

Gut and Metabolic Diseases: Opportunities of Probiotic Medicine

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Laura Mahdi, Mohamad Khalil

Agenda of 23.10.26

- Thanks!
- Microbiota-gut-systemic axis
- Metabolic aspects
- Probiotic chances
- The future



Annarita, Laura!



Anita!

microorganisms

15 November 2024

Review

Unraveling the Role of the Human Gut Microbiome in Health and Diseases

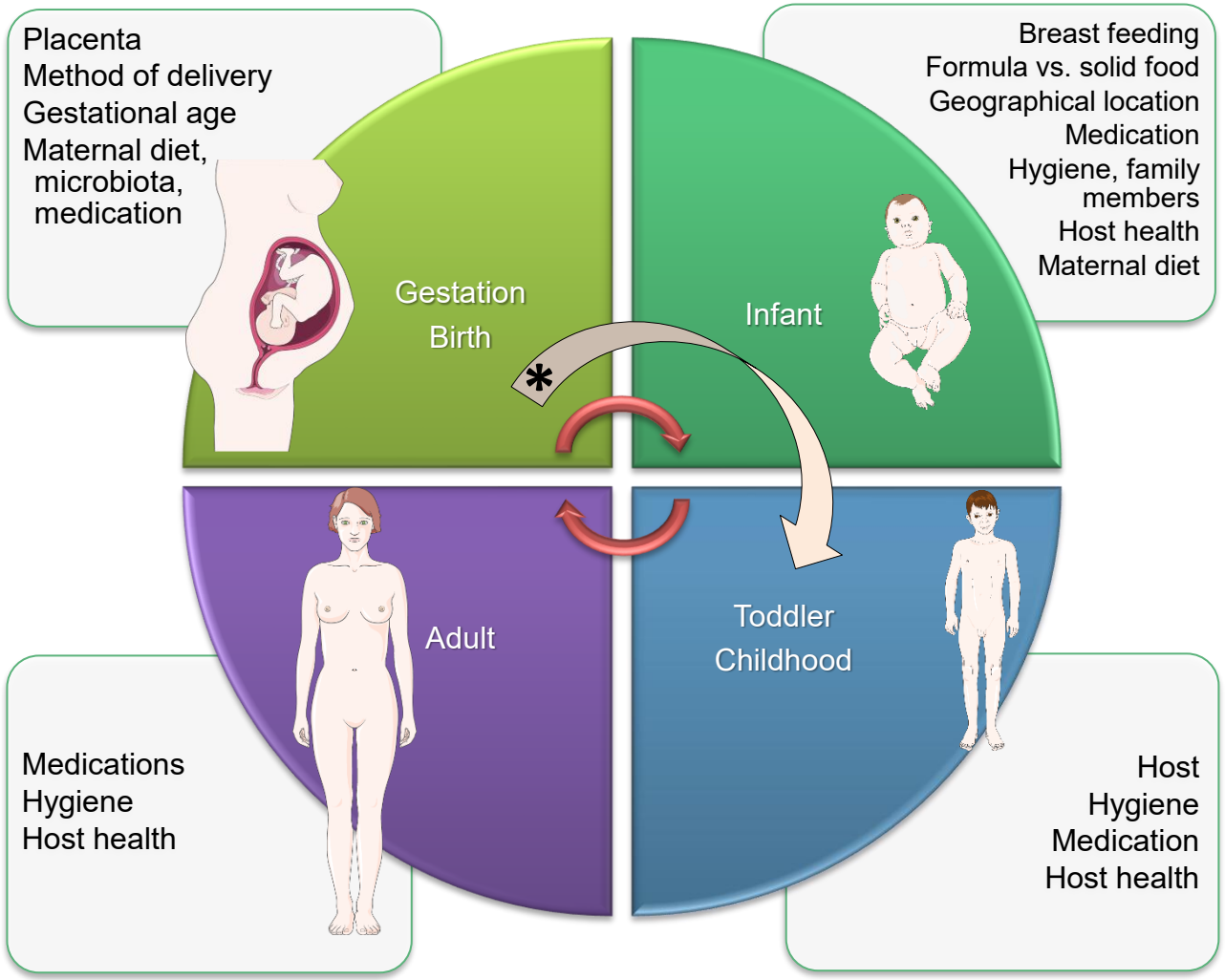
Mohamad Khalil [1,†], Agostino Di Ciaula [1,†], Laura Mahdi [1], Nour Jaber [1], Domenica Maria Di Palo [2], Annarita Graziani [3], Gyorgy Baffy [4,5] and Piero Portincasa [1,*]

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2 Division of Hygiene, Department of Interdisciplinary Medicine, University of Bari Aldo Moro, Piazza Giulio Cesare 11, 70124 Bari, Italy; domenicamaria.dipalo@policlinico.ba.it
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* Correspondence: piero.portincasa@uniba.it
† These authors contributed equally to this work.

Gut microbes in metabolic disturbances. Promising role for therapeutic manipulations?

European Journal of Internal Medicine 2023

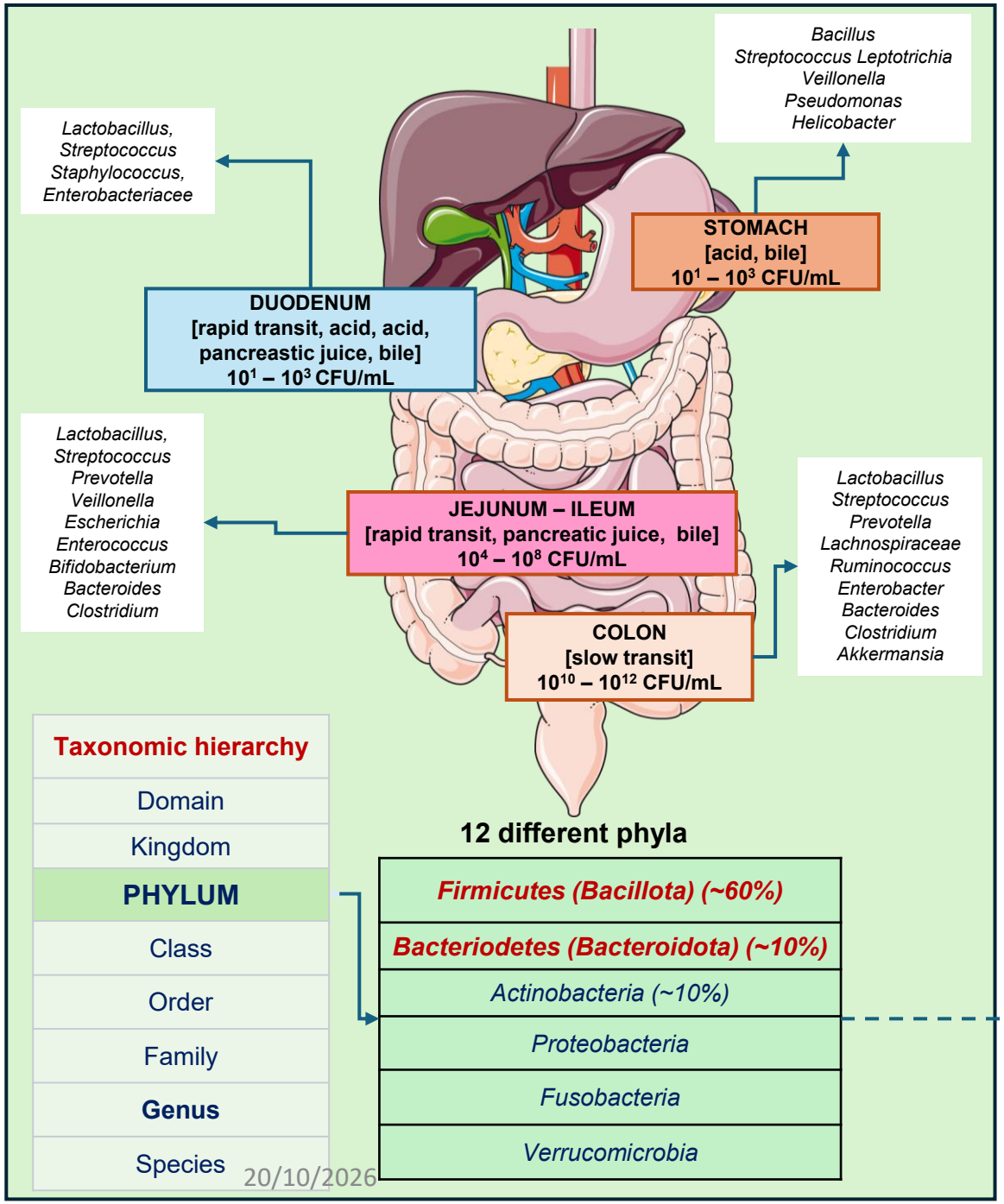
Portincasa P, Khalil M, Graziani A, Frühbeck G, Baffy G, Garruti G, Di Ciaula A, Bonfrate L.



20/10/2026

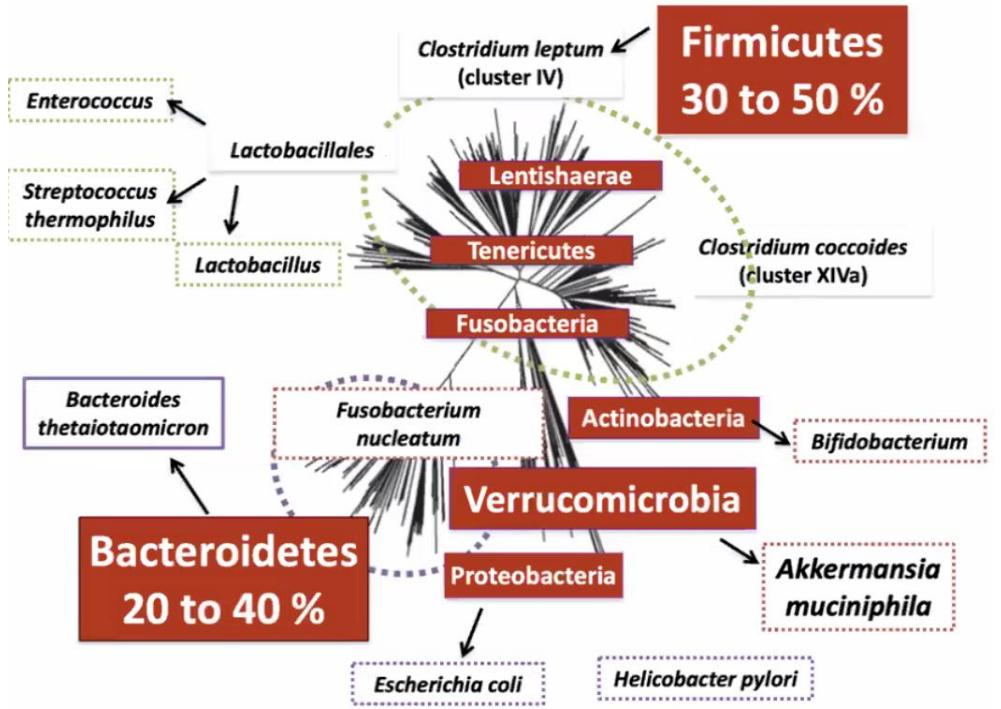
*** Chance for microbiota modulation**

04.10.24



Eubiosis

~600,000 genes
Few (1%) Archaea, fungi
Many protists, viruses/phages



Essential ecological features:
stability
resistance
resilience

Hou, K. et al. Sig transduct target ther, 2022

20/10/2026

Khalil, M.; Di Ciaula, A.; Mahdi, L.; Jaber, N.; Di Palo, D.M.; Graziani, A.; Baffy, G.; Portincasa, P. Unraveling the Role of the Human Gut Microbiome in Health and Diseases. *Microorganisms* ***2024, 12, 2333.***

Figure 1

The Gut barrier ~32 m² (colon ~2 m²)

Helander HF, Fändriks L (2014) Surface area of the digestive tract - revisited. Scand J Gastroenterol 49:681–689. https://doi.org/10.3109/00365521.2014.898326

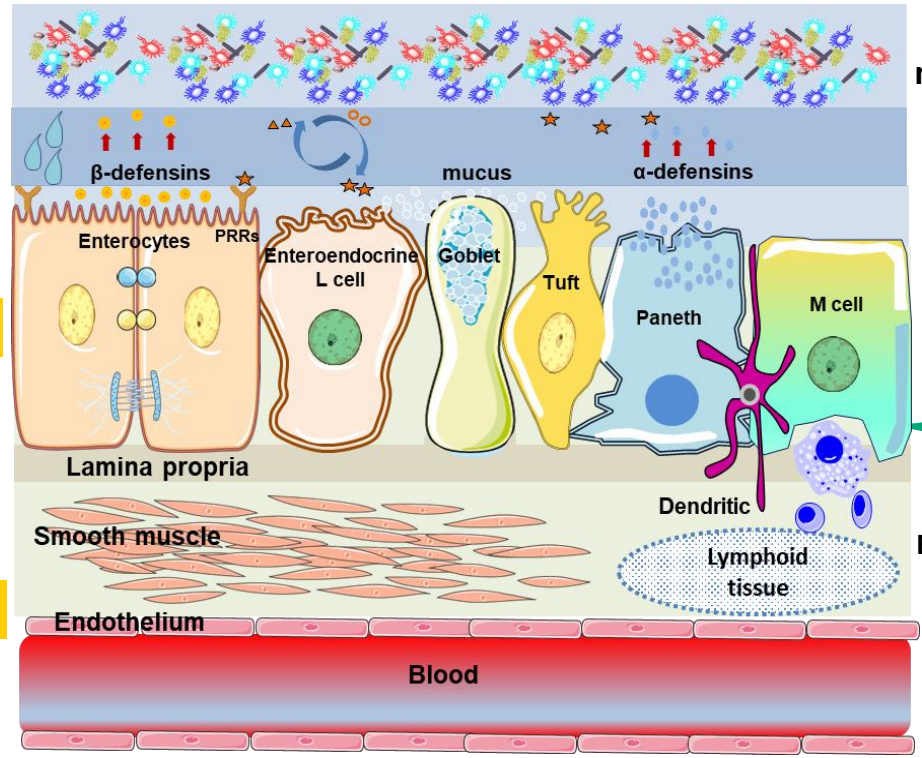
MICROBIAL BARRIER
- Huge collection of microorganisms (10^14) inhabiting the gut
- key role in nutrient and vitamin processing, biotransformation of intestinal primary bile acids

Eubiosis

microbial diversity

1

EPITHELIAL BARRIER
- Enterocytes (β-defensins), Goblet cells (producing mucus), Tufts cells (chemosensory function), Enteroendocrine cells (produce hormones)
- TJ, adherens J
- Permeability



mucin

2

«Bioreactor»

EXTRACELLULAR BARRIER (MUCUS)
- glycosylated proteins (intestinal goblet cells)

IMMUNOLOGICAL BARRIER
- Paneth cells (secretion of antimicrobial peptides α-defensins)
- TLRs – MAMPs (Microbe Associated Molecular Patterns)
- /PAMPs (Pathogen Associated Molecular Patterns)
- Dendritic cells
- Lymphnodes, B/T lymphocytes, Phagocytes

4

5

3

FUNCTIONAL BARRIER
- Motility
- Secretions (acid, bile, pancreatic)

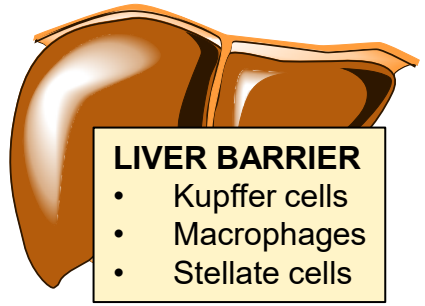
Macrophages
Phagocytes

B-, T-lymphocytes

GUT-VASCULAR BARRIER
- Endothelium associated with pericytes and enteric glial cells, TJ and adherens junctions

6

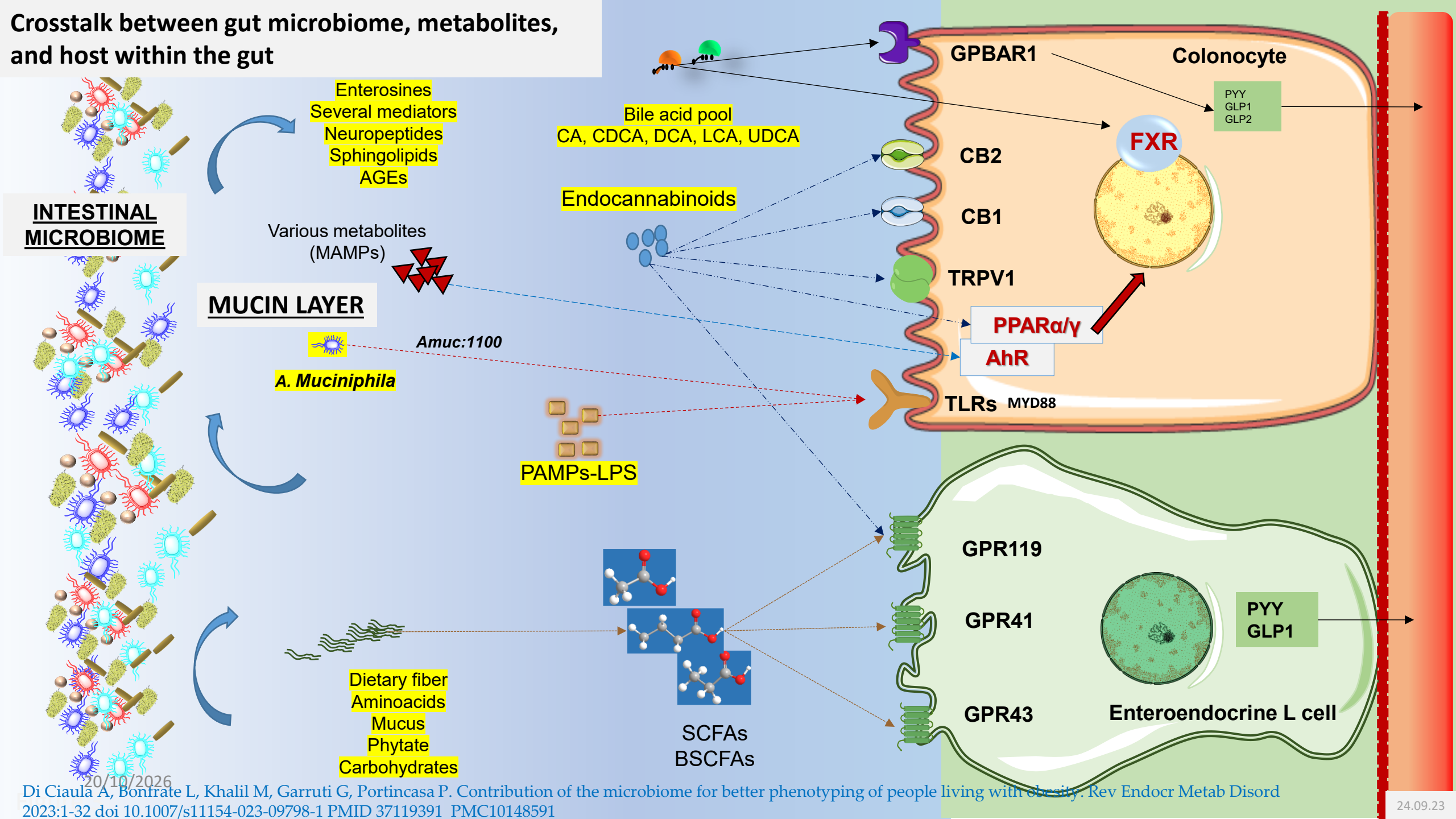
7



LIVER BARRIER
- Kupffer cells
- Macrophages
- Stellate cells

1) Di Ciaula A, Baj J, Garruti G, Celano G, De Angelis M, Wang HH, Di Palo DM, Bonfrate L, Wang DQ, Portincasa P. Liver Steatosis, Gut-Liver Axis, Microbiome and Environmental Factors. A Never-Ending Bidirectional Cross-Talk. J Clin Med 2020;9:2648; 2) Di Ciaula A, Bonfrate L, Khalil M, Garruti G, Portincasa P. Contribution of the microbiome for better phenotyping of people living with obesity. Rev Endocr Metab Disord 2023:1-32 doi 10.1007/s11154-023-09798-1 PMID 37119391 PMC10148591

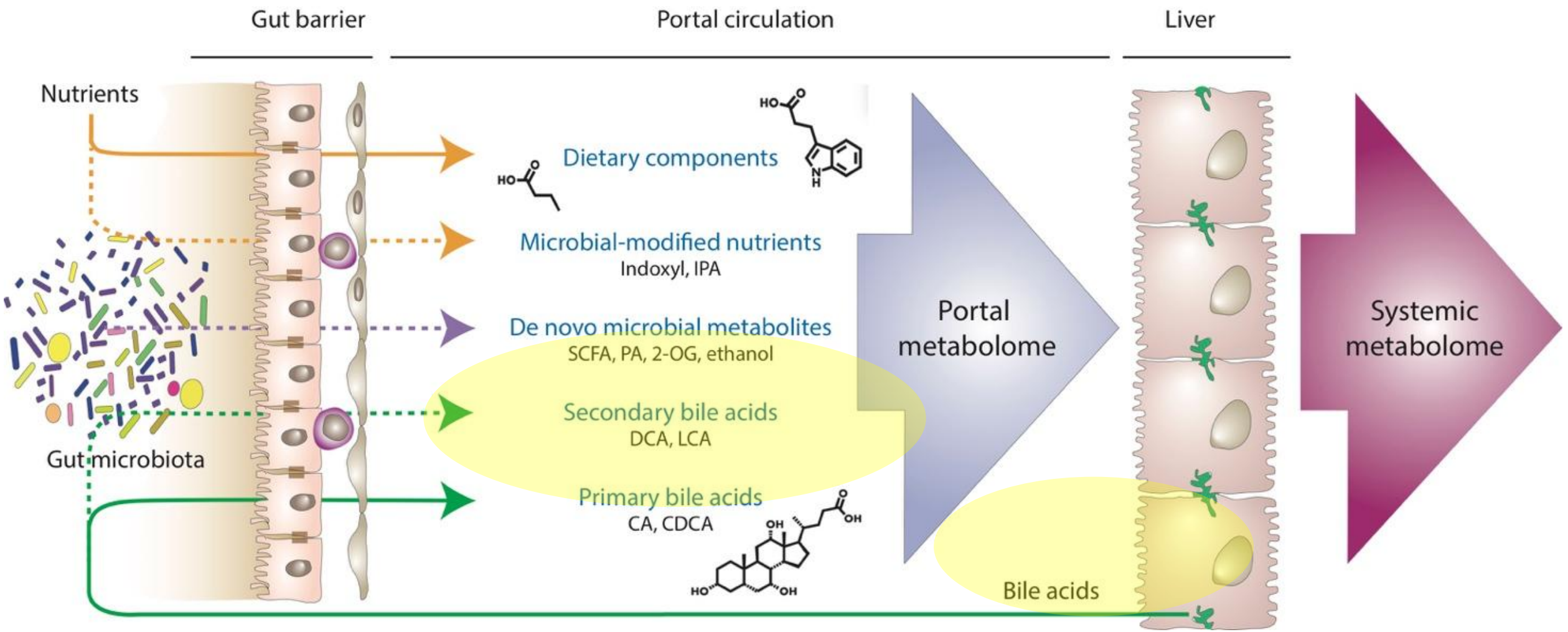
Crosstalk between gut microbiome, metabolites, and host within the gut



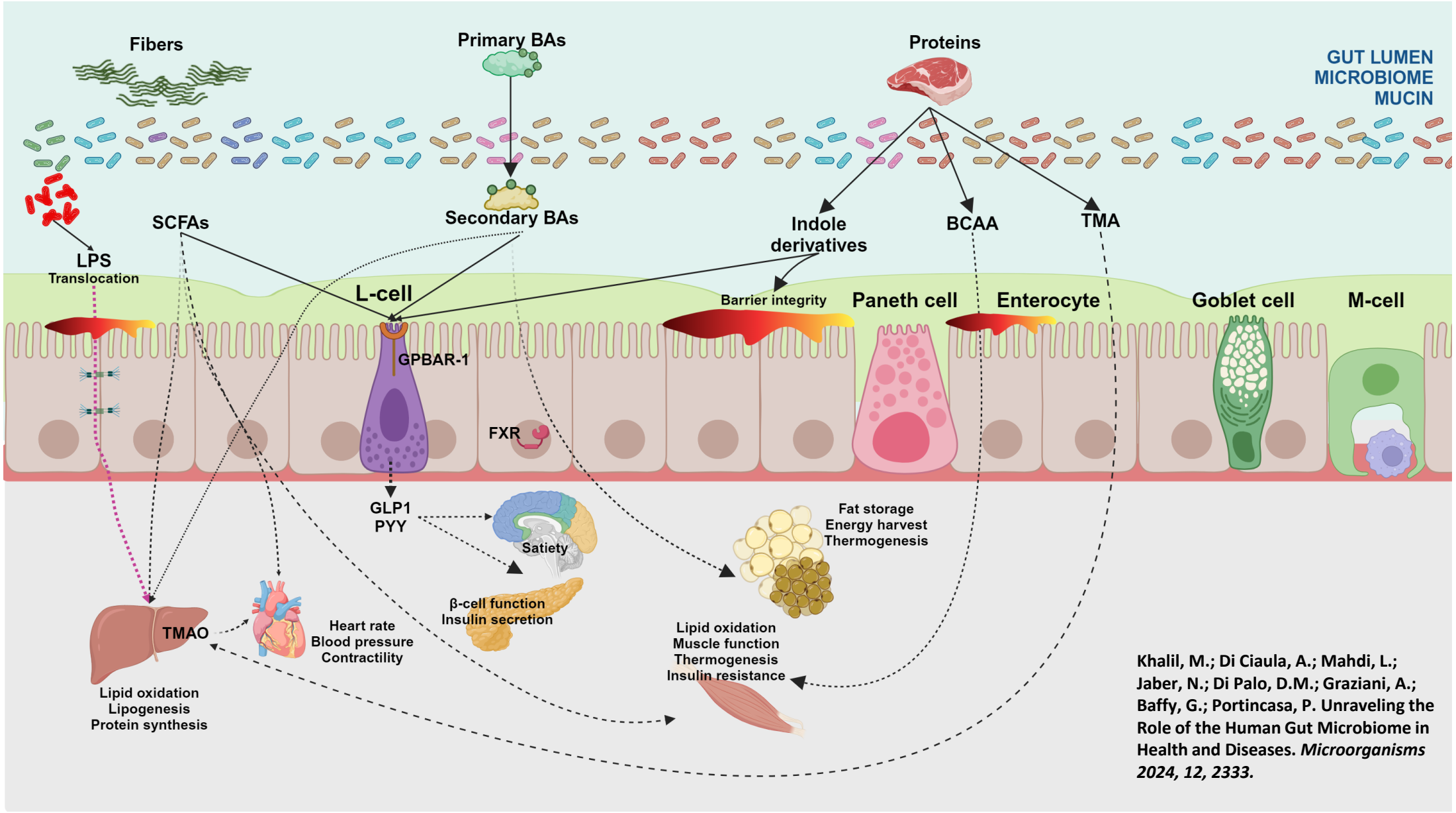
Di Ciaula A, Bonfrate L, Khalil M, Garruti G, Portincasa P. Contribution of the microbiome for better phenotyping of people living with obesity. Rev Endocr Metab Disord 2023:1-32 doi 10.1007/s11154-023-09798-1 PMID 37119391 PMC10148591

The portal and systemic metabolome

Gyorgy Baffy[1,2] and Piero Portincasa[3] **Gut microbiota and sinusoidal vasoregulation in MASLD: a portal perspective**



