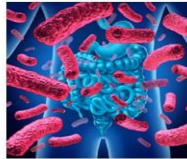


MICROBIOTA INTESTINAL Y SU INFLUENCIA EN EL DESARROLLO DE ENFERMEDADES INFECCIOSAS.

¹ Benítez-Páez, Alfonso

¹ Host-Microbe Interactions in Metabolic Health Laboratory. Centro de Investigación Príncipe Felipe. 46012 Valencia, España.

Memoria en Presentación PowerPoint:



Intestinal microbiota and its influence on infectious diseases

Alfonso Benítez Páez PhD

Host—Microbe Interactions in Metabolic Health Lab [I-71]

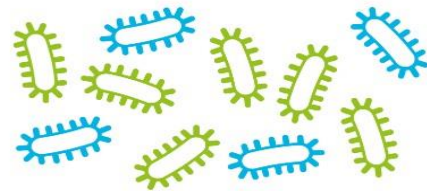
CIPF. Valencia, Spain

 @microbiOMICsLab

 abenitez@cipf.es

Agenda

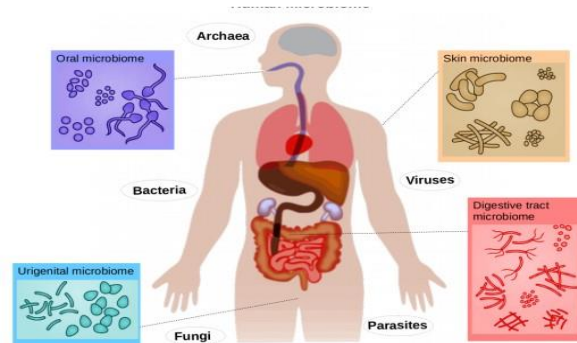
1. Intro (definitions, concepts, and methodological basis)
2. Milestones in microbiome research
3. Microbiota in health and disease
4. Intestinal microbiota & infectious diseases
5. Trends & future directions



1. DEFINITIONS AND CONCEPTS

Microbiota - definition

- Microbiota (**NOT flora**)
 - The ecological community of bacteria, archaea, protists, fungi and viruses species living like commensals, parasites, pathobionts, and pathogenic microorganisms in a particular site, habitat, or niche.



Definitions (I)

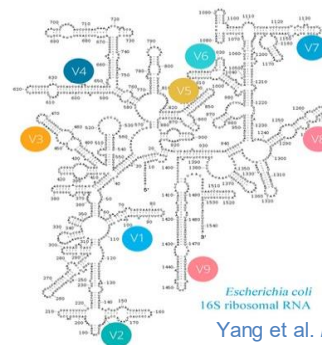
- Microbiome (**≠ microbiota**)
 - The genome of all microbiota components of a certain ecological community of microorganisms.
- (Meta) -genomics, -transcriptomics, -proteomics, -metabolomics
 - Study of the genetic material from a determined ecological community from different points of view (e.g. DNA, RNA, proteins, metabolites).
- Pangenome
 - The full set of genes in a specific clade or taxon.
- Diversity
 - Variability among members of a ecological community. Includes variation in terms of species and their prevalence and abundance.
- Dysbiosis
 - Ambiguous term associated with changes in the microbiota profile with respect to a reference.
AVOID ITS USE!

Definitions (II)

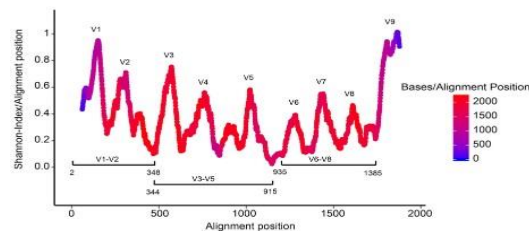
- **Phylotype**
 - In microbiology, a **phylotype** is an environmental DNA sequence or group of sequences sharing more than an arbitrarily chosen level of similarity of a particular gene marker (Moreira D & López-García P, 2011) -> **Non Linnean taxonomy**.
- **Operational Taxonomic Units (OTU)**
 - A set of closely related individuals grouped in a “single **clade**” through numerical taxonomy approaches -> **Linnean taxonomy**.
- **Amplicon sequence variant (ASV)**
 - A term used to refer to individual DNA sequences recovered from a massive sequencing of a marker gene after removal spurious sequences. Equivalent to OTUs, but definition more related to technical variation.
- **Next Generation Sequencing (NGS)– 2nd generation**
 - DNA sequencing platforms based on parallel and massive sequencing approaches (e.g. Illumina, 454, and ion -torrent instruments).
- **Single molecule & realtime sequencing – 3rd generation**
 - DNA sequencing platforms based on parallel and massive sequencing approaches without amplification steps (e.g. PacBio and MinION devices)
- **16S rRNA gene amplicon sequencing IS NOT METAGENOMICS (16ScDNA sequencing IS NOT METATRSCRIPTOMICS)**

Hallmarks of the microbiota analysis

- Principles of microbial ecology dictate two simple query statements: “who’s there”, and “what are they doing”.
- **Who’s there? (only answered by high -resolution methods)**
 - Advances in NGS technology help to solve partially this question.
 - Molecular taxonomy is on fire given the amount of information disclosed recently from molecular markers such as 16S and 23S rRNA genes, and obviously by wide -genome comparisons.
 - Cost-effective approaches to study microbial genomics have positioned the 16S rRNA gene amplicon sequencing as the predominant strategy.



Yang et al. *BMC Bioinformatics* 2016

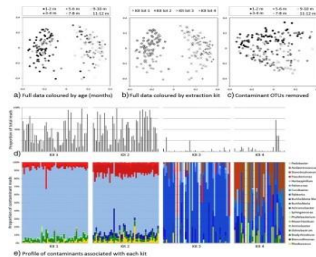


Seedorf et al. *PeerJ* 2014

1

Microbiota assessments - main issues

- Partial evaluation of the 16S rRNA bacterial gene positioned as the cost-effective and predominant strategy of survey.
- Current high-throughput sequencing technology do not offer enough resolution to distinguish species and/or strain identity (DNA read length limitation).

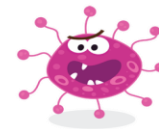


Tummy Buddy

Tummy Baddy



Vs



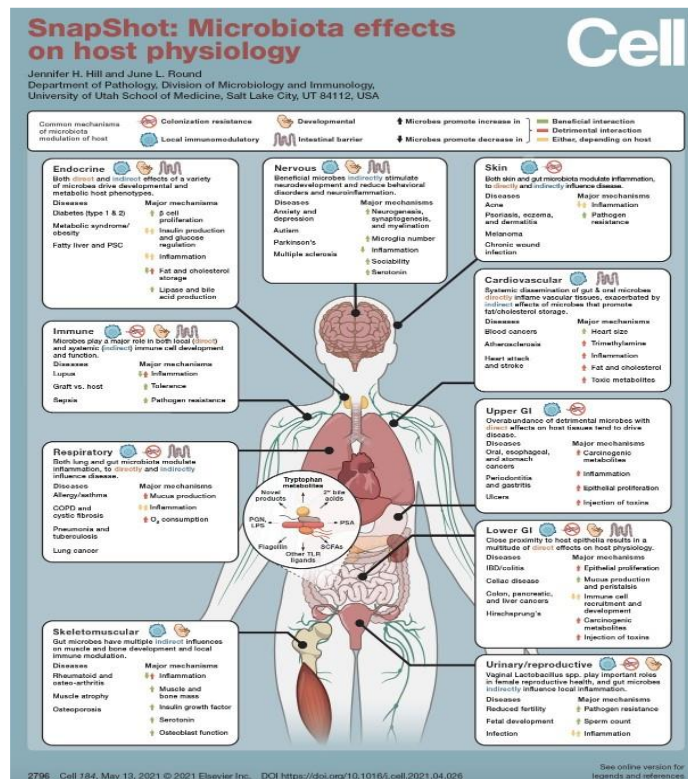
- Multiple technical and data analysis issues generally cause bias, misunderstanding, and wrong results (i.e. “universal” primers, hypervariable regions, OTUs approach, 97% clustering rule of thumb, uneven sequencing effort, DNA extractions).

