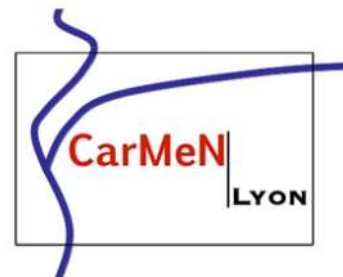


Thyroïde et microbiote intestinal

Journées du GRT – 28 mars 2024

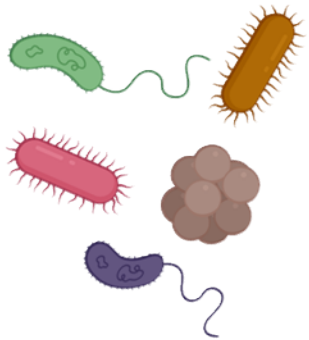
Karim CHIKH, MCU-PH, Biochimie HCL



Le microbiote humain = Ensemble des micro-organismes vivant au sein d'un individu

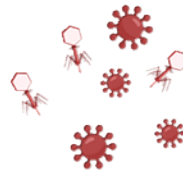
3. 10¹³ cellules ~ 3.10¹³ bactéries
environ 2 kg

Bactéries



Archées

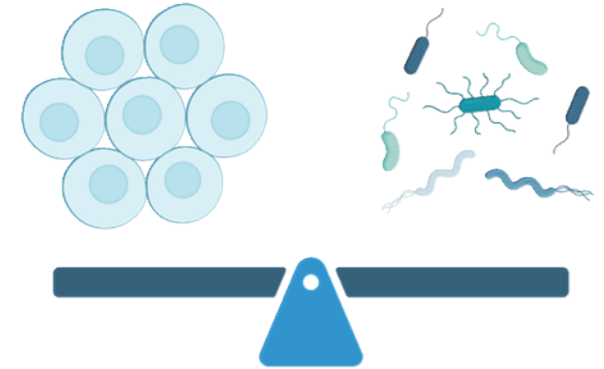
Virus



Champignons



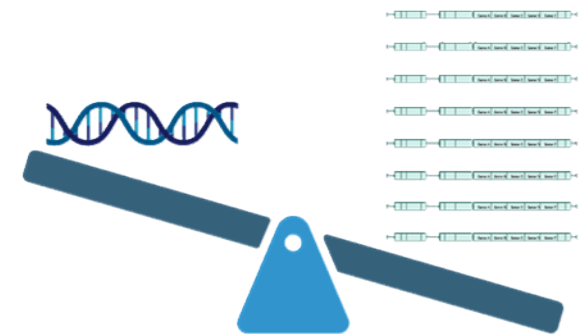
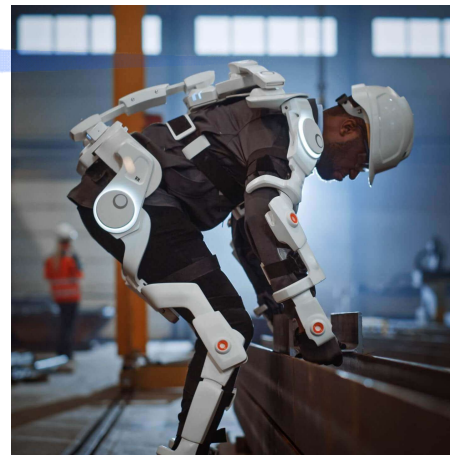
Parasites



Gènes humains < x150 gènes bactériens



10¹¹ bactéries/g de selles



Un microbiote humain – plusieurs éco-systèmes

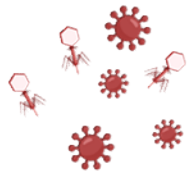
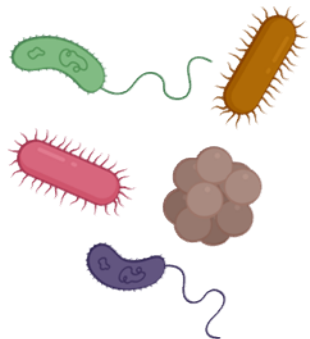
Bactéries

Archées

Virus

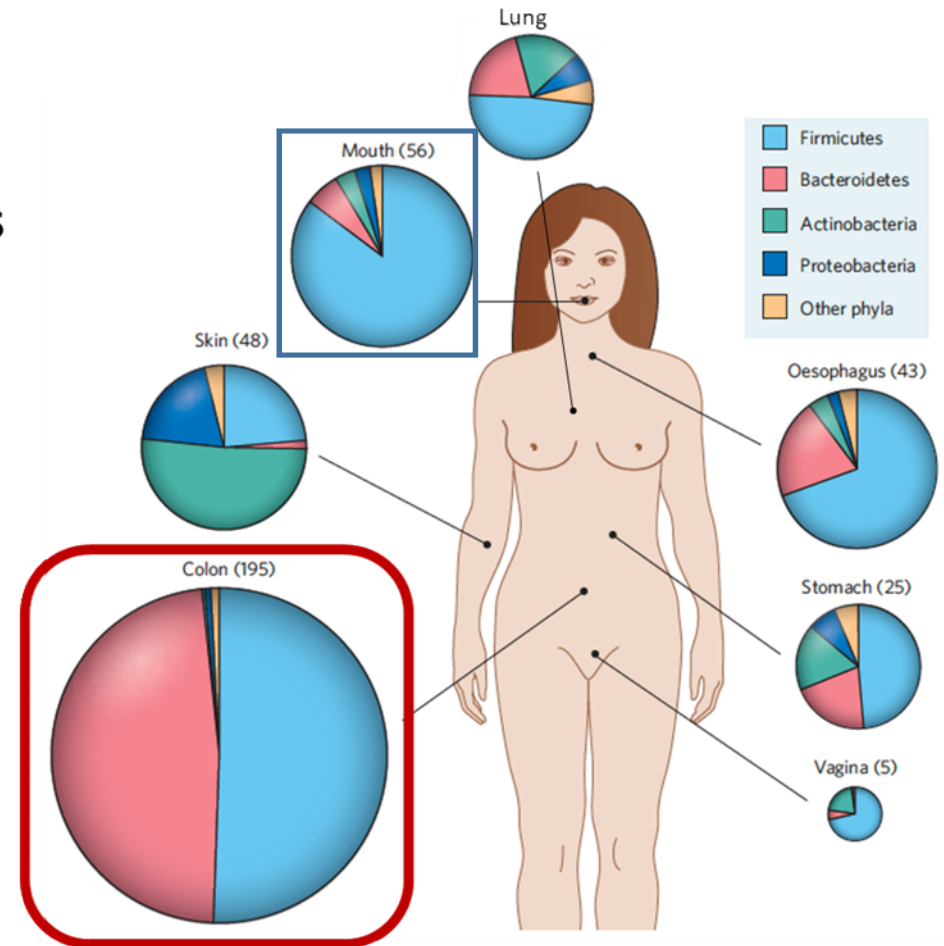
Champignons

Parasites



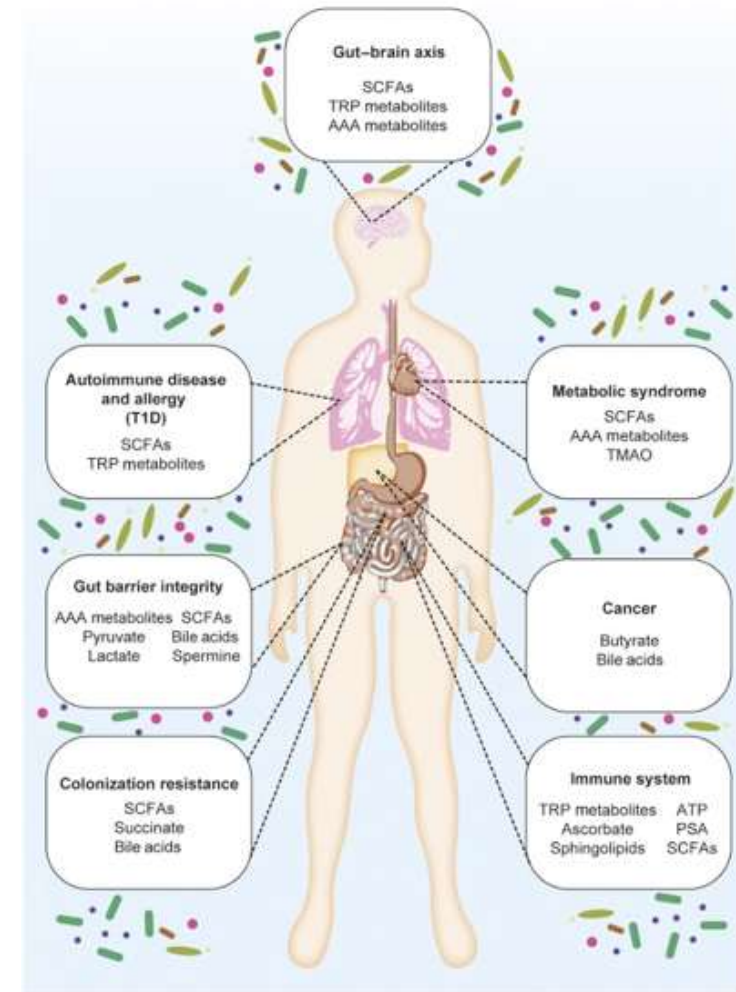
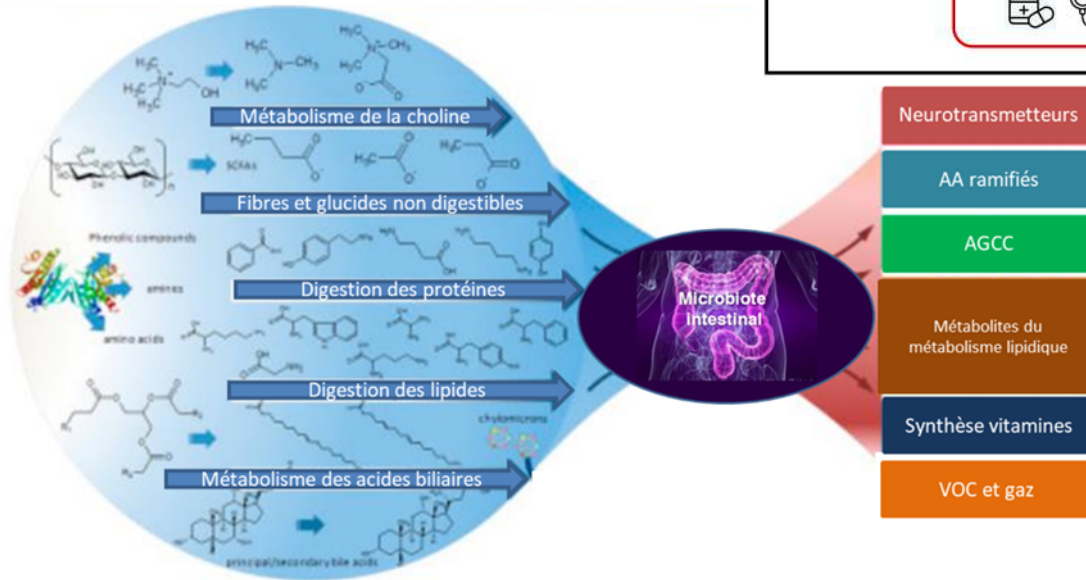
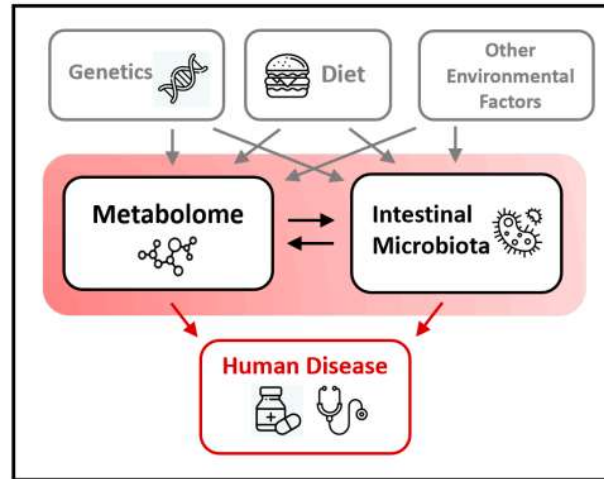
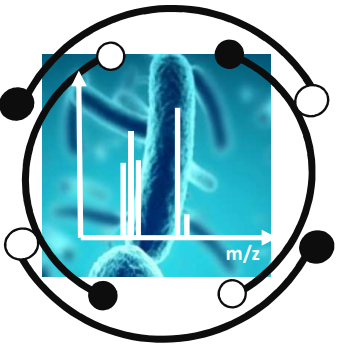
Domaine :	Bactéries
Phylum :	Firmicutes
Classe :	Bacilli
Ordre :	<i>Lactobacillales</i> (Bactéries lactiques)
Famille :	<i>Lactobacillaceae</i>
Genre :	<i>Limosilactobacillus</i>
Espèce :	<i>L. reuteri</i>
Souche :	<i>Limosilactobacillus reuteri</i> DSM 17938

