

**Review Article** 

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# Microbiota A Conceptual Tool for All Uses and Abuses of Science

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## Abstract

The evolution and progress of scientific knowledge does not always bring light and make you understand the interpretation of natural phenomena. Research is often misled by preconceived ideas or superficial interpretations and simplistic conclusions based on observed events or experiments designed to confirm the theories formulated. The more numerous and complex the factors involved in determining a phenomenon, the more uncertain can be the interpretations that are arrived at. It is often the case that gives us the correct answer to the questions we ask ourselves. Scientific discoveries are full of anecdotes linked to the case that provided the key to interpreting the most important laws of the natural sciences.

It is not the case of modern science that studies the composition and effects of the bacterial flora present in the various districts of our body. We're talking about Microbiomica. There is nothing in nature more changeable than bacterial species, so much so that in millions of years, a time negligible compared to the history of our universe, they have given rise to the most numerous and diverse living species, and it is believed to be at the origin of the evolution of life on earth.

Precisely because of their ability to adapt to the most diverse environmental conditions, they have colonized all the terrestrial environments and the depths of the oceans. Well, Microbiomica bases its theories on the power that bacteria in our gut, the Microbiome, has to determine the conditions of our state of well-being or disease. Since the microbiomics relies on the ability to mutate bacteria, and the various compositions of colonies that can form, the pathogenetic cause of many diseases, is doomed to random and inconsistent interpretative results. This article is devoted to the examination of the contradictory interpretations that are encountered in examining the copious specialist literature on the subject.

Keywords: HMicrogenomics, Metagenomics, Microbiome pathogenicity, Intestinal ecosystem, Fecal Microbiota Transplatation, Probiotics

# Introduction

In scientific literature, when a theory or conceptual method of research affects the imagination and lends itself as a means to effectively describe or interpret natural phenomena, is widely used and is taken as the root cause of all observed events. Many of these research methods have been successful and have found the unanimous consent of scientists and researchers, who use them in all cultural manifestations. One for all, the most famous, is the conception of quantum mechanics, which lends itself with its theories and its complex formulas to explain whatever events occur in the universe, microscopically and macroscopically.

This science has assumed cultural dominance in all human knowledge so that the search for every phenomenon, physical or philosophical, is based on the interpretation of gnoseological quantum. The reason for such a great success and unanimous consensus,



in our opinion, is based on the substantial profound cognitive incapacity of our intellectual research tools. The more we broaden and deepen the level of research, with our observations and our acquisitions, the more we become aware of which infinity of phenomena remain totally obscure to us. In this bleak picture of infinite ignorance and obscurity of knowledge that unites mankind, every conception that brings a light and an interpretative glimmer of natural phenomena, rises to the universal law. The epistemological universe is dotted with examples of theories that have been successful, but that in the examination of experience have proved unfounded.

# **Biological Evolution of Bacteria**

Prokaryotic microorganisms, which include Archaeobacteria and Eubacteria, are the most common forms of life in nature and are also the oldest. The unique ability of these organisms to reproduce very easily and quickly allows them to modify their metabolic needs and adapt them to their ecosystem. This was the key to their success in colonizing all terrestrial environments. It is also believed that they are the primordial elements from which life on earth has developed in all its forms. Bacteria, like their descendants, have also undergone the natural forces that have conditioned and conditioned the existence of every living form.

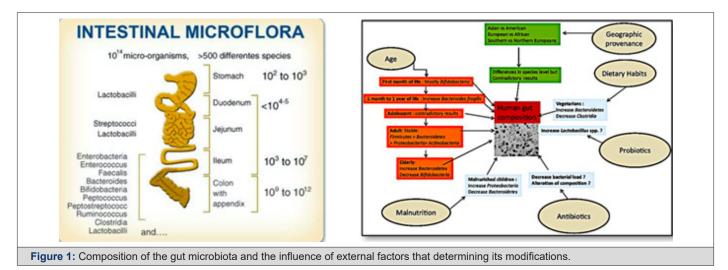
In a nutshell, the natural forces that have conditioned and transformed the terrestrial environment over the millennia have been the astronomical and gravitational events of the planets, the Sun and the Moon, which acting on the orbit of the Earth have modified its solar exposure, that is, the amount of radiation received on Earth, changing the climate accordingly. These astral events were the determining factors that influenced the origin and the biological evolution. Astral factors and cosmic events are translatable, according to quantum mechanics, into electromagnetic and gravitational forces and the effect of radiation from deep space. Regarding the astral factors that have modified the environmental conditions of the earth and consequently the biological evolution, we can summarize with: a) The rhythmic variations of the Earth's orbit related to the movements of rotation and revolution.

b) The gravitational effect of the sun and the moon, the latter acts on the rhythms of the tides and on important life cycles.

c) Insolation by the exposure to the sun's rays of the earth.

d) The reciprocal interaction between the living with their environment.