- DNA extraction kits contamination is recurrently underestimated – special attention in low bacteria load samples.

- SEVERAL STUDIES FOCUSED ON CORRELATIONS (MICROBIOTA DATA VS BIOCHEMICAL PARAMETERS)
- CORRELATION DOES NOT IMPLY CAUSATION

1

Microbiota is in everywhere





2. MILESTONES IN MICROBIOME RESEARCH

2

Unlimited biodiversity

nature
biotechnology

An international human

nature microbiology **ARTICLES**
DOI: 10.1038/s41564-017-0012-7

OPEN
Creative Commons Attribution

ARTICLE
Junhua Li^{1-3,†}, Manimozhiya Chaysavanh³, Suisha Liang¹, Sherif Edris^{1,†}, Karsten Krist Donovan¹, MetaHIT Consortium, Paul N. I...

ARTICLE
Stephen Nayfach^{1,2,†}, Alexandre Almeida^{1,2,†}, Trevor D. Lawley² & Robert D. Finn^{1,2,†}

Resource
Extensive L Revealed b Spanning A
Edoardo Pasoli¹, Francesco Beghini¹, Paolo Casey DuLong¹, Xochitl and Nicola Segata^{1,2,†}

nature biotechnology **RESOURCE**
https://doi.org/10.1038/s41587-020-0603-3

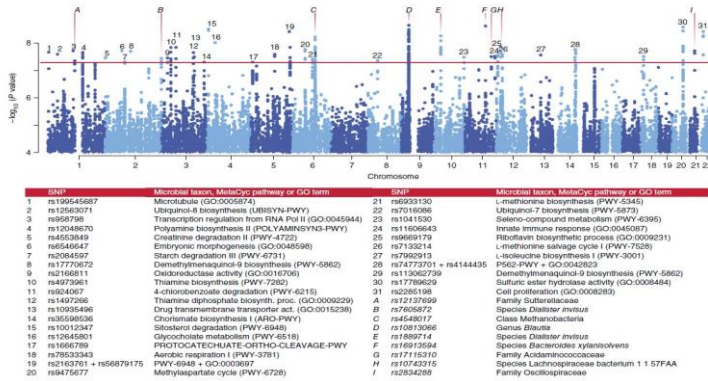
OPEN
A unified catalog of 204,938 reference genomes from the human gut microbiome
Alexandre Almeida^{1,2,†}, Stephen Nayfach^{1,4}, Miguel Boland¹, Francesco Strozzi¹, Martin Beracochea¹, Zhou Jason Shi^{1,7}, Katherine S. Pollard^{1,2,3,9,10,11}, Ekaterina Sakharova¹, Donovan H. Parks¹², Philip Hugenholtz¹², Nicola Segata¹³, Nikos C. Kyrpides^{3,4} and Robert D. Finn^{1,2,†}

Cell

Impact of human genetics on microbiota

The effect of host genetics on the gut microbiome

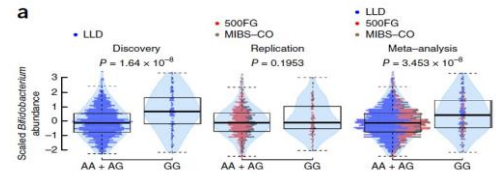
Marc Jan Bonder^{1,19}, Alexander Kurilshikov^{1-3,19}, Etti F Tigheleaar^{1,4}, Zlatan Mujagic^{4,5}, Floris Imhann⁶, Arnau Vich Vila⁶, Patrick Deelen^{1,7}, Tommi Vatanen^{8,9}, Melanie Schirmer^{8,10}, Sanne P Smekens^{11,12}, Daria V Zhernakova¹, Soesma A Jankipersadsing^{1,13}, Martin Jaeger^{11,12}, Marije Oosting^{11,12}, Maria Carmen Ceuil^{1,18}, Ad A M Masclee⁴, Morris A Swertz^{1,7}, Yang Li¹, Vinod Kumar¹, Leo Joosten^{11,12}, Hermie Harmsen¹⁴, Rinse K Weersma⁶, Lude Franke¹, Marten H Hofker¹³, Rannik J Xavier^{8,15-17}, Daisy Jonkers⁵, Mihai G Netea^{11,15}, Cisca Wijmenga¹, Jingyuan Fu^{1,13,20} & Alexandra Zhernakova^{1,4,20}



Nature Genetics 48;1407–1412 (2016)

• Microbiota associated with C-type lectin genes – Chr2 (inflammation, cell-to-cell interaction, bind microbiota, cytokine production)

• *Bifidobacterium* links with hypolactasia allele (G/G) at the LCT gene.



Microbiota covariates

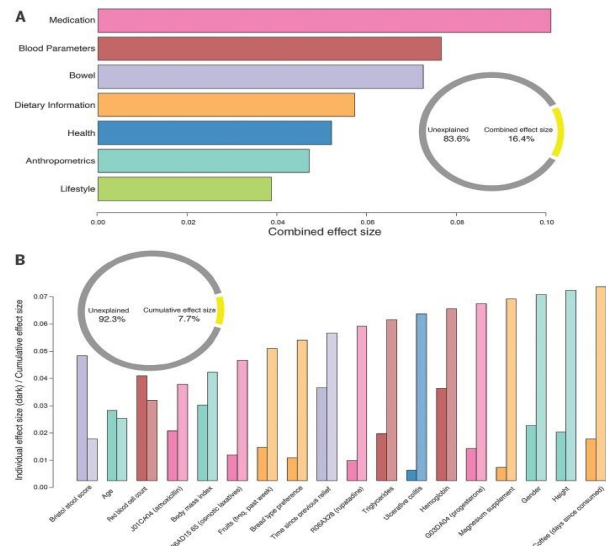
MICROBIOME

Population-level analysis of gut microbiome variation

Gwen Falony^{1,2,*}, Marie Joossens^{1,2,3,*}, Sara Vieira-Silva^{1,2,*}, Jun Wang^{1,2,*}, Youssef Darzi^{1,2,3}, Karoline Faust^{1,2,3}, Alexander Kurilshikov^{4,5}, Marc Jan Bonder⁶, Mirela Valles-Colomer^{1,2}, Doris Vandepitte^{1,2,3}, Raul V. Tito^{1,2,3}, Samuel Chaillon^{1,2,3}, Leon Ryymenans^{1,2,3}, Chloé Verspecht^{1,2}, Lise De Sutter^{1,2,3}, Gipsi Lima-Mendez^{1,2}, Kevin D'Hoe^{1,2,3}, Karl Jonckheere^{2,3}, Daniel Homola^{2,3}, Roberto Garcia^{2,3}, Etti F. Tigheleaar^{4,7}, Linda Eckhardt^{2,3}, Jingyuan Fu^{4,8}, Liesbet Hendrickx^{1,2}, Alexandra Zhernakova^{4,7}, Cisca Wijmenga⁶, Jeroen Raes^{1,2,3,†}

Fecal microbiome variation in the average, healthy population has remained under-investigated. Here, we analyzed two independent, extensively phenotyped cohorts: the Belgian Flemish Gut Flora Project (FGFP; discovery cohort; $N = 1106$) and the Dutch LifeLines-DEEP study (LLDeep; replication; $N = 1135$). Integration with global data sets (N combined = 3948) revealed a 14-genera core microbiota, but the 664 identified genera still underexplored total gut diversity. Sixty-nine clinical and questionnaire-based covariates were found associated to microbiota compositional variation with a 92% replication rate. Stool consistency showed the largest effect size, whereas medication explained largest total variance and interacted with other covariate-microbiota associations. Early-life events such as birth mode were not reflected in adult microbiota composition. Finally, we found that proposed disease marker genera associated to host covariates, urging inclusion of the latter in study design.