Principal modulatory effects of gut microbiome on host metabolism

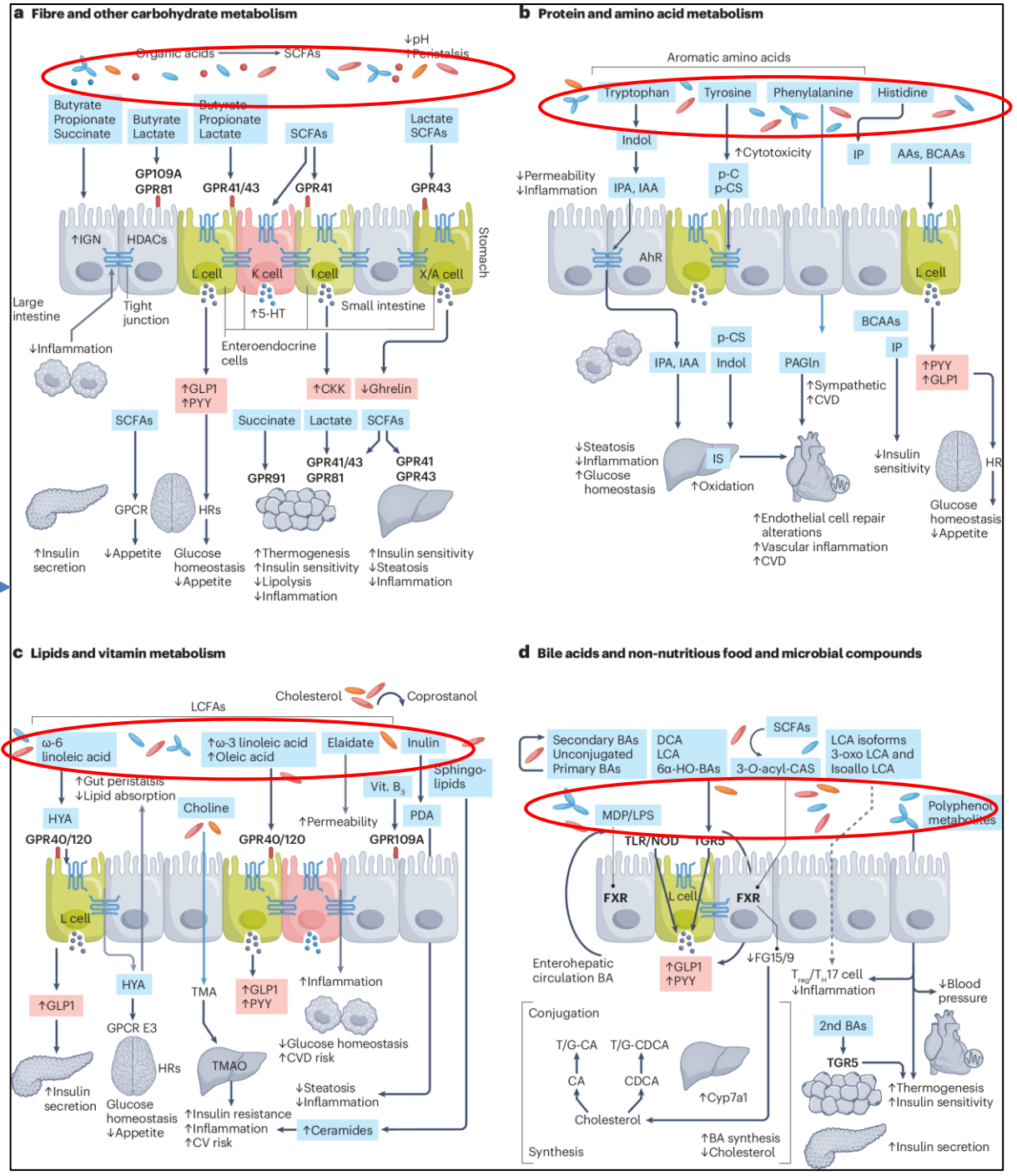


Khalil, M.; Di Ciaula, A.; Mahdi, L.; Jaber, N.; Di Palo, D.M.; Graziani, A.; Baffy, G.; Portincasa, P. Unraveling the Role of the Human Gut Microbiome in Health and Diseases. *Microorganisms 2024, 12, 2333.*

Figure 4

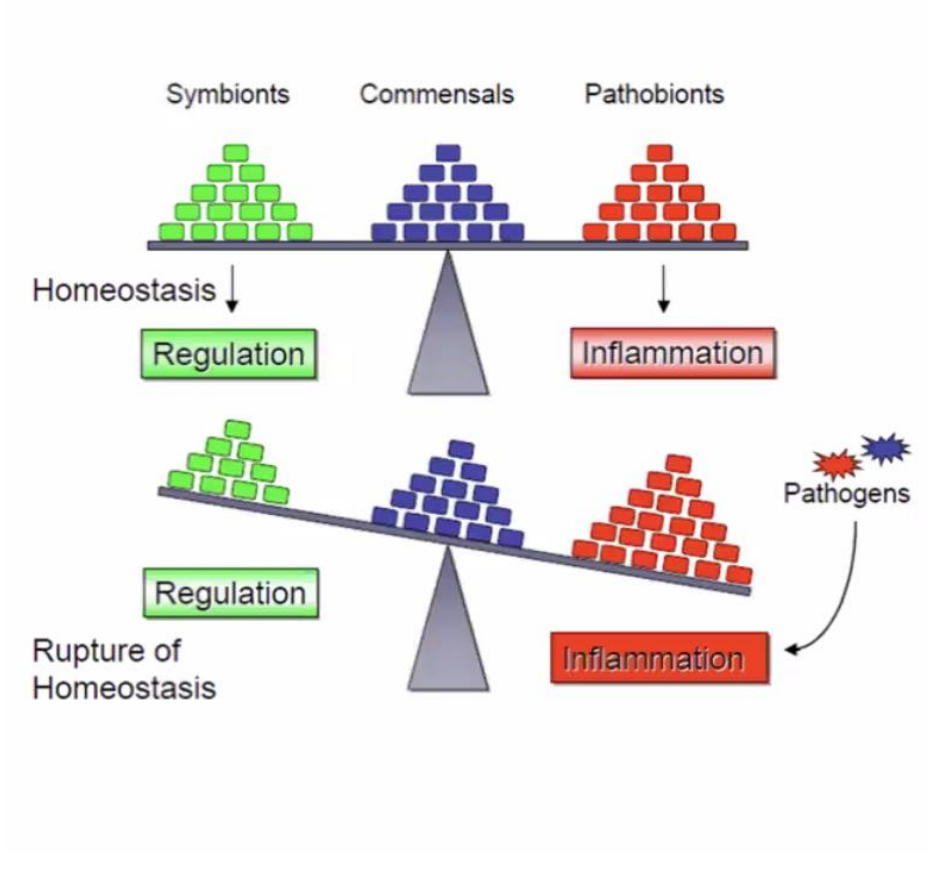
Gut microbiome-produced metabolites from dietary sources or synthesized *de novo* affect different aspects of cardiometabolic health

Microbiota always in business!



Sanz, Y.; Cryan, J.F.; Deschasaux-Tanguy, M.; Elinav, E.; Lambrecht, R.; Veiga, P. The gut microbiome connects nutrition and human health. *Nature Reviews Gastroenterology & Hepatology* ***2025, 22, 534–555, doi:10.1038/s41575-025-01077-5.***

From Eubiosis to Dysbiosis



Eubiosis: healthy relationship among commensal gut microbes and the host

- **High diversity**
- **Functional redundancy**
- **Stability**

Dysbiosis: imbalance in the microbiota with changed composition and functional activities

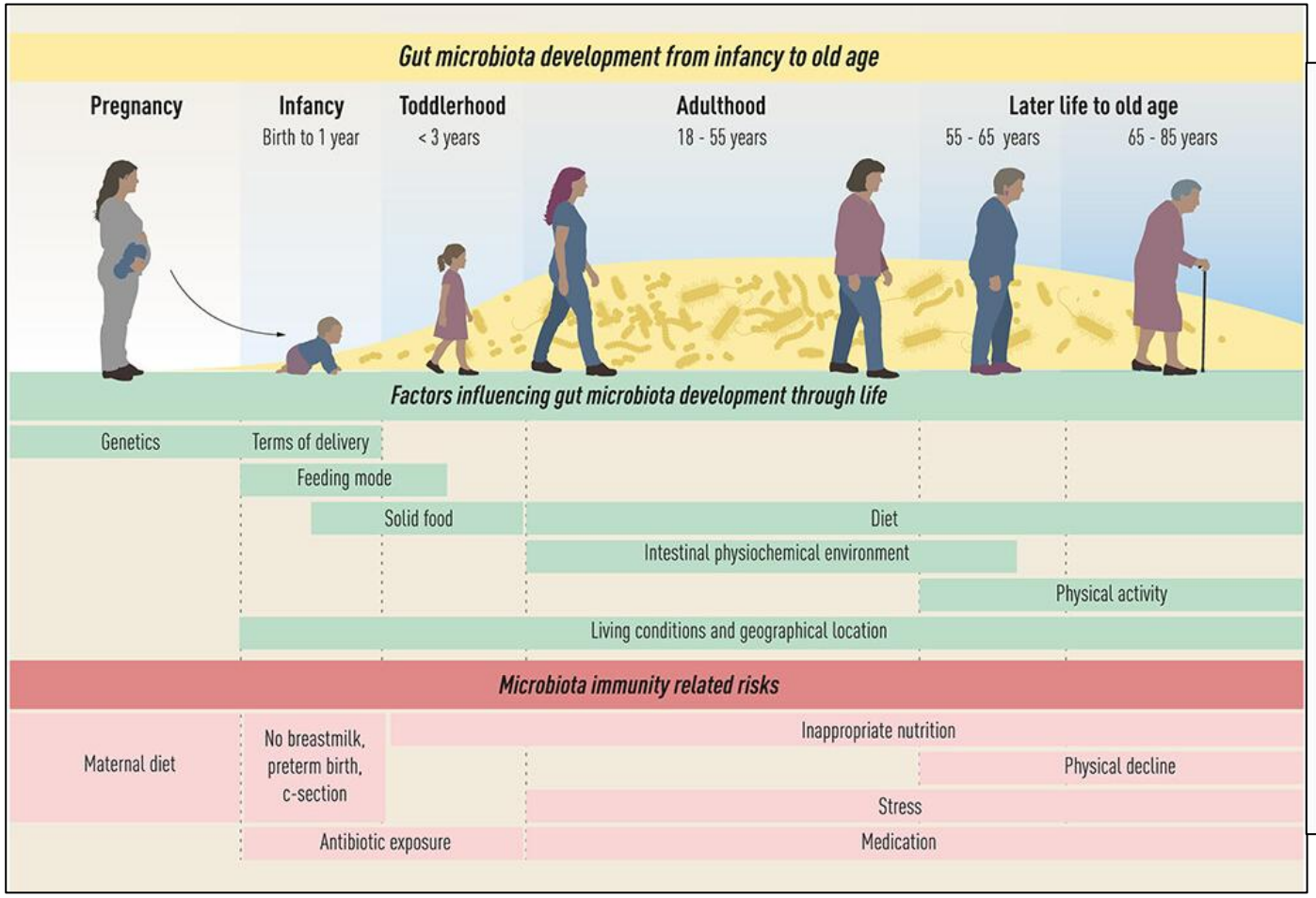
- **Low diversity**
- **Depletion of beneficial health-associated taxa (SCFA producers)**
- **Enrichment in pathobionts**
- **Increase in mucin degraders**
- **Increase in bacteria with LPS endotoxins (Proteobacteria)**

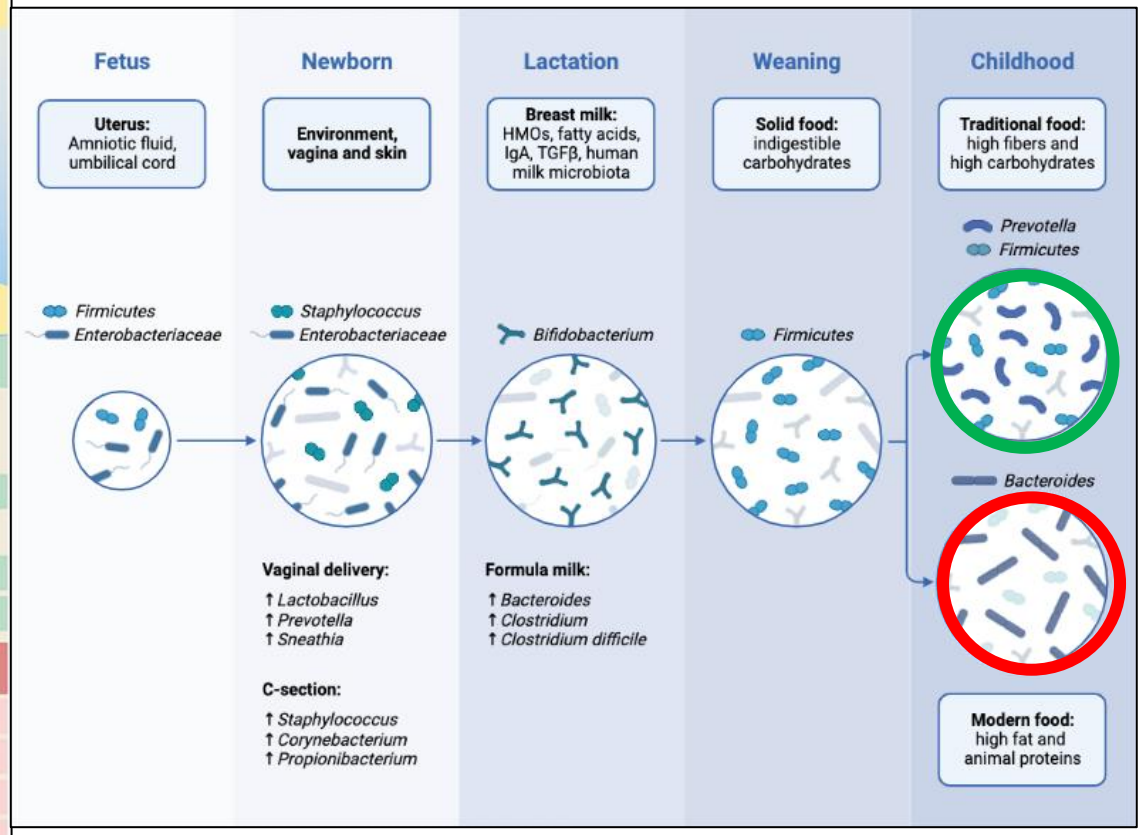
Symbionts: living in symbiosis with another organism or each other.

Commensal: act on the host's immune system → protective responses that prevent colonization and invasion by pathogens

Pathobionts: potential pathogenic influence on the host

Gut microbiota development across the lifespan









Schoultz I, et al. Gut microbiota development across the lifespan: Disease links and health-promoting interventions. Journal of Internal Medicine. 2025.

19.03.26

Crosstalk between microbiome and gut barrier

Khalil, M.; Di Ciaula, A.; Mahdi, L.; Jaber, N.; Di Palo, D.M.; Graziani, A.; Baffy, G.; Portincasa, P. Unraveling the Role of the Human Gut Microbiome in Health and Diseases. *Microorganisms* ***2024, 12, 2333***

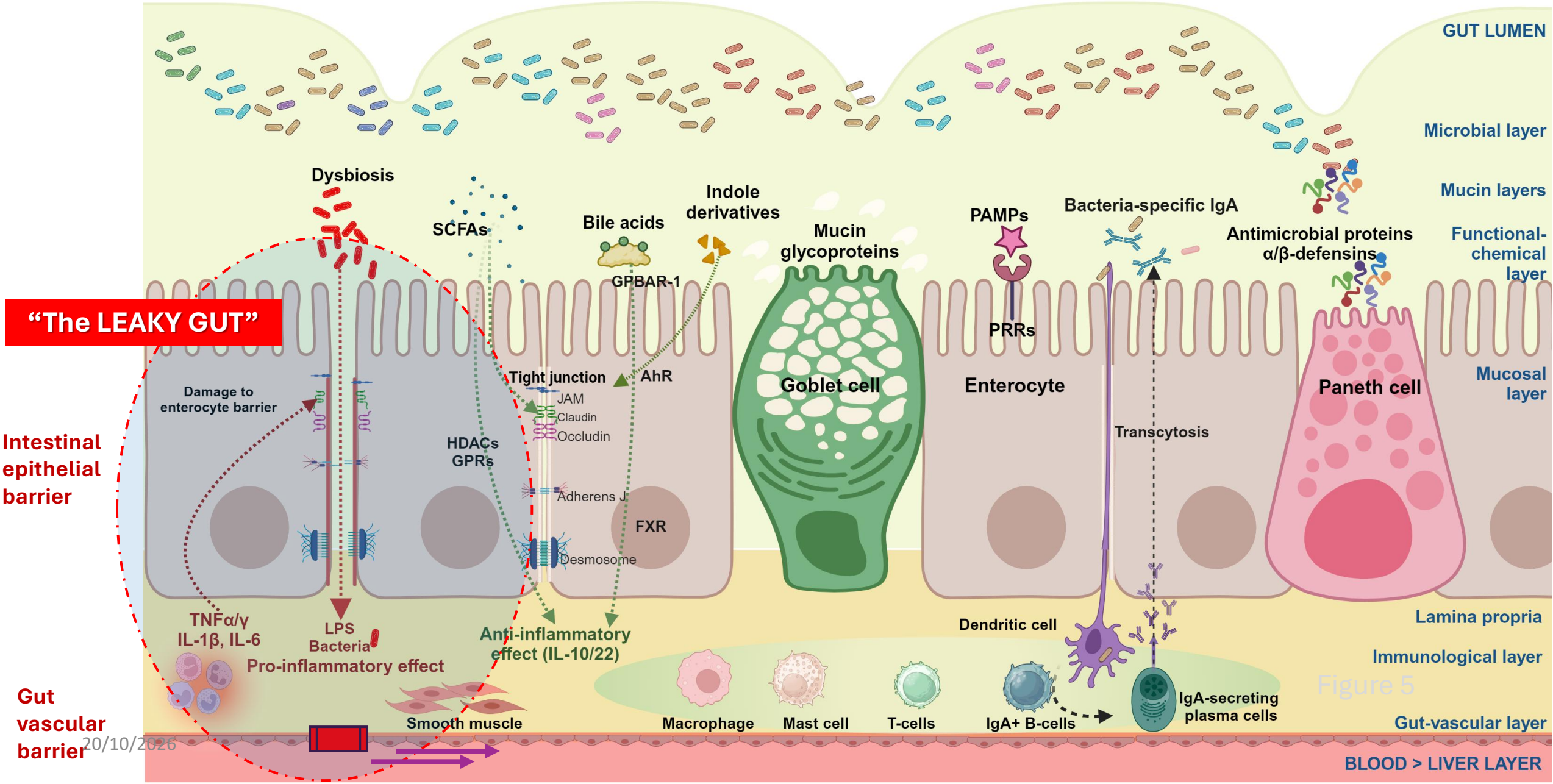
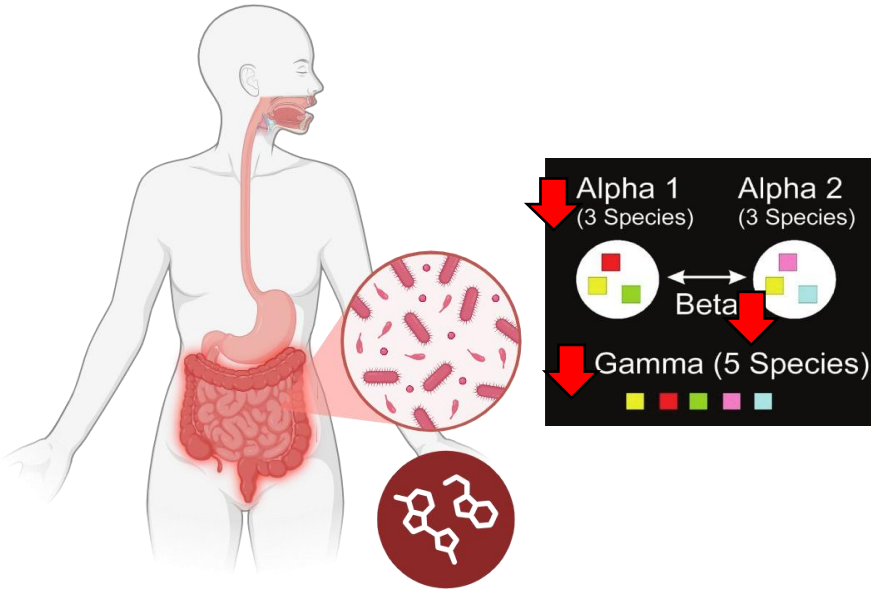
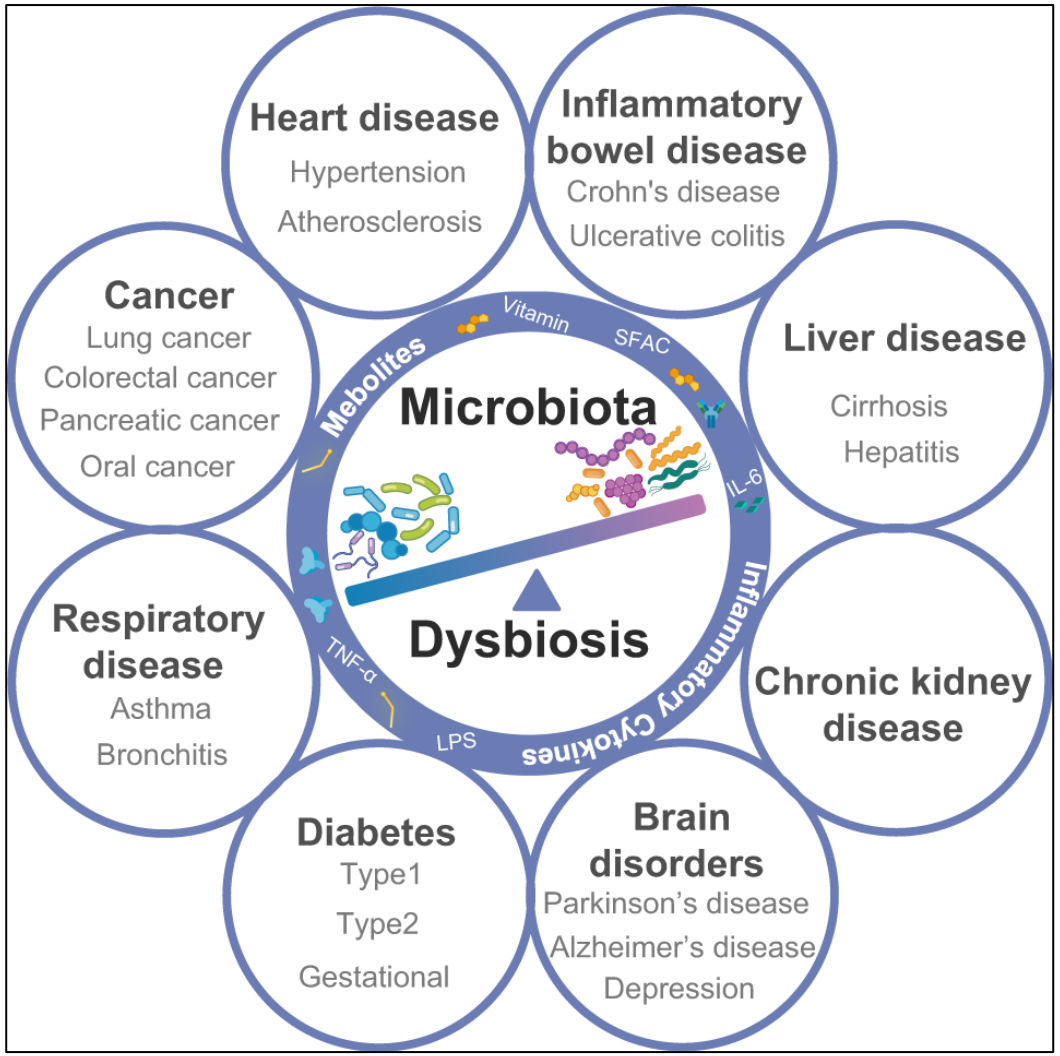


Figure 5

Impact of dysbiosis on global health? YES

Deranged
- taxonomic &
- functional features





Hou, K., Wu, ZX., Chen, XY. et al. Microbiota in health and diseases. Sig Transduct Target Ther 7, 135 (2022)

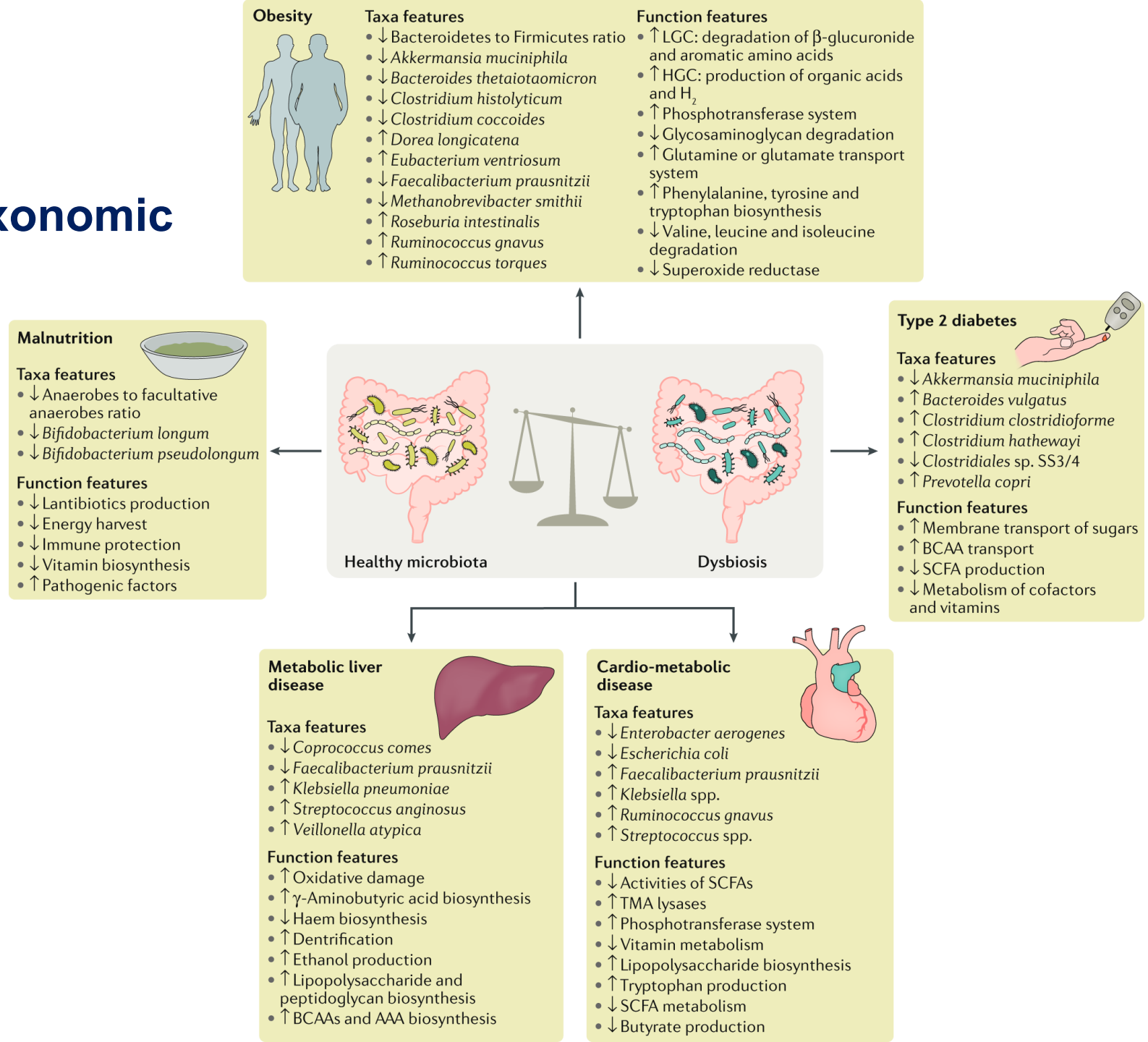
Background

- Many metabolic disorders, e.g.
  - type 2 Diabetes (T2D),
  - obesity
  - metabolic dysfunction-associated steatotic liver disease (MASLD)
  - cardiovascular disorders

are characterised by chronic low-grade systemic inflammation and are potentially related to the gut microbiome.

