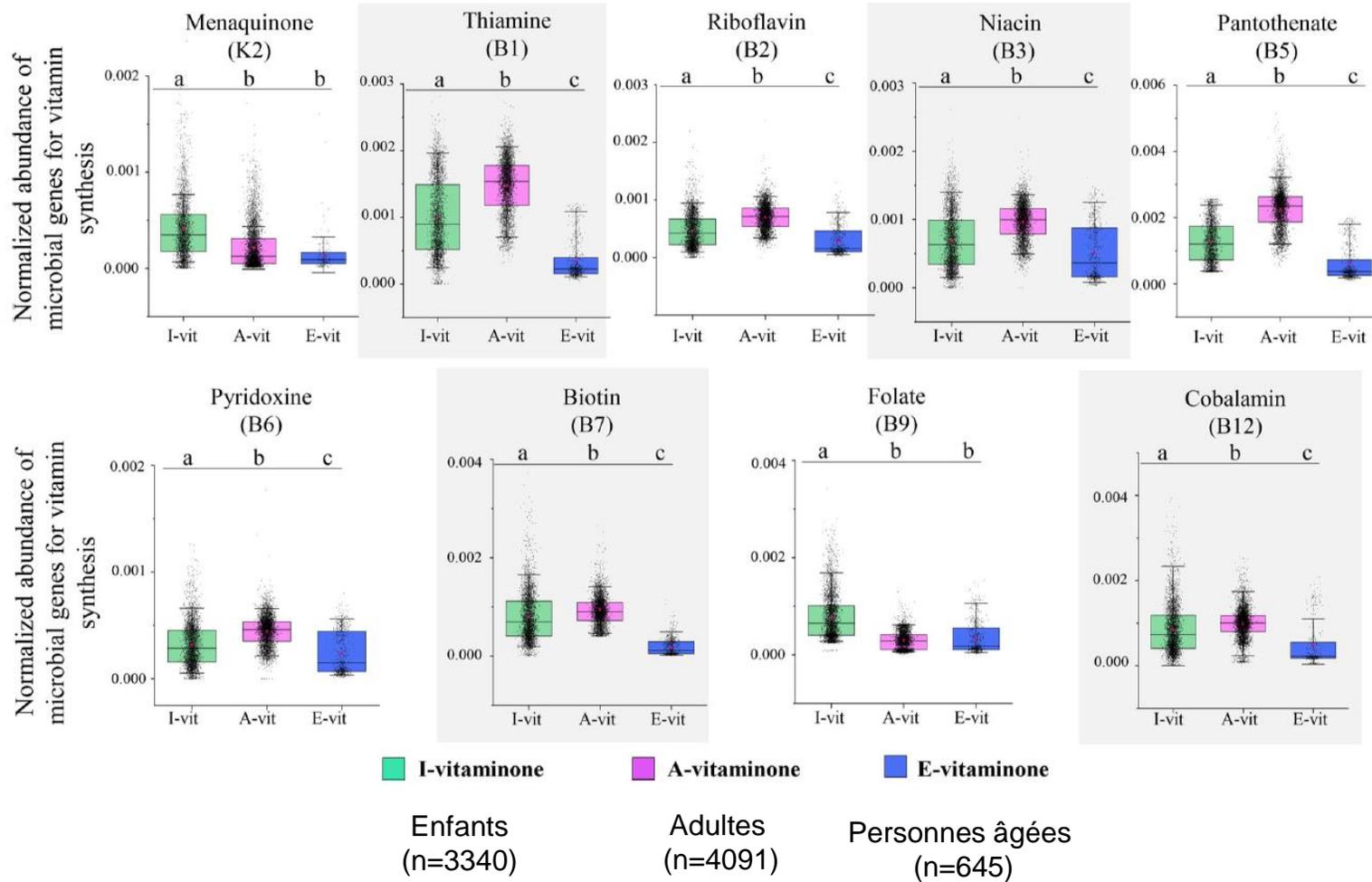


Figure 1 | Distinguishing what is considered a prebiotic with the proposed definition. Prebiotics must be selectively utilized and have adequate evidence of health benefit for the target host. Dietary prebiotics must not be degraded by the target host enzymes. \*The figure shows candidate as well as accepted prebiotics in that levels of evidence currently vary, with FOS and GOS being the most researched prebiotics. CLA, conjugated linoleic acid; PUFA, polyunsaturated fatty acid; FOS, fructooligosaccharides; GOS, galactooligosaccharides; MOS, mannanoligosaccharide; XOS, xylooligosaccharide.

# Le Microbiome Intestinal synthétise des vitamines



## Et la vitamine D ?



Short communication

Short communication: Metabolic synthesis of vitamin D<sub>2</sub> by the gut microbiome

Alex V. Chaves<sup>a</sup>, Mark S. Rybchyn<sup>b</sup>, Rebecca S. Mason<sup>a,b</sup>, David R. Fraser<sup>a,\*</sup>

<sup>a</sup> School of Life and Environmental Sciences, Faculty of Science, The University of Sydney, Sydney, NSW 2006, Australia  
<sup>b</sup> Discipline of Physiology, School of Medical Sciences and Charles Perkins Centre, The University of Sydney, Sydney, NSW 2006, Australia  
<sup>c</sup> Sydney School of Veterinary Science, R.M.C. Gunn Building, The University of Sydney, Sydney, NSW 2006, Australia.

### A B S T R A C T

The origin of vitamin D<sub>2</sub> in herbivorous animals was investigated in vivo in sheep and in bovine as well as mouse gastrointestinal tracts. A high concentration of 25-hydroxyvitamin D<sub>2</sub> in blood plasma of sheep both in summer and winter appeared to be incompatible with the undetectable level of vitamin D<sub>2</sub> in the pasture on which the sheep were grazing. Studies with bovine rumen contents from a cow grazing the same pasture as the sheep, demonstrated an increased concentration of vitamin D<sub>2</sub> on anaerobic incubation in a 'Rusitec' artificial rumen, which was further enhanced when cellulose powder was added as a fermentation substrate. The colon contents of mice that were fed from weaning on a vitamin D-free diet were found to contain vitamin D<sub>2</sub>. The results of these comparative studies in 3 animal species indicated that vitamin D<sub>2</sub> was being generated by microbial anaerobic metabolism in the gastrointestinal tract.

# De nombreuses pathologies sont associées à un déséquilibre du MI...



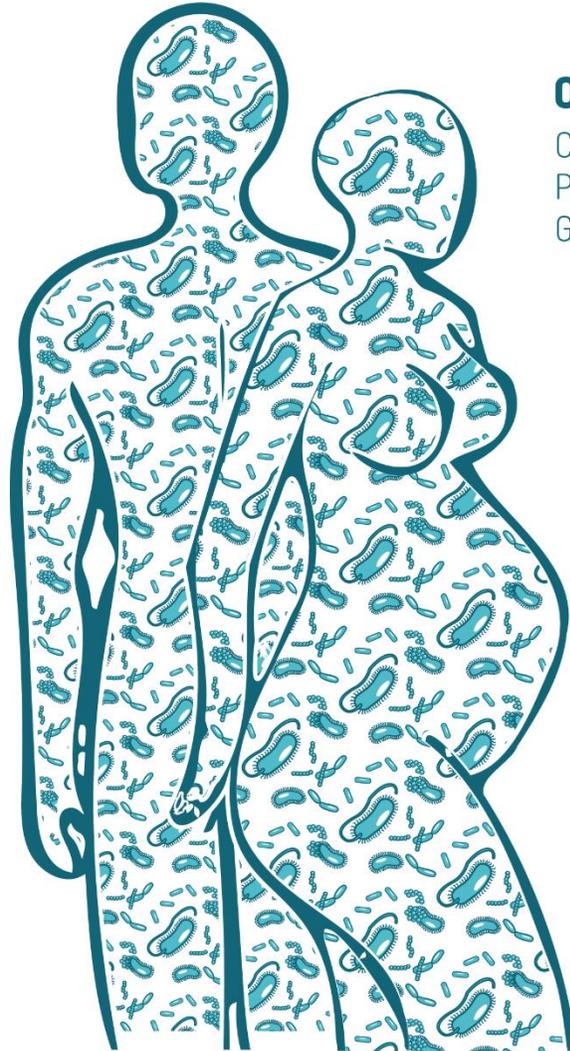
## Skin Microbiome

Allergies  
Acne  
Psoriasis  
Atopic Dermatitis  
Ectodermal Dysplasia  
Skin Cancer



## Gut Microbiome

Obesity ✓  
Metabolic Syndrome ✓  
Diabetes ✓  
C. difficile Infection ✓  
Colorectal Cancer ✓  
Inflammatory Bowel Diseases ✓  
Psychiatric Disorders ✓



## Oral Microbiome

Caries  
Periodontal Diseases  
Gingivitis



## Lung Microbiome

COPD  
Allergies  
Asthma  
Respiratory infections



## Vagina Microbiome

Vaginosis  
Sexually Transmitted Diseases  
Yeast Infection

## ...et une déficience en VitD

Ye *et al.* Lancet Diabetes Endocrinol. 2015

Association between circulating 25-hydroxyvitamin D and incident type 2 diabetes: a mendelian randomisation study

Zheng Ye, Stephen J Sharp, Stephen Burgess, Robert A Scott, Fumiaki Imamura, InterAct Consortium, Claudia Langenberg, Nicholas J Wareham, Nita G Forouhi

Pereira-Santos *et al.* Obes Rev. 2015



Etiology and Pathophysiology

Obesity and vitamin D deficiency: a systematic review and meta-analysis

M. Pereira-Santos ✉, P. R. F. Costa, A. M. O. Assis, C. A. S. T. Santos, D. B. Santos

Zhou *et al.* Int J Cancer. 2021



Cancer Epidemiology

Associations of vitamin D status with colorectal cancer risk and survival

Jian Zhou, Xianxiu Ge, Xikang Fan, Jiayu Wang, Lin Miao ✉, Dong Hang ✉

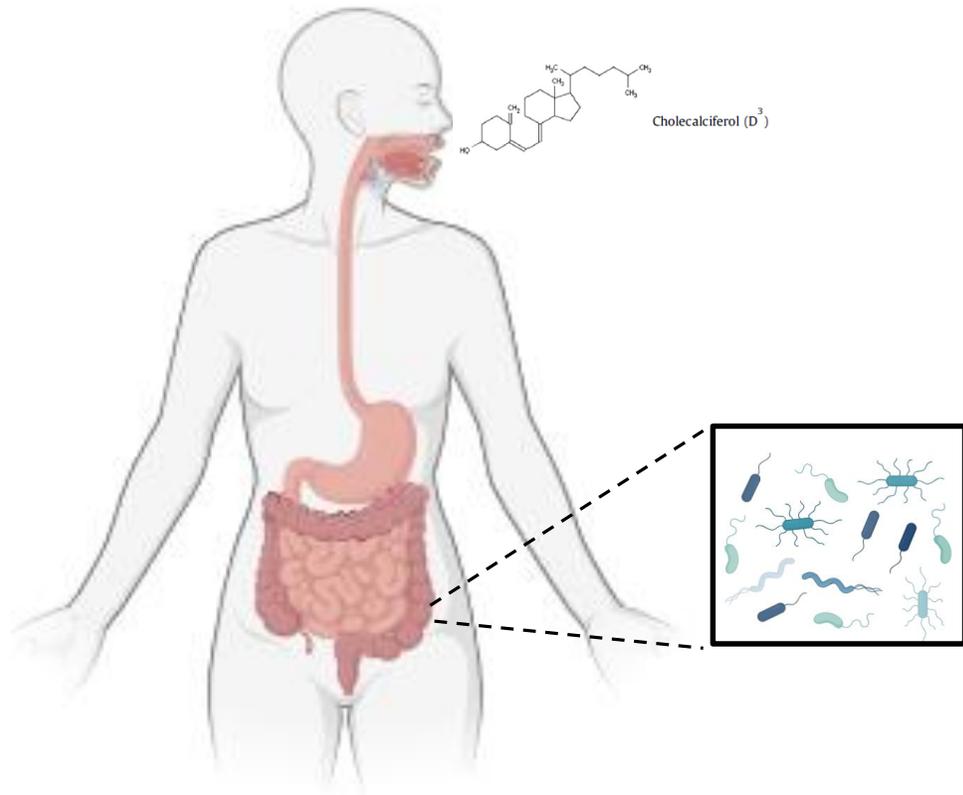
Furuya-Kanamori *et al.* JPEN J Parenter Enteral Nutr. 2017

25-Hydroxyvitamin D Concentrations and Clostridium difficile Infection: A Meta-Analysis

Luis Furuya-Kanamori <sup>1</sup>, Kinley Wangdi <sup>1</sup>, Laith Yakob <sup>2</sup>, Samantha J McKenzie <sup>3</sup>, Suhail A R Doi <sup>1</sup>, Justin Clark <sup>4</sup>, David L Paterson <sup>5</sup>, Thomas V Riley <sup>6</sup>, Archie C A Clements <sup>1</sup>

Adapted from, Belizário JE, Napolitano M. Human microbiomes and their roles in dysbiosis, common diseases, and novel therapeutic approaches. Front Microbiol. 2015;6:1050.

# La vitamine D peut être en contact avec le microbiome du colon



1-50% de VitD non absorbée dans la partie haute de l'intestin

SRB1 (Scavenger Receptor class B type I)  
Cd36 (Cluster differentiation 36)  
NPC1L1 (Niemann-Pick C1 Like 1)

Mol. Nutr. Food Res. 2011, 55, 691-702

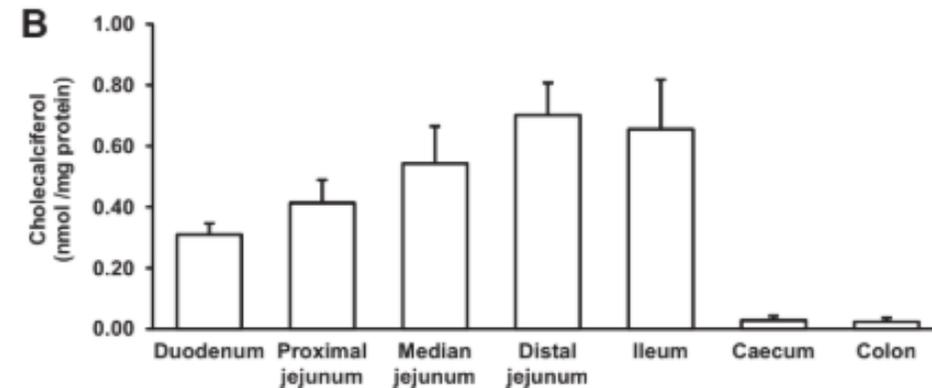
DOI 10.1002/mnfr.201000563

691

RESEARCH ARTICLE

**Vitamin D intestinal absorption is not a simple passive diffusion: Evidences for involvement of cholesterol transporters**

Emmanuelle Reboul<sup>1,2,3</sup>, Aurélie Goncalves<sup>1,2,3</sup>, Christine Comera<sup>4,5</sup>, Romain Bott<sup>1,2,3</sup>, Marion Nowicki<sup>1,2,3</sup>, Jean-François Landrier<sup>1,2,3</sup>, Dominique Jourdeuil-Rahmani<sup>1,2,3</sup>, Claire Dufour<sup>6,7</sup>, Xavier Collet<sup>8</sup> and Patrick Borel<sup>1,2,3</sup>



Goncalves et al. Food chemistry. 2015

THE FASEB JOURNAL • RESEARCH • www.fasebj.org

Degraeve et al. Microbiome (2023) 11:138  
https://doi.org/10.1186/s40168-023-01578-y