Science 29 Apr 2016:
Vol. 352, Issue 6285, pp. 560–564
DOI: 10.1126/science.aad3503

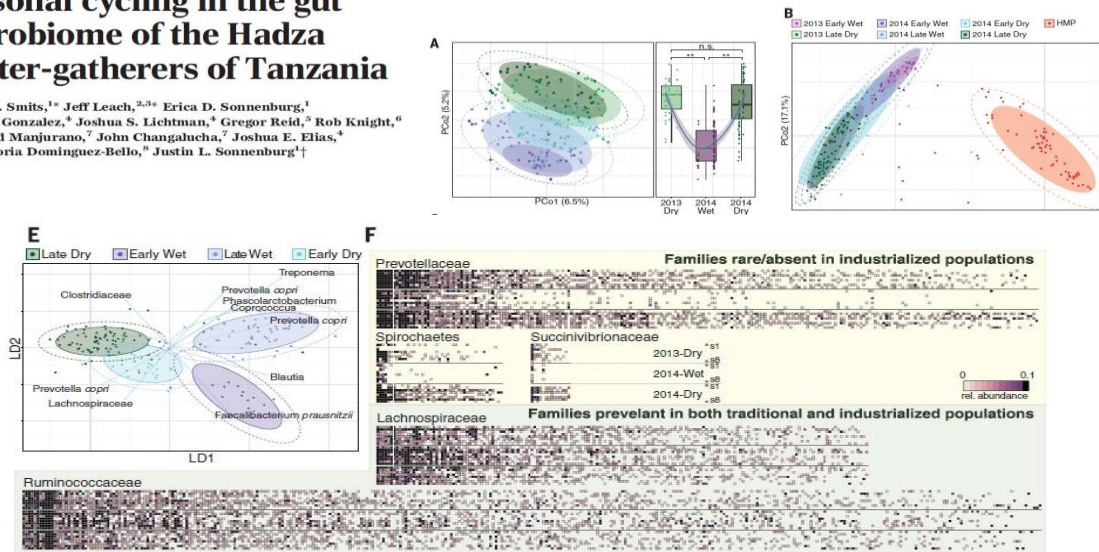


Diet and lifestyle strongly shape the human microbiota

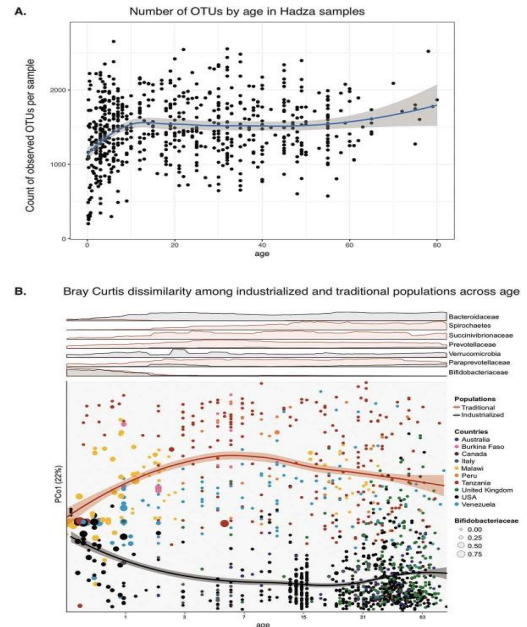
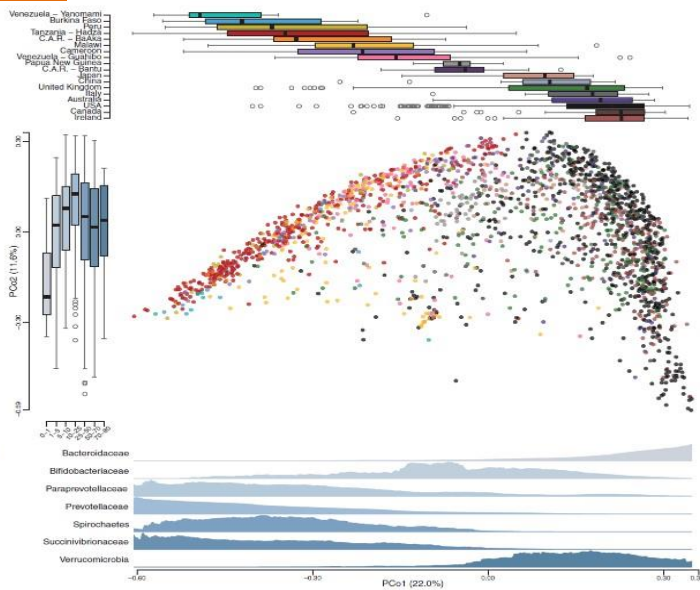
MICROBIOTA

Seasonal cycling in the gut microbiome of the Hadza hunter-gatherers of Tanzania

Samuel A. Smits,^{1*} Jeff Leach,^{2,3*} Erica D. Sonnenburg,¹ Carlos G. Gonzalez,⁴ Joshua S. Lichtman,⁴ Gregor Reid,⁵ Rob Knight,⁶ Alphaxard Manjurano,⁷ John Changalucha,⁷ Joshua E. Elias,⁴ Maria Gloria Dominguez-Bello,⁸ Justin L. Sonnenburg^{1†}



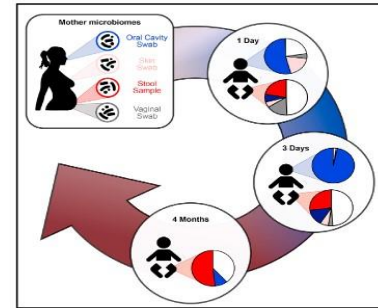
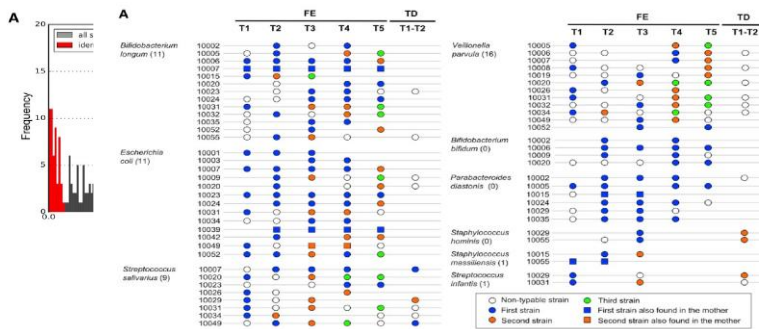
Science. 2017;357:802-806. doi: 10.1126/science.aan4834.