Tracing the biological evolution from bacteria to more complex forms, is outside the scope of this article, for those interested can consult the following synthetic articles [1,2]. Starting from these premises, in this article we are going to examine the literature on the subject of Microbiomics, which concerns the study of the effects produced by the bacterial flora present in our intestines, on the conditions of well-being or disease. We are going to also highlight, the improper use that is made of the Microbiome as an efficient cause of the most diverse pathologies, that is, as a pathogenetic because that embraces most of the diseases that affect mankind and not only. The objective of this review of the literature on the subject is to highlight the profound contradictions and logical conflicts that we encounter by comparing the different conceptions proposed by the individual authors. This is one of the examples I have mentioned above of how well-argued interpretations or conceptions can become universal law. In the scientific universe the conception of the microbiome as an efficient cause of all the phenomena that impact on our health has found a wide consensus. Thanks to this universal truth, we can interpret and cure any pathology and use the acquired laws for the well-being of humanity. The literature examination begins with the list of pathologies of which intestinal dysbiosis is recognized as a pathogenetic cause. Before starting this examination, it is necessary a useful preliminary premise to know what is the average composition of the normal microbiota of man and how it is modified in individual individuals with the passing of years and with the lifestyle, (Figure 1).



Bacteria are the most widespread form of life in nature, although we are unable to observe the wide range of processes in which they are involved. This is due to their extremely small size that do not allow you to observe them with the naked eye. They are also the oldest life form on our planet. In fact, it is hypothesized that they were the first single-celled living beings that appeared about 3.5 billion years ago. Belong to the class of Archea prokaryotic organisms, without nucleus, equipped with the minimum essential requirements to be considered living, or the ability to use materials in the environment to maintain its structure, organization and be able to reproduce. Despite being underestimated, they perform many fundamental functions, either individually or as a community in symbiosis with other organisms in the most diverse fields. Equipped with extreme versatility and adaptability we find them in the most different environments because they reproduce with exponential speed and can change the metabolism in response to environmental changes. They have achieved extraordinary success in colonizing and coexisting with the most diverse living species, from plants to the most complex animals. When this cohabitation allows both cohabiting species to obtain a mutual advantage, we speak about symbiosis, when it is for the benefit of only one species, we speak of parasitism.

Noteworthy is the fact that the bacteria themselves are subject to parasitic attacks by viruses. So much so that they have devised effective defence systems against viral attacks [3,4]. The study of the composite bacterial flora that colonizes our intestines has aroused great interest, since a close relationship has been observed between the quantity and quality of the microorganisms present in it and the state of well-being and disease of the host. The interest has given rise to a new discipline, the Microbiomica, born from the studies of Sergei Nikolaievich Winogradsky (1856-1953), father of Microbial Ecology, which expressed the concept of ecosystem consisting in the balance between microorganisms and their environment, and is one of the principles underlying the Human Microbiome Project: https://hmpdacc.org/. The concept of microbiome is due to the great geneticist and microbiologist Joshua Lenderberg, winner of the Nobel Prize in Medicine in 1958. Understandiing the effective role of the microbiota within the environments in which it lives, it is necessary to know the entire ecosystem and the interactions that take place within it.

## **Intestinal Ecosystem**

The gastrointestinal tract GIT, is a highly specialized organ that allows humans to consume food ingested, including a wide range of foods to meet nutritional needs. In GIT, food is converted into elementary compounds that can be absorbed by the body. GIT organs include the mouth, esophagus, stomach, small intestine and large intestine, as well as the pancreas and liver which secrete in the small intestine substances necessary for food metabolism [5]. The GIT system is connected to the blood, lymphatic and nervous system to facilitate and regulate the intake of food and the digestive process and the distribution of absorbed compounds to the organs of the body. A primary function of GIT is to extract nutrients from the complex mixture of foods consumed. Foods contain more than essential nutrients, and GIT also has a role in selecting, metabolizing, and eliminating excess or toxic non-nutrients. In order to ensure digestive function, many activities contribute to the proper functioning of all digestive phases [6]. These include the nervous control of contractions of the muscles present in the intestinal wall, the supply of blood and lymph to oxygenate the intestinal cells, control the immune system and extract the nutrients to be distributed to the various organs.

