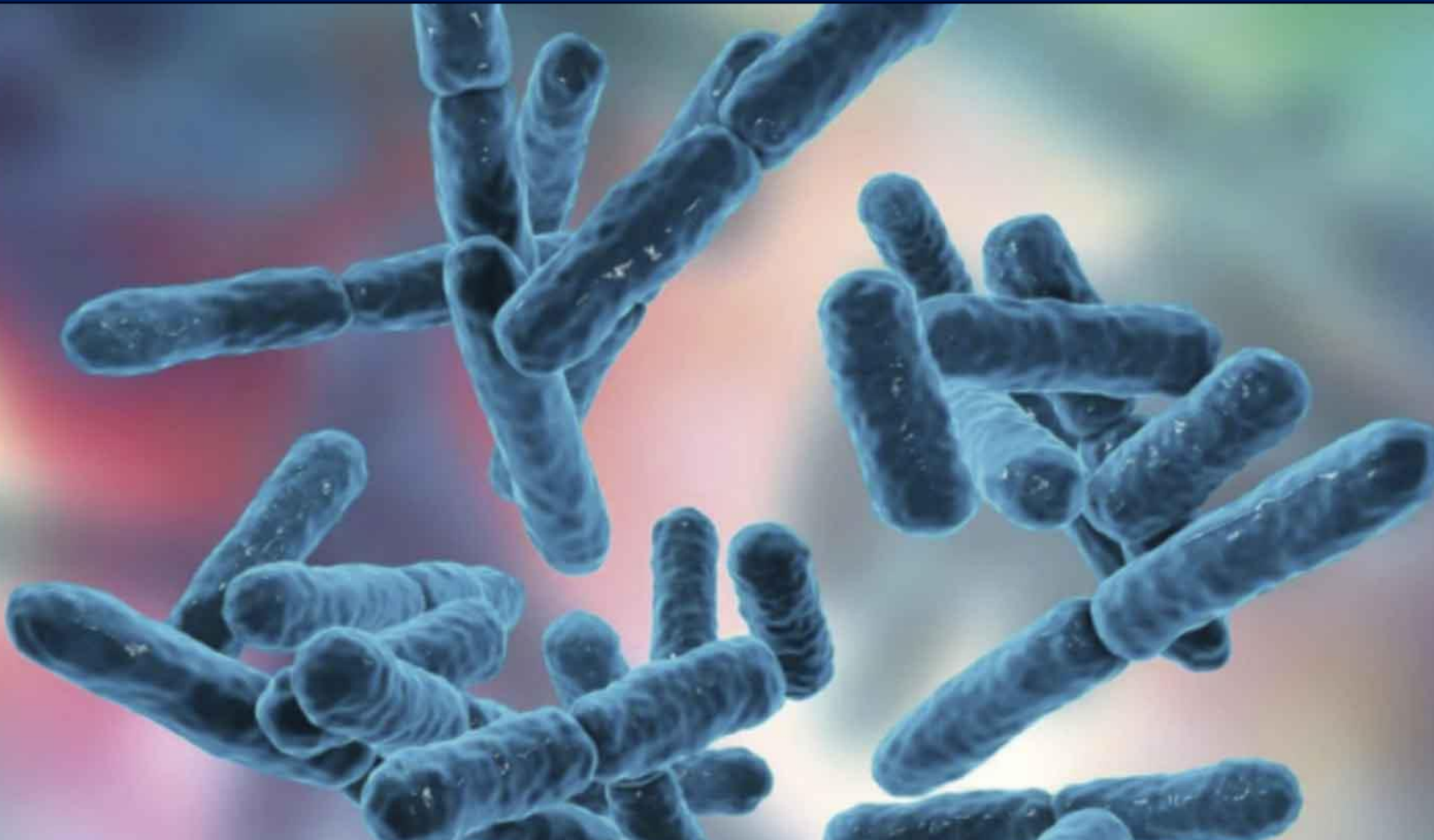


# Bacterias, alimentación y salud: una trilogía fascinante

Daniel Ramón Vidal



CEU

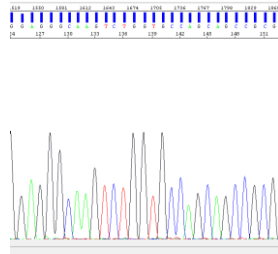
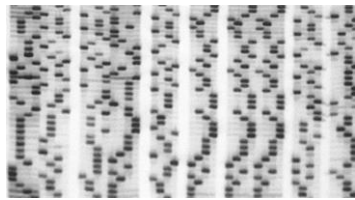
*Universidad  
Cardenal Herrera*

# Todo empezó en febrero del 2001



- El 15 de febrero del 2001 se publicaba en la revista Nature el primer borrador del genoma humano obtenido por el “International Human Genome Project”; un día más tarde, la revista Science publicaba un segundo borrador obtenido por la compañía norteamericana Celera Genomics
- Estas dos publicaciones abrieron la puerta a la necesidad de secuenciar miles de genomas; para ello había que mejorar las técnicas de secuenciación genómica y secuenciar más genomas con menos coste y en menos tiempo
- Obtener estos resultados costó diez años de trabajo de tres mil científicos y una inversión de tres mil millones de dólares

# Las plataformas de secuenciación genómica masiva



1970-90                      1990-2000                      2023

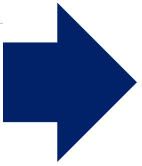
MIT Technology Review 

Biotechnology / DNA Testing

**China's BGI says it can sequence a genome for just \$100**

Super-cheap DNA sequencing could boost cancer screening, prenatal tests, and research into population genetics.