Microbiome

**ABCB1 (P-glycoprotein) regulates vitamin D absorption and contributes to its transintestinal efflux**

Marielle Margier,<sup>\*</sup> Xavier Collet,<sup>†,‡</sup> Cédric le May,<sup>‡,‡</sup> Charles Desmarchelier,<sup>\*</sup> François André,<sup>§</sup> Chantal Lebrun,<sup>¶</sup> Catherine Defoort,<sup>\*,||</sup> Alice Bluteau,<sup>¶</sup> Patrick Borel,<sup>\*</sup> Anne Lespine,<sup>‡,‡</sup> and Emmanuelle Reboul<sup>\*,‡</sup>

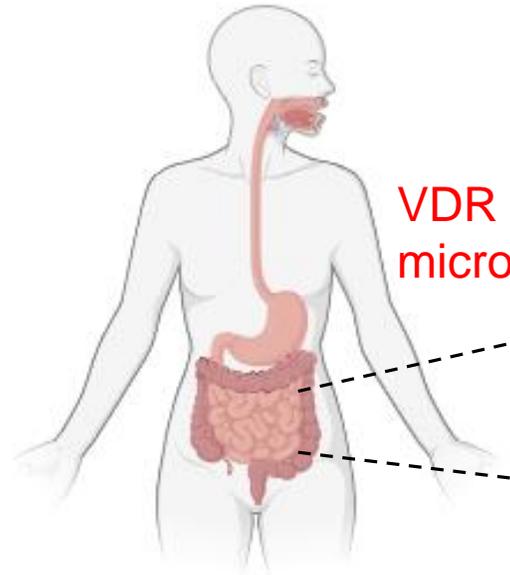
RESEARCH

Open Access

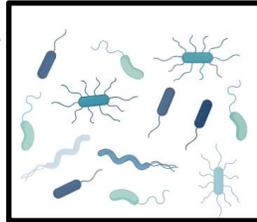
**Gut microbiome modulates tacrolimus pharmacokinetics through the transcriptional regulation of ABCB1**

Alexandra L. Degraeve<sup>1,2</sup>, Vincent Haufroid<sup>3,4</sup>, Axelle Lorient<sup>5</sup>, Laurent Gatto<sup>5</sup>, Vanessa Andries<sup>6,7,8</sup>, Lars Vereecke<sup>6,7,8</sup>, Laure Elens<sup>1,3,†</sup> and Laure B. Bindels<sup>2,9,†</sup>

# Le récepteur nucléaire de la vitamine D (VDR) est exprimé tout le long du tractus gastro-intestinal



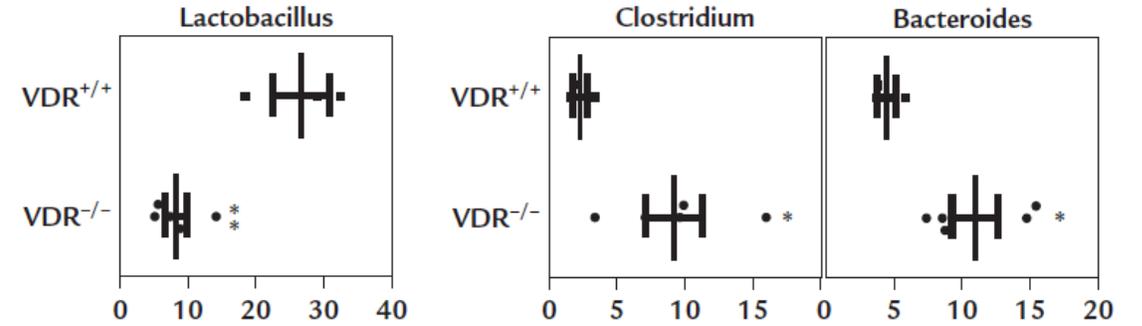
VDR non exprimé par le microbiome intestinal



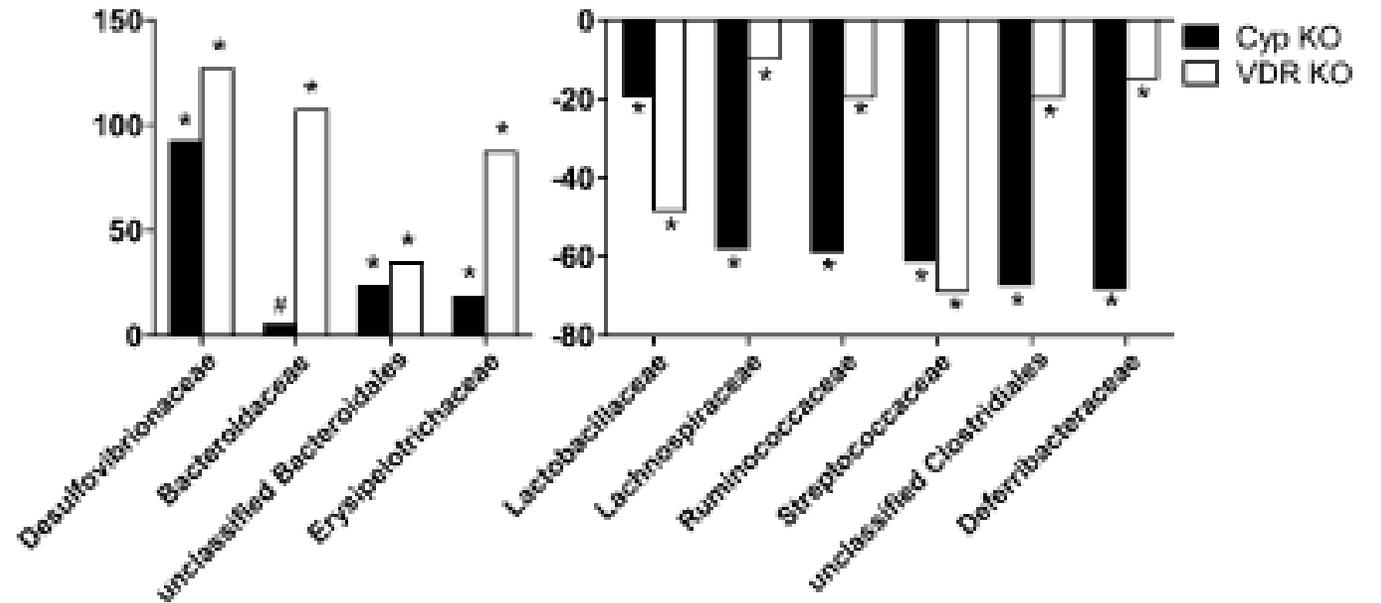
✓ VDR très exprimé dans le tractus gastro-intestinal



KO VDR



↓ *Lactobacillus*, ↑ *Clostridium* et *Bacteroides* (Jin et al. Clin Ther. 2015)



↓ bactéries qui produisent des acides gras à chaîne courte

(Ooi et al. J Nutr. 2013; Wu et al. Gut. 2015)

# Est-ce que le microbiome intestinal régule le métabolisme et/ou l'activité de la VitD ?

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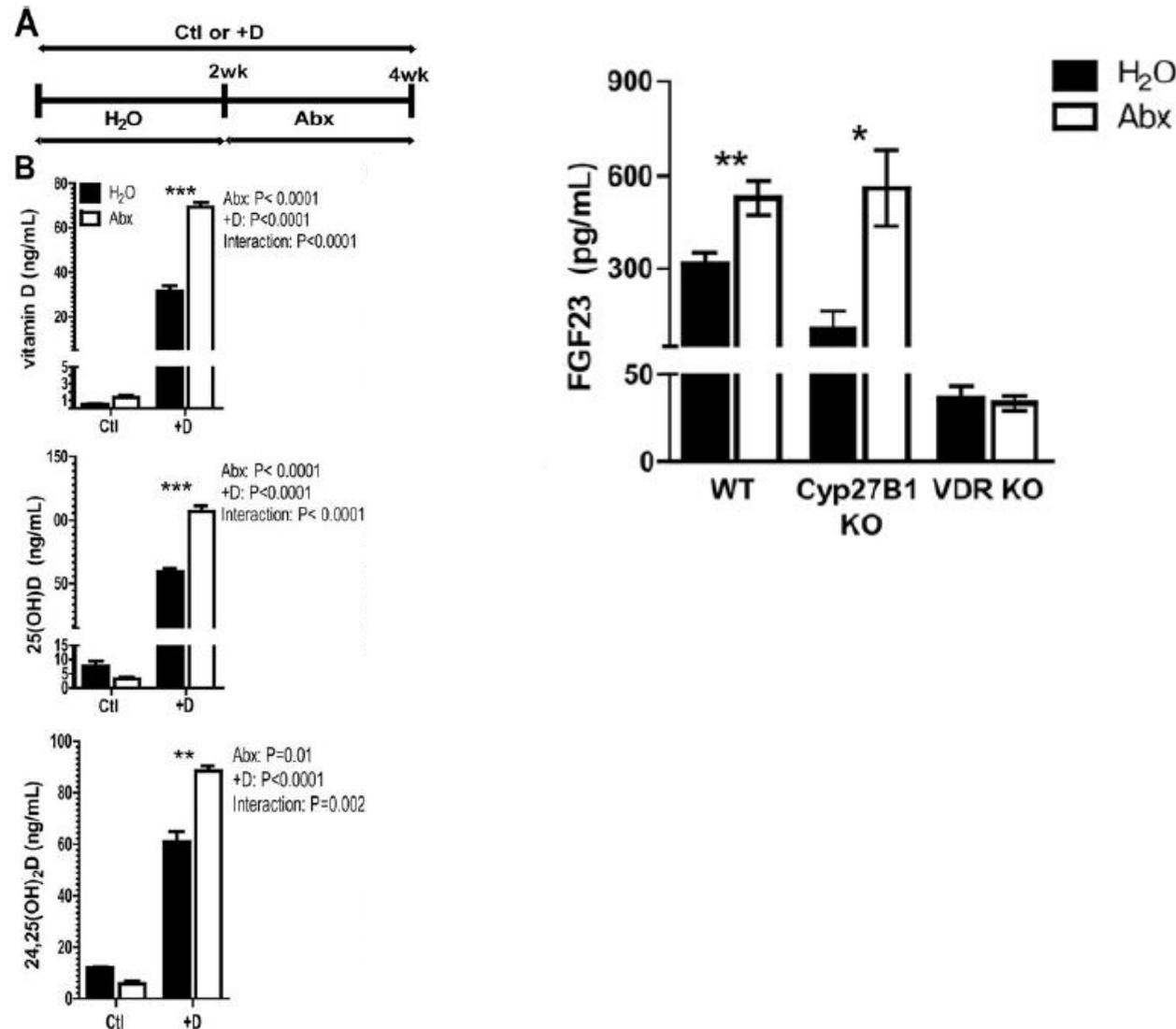


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# Les antibiotiques régulent les niveaux de 25(OH)D, 24,25(OH)<sub>2</sub>D et FGF23

**Cocktail d'antibiotiques (2 semaines):** ampicillin (1g/L), metronidazole (1g/L), neomycin (1g/L), and vancomycin (0.5g/L).



**HHS Public Access**  
 Author manuscript  
*J Nutr Biochem*. Author manuscript; available in PMC 2019 June 01.

Published in final edited form as:  
*J Nutr Biochem*. 2018 June ; 56: 65–73. doi:10.1016/j.jnutbio.2018.01.011.

**Regulation of vitamin D metabolism following disruption of the microbiota using broad spectrum antibiotics**

Stephanie A. Bora<sup>a</sup>, Mary J. Kennett<sup>a</sup>, Philip B. Smith<sup>a,b</sup>, Andrew D. Patterson<sup>a</sup>, and Margherita T. Cantorna<sup>a,\*</sup>

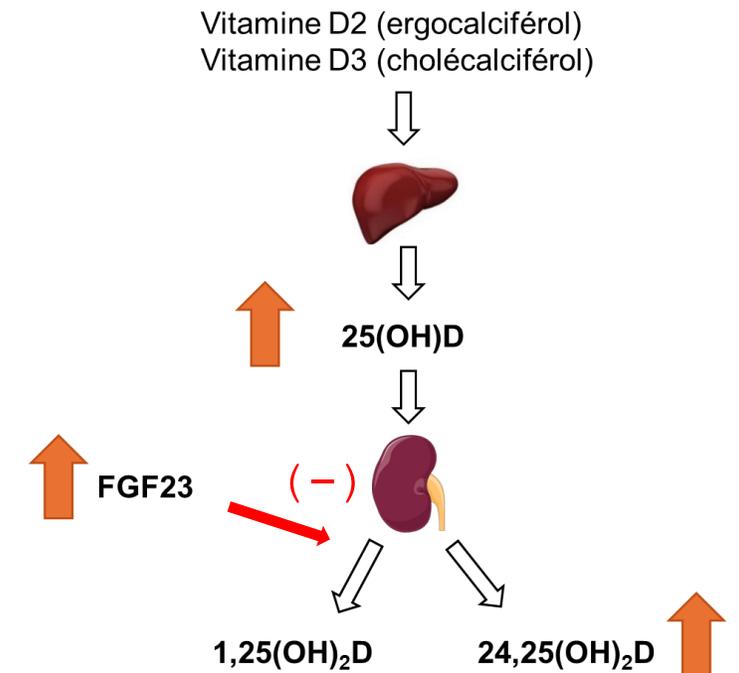


Figure 1. Abx treatments induced vitamin D metabolism

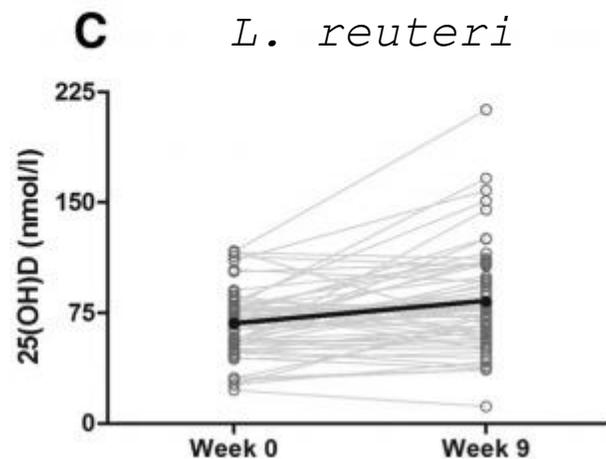
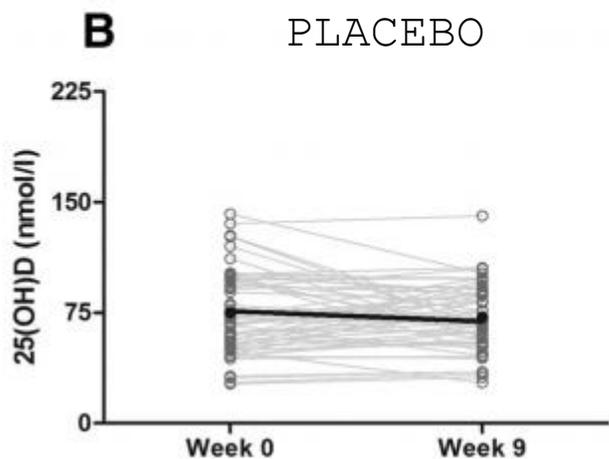
# Certaines bactéries peuvent réguler les niveaux de 25(OH)D