Metabolic diseases

Deranged microbiota taxonomic & functional features

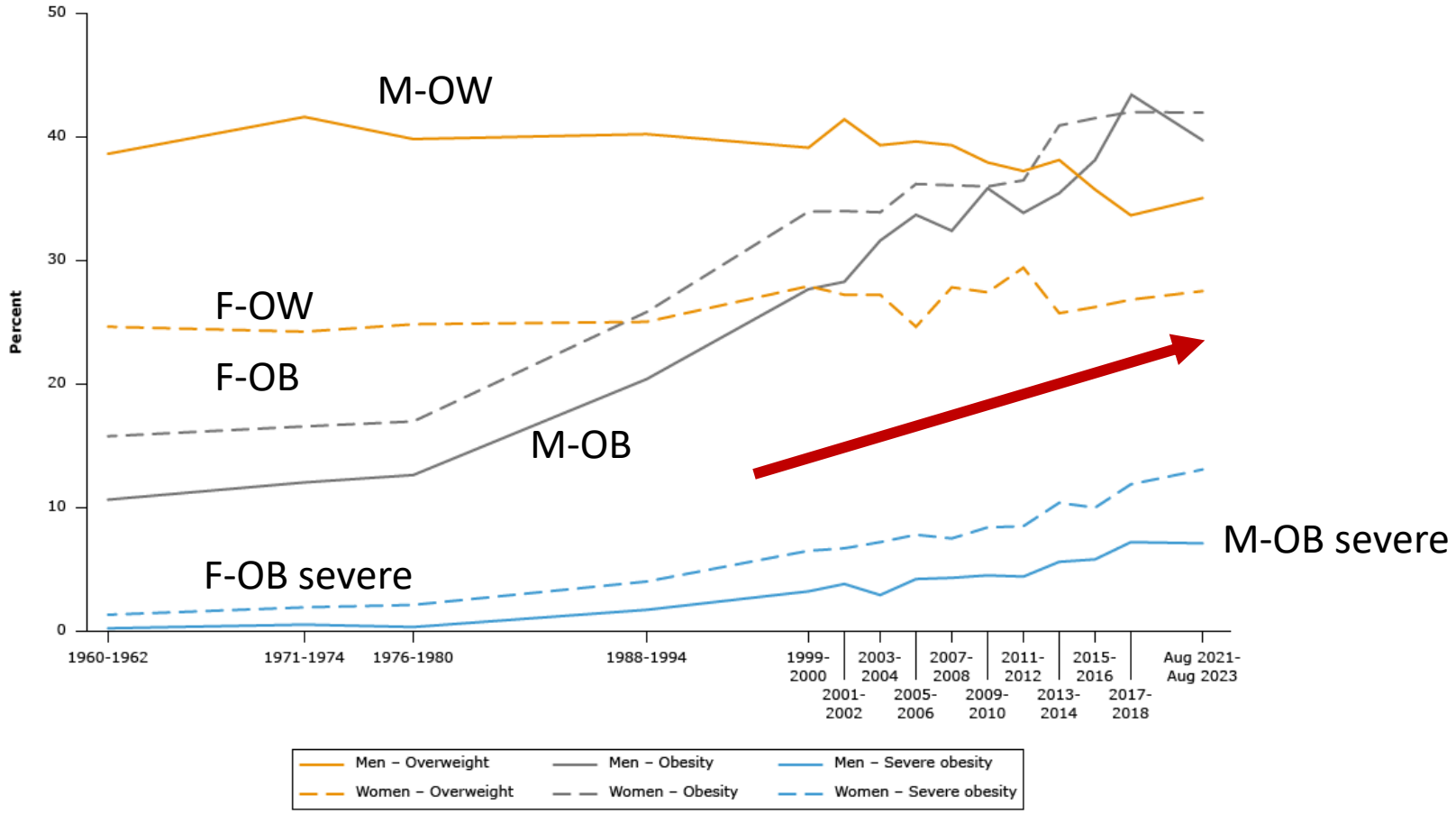


Yong Fan & Oluf Pedersen, 2021

OBESITY

tlq2025

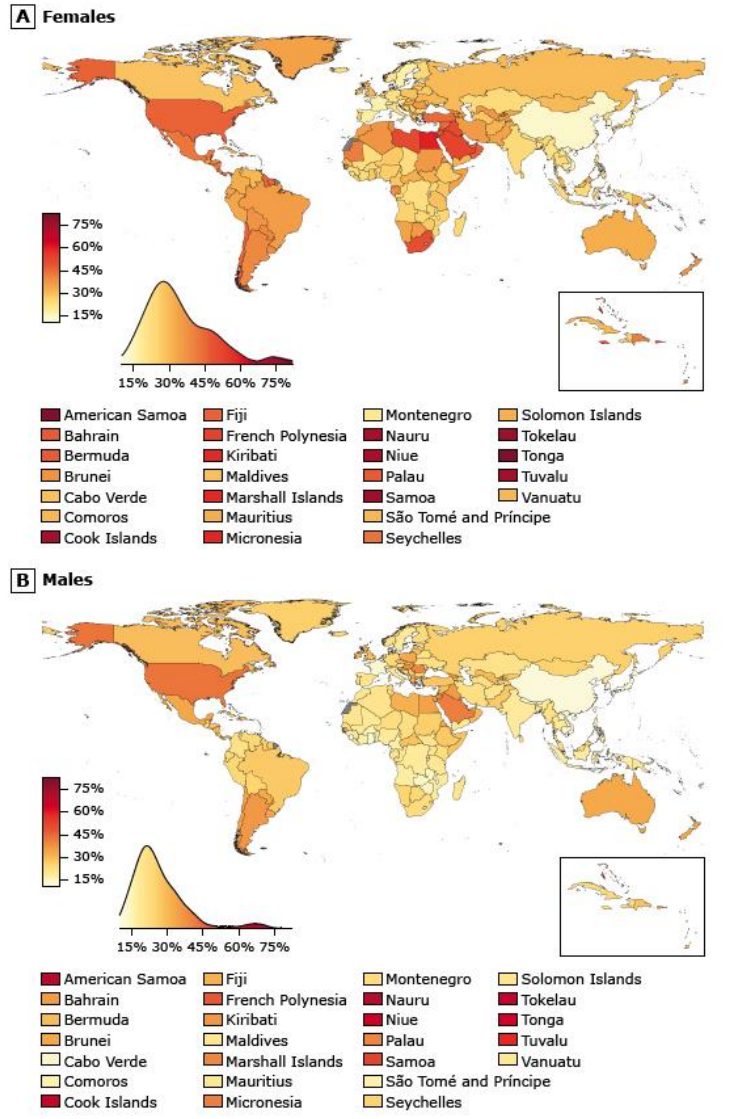
Prevalence of overweight and obesity in the United States over time



Notes: Data are age adjusted by the direct method to the United States Census 2000 estimates using age groups 20 to 39, 40 to 59, and 60 to 74. Overweight is body mass index (BMI) of 25 to 29.9. Obesity is BMI at or above 30. Severe obesity is BMI at or above 40. Pregnant women are excluded from this analysis.

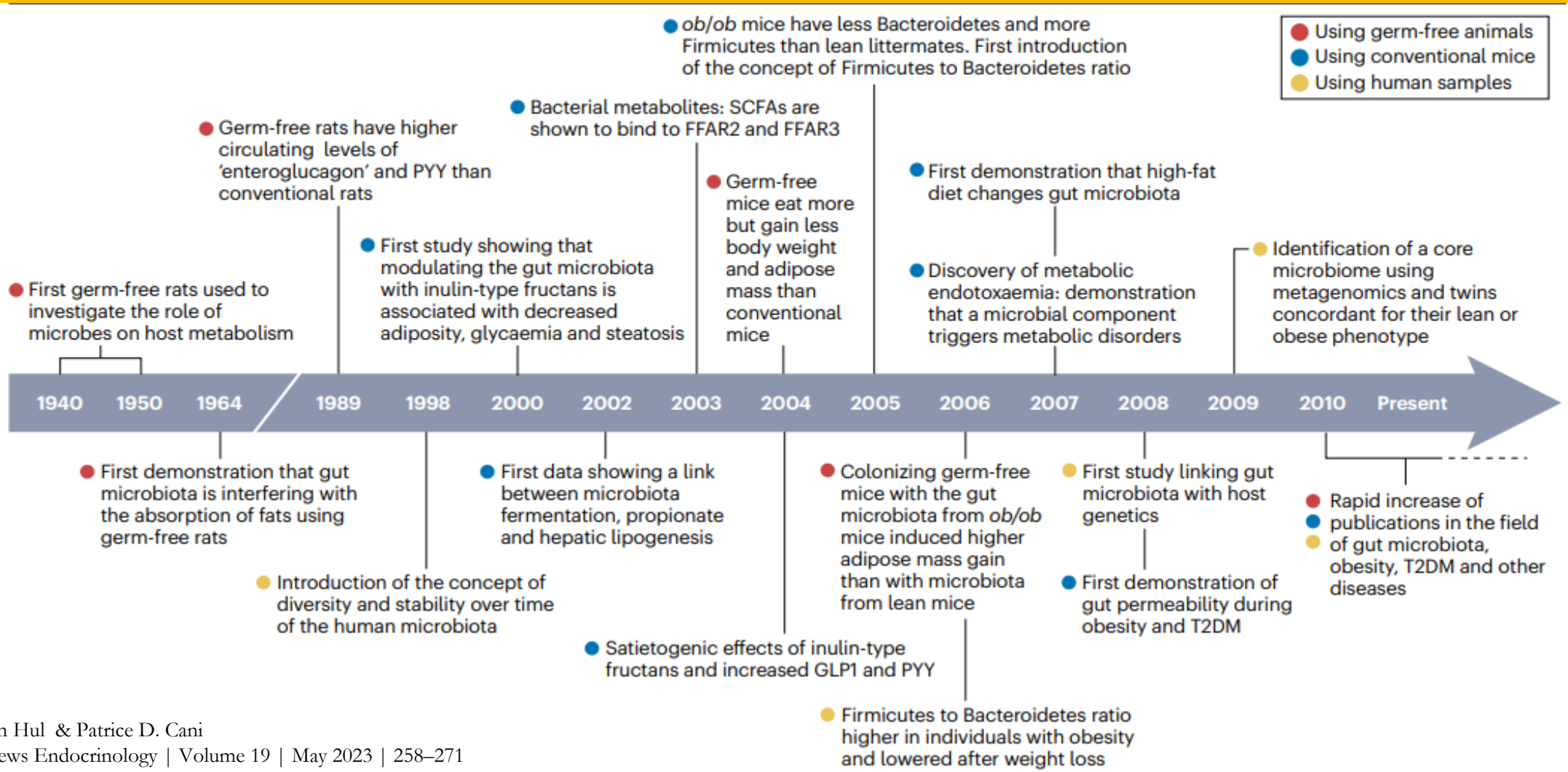
Reproduced from: Fryar CD, Afful J, Saif NT. Health E-Stat 111: Prevalence of overweight, obesity, and severe obesity among adults age 20 and older: United States, 1960–1962 through August 2021–August 2023. National Center for Health Statistics, Centers for Disease Control and Prevention 2026. https://www.cdc.gov/nchs/data/hestat/hestat111.htm (Accessed on April 20, 2026).

Age-standardized prevalence of obesity in adults—2022



From: NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in underweight and obesity from 1990 to 2022: A pooled analysis of 3663 population-representative studies with 222 million children, adolescents, and adults. Lancet 2024; 403:1027. Copyright © 2024 The Authors. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(23)02750-2 (Accessed on May 1, 2024). Reproduced under the terms of the Creative Commons Attribution License 4.0.

Pioneering research in the field of gut microbiota, obesity and related disorders



Matthias Van Hul & Patrice D. Cani
Nature Reviews Endocrinology | Volume 19 | May 2023 | 258–271

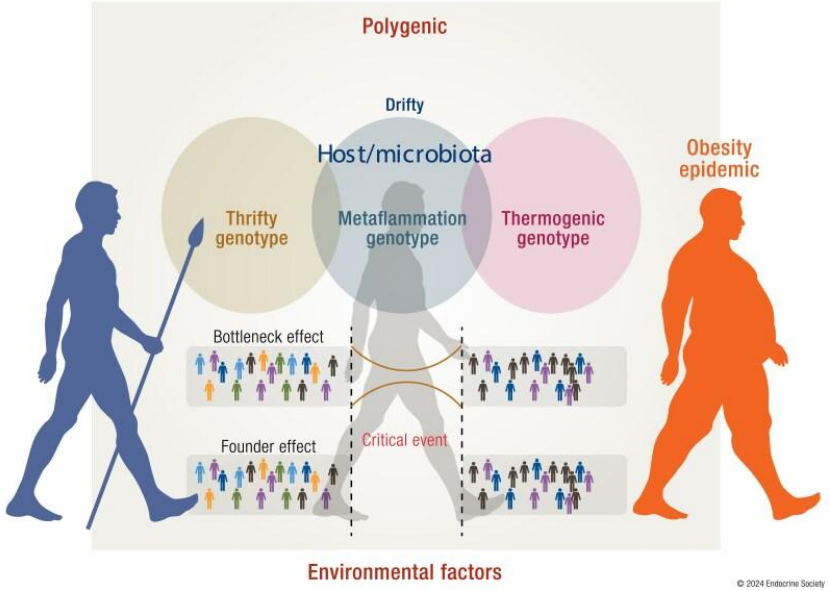
Review > Endocr Rev. 2025 Mar 11;46(2):300-316. doi: 10.1210/endrev/bna

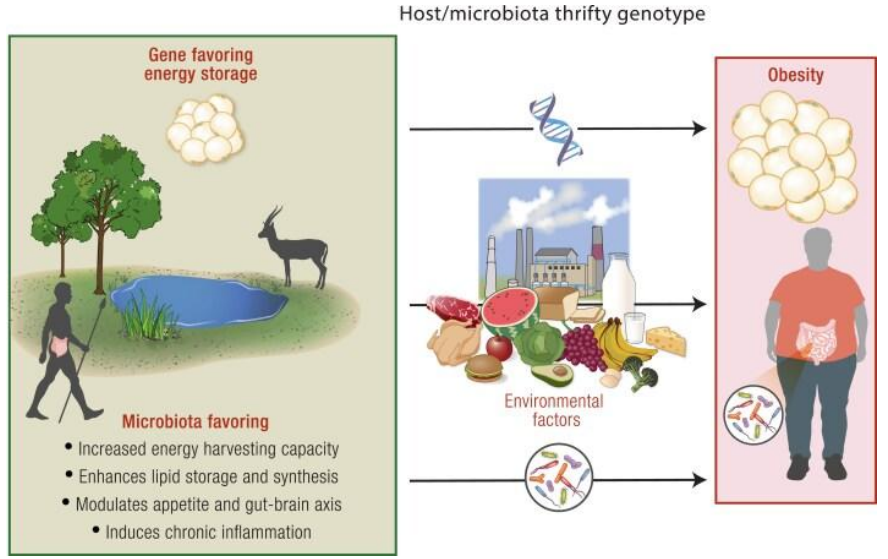
The Microbiota and Evolution of Obesity

Mario J A Saad [1], Andrey Santos [1]

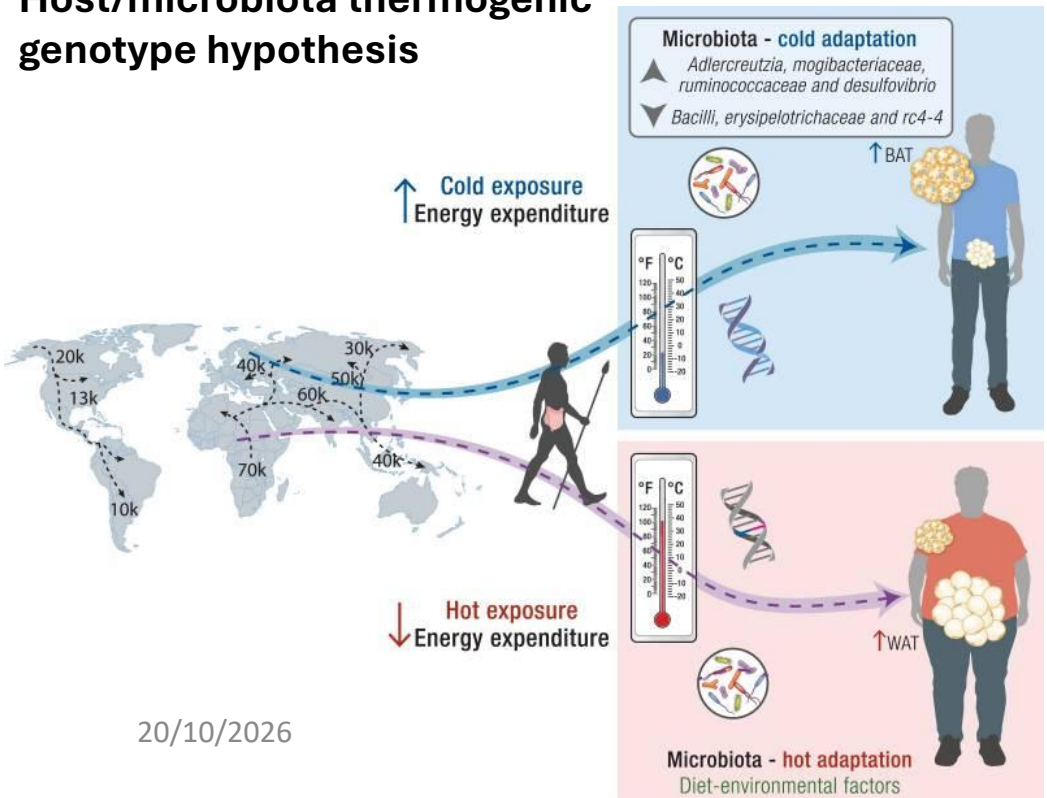
Affiliations + expand

PMID: 39673174 PMCID: PMC11894537 DOI: 10.1210/endrev/bnae033

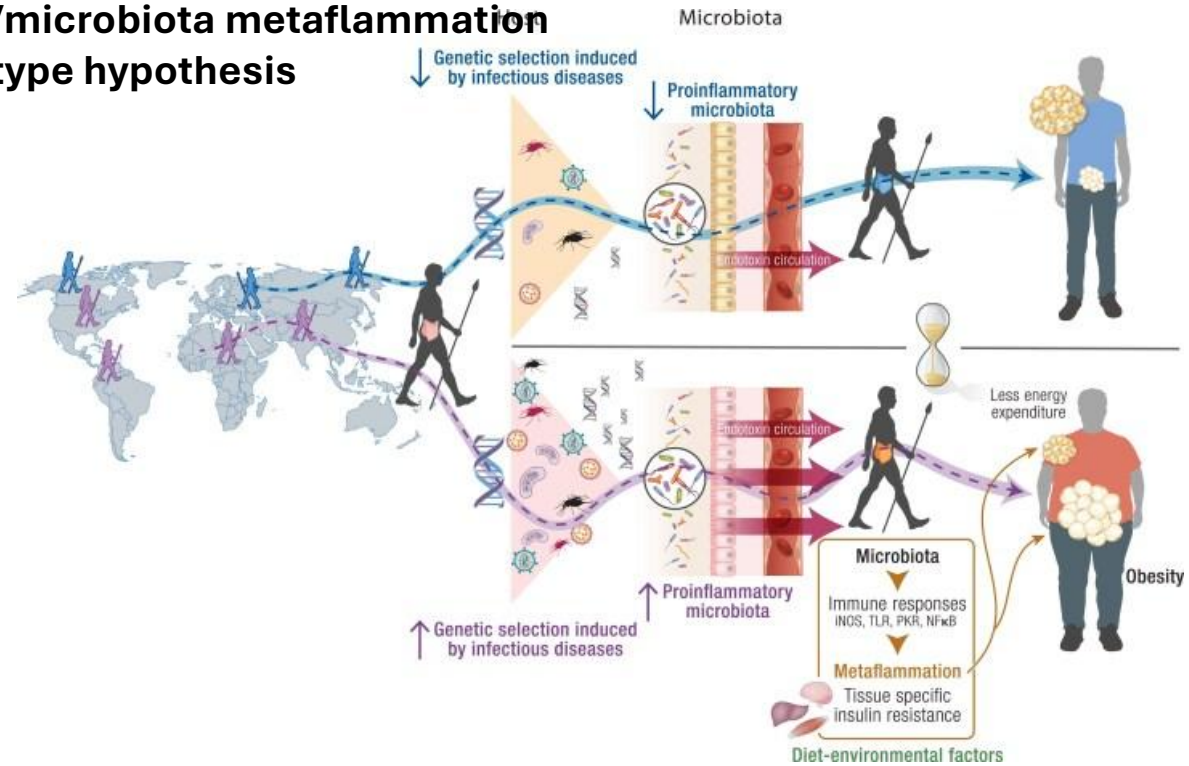




Host/microbiota thermogenic genotype hypothesis



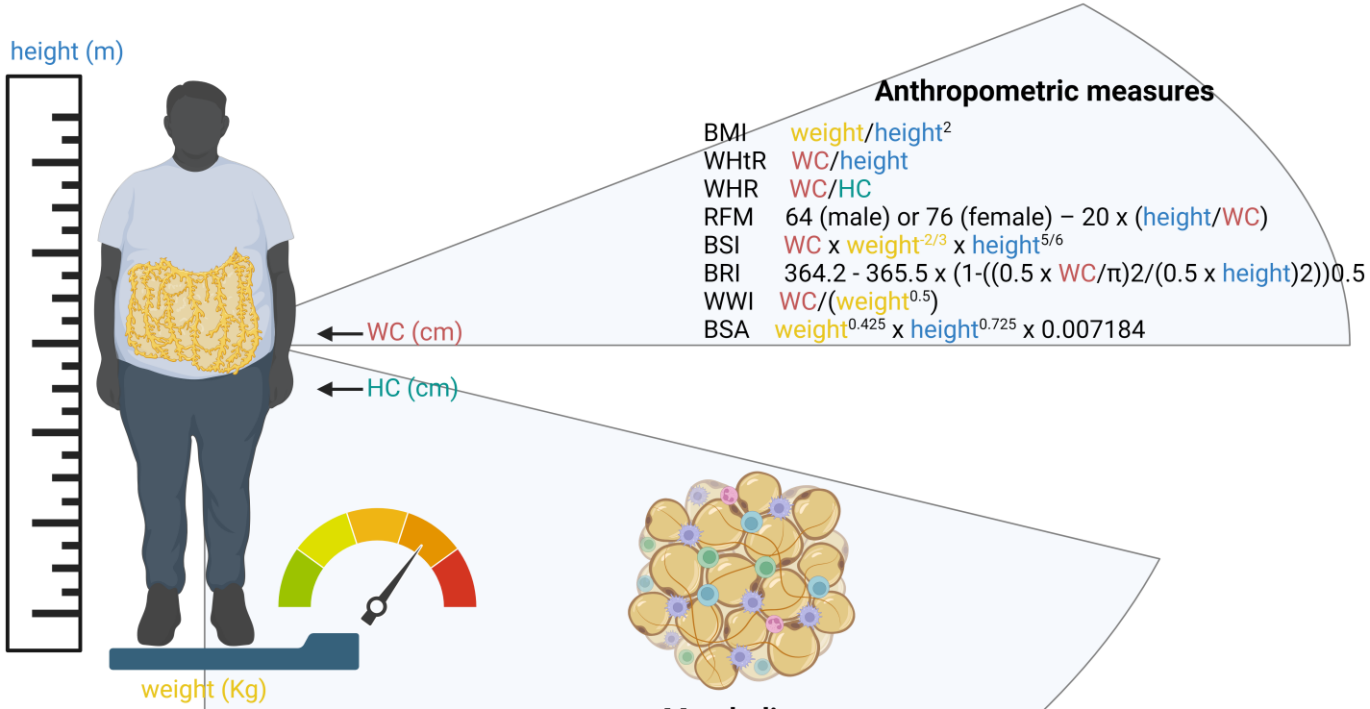
Host/microbiota metaflammation genotype hypothesis



ESCI
EUROPEAN SOCIETY FOR CLINICAL INVESTIGATION



Summary of contemporary methods for obesity assessment/phenotyping



Heterogeneity of obesity.
Better definition "obesities"

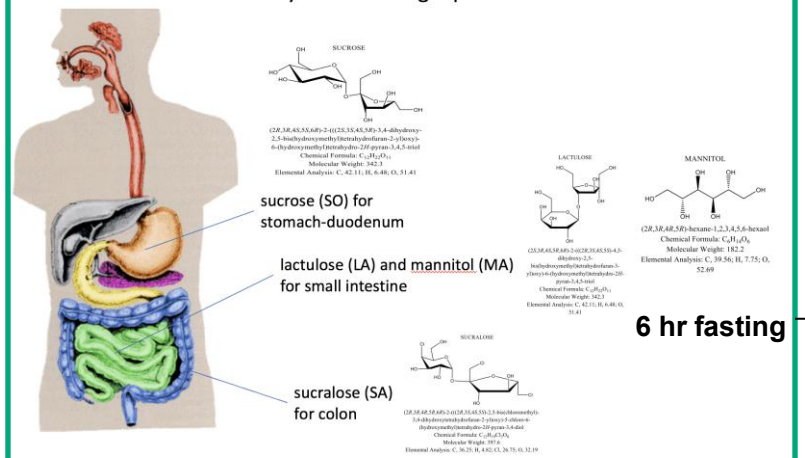
Carbone....Garruti et al Eur J Clin Invest. 2025;00:e70059. https://doi.org/10.1111/eci.7005

Panenteric permeability “LEAKY GUT”
Urinary recovery of selectively absorbed sugars

Di Palo, Portincasa et al, Nutrients 2020

Clinica Medica «A. Murri»
University of Bari

ORAL INGESTION

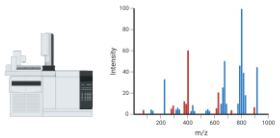


- Sucrose (stomach)
- LAct/MAnn (ileum)
- **Sucralose** **(colon)**

6 hr fasting

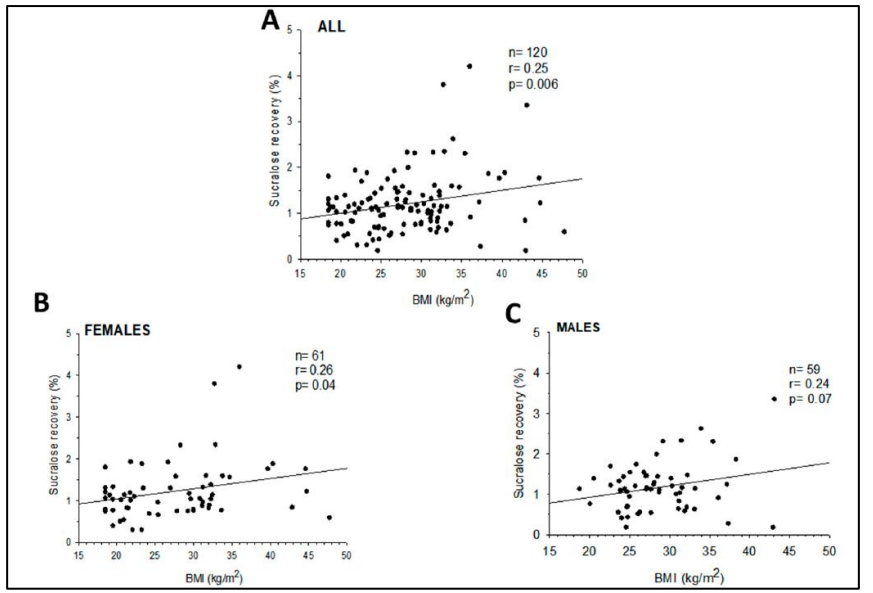


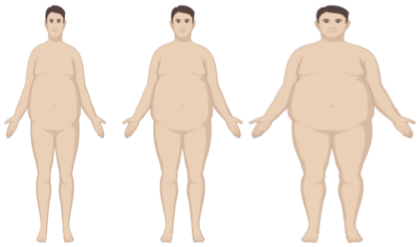
URINARY RECOVERY

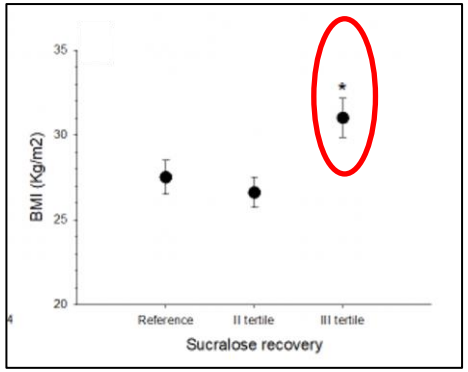


MS-GC

Increased colonic permeability with obesity



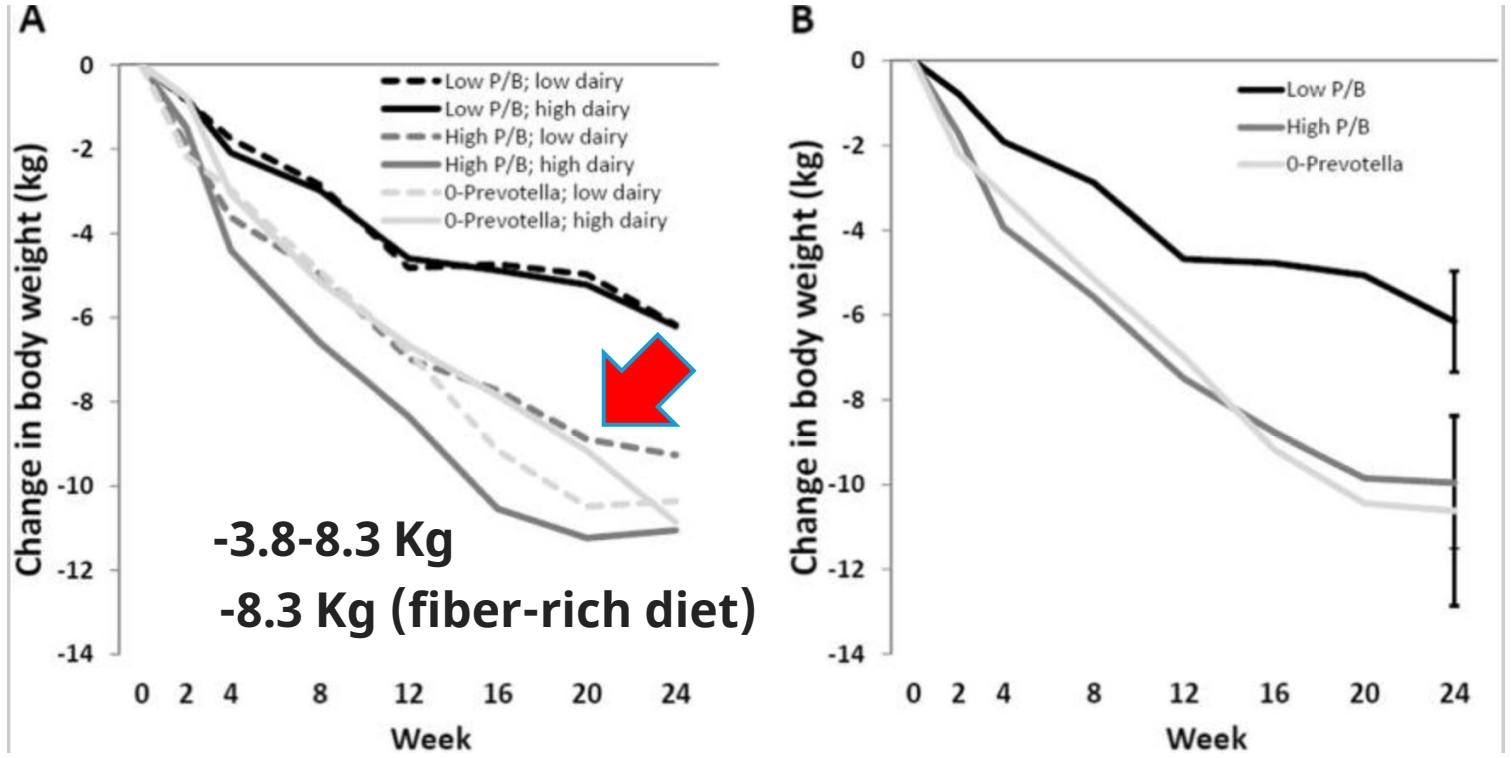




Prevotella-to-*Bacteroides* ratio predicts body weight and fat loss success on 24-week diets

Individuals with a higher gut *Prevotella* to *Bacteroides* ratio lost significantly more weight on a calorie-restricted, high-fiber diet





Hjorth MF et al, Int J Obes (Lond). 2019;43(1):149

Type 2 Diabetes

tlq2025

ARTICLE

doi:10.1038/nature11450

Qin J, Li Y, Cai Z, et al. A metagenome-wide association study of gut microbiota in type 2 diabetes. Nature. 2012;490(7418):55-60. doi:10.1038/nature11450.