by Antonio Regalado Feb 26, 2020



<200 bases  
1 lectura  
200 bases

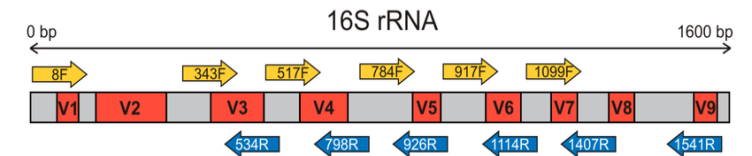
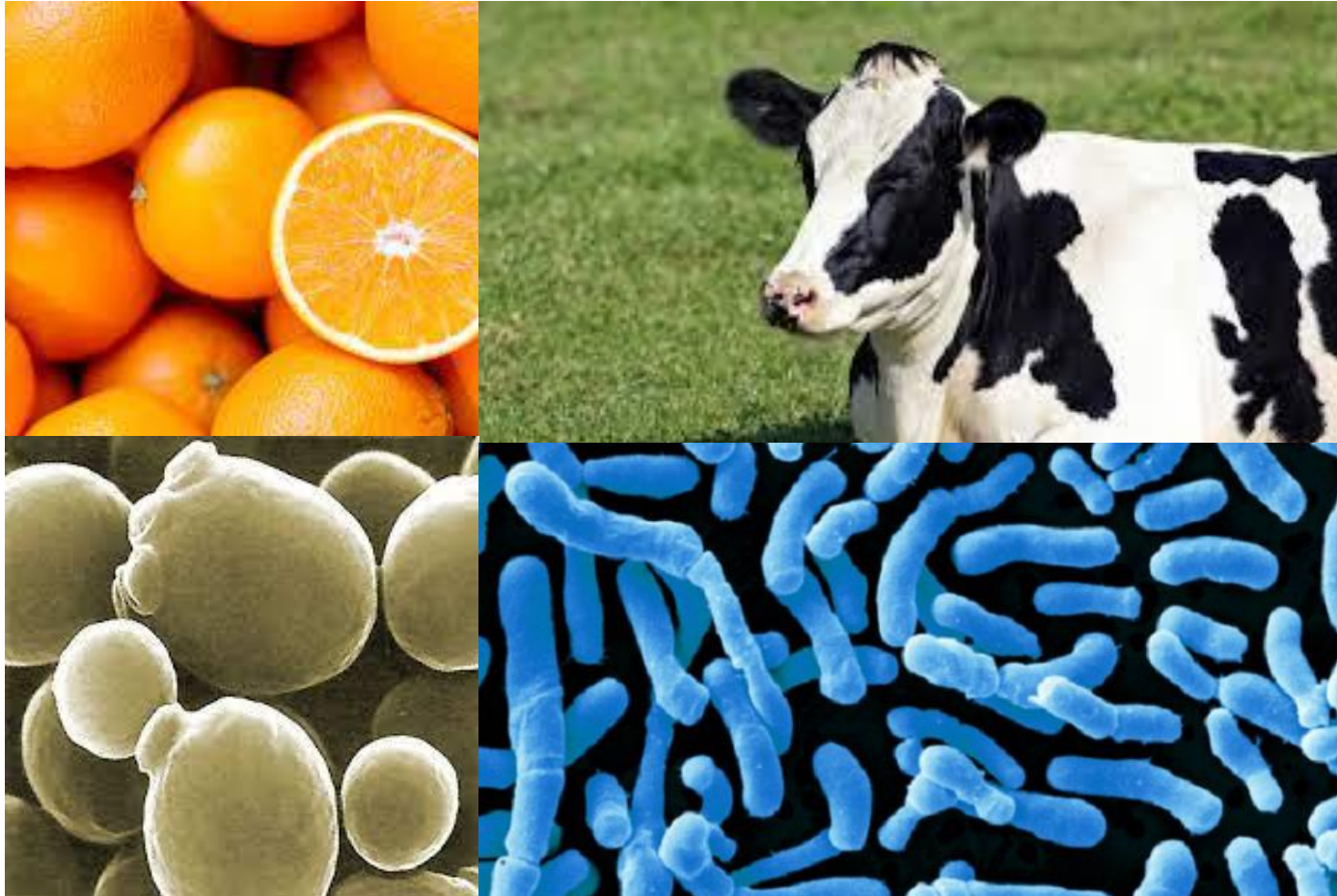
<400 bases  
100 lecturas  
4X10<sup>4</sup> bases

600 bases  
2.5 X 10<sup>7</sup> lecturas  
1.5 X 10<sup>10</sup> bases

600 bases  
5.2 X 10<sup>10</sup> lecturas  
3 X 10<sup>17</sup> bases

4 X 10<sup>6</sup> bases  
5 x 10<sup>10</sup> lecturas  
2 X 10<sup>16</sup> bases

# Genomas humanos...y de cualquier ser vivo



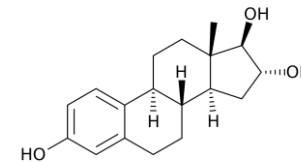
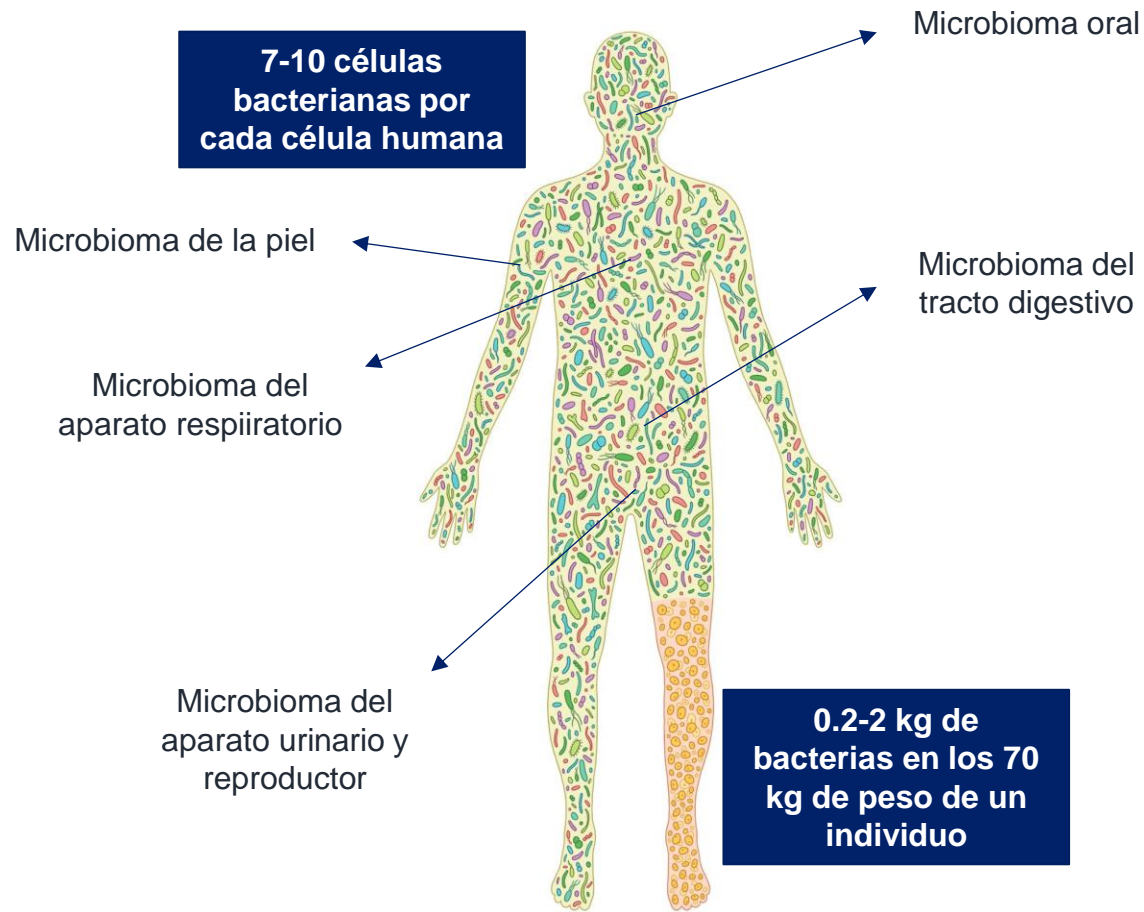
200000 genomas  
bacterianos secuenciados