	Placebo (n 61)	<i>L. reuteri</i> (n 66)	<i>P</i>
	Mean (SD)	Mean (SD)	
Vitamin A (µmol/l)			
Week 0	1.96 (0.53)	1.90 (0.47)	0.360 <sup>a</sup>
Week 9	2.01 (0.53)	1.91 (0.39)	
25(OH)D (nmol/l)			
Week 0	75.12 (27.68)	67.91 (22.14)	0.003 <sup>a</sup>
Week 9	71.93 (22.05)	82.64 (35.52)	
Vitamin E (µmol/l)			
Week 0	32.24 (4.90)	33.15 (2.89)	0.852 <sup>b</sup>
Week 9	33.96 (5.61)	34.63 (6.39)	
β-carotene (µmol/l)			
Week 0	0.55 (0.40)	0.60 (0.49)	0.790 <sup>a</sup>
Week 9	0.55 (0.37)	0.59 (0.46)	
Calcium (mmol/l)			
Week 0	2.35 (0.09)	2.34 (0.07)	0.100 <sup>a</sup>
Week 9	2.36 (0.11)	2.33 (0.07)	
Phosphate (mmol/l)			
Week 0	1.18 (0.22)	1.19 (0.18)	0.312 <sup>a</sup>
Week 9	1.17 (0.18)	1.16 (0.18)	

<sup>a</sup>Two-factor repeated measures ANOVA on log-transformed values

<sup>b</sup>Two-factor repeated measures ANOVA

25(OH)D, 25-hydroxyvitamin D



RCT healthy hypercholesterolemic adult men and women between the ages of 20 and 75 years old

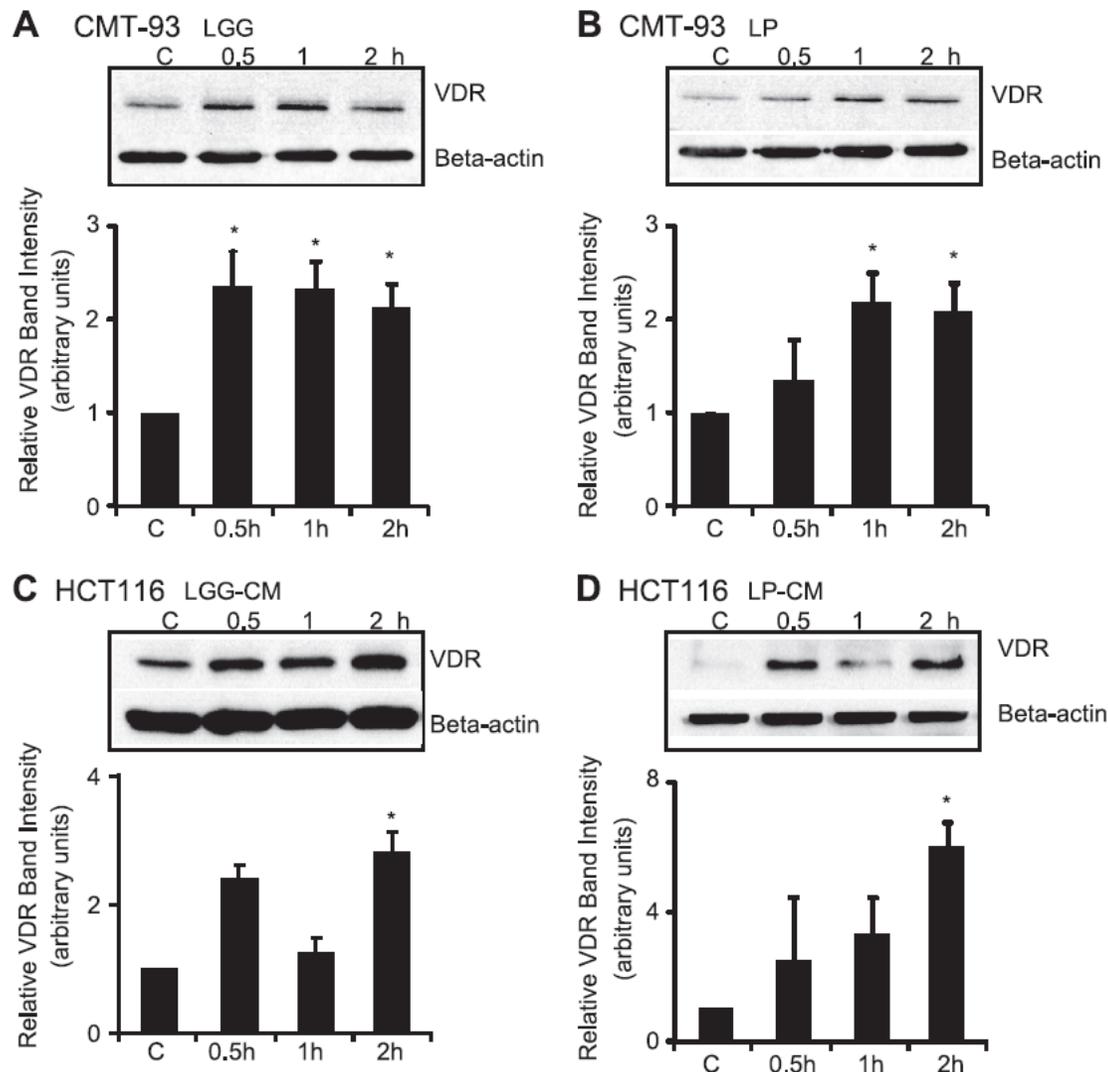
*L. reuteri* (2.9 × 10<sup>9</sup> colony-forming units

per capsule)

13 weeks

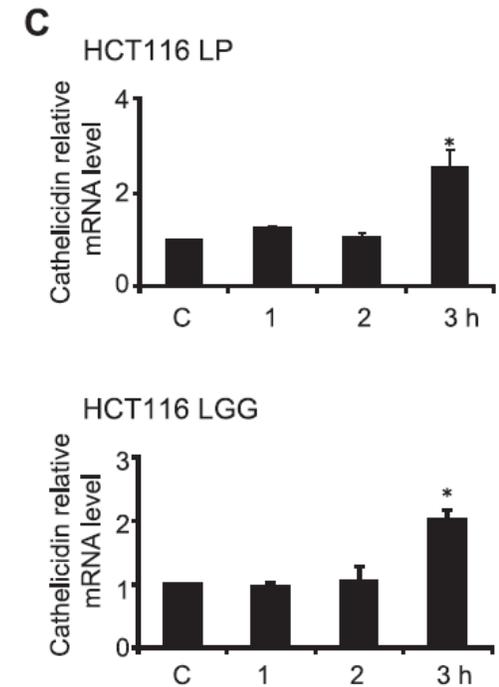
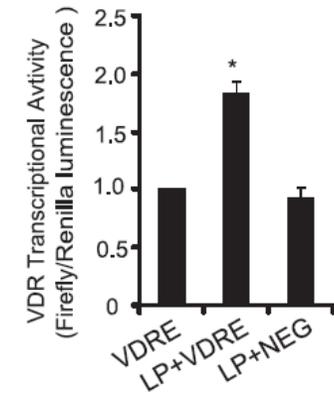
	Mean (SD)		<i>P</i>
	Placebo (n = 61)	<i>L. reuteri</i> (n = 66)	
Energy, kcal/d			
wk 0	2033.1 (642.5)	2074.8 (690.0)	.85 <sup>b</sup>
wk 9	1999.7 (621.0)	2024.6 (586.5)	
Lipids, kcal/d			
wk 0	710.0 (258.5)	770.5 (333.5)	.22 <sup>b</sup>
wk 9	744.8 (301.7)	741.0 (276.5)	
Proteins, kcal/d			
wk 0	345.6 (115.5)	351.3 (116.4)	.87 <sup>b</sup>
wk 9	339.7 (104.3)	345.8 (100.1)	
Carbohydrates, kcal/d			
wk 0	977.5 (343.6)	953.0 (361.2)	.44 <sup>b</sup>
wk 9	915.2 (321.8)	937.8 (295.7)	
Vitamin A, µg/d <sup>a</sup>			
wk 0	554.5 (401.7–843.4)	575.1 (450.9–834.3)	.70 <sup>c</sup>
wk 9	540.8 (394.7–832.0)	542.9 (413.4–772.4)	
Retinol, µg/d <sup>a</sup>			
wk 0	308.5 (206.6–595.3)	345.2 (243.6–484.0)	.68 <sup>c</sup>
wk 9	348.8 (224.2–522.4)	339.4 (241.9–477.7)	
Carotenoids, mg/d <sup>a</sup>			
wk 0	2.51 (1.05–3.81)	1.86 (0.96–4.27)	.90 <sup>c</sup>
wk 9	2.28 (0.96–3.21)	2.13 (0.93–3.61)	
Vitamin D, µg/d <sup>a</sup>			
wk 0	1.26 (0.52–2.25)	1.31 (0.72–2.29)	.26 <sup>c</sup>
wk 9	1.10 (0.57–2.07)	1.09 (0.69–1.70)	
Vitamin E, mg/d <sup>a</sup>			
wk 0	9.96 (7.17–11.72)	10.12 (7.62–13.27)	.51 <sup>c</sup>
wk 9	9.59 (6.71–12.66)	9.90 (7.53–12.78)	

# Certaines bactéries peuvent réguler l'expression et l'activité du VDR dans la cellule intestinale



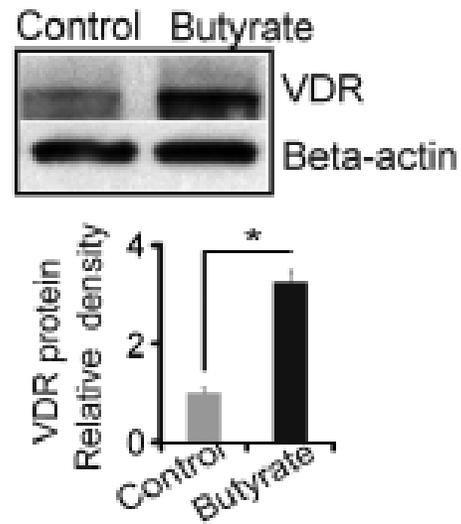
*Lactobacillus rhamnosus* strain GG (LGG)  
*Lactobacillus plantarum* (LP)

Fig. 1. Probiotics *Lactobacillus rhamnosus* strain GG (LGG) and *Lactobacillus plantarum* (LP) increased vitamin D receptor (VDR) protein expression in vitro. **A:** LGG increases VDR protein expression in mouse epithelia CMT-93 cells. **B:** LP increases VDR protein expression in CMT-93 cells. **C:** LGG conditioned medium (CM) increases VDR protein expression in human epithelial HCT116 cells. **D:** LP CM increases VDR protein expression in HCT116 cells. Cells were treated with indicated time course. Three separate experiments with 3 replicates each, \* $P < 0.05$ , compared with control (C).

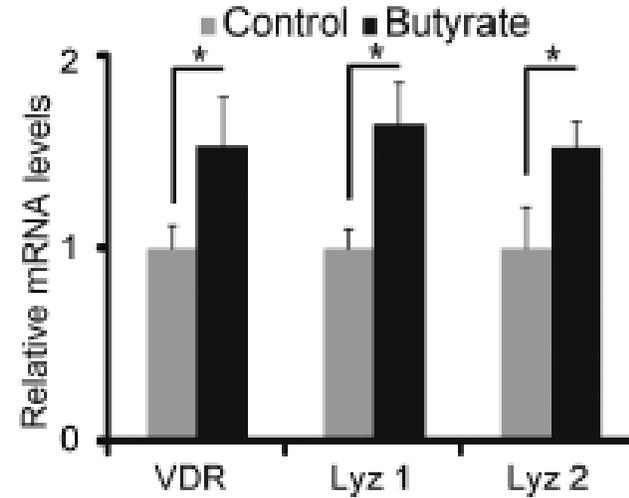


# Des métabolites bactériens peuvent réguler l'expression du VDR dans la cellule intestinale

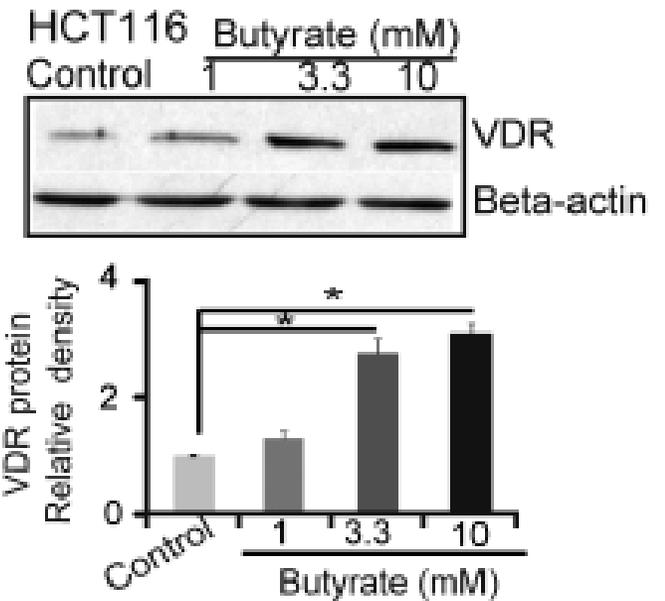
## A MEFs



## B MEFs

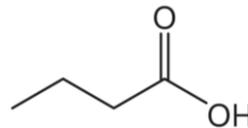


## C HCT116



Mouse embryonic fibroblasts (MEFs)

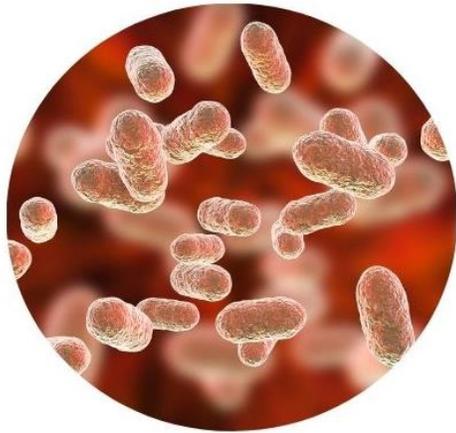
# Est-ce que le microbiome intestinal régule le métabolisme et/ ou l'activité de la VitD ?