Within the intestinal cavity are secreted hormones and enzymatic digestive substances and is secreted mucus and acidic substances that must ensure the correct pH for enzymatic activity. So, it is a complex ecosystem of which the microbiome component occupies an important but not primary position. And it is from the balance of all the components that the state of well-being derives [7]. Here lies the essence of the homeostatic maintenance of the balance of the intestinal flora and the entire ecosystem. The focus of research on the only microbial component, a concept defined bacterium-centric, has produced the inconsistencies that we will show in this work. Few, if any, works have considered with equal interest the effects of fungi or viruses present in the microbiota, as possible causes of the examined pathologies. As well as other possible causes could be additives present in all foods and never considered when examining intestinal function [8,9].

# Conditions Affecting the Balance of the Microbiota

The first fundamental criticism that we can raise to the bacterium-centric research method is the elementary observation, repeatedly expressed in this work, that bacteria continuously change their metabolism in response to changing environmental conditions. Therefore, their role is basically passive and the composition of the flora present in the gut or in other ecosystems is the result of their adaptation to environmental conditions [10-14]. Thus antibiotic-resistant bacteria acquire this characteristic after chronic administration of antibiotics, and still anaerobic or thermophilic bacteria have adapted their metabolism to the particular environmental conditions, and certainly they were not the cause of such conditions. Even treatments with probiotics demonstrate that it is possible to change the intestinal microbiota with the intake of specific bacterial strains, which however do not change the condition of the intestinal endothelium. Diet [15-18], antibiotic therapy, ethnicity [19-20] and host age [21-22] are crucial in drastically changing the balance and composition of the microbiota. This once again shows that the composition of the microbiome is the epiphenomenon of natural or pathological interventions and modifications that occur in the intestine.

# Metagenomic Genetic Composition of the Microbiota

The presence and recognition of the various genomes present in the microbiome is obtained by sequencing the genomes present in the intestinal lumen using the taxonomic reference system called Metagenomica. Sequencing consists of deciphering ribosomal RNA (rRNA), especially the 16S gene rRNA for bacteria and Archea and the 18S gene rRNA for eukaryotic microbial organisms.

Overcoming classical microbiology techniques to identify microorganisms involves the use of total genomic DNA extracted from a matrix of various nature and the sequencing of 16S rDNA. In this way it is possible to study the bacterial communities living in different habitats without having to isolate them individually.

## rRNA16S and Bacterial Phylogeny

The main focus was on 16S rRNA sequences of bacterial ribosomes. Due to the restrictions on the structure of rRNA, which must assume a defined secondary structure and must interact with different proteins in order to form a functional ribosome, the rate of variation of the genes encoding rRNA is much lower than that of the other genes. As we have said earlier, all bacterial species mutate with ease to better adapt to environmental conditions, this is a distinctive feature of these living organisms. Mutations consist of small variations in the genome which remains substantially identical with respect to the distinctive characteristics of the species. So that of the same bacterial species exist different types that can be recognized by the analysis of their genome, they can be "typed" as they say, in scientific terms [23-25]. Then of the same bacterial species of distinguish different types, for example of the Salmonella species are distinguished N types each with a different genetic sequence for small nucleotide bases, which give the bacterial species different properties that may be useful or harmful to the host. In

#### Table 1

other words, there are "good" bacteria and "bad" bacteria. Although metagenomics is widely used in the sequencing of bacterial species in the gut or other microbiome, the method has been the subject of much criticism [26-27].

### **Literature Review**

In this paragraph we are going to report the conclusions of the literature with the lists of pathologies of which some bacterial groups would be responsible. Since the analysis covers the most varied pathologies, it is difficult to compare microbiota-pathology individually considered, therefore may list them directly from the articles examined. The literature examination was initially focused on the microbiota-cancer relationship of the colorectal tract, but since in the many articles examined reference is made to the link between bacterial groups sequenced in the tumor pathology with other pathologies, it was natural to extend the investigation of the pathogenetic connection to these too. The partial result is presented in the tables (Table 1-3).