Lavelle & Sokol, Mol Genet IBD, 2019



Dethlefsen *et al*, Nature 2007
 Donaldson *et al*, Nat. Rev. Microb, 2015

Interactions hôte-microbiote : activités métaboliques et communication à distance



Publications « Thyroïde et microbiote intestinal »

NIH National Library of Medicine
National Center for Biotechnology Information

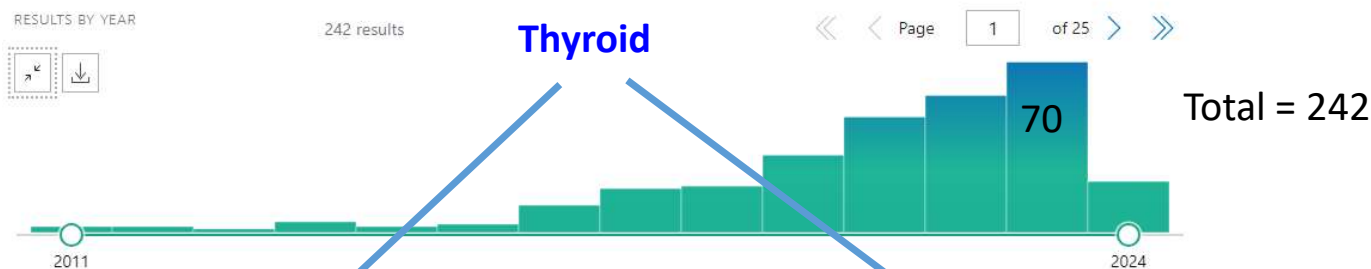
PubMed®

thyroid and gut microbiota

Search

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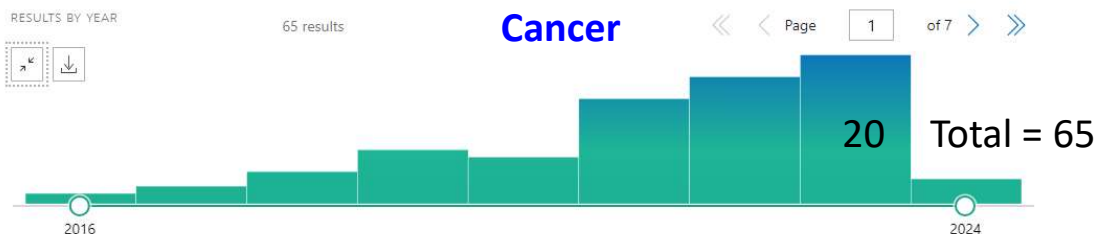
PubMed®

thyroid cancer and gut microbiota

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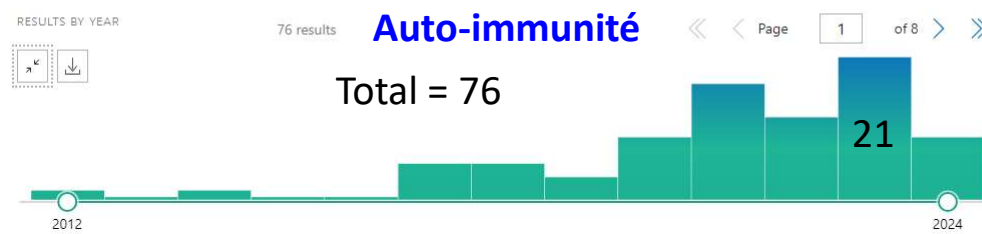
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thyroid and autoimmunity and gut microbiota

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Essais cliniques thyroïde et microbiote intestinal

<https://clinicaltrials.gov/>

Focus Your Search (all filters optional)	Hide <<
Condition/disease ⓘ	

Search Results

6 : Chine; 1 : Italie

Viewing 1-7 out of 7 studies

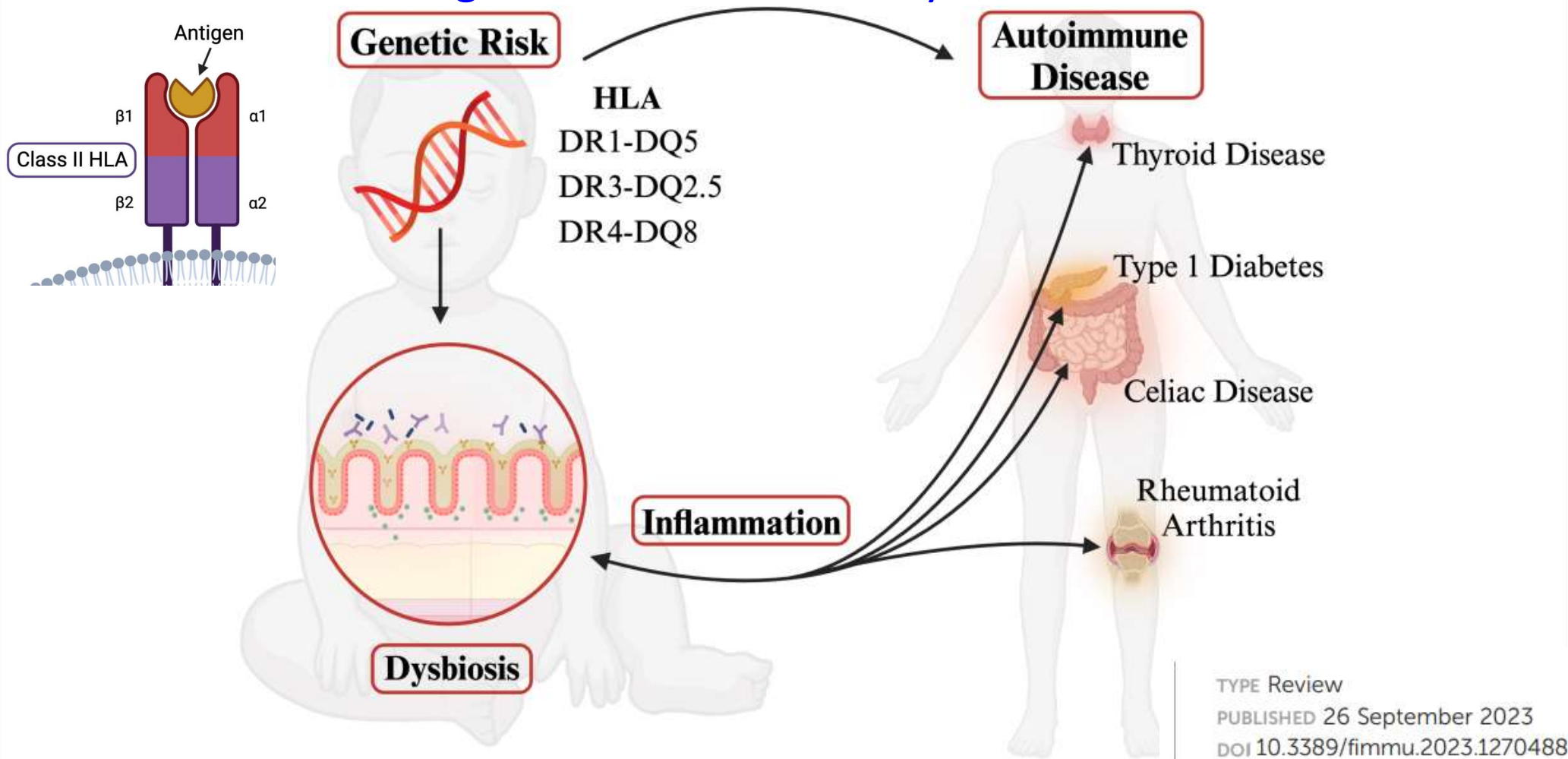
Showing results for: **Thyroid Diseases** | Other terms: **Microbiota**

> [BMJ Open. 2023 Sep 14;13\(9\):e073971. doi: 10.1136/bmjopen-2023-073971.](#)

Protocol for a double-blinded randomised controlled trial to assess the effect of faecal microbiota transplantations on thyroid reserve in patients with subclinical autoimmune hypothyroidism in the Netherlands: the IMITHOT trial

Aline C Fenneman ^{1 2}, Elena Rampanelli ³, Anne H van der Spek ², Eric Fliers ², Max Nieuwdorp ³

Variants des gènes HLA classe II et dysbiose intestinale?



TYPE Review
PUBLISHED 26 September 2023
DOI 10.3389/fimmu.2023.1270488

GRAPHICAL ABSTRACT
Graphical representation of central hypothesis.