- ✓ 25 (OH) D
- ✓ 24, 25 (OH)<sub>2</sub>D
- ✓ FGF23
- ✓ VDR

# Est-ce que la VitD régule la composition et/ou fonction du microbiome intestinal ?

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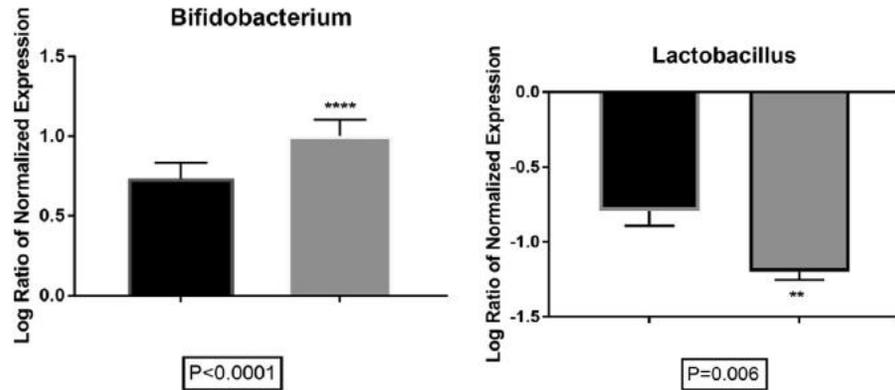


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# La supplémentation en VitD augmente l'abondance relative des bifidobactéries

50 adolescentes en bonne santé,  
santé,  
50 000IU/ wk, 9 semaines  
6% > 30ng/mL avant,  
versus 68% après

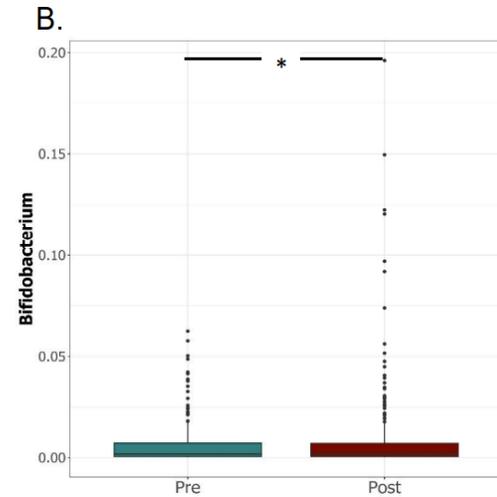
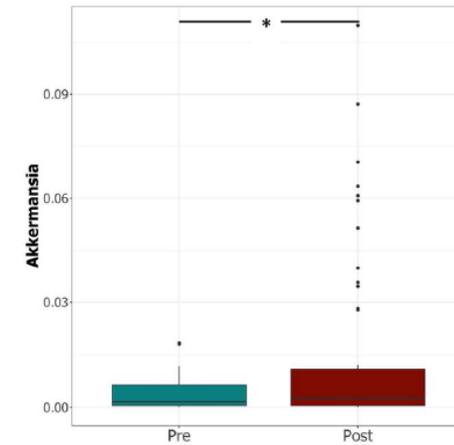
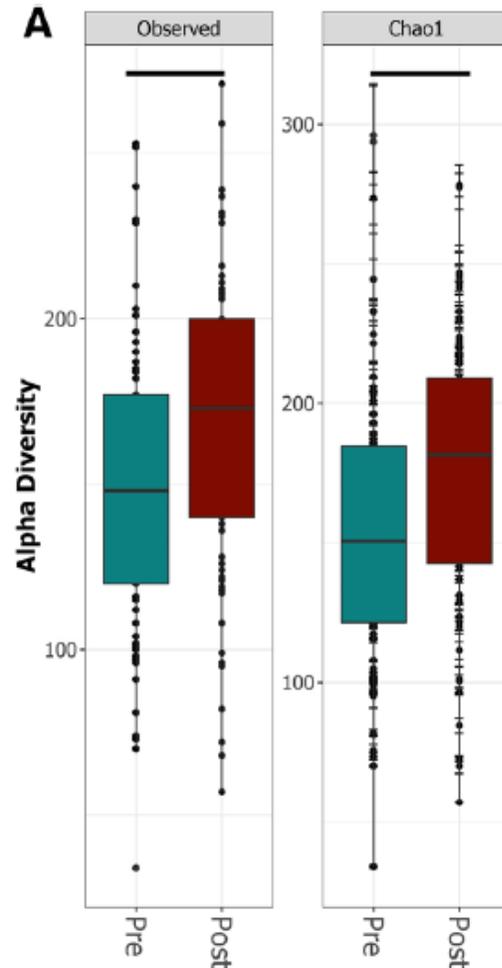


Tabatabaeizadeh *et al.* Clin Nutr ESPEN. 2020

50 femmes en bonne santé (VitD  
déficience),  
50 000IU/ wk, 12 semaines

69% > 30

vention



Singh *et al.* Sci Rep. 2020

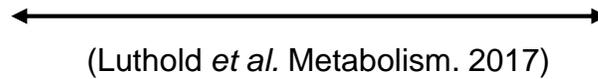
# Des associations retrouvées entre des métabolites de VitD et le microbiome intestinal



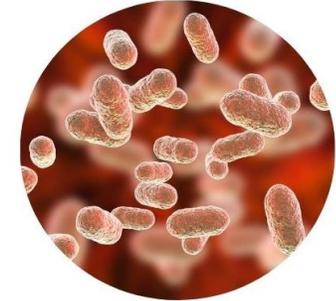
↓ 25(OH)D



Adultes en bonne santé



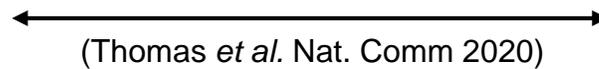
(Luthold *et al.* Metabolism. 2017)



↑ LPS  
↓ *Coprococcus*  
↑ *Bifidobacterium*



Hommes (n=567)



(Thomas *et al.* Nat. Comm 2020)

↑ 1,25(OH)<sub>2</sub>D

↑ diversité bactérienne  
↑ bactéries produisant du butyrate  
(genres appartenant aux familles  
Lachnospiraceae et Ruminococcaceae)

# Est-ce que la VitD régule la composition et/ou fonction du microbiome intestinal ?

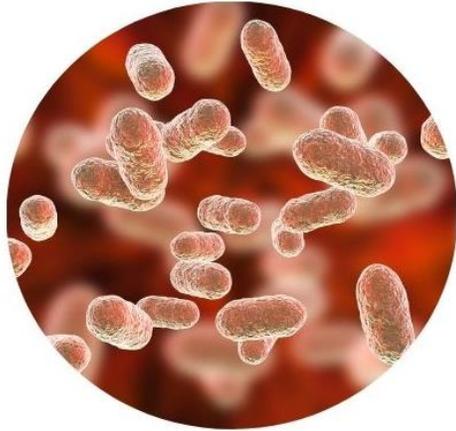
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Bifidobacterium ?  
Akkermansia ?  
Producteurs d'acides  
gras à chaîne courte ?

# Est-ce que la VitD régule la composition et/ou fonction du microbiome intestinal ?

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Récepteur nucléaire  
de la vitD non  
exprimé



?

Via un effet direct ?



# Est-ce que la VitD régule la composition et/ou fonction du microbiome intestinal ?

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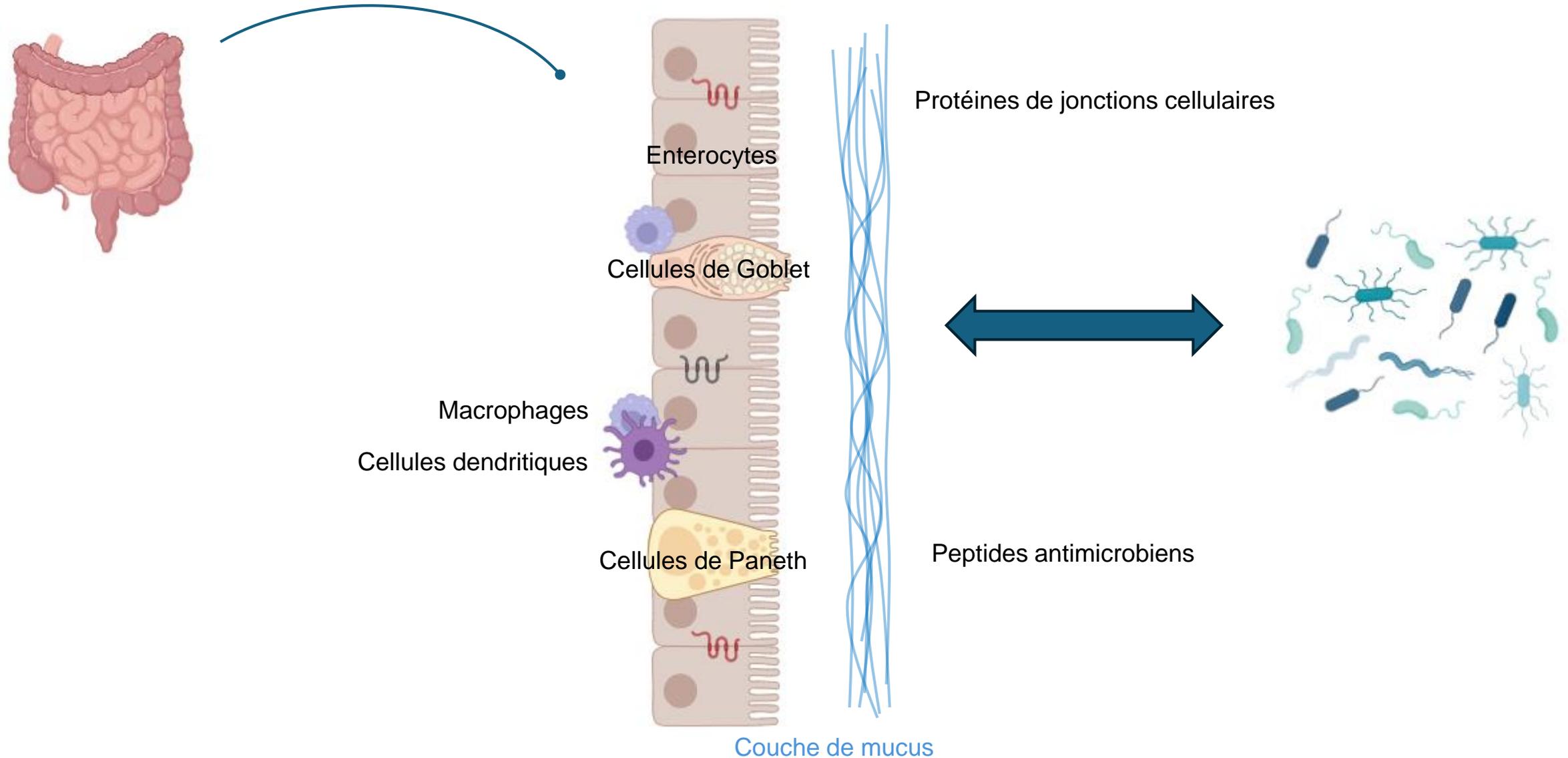


?



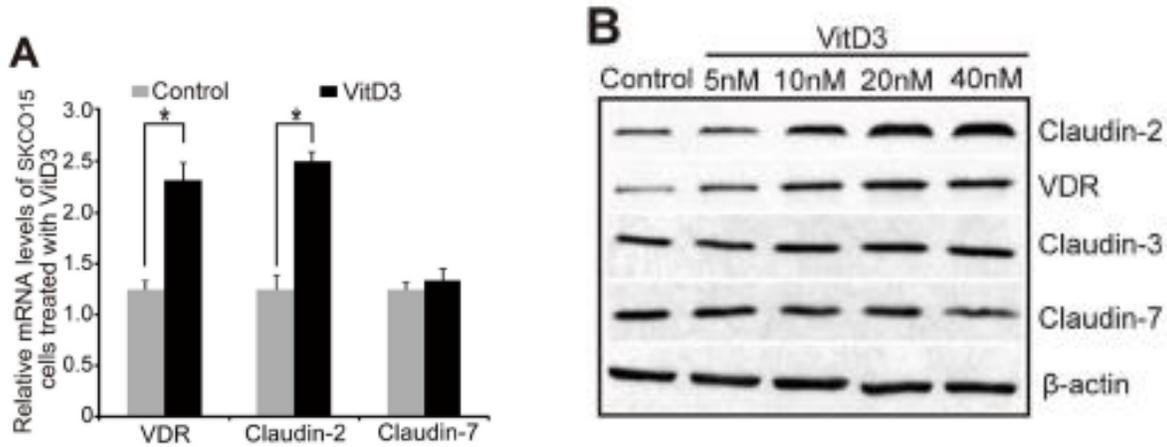
Via un effet indirect ?

# Est-ce que la VitD influence la communication entre la barrière de l'intestin et le MI ?

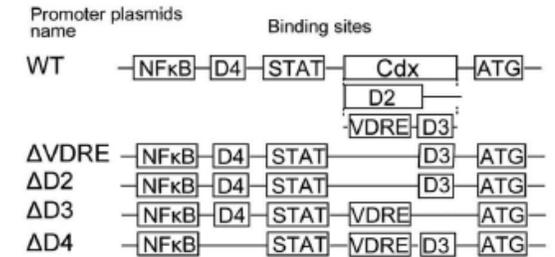


# La VitD régule certaines protéines de jonctions serrées

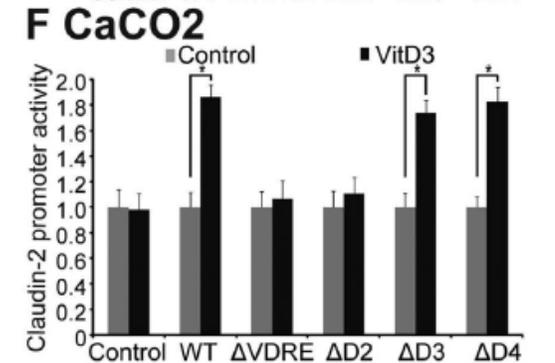
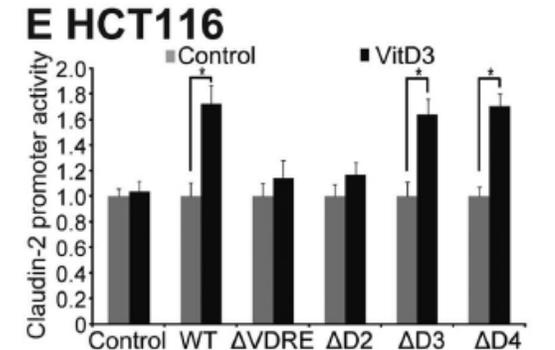
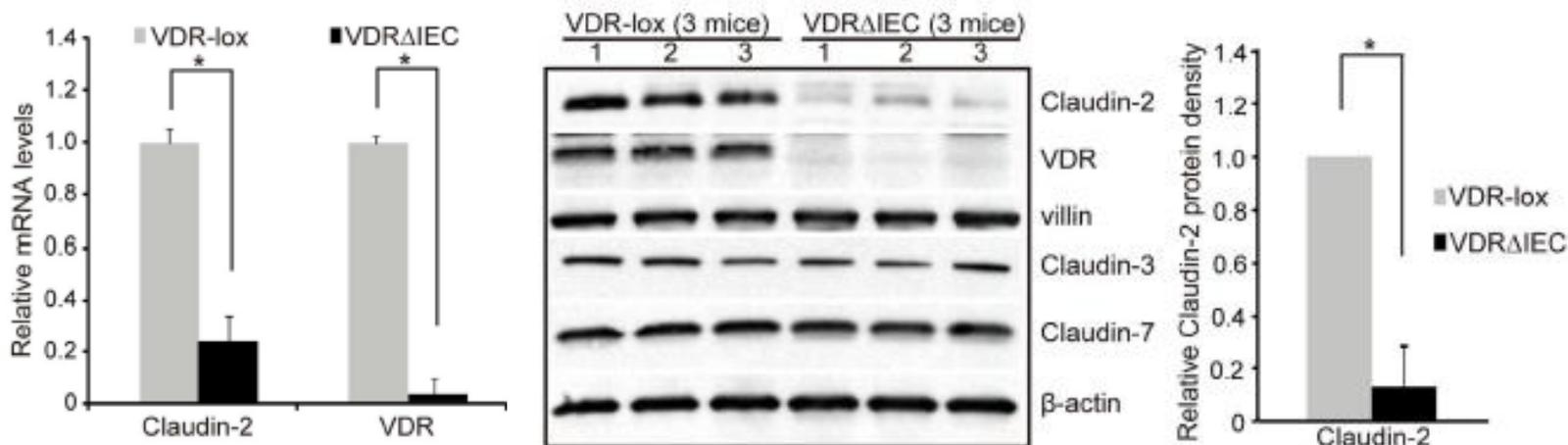
➤ Traitement de cellules épithéliales du colon avec la vitD3