Disease	Name of Prevalent Bacteria
Symptomatic atherosclerosis	Escherichia coli - Eubacterium rectale - Eubacterium siraeum Faecalibacterium prausnit- zii - Ruminococcus bromii Ruminococcus sp. 5_1_39BFAA
Type 2 diabete	Akkermansia muciniphila - Bacteroides intestinalis Bacteroides sp. 20_3 - Clostridium bol- teae Clostridium ramosum - Clostridium sp. HGF2 Clostridium symbiosum - Colstridium hathewayi Desulfovibrio sp. 3_1_syn3-Eggerthella lenta Escherichia coli
Obesity/IBD/CD	Acidimicrobidae ellin 7143 - Actinobacterium GWS-BW-H99 Actinomyces oxydans - Bacillus licheniformis Drinking water bacterium Y7 - Gamma proteobacterium DD103 Nocardioides sp. NS/27 - Novosphingobium sp. K39 Pseudomonas straminea - Sphingo- monas sp. A01
Colorectal cancer	Acinetobacter johnsonii - Anaerococcus murdochii Bacteroides fragilis - Bacteroides vulgatus Butyrate-producing bacterium A2-166 - Dialister pneumosintes Enterococcus faecalis - Fusobacterium nucleatum E9_12 Fusobacterium periodonticum - Gemella mor- billorum Lachnospira pectinoschiza - Parvimonas micra ATCC 33270 Peptostreptococcus stomatis - Shigella sonnei

Note\*: Rahul S Mandal, et al; Metagenomic Surveys of Gut Microbiota, July 2015 Genomics Proteomics & Bioinformatics 13(3).

## Table 2

Human Disease	Related Microorganisms
Atopic dermatitis	Staphylococcucus aureus, Cutibacterium, Streptococcus, Acinetobacter, Gemella
Cystic fibrosis	Streptococcus species
Depression	Coprococcus, Sellimonas, Clostridium, Hungatella
Autism	Clostridium bolteae
Asthma	Clostridia, Proteobacteria
Obesity	Actinobacteria, Bacteroidetes
Tuberculosis	Mycobacterium tuberculosis, Bacteroidesfragilis, Prevotella, Enterococcus
Periodontal diseases	Spirochaetes, Synergistetes, Bacteroidetes
Dental caries	Streptococcus rnutans, Lactobacillus spp., Candida albicans
Oral cancer	Streptococcus species
Esophageal cancer	Tannerellaforsythia, Porphyromonas gingivalis
Cardiovascular disease	Campylobacter rectus, Porphyromonas gingivalis, Porphyromonas endodontalis, Prevotella inter- media
Rheumatoid arthritis	Veillonella, Atopobium, Prevotella, Leptotrichia
Parkinson's disease	Lachnospiraceae, Faecalibacterium, Lactobacillus, Akkermansia, Bifidobacterium

Alzheimer's disease	Spirochaetes
Diabetes	Aggregatibacter, Neisseria, Gemella, Selenomonas, Actinomyces, Fusobacterium, Streptococcus

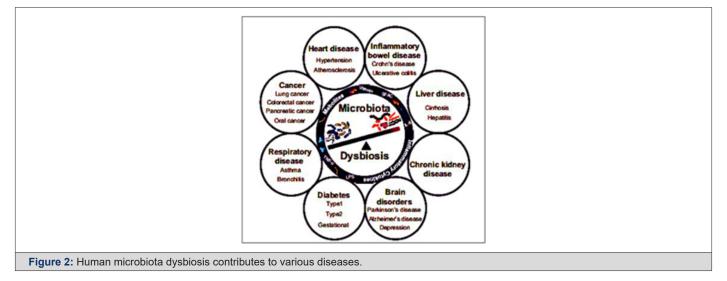
Note\*: Athanasopoulou K, Adamopoulos PG, Scorilas A. Unveiling the Human Gastrointestinal Tract Microbiome: The Past, Present, and Future of Metagenomics. Biomedicines 2023, 11, 827.