A metagenome-wide association study of gut microbiota in type 2 diabetes

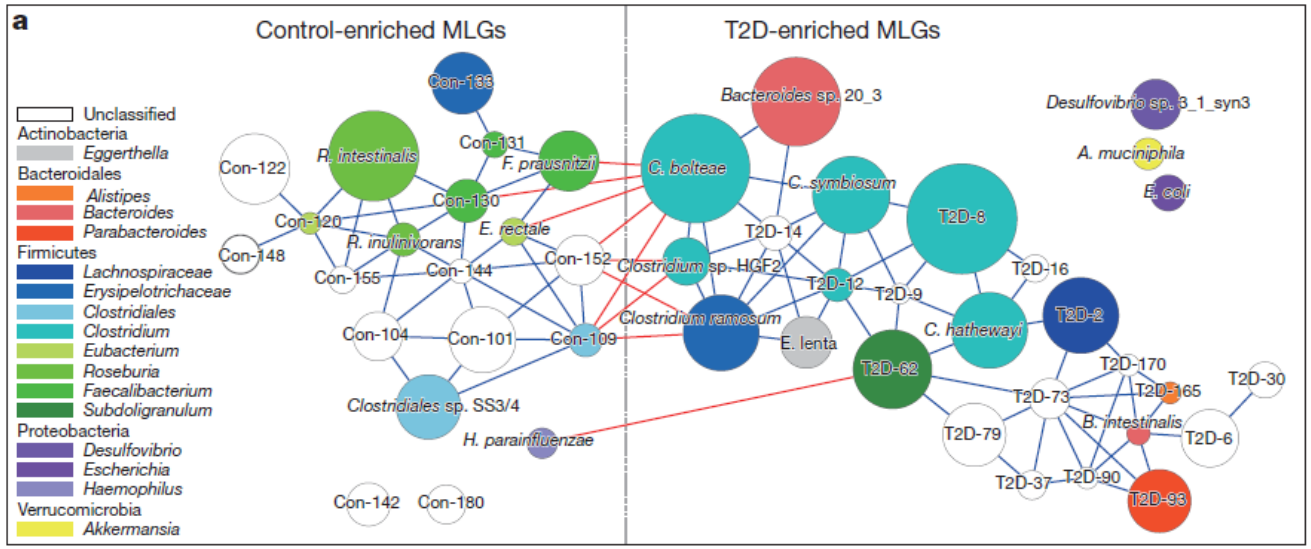
Junjie Qin[1]*, Yingrui Li[1]*, Zhiming Cai[2]*, Shenghui Li[1]*, Jianfeng Zhu[1]*, Fan Zhang[3]*, Suisha Liang[1], Wenwei Zhang[1], Yuanlin Guan[1], Dongqian Shen[1], Yangqing Peng[1], Dongya Zhang[1], Zhuye Jie[1], Wenxian Wu[1], Youwen Qin[1], Wenbin Xue[1], Junhua Li[1], Lingchuan Han[3], Donghui Lu[3], Peixian Wu[3], Yali Dai[3], Xiaojuan Sun[2], Zesong Li[2], Aifa Tang[2], Shilong Zhong[4], Xiaoping Li[1], Weineng Chen[1], Ran Xu[1], Mingbang Wang[1], Qiang Feng[1], Meihua Gong[1], Jing Yu[1], Yanyan Zhang[1], Ming Zhang[1], Torben Hansen[5], Gaston Sanchez[6], Jeroen Raes[7,8], Gwen Falony[7,8], Shujiro Okuda[7,8], Mathieu Almeida[9], Emmanuelle LeChatelier[9], Pierre Renault[9], Nicolas Pons[9], Jean-Michel Batto[9], Zhaoxi Zhang[1], Hua Chen[1], Ruifu Yang[1,10], Weimou Zheng[1], Songgang Li[1], Huanming Yang[1], Jian Wang[1], S. Dusko Ehrlich[9], Rasmus Nielsen[6], Oluf Pedersen[5,11,12], Karsten Kristiansen[1,13] & Jun Wang[1,5,13]

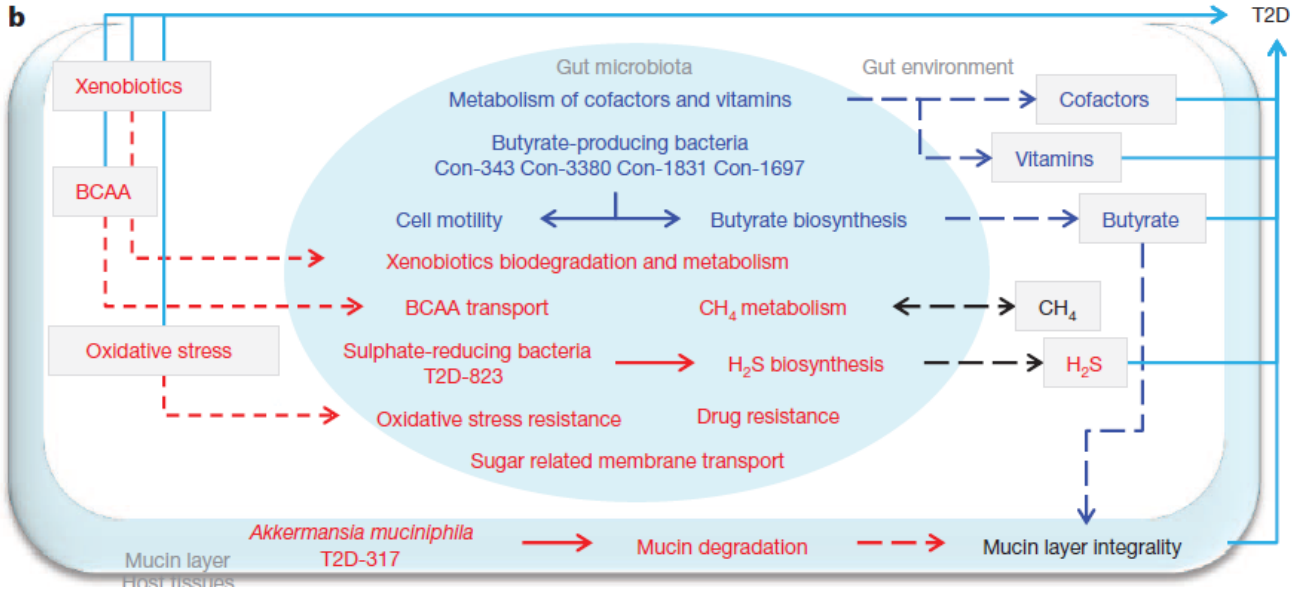
- Metagenome-wide association study (MGWAS)
- 345 Chinese subjects
- 60,000 type-2 diabetes-associated markers identified
- Convincing microbiome signature in type 2 Diabetes

tlg2025

Taxonomic and functional characterisation of gut microbiota in T2D

Qin J, Li Y, Cai Z, et al. A metagenome-wide association study of gut microbiota in type 2 diabetes. Nature. 2012;490(7418):55-60. doi:10.1038/nature11450.





MLGs,
Metagenomic linkage group

Red text = Enriched functions
Includes oxidative stress = inflammation

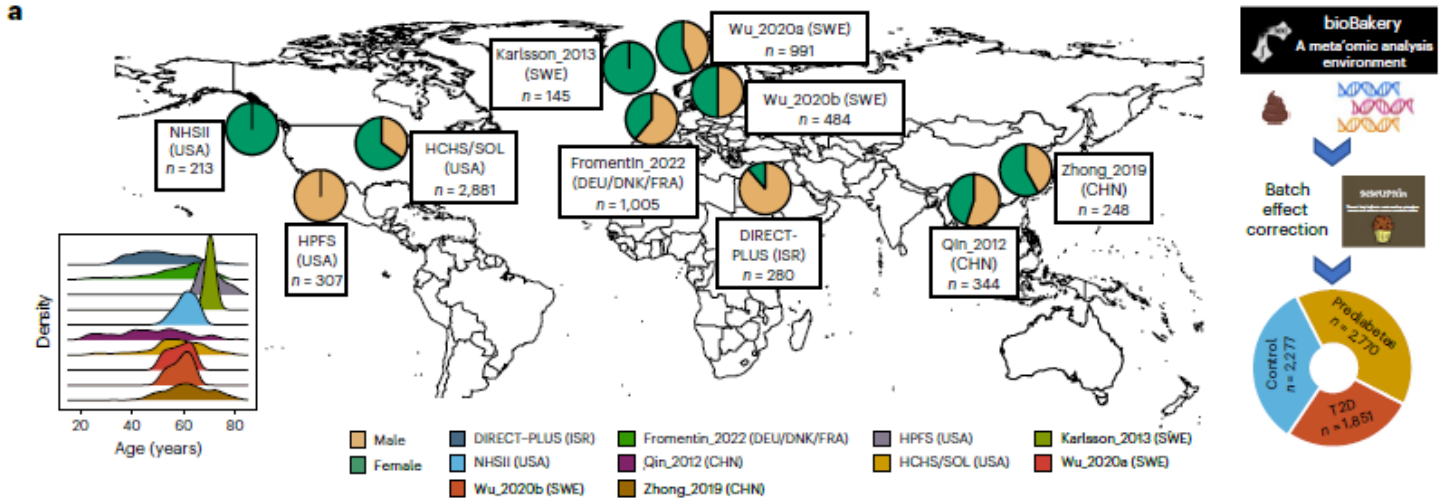
Blue text = Decreased functions

tlg2025

Strain-specific gut microbial signatures in type 2 diabetes identified in a cross-cohort analysis of 8,117 metagenomes

- 8,117 metagenomes from 10 cohorts (T2D, prediabetes, controls)
- Dysbiosis in 19 phylogenetically diverse species, e.g. *Clostridium bolteae, Butyrovibrio crossotus*
- Disturbed microorganisms also contributed to perturbations in glucose metabolism
- 27 species that explain inter-individual differences in T2D risk, such as *Eubacterium rectale*
- Study shows robust cross-cohort microbial signatures in T2DM

Overview of microbial community structure associated with T2D

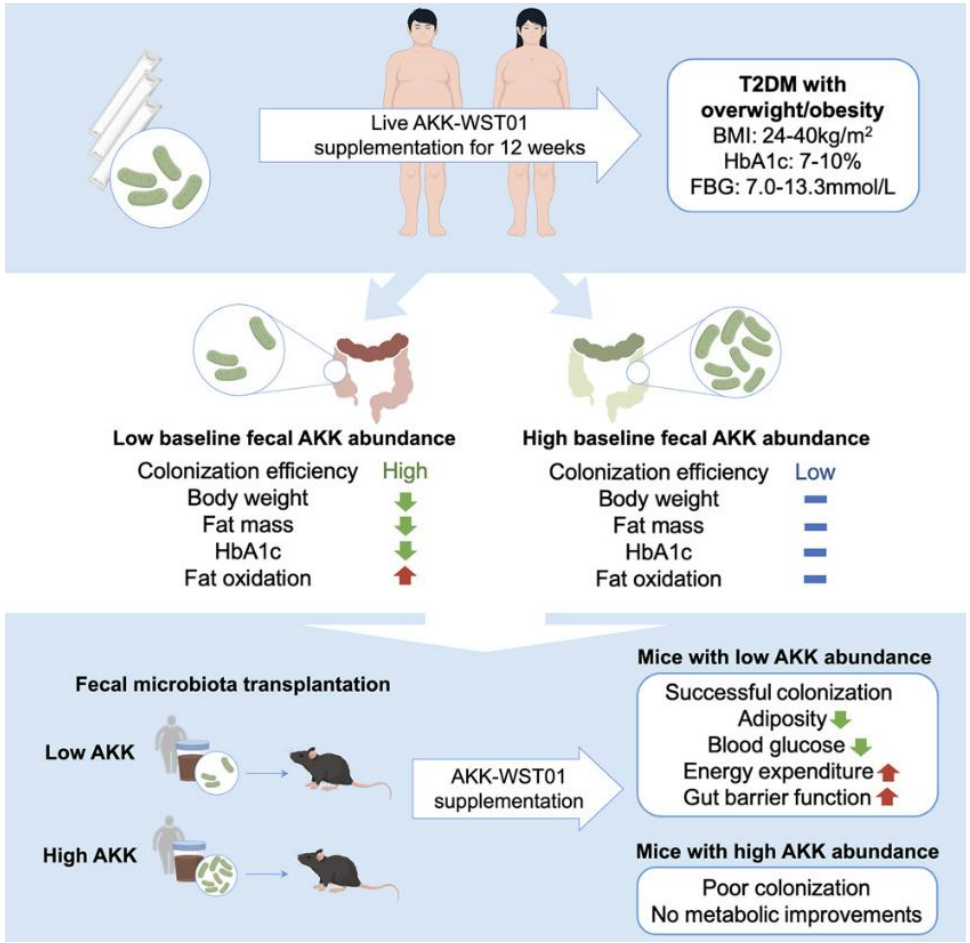


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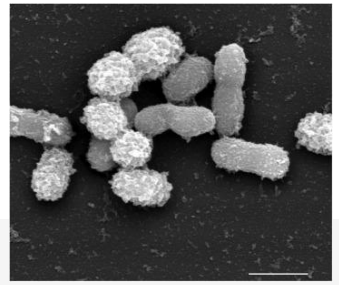
Mei Z, Wang F, Bhosle A, et al. Strain-specific gut microbial signatures in type 2 diabetes identified in a cross-cohort analysis of 8,117 metagenomes. Nat Med. 2024;30(8):2265-2276. doi:10.1038/s41591-024-03067-7

Akkermansia muciniphila supplementation in patients with overweight/obese type 2 diabetes: Efficacy depends on ist baseline levels in the gut

Zhang Y, Liu R, Chen Y, et al. Akkermansia muciniphila supplementation in patients with overweight/obese type 2 diabetes: Efficacy depends on its baseline levels in the gut. Cell Metab. 2025;37(3):592-605.e6. doi:10.1016/j.cmet.2024.12.010



58 participants/12 weeks



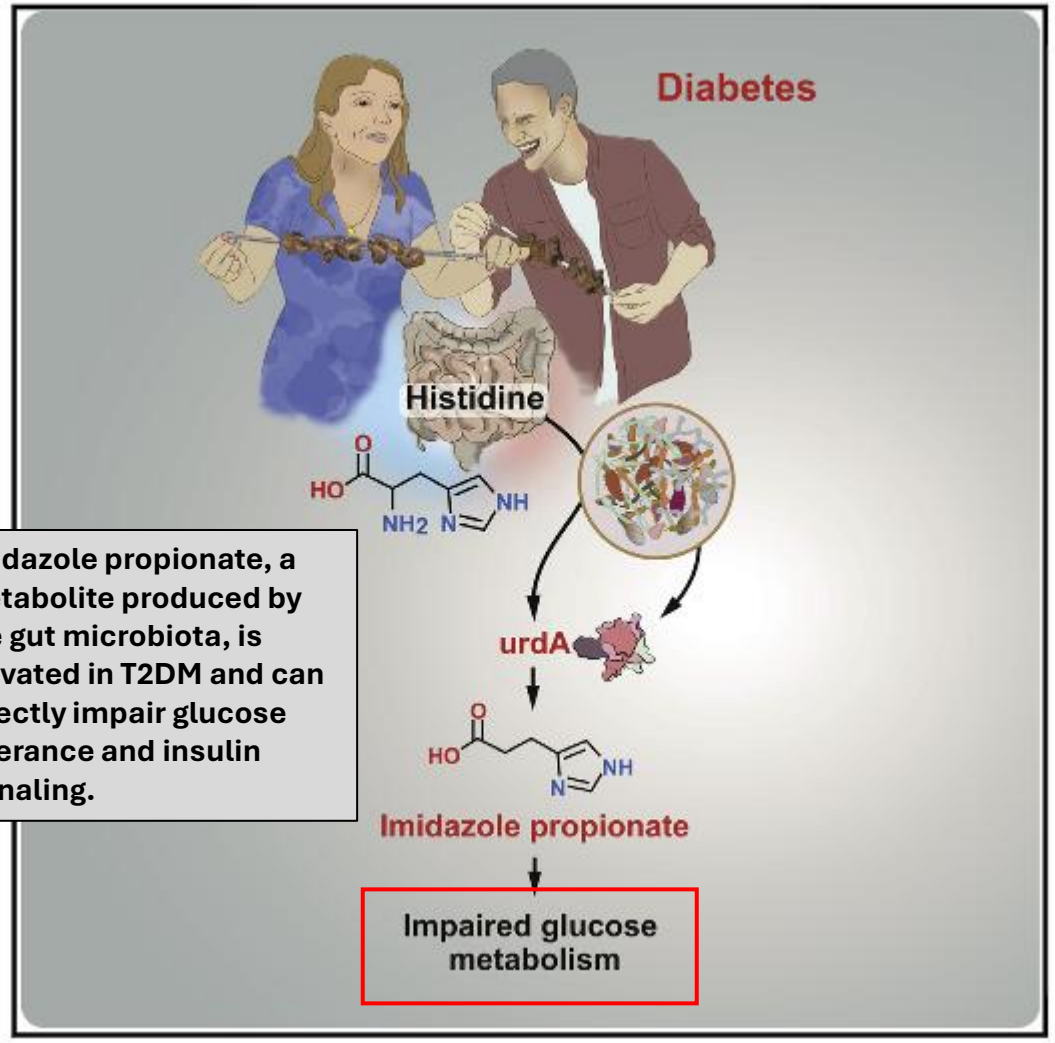
Highlights

- AKK-WST01 supplementation successfully colonizes in low *A.muciniphila* participants
- AKK-WST01 improves weight and metabolism in low *A.muciniphila* patients with T2D
- AKK-WST01 increases fat oxidation in low *A.muciniphila* patients with T2D
- AKK-WST01 improves metabolic homeostasis in mice with low *A.muciniphila*

tlg2025

Microbially Produced Imidazole Propionate Impairs Insulin Signaling through mTORC1

Koh A, Molinaro A, Ståhlman M, et al. Microbially Produced Imidazole Propionate Impairs Insulin Signaling through mTORC1. Cell. 2018;175(4):947-961.e17. doi:10.1016/j.cell.2018.09.055



Imidazole propionate, a metabolite produced by the gut microbiota, is elevated in T2DM and can directly impair glucose tolerance and insulin signaling.

Association with ImP	Microbial Features (Indicators or Bacteria)	Reference
ImP-producing bacteria	The bacteria with "Y"- or "M"-UrdA homologs: *Aerococcus urinae, Streptococcus mutans, Anaerococcus prevotii, Adlercreutzia quolifaciens, Eggerthella lenta, Lactobacillus paraplantarum, Brevibacillus laterosporus, Shewanella oneidensis.*	(12)
Positively correlated with ImP levels	Bacteroides 2 enterotype	(13)
	Lactobacillus: *L. gasseri, L. fermentum, L. plantarum, L. amylovorus, L. crispatus, L. iners.*	(12, 13, 17, 18, 20, 30, 71, 87)
	Streptococcus: *S. mutans, S. parasanguinis, S. gallolyticus, S. anginosus, S. oralis, S. gordonii, S. agalactiae.*	
	Clostridium: *C. bolteae, C. symbiosum, C. ramosum, C. scindens, C. bartlettii, C. spiroforme, C. clostridioforme, Flavonifractor plautii.*	
	Bifidobacterium: *B. longum, B. dentium, B. breve, B. reuteri*	
	Bacteroides: *B. xylanisolvens, B. vatus, B. dorei vulgatus, B. faecis.*	
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Negatively correlated with ImP levels	Microbiome gene count (607,000 threshold)	(13)
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Zeng, Y.; Wu, Q.; Guo, M.; Teng, F.; Jiang, C.; Chen, J.; Tan, X.; Zeng, C.; Long, Y.; Law, B.Y.-K.; Xu, Y. Gut microbiota-derived imidazole propionate: an emerging target for the prevention and treatment of cardiometabolic diseases. *Frontiers in Endocrinology* ***2025, 16, doi:10.3389/fendo.2025.1409119.***

tlg2025

Gut-liver axis: prototypic area of interactions of gut microbiota with Immunity

tlq2025

nutrients

Microbiota associated gut liver mechanisms implicated in MASLD/MASH

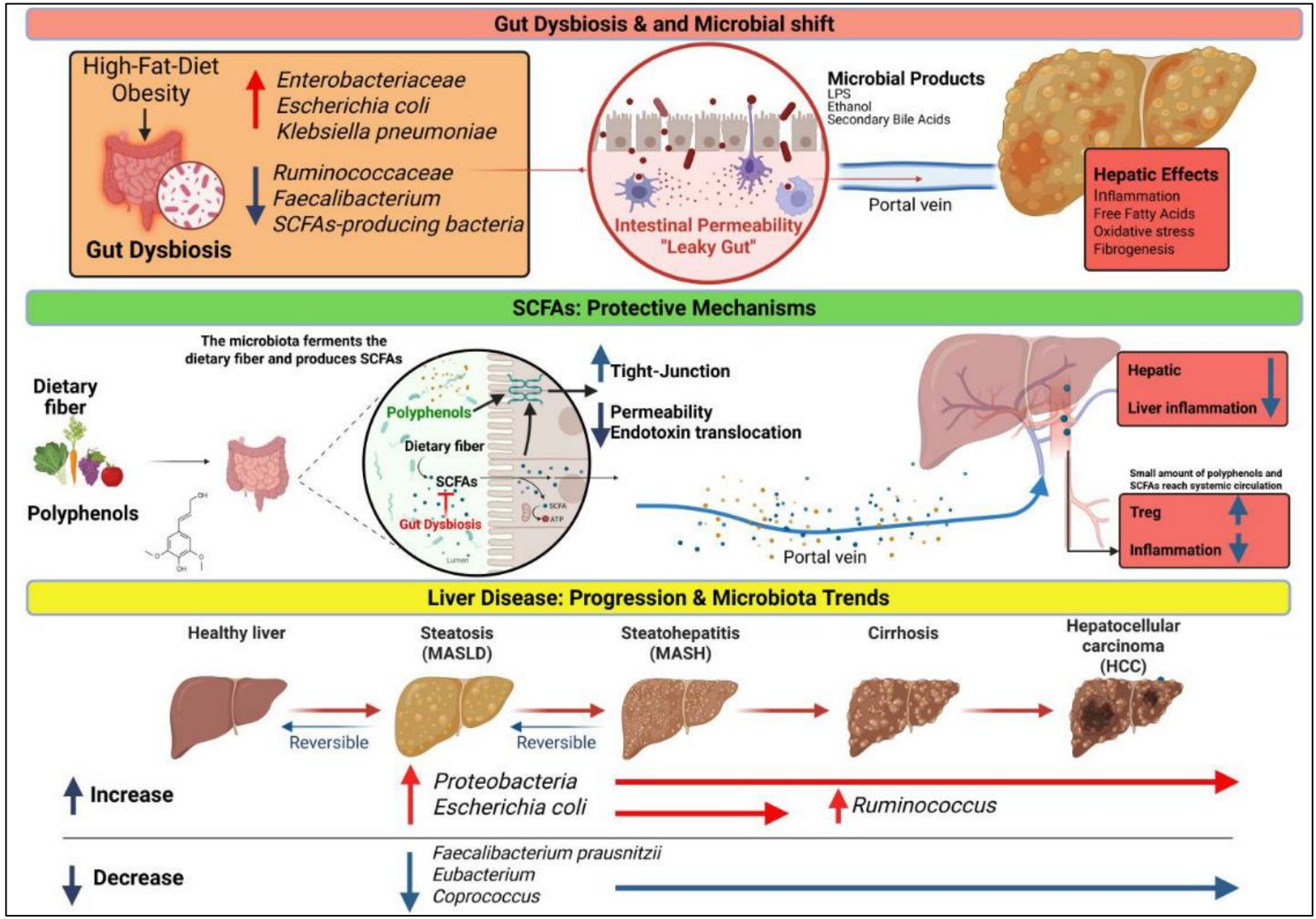
Review

Targeting the Human Gut Microbiota—Between Conventional Therapy and Precision Genetic Engineering

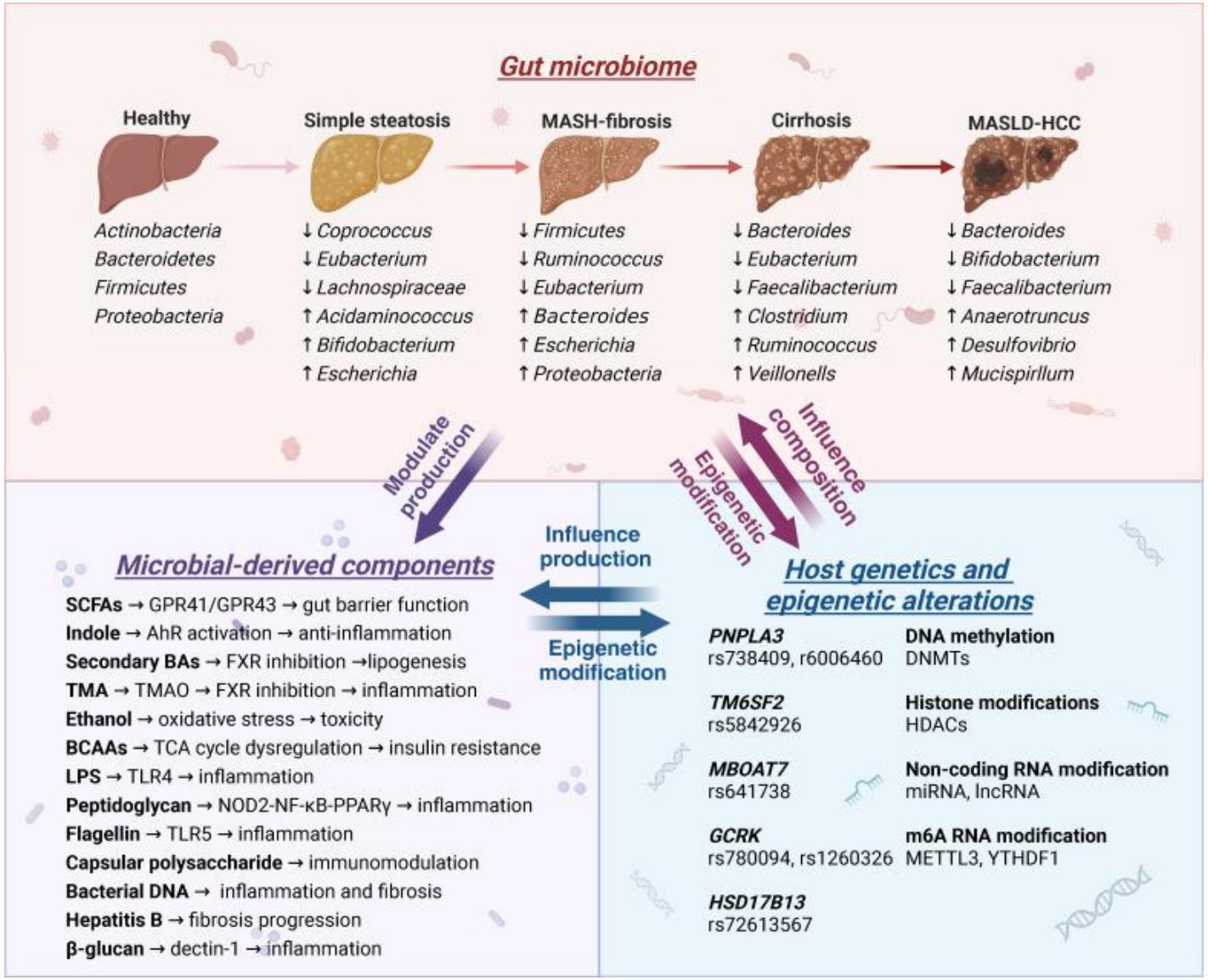
Naomi-Adina Ciurea [1,2,†], Laura Mahdi [3,†], Annarita Graziani [4], Agostino Di Ciaula [3], Piero Portincasa [3,*] and Mohamad Khalil [3]

[1] Department of Internal Medicine, "George Emil Palade" University of Medicine, Pharmacy, Science and Technology of Targu Mures, 540139 Targu Mures, Romania; naomi-adina.macaru@umfst.ro
[2] Doctoral School of Medicine and Pharmacy, "George Emil Palade" University of Medicine, Pharmacy, Sciences and Technology of Targu Mures, 38 Gheorghe Marinescu Street, 540139 Targu Mures, Romania
[3] Clinica Medica A. Murri, Department of Precision and Regenerative Medicine and Ionian Area (DiMePre-J), University of Bari Aldo Moro, Piazzale G. Cesare 11, 70124 Bari, Italy; laura.mahdi@uniba.it (L.M.); agodiciaula@gmail.com (A.D.C.); mohamad.khalil@uniba.it (M.K.)
[4] Institut AllergoSan Pharmazeutische Produkte Forschungs-und Vertriebs GmbH, 8055 Graz, Austria; graziani@allergosan.at
* Correspondence: piero.portincasa@uniba.it
† These authors contributed equally to this work.