➤ VDRE présent sur le promoteur de claudin-2



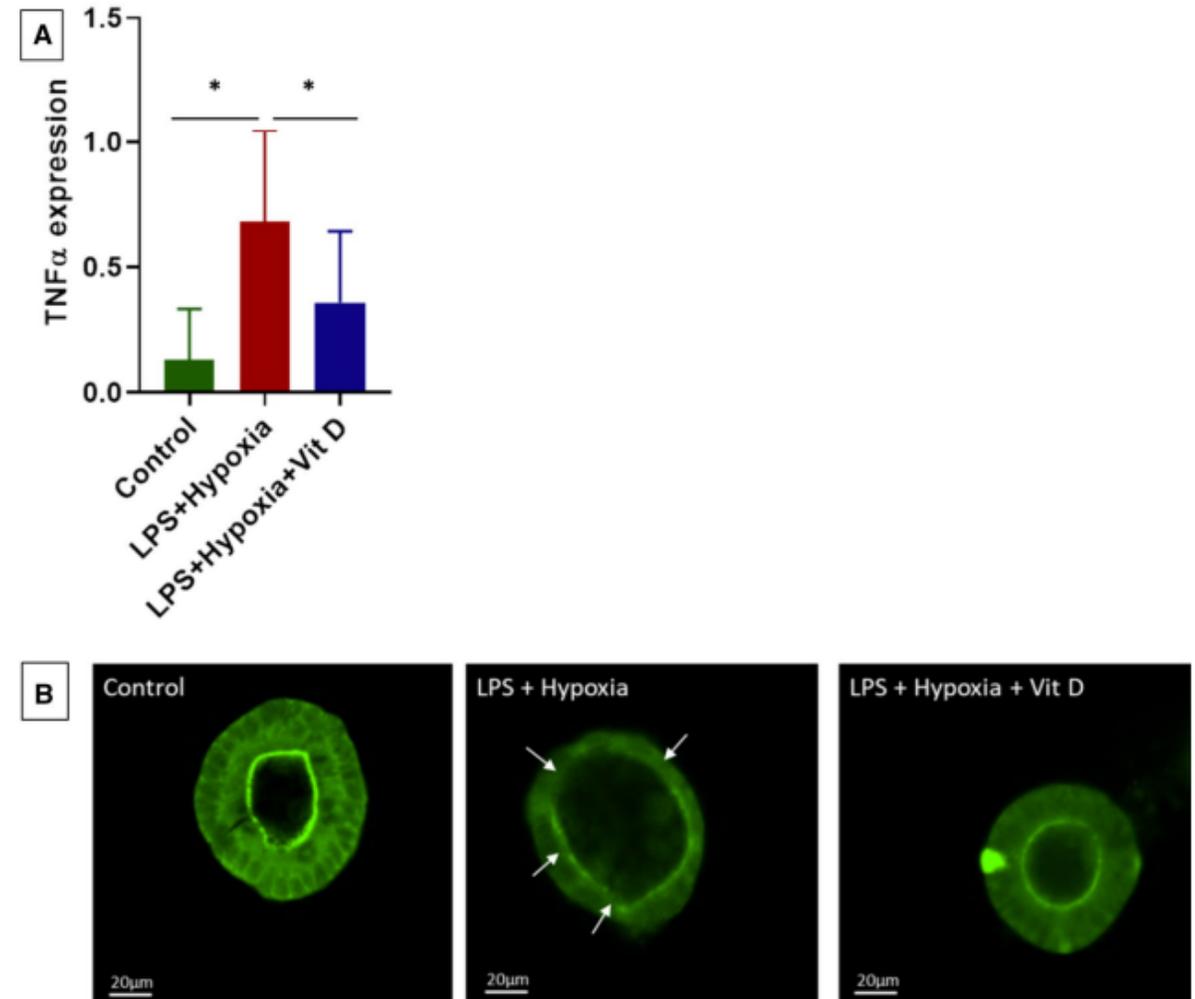
➤ Inactivation constitutive du récepteur nucléaire de la VitD dans l'intestin



# La VitD régule certaines protéines de jonctions serrées

➤ Traitement des organoïdes avec du LPS et de la VitD.

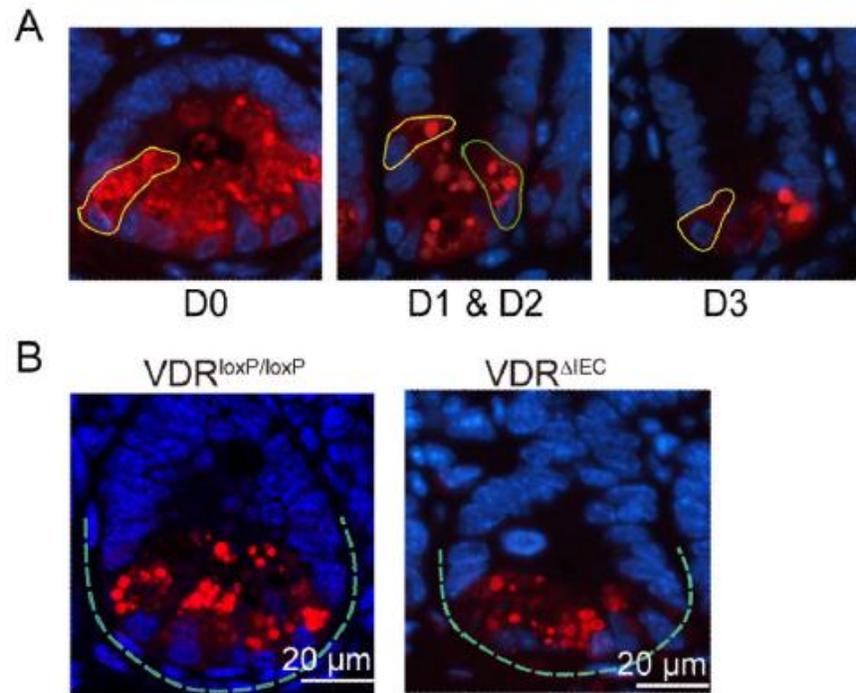
➤ Effets sur la protéine de jonction cellulaire zo1



**Fig.3** Organoid inflammation and tight junction disruption were prevented by vitamin D. **a** Gene expression of inflammation marker TNF $\alpha$  in intestinal organoids Real-time polymerase chain reaction for inflammation markers TNF $\alpha$  in control intestinal organoids and organoids subjected to LPS+Hypoxia and LPS+Hypoxia+Vit D. **b** Immunofluorescence staining micrographs of tight junction protein in intestinal organoids Immunofluorescence staining micrographs of

tight junction ZO-1. ZO-1 protein formed a distinct ring in the control organoid and it was disrupted in LPS and hypoxia-treated organoids as indicated by white arrows. Organoids treated with vitamin D showed similar ring structure as control organoids. Experiments were independently repeated three times.  $p < 0.05$  was considered significant

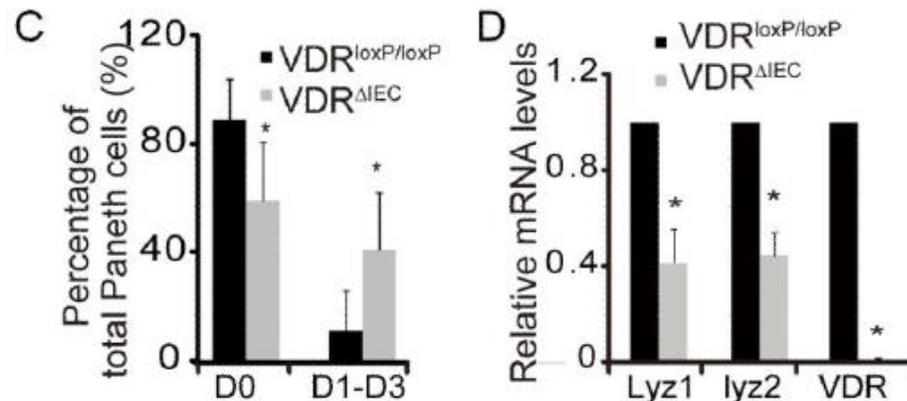
# L'absence de VDR induit des cellules de Paneth anormales



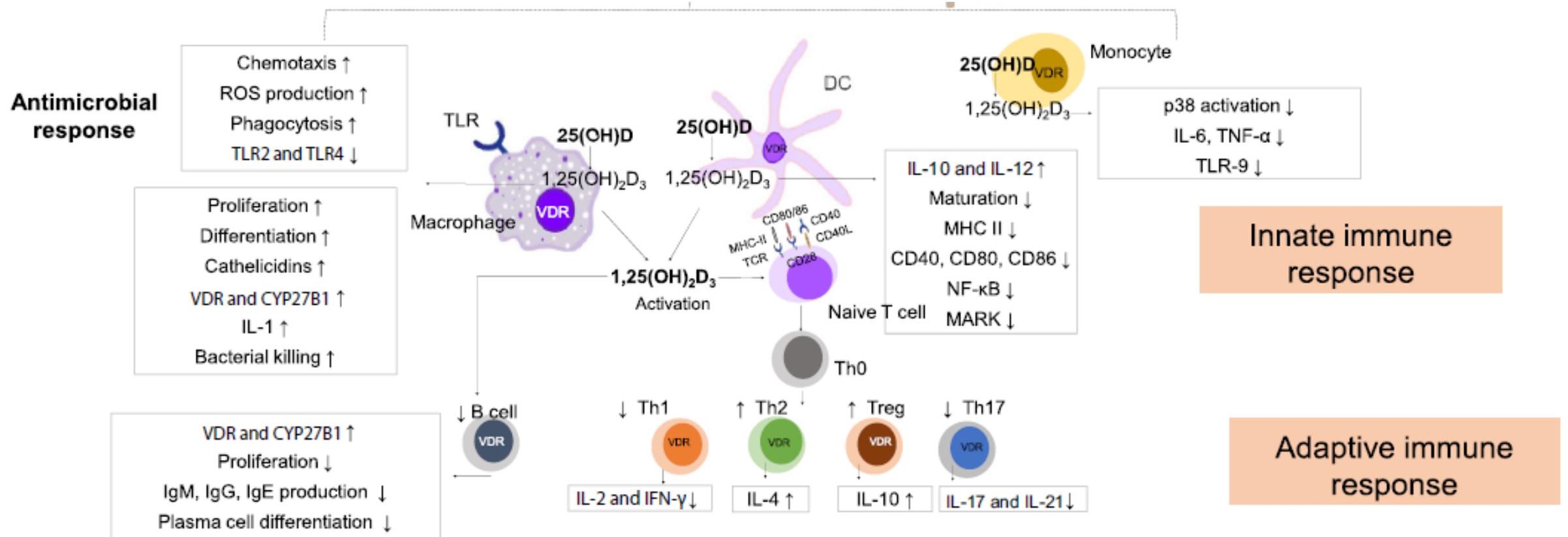
1/ Le nombre de cellules de Paneth diminue dans l'iléon des souris n'exprimant pas le VDR dans l'intestin (comparées aux souris contrôles)

2/ L'absence de VDR dans l'épithélium intestinal induit des cellules de Paneth anormales.

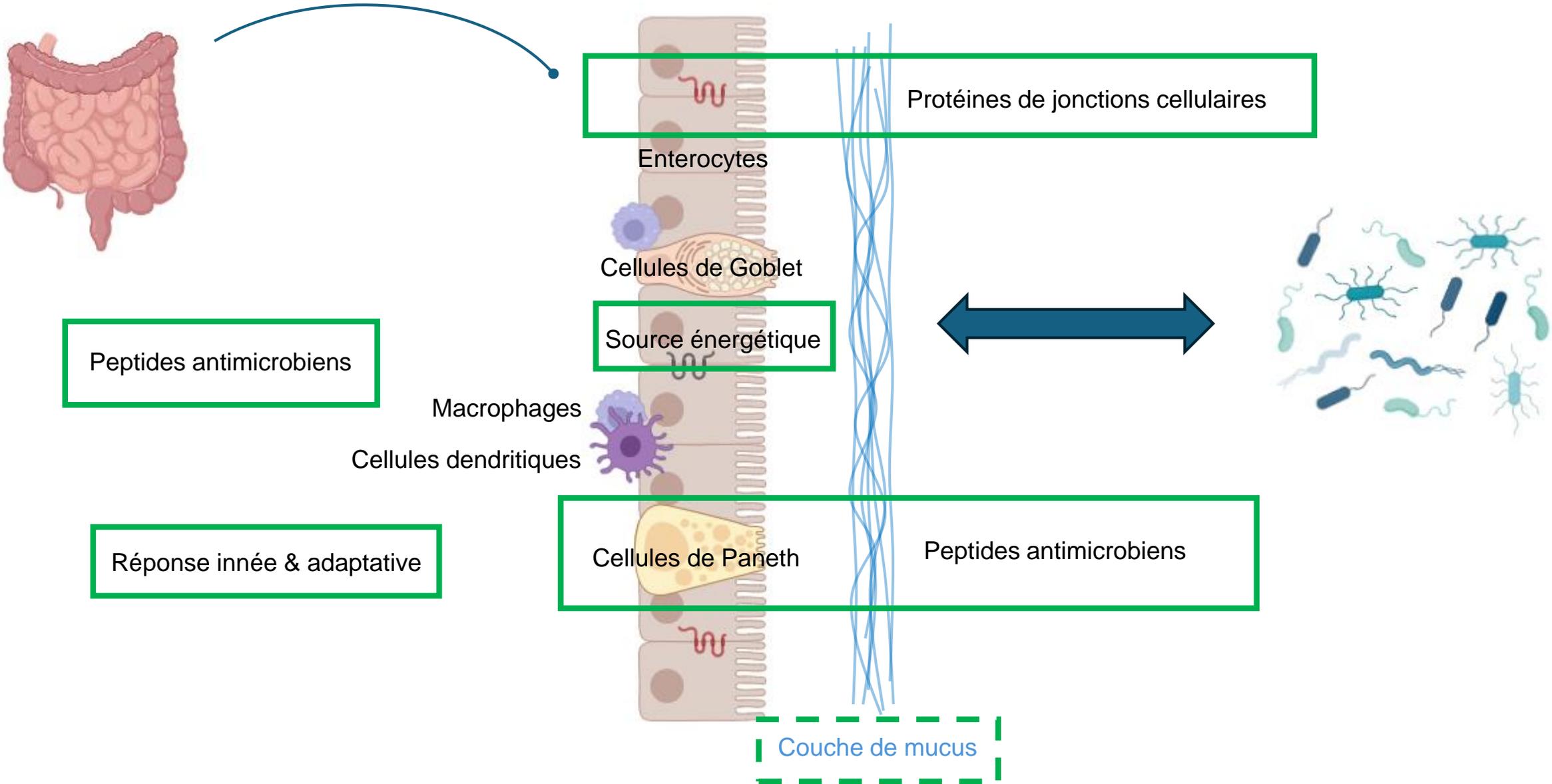
3/ Les capacités antimicrobiennes des cellules de Paneth sont altérées en absence de VDR



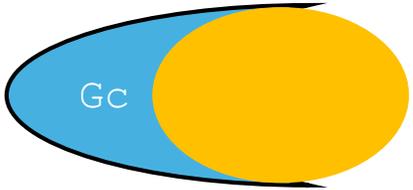
# La VitD régule les réponses immunitaires innées et adaptatives