# El increíble mundo microbiano

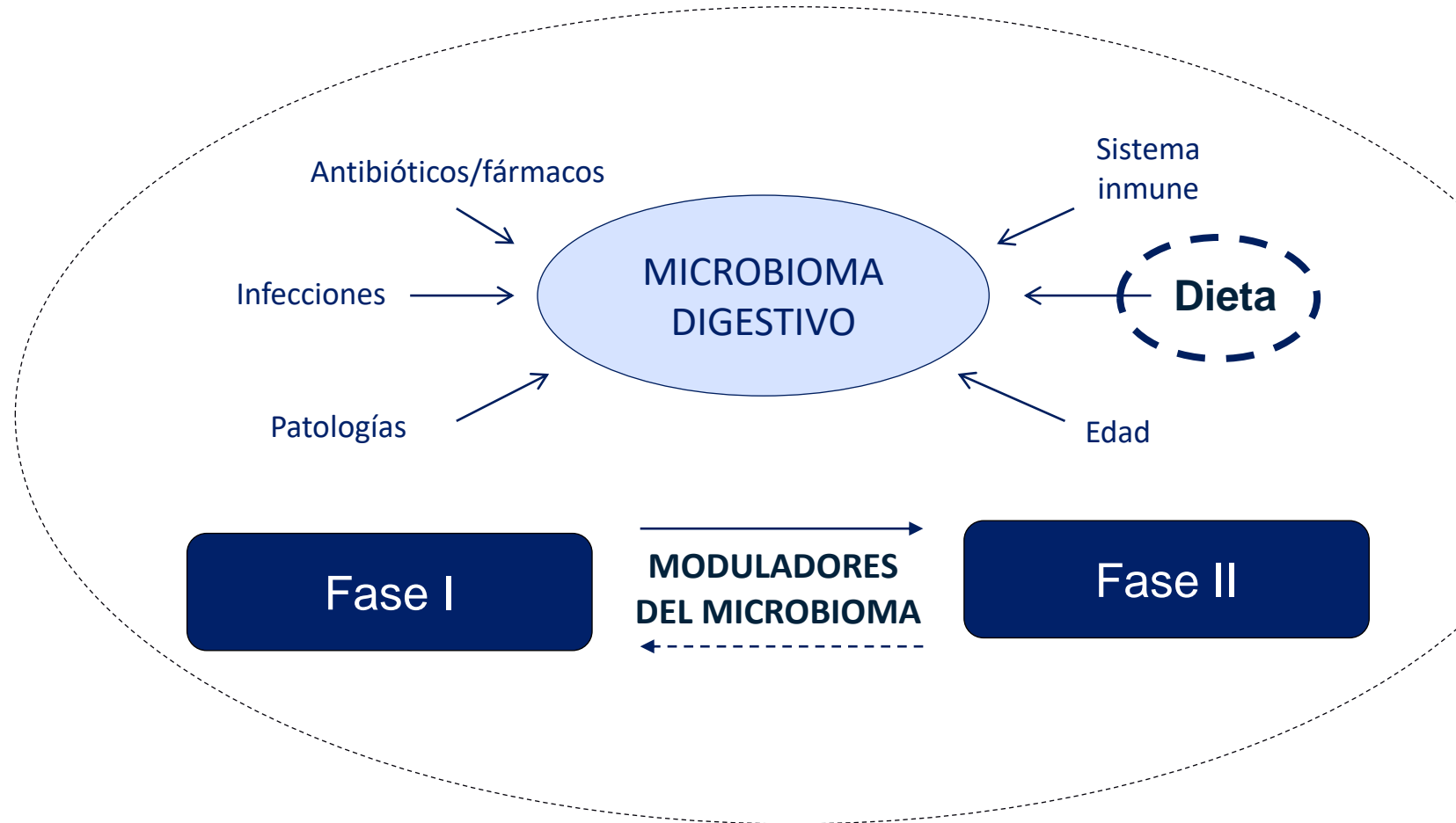


- Las bacterias son ubicuas; hay bacterias en los sitios más inhóspitos: en los lagos helados de la Antártida, en los geiseres del Parque Nacional de Yellowstone o en el desierto de Atacama
- Se calcula que en 1 gramo de tierra hay 10 millones de bacterias y en un mililitro de agua de un río 1 millón
- Son los seres vivos más numerosos en el planeta; se calcula que en la Tierra hay del orden de  $5 \times 10^{30}$  bacterias (5 quintillones = 5 billones de trillones),
- Por cada humano tocamos a  $6.4 \times 10^{20}$  bacterias (640 trillones de bacterias/humano)

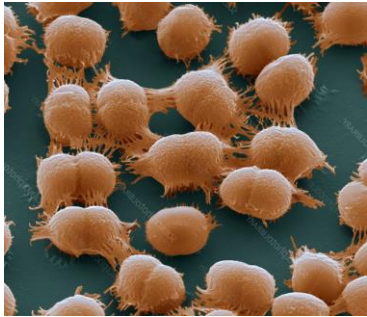
# El microbioma humano



# Moduladores del microbioma



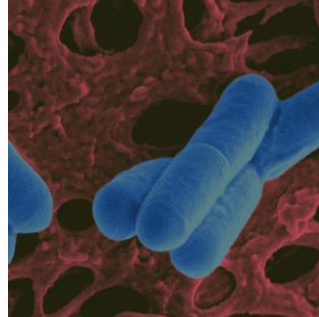
# La “limitada” primera generación de moduladores



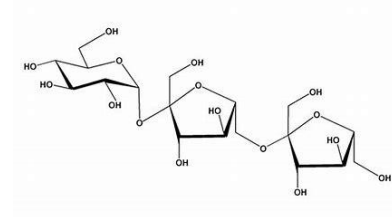
*Bacillus*



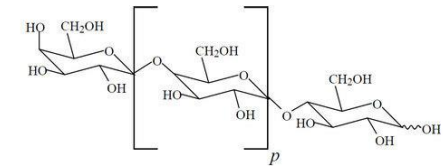
*Bifidobacterium*



*Lactobacillus*



FOS

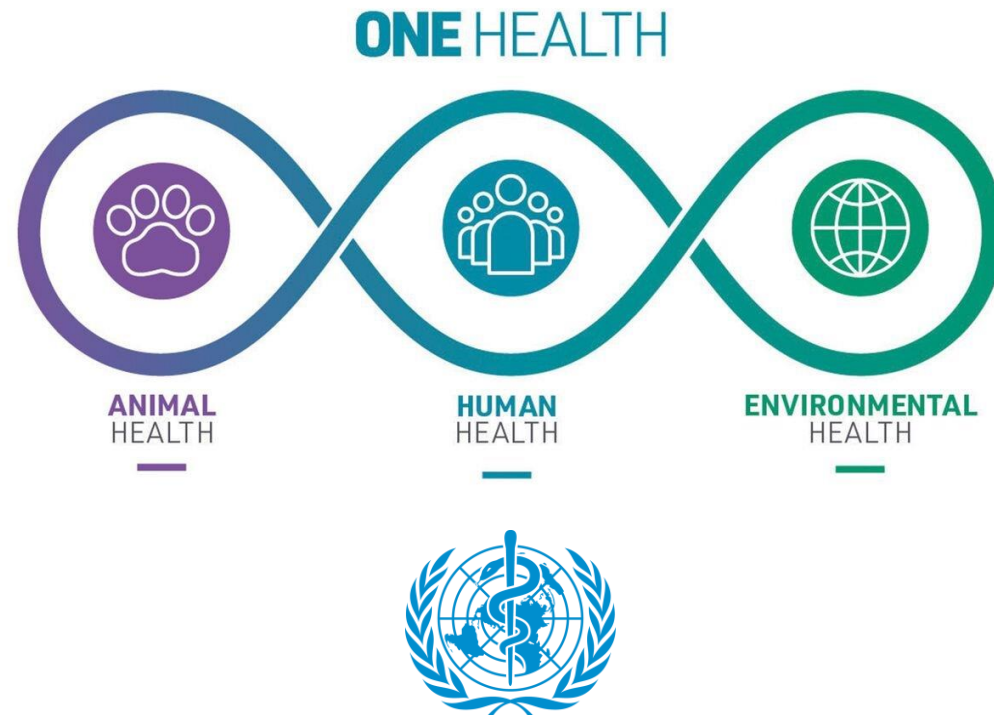


GOS

Probióticos, prebióticos y sinbióticos



# Para el futuro necesitamos un abordaje distinto



# Muchas oportunidades



## Moduladores de 1ª generación

*Bacillus*  
*Bifidobacterium*  
*Lactobacillus*  
*Saccharomyces*  
FOS  
GOS  
HMO