 **frontiers** | Frontiers in **Immunology**

Axe intestin-thyroïde et mécanismes hypothétiques

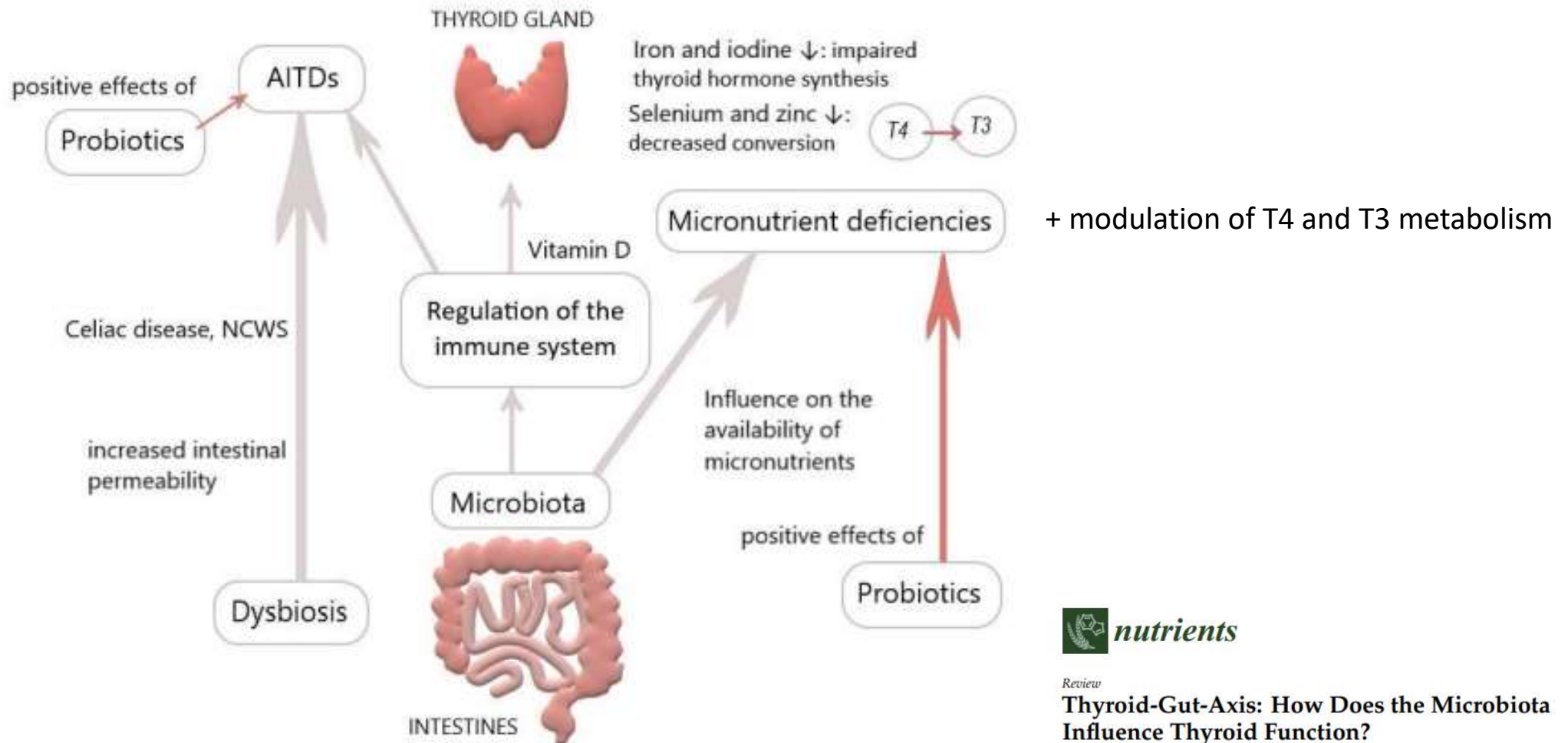
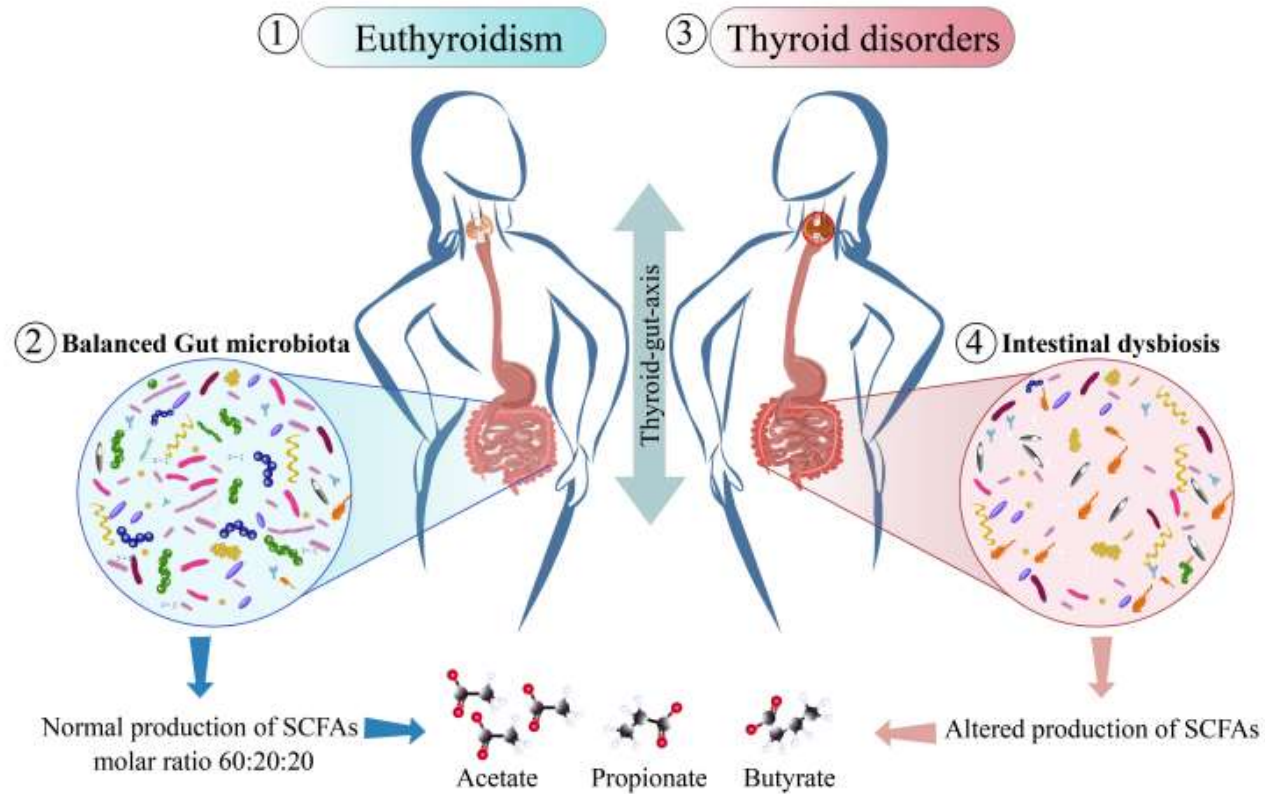


Figure 1. Overview of the influence of the gut on the thyroid (personal figure).

Axe intestin-thyroïde et production de SCFA



TYPE Review
PUBLISHED 30 June 2023
DOI 10.3389/fendo.2023.1192216

The Role of the Microbiota in Graves' Disease and Graves' Orbitopathy

Jueyu Hou^{1,2†}, Yunjing Tang^{1,2†}, Yongjiang Chen^{3†} and Danian Chen^{1,2*}

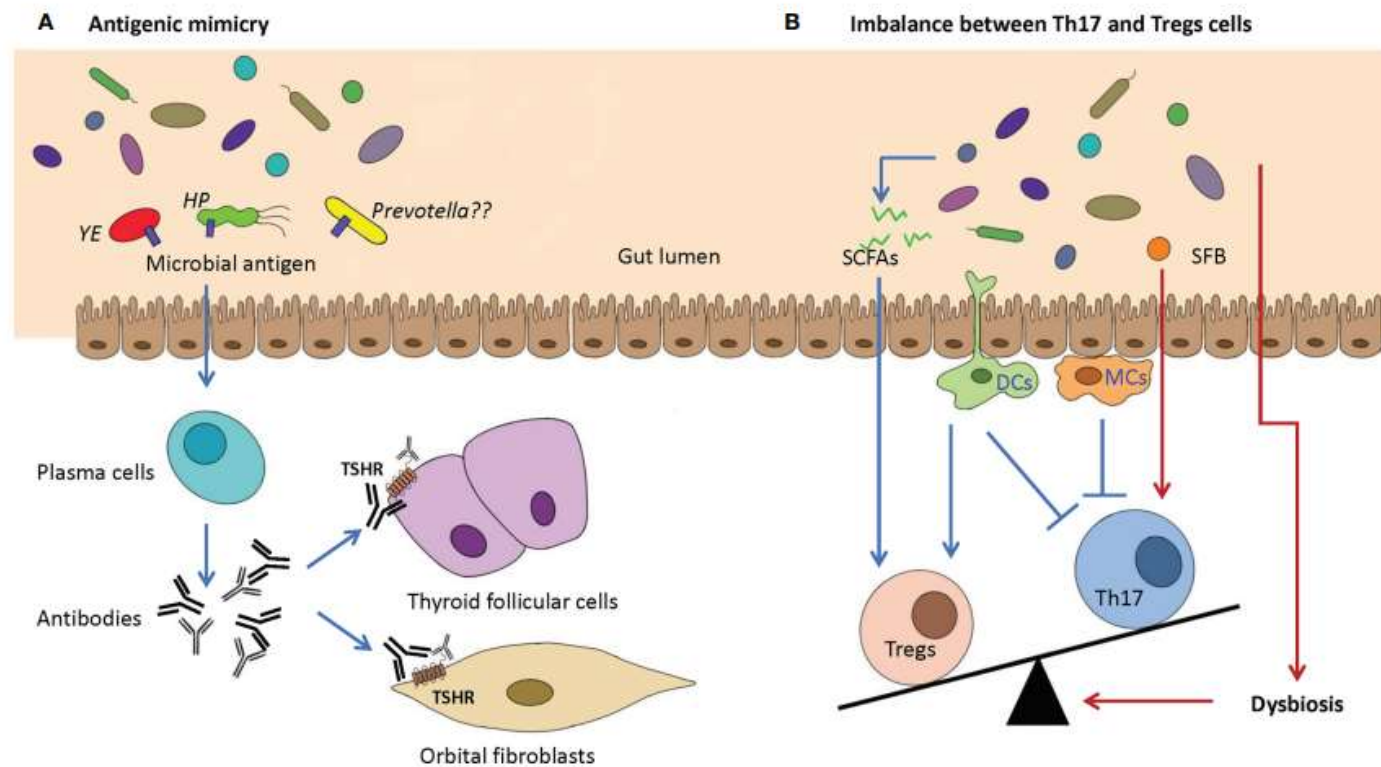


FIGURE 3 | Two potential proposed mechanisms of GD/GO are caused by dysbiosis of the gut microbiome. **(A)** Antigenic mimicry. Antigenic mimics in the gut microbiome, which have a highly similar structure or sequence with the autoantigens (e.g., TSHR), could activate plasma cells to produce antibodies that can bind TSHR on the thyroid follicular cells and orbital fibroblasts. Possible pathogenic microbes include *Yersinia enterocolitica* (YE), *Helicobacter pylori* (HP), and *Prevotella*. **(B)** Imbalance between Th17 and Tregs cells. Intestinal dysbiosis may cause the absence of beneficial microbiota and the reduction in beneficial anti-inflammatory metabolites such as SCFAs, which can increase the production of Tregs. SFB can promote the differentiation and maturation of Th17 cells. The imbalance between Th17 and Tregs cells can indirectly promote the progression of GD/GO. TSHR, thyroid-stimulating hormone receptor; SCFA, short-chain fatty acids; SFB, segmented filamentous bacteria.

Composition du microbiote et auto-immunité thyroïdienne

Association Between Gut Microbiota and Autoimmune Thyroid Disease: A Systematic Review and Meta-Analysis

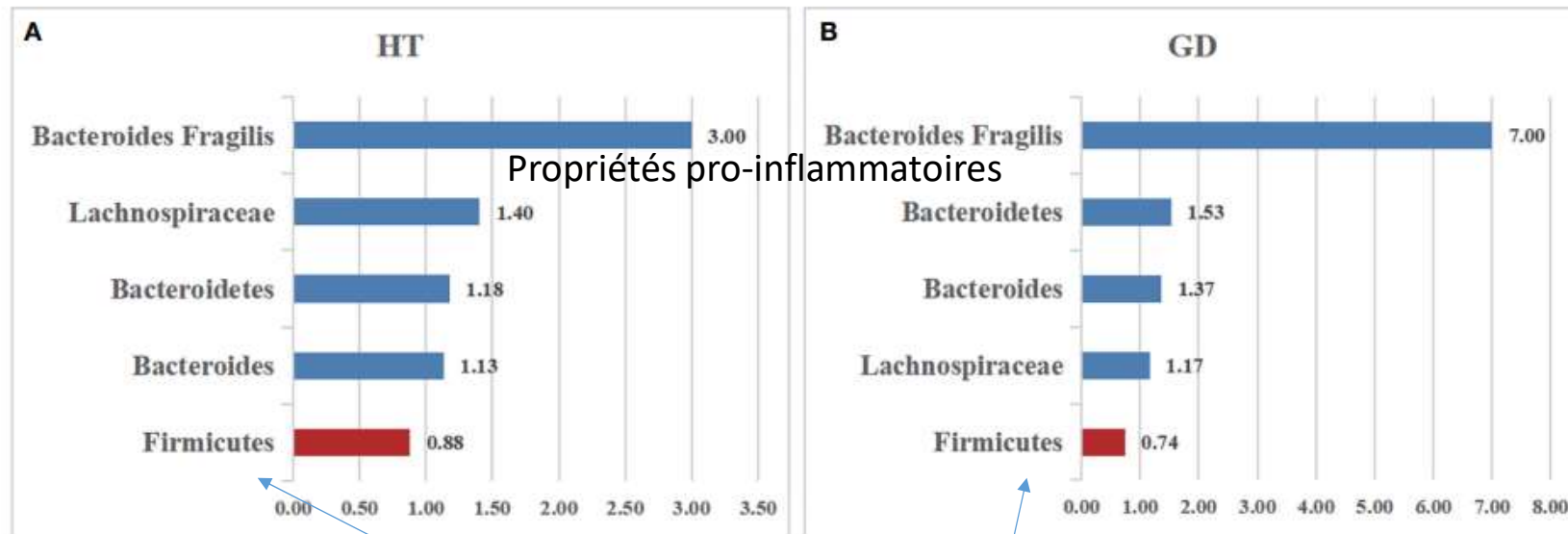
Boshen Gong, Chuyuan Wang, Fanrui Meng, Haoyu Wang, Bo Song, Yang Yang and Zhongyan Shan*

8 études sélectionnées
196 patients / 160 contrôles

Author	Country	AITD(n)
Zhao (21)	China	28
Zawawy (32)	Egypt	20
Ishaq (25)	China	29
Cornejo (28)	Spain	18
Ishaq (26)	China	27
Jiang (30)	China	45
Chen (29)	China	15
Zhou (33)	China	14

AITD, autoimmune thyroid disease.