# La VitD influence la communication bidirectionnelle entre la barrière de l'intestin et le MI



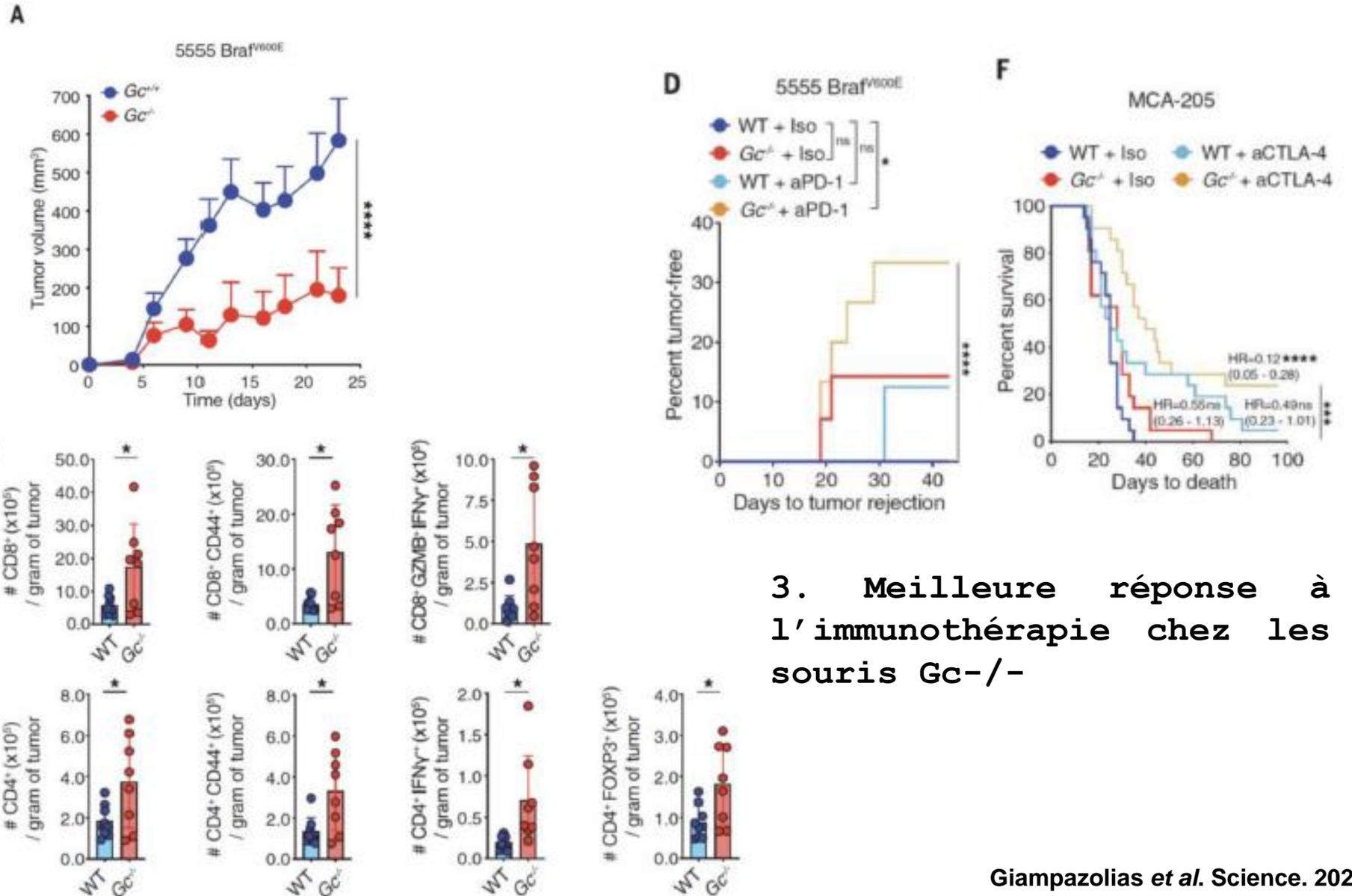
# Un exemple récent de l'effet indirect de la VitD sur le microbiome intestinal



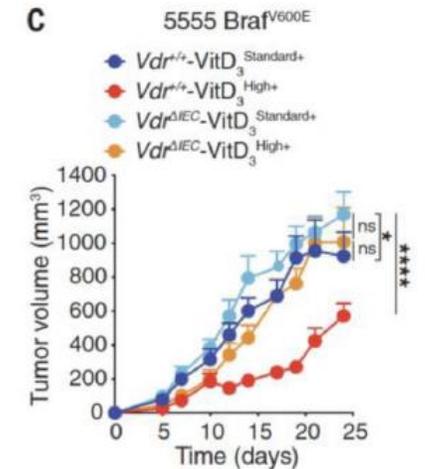
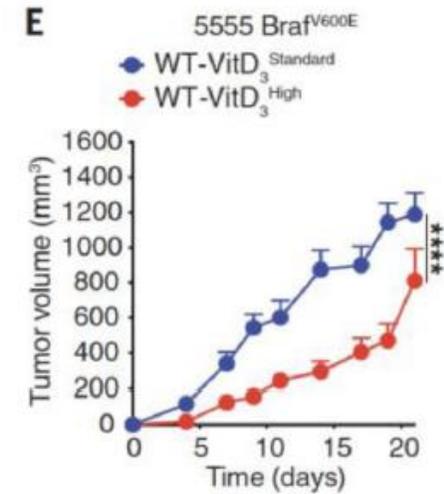
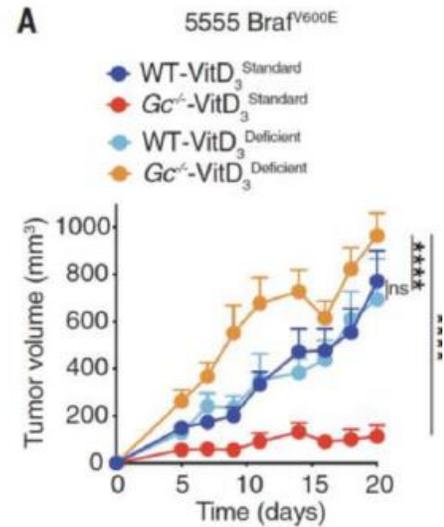
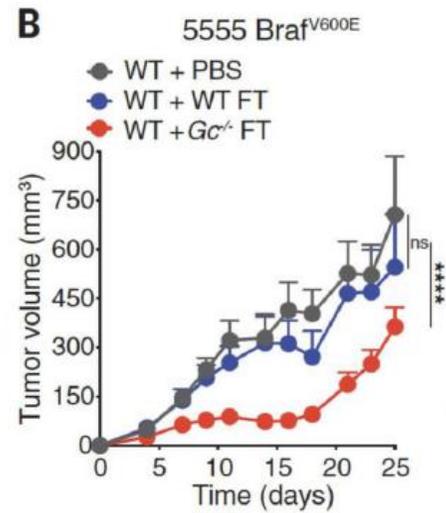
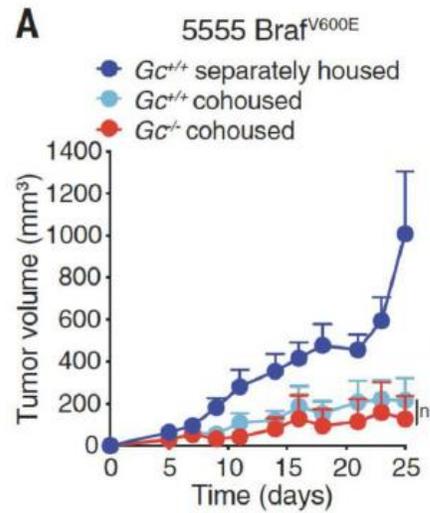
1. Les souris  $Gc^{-/-}$  contrôlent mieux la croissance tumorale

2. Infiltration intra-tumorale des  $CD4^+$   $CD8^+$  augmentée chez les  $Gc^{-/-}$

3. Meilleure réponse à l'immunothérapie chez les souris  $Gc^{-/-}$



# Un exemple récent de l'effet indirect de la VitD sur le microbiome intestinal

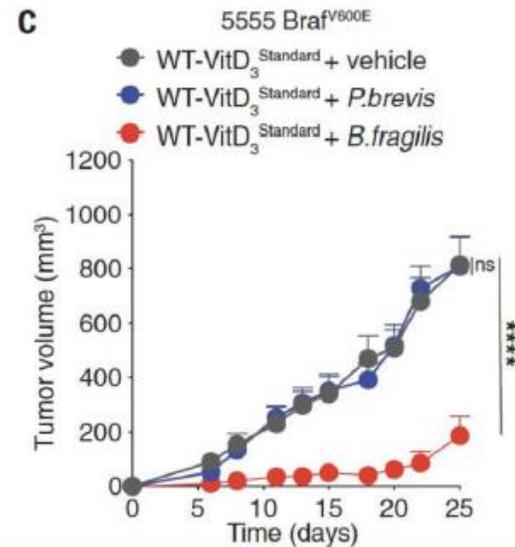
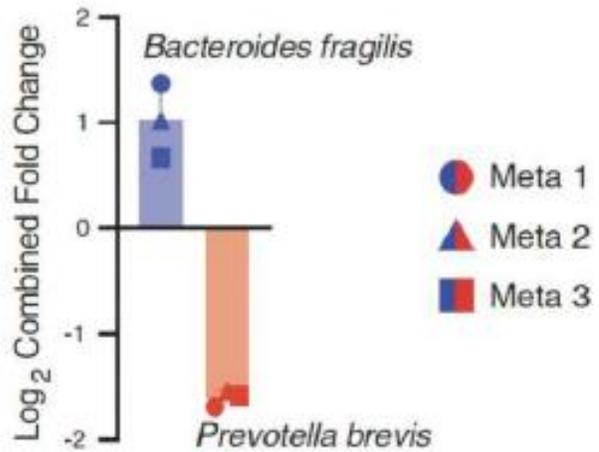


4. La résistance à la croissance tumorale est transférable

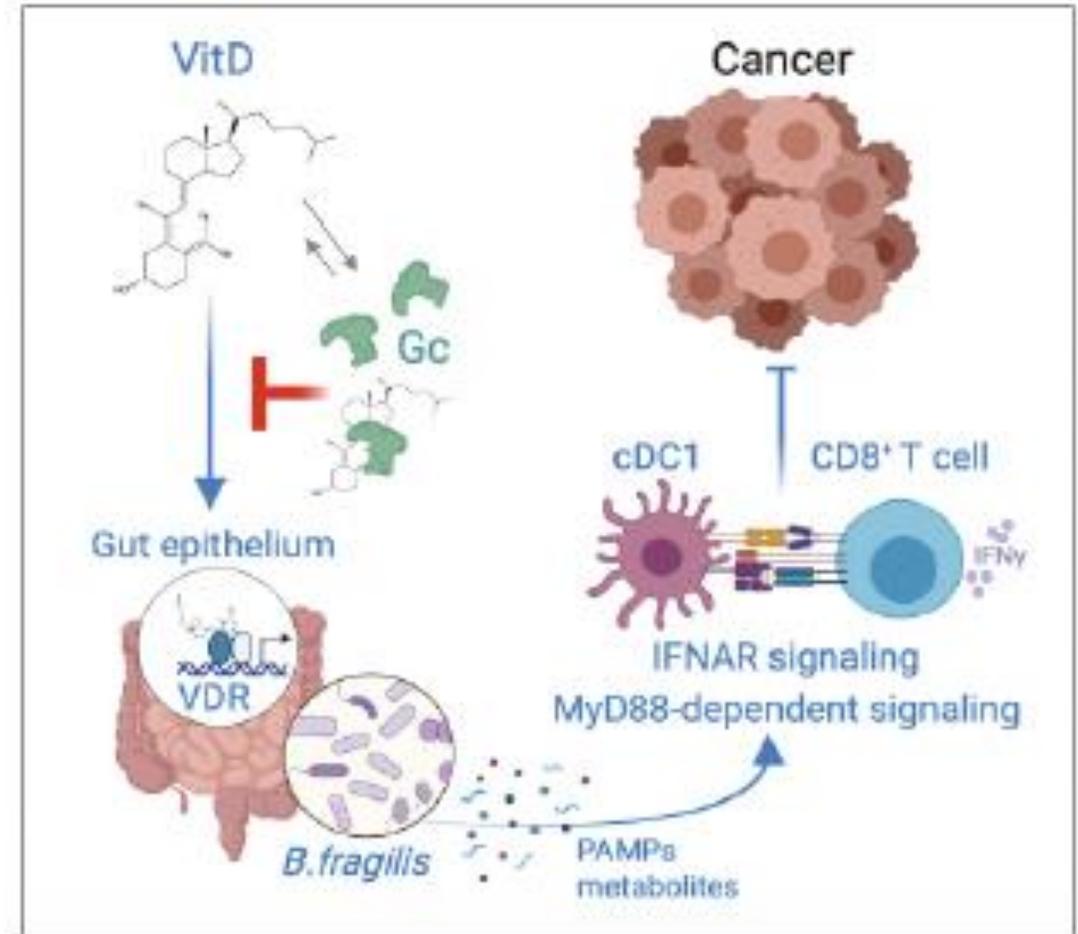
5. L'effet est dépendant de la biodisponibilité de la VitD3...

6. ... et du récepteur VDR dans l'intestin !

# Un exemple récent de l'effet indirect de la VitD sur le microbiome intestinal

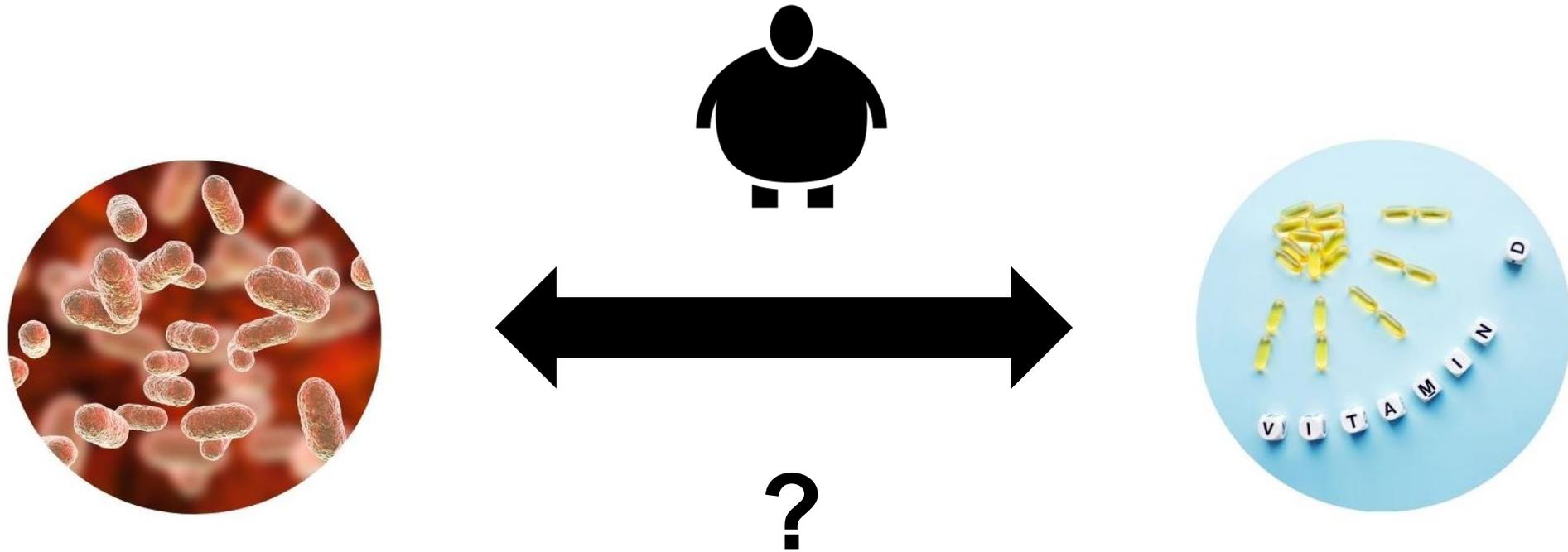


7. Le gavage oral de *Bacteroides fragilis* induit une résistance à la croissance tumorale



# Interactions entre le microbiome intestinal et la vitamine D au cours du syndrome métabolique

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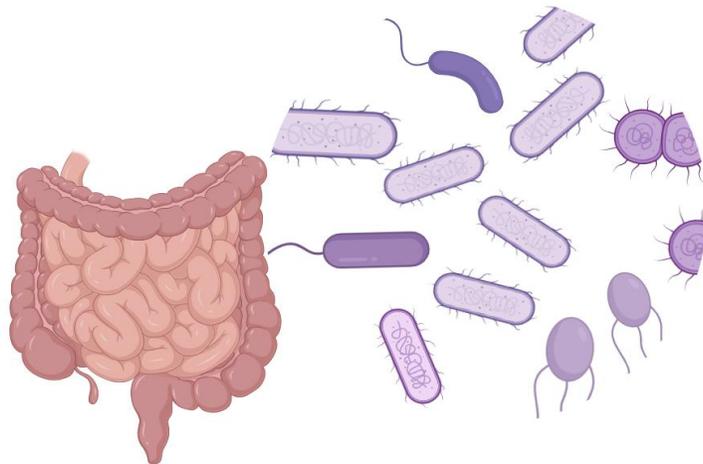
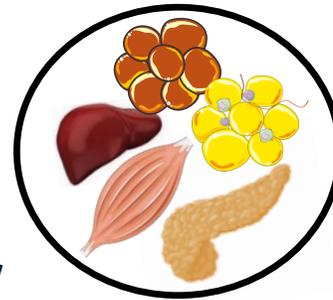
# L'obésité a des causes multifactorielles → a-t-on pris en compte tous les facteurs ?