## Probióticos de 2ª generación

*Akkermansia*  
*E. coli* Nissle  
*Faecalibacterium*  
*Odoribacter*  
*Roseburia*  
“Traditional-healthy” strains

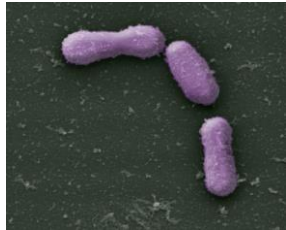
## Nuevos moduladores microbianos

Bacteriocinas  
Exopolisacáridos  
Exovesículas  
GpC rich oligoDNA  
LTA  
Postbióticos  
Proteasas  
Pili  
Péptidos microbianos  
Restos de pared celular  
SCFA

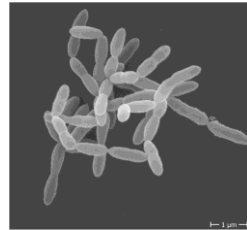
## Nuevos moduladores no microbianos

Antocianos  
Bacteriofagos  
Enzimas líticos de fagos  
Isoflavonas  
Nuevas fibras prebióticas  
Péptidos  
Polifenoles  
Terpenos

# Probióticos anaerobios estrictos



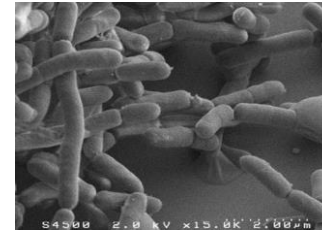
*Akkermansia*



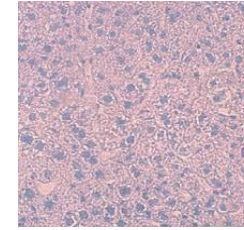
*Christensenella*



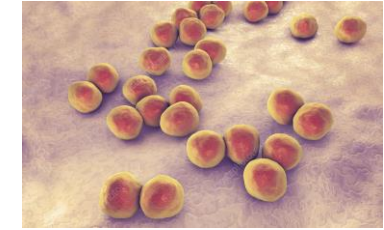
*Clostridium*



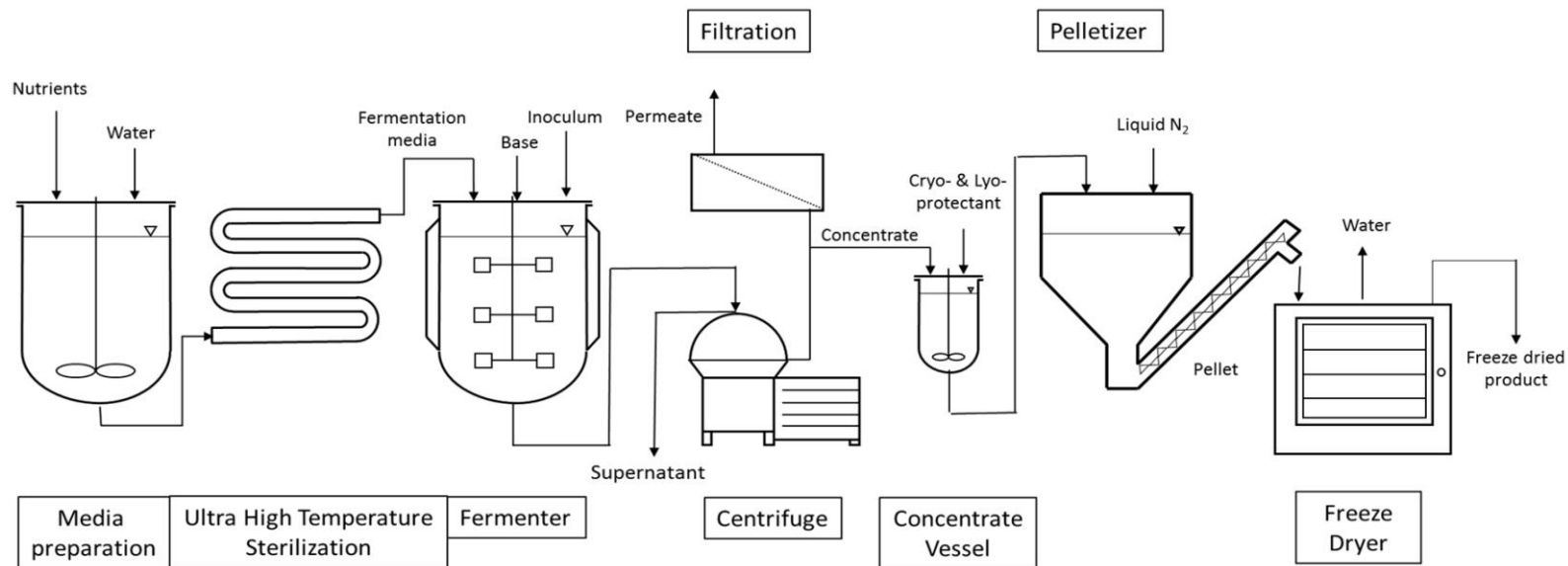
*Faecalibacterium*



*Parabacteroides*



*Veillonella*



*Escherichia coli* Nissle

Diabetes

*Lactobacillus gasseri*

Fenilcetonuria

*Lactobacillus helveticus*

Hiperamonemia

*Lactobacillus rhamnosus*

Inflamación

*Lactococcus lactis*

Patógenos

*Vibrio cholerae*

Metastasis hígado

Zhou et al. *Microb Cell Fact* (2020) 19:56  
<https://doi.org/10.1186/s12934-020-01318-z>

Microbial Cell Factories

REVIEW

Open Access



## Engineering probiotics as living diagnostics and therapeutics for improving human health

Zhao Zhou<sup>1</sup>, Xin Chen<sup>1</sup>, Huakang Sheng<sup>1</sup>, Xiaolin Shen<sup>1</sup>, Xinxiao Sun<sup>1</sup>, Yajun Yan<sup>2</sup>, Jia Wang<sup>1\*</sup> and Qipeng Yuan<sup>1\*</sup>

### Abstract

The gut microbiota that inhabit our gastrointestinal tract are well known to play an important role in maintaining human health in many aspects, including facilitating the digestion and absorption of nutrients, protecting against pathogens and regulating immune system. Gut microbiota dysbiosis is associated with a lot of diseases, such as inflammatory bowel disease, allergy, obesity, cardiovascular and neurodegenerative diseases and cancers. With the increasing knowledge of the microbiome, utilization of probiotic bacteria in modulating gut microbiota to prevent and treat a large number of disorders and diseases has gained much interest. In recent years, aided by the continuous development of tools and techniques, engineering probiotic microbes with desired characteristics and functionalities to benefit human health has made significant progress. In this paper, we summarize the recent advances in design and construction of probiotics as living diagnostics and therapeutics for probing and treating a series of diseases including metabolic disorders, inflammation and pathogenic bacteria infections. We also discuss the current challenges and future perspectives in expanding the application of probiotics for disease treatment and detection. We intend to provide insights and ideas for engineering of probiotics to better serve disease therapy and human health.