#### Table 3

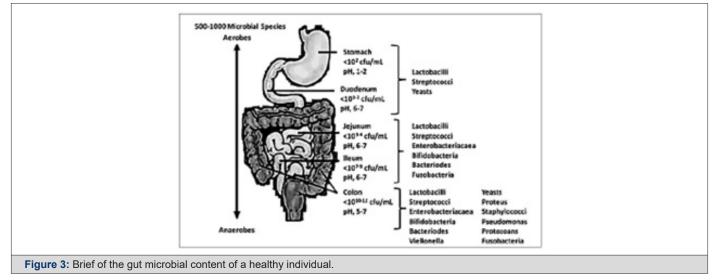
Bacteria	Types of Tumors
Salmonella typhi	↑ Gallbladder cancer
Helicobacter pylori	↑ Gastric cancer
Uropathogenic Escherichia coli	↑ Prostate cancer
Escherichia coli (strain CPI)	↑ Prostate cancer
Escherichia coli	↑ Bladder cancer
Bacteroides vulgatus, Bacteroides stercoris	↑ Colorectal cancer
Lactobacillus acidophilus, Lactobacillus S06, and Eubacterium aerofaciens	↓ Colorectal cancer
Fusobacteria, Leptotrichia genus	↓ Pancreatic cancer
Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans	↑ Pancreatic cancer
↑↑↑ Enterotoxigenic Bacteroides <i>fragilis</i>	Colorectal cancer
↑↑↑ Fusobacterium nucleatum	Colorectal cancer
↑↑↑ Porphyromonas gingivalis, Fusobacterium nucleatum	Oral squamous cell carcinoma
↑↑↑ Enterobacteriaceae	Stomach cancer
↓↓↓ Bifidobacteriaceae	Rectal neoplasm
↑↑↑ Capnocytophaga,Veillonella (in saliva)	Lung cancer

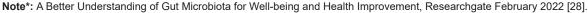
Note\*: Emerging role of human microbiome in cancer development and response to therapy: special focus on intestinal microflora, Hourieh Sadrekarimi.

There is also a substantial literature describing the pathogenetic role of the microbiome in many other diseases that affect practically all areas of medicine and psychiatry, without neglecting those more specific related to the gastroenteric tract. Listing these articles would be extremely tedious and scientifically inconclusive. Even from a superficial look of the above tables it can be observed that identical bacterial groups are considered the pathogenetic factors of different pathologies. If we want to adhere with scientific scrupulousness and without prejudice to the arguments set out in the articles reported, the contradiction between the pathogenetic role of certain microbiomes and the multiplicity of pathologies for which they would be responsible remains evident, Figure 2 gives a plastic image of this concept. In other words, how is it possible that the same bacteria cause such different pathologies as cardiocirculatory, metabolic, cancerous, autism, etc.? It would be interesting, even if very laborious, to examine and extend these singular coincidences with a computerized investigation. But if the hypotheses that have emerged from the reported literature are clearly of dubious scientific value, the aspect that makes them totally absurd is that the same pathogenetic species reported in the tables at the same time play a positive role for the well-being and we find them constantly in healthy people, [28,29] (Figure 2,3).



Note\*: Kaijian Hou, et al. Microbiota in health and diseases, Springer Nature 23 April 2022.





Supported by these scientific assumptions nowadays the treatment with specific bacterial strains has entered the common use for the prevention of many pathologies, with the use of probiotics. Probiotics, together with prebiotics, are currently the most widespread products in the nutraceutical market in Europe, which has reached a record value of 1,900 billion euros [30]. Such an extensive use of nutraceutical products requires the utmost rigour in respect of the rules of production and the correct information concerning them. Unfortunately, the rules are often not respected. IPA, the International Probiotics Association, calls on all manufacturers to use product labelling responsibly [31]. The great success achieved by these products has stimulated many Authors to go beyond the treatment with probiotics, and have proposed and adopted the treatment with bacterial strains of fecal origin, Fecal Microbiota Transplantation [32-37]. By this procedure we'd like want to add or replace, speaking about substitution therapy, to the resident microbiome of the subjects in treatment, the microbiome extracted from the feces containing the selected bacterial strains to be implanted. Many authors consider this practice to be immoral and immoral, not to mention ineffective. The question remains how is the therapy administered, in liquid, solid or spreadable form? We are willing to do anything to improve our health, but you are not proposing to ingest other people's feces.