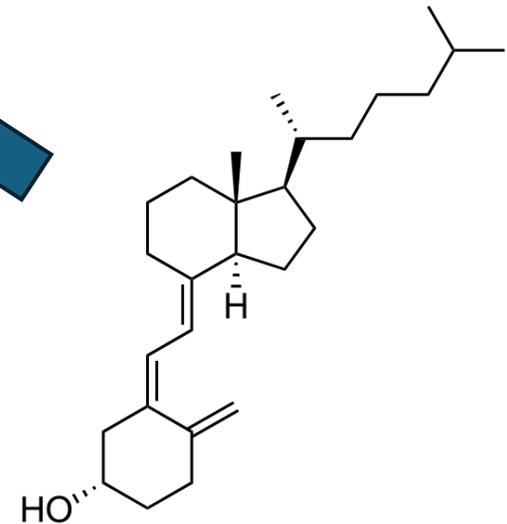
En 2022: **1 personne sur 8** dans le monde était atteinte d'obésité (WHO)

En 2050: prédiction de **1 personne sur 2** (GBD 2021 Adult BMI Collaborators. Lancet. 2025)

**Causes multifactorielles** et encore incomplètement comprises (Rubino et al. Lancet Diabetes Endocrinol. 2025)



**Microbiote Intestinal**



**Vitamine D  
(VitD)**

# Un déséquilibre du MI est observé au cours du syndrome métabolique

## ↓ Diversité bactérienne

### ↓ Bactéries « bénéfiques »

*Bifidobacterium* (immunité)

*F. prausnitzii* (anti-inflammatoire, butyrate)

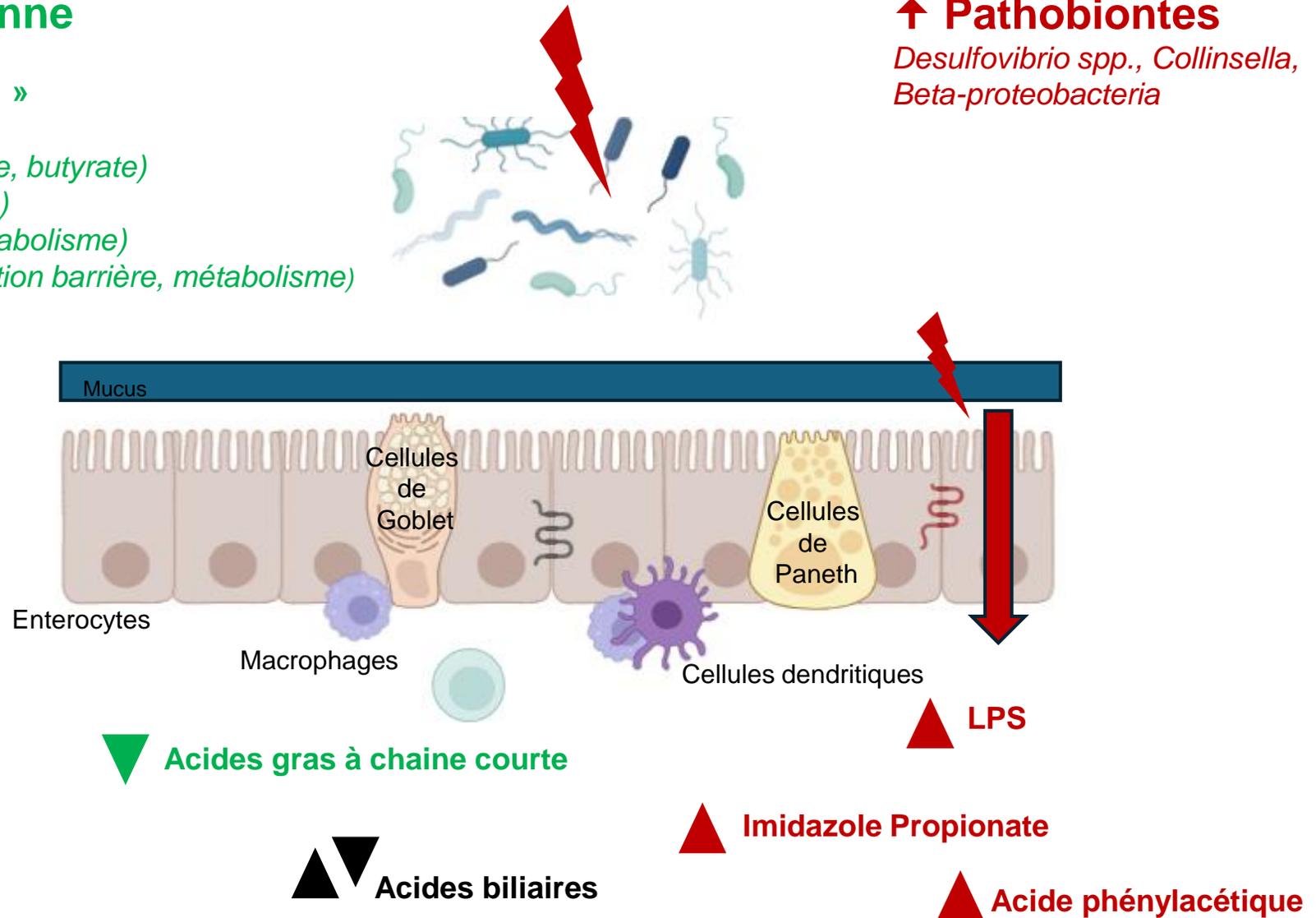
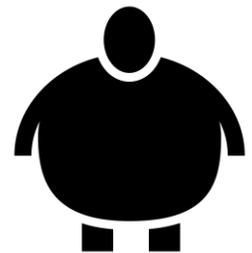
*Roseburia intestinalis* (butyrate)

*Dysosmobacter welbionis* (métabolisme)

*Akkermansia muciniphila* (fonction barrière, métabolisme)

## ↑ Pathobiontes

*Desulfovibrio* spp., *Collinsella*,  
*Beta-proteobacteria*

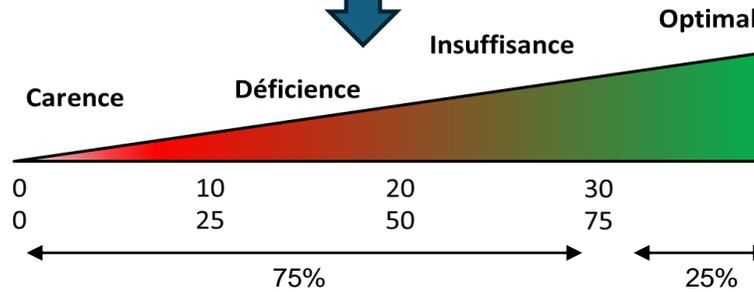
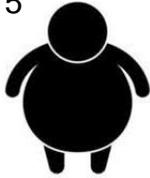


# La triade Métabolisme – Microbiome - Micronutriments

Vitamine D2 (ergocalciférol)  $\Rightarrow$    $\Rightarrow$  25(OH)D  $\Rightarrow$    $\Rightarrow$  1,25(OH)<sub>2</sub>D

## Niveaux plus faibles de 25(OH)D

Pereira-Santos *et al.* Obes. Rev. Off. J. Int. Assoc. Study Obes. 2015



Population générale :  
Cui *et al.* Front. Nutr. 2013;  
Etude Esteban 2015

## Effets de la supplémentation en VitD

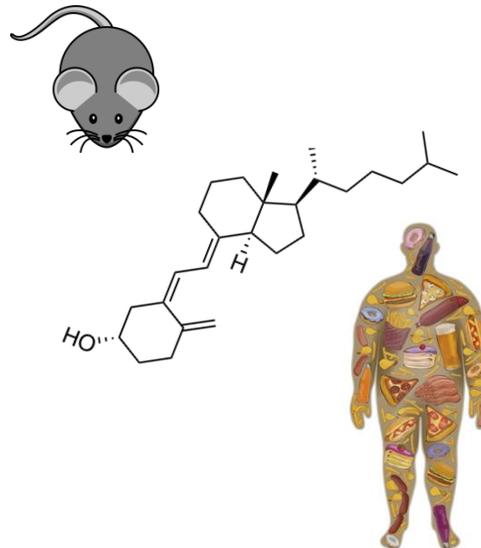


Inflammation



Homéostasie glucidique et lipidique

Marcotorchino *et al.* J Nutr Biochem. 2014  
Karkeni *et al.* Endocrinology. 2015  
Karkeni *et al.* Epigenetics. 2018  
Bonnet *et al.* J Steroid Biochem Mol Biol. 2019  
Marziou *et al.* Nutrients. 2020  
Payet *et al.* Mol Nutr Food Res. 2023  
Payet *et al.* Biofactors. 2025



Expression de gènes proinflammatoires



Homéostasie du glucose

Lontchi-Yimagou *et al.* Mol. Metab. 2020

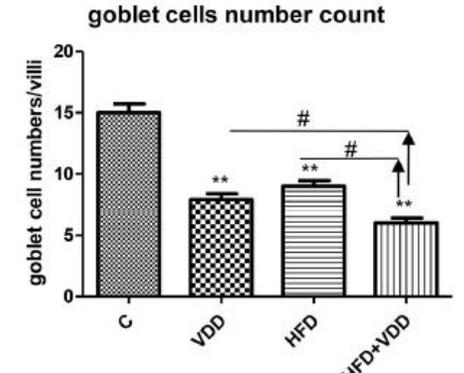
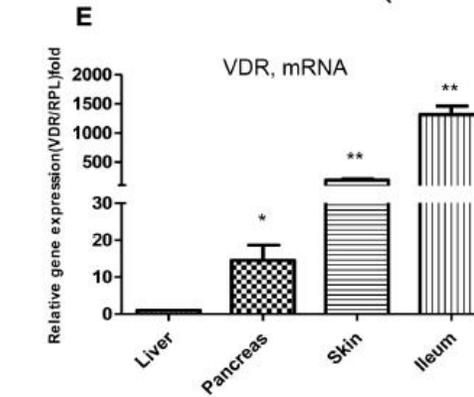
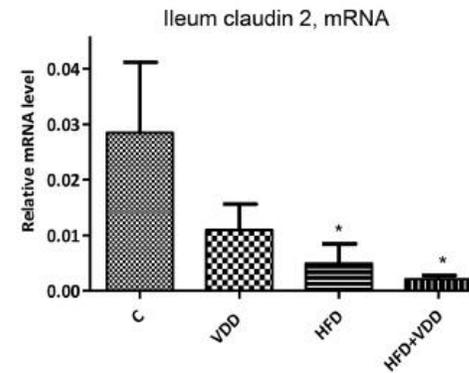
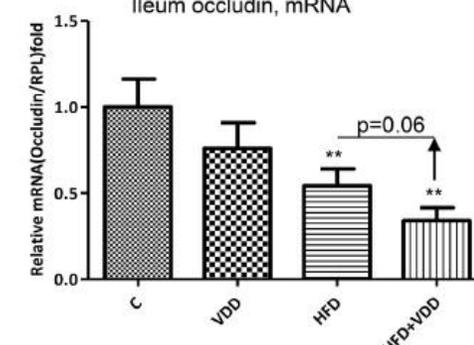
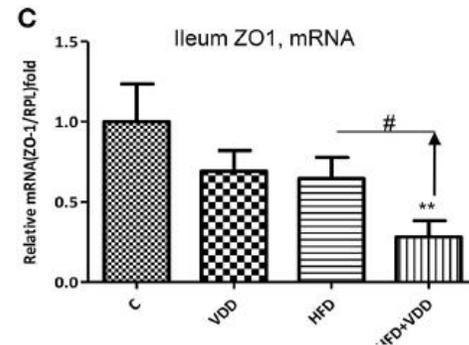
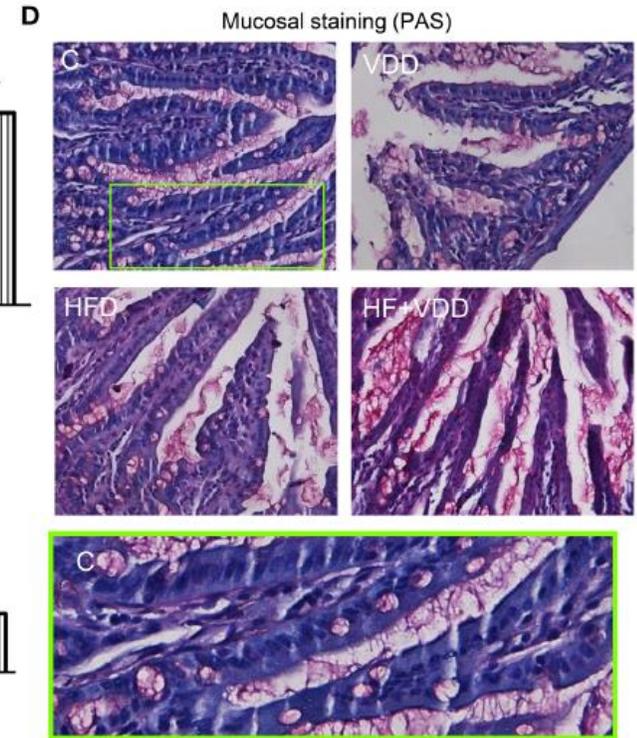
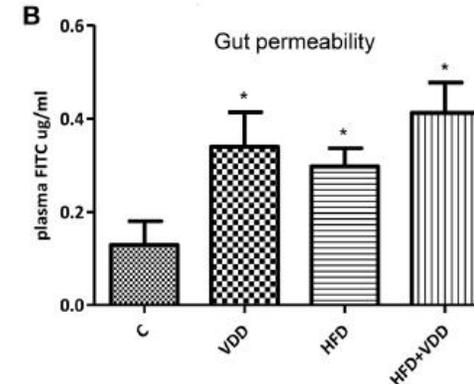
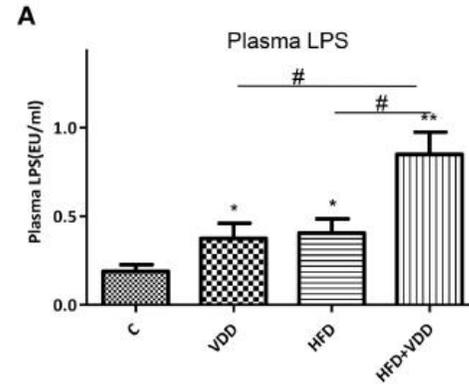
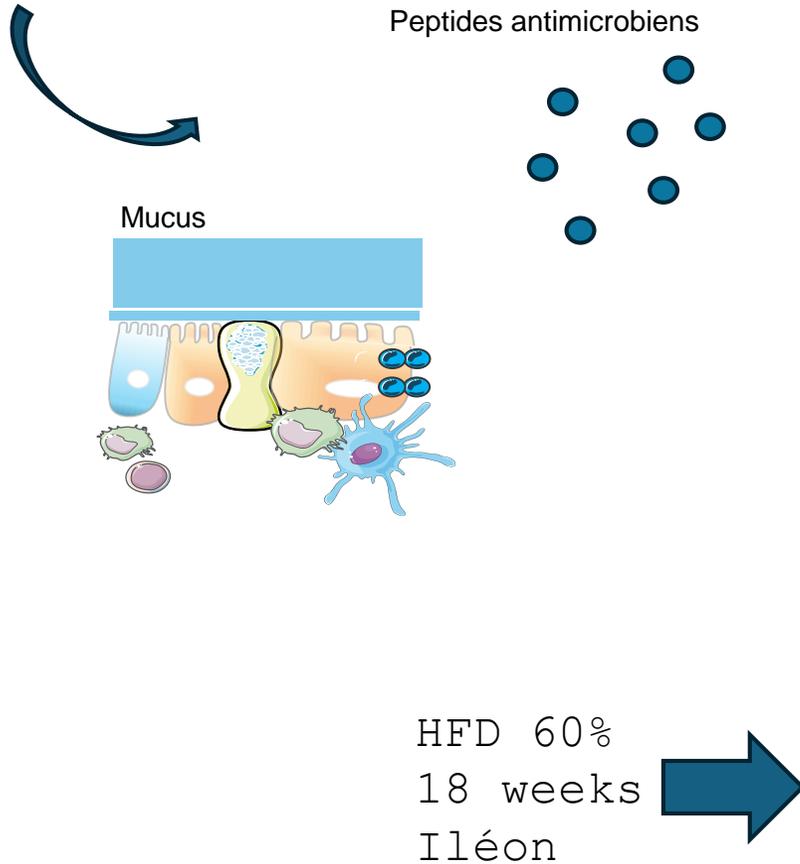
Méta-analyse (39RCT- n=2982 T2D)