**Keywords:** Probiotics, Metabolic engineering, Synthetic biology, Microbiome

### Background

The human gastrointestinal tract harbors complex and diverse microbes that act as a key factor in maintaining the homeostasis of the intestinal microenvironment [1]. It is estimated that approximately  $10^{13}$ – $10^{14}$  bacterial cells from more than 1000 different species are present in gut, which form a natural ecosystem in the human body [2]. Those commensal bacteria can utilize the nutrients in the gut to produce metabolites to form a host-microbe metabolic axes [3]. Within those metabolic axes, it is able to regulate nutrient absorption, energy metabolism and various physiological processes in host [4]. Recently, study of interaction between gut flora and human host

has gained much interest. More and more evidence indicated that gut microbiota plays an important role in human health and diseases [5]. On the one hand, the human gut microbiota contributes to supply essential healthy nutrients, digestion of food, reduction of inflammation and breakdown of toxins, promotes hematopoiesis and enteric nerve function, and regulates the host's immune system [6]. On the other hand, the abnormal changes of the gut ecosystem are associated with pathological conditions such as atherosclerosis, hypertension, heart failure, chronic kidney disease, obesity, diabetes and cancer [7–15]. In addition, the composition of the gut microbiota in humans can indicate the disease risk or development [16, 17]. It has been reported that diet can significantly alter the gut microbiota composition, other factors including host genetics, infections, the use of antibiotics, immunosuppressive therapy and other means of treatment also contribute to the composition and effect of the gut flora [18, 19].

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## CONSENSUS STATEMENT

OPEN



### The International Scientific Association of Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of postbiotics

Seppo Salminen<sup>1,2</sup>, Maria Carmen Collado<sup>3</sup>, Akihito Endo<sup>4</sup>, Colin Hill<sup>4,5</sup>, Sarah Lebeer<sup>6</sup>, Eamonn M. M. Quigley<sup>7</sup>, Mary Ellen Sanders<sup>8</sup>, Raanan Shamir<sup>9,10</sup>, Jonathan R. Swann<sup>11,12</sup>, Hania Szajewska<sup>13</sup> and Gabriel Vinderola<sup>14</sup>

**Abstract** | In 2019, the International Scientific Association for Probiotics and Prebiotics (ISAPP) convened a panel of experts specializing in nutrition, microbial physiology, gastroenterology, paediatrics, food science and microbiology to review the definition and scope of postbiotics. The term 'postbiotics' is increasingly found in the scientific literature and on commercial products, yet is inconsistently used and lacks a clear definition. The purpose of this panel was to consider the scientific, commercial and regulatory parameters encompassing this emerging term, propose a useful definition and thereby establish a foundation for future developments. The panel defined a postbiotic as a "preparation of inanimate microorganisms and/or their components that confers a health benefit on the host". Effective postbiotics must contain inactivated microbial cells or cell components, with or without metabolites, that contribute to observed health benefits. The panel also discussed existing evidence of health-promoting effects of postbiotics, potential mechanisms of action, levels of evidence required to meet the stated definition, safety and implications for stakeholders. The panel determined that a definition of postbiotics is useful so that scientists, clinical trialists, industry, regulators and consumers have common ground for future activity in this area. A generally accepted definition will hopefully lead to regulatory clarity and promote innovation and the development of new postbiotic products.

The past few decades have demonstrated unequivocally the importance of the human microbiota to both short-term and long-term human health. Early programming of the microbiota and immune system during pregnancy, delivery, breastfeeding and weaning is important and determines adult immune function, microbiome and overall health<sup>1</sup>. We have also seen rapid growth in the number of products that claim to affect the functions and composition of the microbiota at different body sites to benefit human health.

Improving human health through modulation of microbial interactions during all phases of life is an evolving concept that is increasingly important for consumers, food manufacturers, health-care professionals and regulators. Microbiota-modulating dietary interventions include many fermented foods and fibre-rich dietary regimens, as well as probiotics, prebiotics and synbiotics, some of which are available as drugs and medical devices, as well as foods<sup>2</sup>. The rich, diverse

microbial ecosystems and immune cells inhabiting all mucosal and cutaneous surfaces provide targets for intervention, with the goals of reducing the risk of diseases and improving health status<sup>3</sup>. Consensus definitions of probiotics, prebiotics and synbiotics have been published previously. Probiotics are "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host"<sup>4</sup>, whereas a prebiotic is a "substrate that is selectively utilized by host microorganisms conferring a health benefit"<sup>5</sup>. A synbiotic, initially conceived as a combination of both probiotics and prebiotics, has now been defined as "a mixture comprising live microorganisms and substrate(s) selectively utilized by host microorganisms that confers a health benefit on the host"<sup>6</sup>. The concept of postbiotics is related to this family of terms and is emerging as an important microorganism-derived tool to promote health.

Probiotics are by definition alive and required to have an efficacious amount of viable bacteria at the

- Un postbiótico es “una preparación de microorganismos inanimados y/o sus componentes que confiere un beneficio para la salud del huésped”
- Pueden vehiculizarse en cualquier alimento o bebida, aunque sufran un tratamiento térmico
- No son un riesgo para personas inmunodeprimidas

\*e-mail: sepsa@utu.fi  
<https://doi.org/10.1038/s41575-021-00440-6>



## Gut microbiota targeted nanomedicine for cancer therapy: Challenges and future considerations

Muhammad Shahid Riaz Rajoka<sup>a,1</sup>, Hafiza Mahreen Mehwish<sup>a,1</sup>, Yongai Xiong<sup>a</sup>, Xun Song<sup>a</sup>, Nazim Hussain<sup>b</sup>, Qinchang Zhu<sup>a,c,\*</sup>, Zhendan He<sup>a,c,1</sup>

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<sup>b</sup> Centre for Applied Molecular Biology (CAMB), University of the Punjab, Lahore 55000, Pakistan  
<sup>c</sup> School of Pharmacy, Shenzhen Technology University, Shenzhen, 518060, PR China

### ARTICLE INFO

**Keywords:**  
 Gut microbiota  
 Cancer  
 Nanomaterials  
 Microbiome  
 Microbiota variability

### ABSTRACT

**Background:** Nanomedicine has become one of the most promising technologies to modernize the traditional food. However, not only the public perception of the new technology is uncertain, but also the regulators have not yet to agree on how to apply globally. The gastrointestinal tract microbiota and its genes (the microbiome) are considered a fundamental part of the human body. The gut microbiota is a major part of the host microbiome and contains approximately  $3 \times 10^{13}$  bacterial cells in a commensal relationship with the host. However, once the gastric ecosystem is altered, various bacterial species (e.g., antibiotic-resistant *Enterococcus* and *Clostridium difficile*) can increase and develop pathogenic phenotypes. Recent evidence suggests that the gut microbiota is involved in carcinogenesis and can enhance the activity, efficacy, and toxicity of anticancer therapies. Recently, there is fast-growing concern regarding the effect of nanoparticles on the human gut microbiome. Nanomaterials can enter the human body via skin contact, ingestion, and inhalation.