Diversité bactérienne augmentée dans HT et diminuée dans GD



Propriétés pro-inflammatoires

Lactobacillus et bifidobacteries
Propriétés anti-inflammatoires

doi: 10.3389/fendo.2021.774362

Gut Microbiome Associated With Graves Disease and Graves Orbitopathy: The INDIGO Multicenter European Study

Filippo Biscarini, Giulia Masetti, Ilaria Muller, Hedda Luise Verhasselt, Daniela Covelli, Giuseppe Colucci, Lei Zhang, Mohd Shazli Draman, Onyebuchi Okosieme, Pete Taylor, Chantal Daumerie, Maria-Cristina Burlacu, Michele Marino, Daniel George Ezra, Petros Perros, Sue Plummer, Anja Eckstein, Mario Salvi,[✉] Julian R Marchesi,[✉] and Marian Ludgate

United Kingdom (Cardiff, Merthyr Tydfil, Newcastle Upon Tyne, and Moorfields), **Italy** (Milan and Pisa), **Belgium** (Brussels), and **Germany** (Essen)

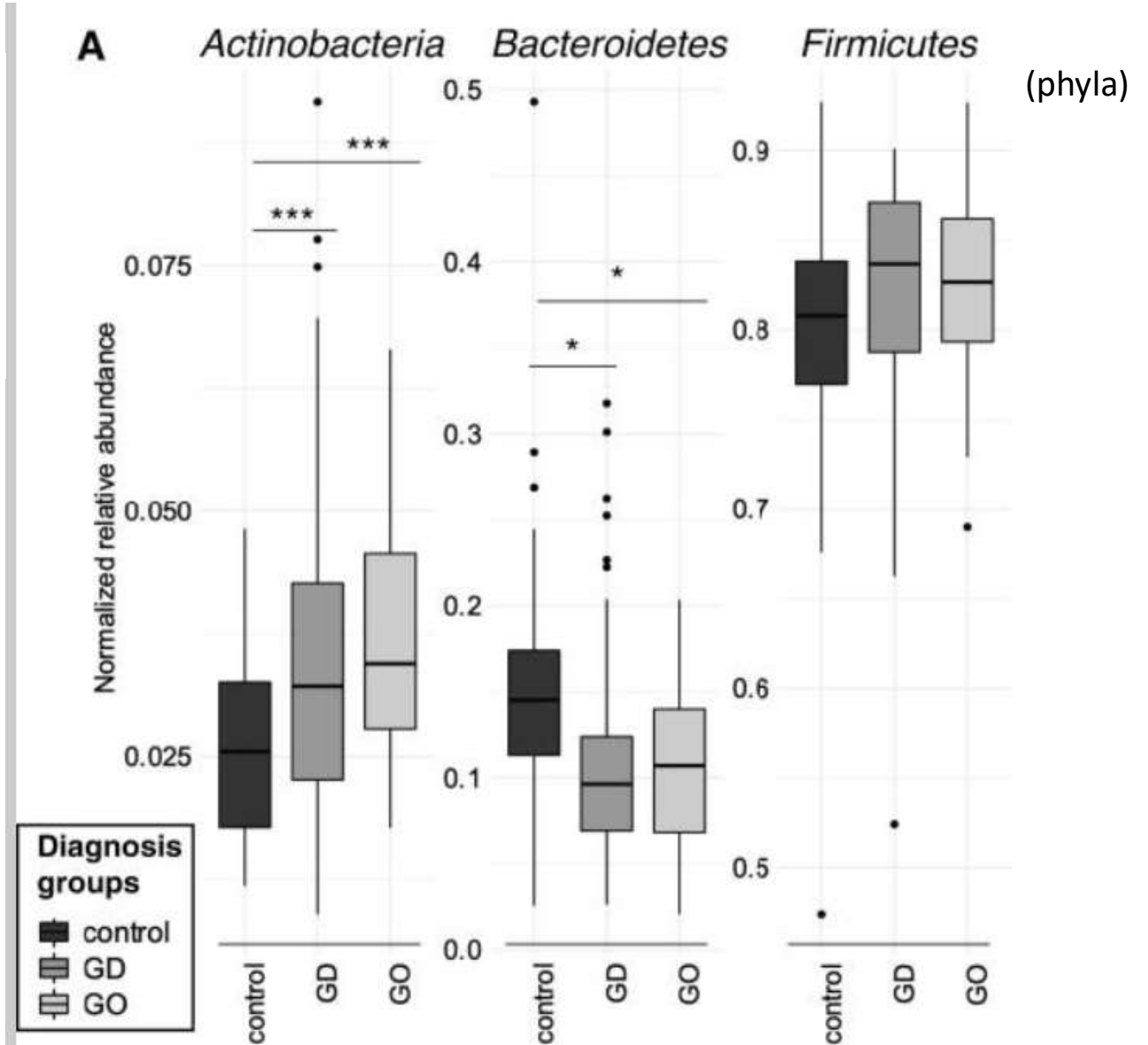
Characteristics of 59 patients with Graves disease, 46 patients with Graves orbitopathy, and 41 healthy controls at recruitment

	Controls n = 41	GD n = 59	GO n = 46
Demographic			
Age (mean, SD), y	46.08 (13.45)	46.39 (14.38)	47.04 (11.43)
Female (%)	32 (78.05%)	53 (89.83%)	40 (86.96)
White (%)	41 (100%)	50 (84.75%)	38 (82.60%)
Current smokers (%)	6 (14.63%)	8 (13.56%)	15 (32.60%)
Thyroid status			
Hyperthyroid (%)	0 (0%)	54 (91.53%)	35 (76.09%)
Hypothyroid (%)	0 (0%)	1 (1.65%)	0 (0%)
Euthyroid (%)	41 (100%)	4 (6.77%)	11 (23.91%)
Orbitopathy status			
No sign (%)	41 (100%)	59 (100%)	0 (0%)
Mild (%)	—	—	36 (78.26%)
Moderate-severe (%)	—	—	10 (21.74%)

Traités + non traités

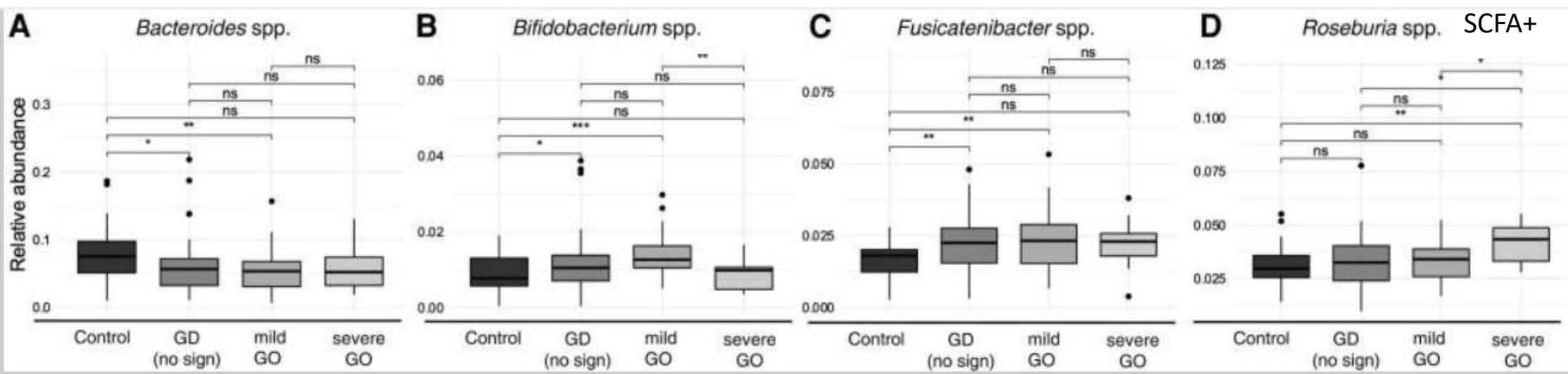
Gut Microbiome Associated With Graves Disease and Graves Orbitopathy: The INDIGO Multicenter European Study

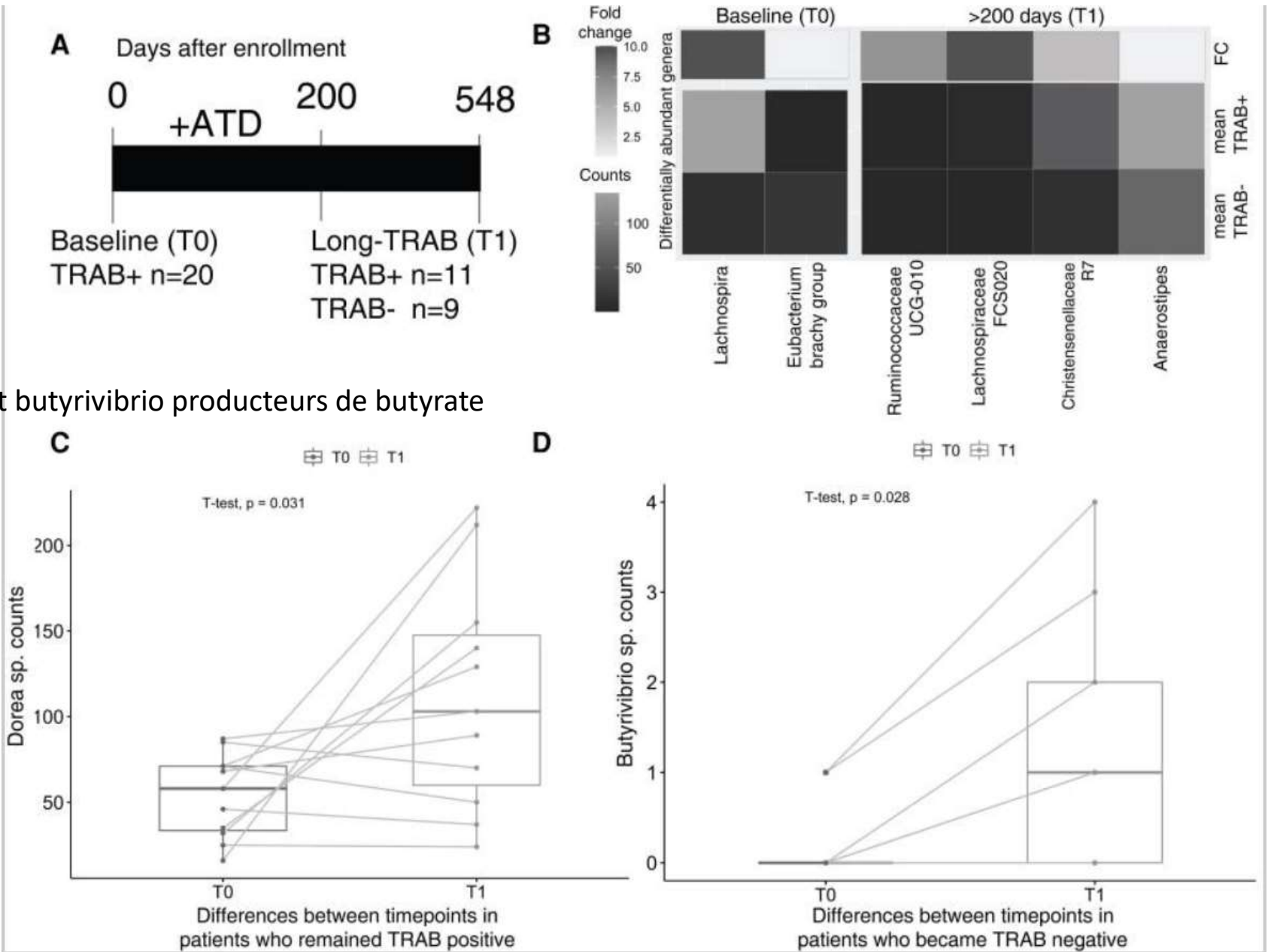
Filippo Biscarini, Giulia Masetti, Ilaria Muller, Hedda Luise Verhasselt, Danila Covelli, Giuseppe Colucci, Lei Zhang, Mohd Shazli Draman, Onyebuchi Okosieme, Pete Taylor, Chantal Daumerie, Maria-Cristina Burlacu, Michele Marino, Daniel George Ezra, Petros Perros, Sue Plummer, Anja Eckstein, Mario Salvi, Julian R Marchesi, and Marian Ludgate



