MESA I:
ACTUALIZACIÓN EN ENFERMEDADES INFECCIOSAS

Dra. Patricia Pérez-Matute

Unidad Predepartamental de Enfermería. Facultad de Ciencias de la Salud. Universidad de La Rioja

Unidad de Enfermedades Infecciosas, Microbiota y Metabolismo. Centro de Investigación Biomédica de La Rioja (CIBIR)

Hospital Universitario San Pedro

carmen-patricia.perez@unirioja.es

CSIC
Consejo Superior de Investigaciones Científicas

UNIVERSIDAD DE LA RIOJA

CIBIR
Centro de Investigación Biomédica de La Rioja

Hospital San Pedro

¿Qué aporta el estudio de la microbiota a las enfermedades infecciosas?

Dra. Patricia Pérez-Matute

Unidad Predepartamental de Enfermería. Facultad de Ciencias de la Salud. Universidad de La Rioja

Unidad de Enfermedades Infecciosas, Microbiota y Metabolismo. Centro de Investigación Biomédica de La Rioja (CIBIR)

Hospital Universitario San Pedro

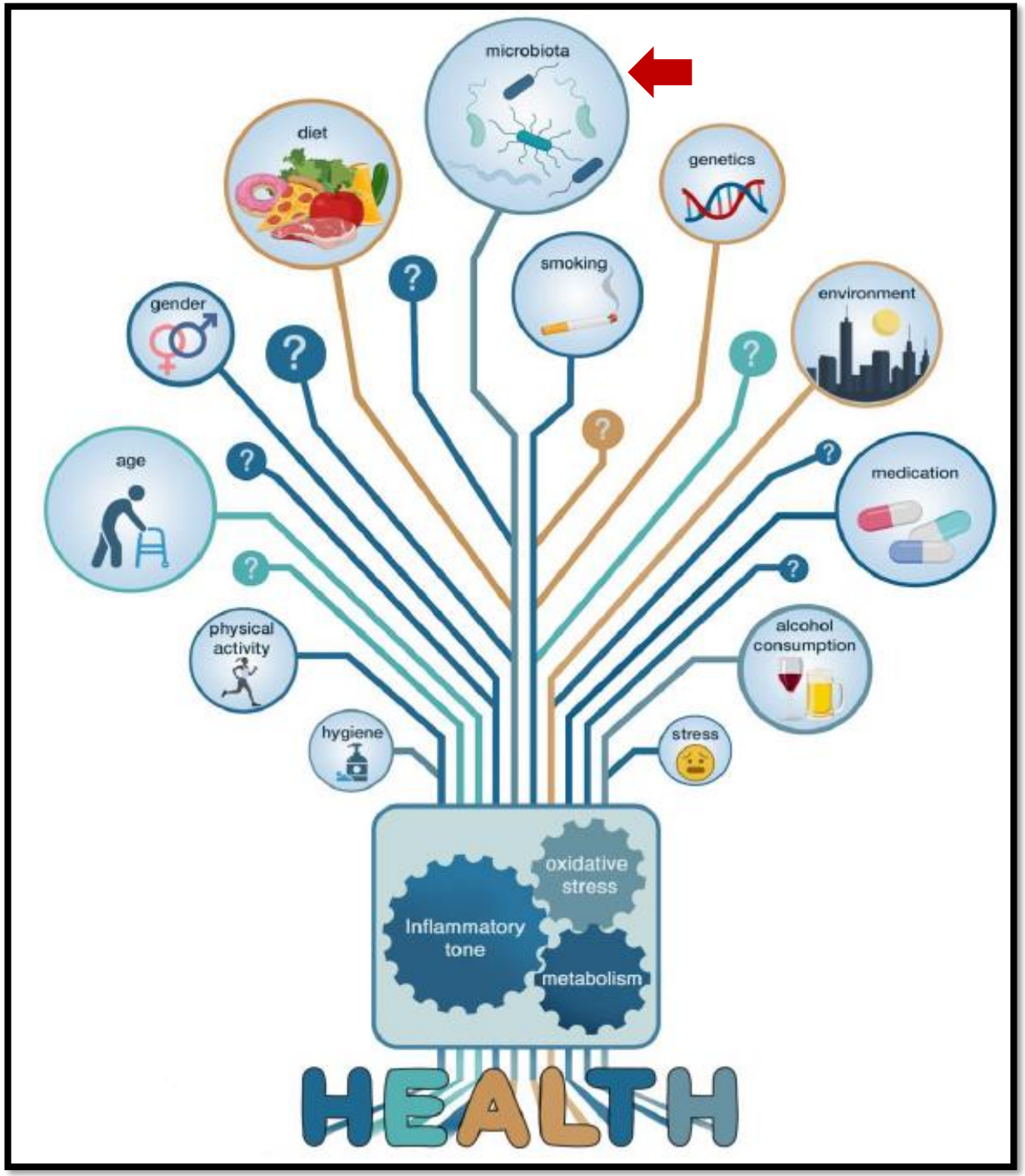
carmen-patricia.perez@unirioja.es

CSIC
Consejo Superior de Investigaciones Científicas

UNIVERSIDAD DE LA RIOJA

CIBIR
Centro de Investigación Biomédica de La Rioja

Hospital San Pedro



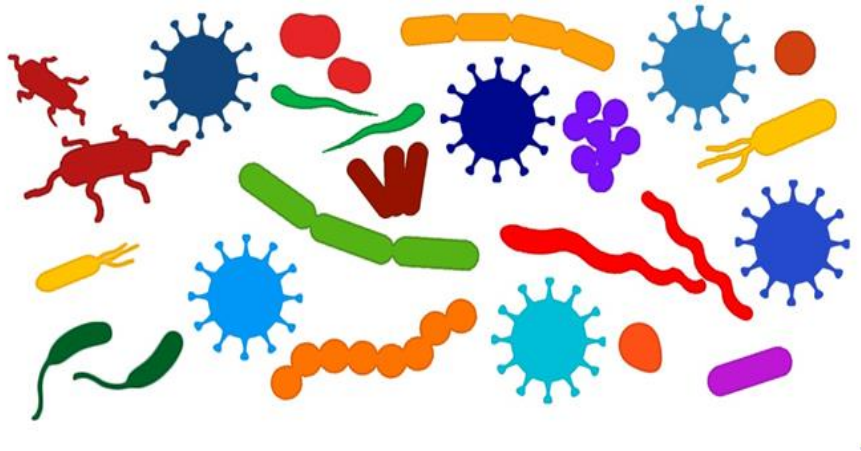
Cani et al., Microorganisms, 2021

Microbiota

Bacterias

Hongos

Protozoos

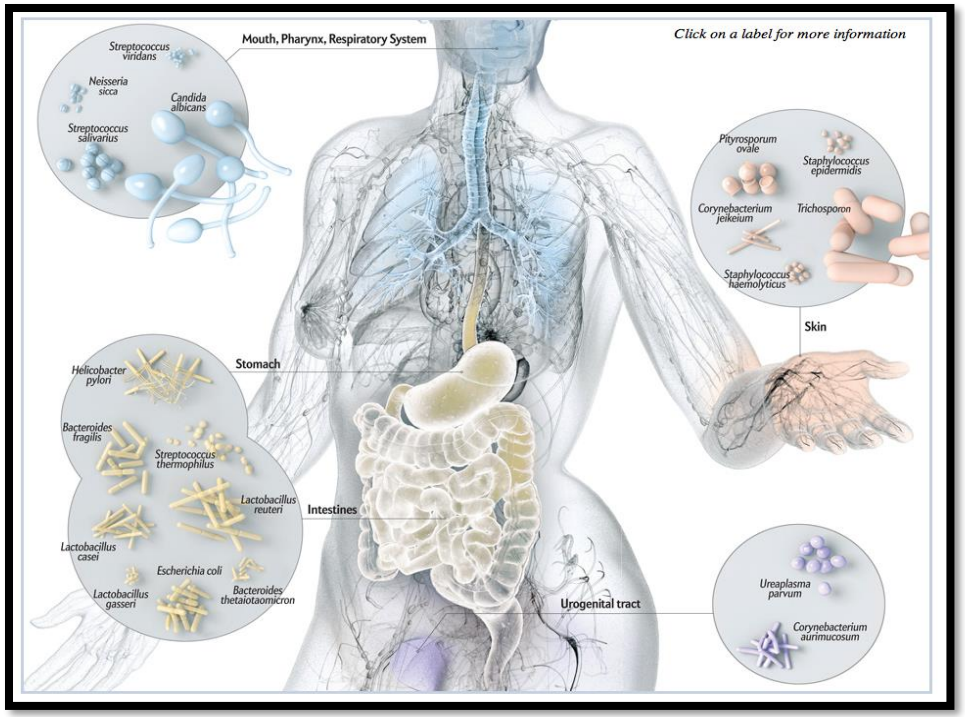


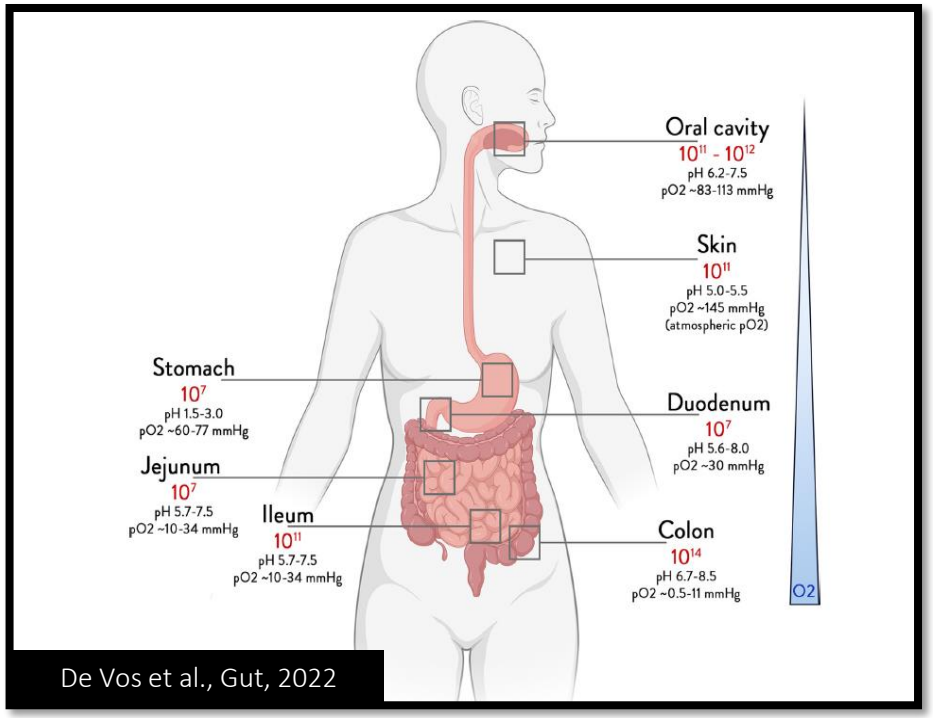
Arqueas

Virus

Conjunto de microorganismos estructurados en comunidades que viven e interactúan en nuestro organismo

Ser humano como «SUPER organismo»





De Vos et al., Gut, 2022

BACTERIAS
Bacteroides
&
Firmicutes

HONGOS
Candida
Penicillium
Wallemia
Cladosporium
Saccharomyces

VIRUS
Caudovirales

UNIVERSIDAD DE LA RIOJA

Hospital San Pedro

CIBIR
Centro de Investigación Biomédica de La Rioja

ÚLTIMO ÓRGANO DEL CUERPO

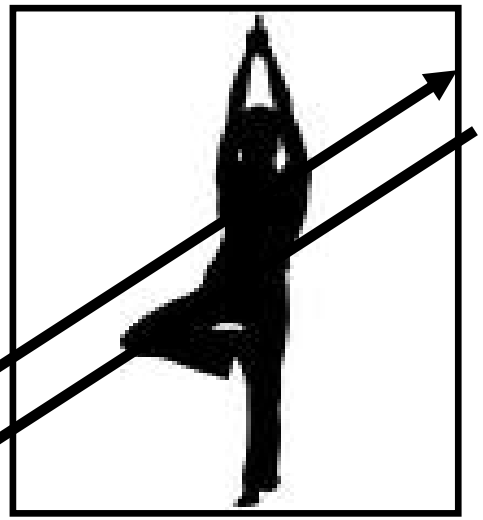
Funciones

- Procesar componentes digeribles e indigeribles de la dieta como los polisacáridos de las plantas
- Mantenimiento de la barrera epitelial y capa de moco intestinal desde el nacimiento
- Competencia con las bacterias patógenas
- Producción de ácidos grasos de cadena corta,…
- Síntesis de vitamina K y ácido fólico
- Maduración del sistema inmune innato
- Metabolismo de las sales biliares
- Metabolismo de sustancias tóxicas y carcinogénicas

https://goo.gl/images/RJ5wQp

Eubiosis *vs.* disbiosis

Bacterias perjudiciales-patógenos



Microorganismos "beneficiosos"

Diversidad

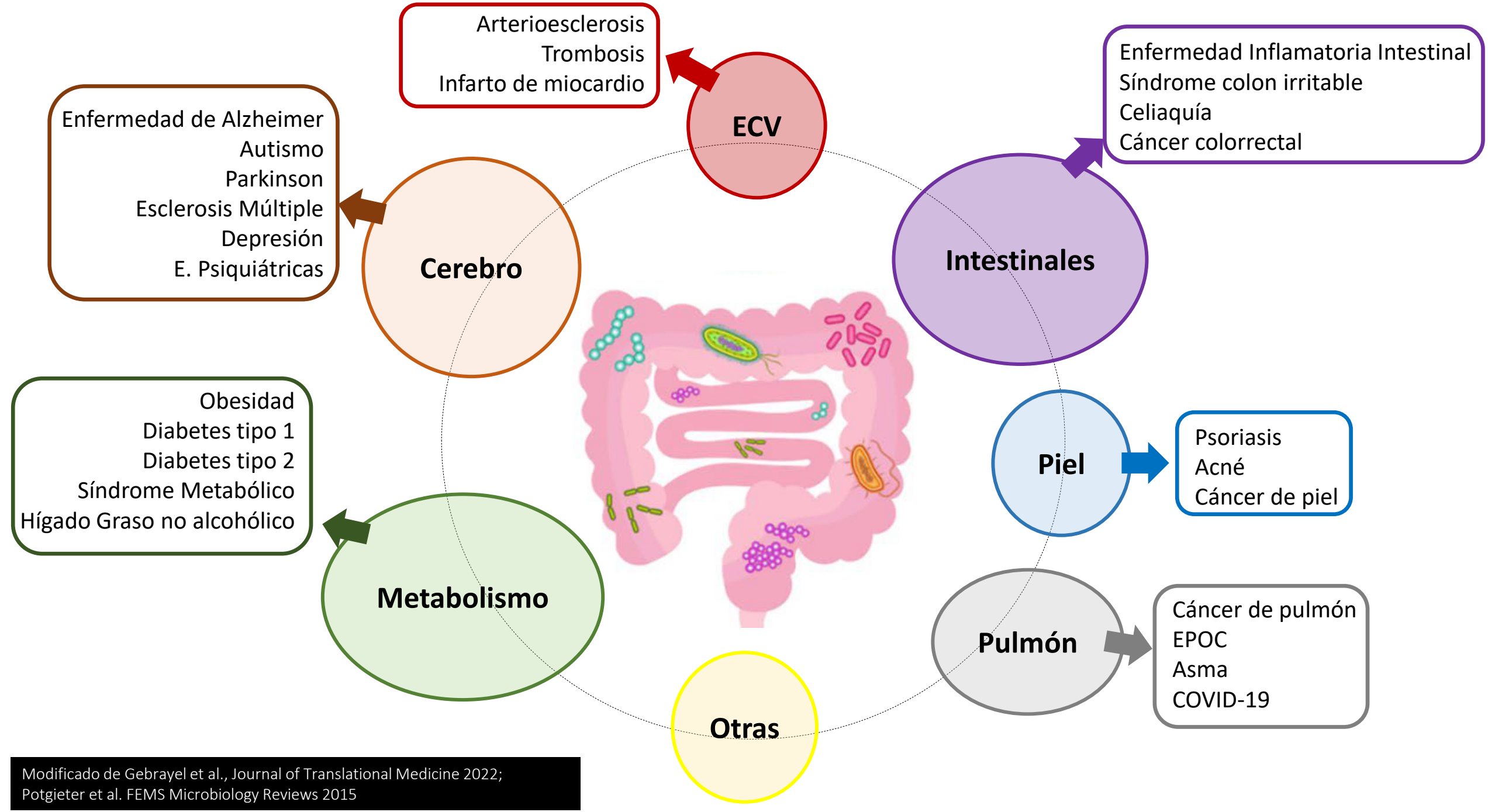
DISBIOSIS

UNIVERSIDAD DE LA RIOJA

Hospital San Pedro

CIBIR Centro de Investigación Biomédica de La Rioja

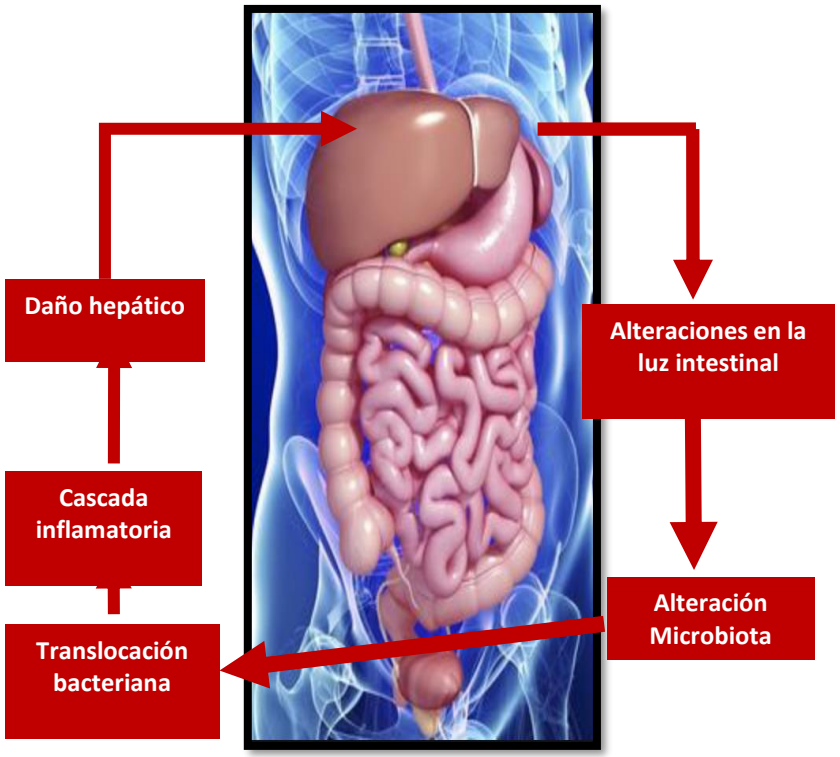
Diferentes causas pueden romper ese equilibrio ⟶ DISBIOSIS



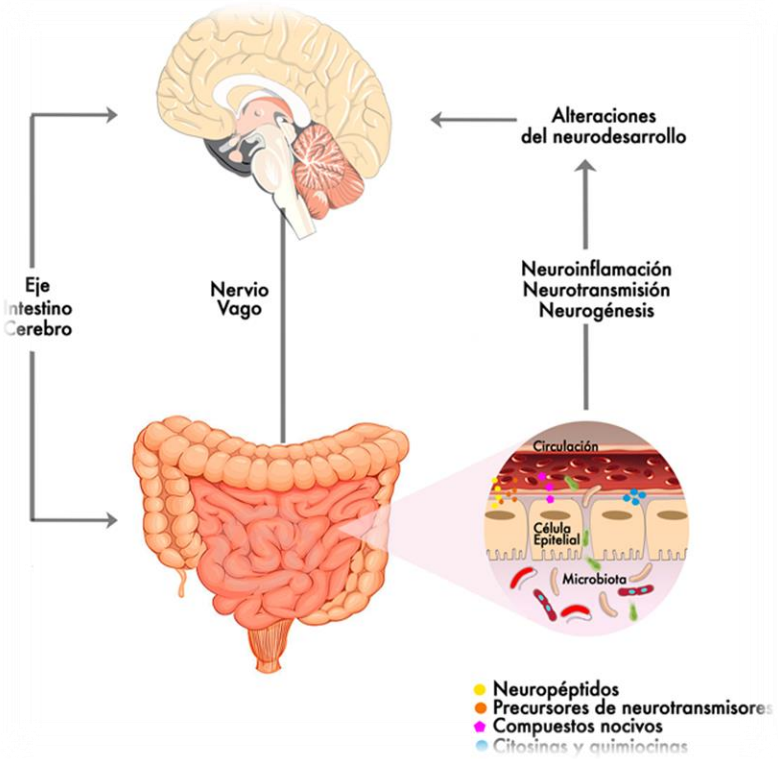
Modificado de Gebrayel et al., Journal of Translational Medicine 2022;
Potgieter et al. FEMS Microbiology Reviews 2015

Microbiota y ejes sistémicos

Eje intestino-hígado

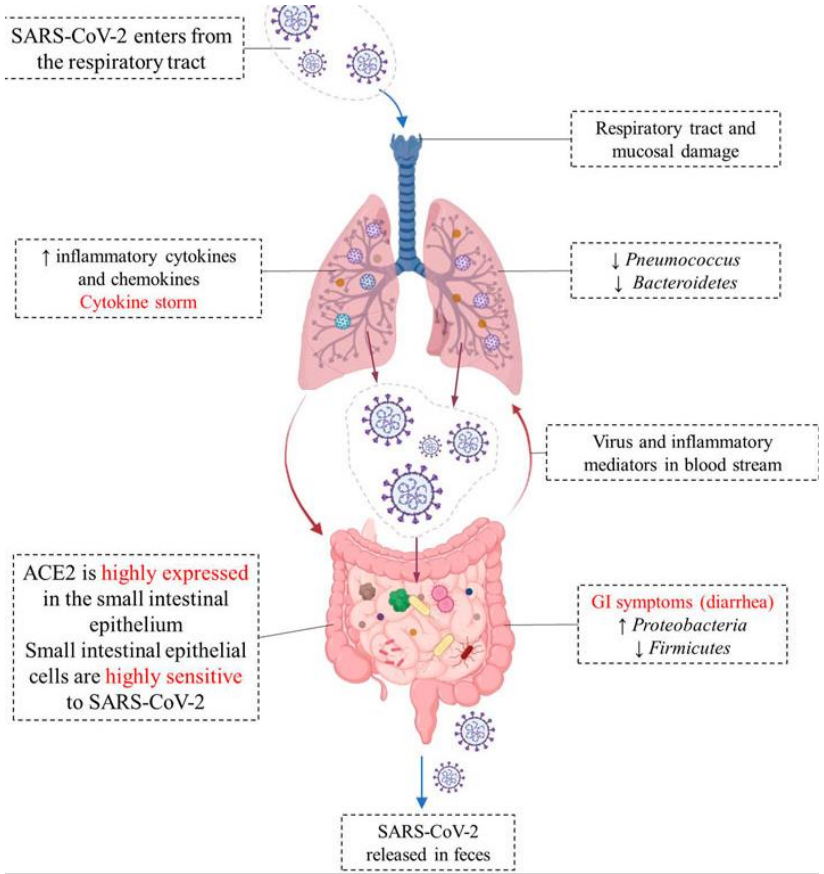


Eje intestino-cerebro



Richarte et al., Neurologia, 2018

Eje intestino-pulmón



Xu et al., Frontiers in Pharmacology, 2022

...