Ciurea N-A, Mahdi L, Graziani A, Di Ciaula A, Portincasa P, Khalil M (**2026**) Targeting the Human Gut Microbiota—Between Conventional Therapy and Precision Genetic Engineering. Nutrients 18:1958.



Risk factors in MASLD and the intricate interplay between gut microbiome, microbial metabolites, and host genetics and epigenetics



Ha S, Wong VW, Zhang X, Yu J. Interplay between gut microbiome, host genetic and epigenetic modifications in MASLD and MASLD-related hepatocellular carcinoma. *Gut*. 2024;74(1):141-152. Published 2024 Dec 10.

MASLD: a role for gut microbiota & metabolites

	metabolites	positive effects	negative effects
BAs	DCA	enhance the secretion of serum GLP-1 [124]	inhibit mitophagy, accelerate inflammation and induce pyroptosis [122]
	UDCA TUDCA	remodel liver inflammation and reverse liver fibrosis [125] regulate intestinal stabilization and inhibit gut lipid absorption [126] reverse TCDCA-induced lipid dysmetabolism [127]	
	TCDCA		enhance the liver weight/body weight ratio, hepatic triglyceride and total cholesterol levels [127] enhance the activity of HSC and facilitate the transcription of hepatic fibrosis gene [128]
	HDCA	promote to activate PPARα and FXR signaling of liver and regulate the synthetases of BAs [129] increase nuclear PPARα accumulation [130]	
SCFAs	acetic acids	stimulate free fatty acid receptor 2, improve insulin resistance and lipid metabolism in liver [133] alleviate hepatic inflammation and tissue damage [134] induce cell cycle arrest and cell apoptosis, reduce tumor volume and tumor weight in NAFLD-HCC [136]	offer an additional lipogenic precursor [132]
	propionic acids	weaken acetate induced fat accumulation [132] suppress hepatic macrovesicular steatosis, inflammatory aggregates and collagen content [137]	induce insulin resistance, hyperinsulinemia and weight gain [138]
LPS			inhibit the expression of microsomal triglyceride transfer protein and apolipoprotein B, and ultimately facilitate triglycerides accumulation and steatosis [140] enhance lipid accumulation and content of free fatty acids, raise FFA-induced NAFLD cells apoptosis [141] involve the genesis of NAFLD [143] profibrotic cytokines and impair hepatocyte y [144]

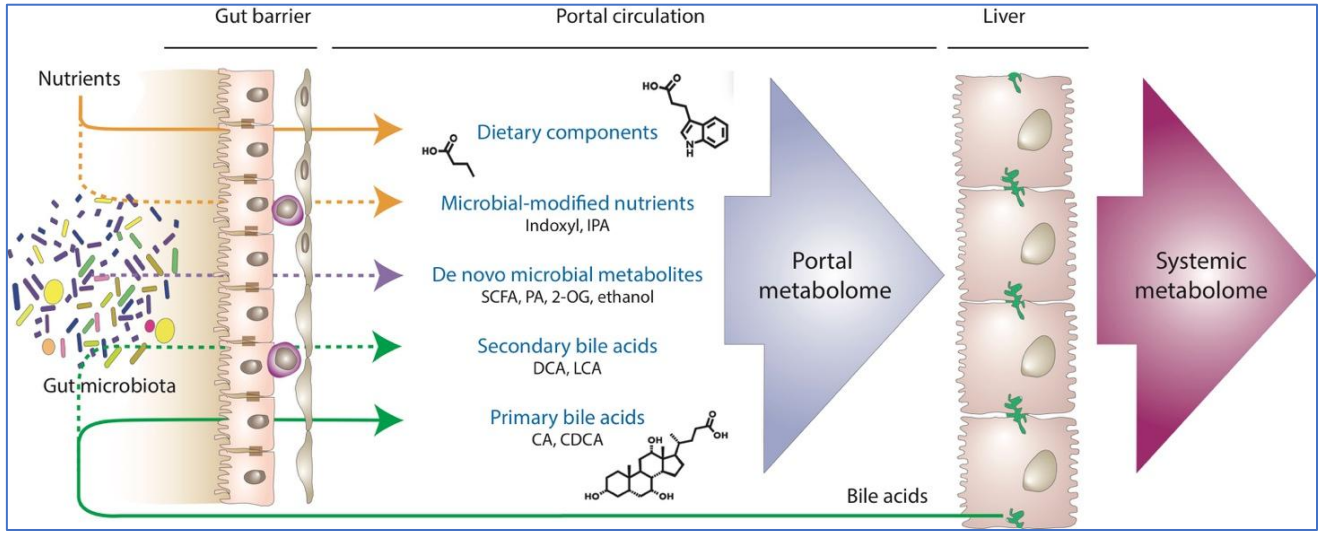
Animal vs. Human studies

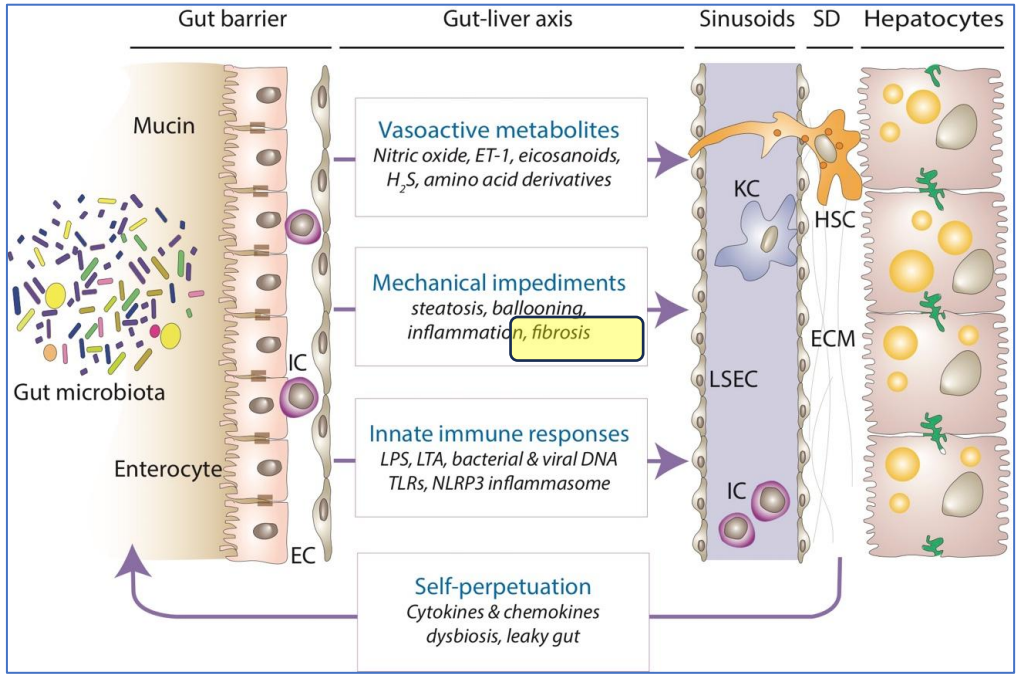


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Li, N.; Zhao, C.; Zhang, P.; Wu, S.; Dou, X.; Xu, S.; Zhang, X.; Peng, C.; Xie, Y.; Huang, S.; Zhou, L.; Shen, Y.; Wang, L.; Wang, J.; Yu, C. The role of gut microbiota associated metabolites in digestive disorders. *Engineered Regeneration* ***2024, 5, 228–246, doi:https://doi.org/10.1016/j.engreg.2024.04.003.***

Baffy G, and Portincasa P.
Gut Microbiota and Sinusoidal Vasoregulation in MASLD: A Portal Perspective.
Metabolites. 2024;14(6):324.







Gyorgy Baffy, Harvard, Boston USA

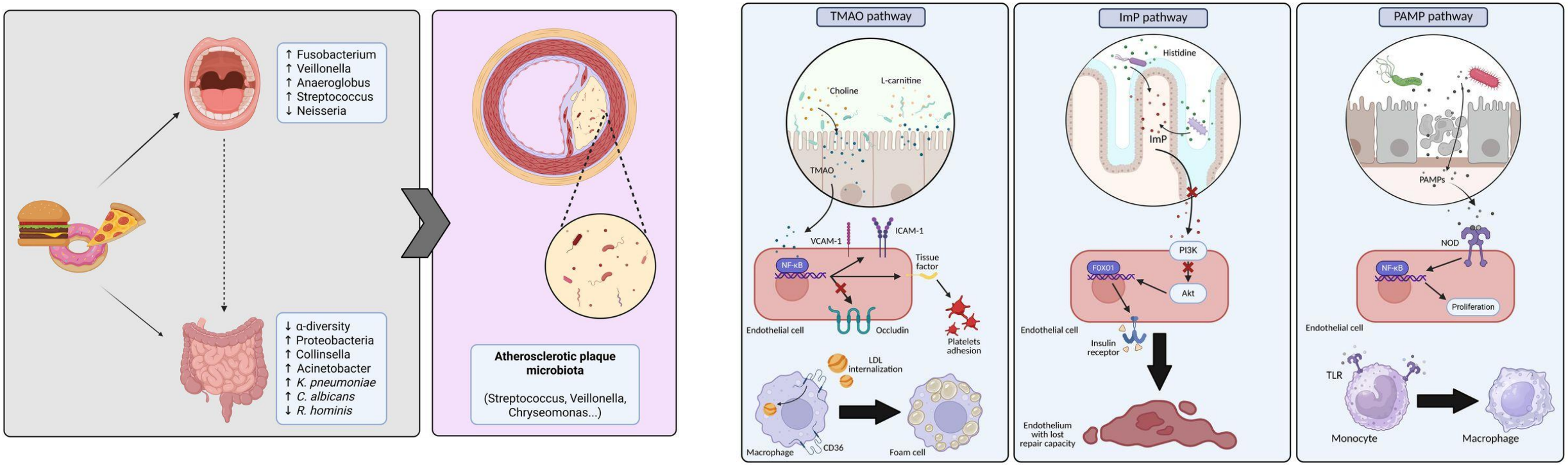
EC	endothelial cell;
ECM	extracellular matrix;
ET-1	endothelin-1;
H_2S	hydrogen sulfide;
HSC	**hepatic stellate cell;**
IC	**immune cells;**
KC	**Kupffer cell;**
LPS	lipopolysaccharide;
LSEC	**liver sinusoidal endothelial cell**
LTA	lipoteichoic acid; ;
NLRP3	nucleotide-binding domain, leucine-rich–containing family, pyrin domain–containing-3;
SD	space of Disse.

Cardiovascular diseases, chronic inflammation and microbiome

Gut microbiota and Atherosclerosis

Fusco W, Adolph T, Cammarota G, Gasbarrini A, Ianiro G, Tilg H. Gut microbiota and atherosclerosis. Gut. Published online July 11, 2025. doi:10.1136/gutjnl-2025-335610

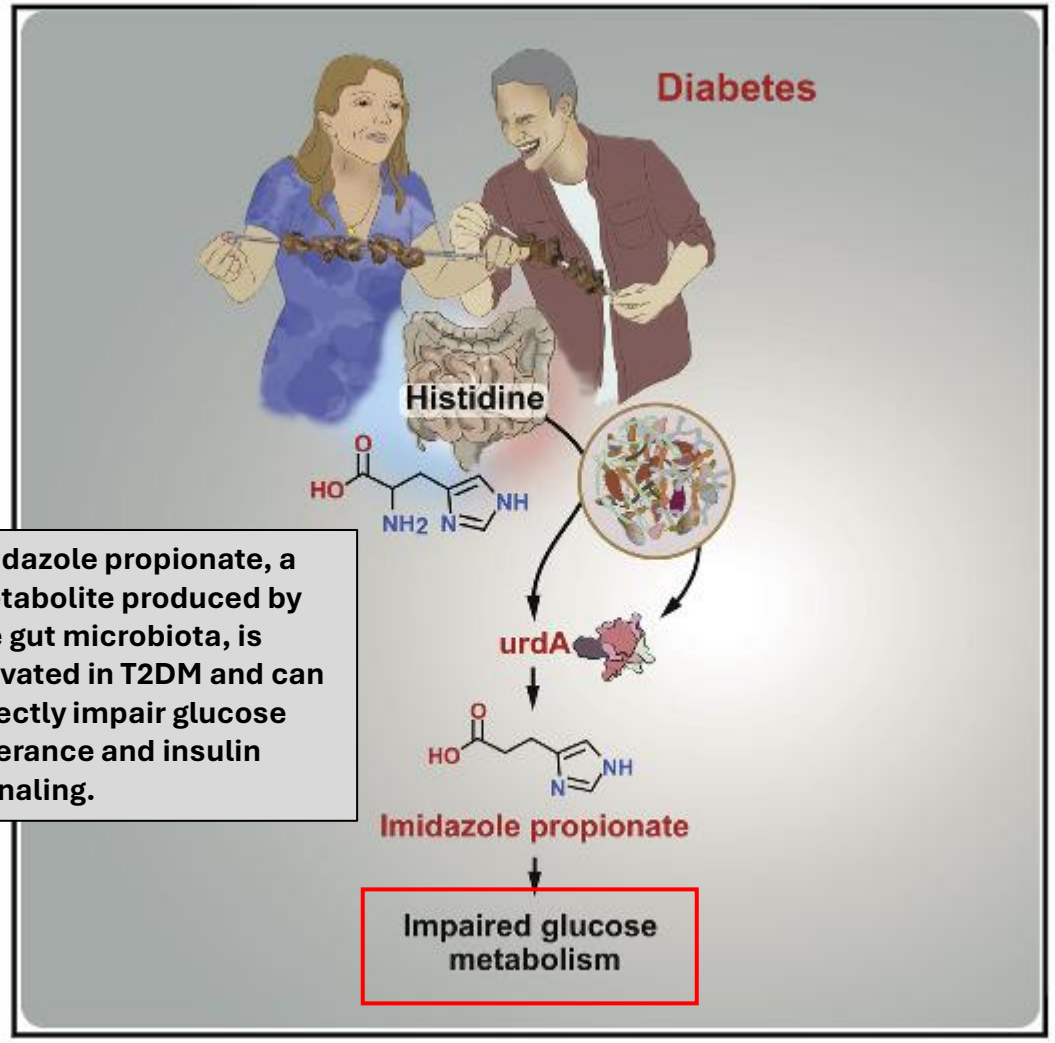
Association between gut microbiota and atherosclerosis



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Microbially Produced Imidazole Propionate Impairs Insulin Signaling through mTORC1

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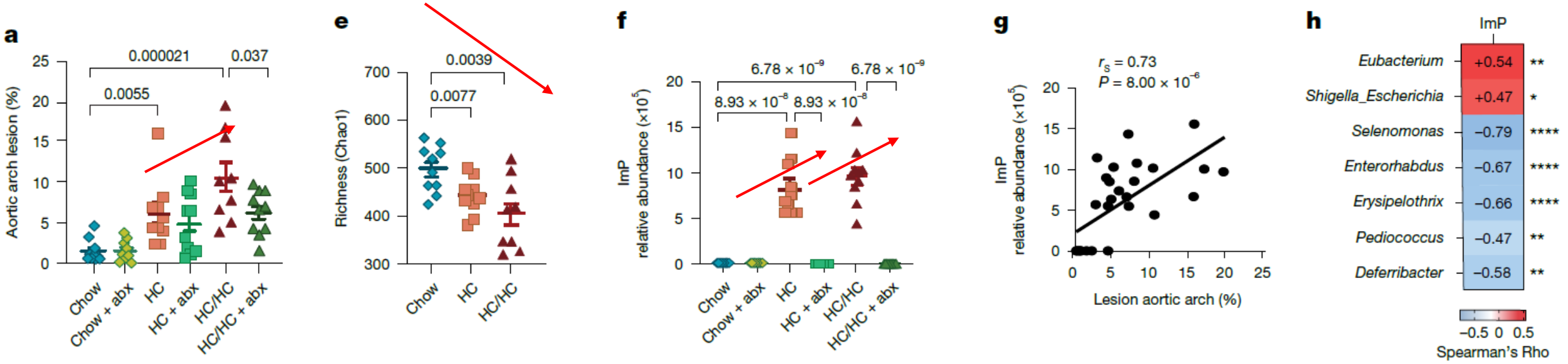
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tlg2025

Imidazole propionate is a driver and therapeutic target in Atherosclerosis



ImP as a microbiota-dependent metabolite that is associated with atherosclerosis.

Apoe$^{-/-}$ mice were fed a chow, HC or HC + choline-enriched diet +/- antibiotics

Mastrangelo A, Robles-Vera I, Mañanes D, et al. Imidazole propionate is a driver and therapeutic target in atherosclerosis. Nature. 2025;645(8079):254-261. doi:10.1038/s41586-025-09263-w

tlg2025



Gut and Metabolic Diseases: Opportunities of Probiotic Medicine

Piero Portincasa

MD, PhD, Dr honoris Causa, AGAF
Department of Precision and Regenerative Medicine and Jonian Area (DiMePre-J)
University "Aldo Moro" Bari, ITALY

Laura Mahdi, Mohamad Khalil

European Journal of Internal Medicine 119 (2024) 13–30

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journal homepage: www.elsevier.com/locate/ejim



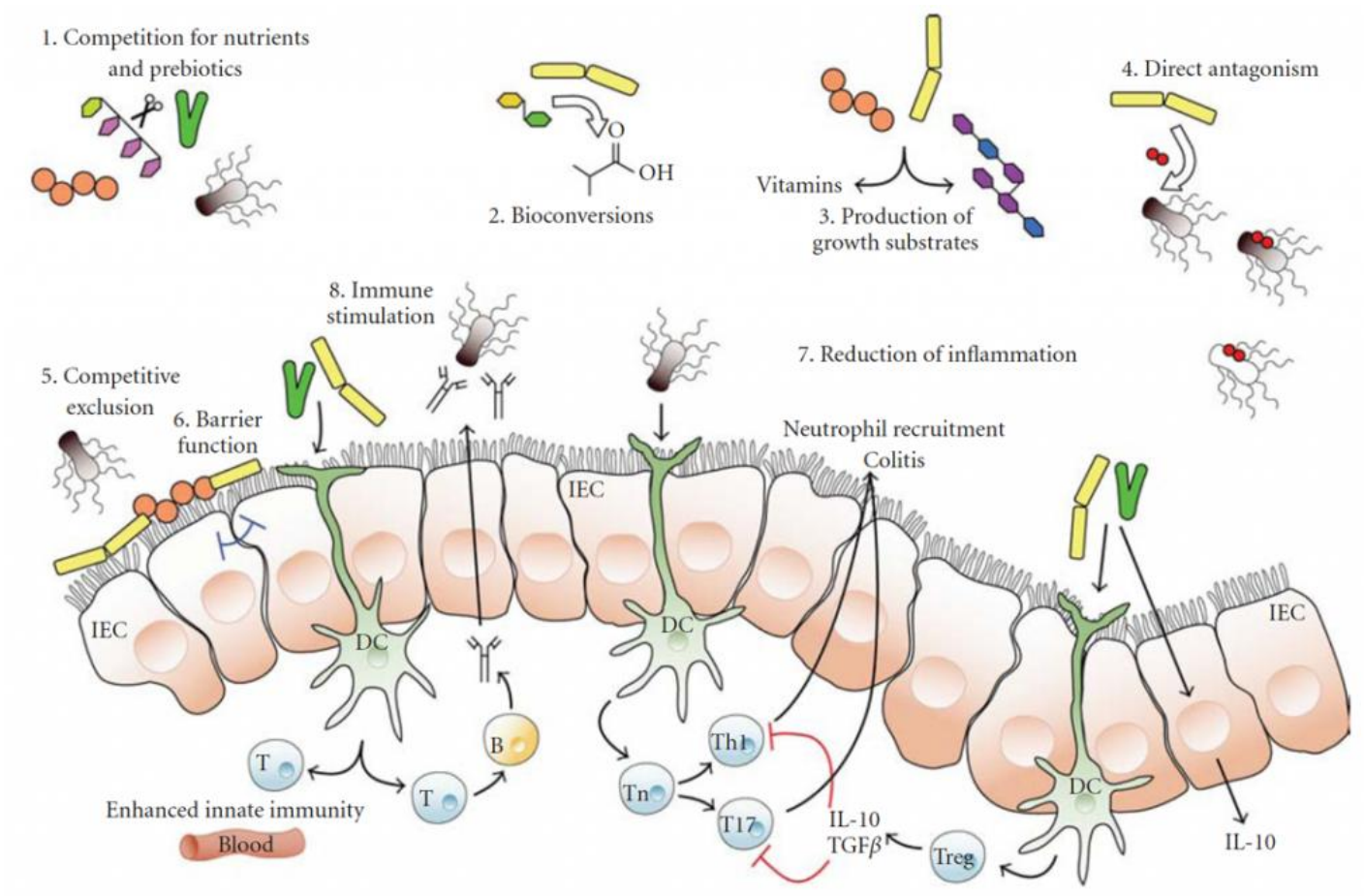
Review Article

Gut microbes in metabolic disturbances. Promising role for therapeutic manipulations?

Piero Portincasa [a,1,*], Mohamad Khalil [a,1], Annarita Graziani [b], Gema Frühbeck [c,d,e,f], Gyorgy Baffy [g], Gabriella Garruti [h], Agostino Di Ciaula [a,*], Leonilde Bonfrate [a]

[a] *Clinica Medica "A. Murri", Department of Precision and Regenerative Medicine and Ionian Area (DiMePre-J), University of Bari "Aldo Moro" Medical School, Policlinico Hospital, Piazza G. Cesare 11, Bari 70124, Italy*
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[d] *CIBER Fisiopatología de la Obesidad y Nutrición (CIBEROBN), ISCIII, Pamplona, Spain*
[e] *Obesity and Adipobiology Group, Instituto de Investigación Sanitaria de Navarra (IdiSNA), Pamplona, Spain*
[f] *Department of Endocrinology & Nutrition, Clínica Universidad de Navarra, Pamplona, Spain*
[g] *Department of Medicine, VA Boston Healthcare System and Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02130, USA*
[h] *Section of Internal Medicine, Endocrinology, Andrology and Metabolic Diseases, Department of Precision and Regenerative Medicine and Ionian Area (DiMePre-J), University of Bari Medical School, Bari 70124, Italy*

Mechanism of action of probiotics



Pattanaik et al., Indian J. Comp. Microbiol. Immunol. Infect. Dis.2022

Table 1
Studies on variety of diseases in human and animal models treated using probiotics.

S/N	Disease Model	Probiotic Strain	Outcomes	References
1	Rheumatoid Arthritis	*Lactobacillus casei*	Reduced joint inflammation, decreased pro-inflammatory cytokines, improved clinical arthritis scores	(Noto Llana et al., 2013)
2	Inflammatory Bowel Disease (IBD)	*Lactobacillus rhamnosus* GG	Reduced colonic inflammation, decreased cytokine production, improved gut barrier function	(Madsen et al., 2001)
3	Gastric Ulcers	*Lactobacillus acidophilus*	Accelerated healing of gastric ulcers, reduced ulcer area, decreased *Helicobacter pylori* colonization	(Enany & Abdalla, 2015)
4	Hypertension	*Lactobacillus helveticus*	Reduced blood pressure, decreased angiotensin-converting enzyme (ACE) activity	(Aihara et al., 2005)
5	Type 1 Diabetes	*Bifidobacterium lactis*	Delayed onset of diabetes, reduced pancreatic inflammation, modulated immune response	(Calcinaro et al., 2005)
6	Colorectal Cancer	*Lactobacillus casei* Shirota	Suppressed tumor growth, reduced inflammation, improved immune response	(Baken et al., 2006)
7	Allergic Asthma	*Lactobacillus rhamnosus*	Reduced airway inflammation, decreased Th2 cytokine levels, lower eosinophil counts	(Spacova et al., 2019)
8	Hypercholesterolemia	*Lactobacillus plantarum*	Lowered serum cholesterol levels, reduced lipid absorption, increased bile acid excretion	(Fuentes et al., 2016)
9	Atherosclerosis	*Bifidobacterium longum*	Reduced atherosclerotic lesions, decreased cholesterol levels, improved lipid profiles	(Chan et al., 2016)
10	Chronic Kidney Disease (CKD)	*Lactobacillus acidophilus* and *Bifidobacterium longum*	Reduced uremic toxins, improved renal function, decreased oxidative stress	(Borges et al., 2018)
11	Obesity and Metabolic Syndrome	*Lactobacillus gasseri* SBT2055	Reduced body weight gain, decreased fat accumulation, improved insulin sensitivity	(Kadooka et al., 2010)
12	Anxiety and Depression	*Lactobacillus rhamnosus* JB−1	Reduced anxiety- and depression-like behavior, altered GABA receptor expression in the brain	(Bravo et al., 2011)
13	Alzheimer's Disease	*Bifidobacterium breve* A1	Improved cognitive function, reduced amyloid-beta accumulation, decreased neuroinflammation	(Abdelhamid et al., 2022)

Obayomi et al. "Gut Dysbiosis and Chronic Diseases: Unraveling Contributing Factors, Health Implications, and Therapeutic Interventions." *Food and Humanity*, vol. 5, 2025, article 100892.