Gut Microbiome Associated With Graves Disease and Graves Orbitopathy: The INDIGO Multicenter European Study

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Dorea et butyrivibrio producteurs de butyrate

Article

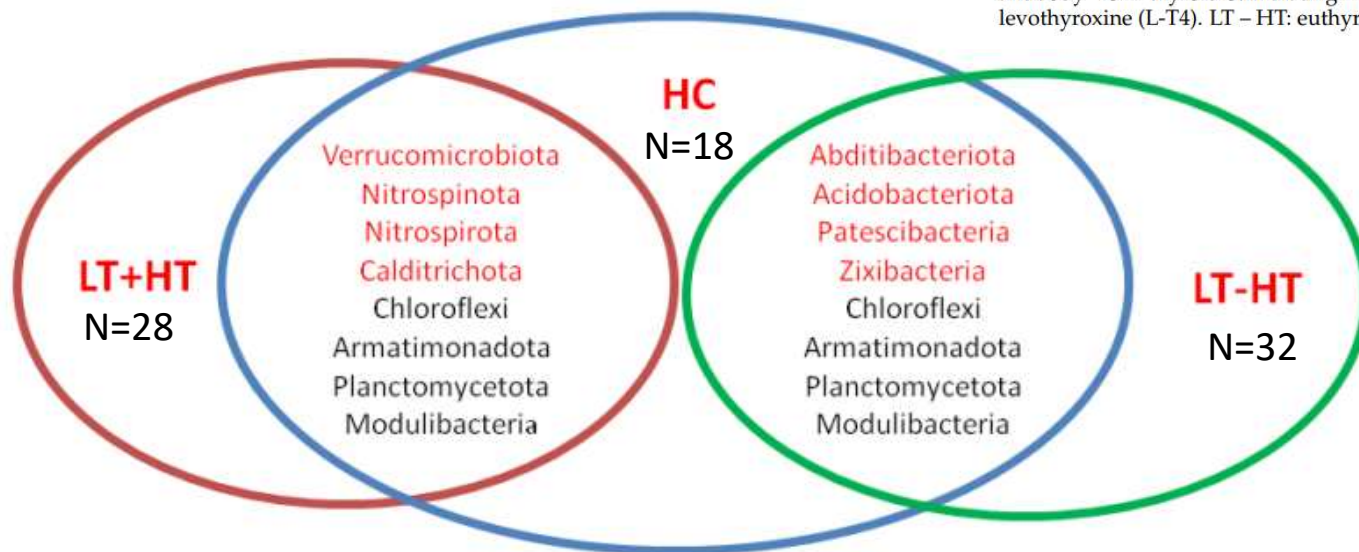
Oral Microbiota Signatures in the Pathogenesis of Euthyroid Hashimoto's Thyroiditis

Mustafa Genco Erdem ¹, Ozge Unlu ², Fatma Ates ³, Denizhan Karis ⁴ and Mehmet Demirci ^{5,*}

Table 1. Demographic characteristics for all participants (Mean + SD *).

	LT – HT (n = 32)	LT + HT (n = 28)	HC (n = 18)	p **
Age (years)	39.4 ± 4.52	39.8 ± 6.04	39.1 ± 5.8	0.893
BMI (kg/m ²)	21.6 ± 2.1	22.4 ± 1.9	20.8 ± 2.3	0.914
TSH (mU/L)	1.86 ± 1.81	2.12 ± 1.94	1.61 ± 1.35	0.785
TPOAb (IU/mL)	265 ± 224	342 ± 274	7.8 ± 4.9	<0.0001

* Values are presented as mean ± standard deviation. ** The Kruskal Wallis test. TPOAb: thyroid peroxidase antibody. TSH: thyroid-stimulating hormone. HT: Hashimoto's thyroiditis. LT + HT: Euthyroid HT treated with levothyroxine (L-T4). LT – HT: euthyroid HT without L-T4 therapy. HC: Healthy control.

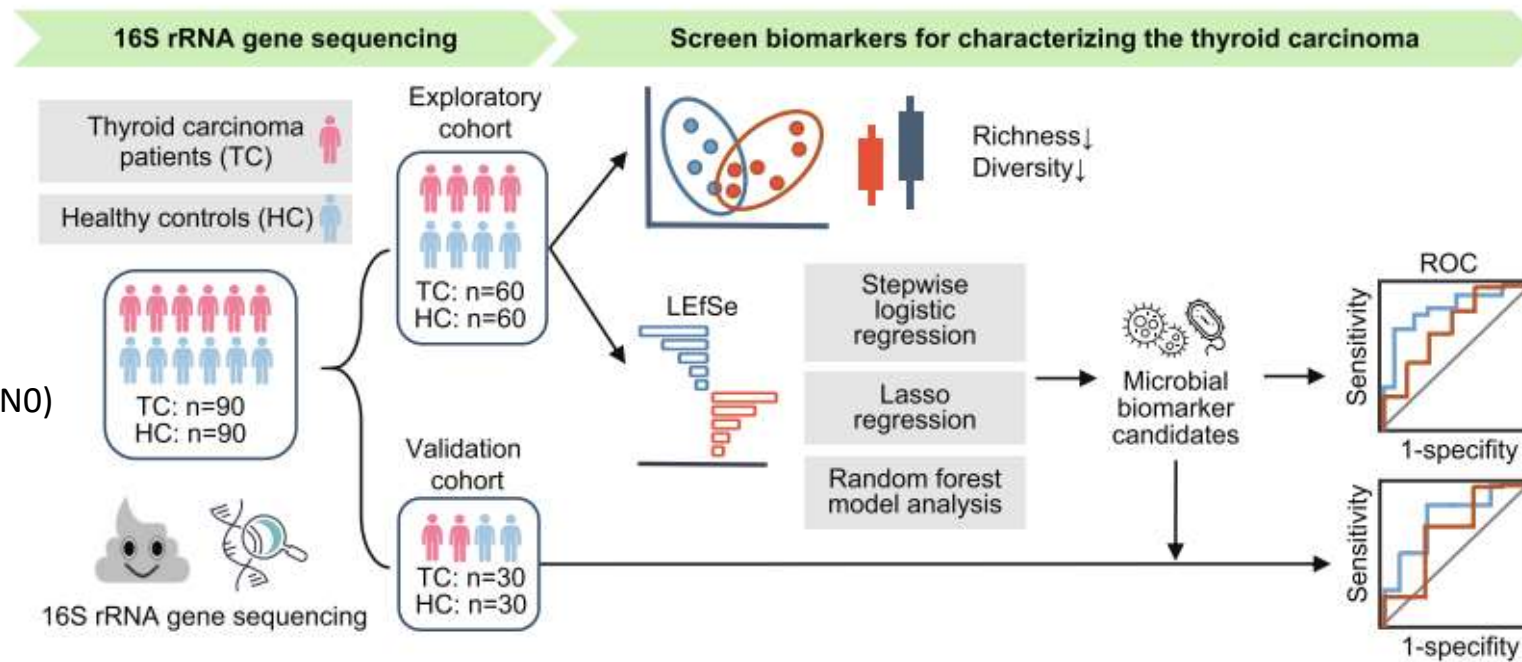


Certains genres bactériens associés à d'autres pathologies auto-immunes

Figure 1. Phyla showing a significant difference between groups. (HT: Hashimoto's thyroiditis. LT + HT: Euthyroid HT treated with levothyroxine (L-T4). LT-HT: euthyroid HT without L-T4 therapy. HC: Healthy control).

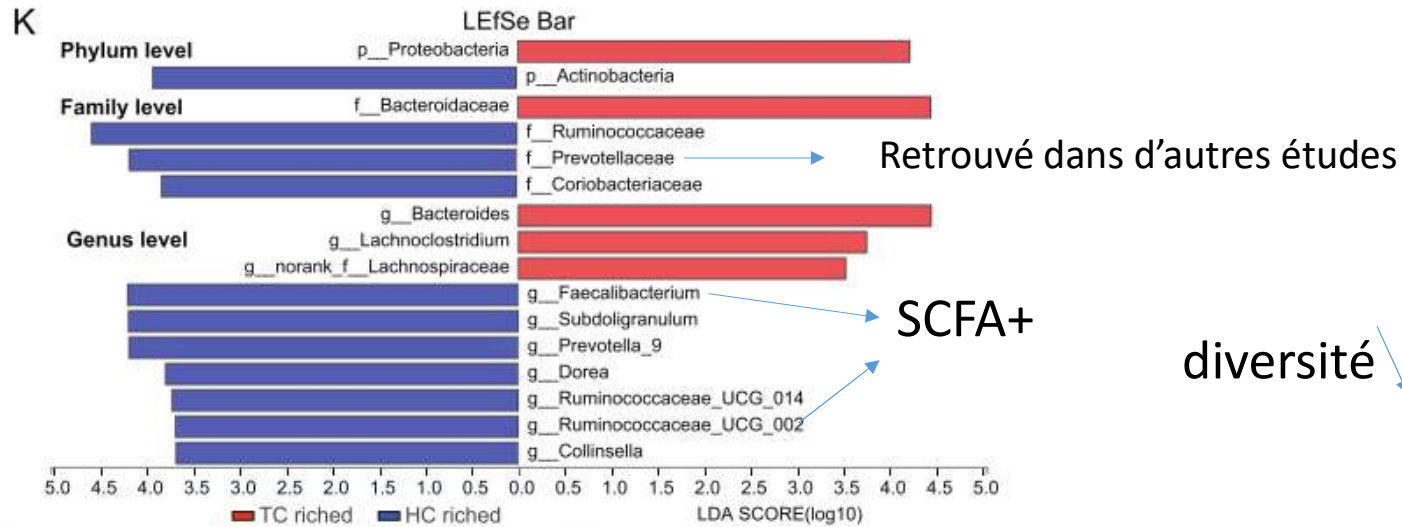
Cancers thyroïdiens et microbiome intestinal