MAMI, MAMI ¿QUIEN FUE PRIMERO, EL HUEVO O NOSOTROS?
¡UH! PREPARATE, CLOTILDE, TU HIJO EMPEZÓ A HACER LAS PREGUNTAS DIFÍCILES
graciosos21.com

Microbiota y Enfermedades Infecciosas

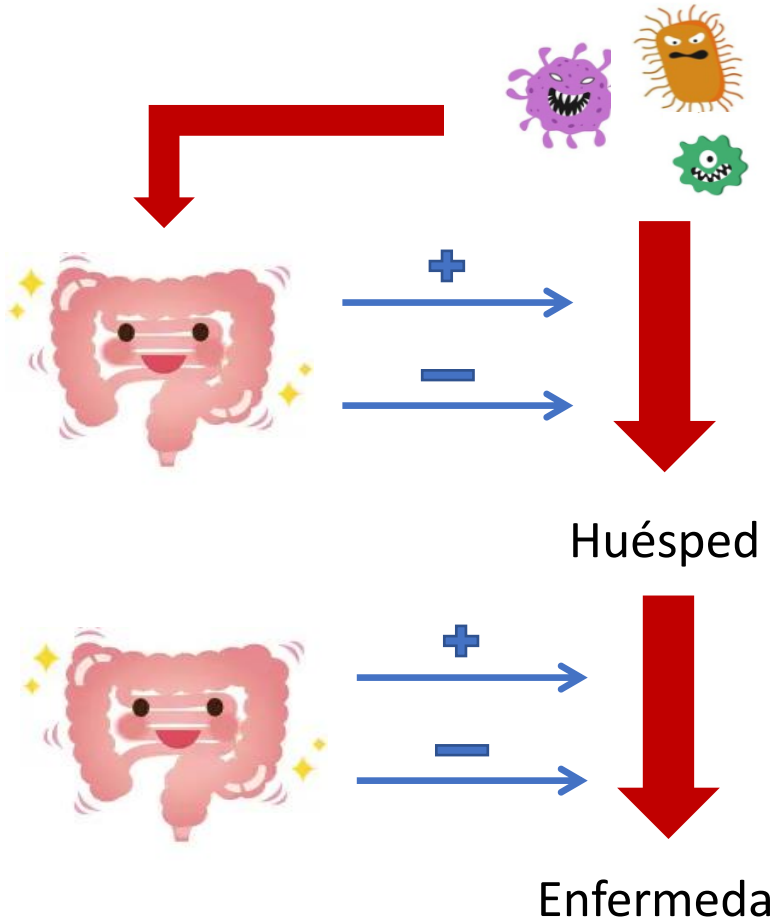
Freepik

https://medicodeguardia11235.wordpress.com/2019/04/04/podcast-disbiosis-intestinal/
Instituto de Microecología

COMUNICACIÓN BIDIRECCIONAL ENTRE «INFECCIÓN» Y MICROBIOTA INTESTINAL

Microbiota y Enfermedades Infecciosas

Susceptibilidad a la infección
Progresión de la infección/enfermedad



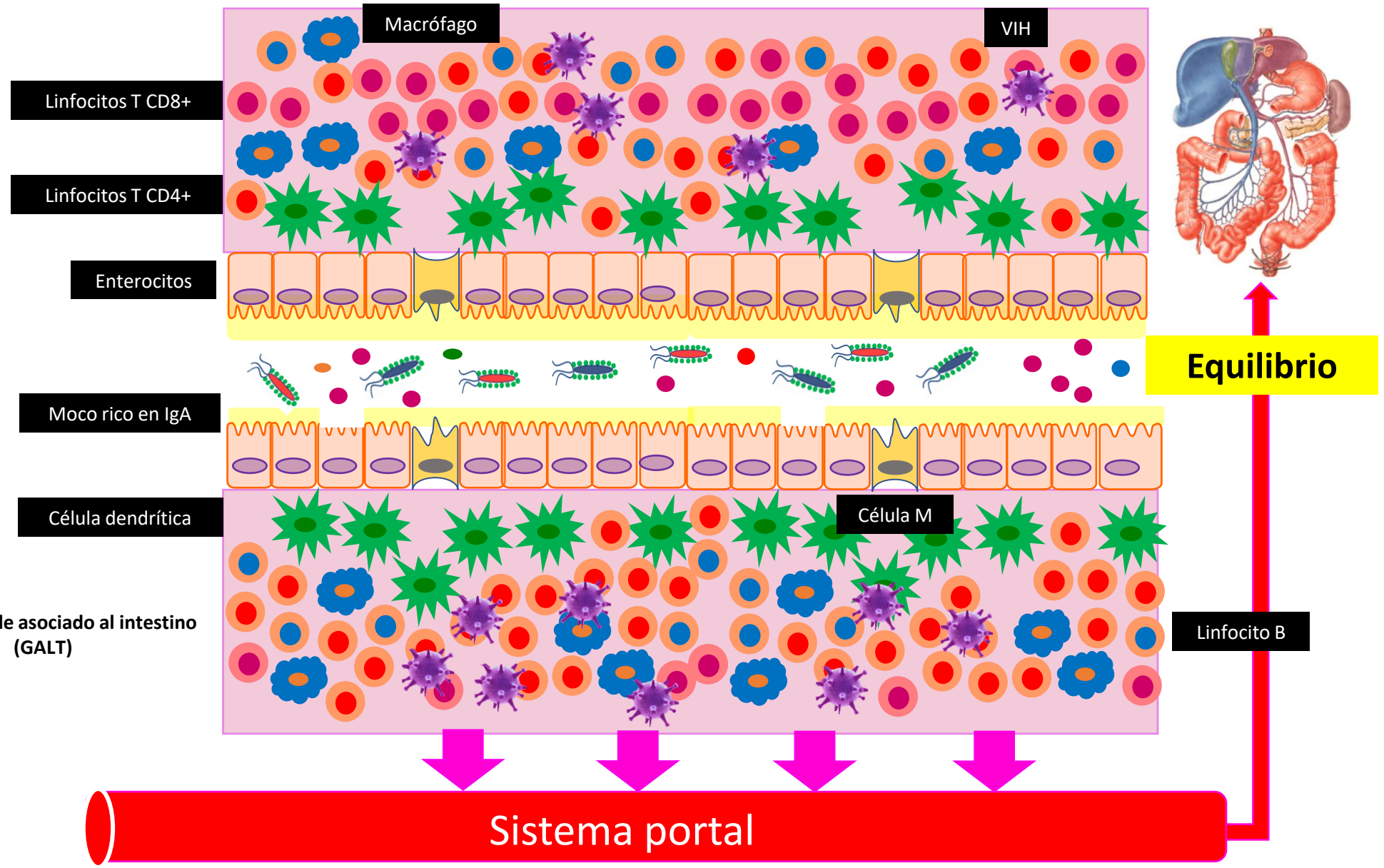
Barrera intestinal

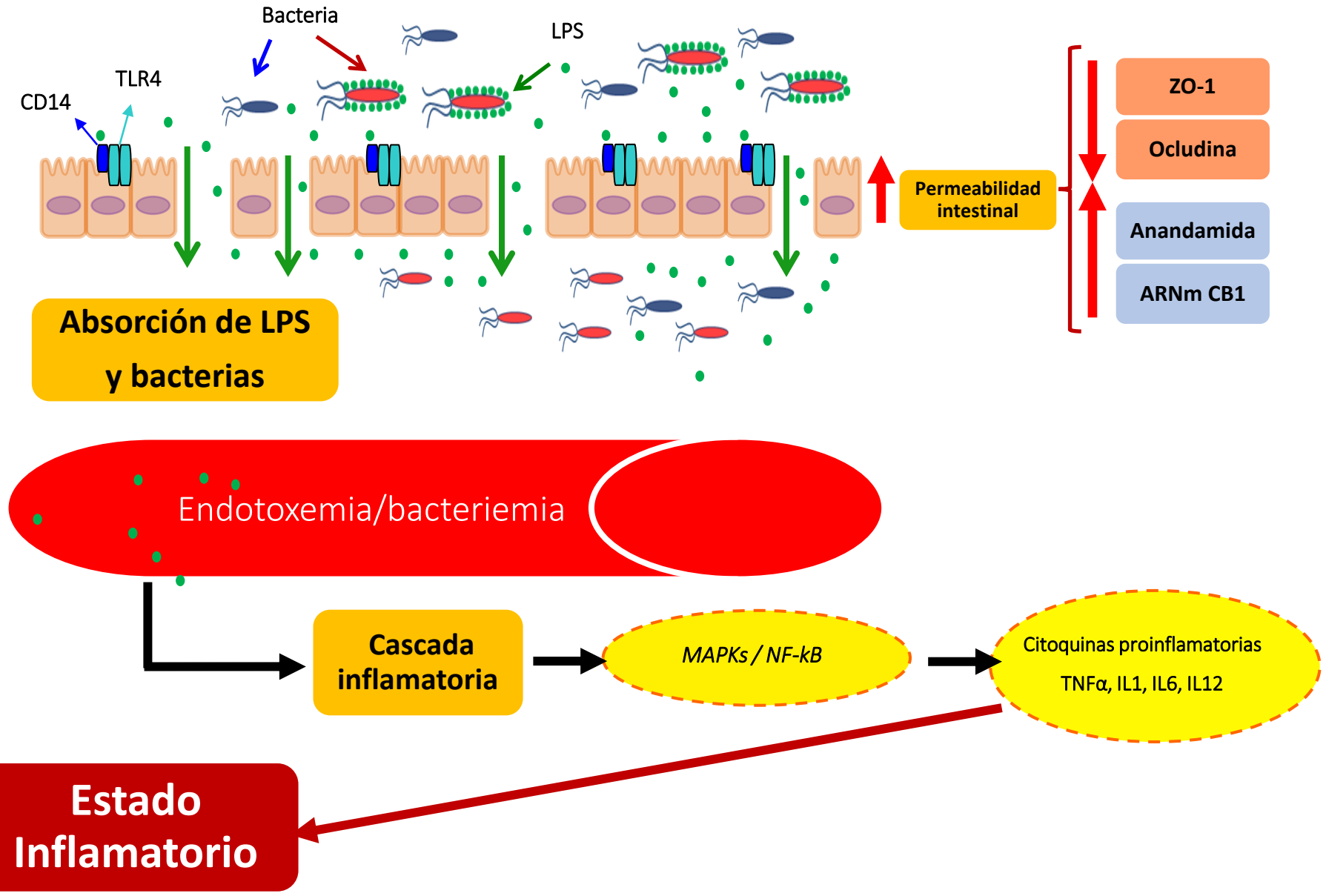
Metabolitos/factores y estimulación del sistema inmune

https://medicodeguardia11235.wordpress.com/2019/04/04/podcast-disbiosis-intestinal/
Instituto de Microecología

Modificado de Mizutani et al., Viruses, 2022

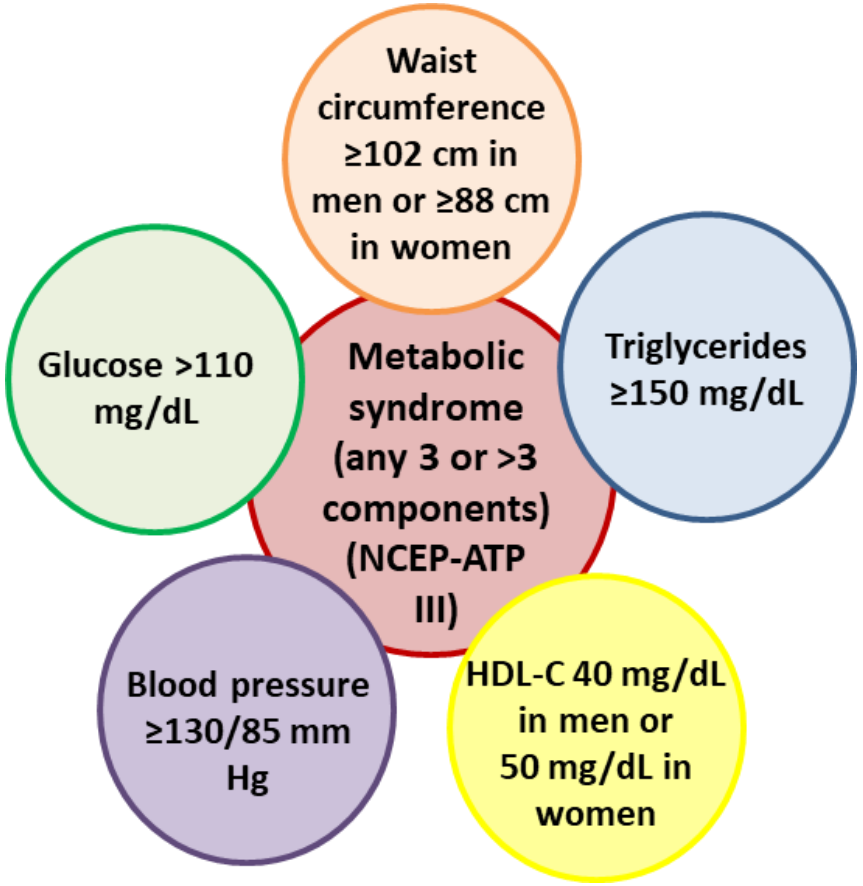
¿Qué ocurre en la infección por el VIH?


Macrófago
VIH
Linfocitos T CD8+
Linfocitos T CD4+
Enterocitos
Moco rico en IgA
Célula dendrítica
Célula M
Tejido linfoide asociado al intestino (GALT)
Equilibrio
Linfocito B
Sistema portal



Villanueva-Millán et al. J Physiol Biochem 2015

Un ejemplo: síndrome metabólico en VIH



Journal of Physiology and Biochemistry (2019) 75:299–309
https://doi.org/10.1007/s13105-019-00673-9

ORIGINAL ARTICLE

Check for updates

Characterization of gut microbiota composition in HIV-infected patients with metabolic syndrome

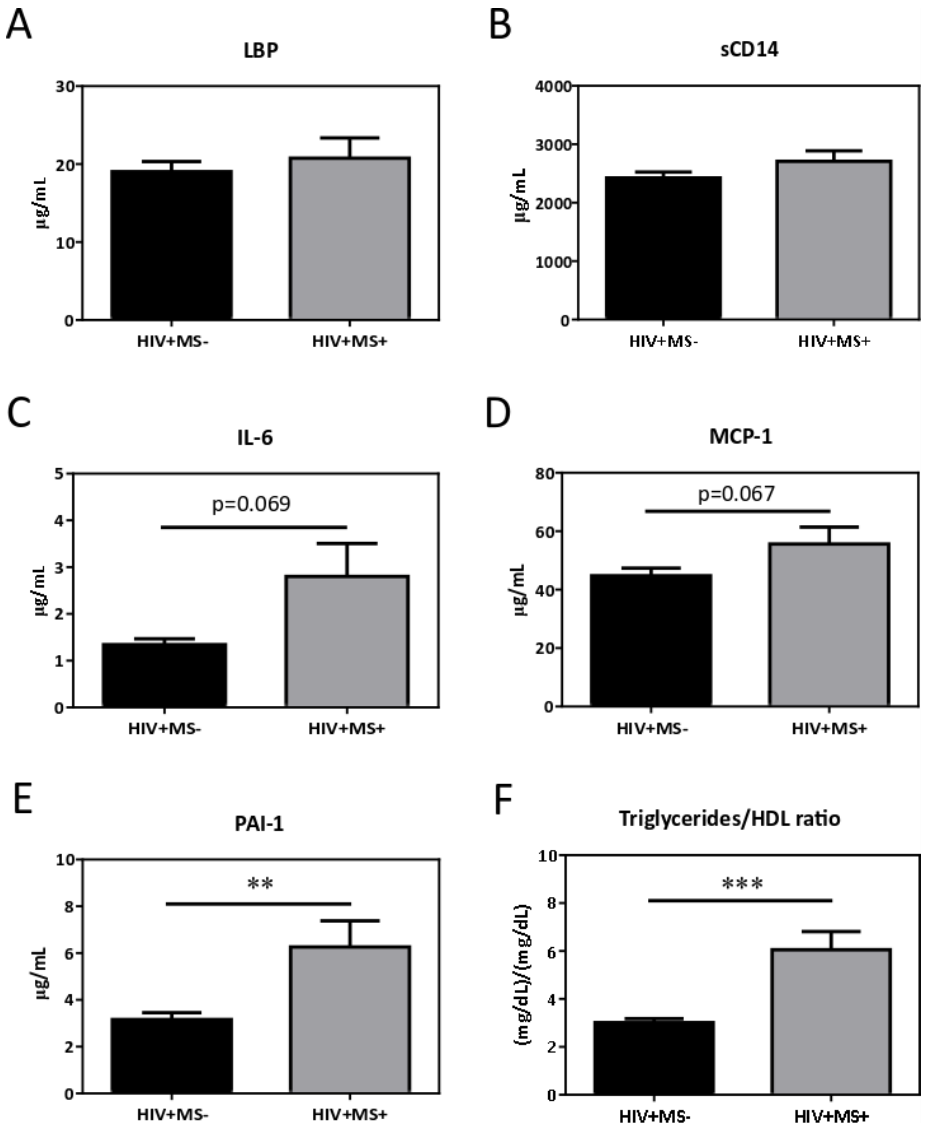
María Jesús Villanueva-Millán[1] · Patricia Pérez-Matute[1] · Emma Recio-Fernández[1] · José-Miguel Lezana Rosales[1] · José-Antonio Oteo[1,2]

Received: 15 October 2018 / Accepted: 6 March 2019 / Published online: 28 March 2019

Abstract
The presence of metabolic syndrome (MS) per se or its separated components in HIV-infected patients contributes to an accelerated aging and increased cardiovascular risk. Gut microbiota (GM) dysbiosis has been linked with chronic inflammation associated with MS in a general non-infected population. However, no studies concerning GM have been performed in HIV-infected patients with MS. The aim of this study was to analyze bacterial translocation, inflammation, and GM composition in HIV-infected patients with and without MS. A total of 51 HIV-infected patients were recruited and classified according to the presence of MS (40 patients without MS and 11 with MS). Markers of bacterial translocation, inflammation, and cardiovascular risk were measured and GM was analyzed using 16S rRNA gene deep sequencing. No differences were observed among both HIV-infected groups in the bacterial translocation markers LBP and sCD14. A tendency to increase the inflammatory markers IL-6 ($p = 0.069$) and MCP-1 ($p = 0.067$) was observed in those patients suffering from MS. An increase in the cardiovascular risk markers PAI-1 ($p = 0.007$) and triglycerides/HDL cholesterol ratio ($p < 0.0001$) was also found in the MS group. No significant changes were observed at phylum level although a decrease in the abundance of seven genera and seven bacterial species, including some anti-inflammatory bacteria, was observed in HIV-infected patients with MS. To summarize, the presence of MS was not accompanied by major changes in GM, although the reduction observed in some anti-inflammatory bacteria may be clinically useful to develop strategies to minimize inflammation and its future deleterious consequences in these HIV-infected patients.

Keywords HIV infection · Metabolic syndrome · Gut microbiota composition · Bacterial translocation · Inflammation · Cardiovascular risk

Prevalencia a nivel global: 16,7-31,3% (Sapula et al., Viruses, 2022)



** *P*<0.01; *** *P*<0.001 *vs*. HIV+MS+

Table 2 The presence of metabolic syndrome in HIV-infected patients was associated with a decrease in the relative abundance of seven genera and seven species in comparison with HIV patients without metabolic syndrome

Phylum	Taxonomic group	Category	FDR
Firmicutes	*Eubacterium*	Genus	0.012
Firmicutes	*Eubacterium eligens*	Species	0.002
Firmicutes	*Faecalibacterium prausnitzii*	Species	0.037
Firmicutes	*Roseburia*	Genus	7.47×10^{-4}
Firmicutes	*Roseburia intestinalis*	Species	0.002
Firmicutes	*Roseburia inulinivorans*	Species	8.85×10^{-4}
Firmicutes	*Ruminococcus*	Genus	3.59×10^{-4}
Firmicutes	*Ruminococcus flavefaciens*	Species	0.002
Firmicutes	*Subdoligranulum*	Genus	0.012
Firmicutes	*Subdoligranulum sp.*	Species	0.002
Proteobacteria	*Desulfovibrio*	Genus	0.019
Proteobacteria	*Sutterella*	Genus	0.002
Proteobacteria	*Sutterella wadsworthensis*	Species	0.002
Actinobacteria	*Coriobacteriales bacterium*	–	0.002
Actinobacteria	*Bifidobacterium*	Genus	0.009

A false discovery rate (FDR) < 0.05 was considered significant

Villanueva-Millán et al. J Physiol Biochem 2019

Disminución de bacterias anti-inflamatorias. PERFIL INFLAMATORIO (Amador-Lara et al., 2022).
Potencial utilidad práctica como «diana» para minimizar el estado inflamatorio y el SM

¿Los ARV impactan en la microbiota?

Bacterioma intestinal: metataxonomía 16s

Villanueva-Millán MJ et al. *Journal of the International AIDS Society* 2017, **20**:21526
http://www.jiasociety.org/index.php/jias/article/view/21526 | http://dx.doi.org/10.7448/IAS.20.1.21526

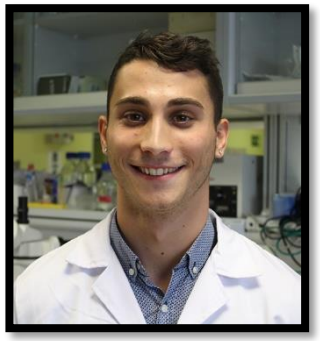
JIAS Journal of the International AIDS Society

Research article

Differential effects of antiretrovirals on microbial translocation and gut microbiota composition of HIV-infected patients

María J. Villanueva-Millán[1], Patricia Pérez-Matute[1§], Emma F
and José A. Oteo[1,2]

[§]**Corresponding author**: Patricia Pérez-Matute, 98, Piqueras Street, Logroño 26006, La