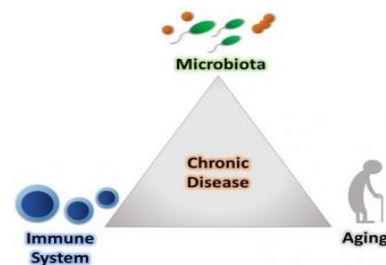
Seeds for the human microbiota

Mother-to-Infant Microbial Transmission from Different Body Sites Shapes the Developing Infant Gut Microbiome

Pamela Ferretti,^{1,2} Edoardo Pasoli,^{1,11} Adrian Tett,^{1,11} Francesco Asnicar,^{1,11} Valentina Gorfer,³ Sabina Fedi,³ Federica Ammanini,¹ Duy Tin Truong,¹ Serena Manara,¹ Moreno Zolfo,¹ Francesco Beghini,¹ Roberto Bertorelli,⁴ Veronica De Sanctis,¹ Ilaria Barietti,² Rosaria Canto,² Rosanna Clementi,² Marina Cologna,² Tiziana Crifo,² Giuseppina Cusumano,² Stefania Gottardi,² Claudia Innamorati,² Caterina Masè,² Daniela Postal,² Daniela Savoi,² Sabrina Duranti,² Gabriele Andrea Lugli,² Leonardo Mancabelli,² Francesca Turrone,² Chiara Ferrario,² Christian Milani,² Marta Mangifesta,^{2,5} Rosaria Anzalone,² Alice Viappiani,¹ Moran Yassour,¹ Hera Vlamakis,¹ Ramnik Xavier,¹ Carmen Maria Collado,¹ Omry Koren,² Saviero Tavecchio,¹ Massimo Soffiati,² Anna Pedrotti,² Marco Ventura,² Curtis Huttenhower,^{1,10} Peer Bork,² and Nicola Segata^{1,12,*}



Cell Host Microbe. 2018;24:133-145.e5



3. MICROBIOTA IN HUMAN DISEASE

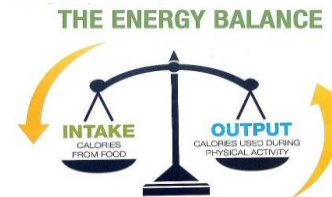
3

Relationship between microbiota & human diseases

- Primary target diseases to study the microbiota:
 - Pandemic diseases (XXI century diseases).
 - Diet-related diseases.
 - Unexplained etiology.
 - Diseases affecting GIT and gut-brain axis interconnection.

3

Overweight and Obesity



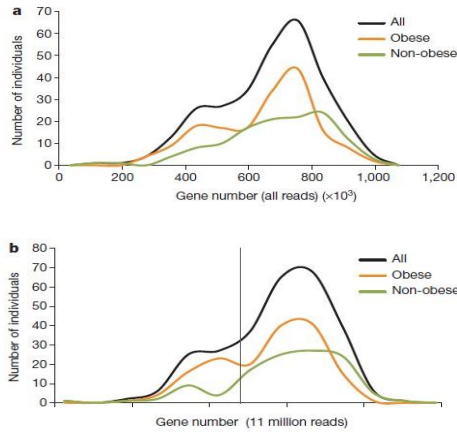
WHO definition

The fundamental cause of obesity and overweight is an energy imbalance between calories consumed and calories expended

WHO obesity fact sheet (June 2021 update)

- 1.9 billion overweight adults (39% world population)
- 650 million obese adults (13% world population)
- 41 million children (<5yo) are overweight
- 340 million children and adolescent are obese
- **OBESITY IS PREVENTABLE**

Gut microbiota in obesity



Richness of human gut microbiome correlates with metabolic markers

Emmanuelle Le Chatelier^{1*}, Trine Nielsen^{2*}, Junjie Qin^{3,4}, Edi Priti^{5*}, Falk Hildebrand^{4,5}, Gwen Falony^{4,5}, Mathieu Almeida¹, Manimozhayan Arumugam^{6,7,8,9}, Jean-Michel Batto¹, Sean Kennedy¹, Pierre Leonard¹, Junhua Li¹⁰, Kristoffer Bundgaard¹, Niels Grarup⁷, Torben Jorgensen^{6,7,10}, Ivan Brandt^{11,12}, Henrik Bjern Nielsen¹, Agnieszka S. Juncker¹³, Marcelo Bertalan¹³, Florence Levenez¹, Nicolas Pons¹, Simon Rasmussen¹³, Shinichi Sunagawa⁴, Julien Tap⁴, Sebastian Tims⁴, Erwin G. Zoetendal¹⁴, Søren Brunak¹⁵, Karine Clément^{15,16,17}, Joël Doré¹⁸, Michiel Kleerebezem¹⁹, Karsten Kristiansen⁹, Pierre Renault¹⁸, Thomas Sichertitz-Ponten²¹, Willem M. de Vos²⁰, Jean-Daniel Zucker^{15,22}, Jeroen Raes²³, Torben Hansen²², MetaHIT consortium[†], Peer Bork^{24,25,26}, S. Dusko Ehrlich⁷ & Oluf Pedersen^{7,26,27,28}

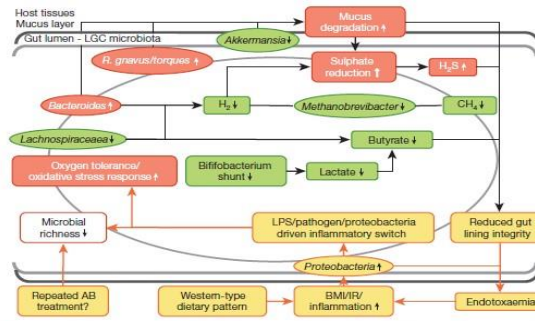
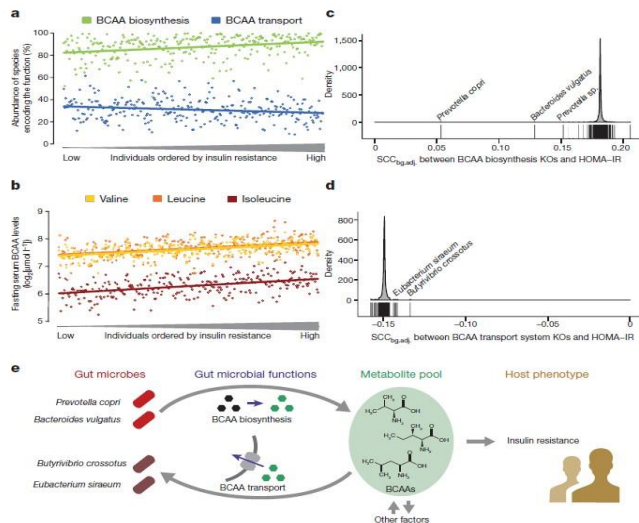


Figure 3 | Functional and phylogenetic shifts in the LGC microbiome. Top, observed increase (red) or decrease (green) of functions and phylogenetic groups. Bottom, potential drivers (yellow) of inflammation related to decreased richness. Left, antibiotic-mediated perturbation of the richness; Right, proteobacterial lipopolysaccharide-mediated perturbation of the richness. AB, antibiotic; IR, insulin resistance.

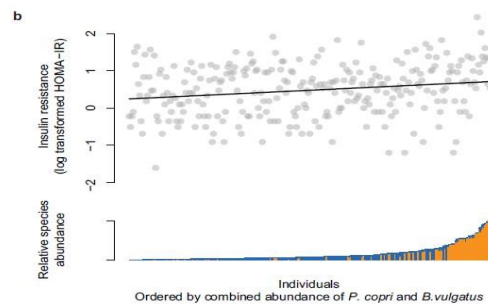
Nature. 2013;500:541-6. doi: 10.1038/nature12506.