**Scope and approach:** In the present review, the recent advances on the role of microbiota and nanomaterials in cancer therapy, the microbiota and their metabolic interventions via nanomaterials, microbial inspiration via nanomaterials, and the challenge associated with using nanomaterials in humans and animals is discussed. In short, this review will focus on the current status and future perspectives of gut microbiota targeted nanotechnology for cancer therapy and cancer-related metabolic diseases.

**Key findings and conclusion:** The changes in the gut microbiota or microbiome play vital roles in human diseases such as cancer. Traditional microbiome treatments have led to improved cancer treatments in some cases; however, problems such as collateral injury to the symbiotic microbiome and reliability of these treatment methods have led to new technological developments designed specifically for cancer microbiota crossing point. Hence, the prosperance of nanomaterials in cancer prevention has led to the idea that nanomaterials can alter the cancer-causing microbes/microbiome and their metabolites as well as alter the cancer microenvironment. Therefore, nanomaterials can be used as novel strategies to treat cancer. However, this emerging research area requires further in vivo clinical trials to determine the exact mechanisms of action involved in treating cancer via nanomaterials. Further studies should explore the connection between nanomaterials, the microbiota, microbial metabolites, cancer and cancer-related microenvironments in animals and humans.

### 1. Introduction

Cancer is now the major cause of death in developing countries

(Arbyn et al., 2020; Jung, Wm, Kang, & Lee, 2019). Despite the therapeutic advances in treating cancer, resistance to chemotherapeutic agents remains the hallmark of cancer therapy. Chemotherapeutic

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<sup>1</sup> Author equally contributed.

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 Available online 1 November 2020  
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Med

CellPress  
OPEN ACCESS

### Clinical and Translational Article

## Heterogeneity in statin responses explained by variation in the human gut microbiome



Prior work has indicated that statin therapy impacts gut microbiome composition and that gut bacteria can metabolize statins, but the clinical implications of these interactions remain unknown. Wilmanski et al. identify robust associations between microbiome composition and on-target and adverse responses to statins, which could prove useful in drug personalization.

Tomasz Wilmanski, Sergey A. Komilov, Christian Diener, ..., Noa Rappaport, Andrew T. Magis, Sean M. Gibbons

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 amagis@sbscience.org (A.T.M.)  
 sgibbons@sbscience.org (S.M.G.)

**Highlights**  
 HMG in blood identified as a potential cross-sectional biomarker for statin responses

Gut microbiome  $\alpha$ -diversity negatively associated with on-target statin responses

Bacteroides-enriched individuals at higher risk of statin-induced metabolic disruption

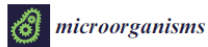
Firmicutes-dominant individuals at lower risk of statin-induced metabolic disruption

Translation to Patients

Wilmanski et al., Med 3, 1–18  
 June 10, 2022 © 2022 The Author(s). Published by Elsevier Inc.  
<https://doi.org/10.1016/j.med.2022.04.007>

# Y además, a lo largo de la cadena agroalimentaria





Article

## Unlocking the Microbiome Communities of Banana (*Musa* spp.) under Disease Stressed (*Fusarium* wilt) and Non-Stressed Conditions

Manoj Kaushal<sup>1,\*</sup>, Rony Swennen<sup>2,3,4</sup> and George Mahuku<sup>1</sup><sup>1</sup> International Institute of Tropical Agriculture (IITA), Mikochei B, Dar es Salaam 34441, Tanzania; g.mahuku@iita.org<sup>2</sup> International Institute of Tropical Agriculture (IITA), Arusha 447, Tanzania; rony.swennen@iitakuven.be<sup>3</sup> Laboratory of Tropical Crop Improvement, Division of Crop Biotechnics, KU Leuven, B-3001 Leuven, Belgium<sup>4</sup> Bioversity International, Willem De Croylaan 42, B-3001 Leuven, Belgium

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**Abstract:** We assessed the diversity, structure, and assemblage of bacterial and fungal communities associated with banana plants with and without *Fusarium oxysporum* f. sp. *cubense* (Foc) symptoms. A total of 117,814 bacterial and 17,317 fungal operational taxonomy units (OTUs) were identified in the rhizosphere, roots, and corm of the host plant. Results revealed that bacterial and fungal microbiota present in roots and corm primarily emanated from the rhizosphere. The composition of bacterial communities in the rhizosphere, roots, and corm were different, with more diversity observed in the rhizosphere and less in the corm. However, distinct sample types i.e., without (asymptomatic) and with (symptomatic) *Fusarium* symptoms were the major drivers of the fungal community composition. Considering the high relative abundance among samples, we identified core microbiomes with bacterial and fungal OTUs classified into 20 families and colonizing distinct plant components of banana. Our core microbiome assigned 129 bacterial and 37 fungal genera to known taxa.

**Keywords:** *Musa*; *Fusarium* wilt; rhizosphere; microbiome diversity; *Fusarium oxysporum* f. sp. *cubense*

### 1. Introduction

Rhizospheric and endophytic microbiota have been shown to significantly improve plant health and development [1,2]. Beneficial microorganisms in the rhizosphere/roots of bananas have been investigated for potential beneficial impacts [3]. Both roots as well as the thin soil layer adhering to roots, called rhizosphere, host diverse microbial communities. To date, however, most research has focused on only a small fraction of a pre-targeted group of the rhizosphere microbiota. Hence information is missing of the entire associated microbial diversity and influencing factors.

Bananas (*Musaceae* spp.) are cultivated throughout the humid tropics and sub-tropics. In sub-Saharan Africa (SSA), bananas are an important component of the diet and a crucial source of income for many small holder farmers. Disease pressure is the major threat threatening banana productivity in the region [4–6]. The devastation of bananas by Panama disease caused by the soil borne *Fusarium oxysporum* f. sp. *cubense* (Foc), lack of pesticides, and appropriate resistant varieties encouraged the search for alternatives to sustain productivity. Foc race 1 is present everywhere in SSA hampering dessert banana (of the *Musa* subgroup AAB) productivity [7]. In addition, Foc race 4 is present in Mozambique [3]. The pathogen can spread from infected to non-infected fields through banana suckers, water, and movement of people. Foc enters through the roots and infects the plant vascular system. Initial disease expression is yellowing of leaves. In later stages, maroon color lines

ORIGINAL RESEARCH  
published: 24 December 2021  
doi: 10.3389/fpls.2021.775722

## The Bacterial Microbiome of the Tomato Fruit Is Highly Dependent on the Cultivation Approach and Correlates With Flavor Chemistry