Metformin Is Associated With Higher Relative Abundance of Mucin-Degrading *Akkermansia muciniphila* and Several Short-Chain Fatty Acid–Producing Microbiota in the Gut

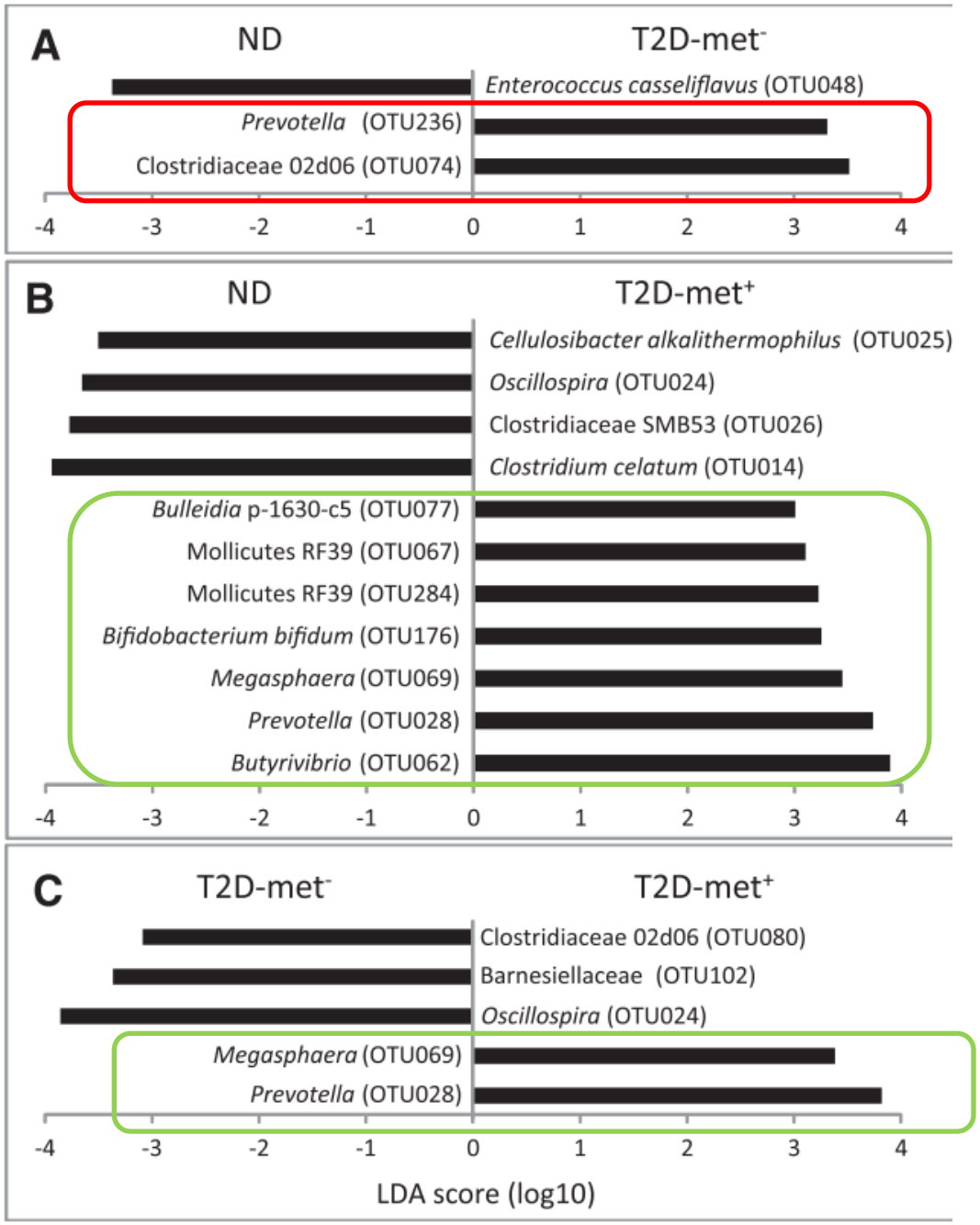
Jacobo de la Cuesta-Zuluaga,[1] Noel T. Mueller,[2] Vanessa Corrales-Agudelo,[1] Eliana P. Velásquez-Mejía,[1] Jenny A. Carmona,[3] José M. Abad,[4] and Juan S. Escobar[1]

Diabetes Care 2017;40:54–62 | DOI: 10.2337/dc16-1324

Table 1—General characteristics of T2D-met$^+$, T2D-met$^-$, and ND participants among community-dwelling Colombian adults

	Group			*P**		
	T2D-met$^+$	T2D-met$^-$	ND	T2D-met$^+$ vs. T2D-met$^-$	T2D-met$^+$ vs. ND	T2D-met$^-$ vs. ND
n	14	14	84	—	—	—
Age (years)	50 ± 10	44 ± 9	47 ± 9	0.11	0.33	0.24
Sex (F/M)	0.36	0.50	0.43	0.70	0.83	0.84
Anthropometry						
BMI (kg/m^2)	31.88 ± 4.63	32.15 ± 6.36	31.11 ± 4.53	0.98	0.56	0.62
Body fat (%)	0.41 ± 0.05	0.41 ± 0.03	0.40 ± 0.04	0.96	0.68	0.58
Waist circumference (cm)	104.6 ± 9.8	102.8 ± 14.2	102.0 ± 11.3	0.70	0.39	0.85
Clinical parameters						
Total cholesterol (mg/dL)	178 ± 51	208 ± 44	187 ± 30	0.11	0.54	0.10
HDL (mg/dL)	40 ± 11	38 ± 6	44 ± 12	0.77	0.21	0.0136
LDL (mg/dL)	105 ± 35	128 ± 39	115 ± 28	0.11	0.31	0.26
VLDL (mg/dL)	38 ± 40	52 ± 52	31 ± 15	0.19	0.64	0.0471
Apolipoprotein B (mg/dL)	102 ± 30	108 ± 30	97 ± 26	0.56	0.55	0.18
Triglycerides (mg/dL)	176 ± 202	244 ± 253	154 ± 75	0.15	0.97	0.07
Fasting glucose (mg/dL)	127 ± 47	145 ± 76	90 ± 10	0.57	0.0047	0.0060
HbA_{1c} [% (mmol/mol)]	6.9 ± 1.4 (52.0 ± 15.3)	7.1 ± 1.7 (54.0 ± 18.6)	5.6 ± 0.3 (38.0 ± 3.3)	0.78	0.0026	0.0047
Fasting insulin (μU/mL)	22.24 ± 12.58	24.24 ± 12.86	15.20 ± 8.79	0.49	0.11	0.0029
Insulin resistance index	2.9 ± 1.5	3.7 ± 3.0	1.9 ± 1.1	0.39	0.0420	0.0018
Leptin (ng/mL)	7.39 ± 6.09	8.34 ± 5.40	7.89 ± 6.14	0.38	0.91	0.25
Adiponectin (μg/mL)	4.59 ± 1.97	4.96 ± 3.22	6.79 ± 3.90	0.91	0.0195	0.07
hs-CRP (mg/L)	2.70 ± 2.53	3.35 ± 2.76	4.04 ± 5.02	0.61	0.21	0.62
Dietary intake						
Energy intake (calories)	1,843 ± 268	1,865 ± 584	1,945 ± 572	0.75	0.61	0.57
Carbohydrate (g)	250 ± 37	260 ± 86	267 ± 88	0.92	0.52	0.68
Protein (g)	74.7 ± 9.1	69.7 ± 13.1	74.1 ± 13.8	0.26	0.85	0.26
Fat (g)	60.7 ± 13.0	60.2 ± 21.3	62.9 ± 17.1	0.64	0.76	0.51
Cholesterol (mg)	336 ± 31	330 ± 41	347 ± 38	0.67	0.28	0.18
Dietary fiber (g)	17.9 ± 4.8	18.6 ± 6.4	17.5 ± 4.8	0.88	0.73	0.64
Stool consistency [*n* (%)]				0.38	0.58	0.50
Hard	4 (28)	2 (14)	13 (15)	—	—	—
Normal	8 (57)	9 (64)	54 (64)	—	—	—
Mushy	2 (14)	1 (7)	13 (15)	—	—	—
Diarrheic	0 (0)	2 (14)	4 (5)	—	—	—

Values presented as mean ± SD. *All *P* values from *t* tests except in sex and stool consistency (χ^2 tests).



SCIENTIFIC REPORTS
nature research

Discovery of a bacterial peptide as a modulator of GLP-1 and metabolic disease

Catherine Tomaro-Duchesneau[1], Stephanie L. LeValley[1], Daniel Roeth[2], Liang Sun[3], Frank T. Horrigan[3], Markus Kalkum[2], Joseph M. Hyser[1] & Robert A. Britton[1*]

SCIENTIFIC REPORTS | (2020) 10:4922 | https://doi.org/10.1038/s41598-020-61112-0

Early work in rodents highlighted the gut microbiota's importance in metabolic disease, including Type II Diabetes Mellitus (T2DM) and obesity. Glucagon-like peptide-1 (GLP-1), an incretin secreted by L-cells lining the gastrointestinal epithelium, has important functions: promoting insulin secretion, insulin sensitivity, and β-cell mass, while inhibiting gastric emptying and appetite. We set out to identify microbial strains with GLP-1 stimulatory activity as potential metabolic disease therapeutics. Over 1500 human-derived strains were isolated from healthy individuals and screened for GLP-1 modulation by incubating bacterial cell-free supernatants with NCI H716 L-cells. Approximately 45 strains capable of increasing GLP-1 were discovered. All GLP-1 positive strains were identified as *Staphylococcus epidermidis* by 16S rRNA sequencing. Mass spectrometry analysis identified a 3 kDa peptide, Hld (delta-toxin), present in GLP-1 positive supernatants but absent in GLP-1 neutral supernatants.

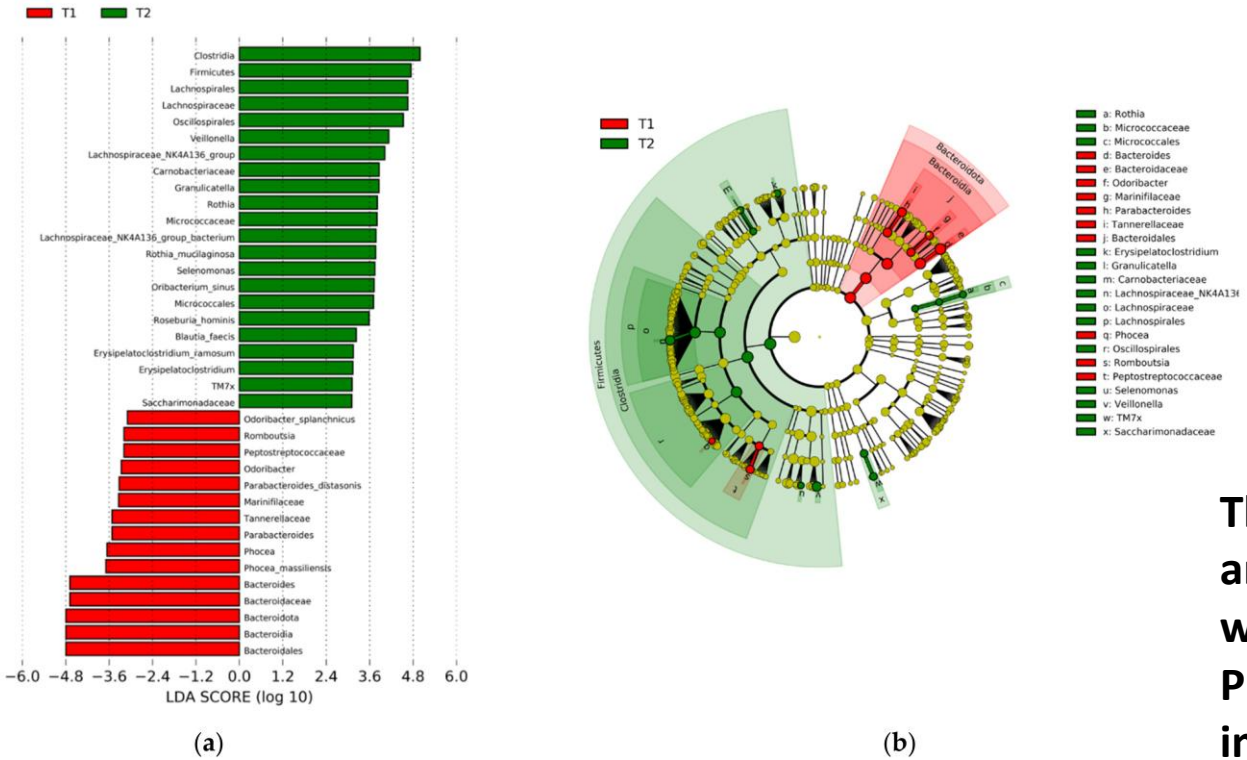
nutrients

MDPI

Article

A Six-Day, Lifestyle-Based Immersion Program Mitigates Cardiovascular Risk Factors and Induces Shifts in Gut Microbiota, Specifically *Lachnospiraceae, Ruminococcaceae, Faecalibacterium prausnitzii*: A Pilot Study

Angelica P. Ahrens [1], Tyler Culpepper [2], Brittany Saldivar [2], Stephen Anton [3], Scott Stoll [4], Eileen M. Handberg [5], Ke Xu [6], Carl Pepine [5], Eric W. Triplett [1] and Monica Aggarwal [5,*]



	Saturday	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday
7:00 to 8:00	Arrival	Blood work, breakfast, free time	Fitness	Fitness	Fitness	Fitness	Blood work, breakfast, free time
8:00 to 9:00			Breakfast	Breakfast	Breakfast	Breakfast	
9:00 to 10:00			What Is Food?	Preventing & Reversing Disease - Part 1	Men's Health (free time for women)	Future of Health; Angiogenesis & Nutrigenomics	
10:00 to 11:00			Break	Break	Women's Health (free time for men)	Break	
11:00 to 12:00		Fitness, free time	Conquer Hunger, Food Addictions, Emotions & Cravings	Preventing & Reversing Disease - Part 2	Break	The Things I Wish My Doctor Learned In Medical School	Fitness, free time
12:00 to 1:00			Break	Break	Strong Bones, Strong Body	Break	
			Beverages	Ingredients and Label Reading		Practical Steps to Success	
		Lunch	Lunch	Lunch	Lunch	Lunch	Lunch
1:00 to 2:00	Registration						
2:00 to 3:00		Total Health Immersion - Why You Are Here	Sauces, Dressings and Dips	Plant-based Culinary Basics and Favorites	Quick and Easy Plant-based Meals	Cooking with The Stoll Family	Relaxation / Depart
3:00 to 4:00		Break	Testimonial	Break	Testimonial	Break	
		Finding Your Why and Freedom!	Fitness / Break	Find Financial Freedom in Your Fridge	Break	Ask the Doctor	
4:00 to 5:00					Dinner Cruise	Appreciations	
		Fitness / Break	Ions from Ocean & Sand	Fitness / Break		Group Picture / Break	
5:00 to 6:00	Welcome Reception						
6:00 to 7:00		Dinner	Dinner	Dinner		Dinner	
7:00 to 8:00	Welcome Dinner						
8:00 to 9:00	Free Time	Movie Night	Free Time	Talent Show	Free Time	Beach Party	

This brief lifestyle-based intervention improved lipids and BP and enhanced known butyrate producers, without significant weight loss.
Promising non-pharmacological preventive strategy for improving cardiovascular health

1. Ahrens AP, Culpepper T, Saldivar B, Anton S, Stoll S, Handberg EM, et al. A Six-Day, Lifestyle-Based Immersion Program Mitigates Cardiovascular Risk Factors and Induces Shifts in Gut Microbiota, Specifically Lachnospiraceae, Ruminococcaceae, Faecalibacterium prausnitzii: A Pilot Study. Nutrients. 2021;13(10).

Singlestrain probiotics vs multistrain probiotics

biology

MDPI

Review

Multi-Strain Probiotics: Synergy among Isolates Enhances Biological Activities

Iliya D. Kwoji [1], Olayinka A. Aiyegoro [2,3], Moses Okpeku [1] and Matthew A. Adeleke [1,*]

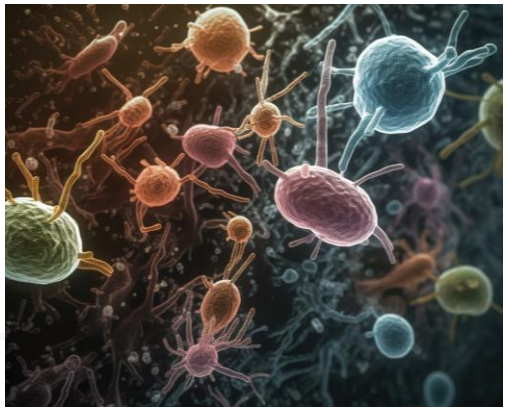
[1] Discipline of Genetics, School of Life Sciences, Westville Campus, University of KwaZulu-Natal, Durban 4000, South Africa; 219094534@stu.ukzn.ac.za (I.D.K.); okpekum@ukzn.ac.za (M.O.)

[2] Gastrointestinal Microbiology and Biotechnology Unit, Agricultural Research Council-Animal Production,

the non-therapeutic use of antibiotics for prophylaxis and growth promotion, especially in animal husbandry. While single-strain probiotics are beneficial to health, multi-strain probiotics might be more helpful because of synergy and additive effects among the individual isolates. This article documents the mechanisms by which multi-strain probiotics exert their effects in managing infectious and non-infectious diseases, inhibiting antibiotic-resistant pathogens and health improvement. The interactions with the host tissues, and modulation of the immune systems. Multi-strain probiotics applications include alleviation of disease conditions, inhibition of pathogens, and restoration of the gastrointestinal microbiome. Despite all these benefits, the potential of using multi-strain probiotics is still not fully explored.

 Iliya D. Kwoji *et al.*, Multi-Strain Probiotics: Synergy among Isolates Enhances Biological Activities. Biology 2021, 10, 322

Multi-strain probiotics



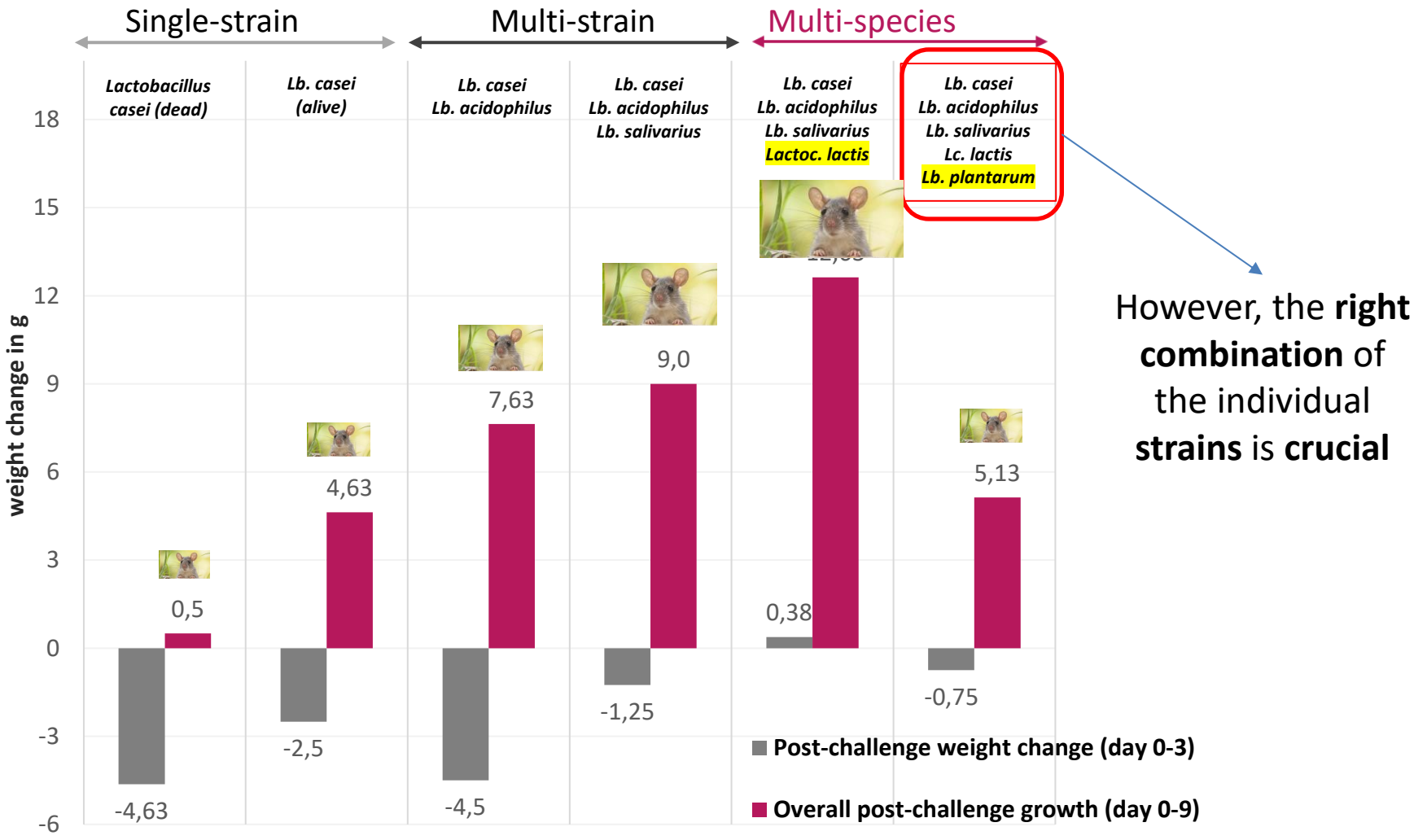
Pros

- **Broader spectrum of action**
  - combination of different and multi-level mechanisms
- **Synergistic effects**
  - increased adhesion, increased pathogen inhibition
- **Increased Resilience**
  - different strains can thrive in varying conditions
  - better colonization and persistence
- **Comprehensive Health Benefits**
  - address multiple health issues simultaneously
  - enhancing gut health, immune function
  - reducing inflammation

Cons

- **Reduced efficacy**
- **Potential antagonistic intra-strain inhibition by different probiotic strains**

The effect of different probiotic treatments on weight change in rats after challenge with *Salmonella Enteritidis*



However, the **right combination** of the individual **strains** is **crucial**

Timmerman HM, *et al*., Monostrain, multistrain and multispecies probiotics--A comparison of functionality and efficacy. Int J Food Microbiol. 2004;96:219–33.

Clinical Nutrition 41 (2022) 365–373

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Meta-analyses

Meta-analysis of randomized controlled trials of the effects of probiotics on type 2 diabetes in adults

Chengcheng Zhang [a, b], Jinchi jiang [a, b, f], Chen Wang [a, b], Sijia Li [a, b], Leilei Yu [a, b], Fengwei Tian [a, b], Jianxin Zhao [a, b], Hao Zhang [a, b, c, d, e], Wei Chen [a, b, c], Qixiao Zhai [a, b, *]

Effects of probiotics on **T2DM**
→ 33 eligible trial

- A median probiotic dose of ~10^9 cfu/day significantly reduced glycated hemoglobin, fasting blood glucose, fasting insulin levels, HOMA index *vs* placebo
- Lack of clinically significant reductions in HbA1c levels, but marginally clinically significant reductions in fasting glucose and fasting insulin levels
- Compared with single-strain and low- dose probiotics, **multi-strain and high-dose probiotics have a greater beneficial effect on glycemic homeostasis**

RESEARCH Open Access

Effects of a multi-strain probiotic supplement for 12 weeks in circulating endotoxin levels and cardiometabolic profiles of medication naïve T2DM patients: a randomized clinical trial

Shaun Sabico[1,2*], Ayah Al-Mashharawi[2], Nasser M. Al-Daghri[2], Sobhy Yakout[2], Abdullah M. Alnaami[2], Majed S. Alokail[2] and Philip G. McTernan[3]

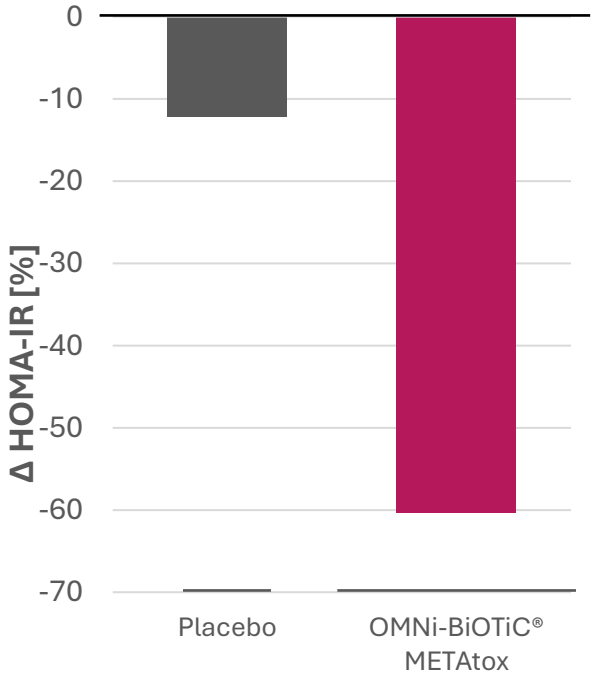
Institut AllergoSan
Competence Center for Mirobiome Research

2017

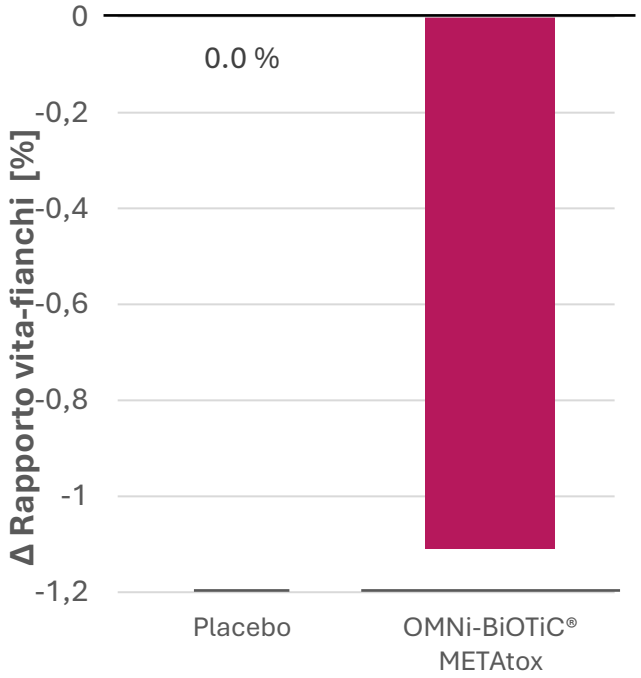
OMNi-BiOTiC® METAtox

Lactobacillus acidophilus W37	*Bifidobacterium bifidum W23*
Levilactobacillus brevis W63	*Bifidobacterium animalis subsp. lactis W52*
Lacticaseibacillus paracasei W56	*Lactococcus lactis subsp. lactis W19*
Ligilactobacillus salivarius W24	*Lactococcus lactis subsp. lactis W58*
Bifidobacterium animalis subsp. lactis W51	

- **Subjects:** 78 Saudi adult patients with T2DM with no comorbidities
- **Treatment for 12 weeks with**: OMNi-BiOTiC® METAtox 2.5 × 10^9 cfu/g twice daily.
- Randomized, double-blind, placebo-controlled trial
- **Parameters**: anthropometric characteristics, cardiometabolic profiles and endotoxin at the beginning and end of surgery



Clinically Significant Reduction in Insulin Resistance (HOMA-IR): -60.4%



Significant improvement in waist-to-hip ratio

Contents lists available at ScienceDirect

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Randomized Control Trials

Effects of a 6-month multi-strain probiotics supplementation in endotoxemic, inflammatory and cardiometabolic status of T2DM patients: A randomized, double-blind, placebo-controlled trial

Shaun Sabico [a, b, *], Ayah Al-Mashharawi [b], Nasser M. Al-Daghri [b], Kaiser Wani [b], Osama E. Amer [b], Danish S. Hussain [b], Mohammed Ghouse Ahmed Ansari [b], Mohammad S. Masoud [b], Majed S. Alokail [b], Philip G. McTernan [c, **]

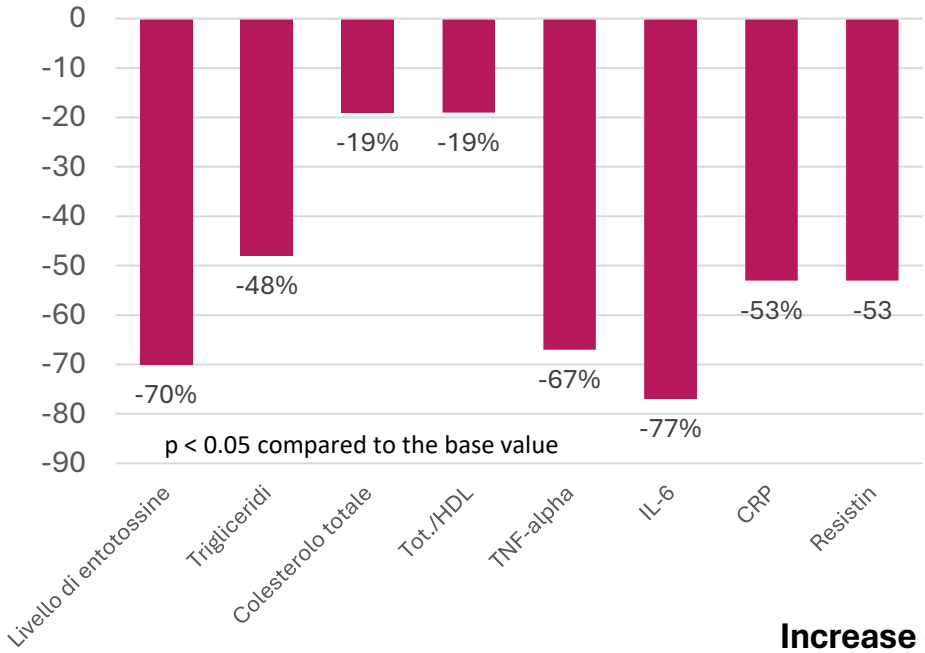
[a] Warwick Medical School, Division of Biomedical Sciences, University of Warwick, UHCW Trust, Clifford Bridge Road, Walsgrave, Coventry, CV2 2DX, UK
[b] Prince Mutaib bin Abdullah Chair for Biomarkers of Osteoporosis, Biochemistry Department, College of Science, King Saud University, Riyadh, 11451, Saudi Arabia
[c] School of Science and Technology, Department of Biosciences, Nottingham Trent University, Nottingham, NG1 8NS, UK

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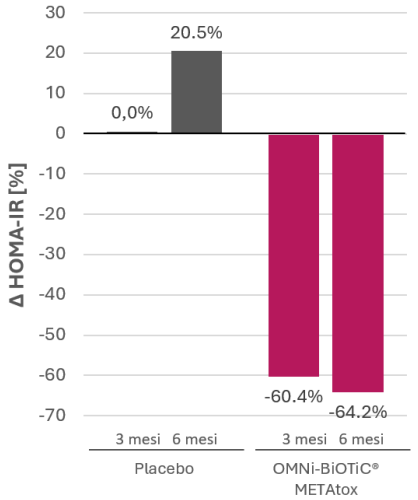
- Subjects: 61 subjects with newly diagnosed type 2 diabetes mellitus aged 30-60 years
-
- Treatment with OMNi-BiOTiC® METAtox (10 x 10^9 cfu) for 6 months, 2 times a day
-
- Randomized, double-blind, placebo-controlled trial
-
- Parameters: Baseline, 3-month, and 6-month measurements of endotoxin, glucose, insulin, HOMA-IR, lipids (Triglycerides, Cholesterol, HDL/LDL), inflammatory markers (TNF-α, IL-6, CRP), and adipocytokines (adiponectin, resistin, leptin)

Sabico S, et al. McTernan PG, Effects of a 6-month multi-strain probiotics supplementation in endotoxemic, inflammatory and cardiometabolic status of T2DM patients: A randomized, double-blind, placebo-controlled trial. Clin Nutr 2018, doi:10.1016/j.clnu.2018.08.009.