Microbe-host metabolic cross-talk



Human gut microbes impact host serum metabolome and insulin sensitivity

Helle Krogh Pedersen^{1*}, Valborg Gudmundsdottir^{1*}, Henrik Bjern Nielsen^{1*}, Tiina Hyötylainen^{2,3,4*}, Trine Nielsen^{2,4}, Benjamin A. H. Jensen⁵, Kristoffer Bundgaard¹, Falk Hildebrand^{7,8,9}, Edi Priti^{10,11}, Gwen Falony^{12,13}, Emmanuelle Le Chatelier¹⁴, Florence Levenez¹⁵, Joël Doré^{16,17}, Jarmo Mattila¹⁸, Damian R. Plichta¹, Paivi Pohjo¹⁹, Lars I. Hellgren¹, Manimozhayan Arumugam²⁰, Shinichi Sunagawa²¹, Sara Vieira Silva²², Torben Jorgensen^{23,24}, Jacob Bak Holm²⁵, Kajetan Trzask²⁶, MetaHIT Consortium[†], Susanne Brix²⁷, Jeroen Raes^{28,29}, Jun Wang^{30,31,32,33}, Torben Hansen^{32,33}, Peer Bork^{34,35,36}, Søren Brunak³⁷, Matej Orešić^{3,4,14}, S. Dusko Ehrlich^{10,28} & Oluf Pedersen^{7,27}



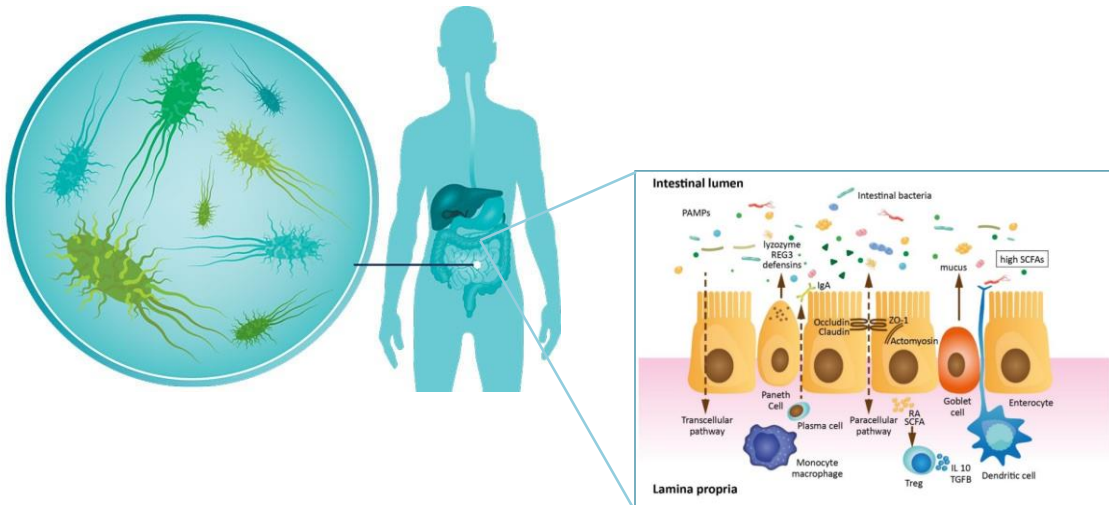
Nature. 2016;535:376-81.



4. INTESTINAL MICROBIOTA & INFECTIOUS DISEASES

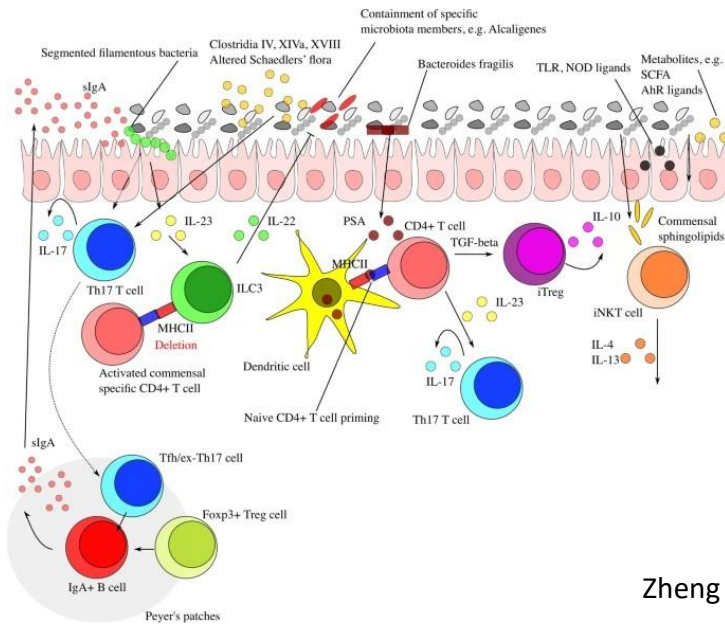
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The GIT is a microbe highway



4

Intestinal microbiota-immunity interplay

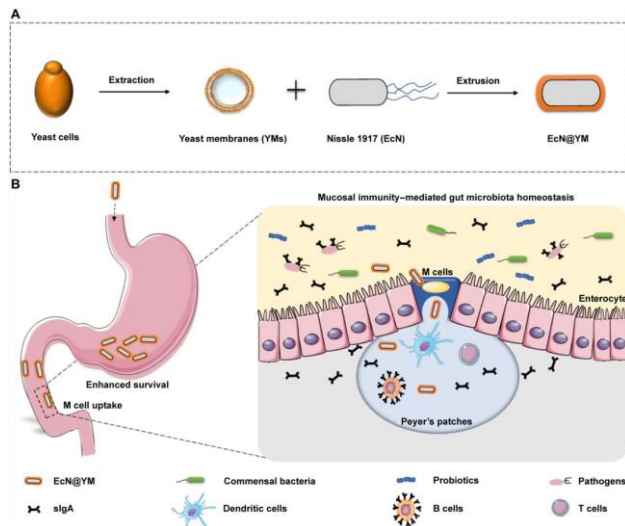


Some immune cells are directly induced from gut microbes (**Th17** - potent immunomodulatory effector cells)

Zheng et al. Cell Research 2020;30:492-506.

4

Gut microbiota regulates gut immune homeostasis



Lin t al. Sci Adv 2021;7: eabf0677

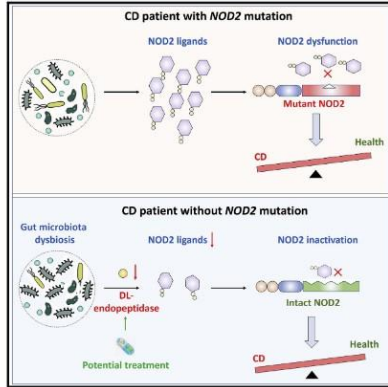
Gut microbiota subcellular components as therapeutics

Article

Cell Host & Microbe

Gut microbial DL-endopeptidase alleviates Crohn's disease via the NOD2 pathway

Graphical abstract



Authors

Jie Gao, Xinmei Zhao, Shixian Hu, ..., Rinse K. Weersma, Xiaolong He, Hongwei Zhou

Correspondence

r.k.weersma@mdl.umcg.nl (R.K.W.), hxl2027315@smu.edu.cn (X.H.), biodegradation@gmail.com (H.Z.)

In brief

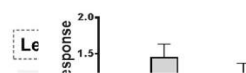
Gao et al. show that Firmicutes-derived DL-endopeptidase generates NOD2 ligands in the gut and that it is depleted globally in CD patients. The gut microbiota from CD patients with low DL-endopeptidase activity increased colitis susceptibility in mice. Importantly, restoring NOD2 ligands by administering DL-endopeptidase, DL-endopeptidase-producing probiotics, or mifamurtide exerts anti-colitis effects via NOD2.

Cell Host Microbe 2022;30:1435-1449.