Carolina Escobar Rodriguez<sup>1</sup>, Johannes Novak<sup>2\*</sup>, Franziska Buchholz<sup>3</sup>, Pia Uetz<sup>4</sup>, Laura Bragagna<sup>1</sup>, Marija Gumzo<sup>1</sup>, Ljivo Antoniali<sup>5</sup> and Birgit Mitter<sup>2</sup><sup>1</sup>FFG2S GmbH – Austrian Competence Centre for Food and Food Quality, Safety and Innovation, Tulln, Austria; <sup>2</sup>Institute of Applied Botany and Pharmacognosy (IAB), Veterinary University of Vienna, Vienna, Austria; <sup>3</sup>Center for Health & Biosciences, Biosciences Unit, AIT Austrian Institute of Technology GmbH, Tulln, Austria

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on the Cultivation Approach and  
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The modes of interactions between plants and plant-associated microbiota are manifold, and secondary metabolites often play a central role in plant-microbe interactions. Abiotic and biotic (including both plant pathogens and endophytes) stress can affect the composition and concentration of secondary plant metabolites, and thus have an influence on chemical compounds that make up for the taste and aroma of fruit. While the role of microbiota in growth and health of plants is widely acknowledged, relatively little is known about the possible effect of microorganisms on the quality of fruit of plants they are colonizing. In this work, tomato (*Solanum lycopersicum* L.) plants of five different cultivars were grown in soil and in hydroponics to investigate the impact of the cultivation method on the flavor of fruit, and to assess whether variations in their chemical composition are attributable to shifts in bacterial microbiota. Ripe fruit were harvested and used for bacterial community analysis and for the analysis of tomato volatiles, sugars and acids, all contributing to flavor. Fruit grown in soil showed significantly higher sugar content, whereas tomatoes from plants under hydroponic conditions had significantly higher levels of organic acids. In contrast, aroma profiles of fruit were shaped by the tomato cultivars, rather than the cultivation method. In terms of bacterial communities, the cultivation method significantly defined the community composition in all cultivars, with the bacterial communities in hydroponic tomatoes being more variable than those in tomatoes grown in soil. Bacterial indicator species in soil-grown tomatoes correlated with higher concentrations of volatiles described to be perceived as “green” or “pungent.” A soil-grown specific reproducibly occurring ASV (amplicon sequence variants) classified as *Bacillus* detected solely in “Solarino” tomatoes, which were the sweetest among all cultivars, correlated with the amount of aroma-relevant volatiles as well as of fructose and glucose in the fruit. In contrast, indicator bacterial species in hydroponic-derived tomatoes correlated with aroma compounds with “sweet” and



# ¿Es posible modificar el microbioma de las partes comestibles de las plantas?



Eric Schott

Gerardo Toledo



## scientific reports

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### The Edible Plant Microbiome represents a diverse genetic reservoir with functional potential in the human host

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Plant microbiomes have been extensively studied for their agricultural relevance on growth promotion and pathogenesis, but little is known about their role as part of the diet when fresh fruits and vegetables are consumed raw. Most studies describing these communities are based on 16S rRNA gene amplicon surveys, limiting our understanding of the taxonomic resolution at the species level and functional capabilities. In this study, we characterized microbes colonizing tomatoes, spinach, brined olives, and dried figs using shotgun metagenomics. We recovered metagenome-assembled genomes of novel lactic acid bacteria from green olives and identified high intra- and inter-specific diversity of *Pseudomonas* in tomatoes. All samples were colonized by *Pseudomonas*, consistent with other reports with distinct community structure. Functional characterization showed the presence of enzymes involved in vitamin and short chain fatty acid metabolism and degradation of diverse carbohydrate substrates including plant fibers. The dominant bacterial members were isolated, sequenced, and mapped to its metagenome confirming their identity and indicating the microbiota is culturable. Our results reveal high genetic diversity, previously uncultured genera, and specific functions reflecting a likely plant host association. This study highlights the potential that plant microbes can play when consumed as part of our diet and proposes these as transient contributors to the gut microbiome.

Advancements in molecular methods over the past 30 years have expanded our knowledge of the vast extent of biological diversity on earth. The use of 16S rRNA gene sequences has enabled characterization of microbial communities in a wide range of habitats including the human body and in fluids including stool, prompting establishment of the microbiome field and industry. Diet has been identified as one of the main variables shaping the gut microbiome, as dietary intervention studies have demonstrated that the gut microbiota composition can reflect variations in food consumption despite inter-individual variation and the heterogeneous nature of stool that complicates representative sample collection<sup>1–3</sup>.

In contrast to the efforts aimed to describe the microbiota in stool, very little exploration has been conducted in our foods and the microbes consumed in a typical diet<sup>4</sup>. Most of what we know about food microbiomes, especially as it relates to fresh fruits and vegetables, is related to agricultural pathogens and toxins. However, the recognition that our diets contain potentially beneficial bacteria and fungi is a new concept. Berg et al.<sup>5</sup> coined the term *Edible Plant Microbiome* to identify the types of taxa, compartments, and plant groups that carry live microbes in our diets, especially when eaten raw. The overall view is that microbes colonizing internal and external plant tissues can play a role in human nutrition and health and provide insights of co-adaptation processes between plants, animals, and their microbiomes. For example, Wasserman et al.<sup>6</sup> studied the microbiomes of cruciferous vegetables and showed they provide protection against fungal plant pathogens and anticancer molecules to the human host, indicating an important relationship between the plant host and its microbiota. Plant-associated bacteria play crucial roles in their hosts, including beneficial effects on the production of secondary plant metabolites, protection against pathogen colonization, plant growth promotion, among others<sup>7,8</sup>.

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# Mejoras de rendimiento, calidad y sostenibilidad en animales de granja



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Microbiome

RESEARCH

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## Multi-omics reveals that the rumen microbiome and its metabolome together with the host metabolome contribute to individualized dairy cow performance

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### Abstract

**Background:** Recently, we reported that some dairy cows could produce high amounts of milk with high amounts of protein (defined as milk protein yield [MPY]) when a population was raised under the same nutritional and management condition, a potential new trait that can be used to increase high-quality milk production. It is unknown to what extent the rumen microbiome and its metabolites, as well as the host metabolisms, contribute to MPY. Here, analysis of rumen metagenomics and metabolomics, together with serum metabolomics was performed to identify potential regulatory mechanisms of MPY at both the rumen microbiome and host levels.

**Results:** Metagenomics analysis revealed that several *Prevotella* species were significantly more abundant in the rumen of high-MPY cows, contributing to improved functions related to branched-chain amino acid biosynthesis. In addition, the rumen microbiome of high-MPY cows had lower relative abundances of organisms with methanogen and methanogenesis functions, suggesting that these cows may produce less methane. Metabolomics analysis revealed that the relative concentrations of rumen microbial metabolites (mainly amino acids, carboxylic acids, and fatty acids) and the absolute concentrations of volatile fatty acids were higher in the high-MPY cows. By associating the rumen microbiome with the rumen metabolome, we found that specific microbial taxa (mainly *Prevotella* species) were positively correlated with ruminal microbial metabolites, including the amino acids and carbohydrates involved in glutathione, phenylalanine, starch, sucrose, and galactose metabolism. To detect the interactions between the rumen microbiome and host metabolism, we associated the rumen microbiome with the host serum metabolome and found that *Prevotella* species may affect the host's metabolism of amino acids (including glycine, serine, threonine, alanine, aspartate, glutamate, cysteine, and methionine). Further analysis using the linear mixed effect model estimated contributions to the variation in MPY based on different omics and revealed that the rumen microbial composition, functions, and metabolites, and the serum metabolites contributed 17.81, 21.56, 29.76, and 26.78%, respectively, to the host MPY.