Dres. MJ Villanueva-Millán y P. Villoslada-Blanco

Infect Dis Ther (2022) 11:1541–1557
https://doi.org/10.1007/s40121-022-00654-4

Check for updates

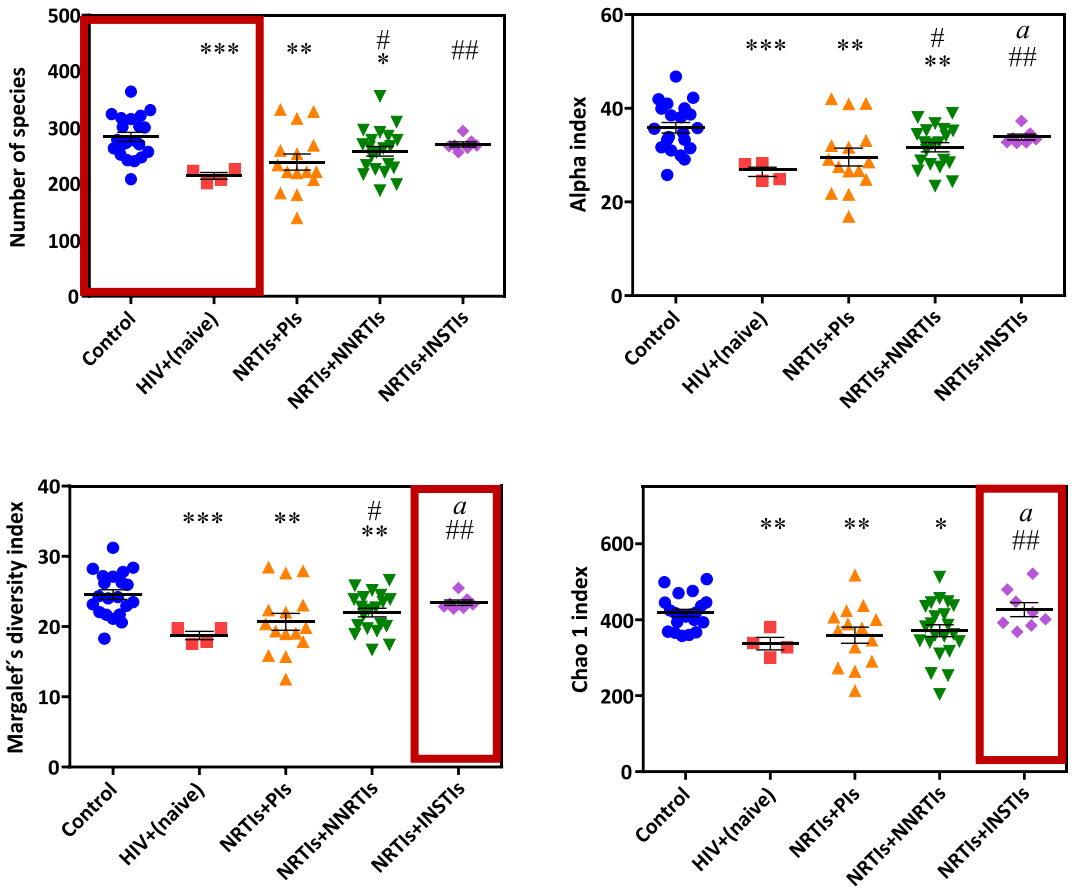
ORIGINAL RESEARCH

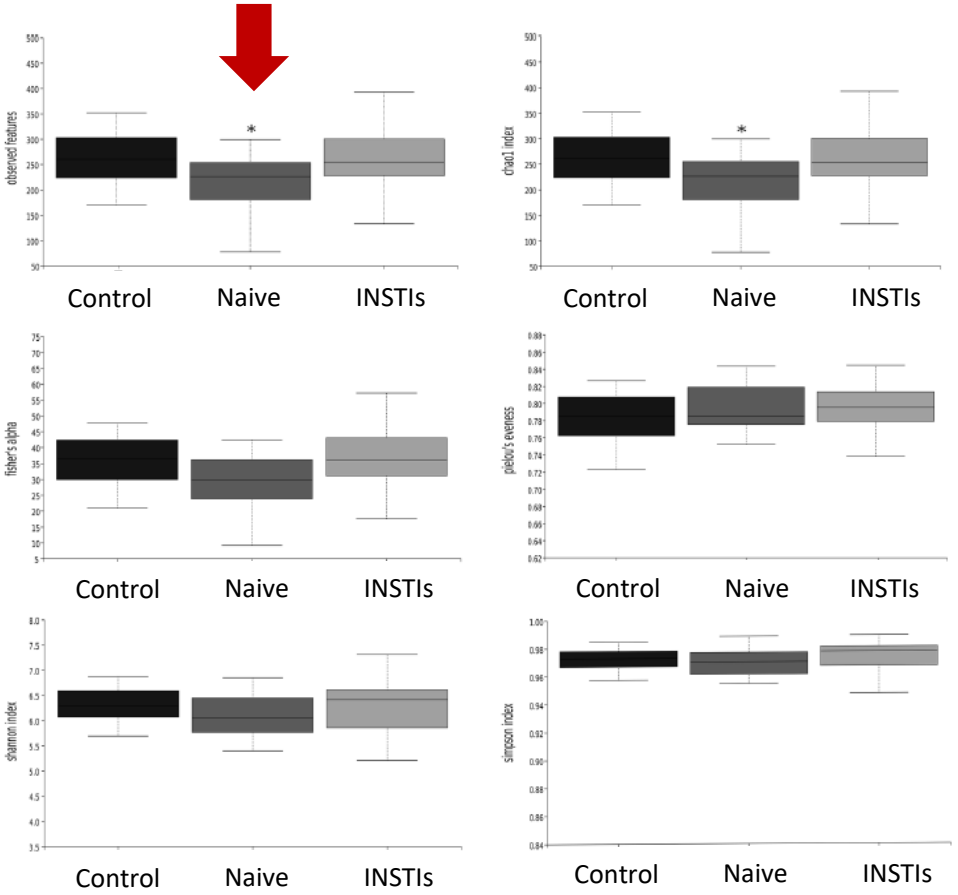
Integrase Inhibitors Partially Restore Bacterial Translocation, Inflammation and Gut Permeability Induced by HIV Infection: Impact on Gut Microbiota

Pablo Villoslada-Blanco · Patricia Pérez-Matute · María Íñiguez ·
Emma Recio-Fernández · Pilar Blanco-Navarrete · Luis Metola ·
Valvanera Ibarra · Jorge Alba · María de Toro · José A. Oteo

Received: March 24, 2022 / Accepted: May 4, 2022 / Published online: May 26, 2022

Alfa diversidad



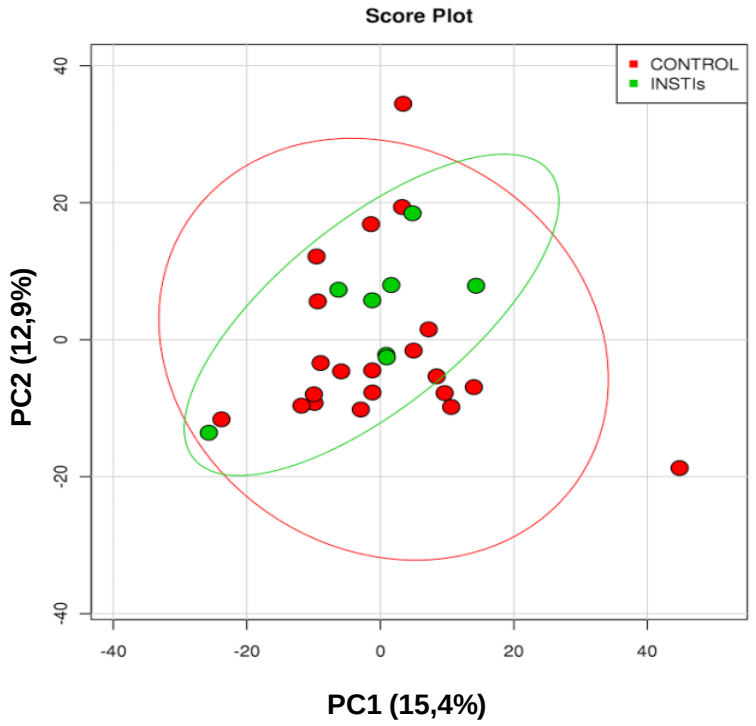


*P<0.05; ** P<0.01; *** P<0.001 *vs*. control, # P<0.05; ## P<0.01 *vs*. HIV+(naive), ^{a}P<0.05 *vs*. NRTIs+PIs

Villanueva-Millán et al., JIAS, 2017
Villoslada-Blanco et al., Infect Dis Ther, 2022

Pacientes VIH tienen menos diversidad bacteriana. INSTIs (RAL) lo revierten.

Beta-diversidad y abundancia relativa



Control vs. Naïve				ART			
Category	Taxonomic group		*W*	Category	Taxonomic group		*W*
				Phylum	Spirochaetes	↑	9
				Phylum	Cyanobacteria	↑	6
Order	Aeromonadales	↑	41	Order	Aeromonadales	↑	42
Genus	*Succinivibrio*	↑	285	Genus	*Succinivibrio*	↑	307
Genus	*Prevotella 2*	↑	285	Genus	*Catenibacterium*	↑	286
Phylum	Verrucomicrobia	↓	9	Phylum	*Bacteroidetes*	↓	4
				Phylum	*Actinobacteria*	↓	4
Genus	*Erysipelotrichaceae UCG-003*	↓	303				
Genus	*Catenibacterium*	↓	292				

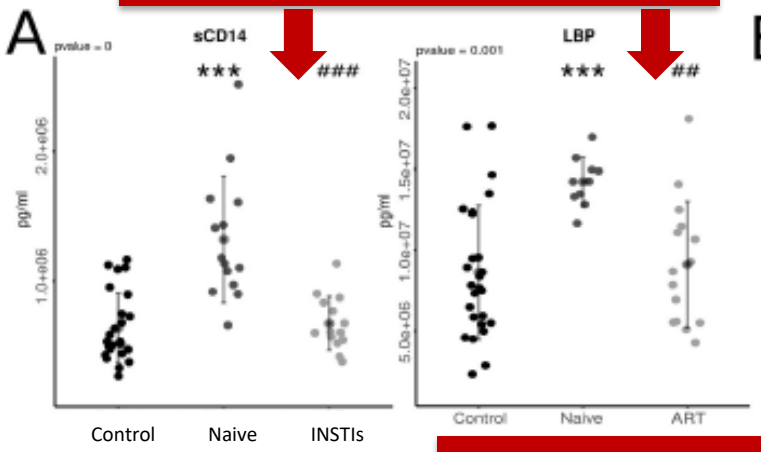
Proteobacteria

Villanueva-Millán et al., JIAS, 2017
Villoslada-Blanco et al., Infect Dis Ther, 2022

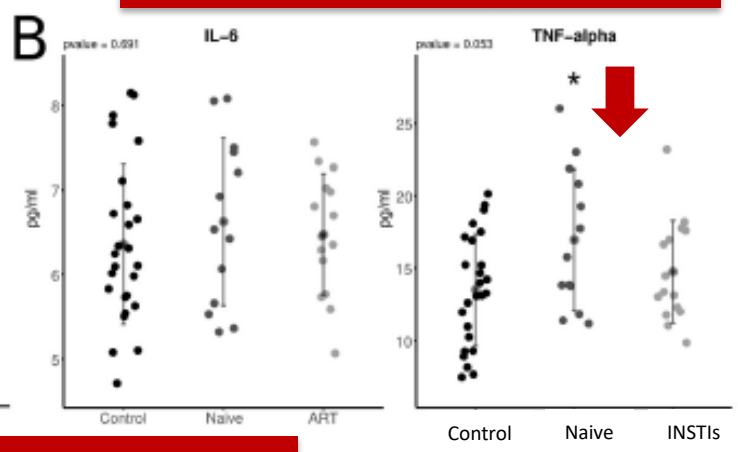
Pacientes con INSTIs presentaron un perfil de su microbiota más parecido a la de los individuos NO infectados.
Restauración parcial de los cambios inducidos por la infección por el VIH

Inflamación, translocación bacteriana y RCV

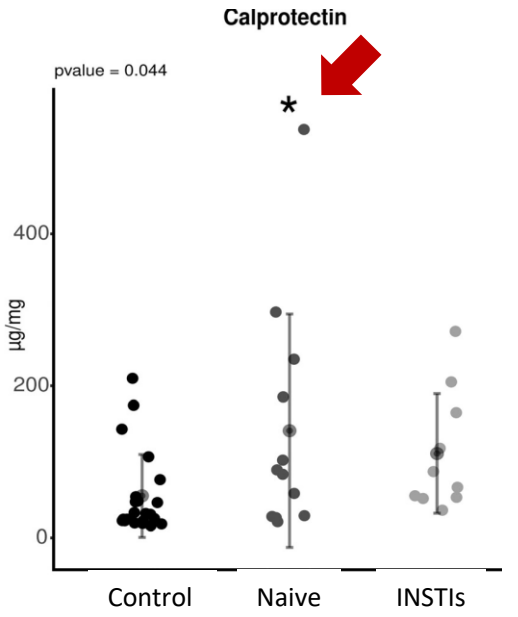
Translocación Bacteriana



Inflamación

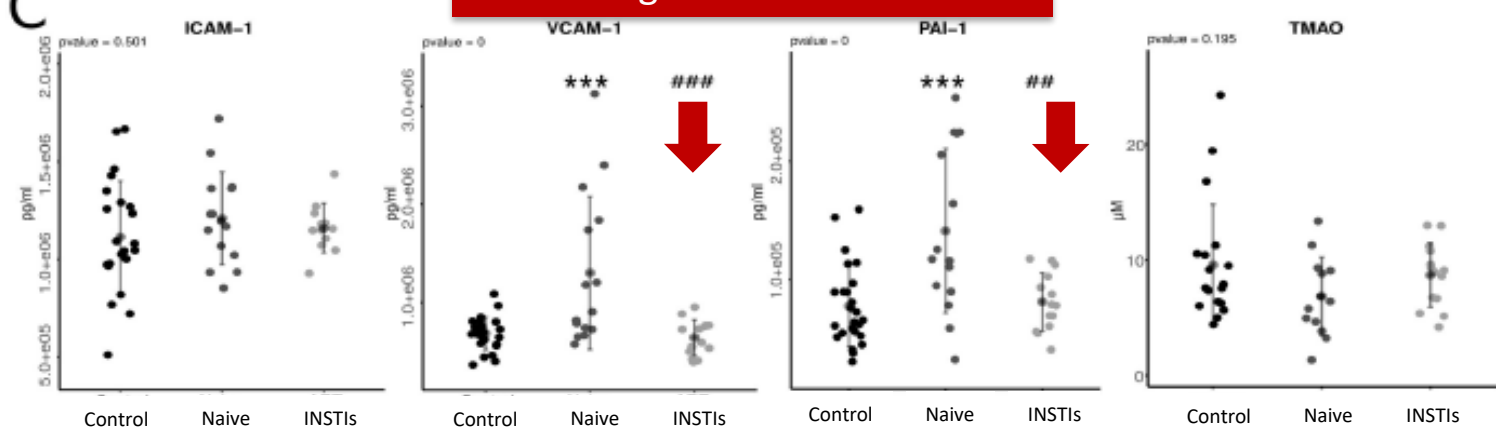


Calprotectina



Villoslada-Blanco et al., Infect Dis Ther, 2022

Riesgo cardiovascular



* p<0.05 *vs.* control
*** p<0.001 *vs.* control
p<0.01 *vs.* naïve
p<0.01 *vs.* naïve

El tratamiento con INSTIs revierte los efectos de la infección por el VIH sobre la translocación bacteriana, permeabilidad intestinal, inflamación y riesgo cardiovascular.

¿Los ARV impactan en el viroma?

Viroma y salud

Published in final edited form as:
Curr Opin Virol. 2019 August ; 37: 37–43. doi:10.1016/j.coviro.2019.05.007.

Virome and bacteriome: Two sides of the same coin

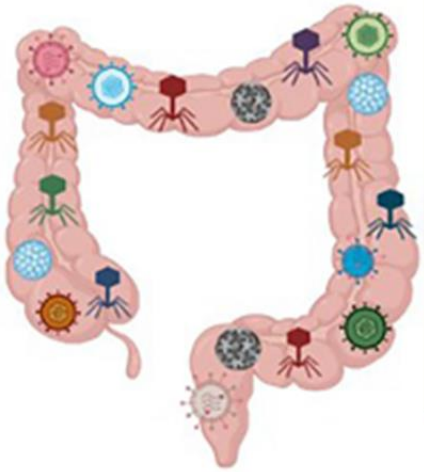
Jonathan Stern[1], **George Miller**[2], **Xin Li**[1], **Deepak Saxena**[1,2]
[1]Department of Basic Science, New York University College of Dentistry, New York NY 10010
[2]S. Arthur Localio Laboratory, Departments of Surgery New York University School of Medicine, New York, NY 10016

Abstract

Although bacterial dysbiosis has been previously associated with carcinogenesis and HIV infection, the impact of the virome and these disease states has been less well studied. In this review, we will summarize what is known about the interplay between both the bacterial and the viral components of the microbiome on cancer and HIV pathogenesis. Bacterial dysbiosis has been associated with carcinogenesis such as colorectal cancer (CRC), hepatocellular carcinoma (HCC), lung cancer, breast cancer, and gastric cancer. The dysbiotic pathogenesis may be species-based or community-based and can have varying mechanisms of carcinogenesis. The human virome was also associated with certain cancers. Viruses, such as cytomegalovirus (CMV), Human herpesvirus 8 (HHV-8), human papilloma virus (HPV), hepatitis B virus (HBV), hepatitis C virus (HCV), and Epstein-Barr virus (EBV), all had associations with cancers. It was also reported that an altered bacteriophage community may lead to carcinogenesis by allowing opportunistic, oncogenic bacteria to proliferate in a gastrointestinal biofilm. This mechanism shows the importance of analyzing the bacteriome and the virome concurrently as their interactions can provide insight into new mechanisms in the pathogenesis of not only cancer, but other diseases as well. The enteric bacteriome was shown to be distinctly altered in immunocompromised HIV-infected individuals and highly active antiretroviral therapy (HAART) was shown to at least partially reverse the alterations that HIV causes in the bacteriome. Studies have shown that the progression to HIV is associated with changes in the plasma concentration of commensal viruses. HIV also act synergistically with multiple other viruses, such as HPV, EBV, varicella zoster virus (VZV), and HHV-8. Although it has been shown that HIV infection leads to enteric virome expansion in humans, most of the research on HIV's effect on the virome was conducted in non-human primates and there is a lack of research on the effect of HAART on the virome. Virome-wide analysis is necessary for identifying novel viral etiologies. There is currently a wealth of information on the bacteriome and its associations with cancer and HIV, but more research should be conducted on the virome's associations and reaction to HAART as well as the bacteriomevirome interactions that may play a major role in pathogenesis and recovery.

Composición del viroma intestinal

Bacteriófagos: 97,7%
Virus eucariotas: 2,1%
Virus Arqueas: 0,1%



Efectos protectores del viroma

AGENTES TERAPÉUTICOS
Enfermedades neurodegenerativas
Cáncer

PROTECCIÓN FRENTE A BACTERIAS PATÓGENAS

Viroma intestinal y enfermedades intestinales

Enfermedad inflamatoria intestinal

Cáncer gástrico y colorrectal

Modificado de Spencer et al., Front Cell Infect Microbiol, 2022

www.nature.com/scientificreports

scientific reports

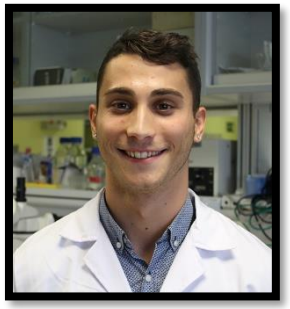
Check for updates

OPEN

Impact of HIV infection and integrase strand transfer inhibitors-based treatment on the gut virome

Pablo Villoslada-Blanco[1], Patricia Pérez-Matute[1]✉, María Íñiguez[1], Emma Recio-Fernández[1], Daan Jansen[2], Lander De Coninck[2], Lila Close[2], Pilar Blanco-Navarrete[3], Luis Metola[4], Valvanera Ibarra[4], Jorge Alba[4], Jelle Matthijnssens[2] & José A. Oteo[1,4]

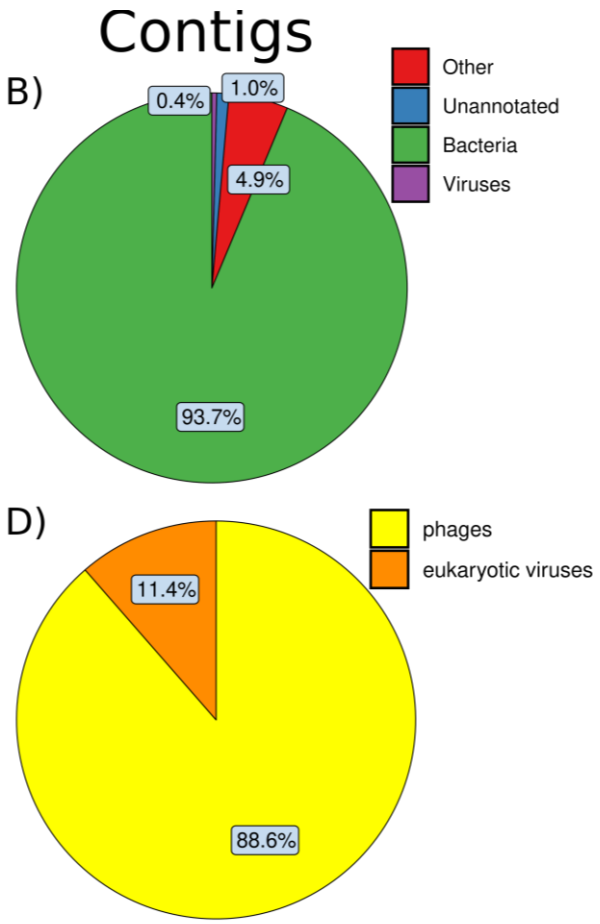
Viruses are the most abundant components of the human gut microbiome with a significant impact on health and disease. The effects of human immunodeficiency virus (HIV) infection on gut virome has been scarcely analysed. Several studies suggested that integrase strand transfers inhibitors (INSTIs) are associated with a healthier gut. Thus, the objective of this work was to evaluate the effects of HIV infection and INSTIs on gut virome composition. 26 non-HIV-infected volunteers, 15 naive HIV-infected patients and 15 INSTIs-treated HIV-infected patients were recruited and their gut virome composition was analysed using shotgun sequencing. Bacteriophages were the most abundant and diverse viruses present in gut. HIV infection was accompanied by a decrease in phage richness which was reverted after INSTIs-based treatment. β-diversity of phages revealed that samples from HIV-infected patients clustered separately from those belonging to the control group. Differential abundant analysis showed an increase in phages belonging to Caudoviricetes class in the naive group and a decrease of Malgrandaviricetes class phages in the INSTIs-treated group compared to the control group. Besides, it was observed that INSTIs-based treatment was not able to reverse the increase of lysogenic phages associated with HIV infection or to modify the decrease observed on the relative abundance of Proteobacteria-infecting phages. Our study describes for the first time the impact of HIV and INSTIs on gut virome and demonstrates that INSTIs-based treatments are able to partially restore gut dysbiosis at the viral level, which opens several opportunities for new studies focused on microbiota-based therapies.