GRAPHICAL ABSTRACT

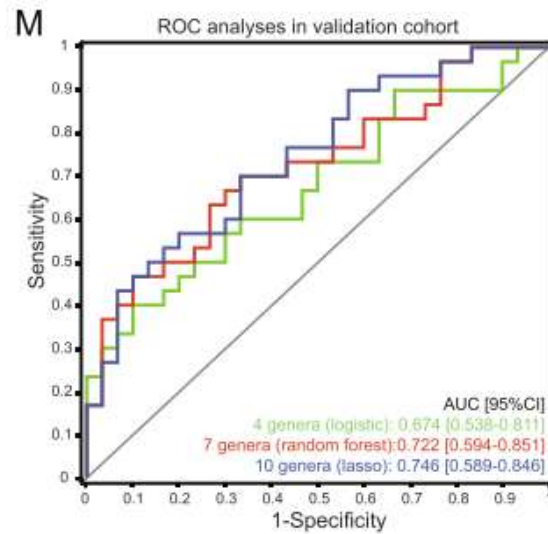
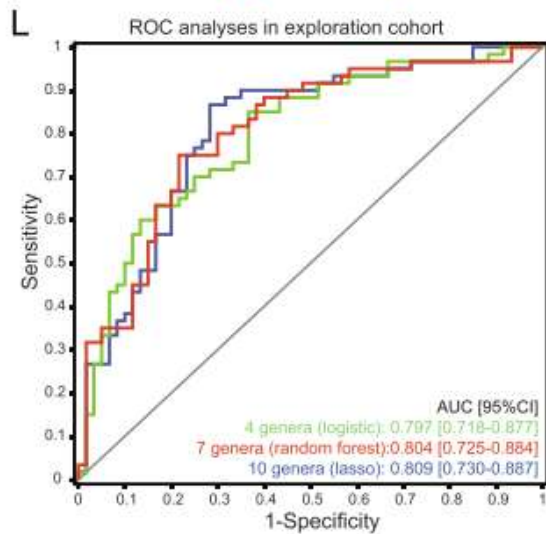


X. Yu, W. Jiang, Russell Oliver Kosik et al. Journal of Advanced Research 35 (2022) 61–70

Cancers thyroïdiens et microbiome intestinal



diversité ↓

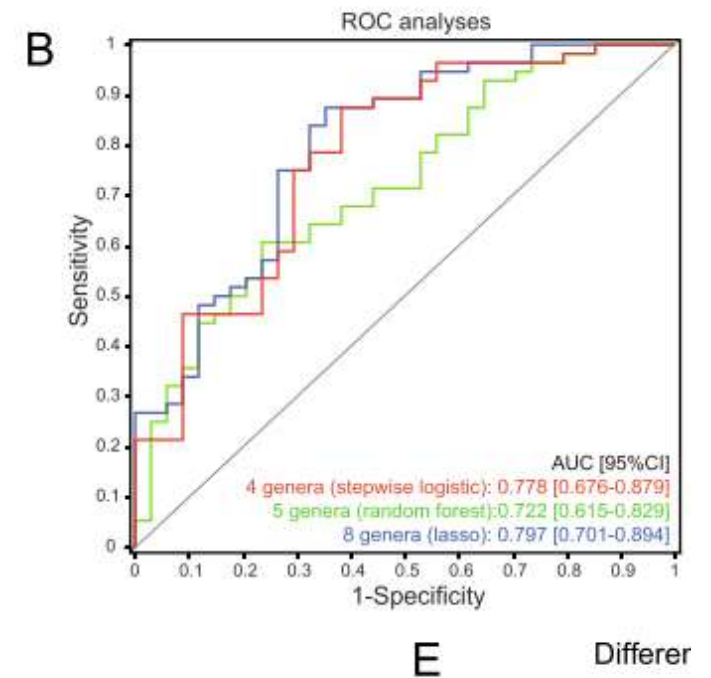
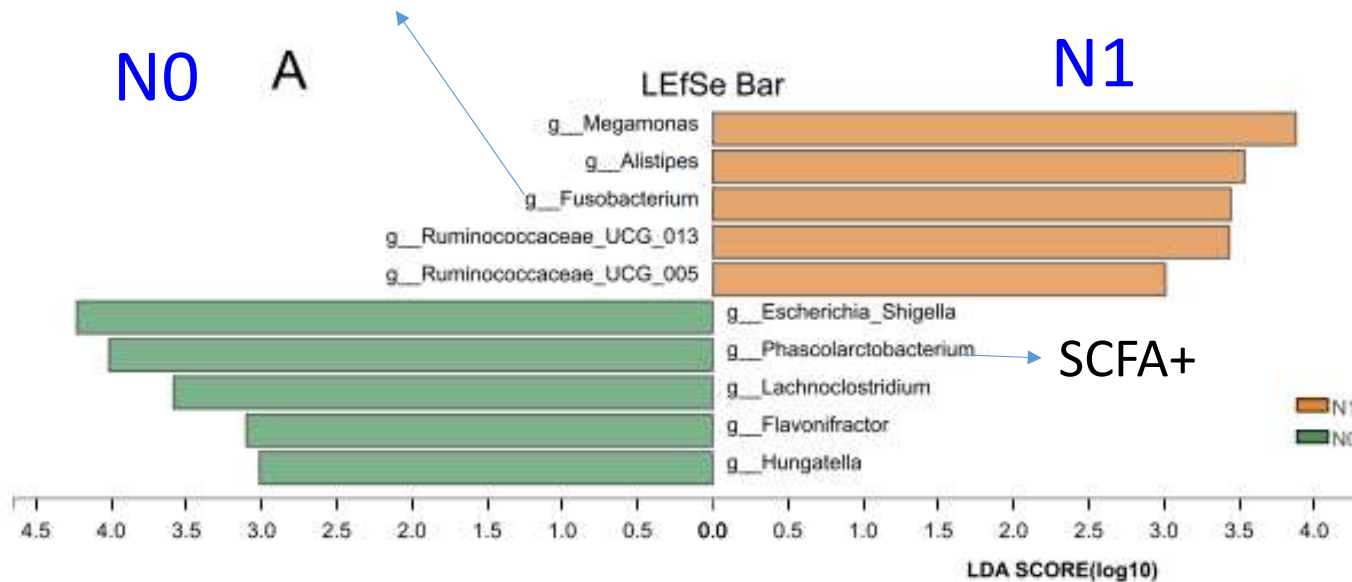


Analyse fonctionnelle liée aux capacités de réparation de l'ADN (base excision repair and nucleotide excision repair)

X. Yu, W. Jiang, Russell Oliver Kosik et al. Journal of Advanced Research 35 (2022) 61–70

Cancers thyroïdiens et microbiome intestinal

Associé aux métastases à distance dans cancer colorectal



X. Yu, W. Jiang, Russell Oliver Kosik et al. Journal of Advanced Research 35 (2022) 61–70

Saliva microbiome changes in thyroid cancer and thyroid nodules patients

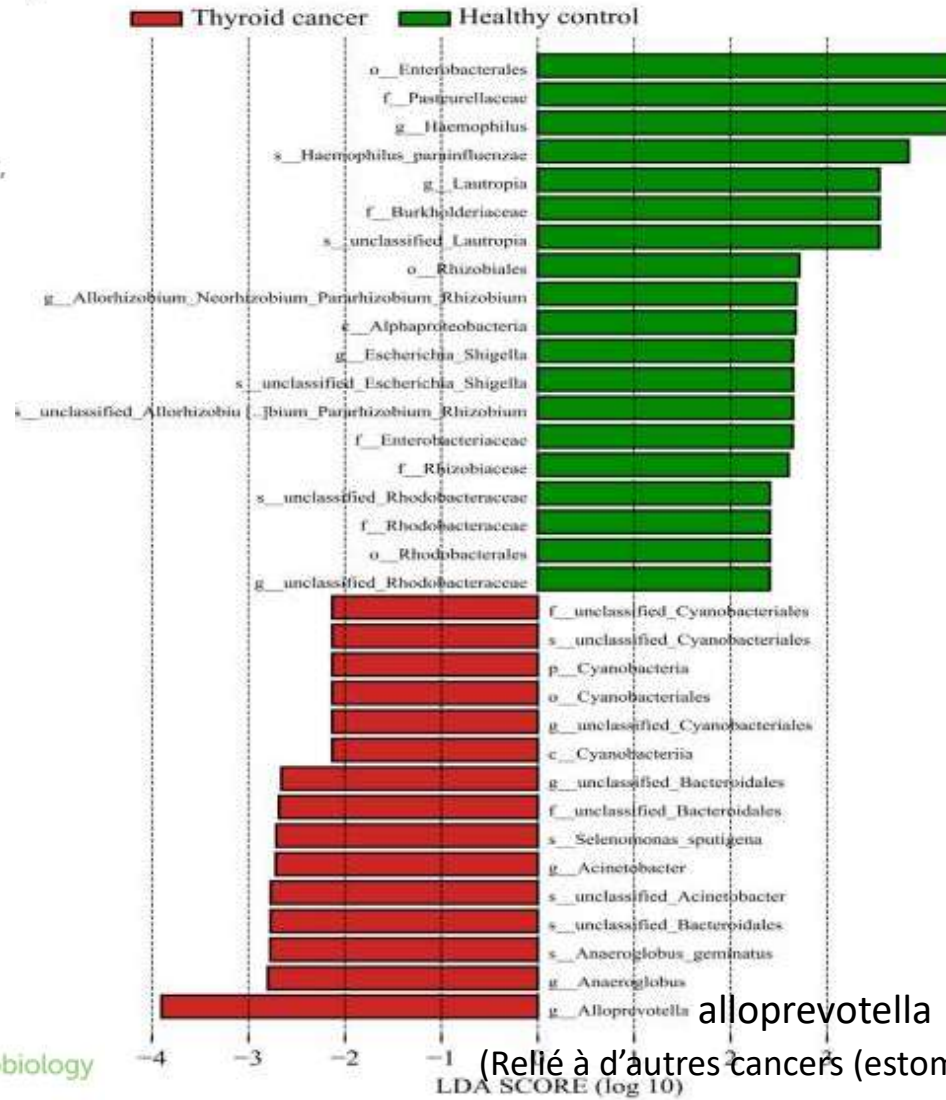
Junjun Jiao^{1†}, Youli Zheng^{2†}, Qingyu Zhang¹, Degeng Xia¹, Li Zhang^{1*} and Ning Ma^{1*}

[†]Hospital of Stomatology, Jilin University, Changchun, China, ²The School and Hospital of Stomatology, Tianjin Medical University, Tianjin, China

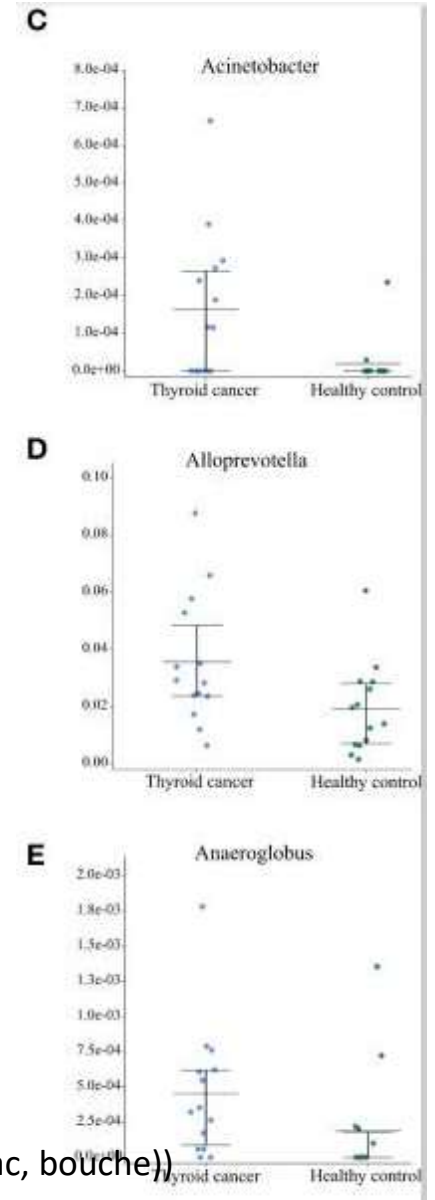
Basic characteristics of participants.