Gut microbiota unbalance impairs intestinal inflammatory tone



RESEARCH ARTICLE
Host-Microbe Biology



Depletion of *Blautia* Species in the Microbiota of Obese Children Relates to Intestinal Inflammation and Metabolic Phenotype Worsening

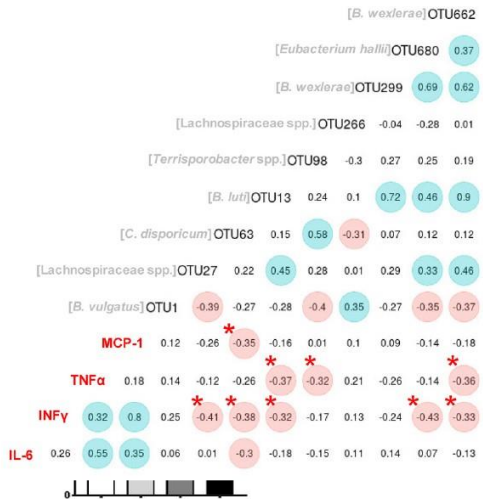
Alfonso Benítez-Páez,^a Eva M. Gómez del Pugar,^a Inmaculada López-Almela,^a Ángela Moya-Pérez,^a Pilar Codoñer-Franch,^{b,c} Yolanda Sanz^a

TABLE 1 Anthropometry and serum biochemistry of children included in this study

Parameter analyzed ^a	Value for child group			P value of statistical analysis ^b		
	Lean (n = 16)	Obese (n = 20)	Obese+IR (n = 15)	Lean vs obese	Lean vs obese+IR	Obese vs obese+IR
Age (yrs)	10.06 ± 0.80	11.30 ± 0.63	13.27 ± 0.66	0.616	0.010	0.152
Sex ^c	Boys, 12; girls, 4	Boys, 10; girls, 10	Boys, 7; girls, 8	0.236	0.329	1.000
BMI (z-score)	1.68 ± 0.08	2.42 ± 0.17	2.76 ± 0.15	0.001	<0.001	0.140
HOMA-IR ^d	1.37 ± 0.13	2.28 ± 0.15	5.18 ± 0.55	0.002	<0.001	<0.001
Glucose (mg/dl)	89.67 ± 1.63	92.15 ± 1.34	87.31 ± 3.97	0.245	0.588	0.208
Insulin (mg/dl)	6.06 ± 0.54	10.38 ± 0.70	25.63 ± 2.04	<0.001	<0.001	<0.001
Total cholesterol (mg/dl)	156.70 ± 6.79	145.50 ± 3.82	160.60 ± 6.05	0.139	0.669	0.042
HDL cholesterol (mg/dl)	50.00 ± 2.54	32.24 ± 2.33	37.36 ± 3.36	<0.001	0.005	0.207
LDL cholesterol (mg/dl)	89.83 ± 7.69	88.00 ± 7.21	64.57 ± 11.89	0.865	0.202	0.233
Triglycerides (mg/dl)	57.17 ± 9.08	78.33 ± 8.39	89.21 ± 6.68	0.118	0.014	0.362

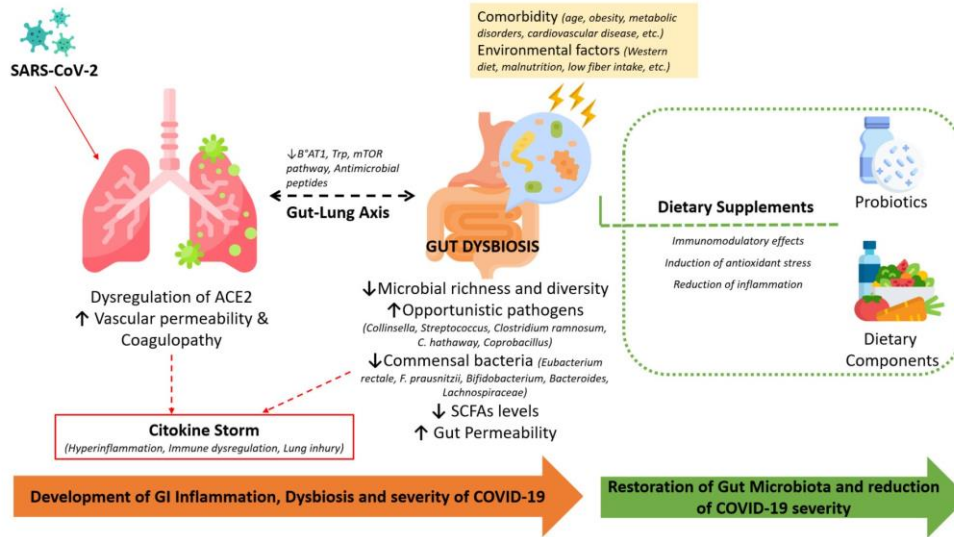
TABLE 2 Immune markers in stool samples of the study children

Marker analyzed ^a	Value for child group			P value of statistical analysis ^b		
	Lean (n = 16)	Obese (n = 20)	Obese+IR (n = 15)	Lean vs obese	Lean vs obese+IR	Obese vs obese+IR
IL-6	17.8 (12.4–51.8)	22.2 (4.0–26.1)	26.4 (11.8–37.3)	0.226	0.925	0.149
IFN-γ	28.5 (19.8–49.2)	192.5 (91.0–273.4)	103.8 (52.0–168.7)	<0.001	0.007	0.055
TNF-α	9.7 (5.7–21.3)	7.8 (7.8–10.5)	33.7 (10.8–70.6)	0.902	0.019	0.004
MCP-1	7.8 (7.8–7.8)	35.9 (12.1–57.9)	21.75 (5.9–49.7)	0.003	0.103	0.427



4

Gut microbiota-immunity axis (Covid-19 case)

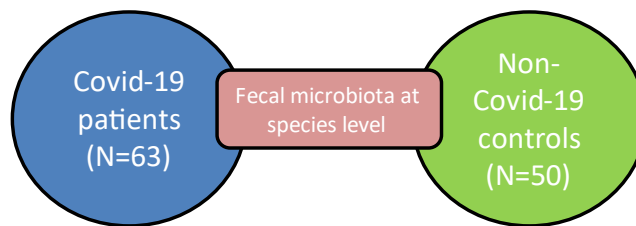


Rocchi et al. Pathogens 2022;11:e1050.

4

Gut microbiota in Covid-19 patients

Unpublished results



Decreasing of central immunomodulatory species:

Faecalibacterium prausnitzii
• *Bacteroides uniformis*

Boost of potential pathogens:

• *Klebsiella pneumoniae*
• *Streptococcus pneumoniae*
• *Enterococcus faecium* / *E. faecalis*

Key gut species lost in Covid-19 patients

► JCI Insight. 2022 Jun 22;7(12):e154722. doi: 10.1172/jci.insight.154722.

Human CD4⁺CD8⁺ Tregs induced by *Faecalibacterium prausnitzii* protect against intestinal inflammation

Sothea Touch ^{1,2}, Emmanuelle Godefroy ³, Nathalie Rolhion ^{1,2}, Camille Danne ^{1,2,4}, Cyriane Ouevray ^{1,2}, Marjolène Straube ^{1,2}, Chloé Galbert ^{1,2}, Loïc Brot ^{1,2}, Iria Alonso Salgueiro ^{1,2}, Sead Chadi ⁴, Tatiana Ledent ¹, Jean-Marc Chatel ⁴, Philippe Langella ⁴, Francine Jotereau ³, Frédéric Altare ³, Harry Sokol ^{1,2,4}

► Gut Microbes. 2020 Nov 9;12(1):1-16. doi: 10.1080/19490976.2020.1826748.