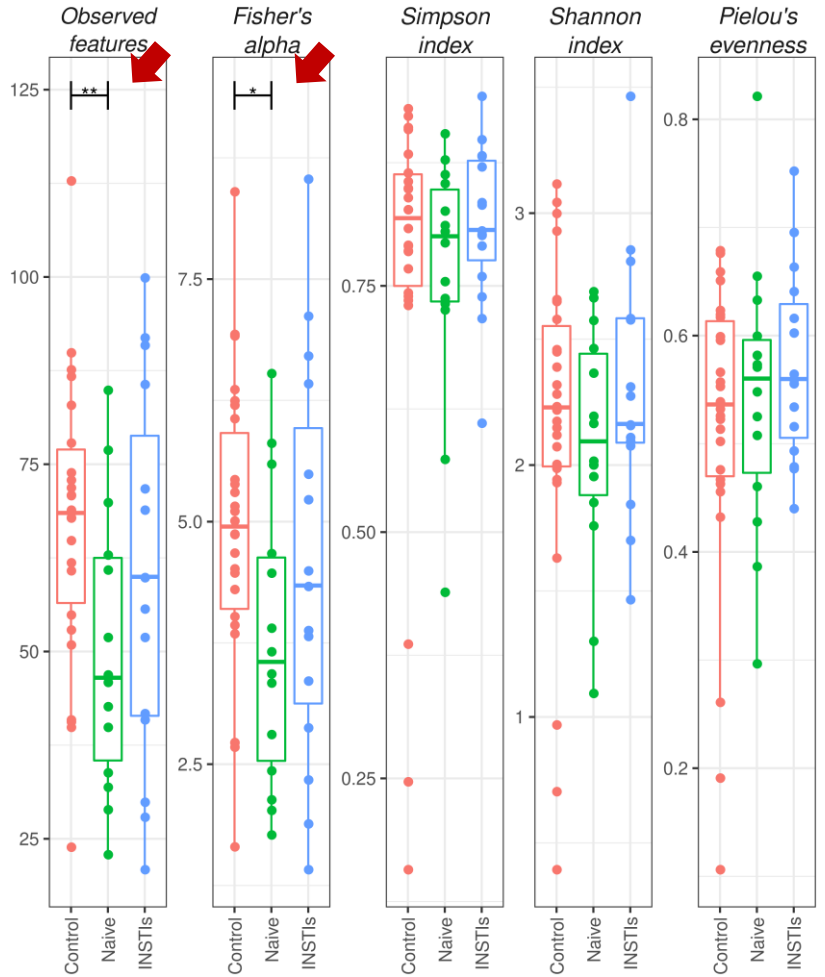


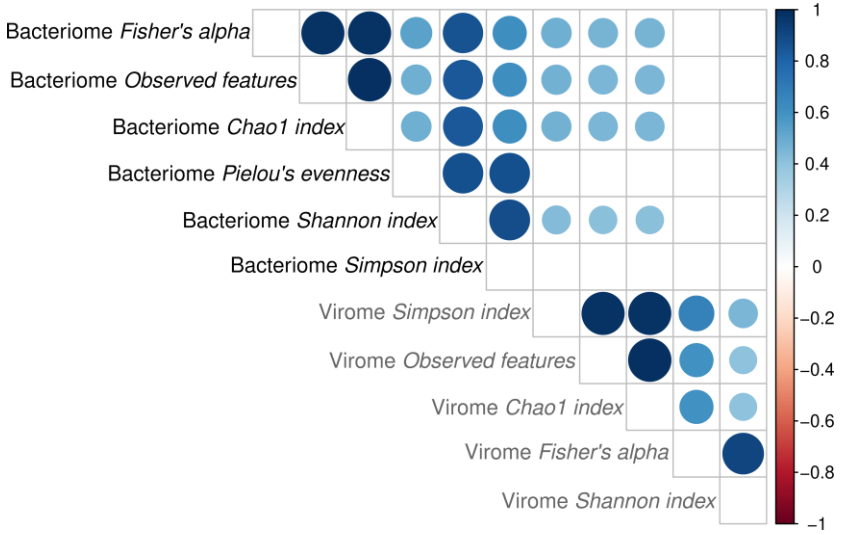
Dr. P. Villoslada-Blanco

KU LEUVEN

Infección por VIH y VIROMA

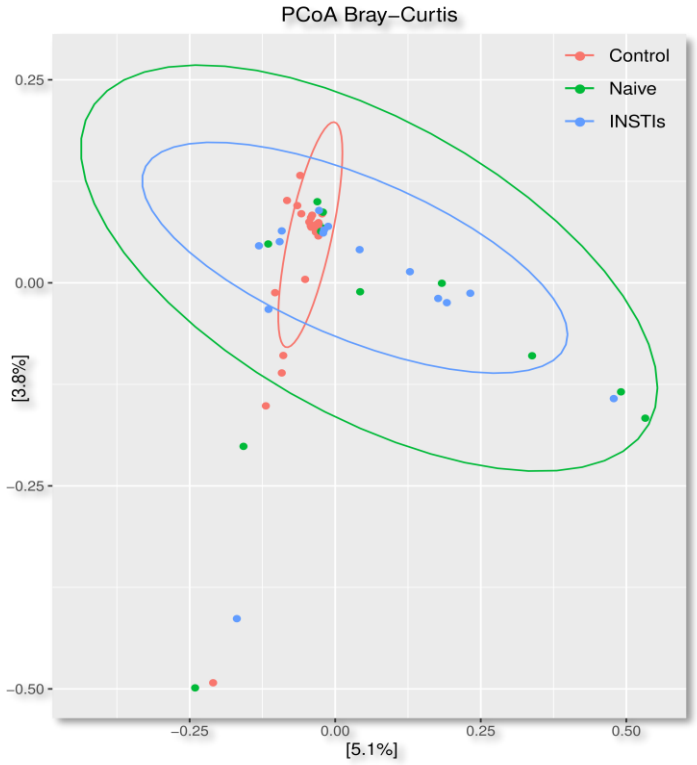




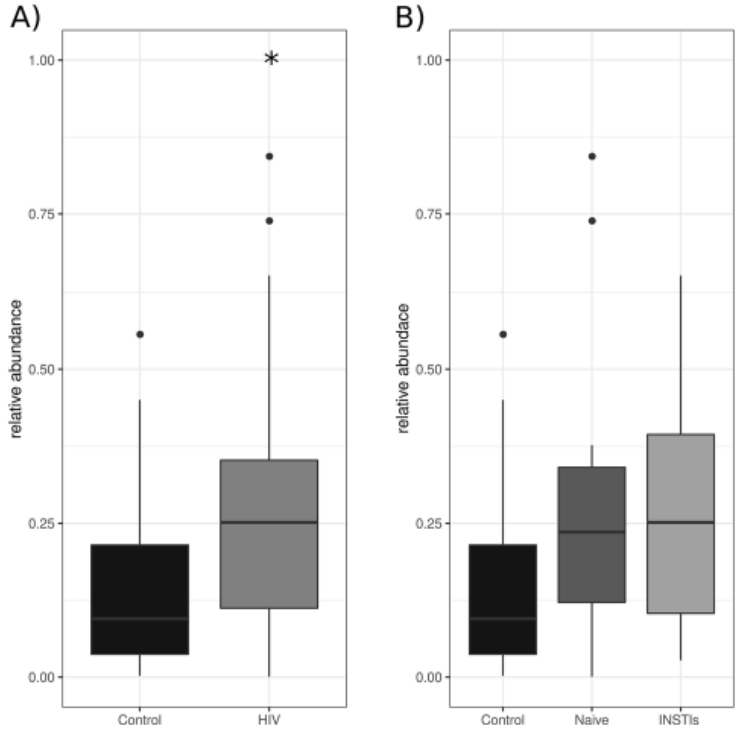


INSTIs revierten la disminución observada en alfa-diversidad en fagos

Infección por VIH y fagos

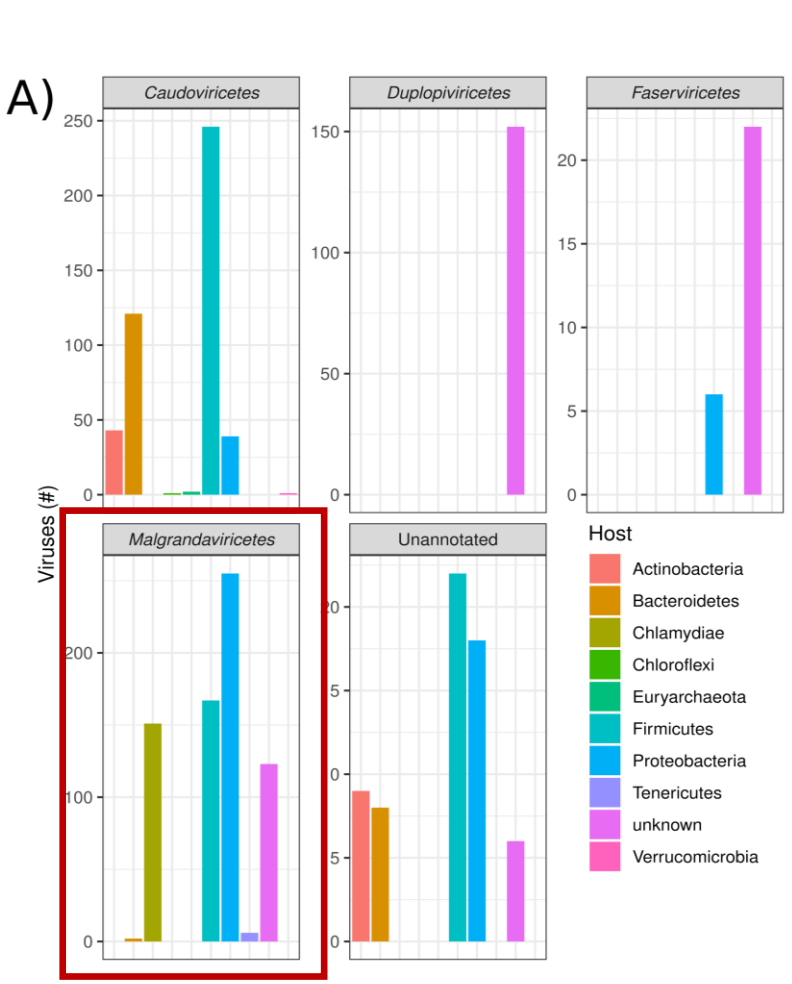


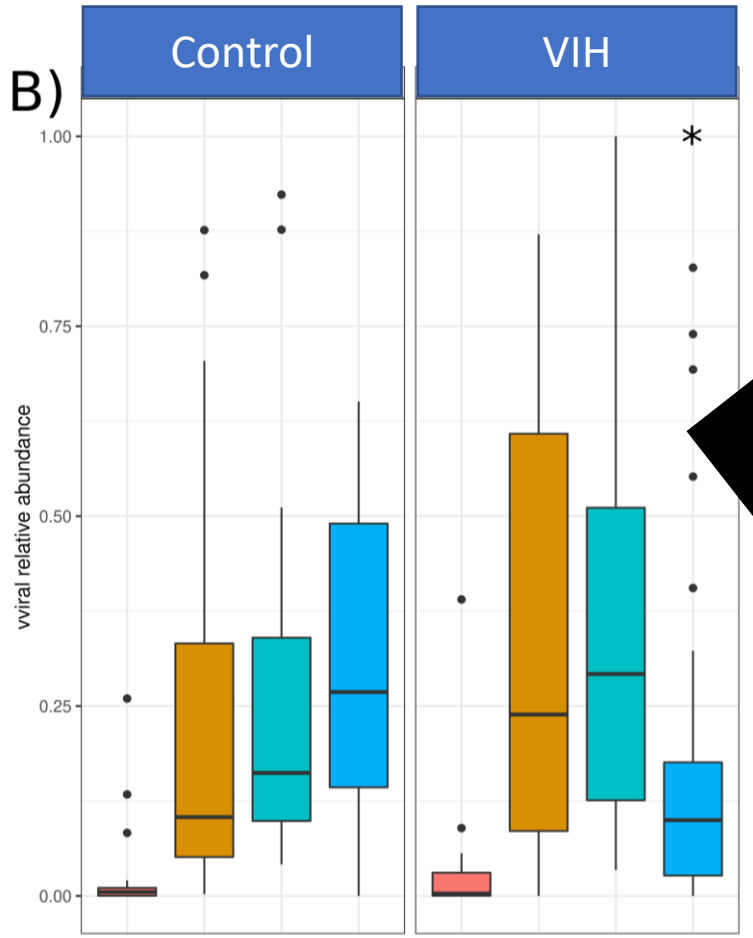
Control vs.							
Naive				INSTIs			
Category	Taxonomic group		padj	Category	Taxonomic group		padj
Phylum	Uroviricota	↑	0.011	Phylum	Phixviricota	↓	<0.001
Class	Caudoviricetes	↑	0.011	Class	Malgrandaviricetes	↓	<0.001

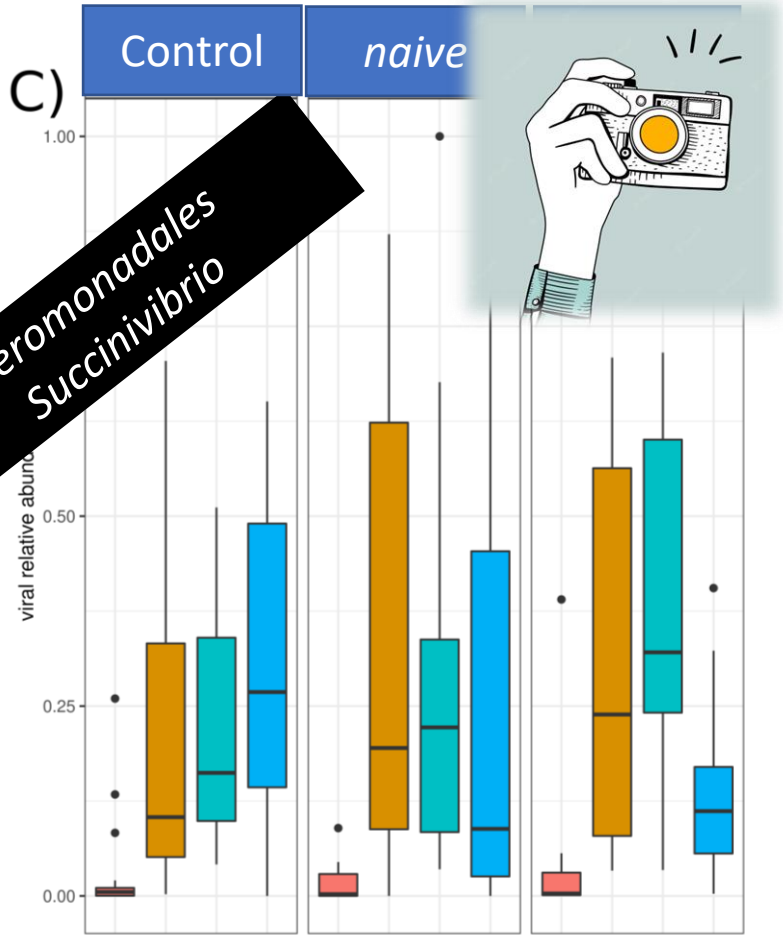


Incremento en la abundancia relativa de fagos lisogénicos no contrarrestado por INSTIs

Predicción del huésped





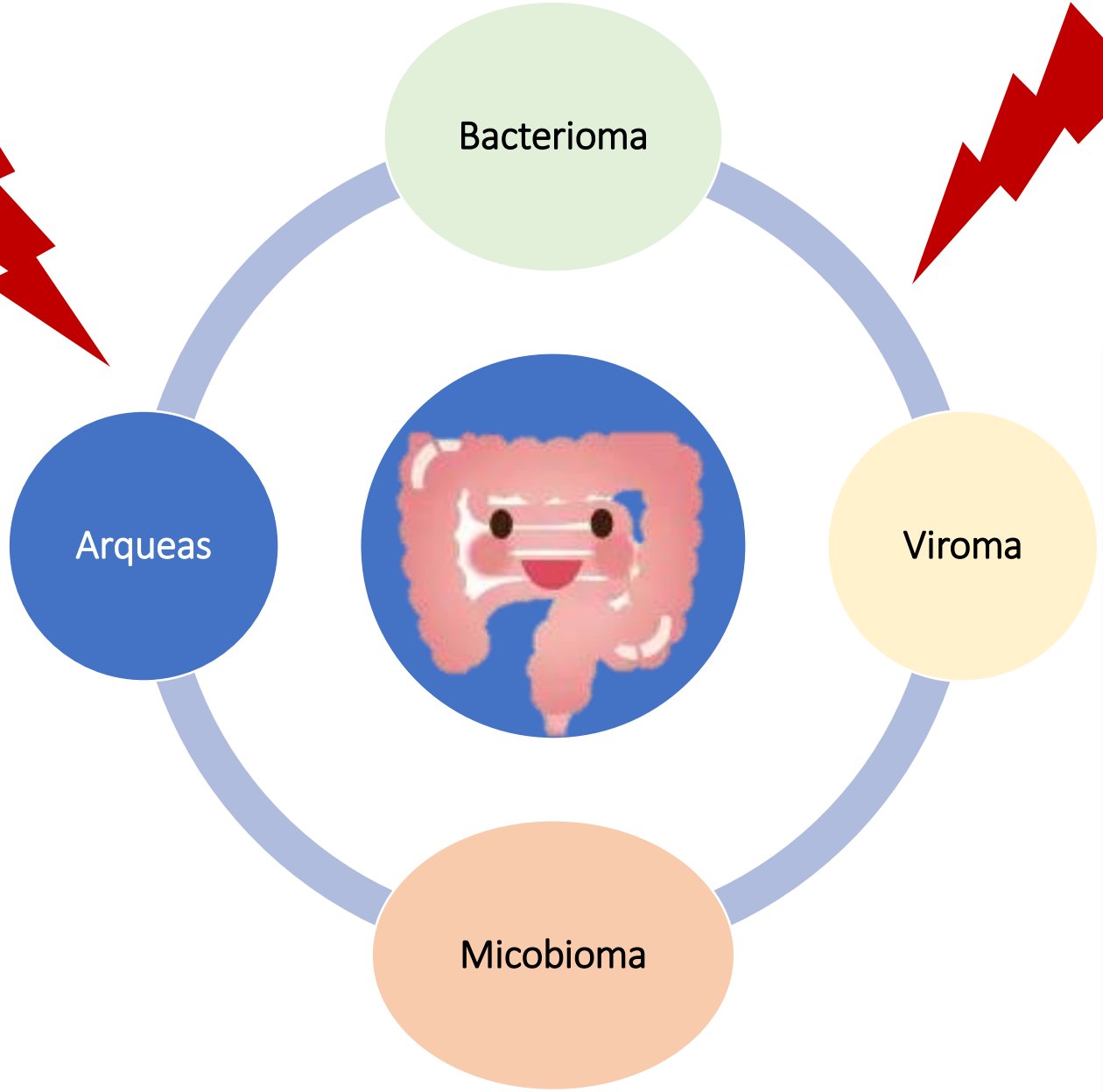


Aeromonadales
Succinivibrio

Los INSTIs no parecen revertir la disminución observada en la abundancia de fagos que infectan a Proteobacteria

VIH

ARV



- Disminuir el estado inflamatorio crónico
- Disminuir la presencia de comorbilidades no-SIDA
- MEJORAR LA CALIDAD DE VIDA DEL PACIENTE

GUT MICROBES
2022, VOL. 14, NO. 1, e2089002 (17 pages)
https://doi.org/10.1080/19490976.2022.2089002

Taylor & Francis
Taylor & Francis Group

RESEARCH PAPER

OPEN ACCESS Check for updates

Interactions among the mycobiome, bacteriome, inflammation, and diet in people living with HIV

María José Gosalbes[a,b], Nuria Jimenéz-Hernandéz[a,b], Elena Moreno[c,d], Alejandro Artacho[b], Xavier Pons[b], Sonia Ruíz-Pérez[b], Beatriz Navia[e], Vicente Estrada[d,f], Mónica Manzano[e], Alba Talavera-Rodriguez[c,d], Nadia Madrid[c,d], Alejandro Vallejo[c,d], Laura Luna[c,d], José A. Pérez-Molina[c,d], Santiago Moreno[c,d], and Sergio Serrano-Villar[c,d]

[a]CIBER de Epidemiología y Salud Pública, Madrid, Spain; [b]Genomics and Health Area, Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana, Valencia, Spain; [c]Department of Infectious Diseases, IRYCIS, Hospital Ramón y Cajal, Madrid, Spain; [d]CIBER de Enfermedades Infecciosas, Madrid, Spain; [e]Department of Nutrition and Food Science, Universidad Complutense de Madrid, Madrid, Spain; [f]HIV Unit, Hospital Clínico San Carlos, Madrid, Spain

ABSTRACT

While the intestinal microbiome seems a major driver of persistent immune defects in people with HIV (PWH), little is known about its fungal component, the mycobiome. We assessed the inter-kingdom mycobiome–bacteriome interactions, the impact of diet, and the association with the innate and adaptive immunity in PWH on antiretroviral therapy. We included 24 PWH individuals and 12 healthy controls. We sequenced the Internal Transcribed Spacer 2 amplicons, determined amplicon sequence variants, measured biomarkers of the innate and adaptive immunity in blood and relations with diet. Compared to healthy controls, PWH subjects exhibited a distinct and richer mycobiome and an enrichment for *Debaryomyces hansenii, Candida albicans*, and *Candida parapsilosis*. In PWH, *Candida* and *Pichia* species were strongly correlated with several bacterial genera, including *Faecalibacterium* genus. Regarding the links between the mycobiome and systemic immunology, we found a positive correlation between *Candida* species and the levels of proinflammatory cytokines (sTNF-R2 and IL-17), interleukin 22 (a cytokine implicated in the regulation of mucosal immunity), and CD8+ T cell counts. This suggests an important role of the yeasts in systemic innate and adaptive immune responses. Finally, we identified inter-kingdom interactions implicated in fiber degradation, short-chain fatty acid production, and lipid metabolism, and an effect of vegetable and fiber intake on the mycobiome. Therefore, despite the great differences in abundance and diversity between the bacterial and fungal communities of the gut, we defined the changes associated with HIV, determined several different inter-kingdom associations, and found links between the mycobiome, nutrient metabolism, and systemic immunity.

ARTICLE HISTORY
Received 2 May 2022
Revised 20 May 2022
Accepted 3 June 2022

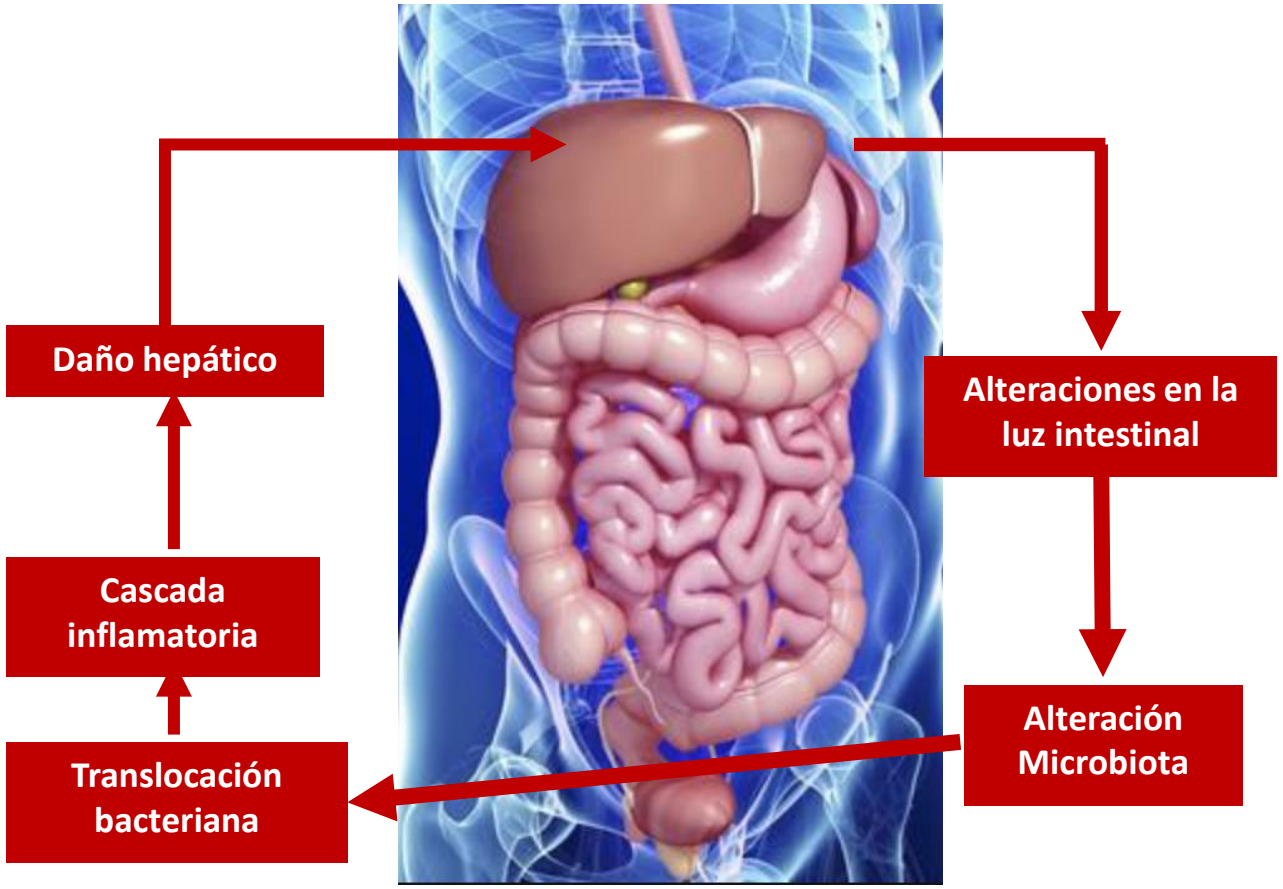
KEYWORDS
Mycobiome; bacteriome; high-throughput sequencing; ITS2; inflammation; diet; HIV

Nuestra experiencia con otras enfermedades infecciosas… VHC

SEI NORTE
SOCIEDAD DE ENFERMEDADES

GILEAD

Eje hígado-intestino



¿Y los ADD?

WJCID World Journal of Clinical Infectious Diseases

Submit a Manuscript: http://www.wjgnet.com/esps/ World J Clin Infect Dis 2017 February 25; 7(1): 1-5

DOI: 10.5495/wjcid.v7.i1.1 ISSN 2220-3176 (online)

EDITORIAL

Is it enough to eliminate hepatitis C virus to reverse the damage caused by the infection?

Patricia Pérez-Matute, José A Oteo

Patricia Pérez-Matute, José A Oteo, Infectious Diseases Department, Center for Biomedical Research of La Rioja (CIBIR)-Hospital San Pedro, 26006 Logroño, La Rioja, Spain

Author contributions: Pérez-Matute P and Oteo JA contributed to this paper.

Conflict-of-interest statement: Authors declare no conflict of interests.