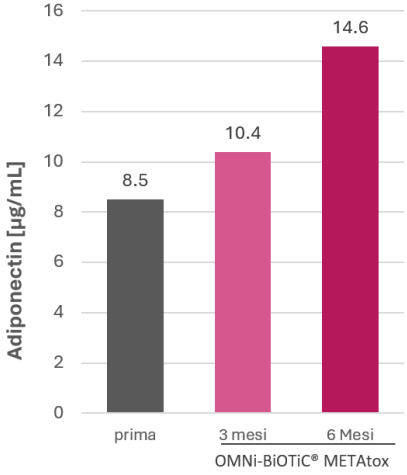
Positive effect of OMNi-BiOTiC® METAtox on cardiometabolic parameters and inflammation



Improved IR in T2DM



Increase of protective adiponectin in T2DM



nutrients

MDPI

OMNi-BiOTiC® METAtox

Article

Dose-Dependent Effects of Multispecies Probiotic Supplementation on the Lipopolysaccharide (LPS) Level and Cardiometabolic Profile in Obese Postmenopausal Women: A 12-Week Randomized Clinical Trial

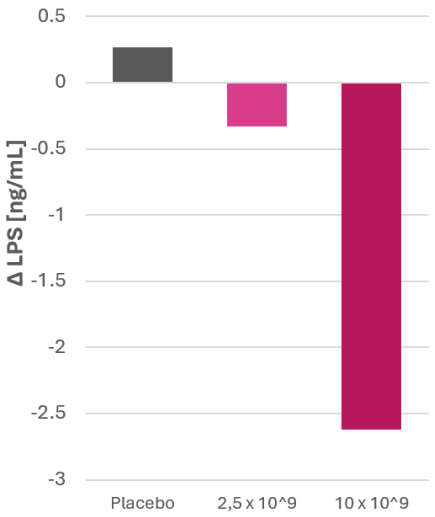
Monika Szulińska [1], Igor Łoniewski [2,*], Saskia van Hemert [3], Magdalena Sobieska [4] and Paweł Bogdański [1]

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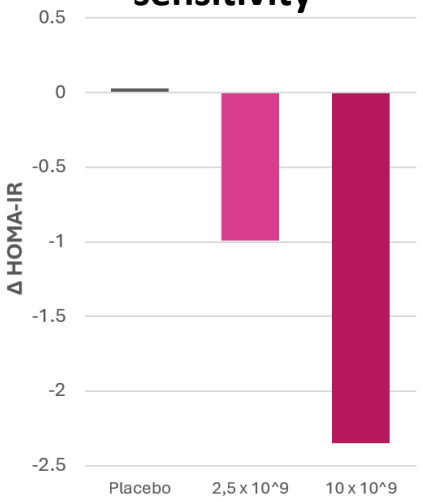
Subjects: 81 overweight women (BMI: 30-45), Age 45-70 years
Treatment: 3 Groups:
High dose of probiotics (10 x 109 cfu)
Low dose of probiotics (2.5 x 109 cfu)
Placebo
For 12 weeks
Randomized, double-blind, placebo-controlled trial
Parameters: Glucose metabolism, Lipid status
Serum LPS level (bacterial toxins)

Szulińska M, et al. Bogdański P, Dose-Dependent Effects of Multispecies Probiotic Supplementation on the Lipopolysaccharide (LPS) Level and Cardiometabolic Profile in Obese Postmenopausal Women: A 12-Week Randomized Clinical Trial. Nutrients 2018.

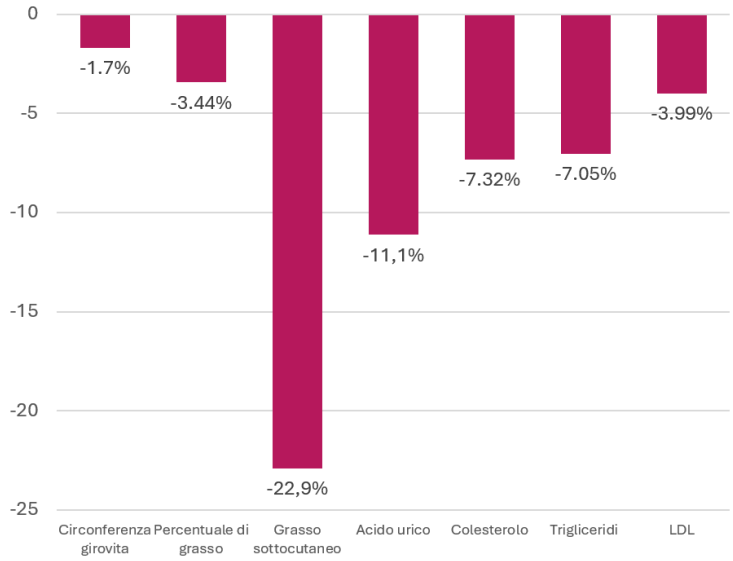
Reduction of LPS levels



Improvement in insulin sensitivity



Improvements of several CVD parameters



European Journal of Nutrition
https://doi.org/10.1007/s00394-019-02135-w

ORIGINAL CONTRIBUTION

Effects of a multispecies synbiotic on glucose metabolism, lipid marker, gut microbiome composition, gut permeability, and quality of life in diabesity: a randomized, double-blind, placebo-controlled pilot study

Angela Horvath[1,2] · Bettina Leber[3] · Nicole Feldbacher[1,2] · Norbert Tripolt[4] · Florian Rainer[1] · Andreas Blesl[1] · Markus Trieb[5] · Gunther Marsche[5] · Harald Sourij[2,4,6] · Vanessa Stadlbauer[1]

Received: 12 June 2019 / Accepted: 4 November 2019
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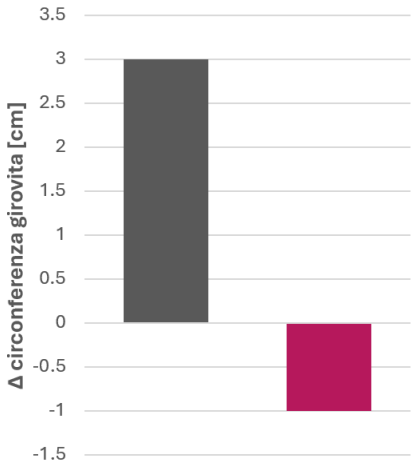
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STUDY DESIGN

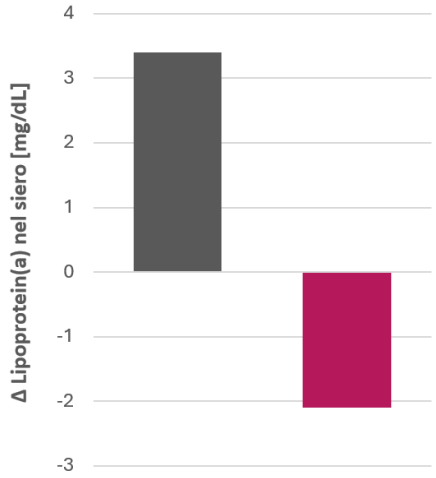
- **Subjects:** 26 patients with type 2 diabetes BMI: 30 – 40 kg/m2
- **Treatment for 6 months with:**
- OMNi-BiOTiC® METAtox 1 × 10^{10} CFU 1 time a day
- OMNi-LOGiC® PLUS 2 g per day
- Randomized, double-blind, placebo-controlled trial
- **Parameters:** glucose metabolism, intestinal permeability (zonulin), lipid markers, neutrophil function, microbiome and quality of life

A. Horvath et al., "Effects of a multispecies synbiotic on glucose metabolism, lipid marker, gut microbiome composition, gut permeability, and quality of life in diabesity: a randomized, double-blind, placebo-controlled pilot study.," Eur. J. Nutr., Nov. 2019.

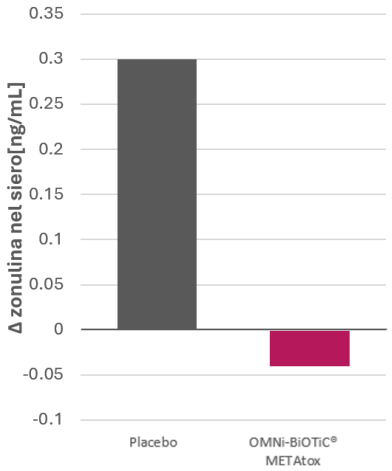
Significant reduction in hip circumference



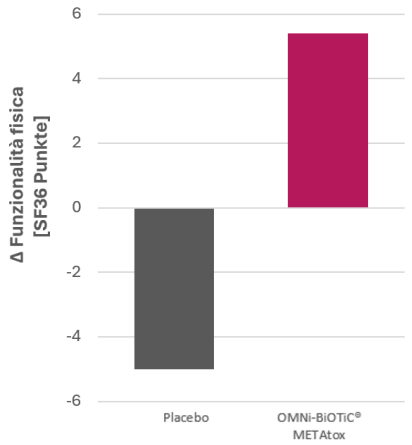
Significant reduction in Lipoprotein



Improvement in intestinal barrier



Improvement in physical aspects



Journal of Clinical Medicine

MDPI

Article

The Multispecies Probiotic Effectively Reduces Homocysteine Concentration in Obese Women: A Randomized Double-Blind Placebo-Controlled Study

Karolina Majewska [1], Matylda Kręgielska-Narożna [1,*], Hieronim Jakubowski [2,3], Monika Szulińska [1] and Paweł Bogdański [1]

[1] Department of Treatment of Obesity, Metabolic Disorders and Clinical Dietetics. University of Medical Sciences in Poznań, Szamarzewskiego Str. 84, 60-569 Poznan, Poland; k.andrzejewska84@wp.pl (K.M.); mszulinska1@wp.pl (M.S.); pawelbogdanski73@gmail.com (P.B.)
[2] Department of Microbiology, Biochemistry and Molecular Genetics, Rutgers University, New Jersey Medical School, International Center for Public Health, 225 Warren Street, Newark, NJ 07103-3535, USA; jakubows@njms.rutgers.edu
[3] Department of Biochemistry and Biotechnology, University of Life Sciences, Dojazd Str. 11, 60-632 Poznan, Poland
* Correspondence: matylda-kregielska@wp.pl; Fax: +48-61-847-8529

Received: 20 February 2020; Accepted: 30 March 2020; Published: 2 April 2020

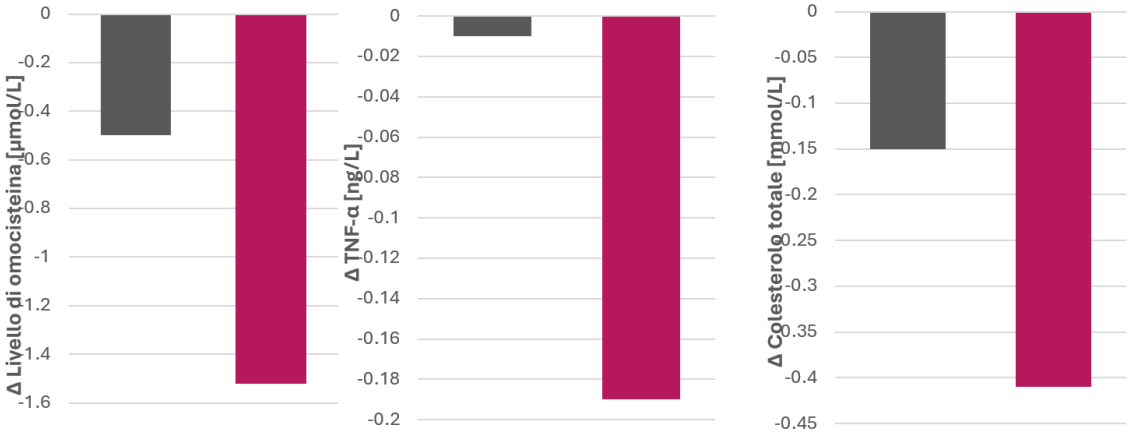
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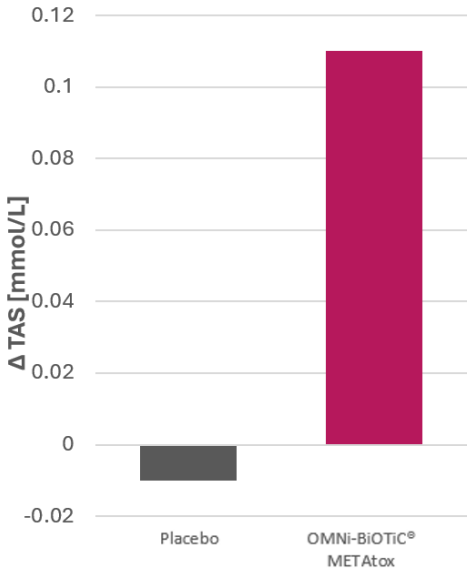
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STUDY DESIGN

- **Subjects**: 50 overweight women (BMI 30-45), 45-70 years old
- **Treatment**: OMNi-BiOTiC® METAtox (10 x 10^9 cfu) for 12 weeks
- Randomized, double-blind, placebo-controlled trial
- **Parameters**: Homocysteine level, Total cholesterol, TNF-alpha, Total antioxidant status

Positive effect on inflammation, CVD risk, and systemic antioxidant status





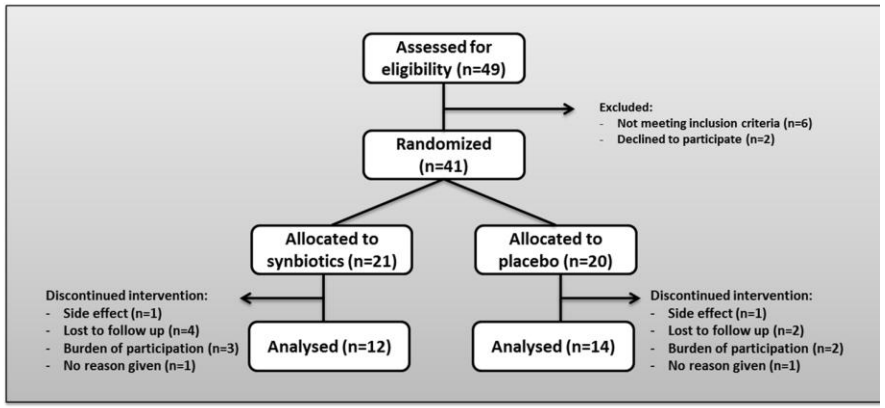
K. Majewska, et al. "The Multispecies Probiotic Effectively Reduces Homocysteine Concentration in Obese Women: A Randomized Double-Blind Placebo-Controlled Study," Journal of Clinical Medicine 2020, Vol. 9, Page 998, vol. 9, no. 4, p. 998, Apr. 2020, doi: 10.3390/JCM9040998.

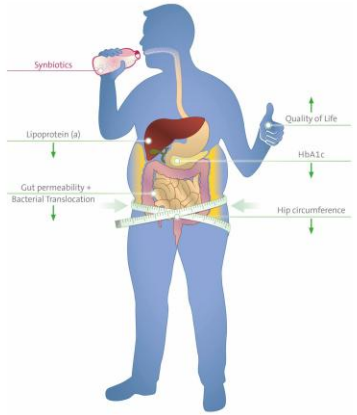
European Journal of Nutrition (2020) 59:2969–2983
https://doi.org/10.1007/s00394-019-02135-w

ORIGINAL CONTRIBUTION

Effects of a multispecies synbiotic on glucose metabolism, lipid marker, gut microbiome composition, gut permeability, and quality of life in diabesity: a randomized, double-blind, placebo-controlled pilot study

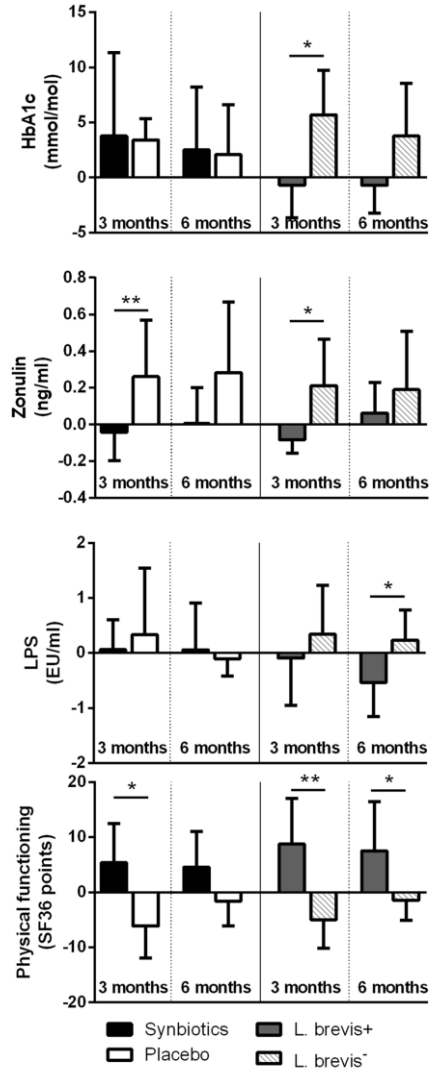
Angela Horvath[1,2] · Bettina Leber[3] · Nicole Feldbacher[1,2] · Norbert Tripolt[4] · Florian Rainer[1] · Andreas Blesl[1] · Markus Trieb[5] · Gunther Marsche[5] · Harald Sourij[2,4,6] · Vanessa Stadlbauer[1]





OMNi-BiOTiC® HETOX **Pro-biotic**

1.5 × 10^10 CFU of a blend
Lactobacillus acidophilus W37
Levilactobacillus brevis W63
Lacticaseibacillus paracasei W56
Ligilactobacillus salivarius W24
Lactococcus lactis subsp. lactis W19
Lactococcus lactis subsp. lactis W58
Bifidobacterium animalis subsp. lactis W51
Bifidobacterium animalis subsp. lactis W52
Bifidobacterium bifidum W23
+
Pre-biotic
Galacto-oligosaccharides, P11 (GOS)
Fructo-oligosaccharides P6 (FOS)
konjac glucomannan P13 (E425)
calcium carbonate (E170)
zinc citrate 3-hydrate
vitamin D3 (cholecalciferol)
vitamin B2 (riboflavin) (E101)



- **A randomized, double-blind, placebo-controlled pilot study in diabesity patients**
- daily dose of a multispecies probiotic and a prebiotic (or a placebo) for **6 months**.
- no changes in glucose metabolism or mixed meal tolerance test responses throughout the study.
- The beneficial effects on hip circumference [− 1 (95% CI − 4; 3) vs +3 (− 1; 8) cm, synbiotics vs. placebo, respectively, $p = 0.04$]
- serum zonulin [− 0.04 (− 0.2; 0.1) vs +0.3 (− 0.05; 0.6) ng/ml, $p = 0.004$)]
- SF36 quality of life assessment [+ 5.4 (− 1.7; 12.5) vs − 5.0 (− 10.1; 0.2) points, $p = 0.02$] after 3 months of intervention
- lipoprotein (a) [− 2.1 (− 5.7; 1.6) vs +3.4 (− 0.9; 7.9) mg/dl, $p = 0.02$] after 6 months.
- No significant differences in alpha or beta diversity of the microbiome between groups or time points.

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Competence Center for Mirobiome Research

UNIVERSITÀ DEGLI STUDI DI BARI ALDO MORO

Dip. di MEDICINA di PRECISIONE e RIGENERATIVA e AREA IONICA

DOTTORATO IN SANITÀ PUBBLICA, MEDICINA CLINICA E ONCOLOGIA

GutMet- Human GUT microbiome from Health to metabolic dysfunction

Synergistic Solutions: Effects of Innovative Synbionts on Intestinal Microbiota and the Management of Diabesity



PhD stud. Dr. Laura Mahdi

Tutor: Prof. Piero Portincasa

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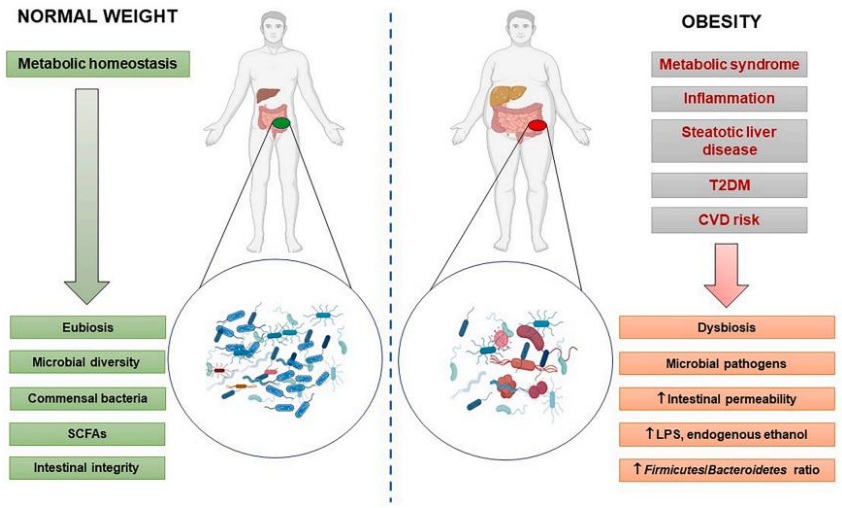
European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Review Article

Gut microbes in metabolic disturbances. Promising role for therapeutic manipulations?