Butyrate mediates anti-inflammatory effects of *Faecalibacterium prausnitzii* in intestinal epithelial cells through *Dact3*

Marion Lenoir ¹, Rebeca Martín ¹, Edgar Torres-Maravilla ¹, Sead Chadi ¹, Pamela González-Dávila ¹, Harry Sokol ^{1,2}, Philippe Langella ¹, Florian Chain ¹, Luis G Bermúdez-Humarán ¹

► Sci Rep. 2021 Jun 3;11(1):11788. doi: 10.1038/s41598-021-90888-y.

Bacteroides uniformis CECT 7771 alleviates inflammation within the gut-adipose tissue axis involving TLR5 signaling in obese mice

Emanuel Fabersani ¹, Kevin Portune ¹, Isabel Campillo ¹, Inmaculada López-Almela ¹, Sergio Montserrat-de la Paz ¹, Marina Romaní-Pérez ¹, Alfonso Benítez-Páez ¹, Yolanda Sanz ²

► Gut Microbes. 2021 Jan-Dec;13(1):1-20. doi: 10.1080/19490976.2020.1865706.

Bacteroides uniformis combined with fiber amplifies metabolic and immune benefits in obese mice

Inmaculada López-Almela ¹, Marina Romaní-Pérez ¹, Clara Bullich-Vilarrubias ¹, Alfonso Benítez-Páez ¹, Eva M Gómez Del Pulgar ¹, Rubén Francés ², Gerhard Liebisch ³, Yolanda Sanz ¹

4 Gut microbiota diversity as trait of gut health

GUT MICROBES
2020, VOL. 12, NO. 1, e1707610 (16 pages)
<https://doi.org/10.1080/19490976.2019.1707610>

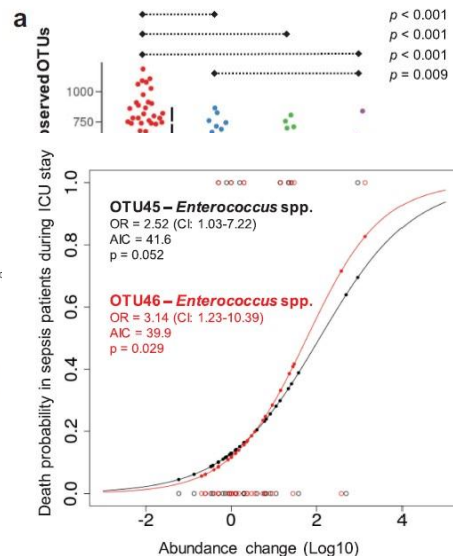
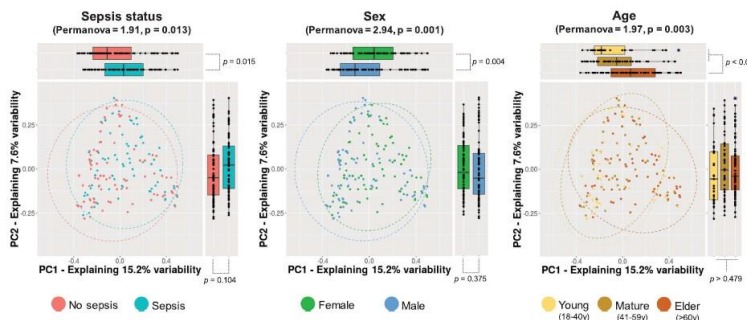
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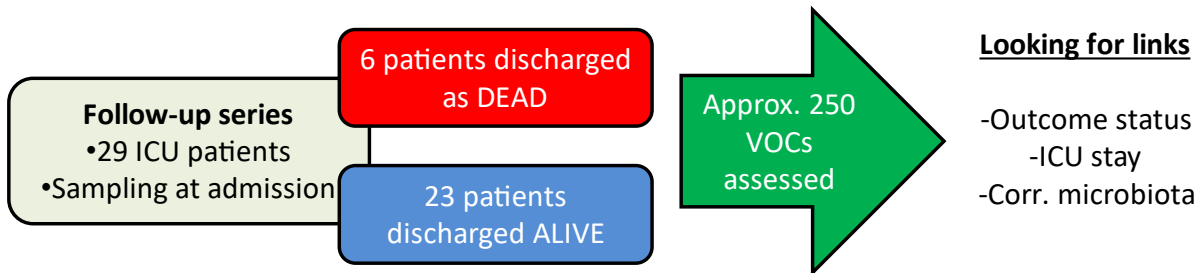
Gut microbiota profiles in critically ill patients, potential biomarkers and risk variables for sepsis

Gloria M. Agudelo-Ochoa ¹, Beatriz E. Valdés-Duque ², Nubia A. Giraldo-Giraldo ³, Ana M. Jaillier-Ramírez ⁴, Adriana Giraldo-Villa ⁵, Irene Acevedo-Castaño ⁶, Mónica A. Yepes-Molina ⁷, Janeth Barbosa-Barbosa ⁸, and Alfonso Benítez-Páez ⁹



4

Insights into the microbiota metabolites



Results:

Indols (skatole), phenols (p-cresol) and mid-chain FAs (valeric and decanoic acid), showed some degree of association with no robust evidence

4

Species-to-species inhibition

Science Translational Medicine Current Issue First release paper

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RESEARCH ARTICLE | BACTERIAL INFECTIONS f t in g

Enterococcal bacteremia in mice is prevented by oral administration of probiotic *Bacillus* spores

PIPAT PIEWNGSAM JANICE CHIOU JOIE LING RYAN LIU PAWIYA PUPA YUE ZHENG AND MICHAEL OTTO [Authors Info & Affiliations](#)

ASM Journals / Applied and Environmental Microbiology / Vol. 87, No. 13
/ Probiotic *Bacillus* Affects *Enterococcus faecalis* Antibiotic Resistance Transfer by Interfering with Pheromone Signaling Cascades

Spotlight Selection | Applied and Industrial Microbiology | Research Article | 11 June 2021 f t in

Probiotic *Bacillus* Affects *Enterococcus faecalis* Antibiotic Resistance Transfer by Interfering with Pheromone Signaling Cascades

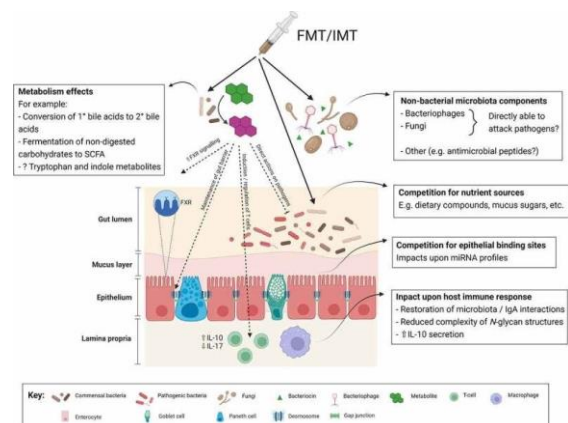
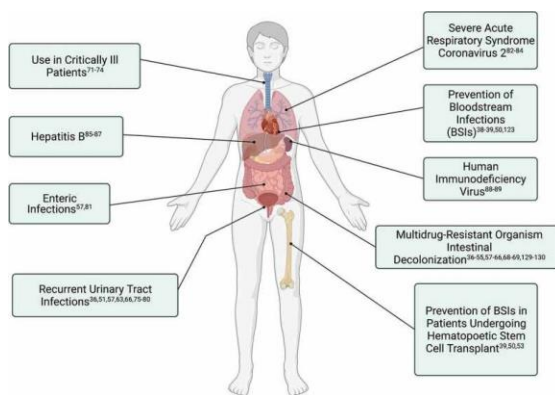
Authors: Yu-Chieh Lin, Eric H.-L. Chen, Rita P.-Y. Chen, Gary M. Dunne, Wei-Shou Hu, Kung-Ta Lee [AUTHORS INFO & AFFILIATIONS](#)



5. FUTURE DIRECTIONS

5

Fecal microbiota transplantation (FMT)



Ghani et al. Gut Microbes 2022;14:e2038856.