Manuscript source: Invited manuscript

Correspondence to: José A Oteo, MD, PhD, Head of the Infectious Disease Department, Center for Biomedical Research of La Rioja (CIBIR)-Hospital San Pedro, c/Piqueras, 98, 26006 Logroño, La Rioja, Spain. jaoteo@riojasalud.es
Telephone: +34-941-278871
Fax: +34-941-298667

Received: August 26, 2016
Peer-review started: August 27, 2016
First decision: October 28, 2016
Revised: November 18, 2016
Accepted: December 1, 2016
Article in press: December 2, 2016
Published online: February 25, 2017

elimination of the HCV from the body through treatment is now possible. However, HCV not only alters the hepatic function. Several extra-hepatic manifestations are present in HCV-infected patients, which increase the mortality rate. Liver and gut are closely associated in what is called the "gut-liver axis". A disrupted gut barrier leads to an increase in bacterial translocation and an activation of the mucosal immune system and secretion of inflammatory mediators that plays a key role in the progression of liver disease towards decompensated cirrhosis in HCV-infected patients. In addition, both qualitative and quantitative changes in the composition of the gut microbiota (GM) and states of chronic inflammation have been observed in patients with cirrhosis. Thus, a successful treatment of HCV infection should be also accompanied by a complete restoration of GM composition in order to avoid activation of the mucosal immune system, persistent inflammation and the development of long-term complications. Evaluation of GM composition after treatment could be of interest as a reliable indicator of the total or partial cure of these patients. However, studies focused on microbiota composition after HCV eradication from the body are lacking, which opens unique opportunities to deeply explore and investigate this exciting field.

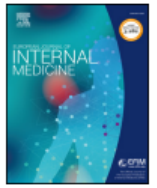
Key words: Hepatitis C infection; Inflammation; Virus eradication; Direct-acting antivirals; Gut microbiota

European Journal of Internal Medicine 67 (2019) 47–58

Contents lists available at ScienceDirect

European Journal of Internal Medicine

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



Original Article

Short-term effects of direct-acting antiviral agents on inflammation and gut microbiota in hepatitis C-infected patients

Patricia Pérez-Matute[a,*], María Íñiguez[a], María J. Villanueva-Millán[a,1], Emma Recio-Fernández[a], Aitana Morano Vázquez[b], Sheila Castro Sánchez[c], Luís E. Morano[c,d], José A. Oteo[a,e]

[a] Infectious Diseases, Microbiota and Metabolism Unit, Infectious Diseases Department, Center for Biomedical Research of La Rioja (CIBIR), Logroño, (La Rioja), Spain
[b] Preventive Medicine, Hospital 12 October, Madrid, Spain
[c] Fundación Biomédica Galicia Sur, Instituto de Investigación Sanitaria Galicia Sur, Vigo, (Galicia), Spain
[d] Infectious Diseases Department, Hospital Universitario Álvaro Cunqueiro, Vigo, (Galicia), Spain
[e] Infectious Diseases Department, Hospital Universitario San Pedro, Logroño, (La Rioja), Spain

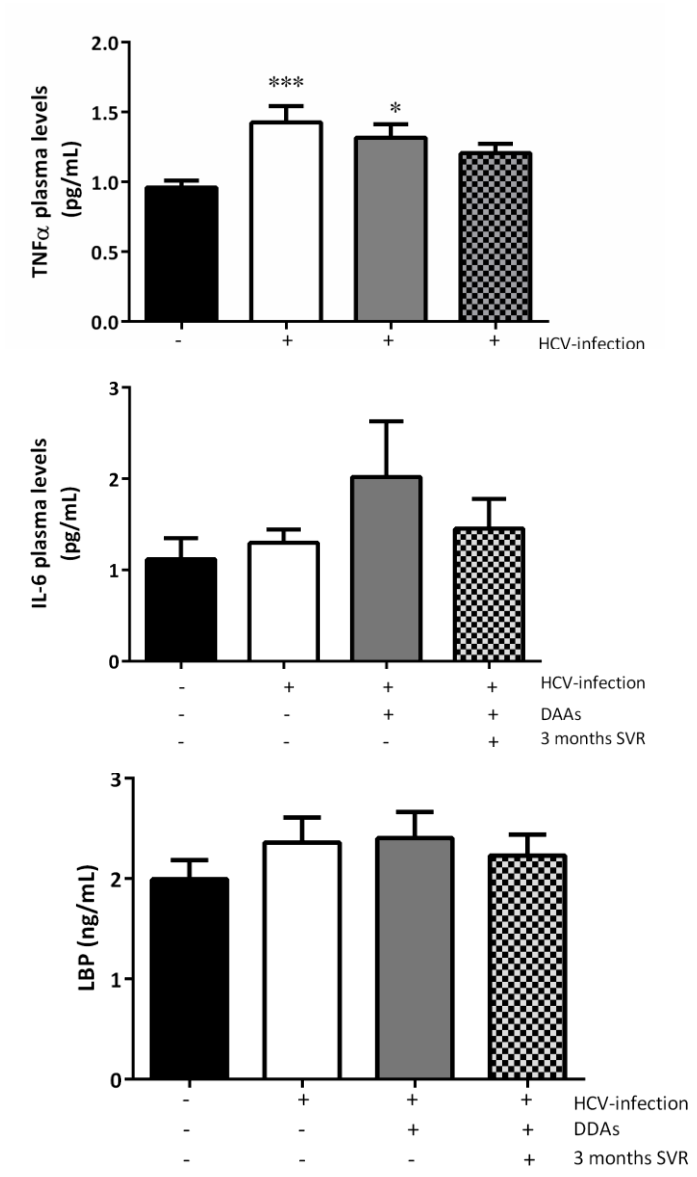
ARTICLE INFO

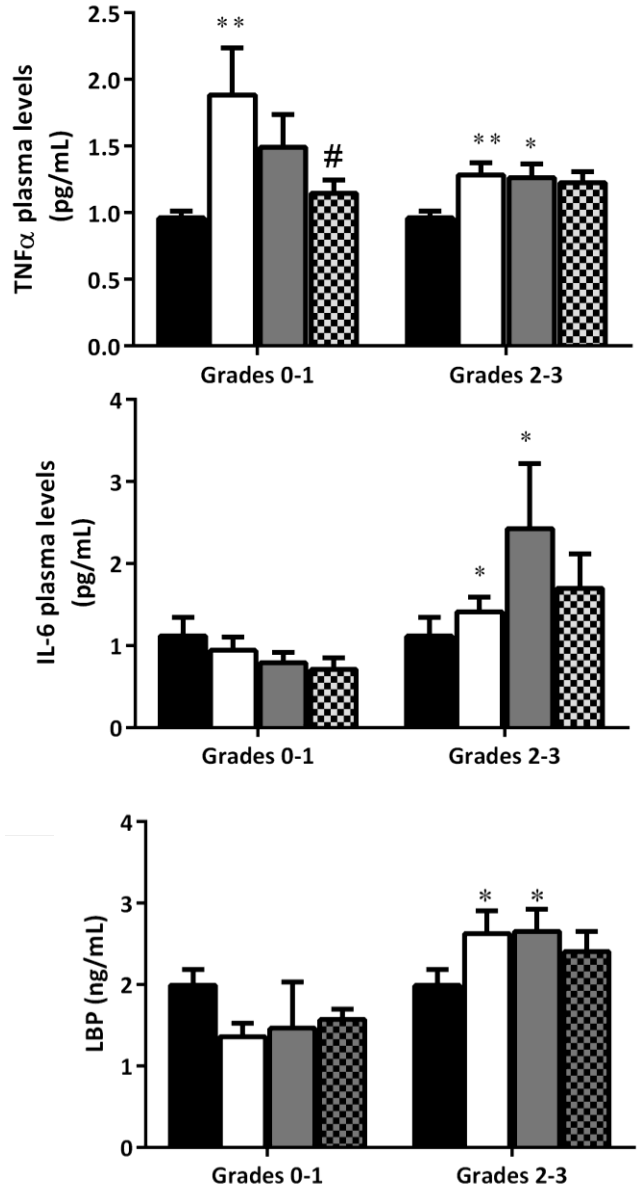
Keywords:
Hepatitis C
Direct-acting antivirals
Gut microbiota
Inflammation
Fibrosis degree

ABSTRACT

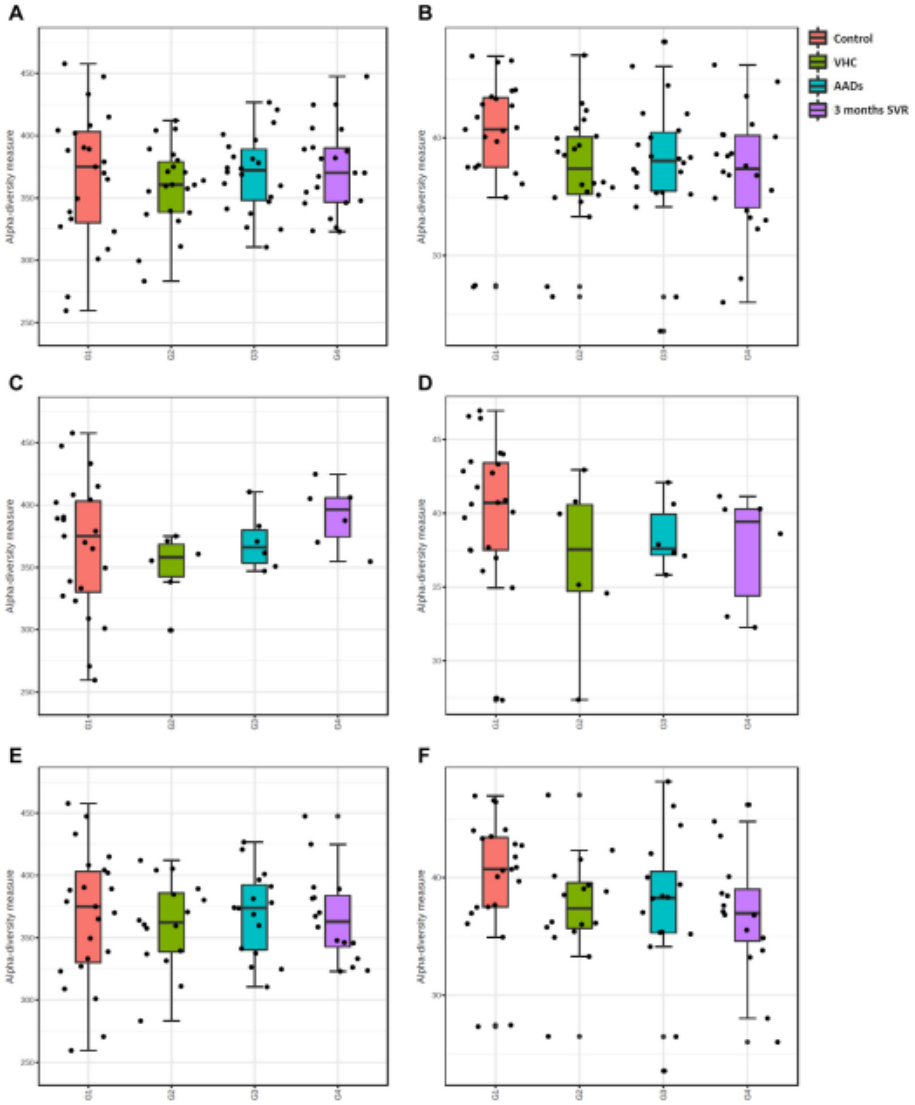
Liver damage is associated with gut dysbiosis. New direct-acting antiviral agents (DAAs) are able to eradicate hepatitis C virus (HCV) from the body. However, the short and medium-term effects of DAAs at gut level before advanced liver damage occurs have not been evaluated yet. Thus, we investigated the impact of HCV and DAAs on gut microbiota composition (GM) and systemic inflammation. To achieve this objective, twenty-three non HCV-infected controls and 22 HCV-infected patients were recruited. Only non-cirrhotic patients (fibrosis stage 0–3) were included to avoid the direct impact of cirrhosis and portal hypertension on gut. The HCV-groups were evaluated before the treatment, after completing DAAs treatment and after 3 months. Fecal bacterial 16S rDNA was ultrasequenced and several biochemical/metabolic/inflammatory parameters were quantified. HCV infection was accompanied by a significant increase in TNFα plasma levels. DAAs were able to reduce this increase, especially in lower fibrosis grades. HCV infection was not accompanied by dramatic changes in α-diversity and was not recovered after HCV negativization, although a complete restoration was observed in lower fibrosis degrees. Six phyla, 15 genera and 9 bacterial species resulted differentially abundant among the groups. These differences were almost blunted with lower fibrosis. In summary, neither the usage of DAAs nor 3 months in sustained viral response were able to counteract the changes induced by HCV at gut level. The partial restoration observed in inflammation and α-diversity was only observed in low fibrosis degrees. Thus, it is urgent to begin treatment with DAAs as soon as possible.

Inflamación y translocación bacteriana





Pacientes no cirróticos (n=22)



		All fibrosis degrees	Abundance in HCV-patients	Do DAAs restore?	F0–1 fibrosis degree	F2–3 fibrosis degree
Phylum	Genera	FDR			FDR	FDR
Actinobacteria	*Collinsella*	2.04e-6	↑	No	0.0286	2.25e-6
Firmicutes	*Blautia*	2.04e-6	↑	No	0.0034	2.32e-5
Actinobacteria	*Actinomyces*	1.09e-4	↑	No	0.0276	2.07e-4
Actinobacteria	*Bifidobacterium*	1.09e-4	↑	No	0.0093	5.67e-4
Firmicutes	*Lachnospira*	2.43e-4	↓	Yes	–	1.12e-4
Firmicutes	*Coprococcus*	1.09e-4	↑	No	–	1.17e-4
Firmicutes	*Lactobacillus*	2.43e-4	↑	No	–	2.32e-5
Firmicutes	*Megasphaera*	1.64e-4	↑	No	–	9.91e-5
Firmicutes	*Acidaminococcus*	1.091e-4	↑	No	0.0342	1.04e-4
Firmicutes	*Streptococcus*	0.0012	↑	No	0.0462	0.0055
Firmicutes	*Turicibacter*	0.0016	↑	No	–	0.0056
Firmicutes	*Dorea*	0.0046	↑	Yes	–	0.0058
Firmicutes	*Clostridium*	0.0267	↑	No	–	0.0146
Firmicutes	*Veillonella*	0.0274	↑	No	–	–
Verrucomicrobia	*Akkermansia*	0.0426	↑	No	–	0.0076
Actinobacteria	*Adlercreutzia*	–		–	0.0342	–
Proteobacteria	*Klebsiella*	–		–	–	0.0257

A false discovery rate (FDR) < 0.05 was considered significant. FDR was obtained comparing the four groups using Kruskal Wallis test (Controls vs HCV-infected patients prior treatment, after finishing DAAs and after 3 months with SVR).

Pérez-Matute et al., Eur J Intern Med, 2019

Ni el empleo de AAD ni 3 meses en RVS fueron capaces de contrarrestar los principales cambios inducidos por el VHC en pacientes no cirróticos. El restablecimiento parcial observado en la inflamación (niveles de TNFα) y la α-diversidad sólo se observó en **grados bajos de fibrosis. Iniciar el tratamiento lo antes posible y monitorizar a los pacientes incluso después de la erradicación del VHC.**

www.nature.com/scientificreports

scientific reports

Check for updates

OPEN

Compositions of gut microbiota before and shortly after hepatitis C viral eradication by direct antiviral agents

Yao-Chun Hsu[1,2,3,4,10], Chih-Cheng Chen[5,10], Wei-Hsiang Lee[3], Chi-Yang Chang[4], Fu-Jen Lee[4], Cheng-Hao Tseng[5], Tzu-Haw Chen[1], Hsiu J. Ho[3], Jaw-Town Lin[1] & Chun-Ying Wu[4,6,7,8,9]✉

It is unclear whether dysbiosis in hepatitis C virus (HCV) infected patients results from the viral infection per se or develops as a result of hepatic dysfunction. We aimed to characterize compositions in gut microbiome before and shortly after HCV clearance. In this prospective cohort study, adult patients with confirmed HCV viremia were screened before receiving direct antiviral agents. Those with recent exposure to antibiotics or probiotics (within one month), prior abdominal surgery, or any malignancy were ineligible. Stool was collected before antiviral therapy started and at 12 weeks after the treatment completed. From the extracted bacterial DNA, 16 s rRNA gene was amplified and sequenced. Each patient was matched 1:2 in age and sex with uninfected controls. A total of 126 individuals were enrolled into analysis. The gut microbiome was significantly different between HCV-infected patients ($n = 42$), with or without cirrhosis, and their age-and sex-matched controls ($n = 84$) from the levels of phylum to amplicon sequence variant (all p values < 0.01 by principal coordinates analysis). All patients achieved viral eradication and exhibited no significant changes in the overall composition of gut microbiome following viral eradication (all p values > 0.5), also without significant difference in alpha diversity (all p values > 0.5). For the purpose of exploration, we also reported bacteria found differently abundant before and after HCV eradication, including *Coriobacteriaceae*, *Peptostreptococcaceae*, *Staphylococcaceae*, *Morganellaceae*, *Pasteurellaceae*, *Succinivibrionaceae*, and *Moraxellaceae*. Gut microbiota is altered in HCV-infected patients as compared with uninfected controls, but the overall microbial compositions do not significantly change shortly after HCV eradication.

2022

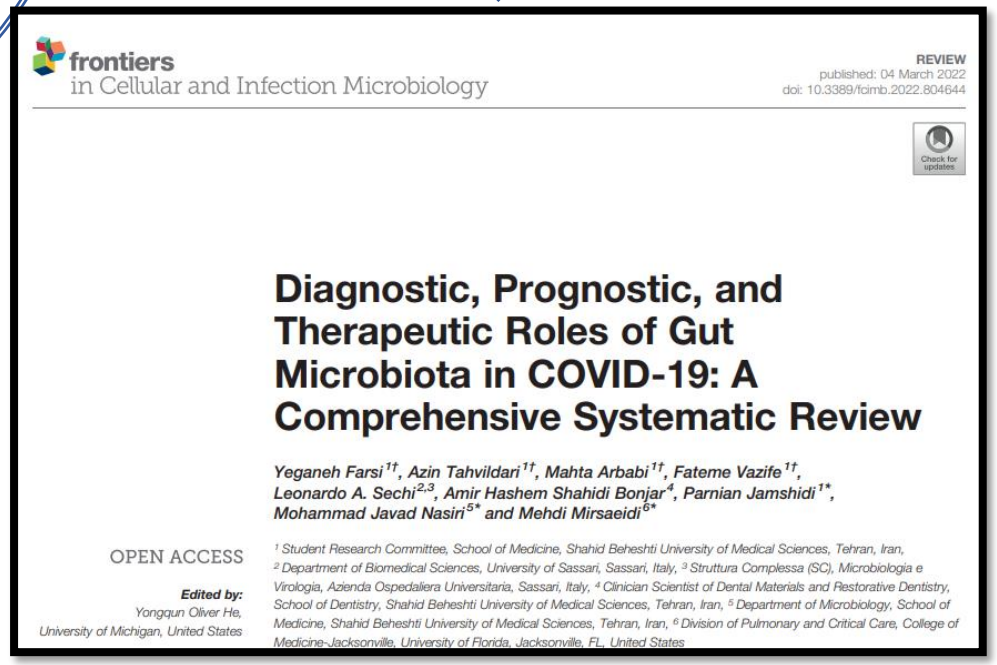
¿Para qué me sirve a mí como clínico?

Con el permiso del Dr. Oteo, Hospital Universitario San Pedro

¿Para qué me sirve a mí como clínico?

«Marcador» de enfermedad??...

¡evolución/pronóstico!



frontiers in Cellular and Infection Microbiology

REVIEW
published: 04 March 2022
doi: 10.3389/fcimb.2022.804644

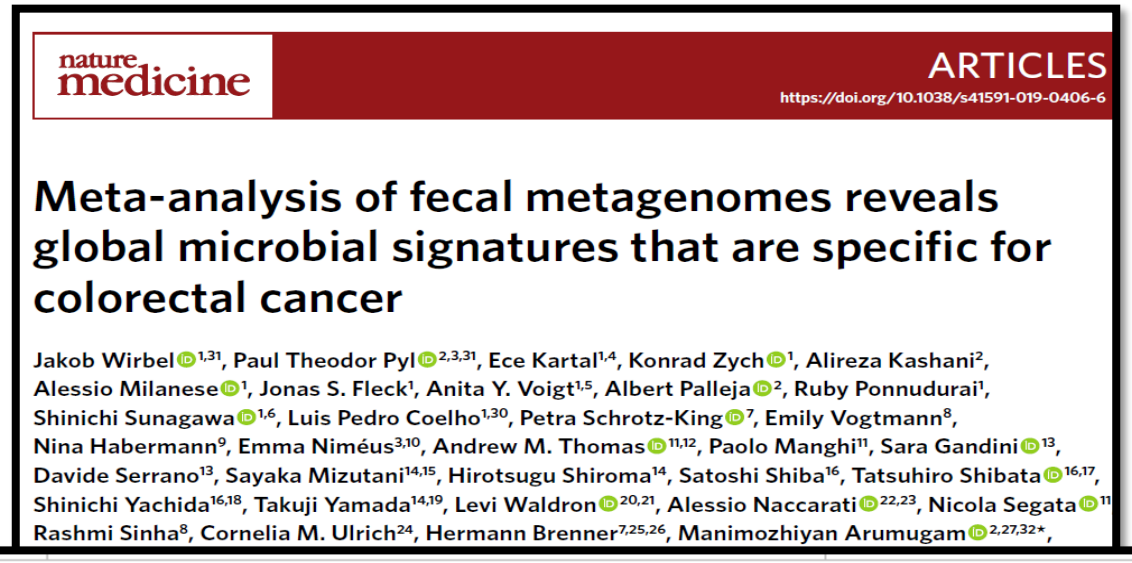
Diagnostic, Prognostic, and Therapeutic Roles of Gut Microbiota in COVID-19: A Comprehensive Systematic Review

Yeganeh Farsi[1†], Azin Tahvildari[1†], Mahta Arbabi[1†], Fateme Vazife[1†], Leonardo A. Sechi[2,3], Amir Hashem Shahidi Bonjar[4], Parnian Jamshidi[1], Mohammad Javad Nasiri[5*] and Mehdi Mirsaeidi[6*]*

OPEN ACCESS

Edited by:
Yongqun Oliver He,
University of Michigan, United States

[1] Student Research Committee, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran, [2] Department of Biomedical Sciences, University of Sassari, Sassari, Italy, [3] Struttura Complessa (SC), Microbiologia e Virologia, Azienda Ospedaliera Universitaria, Sassari, Italy, [4] Clinician Scientist of Dental Materials and Restorative Dentistry, School of Dentistry, Shahid Beheshti University of Medical Sciences, Tehran, Iran, [5] Department of Microbiology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran, [6] Division of Pulmonary and Critical Care, College of Medicine-Jacksonville, University of Florida, Jacksonville, FL, United States