(Continued on next page)

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SCIENCE ADVANCES | RESEARCH ARTICLE

ORGANISMAL BIOLOGY

## A heritable subset of the core rumen microbiome dictates dairy cow productivity and emissions

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A 1000-cow study across four European countries was undertaken to understand to what extent ruminant microbiomes can be controlled by the host animal and to identify characteristics of the host rumen microbiome axis that determine productivity and methane emissions. A core rumen microbiome, phylogenetically linked and with a preserved hierarchical structure, was identified. A 39-member subset of the core formed hubs in co-occurrence networks linking microbiome structure to host genetics and phenotype (methane emissions, rumen and blood metabolites, and milk production efficiency). These phenotypes can be predicted from the core microbiome using machine learning algorithms. The heritable core microbes, therefore, present primary targets for rumen manipulation toward sustainable and environmentally friendly agriculture.

### INTRODUCTION

Hosting one of the most complex microbial communities known to man, the rumen has long attracted the keen interest of microbiologists. Physiologists and nutritionists also understand the pivotal role of the rumen in digesting fibrous feed and providing nutrients to the host animal. These activities enable ruminants to provide humans with foods, mainly milk and meat from nonhuman-edible plant material, including industrial by-products, and enable many rural communities worldwide to survive where arable agriculture is impossible. There is an environmental cost, however, in which ruminants, via their ruminal microbiome, produce substantial amounts of the greenhouse gas, methane (1). Furthermore, production effi-

ciency is linked to the composition of the ruminal microbiome, as was previously shown by an association between microbiome components and residual feed intake (2, 3). Characterizing, quantifying, and understanding the role of rumen microbiome are therefore of significant scientific, economic, and environmental interest.

The main members of the rumen microbiome are now well understood. Bacteria, which usually comprise most of the species richness, are widely persistent geographically across multiple ruminant species and individual animals (4), and many species can be considered symbiotic with ruminants, as they provide metabolic activities and products essential for the host (5). Ciliate protozoa, at up to about half the biomass, consist of species that occur uniquely in the rumen (6). Their community abundance and composition across ruminants are much more variable than bacteria; indeed, protozoa may be absent in some animals without detrimental effect to the host (4, 7). Anaerobic fungi are fewer in number but seem to play an important role in breaking down the toughest of plant cell walls (8). Archaea are key players in methane emissions (9).

Generally speaking, the relationship between members of the microbiome and rumen function is reasonably well understood (10). A host genetics microbiome axis of control has also been implied in several studies (11–13), analogous to, but much less detailed than the remarkable advances in our understanding of the role of the heritability of the human gut microbiome and its role in health (14). In the present study, by applying network analysis to a comprehensive array of microbiome, phenotype, and genotype analysis, we have made a significant contribution in transforming the descriptive understanding of the rumen microbiome to a predictive one, using an unprecedentedly large number of animals and measurements. It emerges, as suggested by an earlier, much more restricted study (15) that rumen function and ruminant productivity can be predicted from the abundance of a small number of microorganisms that form part of the core community across geographical breed and dietary differences. As these microbes show significant heritability estimates, e.g., their abundance is explained to a significant

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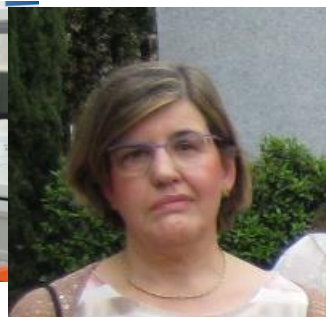
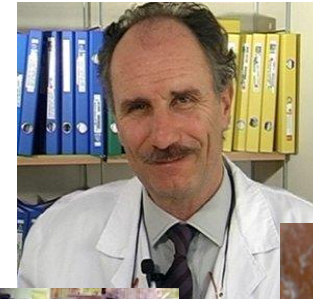
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# Innovando en como vehiculizar probióticos para hacerlos más atractivos en la dieta

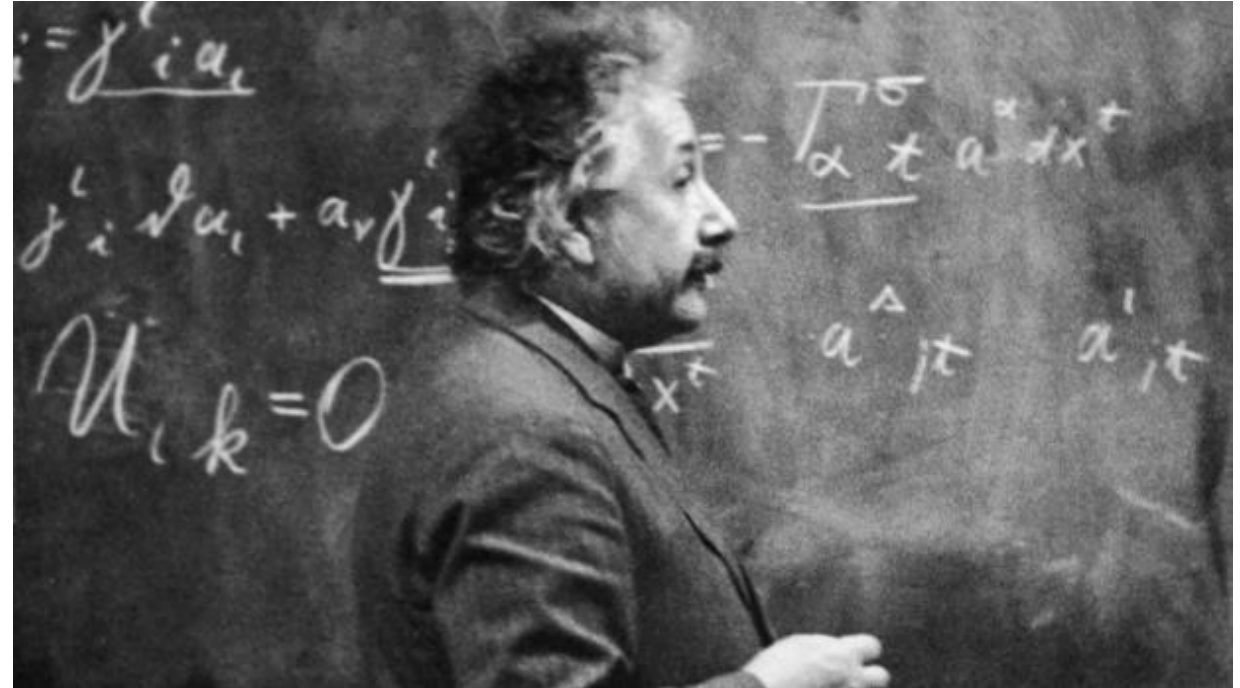


# ¿Está nuestro país bien posicionado para liderar este futuro?





“A lo desconocido no hay que tenerle miedo, simplemente hay que entenderlo” (Marie Curie; 1867-1934)



“Es más fácil desintegrar un átomo que un prejuicio” (Albert Einstein; 1879-1955)