Fecal microbiota transplantation (FMT)



Gastroenterology

Volume 152, Issue 4, March 2017, Pages 799-811.e7



Original Research

Full Report: Clinical—Alimentary Tract

Efficacy of Sterile Fecal Filtrate Transfer for Treating Patients With *Clostridium difficile* Infection

Stephan J. Ott^{1,*}, Georg H. Waetzig^{2,*}, Ateequr Rehman^{3,*}, Jacqueline Moltzau-Anderson^{3,4}, Richa Bharti³, Juris A. Grasis⁵, Liam Cassidy⁶, Andreas Tholey⁶, Helmut Fickenscher⁷, Dirk Seegert⁸, Philip Rosenstiel^{3,9}, Stefan Schreiber^{1,3,9}

Conclusions

A preliminary investigation of 5 patients with CDI shows that transfer of sterile filtrates from donor stool (FFT), rather than fecal microbiota, can be sufficient to restore normal stool habits and eliminate symptoms. This finding indicates that **bacterial components**, **metabolites**, or **bacteriophages** mediate many of the effects of FMT, and that FFT might be an alternative approach, particularly for immunocompromised patients.

Gut microbiota phages

nature microbiology

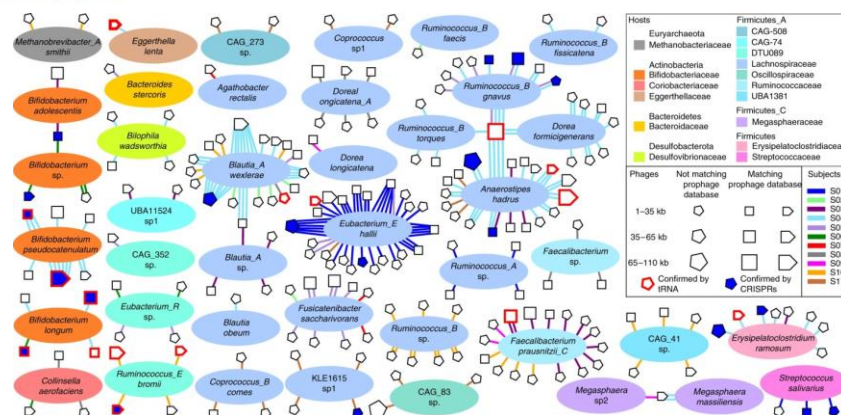
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nature > nature microbiology > articles > article

Article | Published: 05 August 2019

Defining the human gut host–phage network through single-cell viral tagging

Mária Džunková , Soo Jen Low, Joshua N. Daly, Li Deng, Christian Rinke & Philip Hugenholtz



Dietary strategies



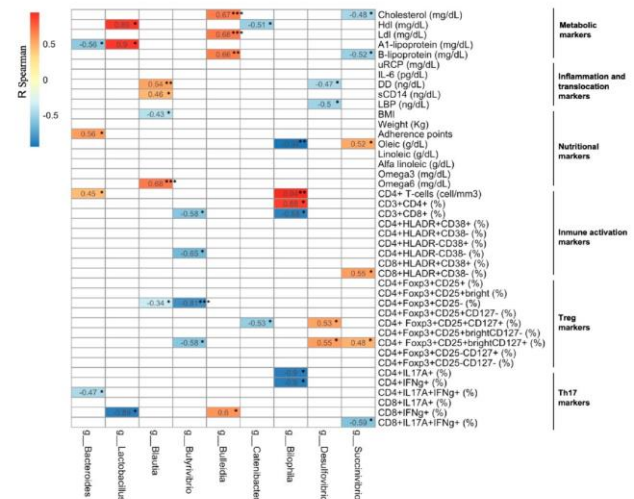
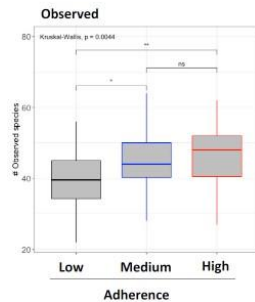
nutrients



Article

Adherence to a Supplemented Mediterranean Diet Drives Changes in the Gut Microbiota of HIV-1-Infected Individuals

Roque Pastor-Ibáñez ¹, Juan Blanco-Heredia ^{2,3,4}, Florencia Etcheverry ^{1,5}, Sonsoles Sánchez-Palomino ¹, Francisco Díez-Fuertes ¹, Rosa Casas ^{6,7}, María Ángeles Navarrete-Muñoz ^{8,9}, Sara Castro-Barquero ^{8,7}, Constanza Lucero ¹, Irene Fernández ^{1,5}, Lorna Leal ^{1,5}, José Miguel Benito ^{8,9}, Marc Noguera-Julian ¹⁰, Roger Paredes ¹⁰, Norma Rallón ^{8,9}, Ramón Estruch ^{6,7}, David Torrents ^{11,12} and Felipe García ^{1,5,*}



Succinivibrio and **Bifidobacterium** abundances were influenced by the adherence to the MD and significantly correlated with **Treg cells**. Conclusion: The **Mediterranean diet improved metabolic parameters, immune activation, Treg function**, and the gut microbiota composition in HIV -1-infected individuals.

Potential probiotic strains

Biomed Res Int. 2022; 2022: 3860896.

Published online 2022 Jan 27. doi: [10.1155/2022/3860896](https://doi.org/10.1155/2022/3860896)

PMCID: PMC8814717

PMID: [35127941](https://pubmed.ncbi.nlm.nih.gov/35127941/)

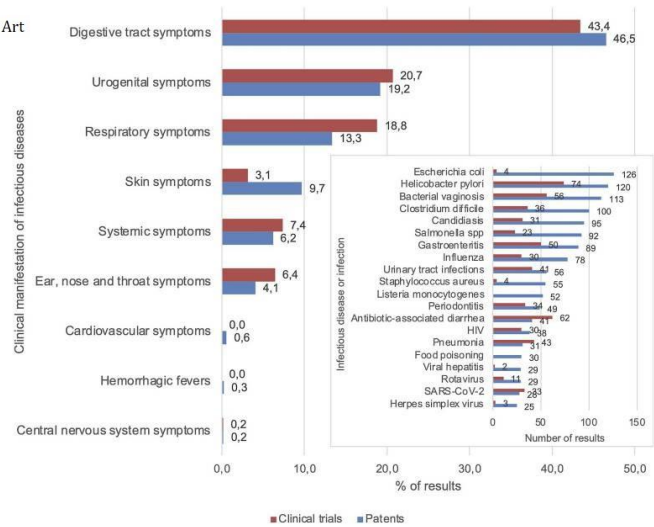
Effectiveness of Multistrain Probiotic Formulation on Common Infectious Disease Symptoms and Gut Microbiota Modulation in Flu-Vaccinated Healthy Elderly Subjects

Anna Sandionigi, ¹ Alessandra De Giani, ¹ Francesco Tursi, ² Angela Michelotti, ² Enza Cestone, ² Silvana Giardina, ² Jessica Zampolli, ¹ and Patrizia Di Gennaro ¹

Potential probiotic strains

Probiotics for the Management of Infectious Diseases: Reviewing the State of the Art

Cato Wiegiers,^{1*} Linda H. M. van de Burghwal, and Olaf F. A. Larsen



Acknowledgements



Thanks for your attention



QUESTIONS?