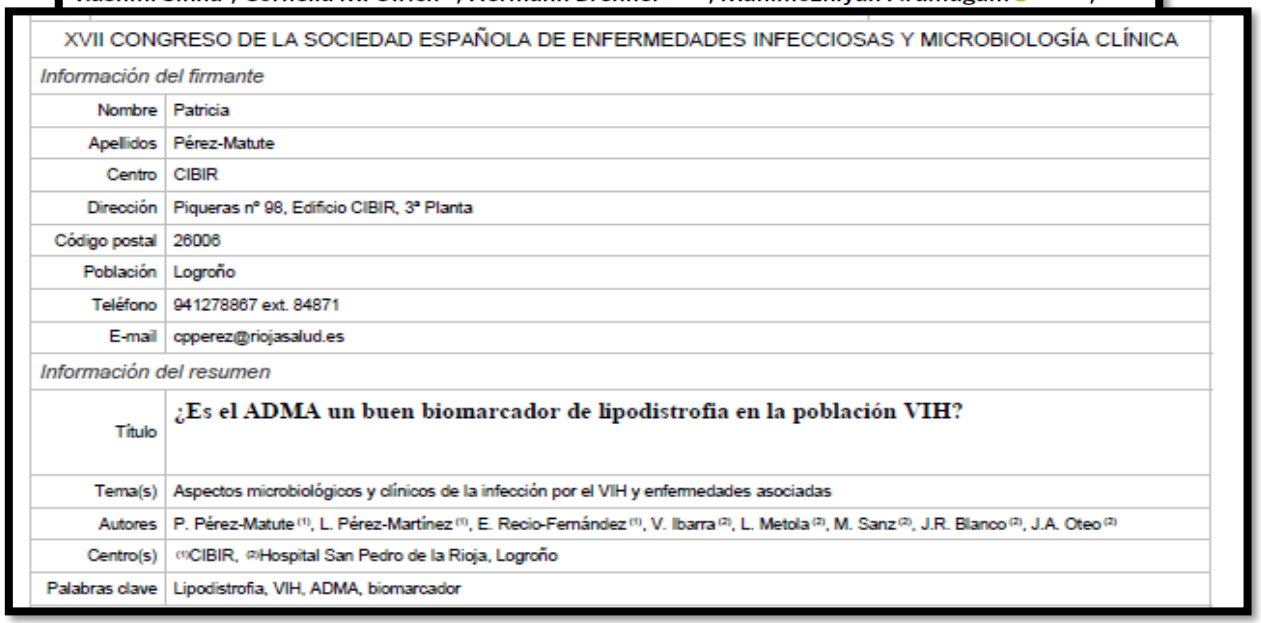
nature medicine

ARTICLES

https://doi.org/10.1038/s41591-019-0406-6

Meta-analysis of fecal metagenomes reveals global microbial signatures that are specific for colorectal cancer

Jakob Wirbel[1,31], Paul Theodor Pyl[2,3,31], Ece Kartal[1,4], Konrad Zych[1], Alireza Kashani[2], Alessio Milanese[1], Jonas S. Fleck[1], Anita Y. Voigt[1,5], Albert Palleja[2], Ruby Ponnudurai[1], Shinichi Sunagawa[1,6], Luis Pedro Coelho[1,30], Petra Schrotz-King[7], Emily Vogtmann[8], Nina Habermann[9], Emma Niméus[3,10], Andrew M. Thomas[11,12], Paolo Manghi[11], Sara Gandini[13], Davide Serrano[13], Sayaka Mizutani[14,15], Hirotsugu Shiroma[14], Satoshi Shiba[16], Tatsuhiro Shibata[16,17], Shinichi Yachida[16,18], Takuji Yamada[14,19], Levi Waldron[20,21], Alessio Naccarati[22,23], Nicola Segata[11], Rashmi Sinha[8], Cornelia M. Ulrich[24], Hermann Brenner[7,25,26], Manimozhiyan Arumugam[2,27,32*],



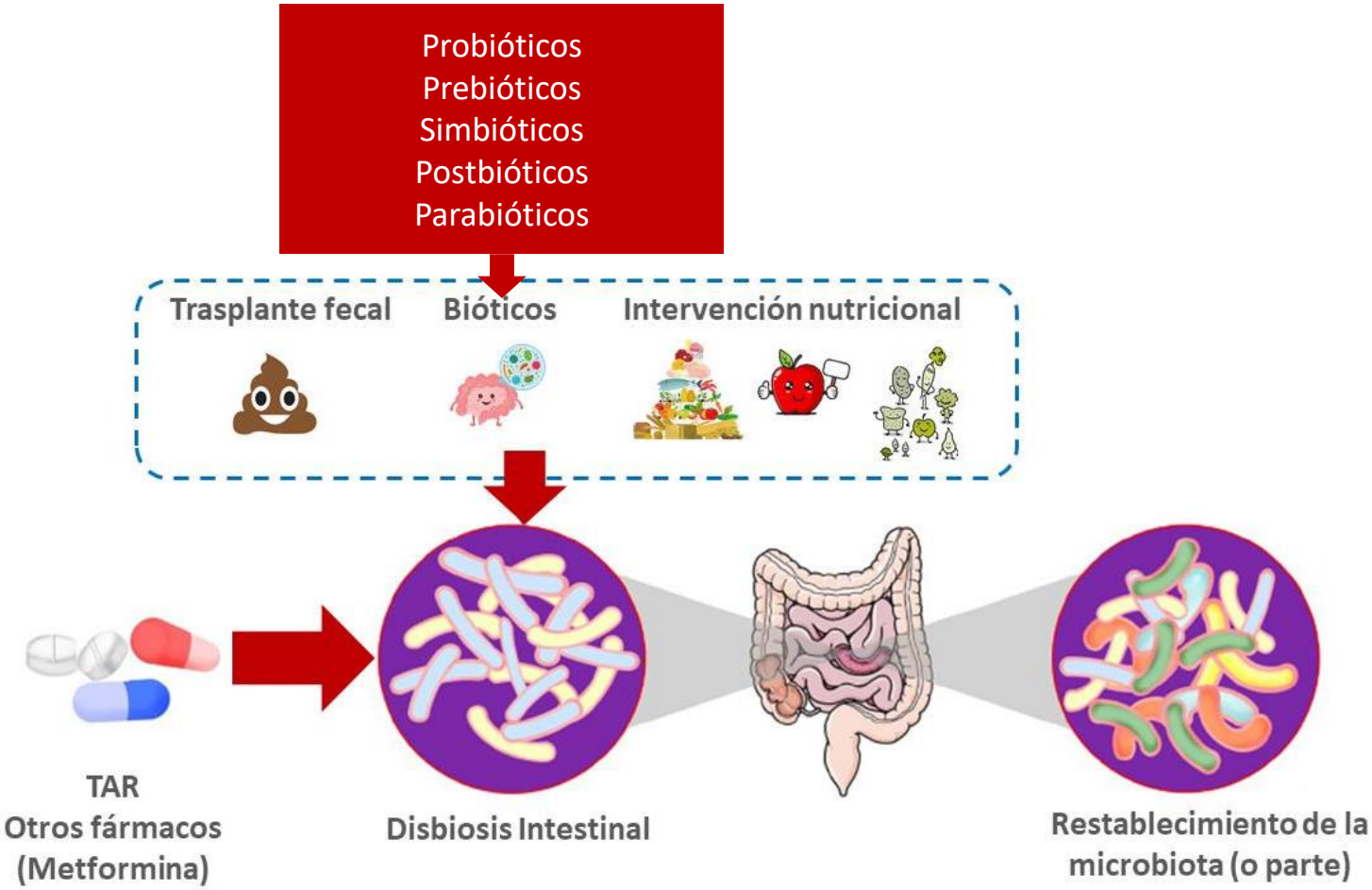
XVII CONGRESO DE LA SOCIEDAD ESPAÑOLA DE ENFERMEDADES INFECCIOSAS Y MICROBIOLOGÍA CLÍNICA

Información del firmante	
Nombre	Patricia
Apellidos	Pérez-Matute
Centro	CIBIR
Dirección	Piqueras nº 98, Edificio CIBIR, 3ª Planta
Código postal	26006
Población	Logroño
Teléfono	941278867 ext. 84871
E-mail	cpperez@riojasalud.es
Información del resumen	
Título	¿Es el ADMA un buen biomarcador de lipodistrofia en la población VIH?
Tema(s)	Aspectos microbiológicos y clínicos de la infección por el VIH y enfermedades asociadas
Autores	P. Pérez-Matute (1), L. Pérez-Martínez (1), E. Recio-Fernández (1), V. Ibarra (2), L. Metola (2), M. Sanz (2), J.R. Blanco (2), J.A. Oteo (2)
Centro(s)	(1)CIBIR, (2)Hospital San Pedro de la Rioja, Logroño
Palabras clave	Lipodistrofia, VIH, ADMA, biomarcador

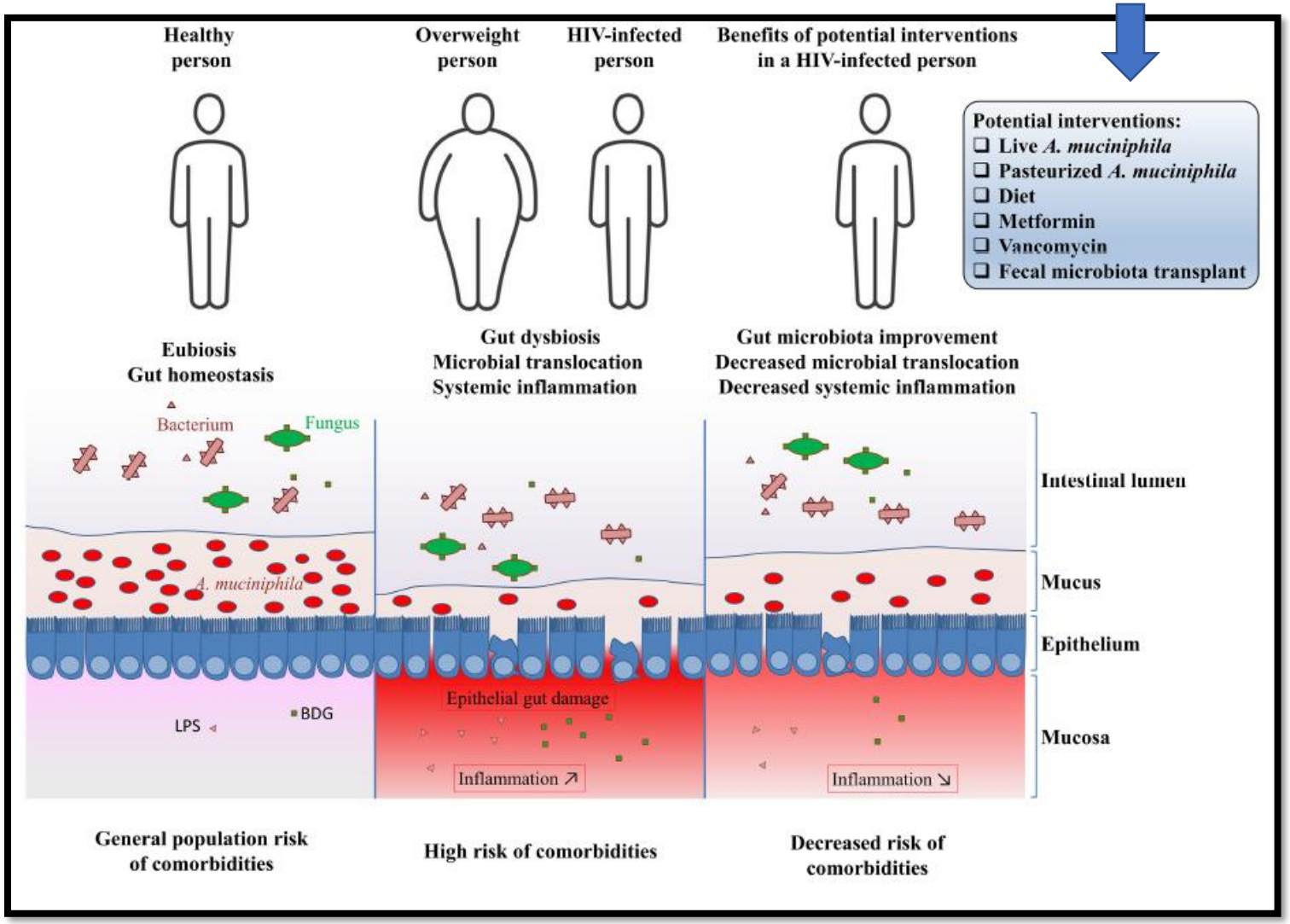
¿Para qué me sirve a mí como clínico?

«Marcador» de evolución/pronóstico

«Diana» terapéutica

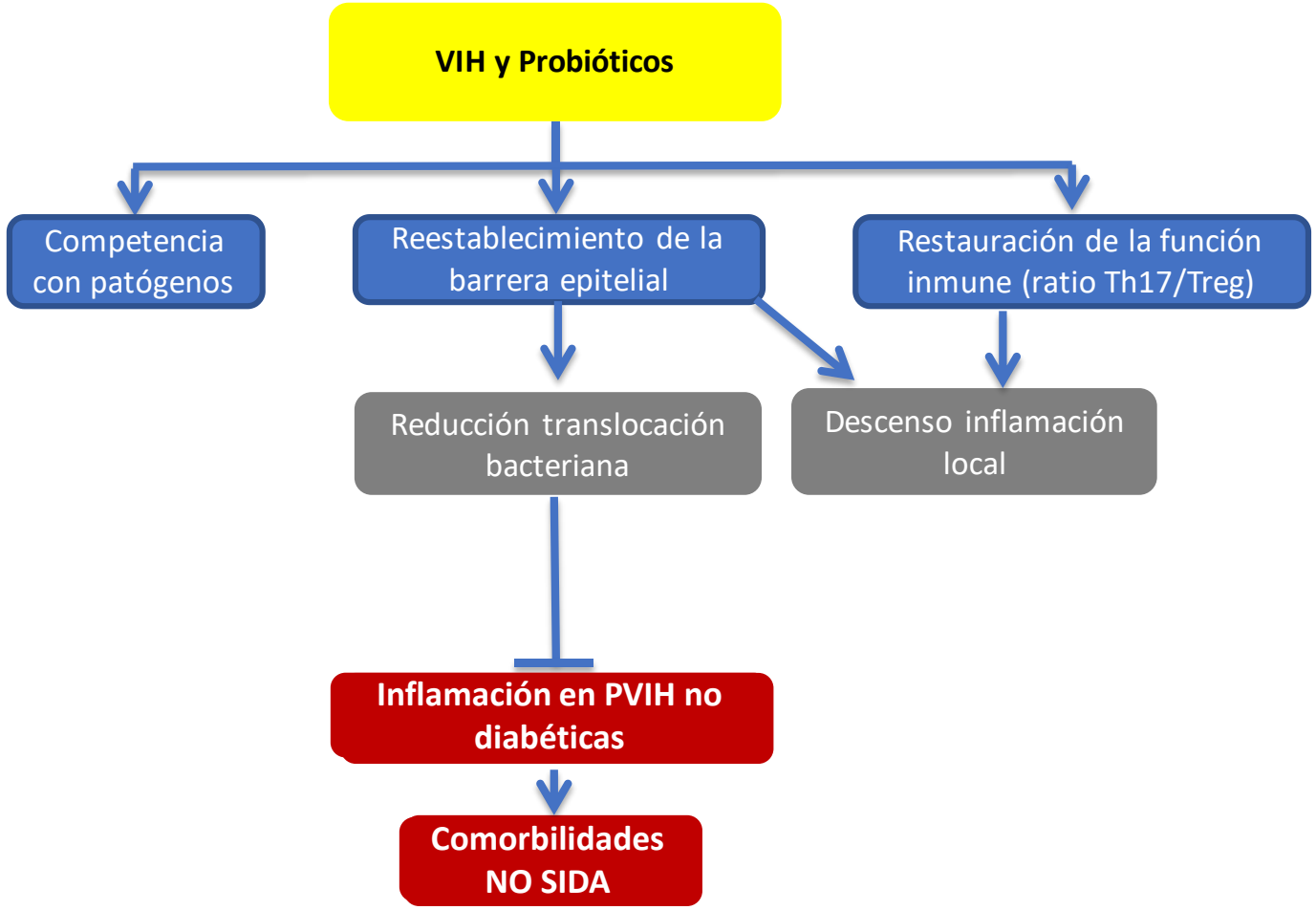


¿Para qué me sirve a mí como clínico?



Ouyang et al., Frontiers in Immunology, 2020

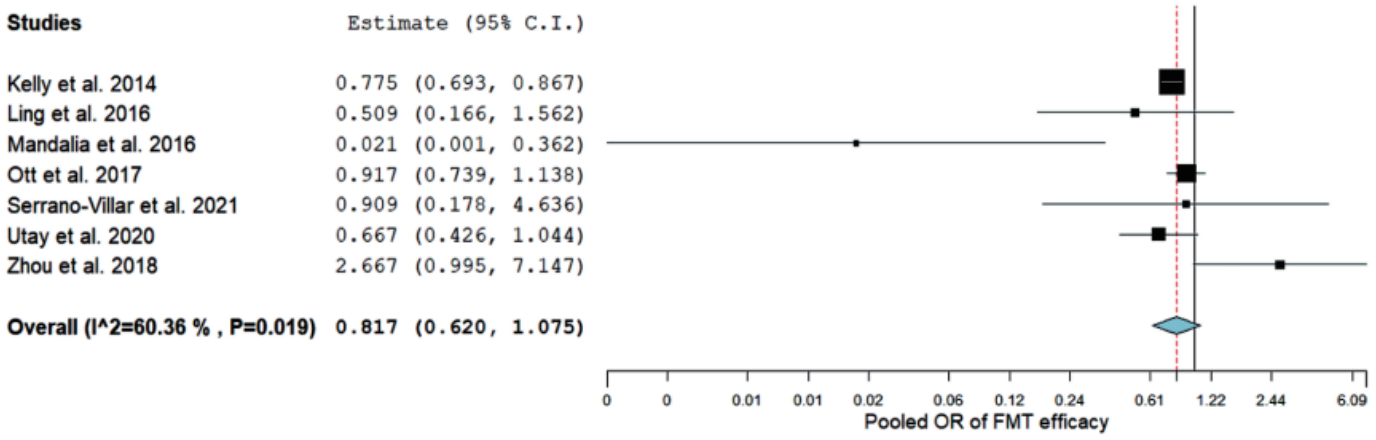
¿Para qué me sirve a mí como clínico?



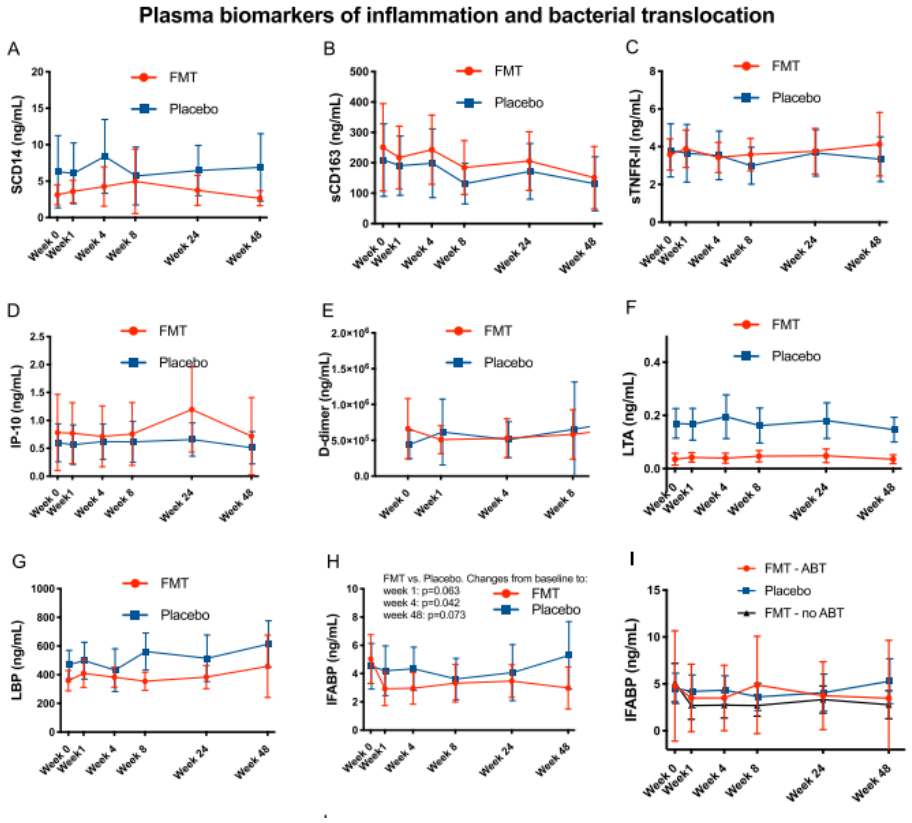
clinicaltrials.gov
D´Angelo et al., Nutrients, 2017

¿Para qué me sirve a mí como clínico?

«*Faecal Transplant and infectious diseases*»: 732 (>50% en los últimos 5 años: 498) mayoría en CD
«*Faecal Transplant and HIV infection*»: 39 (16 revisiones)**METAANÁLISIS de 7 estudios
23/10/2023



Malik & Malik, Gastroenterology research, 2023



Serrano-Villar et al., Randomized Controlled Trial, 2021

Fármacos que actúan sobre la microbiota

Ouyang *et al. AIDS Res Ther* (2020) 17:10
https://doi.org/10.1186/s12981-020-00267-2

AIDS Research and Therapy

REVIEW Open Access

Metformin effect on gut microbiota: insights for HIV-related inflammation

Jing Ouyang[1,2,3], Stéphane Isnard[2,3], John Lin[2,3], Brandon Fombuena[2,3,4], André Marette[5,6], Bertrand Routy[7,8], Yaokai Chen[1*] and Jean-Pierre Routy[2,3,9*]

Open Forum Infectious Diseases

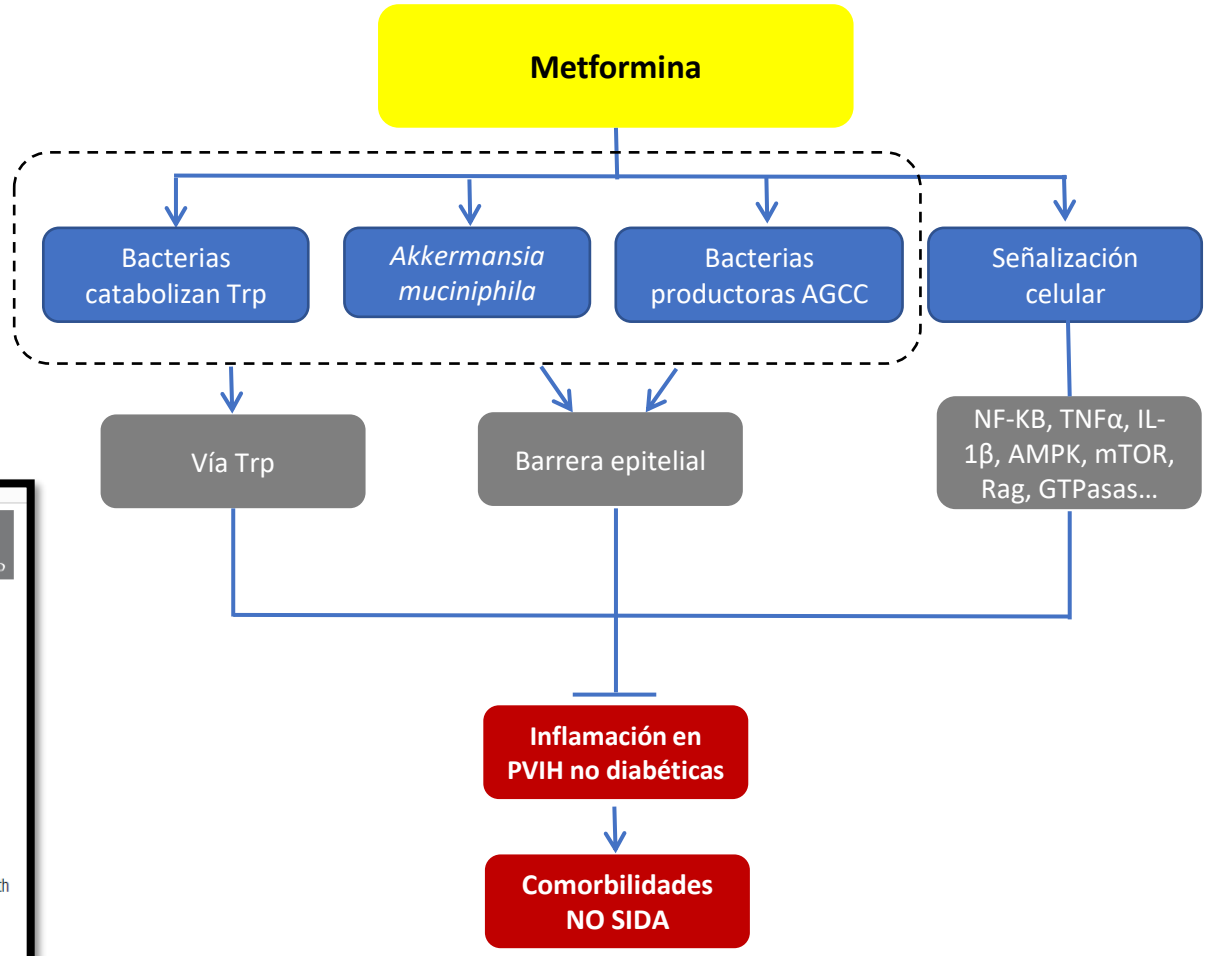
MAJOR ARTICLE

IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

Repurposing Metformin in Nondiabetic People With HIV: Influence on Weight and Gut Microbiota

Stéphane Isnard,[1,2,3] John Lin,[1,2] Brandon Fombuena,[1,2] Jing Ouyang,[1,2,5] Thibault V. Varin,[6] Corentin Richard,[7] André Marette,[6,9] Rayoun Ramendra,[1,2,4] Delphine Planas,[7,8] Laurence Raymond Marchand,[7] Meriem Messaoudene,[7] Claude P. Van der Ley,[10] Ido P. Kema,[10] Darakhshan Sohail Ahmed,[1,2] Yonglong Zhang,[11] Malcolm Finkelman,[11] Bertrand Routy,[7,14] Jonathan Angel,[12] Petronela Ancuta,[7,8] and Jean-Pierre Routy[1,2,13]

[1]Infectious Diseases and Immunity in Global Health Program, Research Institute, McGill University Health Centre, Montreal, Québec, Canada, [2]Chronic Viral Illness Service, McGill University Health Centre, Montreal, Québec, Canada, [3]CIHR Canadian HIV Trials Network, Vancouver, British Columbia, Canada, [4]Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada, [5]Chongqing Public Health Medical Center, Chongqing, China, [6]Institute of Nutrition and Functional Foods, Laval University, Québec City, Québec, Canada, [7]Centre de Recherche du Centre Hospitalier de l'Université de Montréal, Montréal, Québec, Canada, [8]Département de Microbiologie, Infectiologie et Immunologie, Faculté de Médecine, Université de Montréal, Montréal, Québec, Canada, [9]Department of Medicine, Faculty of Medicine, Cardiology Axis of the Québec Heart and Lung Institute, Laval University, Québec City, Québec, Canada, [10]Department of Laboratory Medicine, University Medical Center Groningen, University of Groningen, the Netherlands, [11]Associates of Cape Cod Inc., Falmouth, Massachusetts, USA, [12]The Ottawa Hospital, University of Ottawa, Ottawa, Ontario, Canada, [13]Division of Hematology, McGill University Health Centre, Montreal, Québec, Canada, and [14]Division of Medicine, Department of Hemato-Oncology, University of Montreal Healthcare Center, Montreal, Quebec, Canada



Modificado de Ouyang et al., AIDS Res Ther, 2020
NCT02659306…

¿Terapia de fagos y microbiota?