Variables	Thyroid cancer	Thyroids nodules	Healthy control
Gender (M: F)	11:3	9:0	12:3

TYPE Original Research
 PUBLISHED 11 August 2022
 DOI 10.3389/fcimb.2022.989188



alloprevotella
 (Relié à d'autres cancers (estomac, bouche))

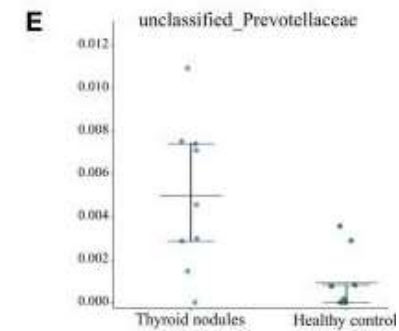
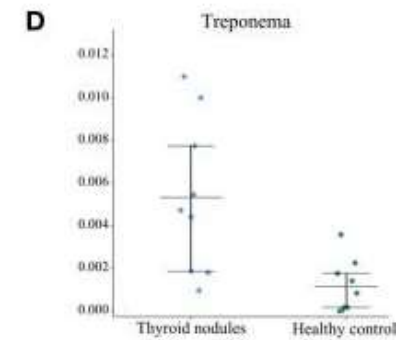
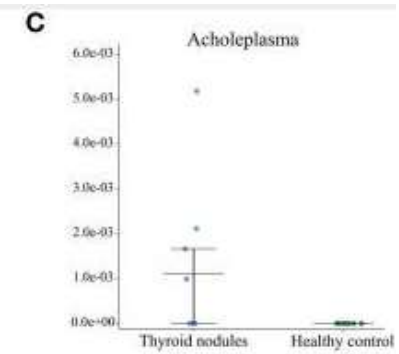
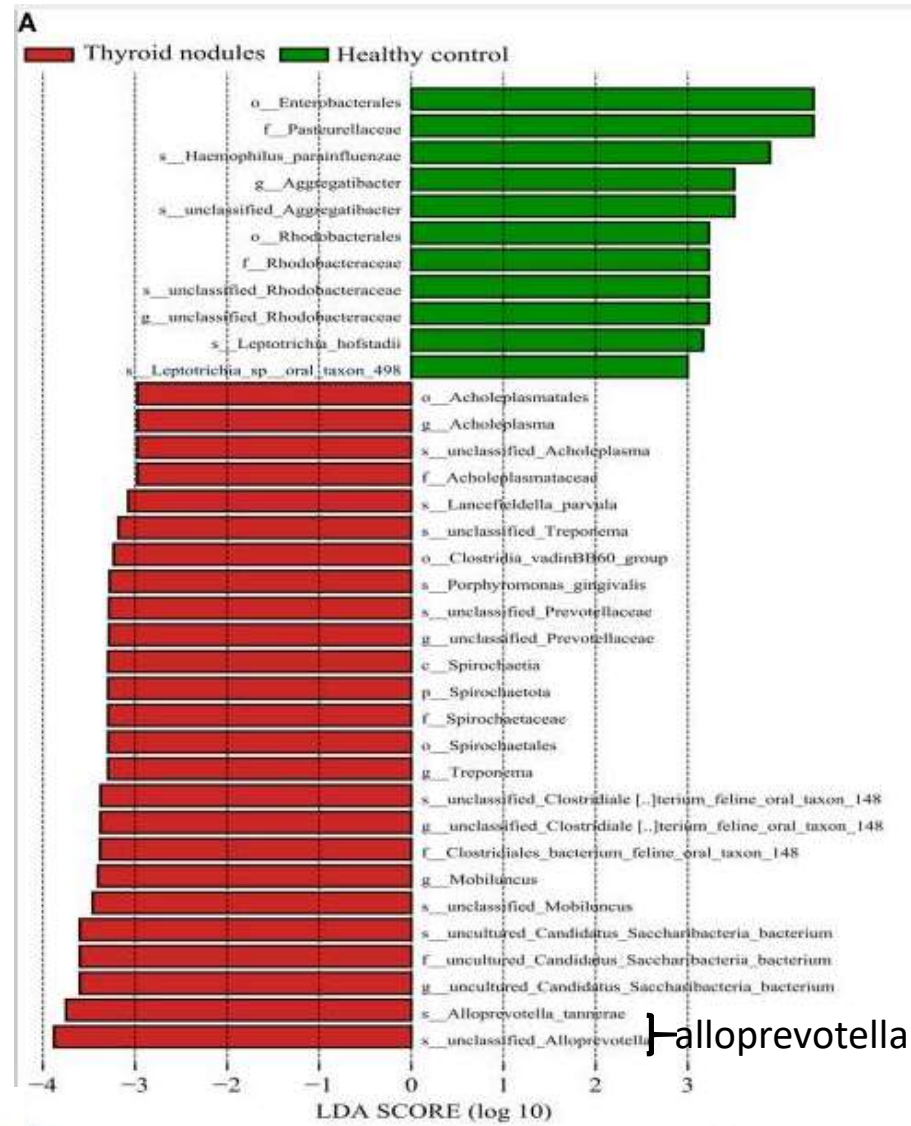


Saliva microbiome changes in thyroid cancer and thyroid nodules patients

Junjun Jiao^{1†}, Youli Zheng^{2†}, Qingyu Zhang¹, Degeng Xia¹, Li Zhang^{1*} and Ning Ma^{1*}

[†]Hospital of Stomatology, Jilin University, Changchun, China, ²The School and Hospital of Stomatology, Tianjin Medical University, Tianjin, China

TYPE Original Research
 PUBLISHED 11 August 2022
 DOI 10.3389/fcimb.2022.989188



Alloprevotella

Cancers thyroïdiens et microbiome intratumoral

ARTICLE

<https://doi.org/10.1038/s42003-022-03814-x>

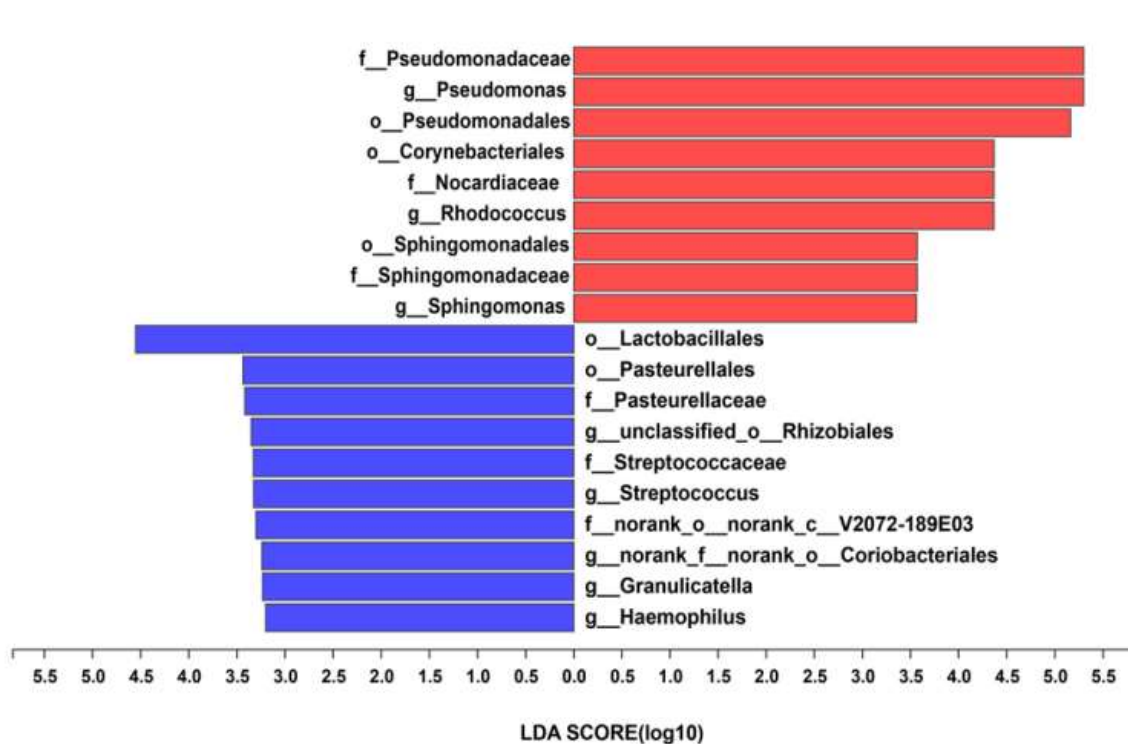
OPEN

Lijuan Yuan^{1,2}, Ping Yang^{1,2}, Gang Wei¹, Xi'e Hu¹, Songhao Chen¹, Jianguo Lu¹, Lin Yang¹, Xianli He¹ & Guoqiang Bao¹

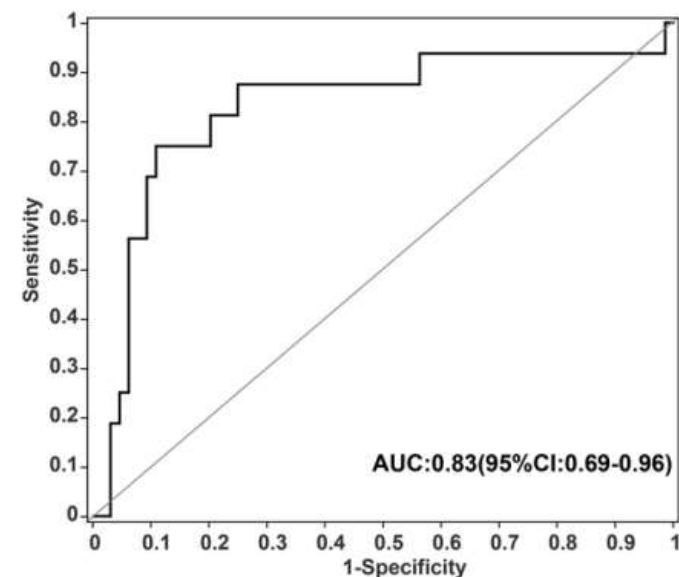
Tumor microbiome diversity influences papillary thyroid cancer invasion

N = 80

h



i



Intérêt des probiotiques ?