# Effect of Therapy on the Microbiota

As we have repeatedly highlighted in this paper, it has become the leitmotif of this elaborate, all bacteria continuously change their metabolic characteristics to adapt to their environment, and the bacteria present in the microbiota are no exception. We have also indicated what are the internal and external factors that act on the intestinal ecosystem of the host or that are adopted by it in order to improve their health conditions. We remember among the external factors the diet, the drugs and the probiotics themselves, etc. Special mention should be made of laxatives that patients use to improve their intestinal functions.

Many studies have linked the use of laxatives and modifications of the microbiota [38-40].

In addition to the direct effect that laxatives cause of "washing" and alteration of the intestinal flora, many researchers do not recommend its prolonged use because this behavior would produce negative effects on the mental health of patients, to the point of causing dementia [41-43]. Conversely, other researchers noted and published that constipation may also be at the root of neurological diseases, such as depression, [44] Alzheimer's [45] and Parkinson's [46-48]. Here there is a problem of therapeutic choice, how do you behave with a constipated patient, who has stubborn constipation? If you do not adopt any treatment you risk, as we have seen, the onset of neurological pathologies, on the other hand if you use laxatives, you risk dementia. This is just one example of the inconsistencies and contradictions present in the literature on this subject, and how each author can support the most absurd hypotheses with learned disquisitions and showing graphs, tables and substantial case studies. I close this review on the microbiome citing part of the numerous literature in which appear the most obvious contradictions that are in conflict with the most elementary and rational logic of scientific investigation. A number of studies agree that certain bacterial colonies are responsible for multiple forms of cancer, while others have an organ-specific predilection [49-56]. What is truly shocking and calls into question our reasoning is that other articles support the efficacy of the microbiome in cancer prevention [57-62], in complete antithesis to the work already mentioned.

## Conclusion

From the critical examination of the scientific hypotheses described in the literature that we have faithfully reported so far, we can conclude that we finally have a new paradigm for medicine and a formidable therapeutic tool. It is the microbiome with which we can understand the origin and pathogenesis of all the evils that afflict humanity and how we can treat them effectively. No type of dysfunction or pathology, from irritable bowel to all types of cancer and even psychiatric diseases, can be traced back to a fundamental dysbiosis of the intestinal microbiome. Thanks to this innovative diagnostic-therapeutic system, we can send to the shredder all the treatments of medicine, semeiotics, pharmacology, and all clinical and imaging investigations used to date, that at most can serve to confirm diagnoses and to monitor the evolution of pathologies under treatment with selected bacterial strains. Moreover, interference or intrusion with other therapeutic means are not allowed, from anti-inflammatory, to antacids or inhibitors of proton pump, and less than ever to antibiotics, antifungals etc. that could alter the microbiota and compromise the examination and metagenomic monitoring of the bacterial flora. Because it takes nothing to completely change the balance and composition of the intestinal environment, to which the intestinal microorganisms should then readjust.

At the end of the day, this is the most absurd, paradoxical aspect that contradicts the whole theoretical building on which the microbiomics is based: an antibiotic or simply an effective laxative is sufficient to completely change the composition of the bacterial flora and with it the evolution and prognosis of any pathology. But even in the particular case that laxatives should be used, care should be taken in their choice and dosage because improper and prolonged use can lead to dementia. In the end it is clear from the interpretations that we have reported that all the hypotheses proposed have no scientific foundation, they are pure and simple intellectual exercises that do not consider all the implications present in the complex phenomena observed. When one comes across certain literature, one becomes overbearing in the conviction that with this type of science everything is possible, even to support absurd and incredible hypotheses.

Following the theses presented in these works, we should recognize that the microscopic beings that make up the microbiome have disrupted centuries of scientific certainties and subverted the rules of logic and the epistemic method of the search for truth. Then we discover that colonies of bacteria have the power to generate all the good and all the evil possible, they are even self-referential because they have conditioned, following the logic of this science, even the thoughts and concepts that concern them in the mind of those who describe them. As well as they can generate heart disease, inflammatory, respiratory, anxiety, depression, autism, etc. Figure 2, they can produce the most extravagant ideas. Then we should not be surprised if we read certain nonsense, because in the end of the absurd conceptions reported in the articles are not the authors responsible, but the microbiome that dwells in them.

## Acknowledgement

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# **Conflict of Interest**

Authors declare that they have no conflicts of interest for this article.

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