Review > Prog Mol Biol Transl Sci. 2023:201:93-118. doi: 10.1016/bs.pmbts.2023.04.005. Epub 2023 May 2.

Phage therapy in gut microbiome

Xingyao Chen [1], Beatriz G Mendes [2], Bruno Secchi Alves [2], Yi Duan [3]

Affiliations + expand

PMID: 37770177 DOI: 10.1016/bs.pmbts.2023.04.005

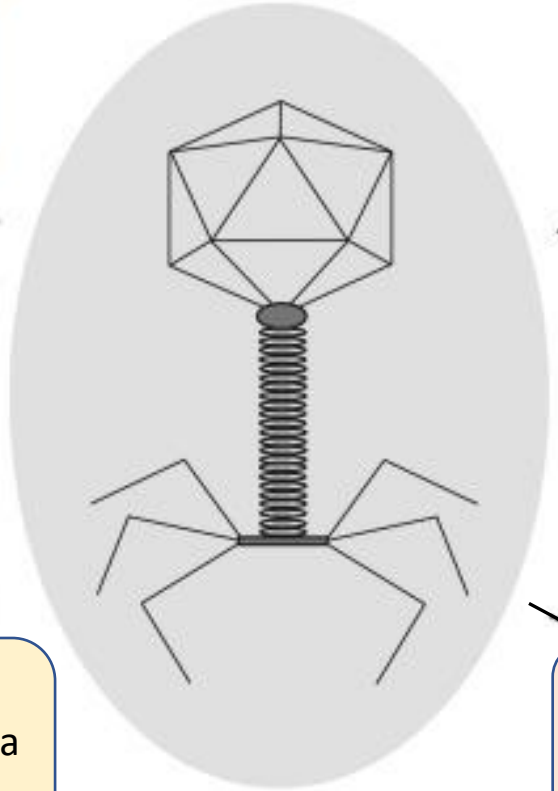
Abstract

Phage therapy, the use of bacteriophage viruses for bacterial infection treatment, has been around for almost a century, but with the increase in antibiotic use, its importance has declined rapidly. There has been renewed interest in revisiting this practice due to the general decline in the effectiveness of antibiotics, combined with improved understanding of human microbiota and advances in sequencing technologies. Phage therapy has been proposed as a clinical alternative to restore the gut microbiota in the absence of an effective treatment. That is due to its immunomodulatory and bactericidal effects against its target bacteria. In the gastrointestinal diseases field, phage therapy has been studied mainly as a promising tool in infectious diseases treatment, such as cholera and diarrhea. However, many studies have been conducted in non-communicable diseases, such as the targeting of adherent invasive Escherichia coli in Crohn's disease, the treatment of Clostridioides difficile in ulcerative colitis, the eradication of Fusobacterium nucleatum in colorectal cancer, the targeting of alcohol-producing Klebsiella pneumoniae in non-alcoholic fatty liver disease, or Enterococcus faecalis in alcohol-associated hepatitis. This review will summarize the changes in the gut microbiota and the phageome in association with some gastrointestinal and liver diseases and highlight the recent scientific advances in phage therapy as a therapeutic tool for their treatment.

Keywords: Bacteriophage; gastrointestinal diseases; microbiota; phage therapy; phageoma.

Llevar fármacos al lugar deseado

Lucha contra infección bacteriana

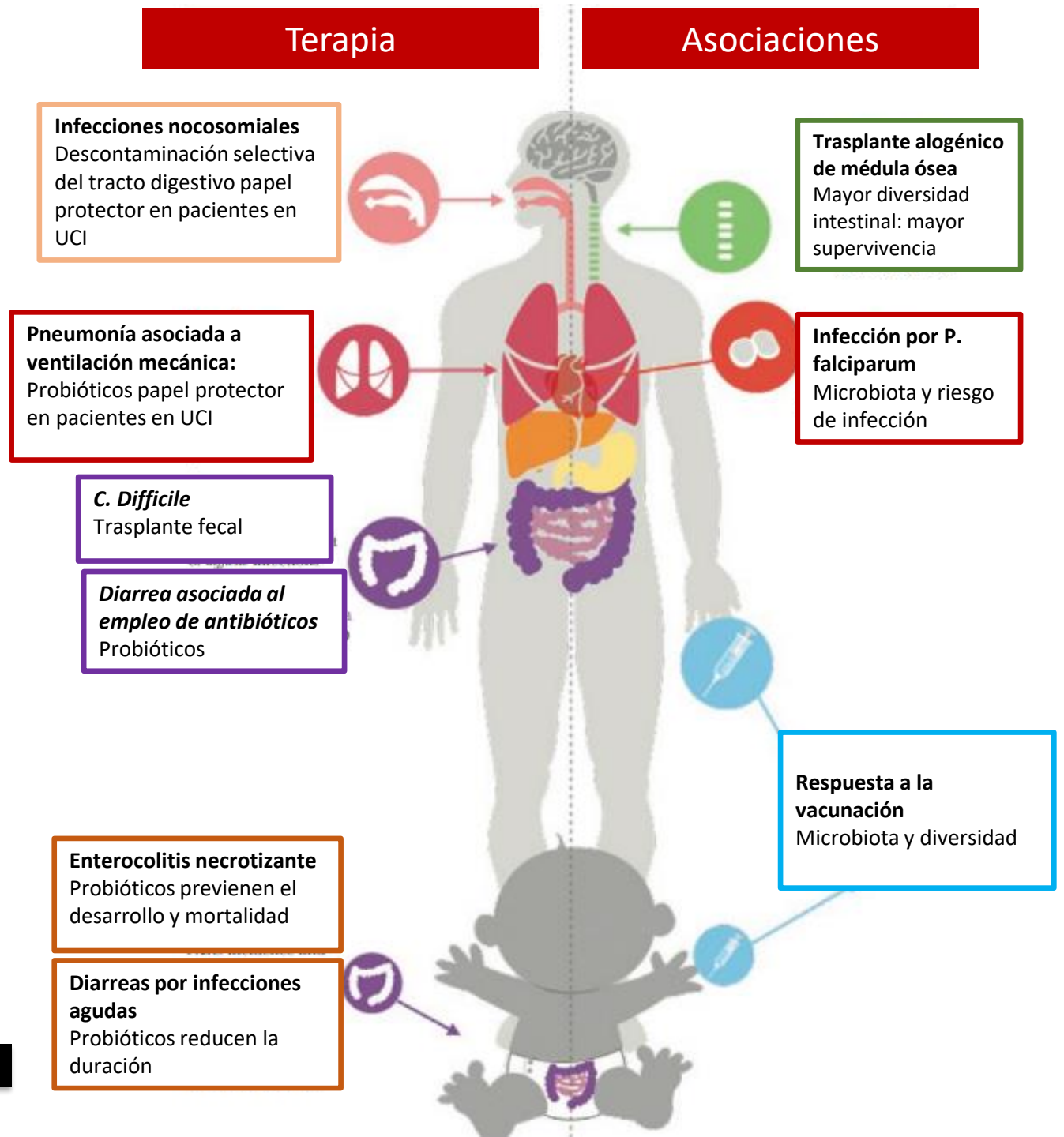


Miembro comensal de la microbiota intestinal

Modula la microbiota intestinal

Chen et al., Prog Mol Biol Transl Sci, 2023

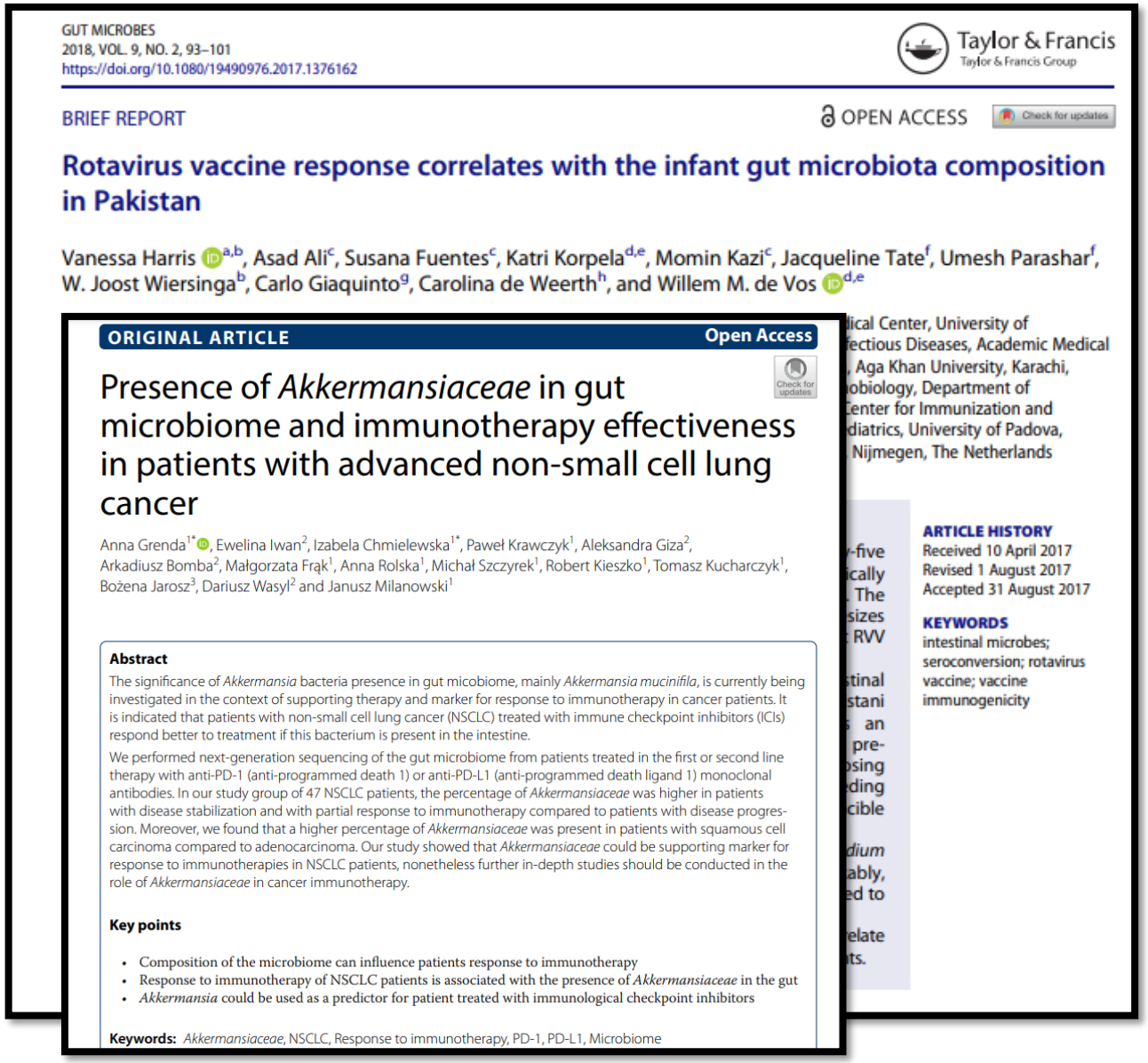
ALGUNOS EJEMPLOS…



Modificado de Harris et al., OFID, 2021

¿Para qué me sirve a mí como clínico?

- «Marcador» de evolución/pronóstico
- «Diana» terapéutica
- «Marcador» de respuesta a tratamientos



GUT MICROBES
2018, VOL. 9, NO. 2, 93–101
https://doi.org/10.1080/19490976.2017.1376162

Taylor & Francis
Taylor & Francis Group

BRIEF REPORT

OPEN ACCESS

Rotavirus vaccine response correlates with the infant gut microbiota composition in Pakistan

Vanessa Harris[a,b], Asad Ali[c], Susana Fuentes[c], Katri Korpela[d,e], Momin Kazi[c], Jacqueline Tate[f], Umesh Parashar[f], W. Joost Wiersinga[b], Carlo Giaquinto[g], Carolina de Weerth[h], and Willem M. de Vos[d,e]

ORIGINAL ARTICLE — Open Access

Presence of *Akkermansiaceae* in gut microbiome and immunotherapy effectiveness in patients with advanced non-small cell lung cancer

Anna Grenda[1*], Ewelina Iwan[2], Izabela Chmielewska[1*], Paweł Krawczyk[1], Aleksandra Giza[2], Arkadiusz Bomba[2], Małgorzata Frąk[1], Anna Rolska[1], Michał Szczyrek[1], Robert Kieszko[1], Tomasz Kucharczyk[1], Bożena Jarosz[3], Dariusz Wasyl[2] and Janusz Milanowski[1]

Abstract

The significance of *Akkermansia* bacteria presence in gut micobiome, mainly *Akkermansia mucinifila*, is currently being investigated in the context of supporting therapy and marker for response to immunotherapy in cancer patients. It is indicated that patients with non-small cell lung cancer (NSCLC) treated with immune checkpoint inhibitors (ICIs) respond better to treatment if this bacterium is present in the intestine.

We performed next-generation sequencing of the gut microbiome from patients treated in the first or second line therapy with anti-PD-1 (anti-programmed death 1) or anti-PD-L1 (anti-programmed death ligand 1) monoclonal antibodies. In our study group of 47 NSCLC patients, the percentage of *Akkermansiaceae* was higher in patients with disease stabilization and with partial response to immunotherapy compared to patients with disease progression. Moreover, we found that a higher percentage of *Akkermansiaceae* was present in patients with squamous cell carcinoma compared to adenocarcinoma. Our study showed that *Akkermansiaceae* could be supporting marker for response to immunotherapies in NSCLC patients, nonetheless further in-depth studies should be conducted in the role of *Akkermansiaceae* in cancer immunotherapy.

Key points

- Composition of the microbiome can influence patients response to immunotherapy
- Response to immunotherapy of NSCLC patients is associated with the presence of *Akkermansiaceae* in the gut
- *Akkermansia* could be used as a predictor for patient treated with immunological checkpoint inhibitors

Keywords: *Akkermansiaceae*, NSCLC, Response to immunotherapy, PD-1, PD-L1, Microbiome

ical Center, University of
fectious Diseases, Academic Medical
, Aga Khan University, Karachi,
obiology, Department of
Center for Immunization and
diatrics, University of Padova,
Nijmegen, The Netherlands

ARTICLE HISTORY
Received 10 April 2017
Revised 1 August 2017
Accepted 31 August 2017

KEYWORDS
intestinal microbes; seroconversion; rotavirus vaccine; vaccine immunogenicity

¿Para qué me sirve a mí como clínico?

DIAGNÓSTICO/ PRONÓSTICO/ EVOLUCIÓN

- **Microorganismos individuales y/o comunidades**
- **Metabolitos**
- **Inteligencia Artificial**

TRATAMIENTO CO-ADJUVANTE

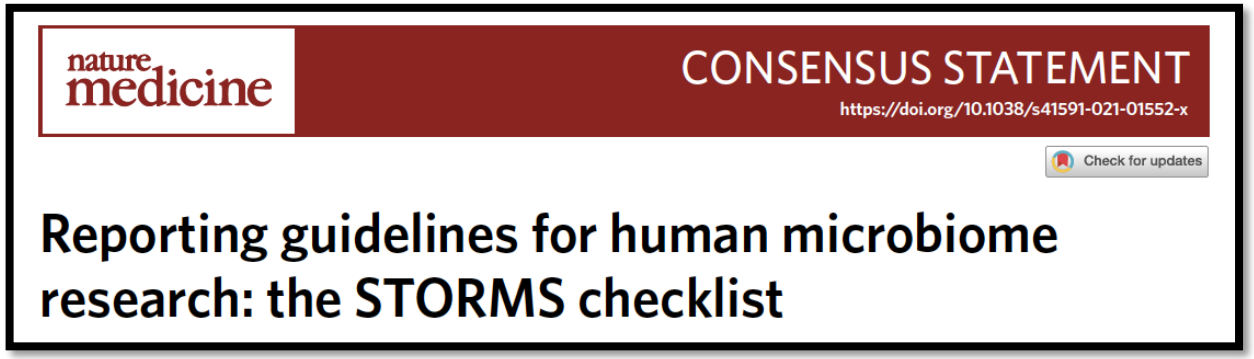
- Modulación específica

MARCADOR DE RESPUESTA A TRATAMIENTOS

"One health"

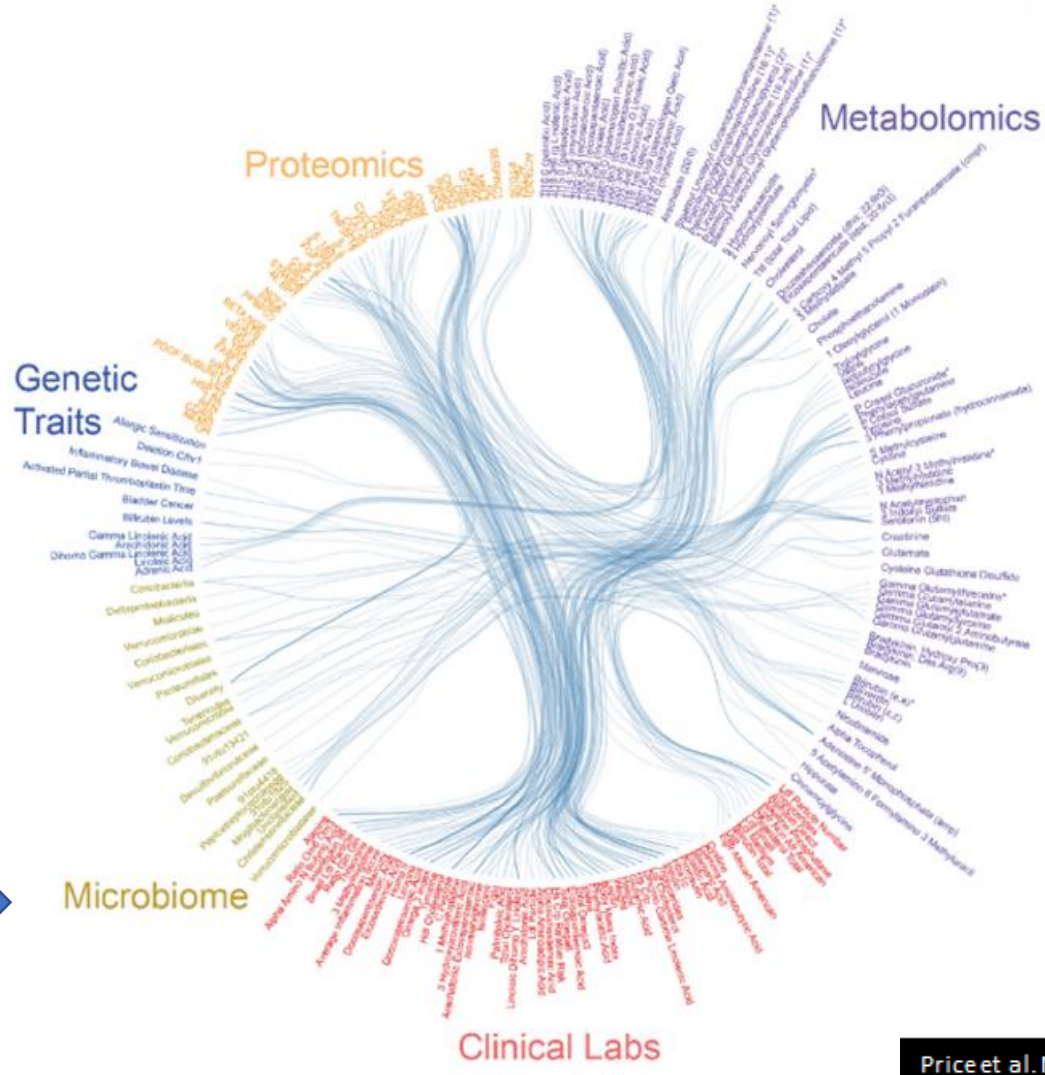
Limitaciones: áreas de mejora

- Se necesitan protocolos «estandarizados» (secuenciación y bioinformática) en los análisis metagenómicos: consensos metodológicos y controles de calidad mediante «mock communities».



- Nuevas metodologías: ¿Están los microorganismos “vivos/funcionales”?
- Es importante estudiar, además del bacterioma, otros componentes de la microbiota en relación estrecha con ellos como son el viroma.
- El intestino muy bien estudiado, pero… ¿qué ocurre con la microbiota oral, pulmonar etc.?