Piero Portincasa [a,1,*], Mohamad Khalil [a,1], Annarita Graziani [b], Gema Frühbeck [c,d,e,f], Gyorgy Baffy [g], Gabriella Garruti [h], Agostino Di Ciaula [a,*], Leonilde Bonfrate [a]



Institut AllergoSan
Competence Center for Mirobiome Research

OMNi-BiOTiC® METAtox

Lactobacillus acidophilus W37	*Bifidobacterium bifidum W23*
Levilactobacillus brevis W63	*Bifidobacterium animalis subsp. lactis W52*
Lacticaseibacillus paracasei W56	*Lactococcus lactis subsp. lactis W19*
Ligilactobacillus salivarius W24	*Lactococcus lactis subsp. lactis W58*
Bifidobacterium animalis subsp. lactis W51	

Improved sugar metabolism

Improved blood fat levels (e.g. cholesterol)

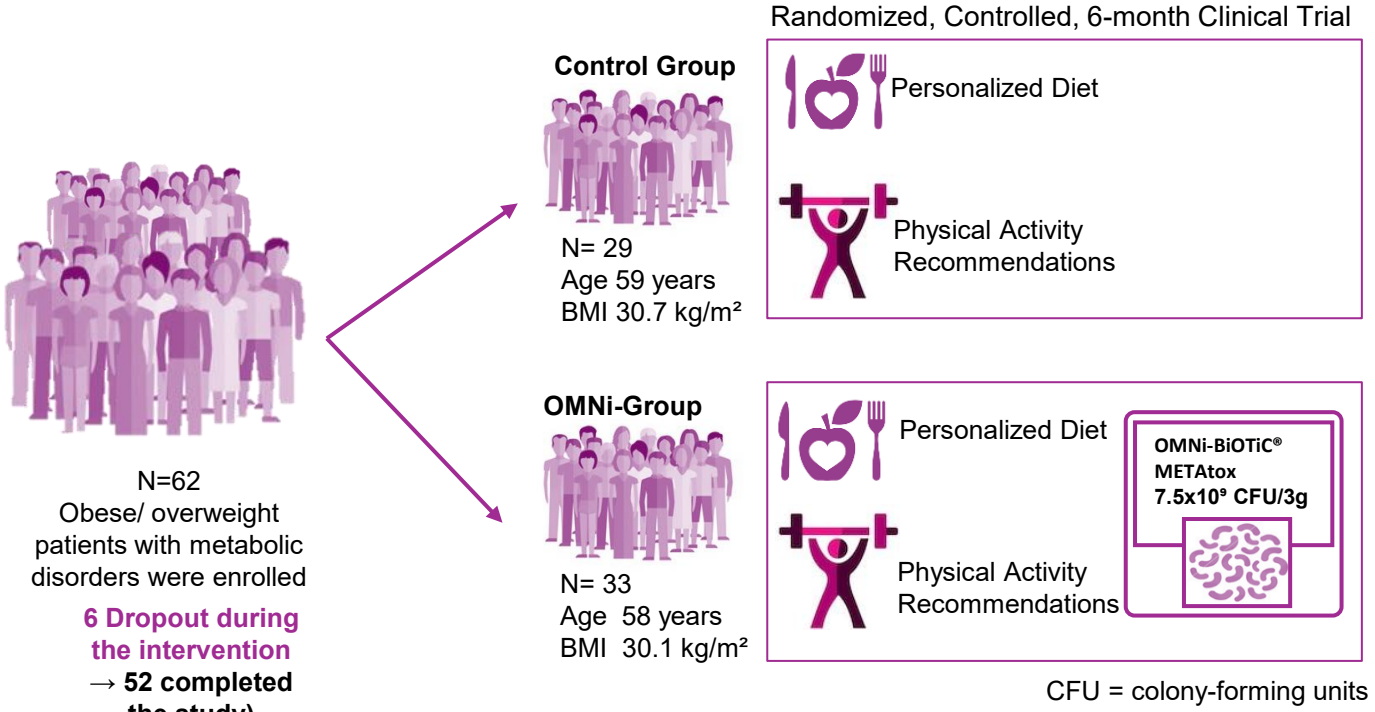
Improved function of the intestinal barrier

Reduced endotoxin exposure

Pure probiotic, multistrain, highly enriched

- 9 human strains
- 3 *Bifido, 6 Lacto*
- ~ 7.5 MLD CFU/pack (3g)

Study Design



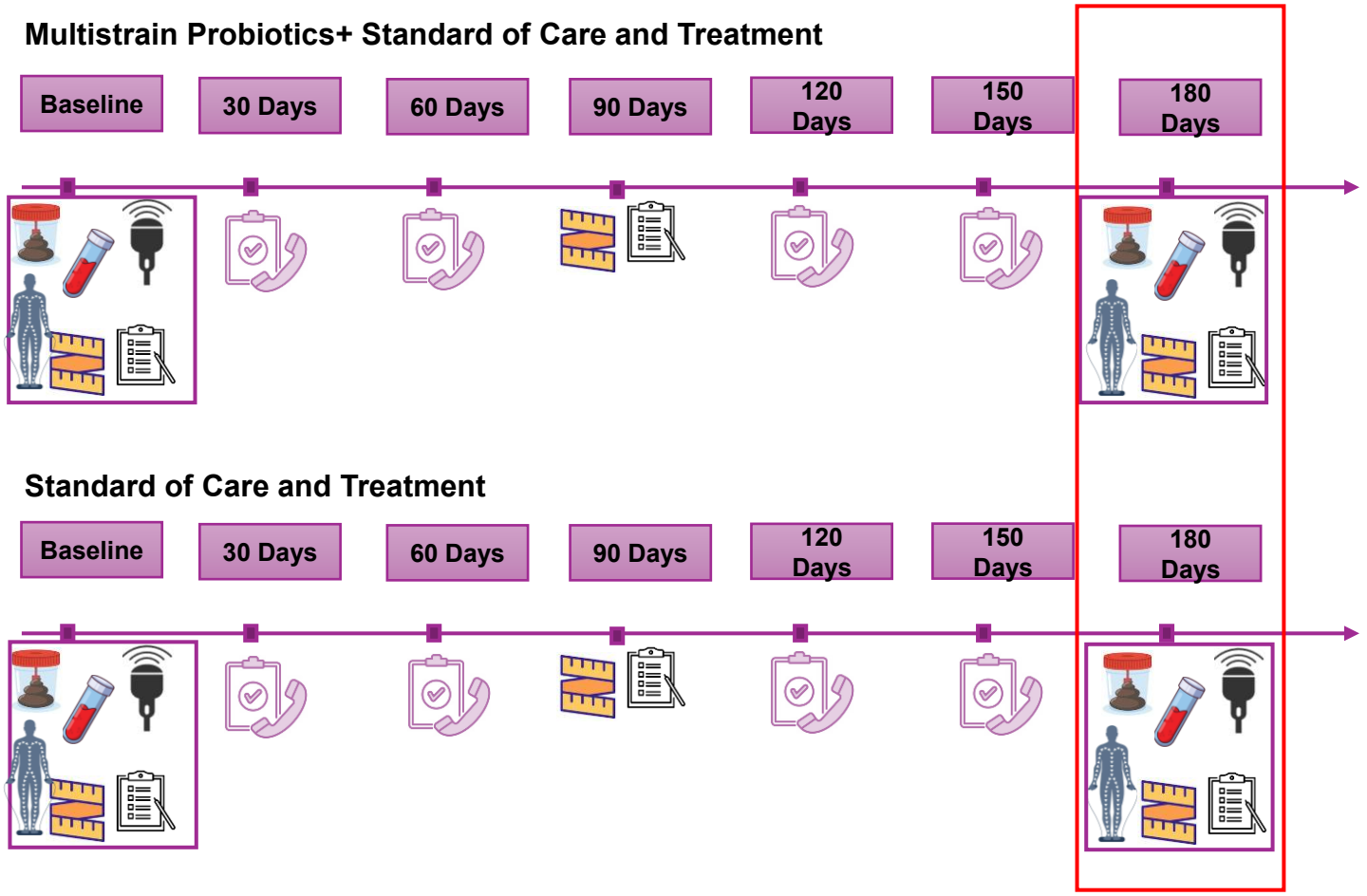
Inclusion Criteria:

- 18 to 65 years.
- GI symptoms (exclusion organic diseases)
- Body Mass Index (BMI) ≥ 25 kg/m².
- Metabolic disorders (MASLD and Type 2 diabetes mellitus)

Exclusion Criteria:

- Patients currently taking antibiotics
- Pregnant or lactating women.
- Severe or uncontrolled medical conditions (e.g., cardiovascular, renal, hepatic disorders
- Patients who have received probiotic or prebiotic supplementation within 3 months before enrollment in the clinical trial.

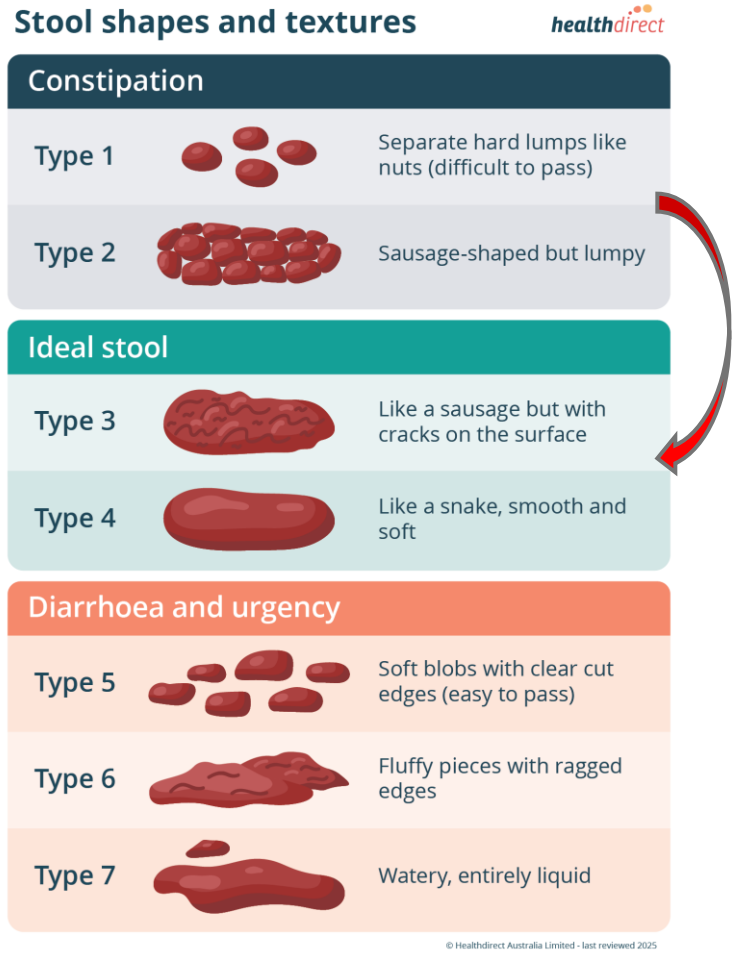
Study Timeline

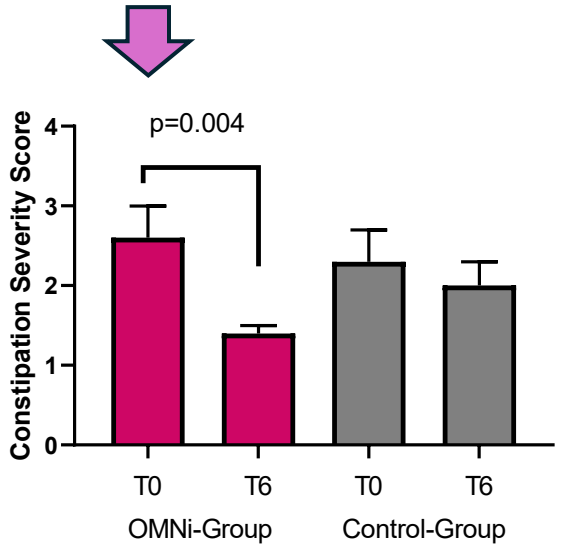


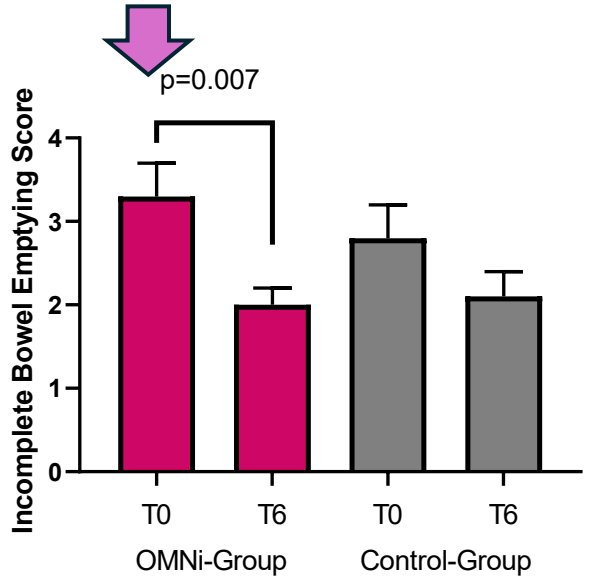
(just concluded)

Bristol Stool Score After 180 Days of Intervention

Bristol Score in OMNi-Group	
T0 (Baseline)	T6 (180 Days)
1	**4**
1	1
1	**5**
1	**4**
2	**4**
2	**3**
2	**3**
2	**4**
2	**3**
2	**4**

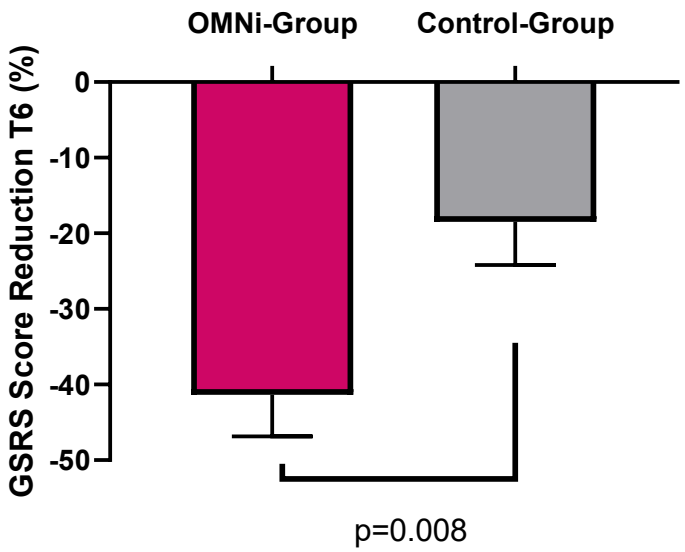


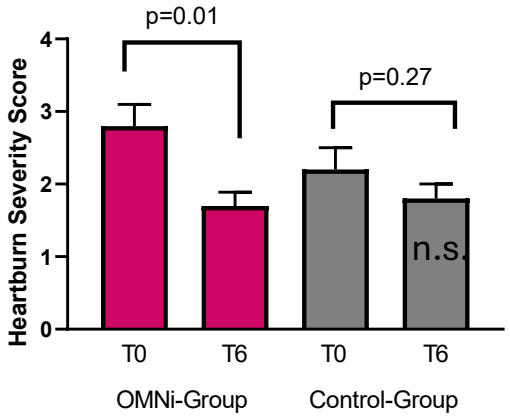


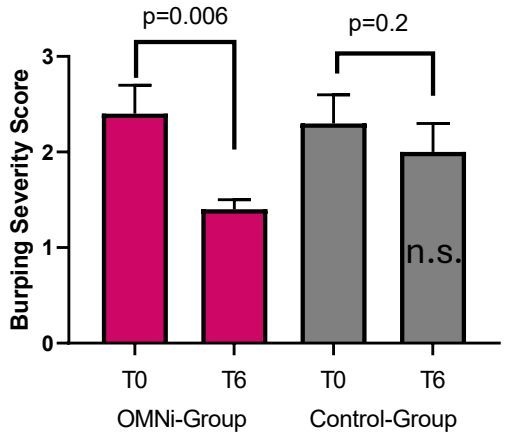


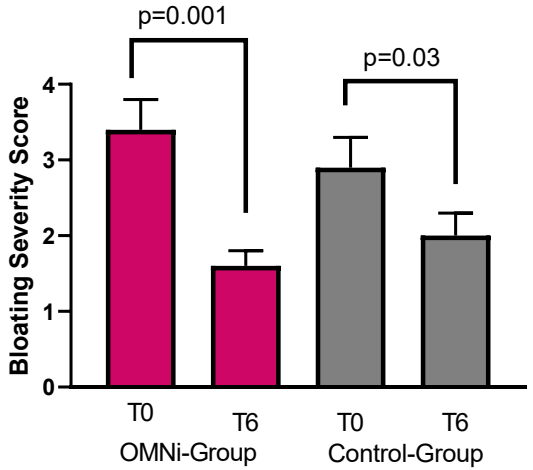
90% of patients who were suffering from constipation improved Bristol scores toward normal

Improvement in gastrointestinal symptoms after 180 days



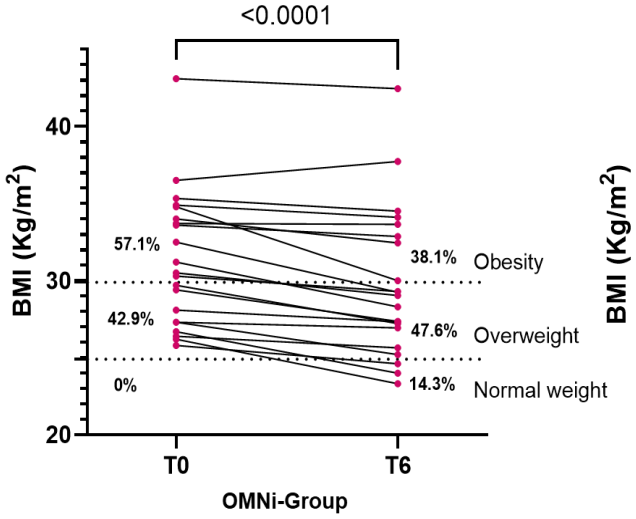


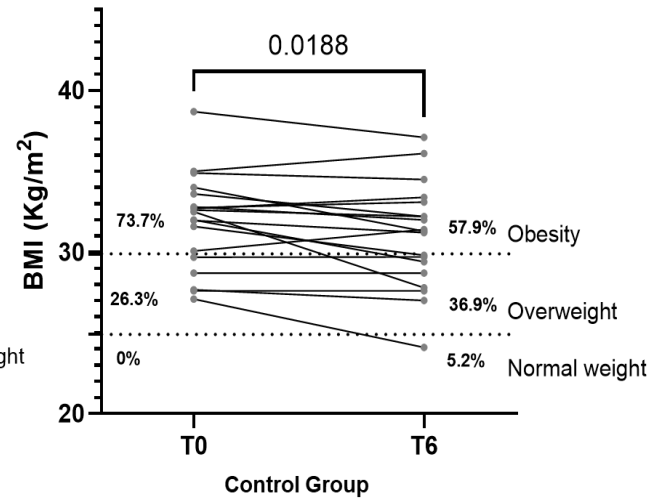


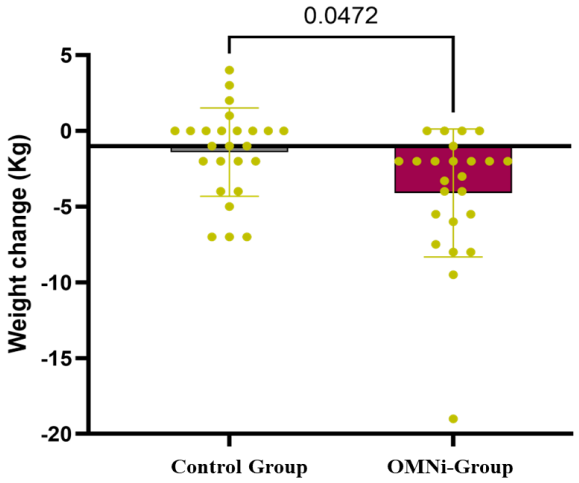


Anthropometric profile after 180 days

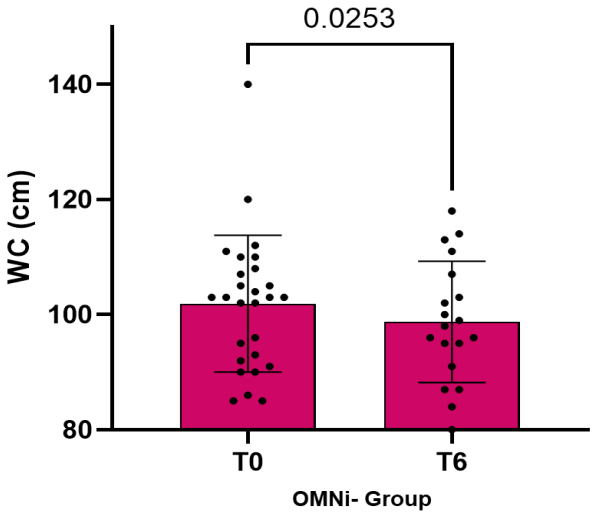
BMI, waist circumference (WC)

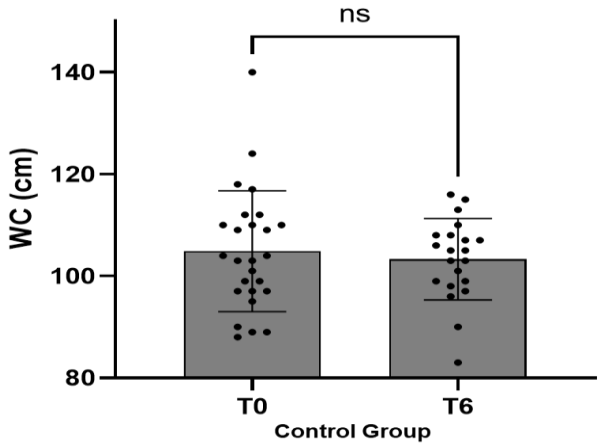


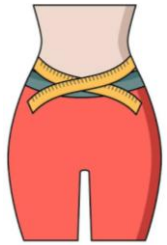










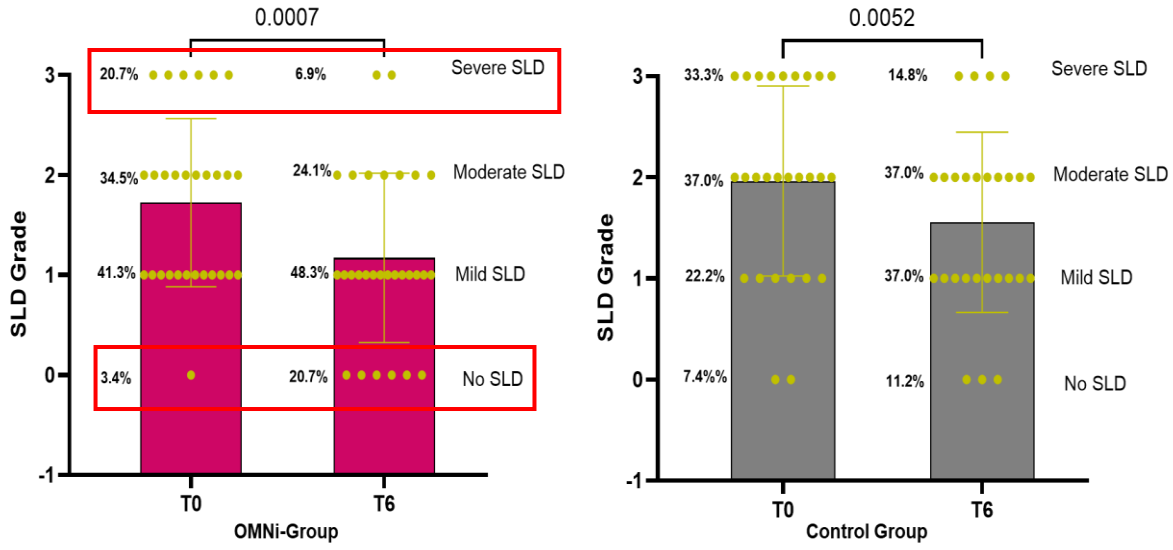


Improvement in subcutaneous and visceral fats after 180 days

	OMNi-Group (N=29)			Control Group (N=27)		
	T0	T6	p-value	T0	T6	p-value
Subcutaneous fat (US, mm)						
Pre-hepatic	14.5 ± 1.4	12.5 ± 0.9	**0.04**	16.4 ± 1.4	15.1 ± 1.4	ns
Pre-pancreatic	16.2 ± 1.2	14.4 ± 0.9	**0.048**	16.3 ± 1.6	14.6 ± 1.2	ns
Pre-aortic	15.3 ± 1.0	16.6 ± 0.9	ns	17.2 ± 1.2	16.5 ± 1.7	ns
Visceral fat (US, mm)						
Pre-hepatic	12.5 ± 1.1	13.4 ± 1.6	ns	14.3 ± 1.3	13.5 ± 2.0	ns
Pre-pancreatic	39.7 ± 2.7	34.3 ± 2.9	0.05	43.2 ± 3.1	41.2 ± 3.8	ns
Pre-aortic	64.6 ± 5.1	54.9 ± 3.8	**0.01**	58.0 ± 5.3	61.5 ± 4.4	ns
Hepato-renal	30.0 ± 2.6	28.3 ± 2.2	ns	32.4 ± 4.4	25.8 ± 1.9	ns
Spleen-renal	30.9 ± 2.8	26.7 ± 2.5	ns	31.3 ± 2.5	26.3 ± 2.1	ns

Amelioration of liver steatosis after 180 days

SLD Grade



In progress

- ELISA (inflammatory, anti-inflammatory, intestinal permeability markers)
- Gut microbiota analysis(16S rRNA)

Effect of OMNi-BiOTiC® on GI symptoms and extra GI symptoms

Portincasa et al. July 2023 – March 2026

~ 500 outpatients





General GI +/- symptoms

~ 150 pts

- Bloating
- Bloating + Gastroesophageal reflux
- Nausea, Belching
- Post-HP eradication symptoms
- Abdominal pain
- Diarrhea
- Constipation
- IBS
- (vaginitis, rosacea)

OMNi-BiOTiC® *6 = 120*

- OMNi-BiOTiC® STRESS Repair
- OMNi-BiOTiC® 10 AAD
- OMNi-BiOTiC® Flora plus

Follow up 1-2 months

Effectiveness

85%
Improvement in **GI symptoms**

Safety



Positive effects of OMNi-BiOTiC® 10 AAD on GI symptoms of patients screened for *Helicobacter Pylori*

Portincasa et al (in progress)

January 2026- August 2026

N=200 (56% females)

Baseline GI symptoms

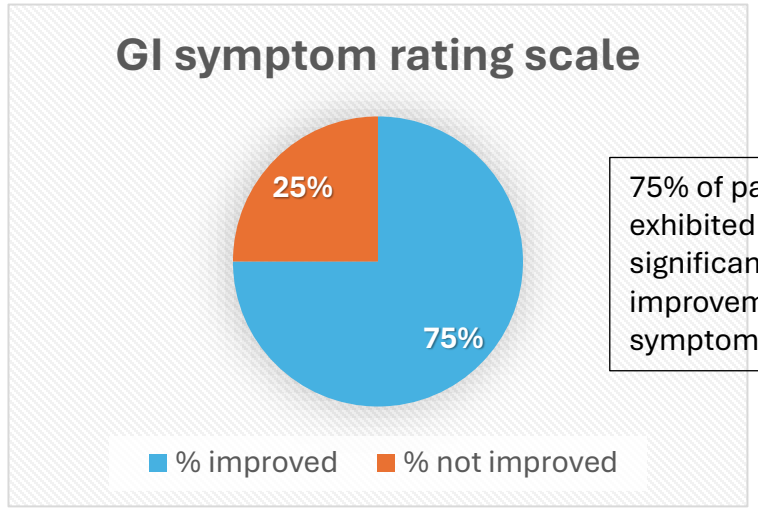
Dyspepsia
Heartburn
Acid reflux
Bloating

screening



50 HP(+)
150 HP(-)

Intervention:
OMNi-BiOTiC® 6-10 AAD daily
for 3 months

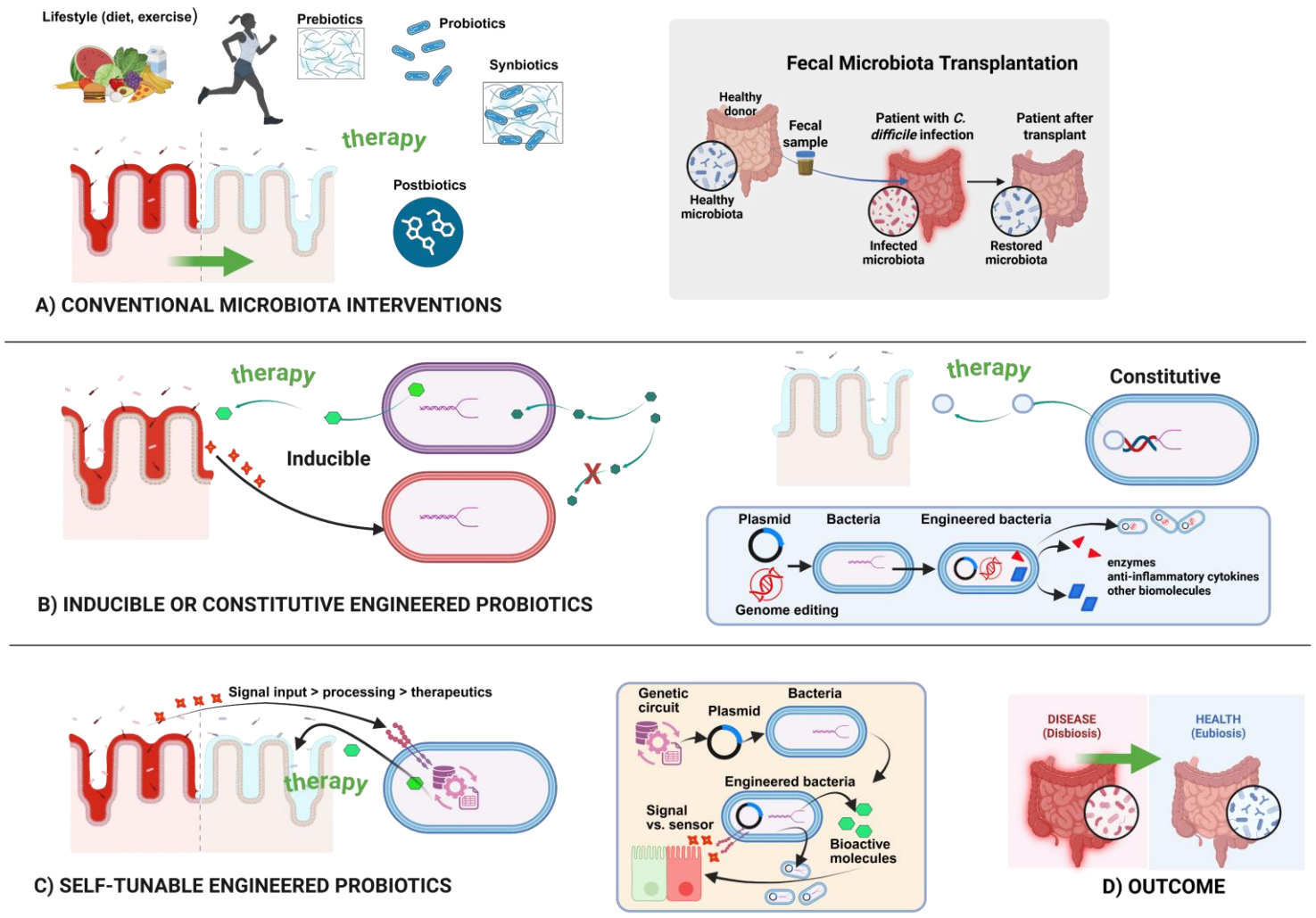


75% of patients exhibited a clinically significant improvement GI symptoms

Safety & Tolerability Profile:
100% well tolerated with zero (0) reported adverse events.

Study in progress to check for the additional effect of eradication

Gut microbiota-targeted interventions?



Ciurea, N.-A.; Mahdi, L.; Graziani, A.; Di Ciaula, A.; Portincasa, P.; Khalil, M. Targeting the Human Gut Microbiota—Between Conventional Therapy and Precision Genetic Engineering. *Nutrients* ***2026, 18, 1958.***

Conclusions

- Metabolism and inflammation are highly intersected phenomena
- Microbiota crucially involved in many noncommunicable disorders
- Microbiome-driven inflammation („**sterile inflammation**“) might play a key role
- Type 2 Diabetes, MASLD or CVD are highly interacted and may have common pathomechanisms involved („**metaflammation**“)
- Several mechanisms have been recently identified, such as endotoxin, TMAO, or ImP
- **Room for probiotic therapy is on the way and increasing**
- **Chance for multistrain probiotics**

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