**Effets sur HbA1c, HOMA-IR, glycémie & insuliniémie à jeun dépend de la durée/ dosage supplémentation ET 25(OH)D basale + BMI**

Chen *et al.* Diabetes Obes. Metab. 2024

# Effet de la modulation de l'apport en VitD sur le microbiome intestinal et les altérations métaboliques induites par un régime HFHS

## Modulation de la teneur en VitD



# La composition du microbiome intestinal est altérée chez les souris déficientes en vitD



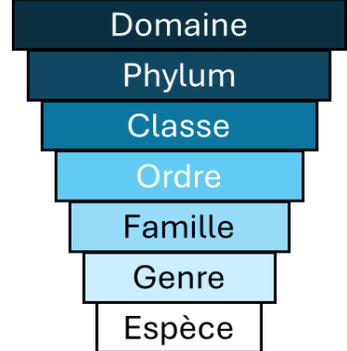
Standard  
10% graisses

– 1250 IU/kg

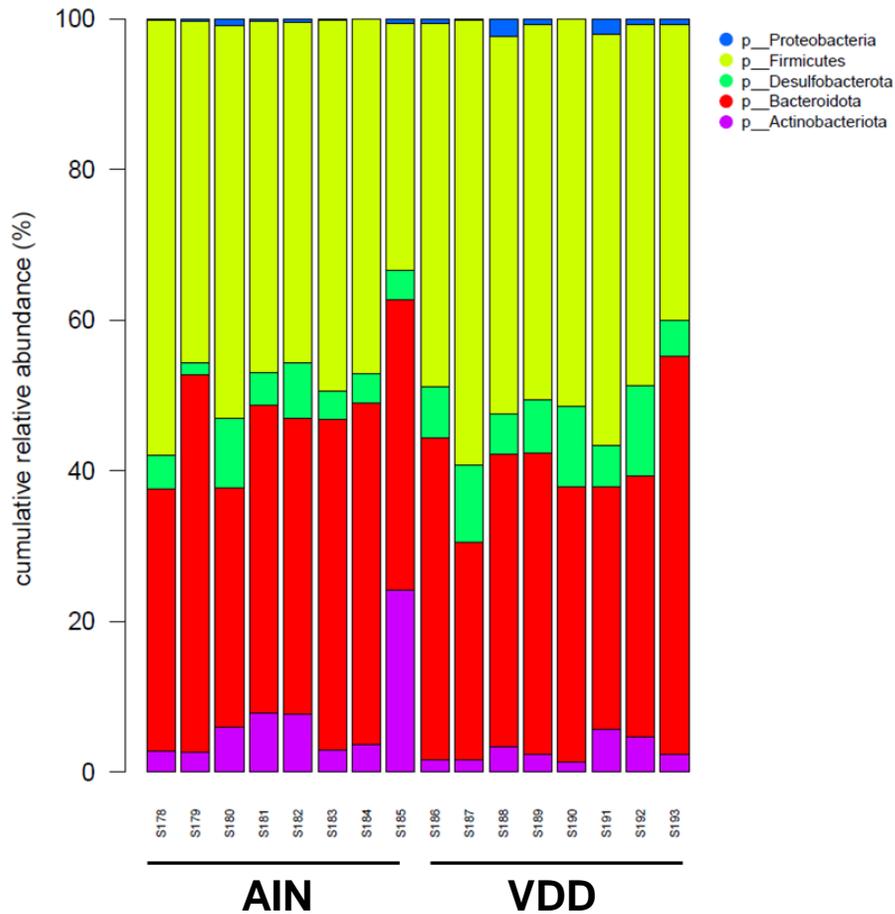
Alimentation

Vitamine D  
dans l'alimentation

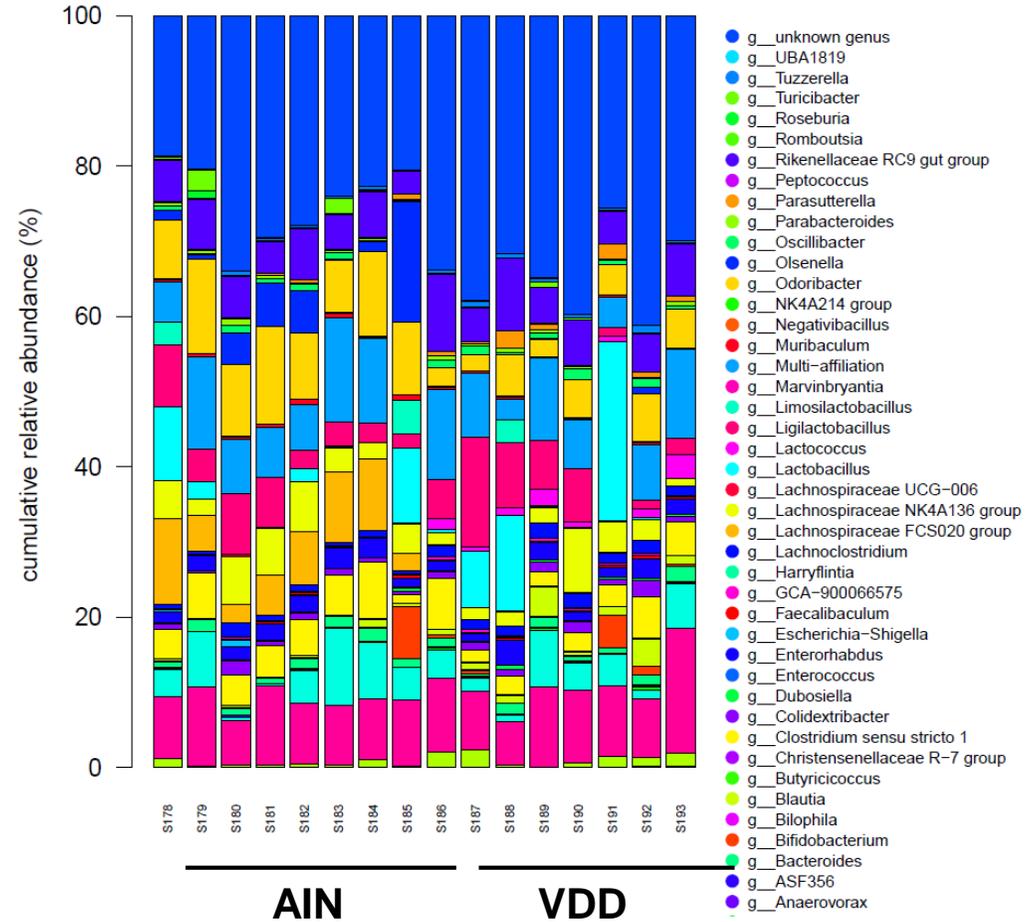
Analyse taxonomique:  
16S rRNA gene sequencing



Taxonomic binning at Phyla level

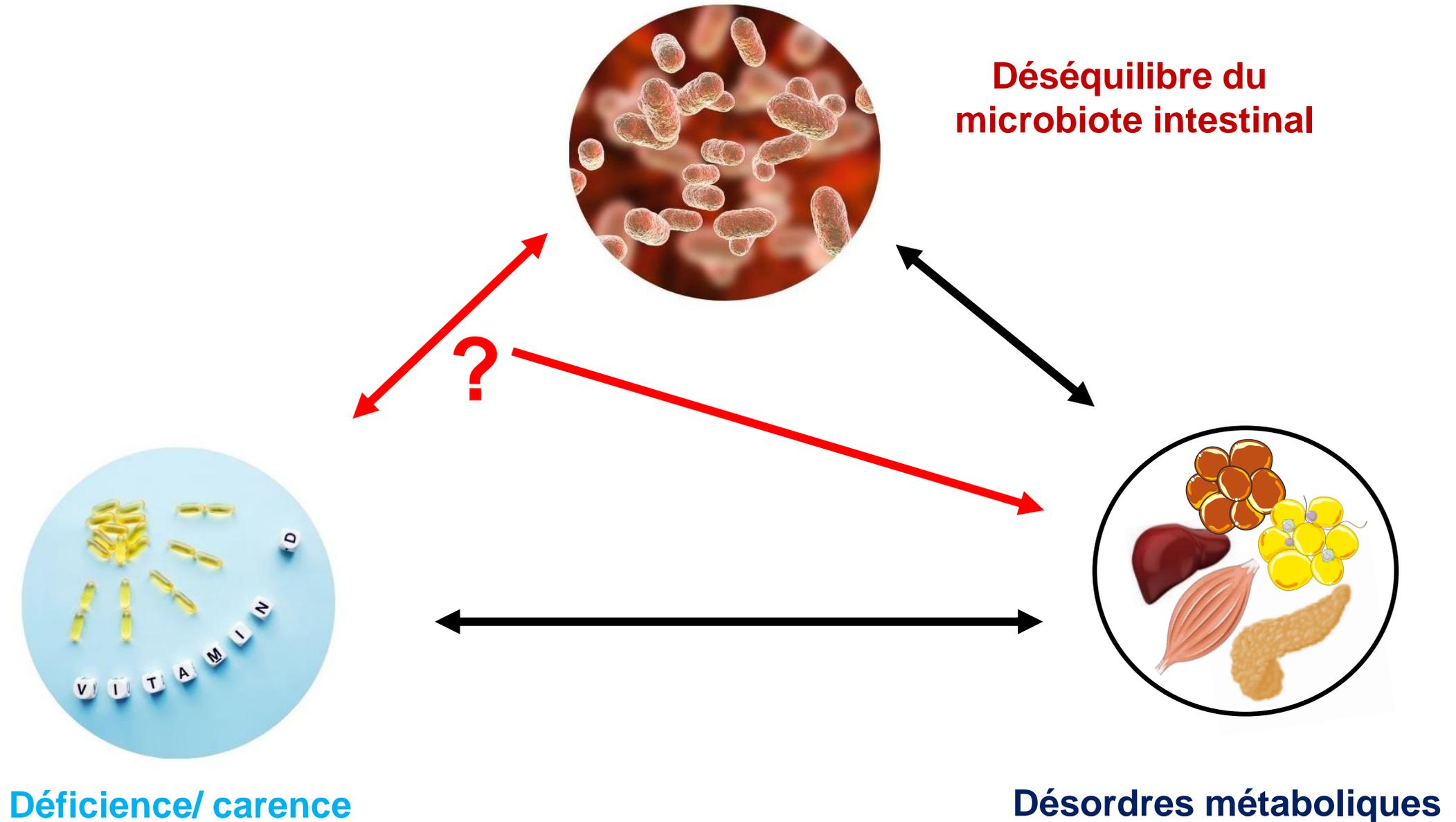


Taxonomic binning at Genus level



# Comprendre les interactions au sein de cette triade est un défi important

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# Messages importants

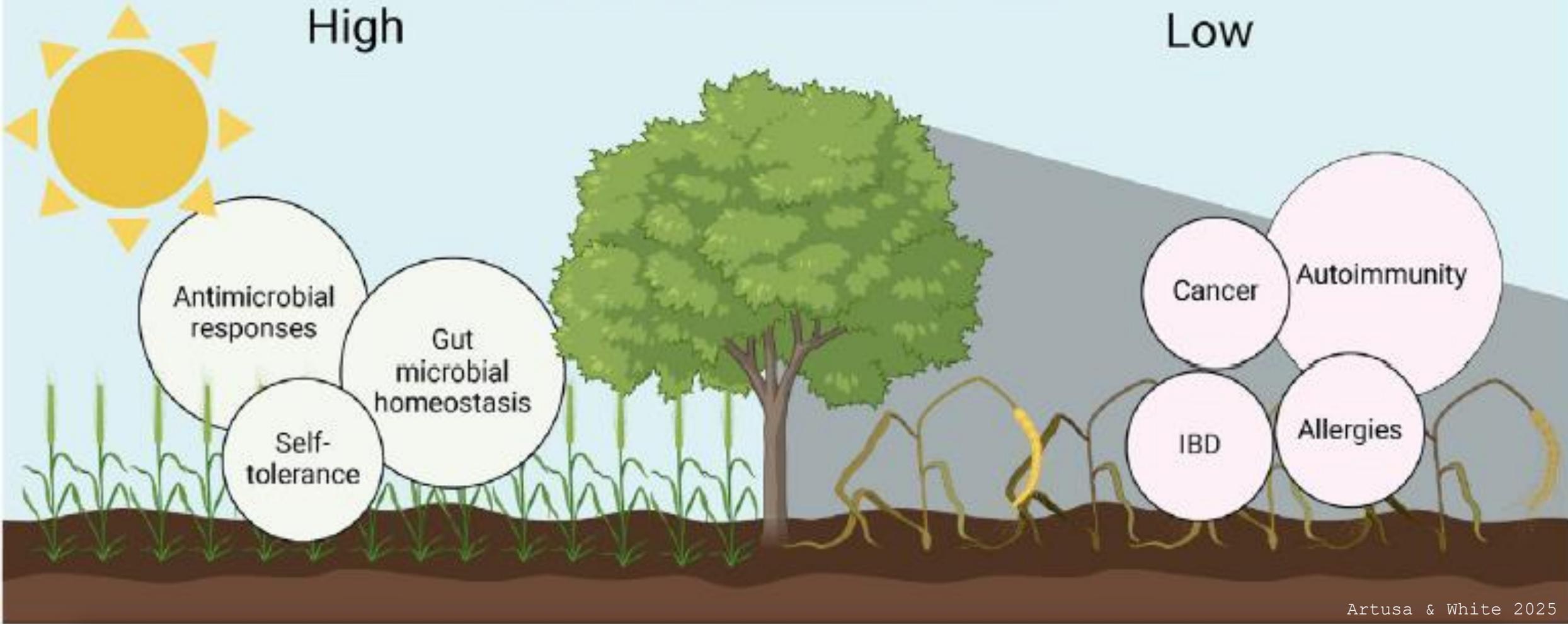
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- Le microbiome intestinal et la Vitamine D jouent un rôle important dans la régulation du métabolisme de l'hôte.
- Le Microbiome intestinal régule le métabolisme de la vitamine D.
- La Vitamine D influence la communication bidirectionnelle entre le microbiome et la barrière intestinale.
- Le statut en 25(OH)D (forme circulante de la vitamine D) mérite plus d'attention dans les études d'intervention.
- **Les interactions Micronutriments – Microbiome constituent un champ de recherche prometteur à approfondir**

# Vitamin D metabolite levels

High

Low



Merci de votre attention