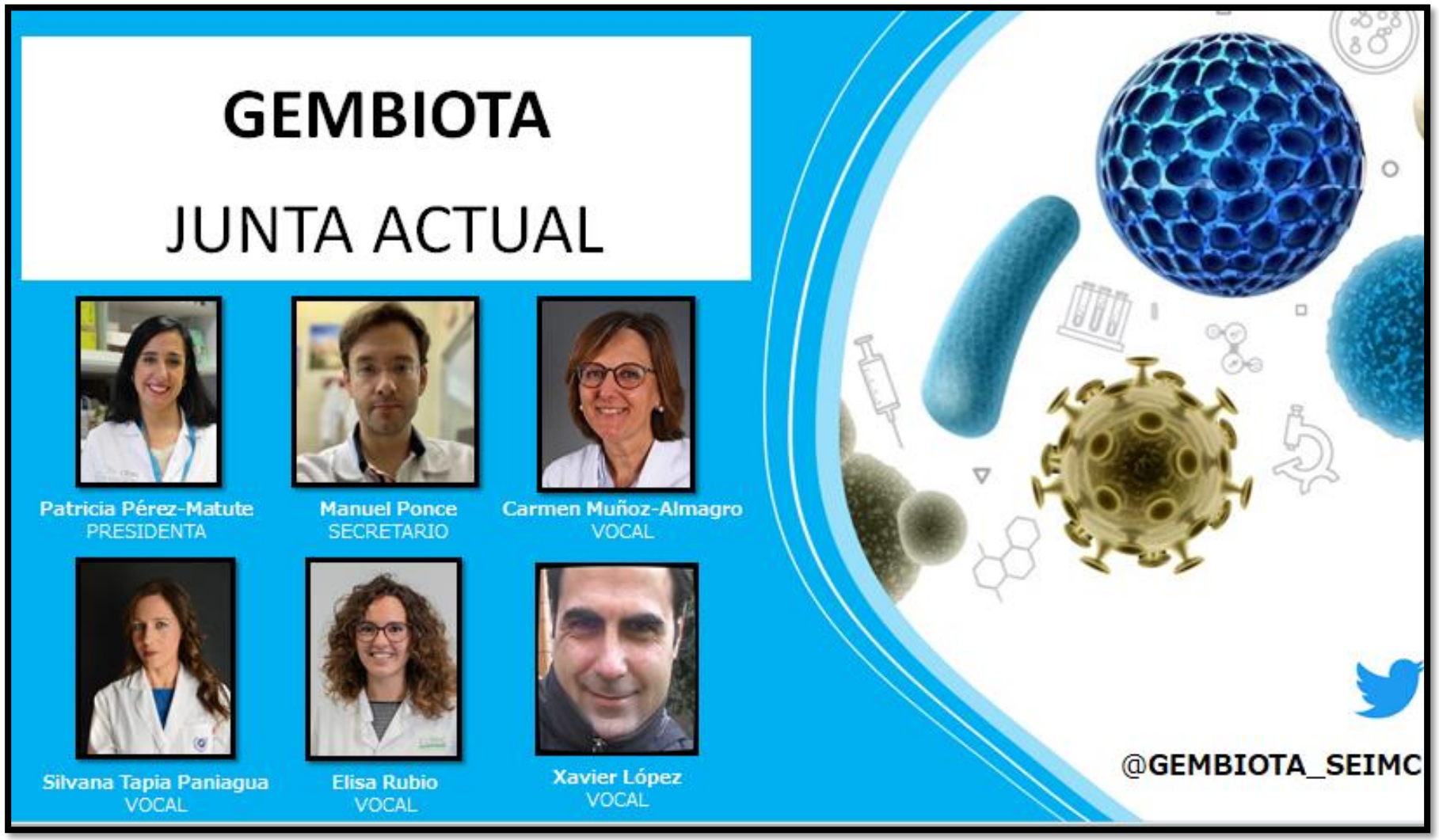
El estudio de la microbiota unido a otros parámetros puede ayudar al desarrollo de una verdadera “medicina personalizada”, así como al desarrollo de terapias coadjuvantes para mejorar la calidad de vida de los pacientes



Price et al. Nat Biotechnol 2017

cost
EUROPEAN COOPERATION IN SCIENCE & TECHNOLOGY

COST ACTION: CA18131
Statistical and machine learning techniques in human microbiome studies.



¡INSCRÍBETE!

https://seimc.org/grupos-de-estudio/gembiota/inscripcion

9 de enero:
Microbiota y Enfermedades Infecciosas

Agradecimientos

MJ. Villanueva-Millán
CEDARS-Sinai, LA (EEUU)

GILEAD

SEI NORTE
SOCIEDAD DE ENFERMEDADES INFECCIOSAS DEL NORTE

Departamento de Enfermedades Infecciosas
Hospital Universitario San Pedro

Luis Metola
Valvanera Ibarra
Jorge Alba
Mercedes Sanz
Sonia Omatos
Estíbaliz Corral
Javier Velasco
José Ramón Blanco

Centro de Salud "Siete Infantes de Lara". Logroño

Pilar Blanco Navarrete

Plataforma de genómica y bioinformática
CIBIR

Hospital Universitario Álvaro Cunqueiro-Vigo

Luis E Morano
Aitana Morano Vázquez
Sheila Castro

Laboratory of Viral Metagenomics
Leuven (Bélgica)

Jelle Matthijnssens
Daan Jansen
Lander De Coninck
Lila Close

Unidad de Enfermedades Infecciosas, Microbiota y Metabolismo.
Unidad Asociada de I+D+i al CSIC por el ICVV (2020-2023)

¿Qué aporta el estudio de la microbiota a las enfermedades infecciosas?

Dra. Patricia Pérez-Matute

Unidad Predepartamental de Enfermería. Facultad de Ciencias de la Salud. Universidad de La Rioja

Unidad de Enfermedades Infecciosas, Microbiota y Metabolismo. Centro de Investigación Biomédica de La Rioja (CIBIR)

Hospital Universitario San Pedro

carmen-patricia.perez@unirioja.es

CSIC
Consejo Superior de Investigaciones Científicas

UNIVERSIDAD DE LA RIOJA

CIBIR
Centro de Investigación Biomédica de La Rioja

Hospital San Pedro

¿La infección por el VIH y los ARV impactan en el “micobioma”?

viruses

MDPI

Article

Characterization of the Intestinal Fungal Microbiome in HIV and HCV Mono-Infected or Co-Infected Patients

Yue Yin [1,†], Maermaer Tuohutaerbieke [1,†], Chengjie Feng [2,†], Xinjie Li [1], Yuqi Zhang [1], Qiang Xu [1], Jing Tu [1], Ence Yang [1], Qinghua Zou [1,*] and Tao Shen [1,*]

[1] Department of Microbiology and Infectious Disease Center, School of Basic Medical Sciences, Peking University, Beijing 100191, China
[2] Department of Microbiology, School of Basic Medical Sciences, Peking University Health Science Center, Beijing 100191, China
* Correspondence: zouqinghua@bjmu.edu.cn (Q.Z.); taoshen@hsc.pku.edu.cn (T.S.)
† These authors contributed equally to this work.

Abstract: Intestinal mycobiome dysbiosis plays an important role in the advancement of HIV- and HCV-infected patients. Co-infection with HCV is an important risk factor for exacerbating immune activation in HIV-infected patients, and gut fungal microbial dysbiosis plays an important role. However, no systematic study has been conducted on the intestinal fungal microbiome of HIV/HCV co-infected patients to date. Patients infected with HIV and HCV, either alone or in combination, and healthy volunteers were included. Stool samples were collected for fungal ITS sequencing and for further mycobiome statistical analysis. We found that the abundance of fungal species significantly decreased in the HIV/HCV co-infection group compared to in the healthy control group, while no significant differences were found in the mono-infection groups. Low-CD4 + T-cell patients in the HIV group and high-ALT-level patients in the HCV group were discovered to have a more chaotic fungal community. Furthermore, the opportunistic pathogenic fungal profiles and fungal inter-correlations in the co-infection group became less characteristic but more complicated than those in the mono-infection groups. Intestinal fungal dysregulation occurs in HIV- and HCV-infected patients, and this dysregulation is further complicated in HIV/HCV co-infected patients.

Keywords: human immunodeficiency virus; hepatitis C virus; intestinal fungal dysbiosis; CD4 + T cells; ALT; opportunistic pathogens

check for updates

Citation: Yin, Y.; Tuohutaerbieke, M.; Feng, C.; Li, X.; Zhang, Y.; Xu, Q.; Tu, J.; Yang, E.; Zou, Q.; Shen, T. Characterization of the Intestinal Fungal Microbiome in HIV and HCV Mono-Infected or Co-Infected Patients. *Viruses* **2022**, *14*, 1811. https://doi.org/10.3390/v14081811

AMERICAN SOCIETY FOR MICROBIOLOGY | mBio®

RESEARCH ARTICLE

Check for updates

Effect of HIV/HAART and Other Clinical Variables on the Oral Mycobiome Using Multivariate Analyses

Paul L. Fidel, Jr.,[a] Zach A. Thompson,[c] Elizabeth A. Lilly,[a] Carolina Granada,[e] Kelly Treas,[a] Kenneth R. Dubois III,[a] Laura Cook,[c] Shahr B. Hashmi,[c] Daniel J. Lisko,[c,d] Chiranjit Mukherjee,[c] Jose A. Vazquez,[e] Michael E. Hagensee,[f] Ann L. Griffen,[b,c] Eugene J. Leys,[c] Clifford J. Beall[c]

[a]Center of Excellence in Oral and Craniofacial Biology, Louisiana State University Health Sciences Center School of Dentistry, New Orleans, Louisiana, USA
[b]Division of Pediatric Dentistry, The Ohio State University College of Dentistry, Columbus, Ohio, USA
[c]Division of Biosciences, The Ohio State University College of Dentistry, Columbus, Ohio, USA
[d]Department of Medicine, University of British Columbia, Vancouver, British Columbia, Canada
[e]Division of Infectious Diseases, Department of Medicine, Augusta University, Medical College of Georgia, Augusta, Georgia, USA

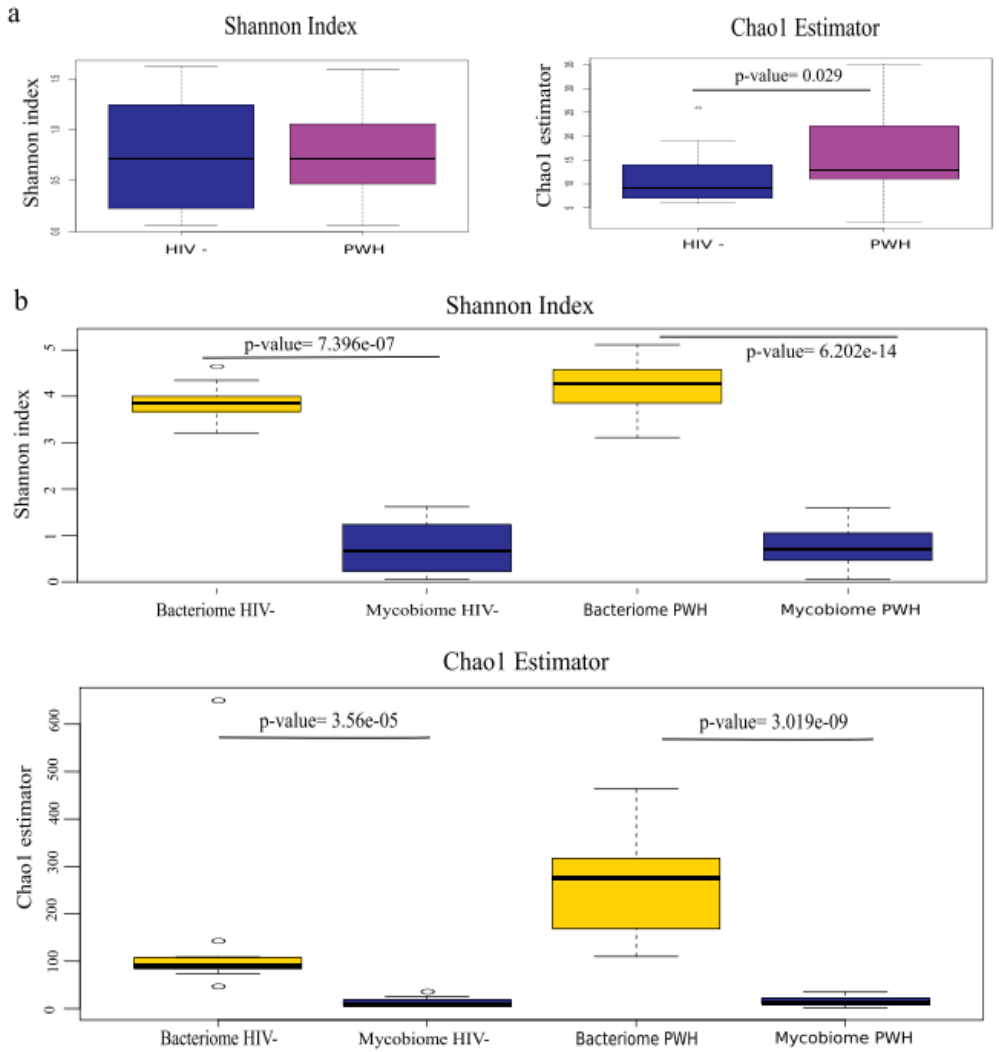


Figure 1. Mycobiome and bacteriome alpha diversity. (a) Shannon diversity index and Chao1 richness estimator of fungal communities from HIV-infected subjects (PWH) and healthy controls (HIV-). (b) Shannon index and Chao1 estimator for mycobiome and bacteriome in PWH and HIV- groups.

Gosalbes et al., Gut Microbes, 2022

Pipeline bioinformático 16S

Análisis 1º

Amplicones región V3-V4 2x300pb

Imaging data ~20GB

- ✓ Conversión demultiplexing

Fastq demultiplexed RAW reads ~100.000/muestra

Análisis 2º

- ✓ Análisis de calidad
- ✓ Eliminar secuencias baja calidad
- ✓ Eliminar adaptadores
- ✓ Eliminar Quimeras
- ✓ Eliminar no bacteriano
- ✓ Unión de pares de reads (merging)

Análisis 2º

Tabla de recuento de **ASVs**

Clustering (97%)

Tabla de **secuencias representativas**

Clasificación bayesiana

silva ngs GREENGENES

Tabla de recuento de **OTUs**

Asignación taxonómica

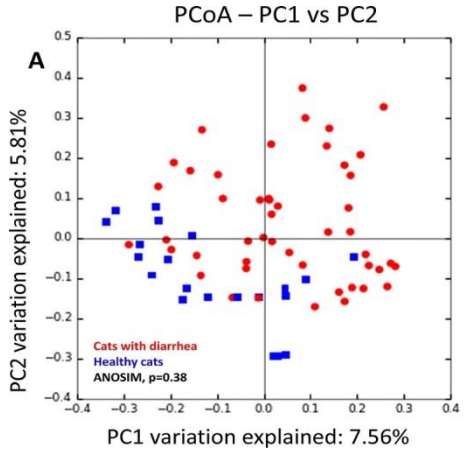
Alineamiento de secuencias (árbol)

Análisis 3º

ANÁLISIS DE DIVERSIDAD

α-div

β-div

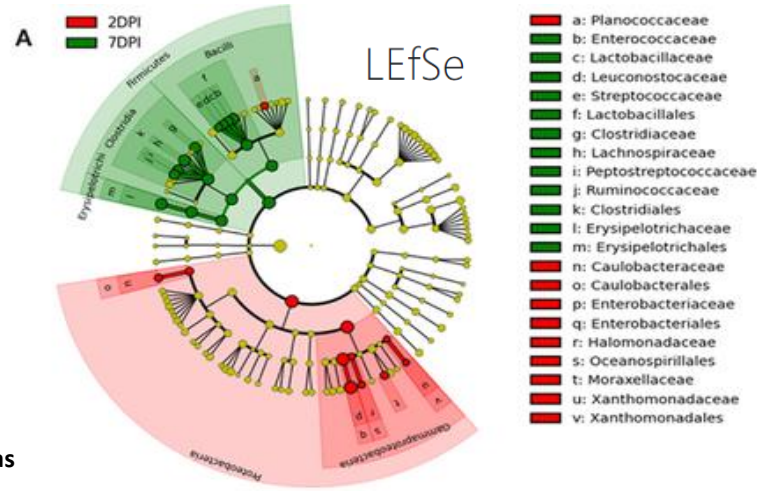


Barplots
Heatmaps

Abundancia diferencial

Rutas metabólicas

Integración con otras -ómicas



Secuenciación: parte II

PLATAFORMA DE SECUENCIACIÓN GENÓMICA DEL CIBIR

FastaQ

~100,000 lecturas/muestra

Calidad por muestra

DADA2

-Eliminar Adaptadores

-Eliminar Lecturas "ruido"

-Eliminar Lecturas repetidas

-Eliminar quimeras

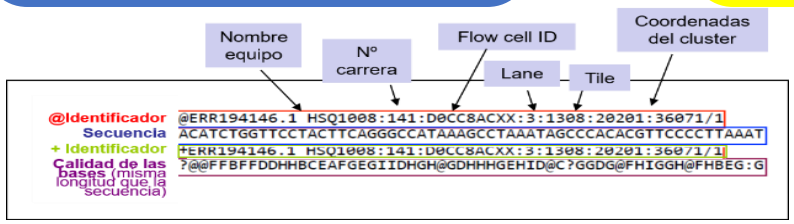
-Une lecturas F+R (~500 pb)

Asignación **ASVs**

(*Amplicon Sequence variants*) (99%)

SILVA

(70%)



Amplicon Sequencing. Exactly.

≠ OTUS*

(*Operational Taxonomic Units*)

QIIME 2 (plataforma bioinformática)

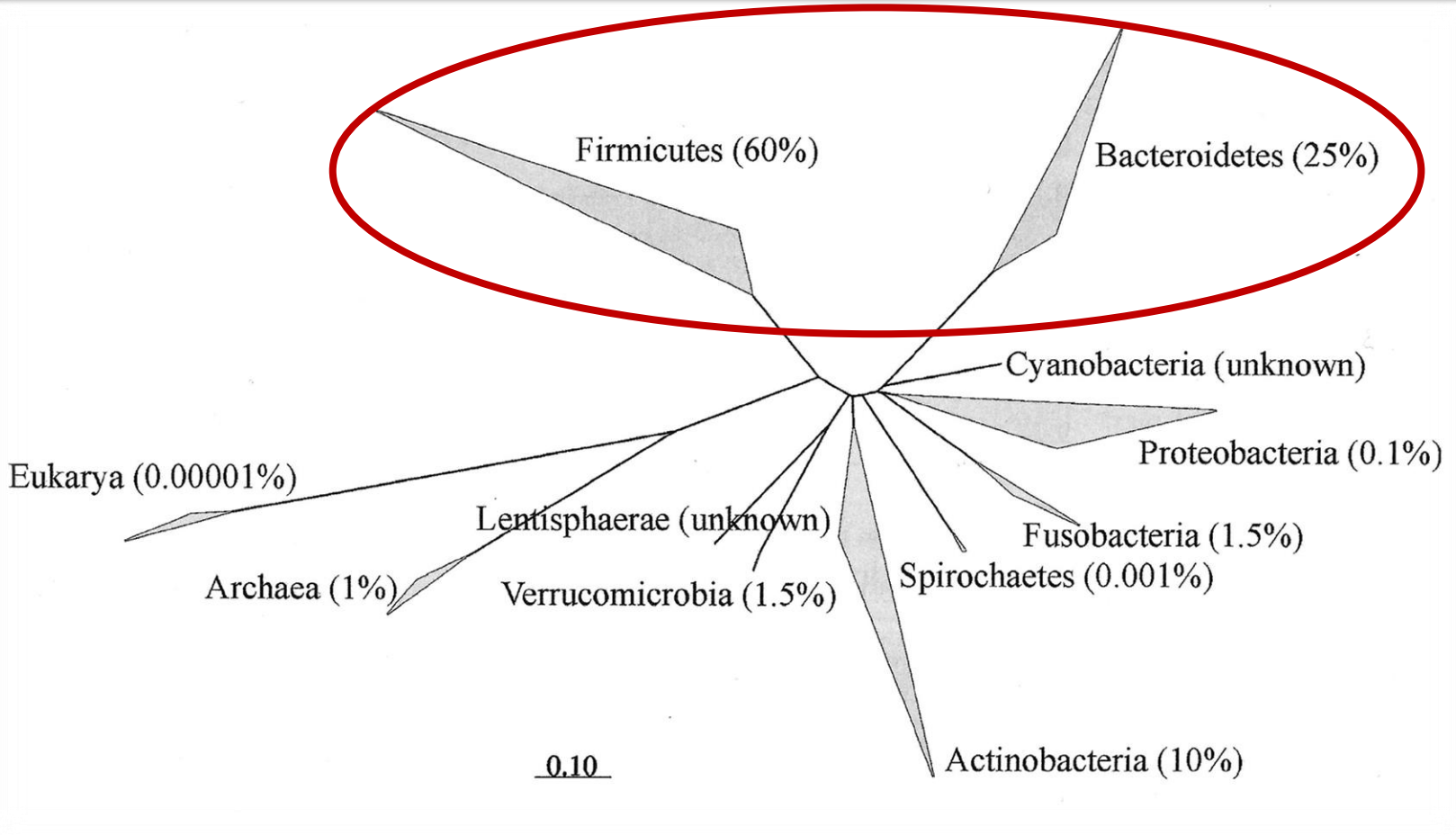
Secuenciación de microbiota: ómicas

B

Method	Advantages	Limitations
Culturome	• High-throughput • Targeted selection • Provides microbial isolates	• Expensive • Laborious • Influenced by media and the environment
Amplicon (16S/18S/ITS)	• Quick analysis • Low-biomass requirement • Applicable to samples contaminated by host DNA	• PCR and primer biases • Resolution limited to genus level • False positive in low-biomass samples
Metagenome	• Taxonomic resolution to species or strain level • Functional potential • Uncultured microbial genome	• Expensive • Time-consuming in analysis • Host-derived contamination
Virome	• Can identify RNA and DNA viruses • Quick diagnosis	• Most expensive • Difficult to analysis • Severe host-derived contamination
Metatranscriptome	• Can identify live microbes • Can evaluate microbial activity • Transcript-level responses	• Complex sample collection and analysis • Expensive and complex in sequencing • Host mRNA and rRNA contamination

TÉCNICAS DE METAGENÓMICA: estudio directo del conjunto de genomas de un determinado entorno (metagenoma) a partir de muestras de ese ambiente, sin necesidad de su aislamiento y cultivo.

How is gut microbiota?



80-90% of the bacteria from the intestinal microbiota belongs to the Phyla Firmicutes (*Clostridium, Lactobacillus, Ruminococcus*) and Bacteroidetes (*Bacteroides, Prevotella*) followed by Actinobacteria (*Bifidobacteria*)

Datos en repositorios

Microbiota composition

Total DNA was obtained by the QiaAmp kit (Qiagen) from the biopsies, from the pellet of saliva after centrifugation, and from 200 µl aliquots of a solution of 0.5 gr of faeces in 5 ml of water. Bacterial composition was determined by PCR amplification of the 16S rDNA V3-V4 region using published primers,[11] whereas the mycobiome was only analyzed in bronchial and saliva of the 16 controls and in a subset of 6 patients by amplification of the ITS-1 region.[12] PCR products were submitted to massive sequencing (2× 300 bp) on a MiSeq (Illumina, San Diego, CA, USA) platform, at FISABIO (Valencia, Spain). Raw sequence data were deposited in GenBank (BioProjects PRJNA586753 and PRJNA586768. QIIME2 software suite (2019.1 distribution)[13] and LEfSE[14] were used for analysis, and adequate negative sequencing controls were added in each process and run. A computational analysis has developed to define the microbiota core that was present in at least 95% of the individuals. This analysis is available at https://github.com/JJ-Lab/Cancer_Lung_Microbiota website.

Bello et al., Arch Bronconeumol, 2021

Infect Dis Ther (2022) 11:1541–1557

Data Availability. The datasets generated during and/or analysed during the current study are available in the NCBI SRA repository, http://www.ncbi.nlm.nih.gov/bioproject/819232.

Villoslada-Blanco et al., Infect Dis Ther, 2022

AADs

Type of treatment (DAAs)	**Ledipasvir/Sofosbuvir:**	**9/22 (40.91%)**
	Ombitasvir/Paritaprevir/Ritonavir + Dasabuvir:	6/22 (27.27%)
	Ombitasvir/Paritaprevir/Ritonavir + Ribavirin:	2/22 (9.09%)
	Sofosbuvir + Daclatasvir:	4/22 (18,18%)
	Ombitasvir/Paritaprevir/Ritonavir + Dasabuvir + Ribavirin:	1/22 (4.55%)