Probiotic *Bifidobacterium longum* supplied with methimazole improved the thyroid function of Graves' disease patients through the gut-thyroid axis

Dongxue Huo^{1,2,3}, Chaoping Cen^{1,3}, Haibo Chang¹, Qianying Ou¹, Shuaiming Jiang², Yonggui Pan², Kaining Chen^{1✉} & Jiachao Zhang^{1,2✉}

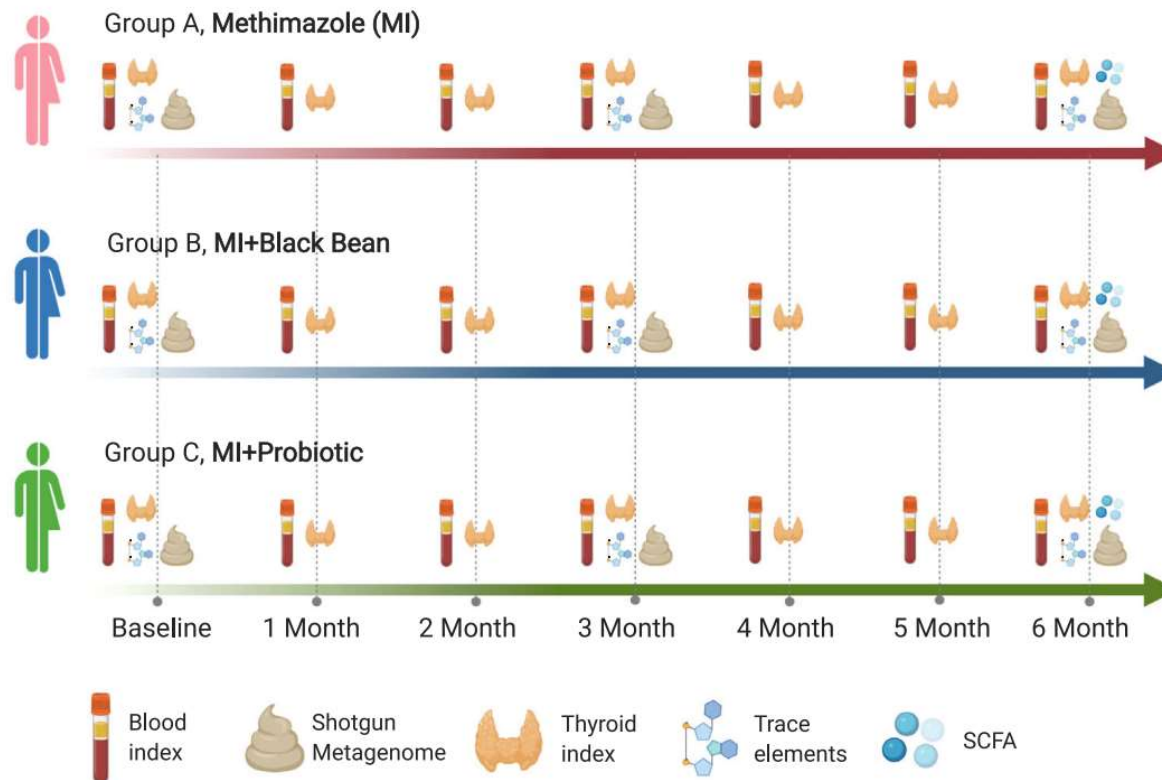


Fig. 1 Experimental design and sampling time points design. We longitudinally tracked blood and thyroid index at every month, gut microbiome determined by shotgun metagenome sequencing, short-chain fatty acids (SCFAs) and trace elements were evaluated at baseline, 3 and 6 months during the 6-month treatment.

communications
biology

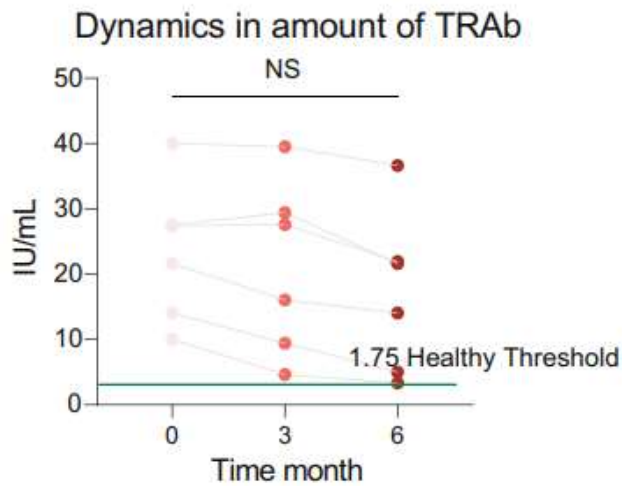
ARTICLE

<https://doi.org/10.1038/s42003-021-02587-z>

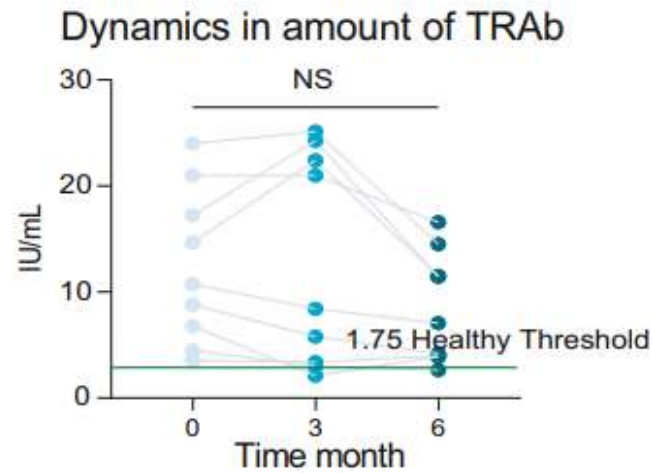
OPEN

Probiotic *Bifidobacterium longum* supplied with methimazole improved the thyroid function of Graves' disease patients through the gut-thyroid axis

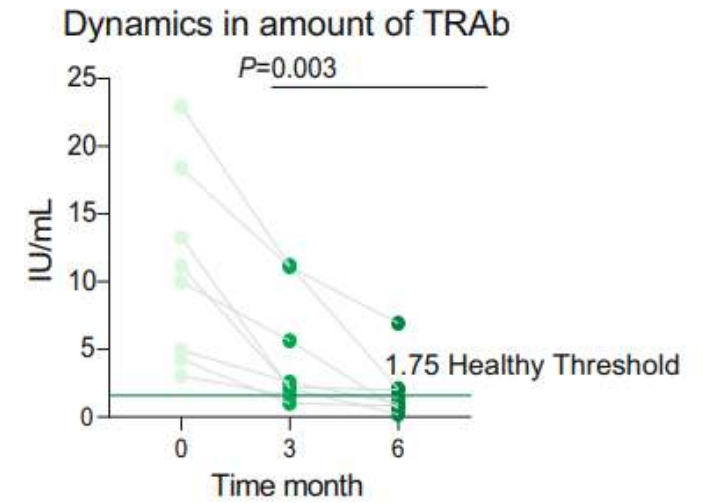
Dongxue Huo^{1,2,3}, Chaoping Cen^{1,3}, Haibo Chang¹, Qianying Ou¹, Shuaiming Jiang², Yonggui Pan², Kaining Chen¹ & Jiachao Zhang^{1,2}



Methimazole (n=8)



Methimazole + black bean (n=9)



Methimazole + *Bifidobacterium longum* (n=9)

SCFA ↑

**communications
biology**

ARTICLE

<https://doi.org/10.1038/s42003-021-02587-z>

OPEN

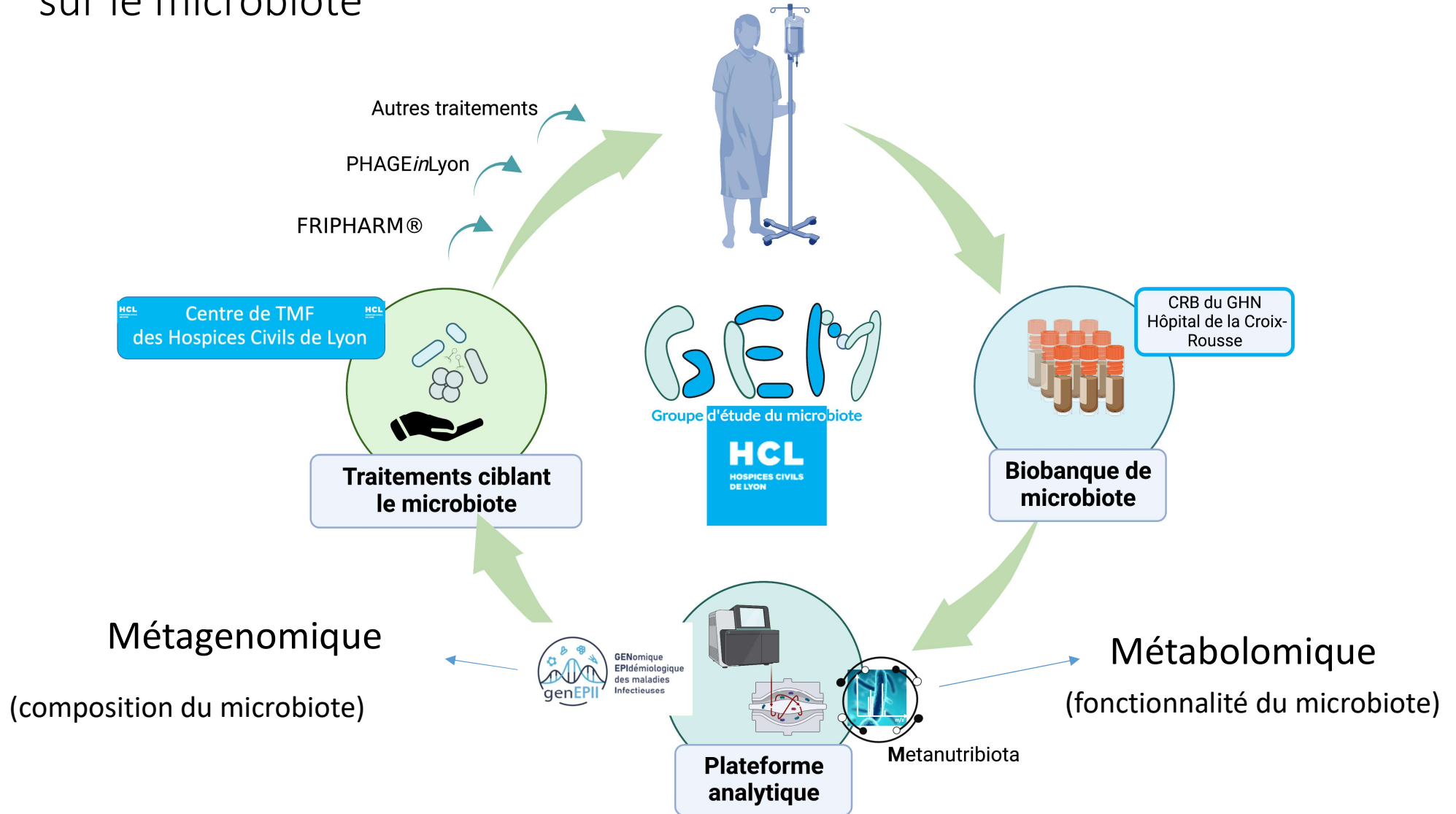
TAKE HOME MESSAGE

- **Les pathologies de la thyroïde sont associées à des modifications de la composition en bactéries de plusieurs microbiomes** : intestinal, buccal, intra-tumoral
- **Les mécanismes sous-jacents restent hypothétiques** : production plus faible de SCFA (butyrate), activation du système immunitaire (balance Treg/Th17), mimétisme antigénique, biodisponibilité en micronutriments (iode, sélénium, zinc, fer).
- **Des études combinant des analyses metagénomiques** éventuellement de plusieurs microbiomes (féces, salive) **et des analyses de métabolomique** (féces, salive, plasma) permettraient de mieux comprendre ces mécanismes

“To add, studies exploring the functional potential of the gut microbiome, including whole genome sequencing and fecal metabolome, are of great importance to be designed.”

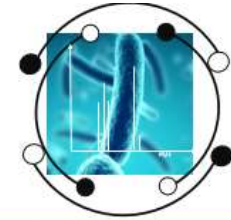
Microbiome Metabolites and Thyroid Dysfunction. J. Clin. Med. 2021, 10, 3609

Aux HCL – Développement d'une plateforme de soin et de recherche intégrée sur le microbiote





Université Claude Bernard  Lyon 1



METANUTRIBIOTA

MERCI POUR VOTRE ATTENTION!!!

karim.chikh@chu-lyon.fr