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#### LETTERS TO THE EDITOR

## Gastrointestinal microbiota and irritable bowel syndrome<sup>☆</sup>



### Microbiota gastrointestinal y síndrome de intestino irritable

The digestive tract of humans and other mammals is inhabited by millions of microorganisms, especially bacteria. This gastrointestinal microbiota is necessary for the good functioning of the digestive process in the host. Recently, Schmulson et al.<sup>1</sup> published a review article on irritable bowel syndrome (IBS) and its relation to the intestinal microbiota, as well as to other clinical and therapeutic aspects. We would like to make some comments on that article that may be of use to the medical community.

First of all, the term «flora» is used on various occasions to refer to methane-producing colonic and fecal microbiota, but this term is incorrect despite its common use in human and veterinary medicine. Second, table 3 not only contains a description of molecular methods for characterizing the intestinal microbiota (the title of the table), but also a description of the 16S subunit of ribosomal RNA and the gene that encodes it, which can be confusing to readers unfamiliar with the subject matter. This same table does not identify what the abbreviation rrs stands for, and the sentence on the use of the variability in 16S for distinguishing proximal and distant organisms is only partially valid, due to the uncertainty in today's bacterial molecular taxonomy.<sup>2</sup> In addition, table 3 only mentions one (pyrosequencing) of several massive sequencing techniques. This is worth mentioning because this technique will soon disappear from the market and therefore many studies have switched to other techniques, such as that of Ilumina.3 Third, the clinical heterogeneity of IBS and the different methods employed for the study of the intestinal microbiota are without a doubt some of the reasons behind our incapacity to establish a microbial composition belonging to IBS. However, it is necessary to emphasize that our main problem lies in the fact that each individual has a unique basal composition of microorganisms that also have qualitative and quantitative variations that are specific to each individual.<sup>4</sup> Fourth, the terms «bifidobacteria», «lactobacilli», «streptococci», and «coliform» are incorrect because in part they do not specify the taxonomic level they belong to. For example, the term «coliform» could refer to specific bacterial species or genera or to a family of *Enterobacteriaceae*. And finally, it would have been very useful if the article had gone into the subject of the use of probiotics and prebiotics as adjunct therapy in treating IBS. There are commercially available products that contain these nutraceuticals that have not been properly validated in clinical or microbiologic studies. This is important due to the possible adverse effects of these products in the clinical development of IBS.<sup>5</sup>

The study of the microbiota that inhabits our digestive tract has the great potential for optimizing the treatment of gastrointestinal problems on the part of the medical community. Now is the time to utilize the knowledge and technology available in this area for the benefit of the millions of patients in Mexico that suffer from IBS and other digestive diseases.

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#### Conflict of interest

The authors declare that there is no conflict of interest.

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# Gastrointestinal microbiota and irritable bowel syndrome; response to García-Mazcorro<sup>★</sup>



## Microbiota gastrointestinal y síndrome de intestino irritable. Respuesta a García-Mazcorro

Mr. Editor:

We thank García-Mazcorro et al. <sup>1</sup> for their interest and comments on our review. <sup>2</sup> In relation to their first point, we completely agree with them concerning the term intestinal «flora». Microbiota is the correct word, defined as the community of living microorganisms residing in a determined ecological niche, and we use it, not only in the title, but throughout the article (79 times to be exact), whereas the less precise but commonly used flora is employed only 5 times. <sup>2</sup>

Secondly, the 16S ribosomal RNA (rRNA) gene is one of the components of the small subunit (30S) of the ribosome and is present in all bacteria and archaea. It is the genetic marker used in bacterial phylogenetic analysis and is widely used in an endless number of studies. This gene sequence is approximately 1,550 bp long and is composed of 9 highly variable regions or hypervariable regions flanked by constant regions. The differences in sequencing of these hypervariable regions make it possible to taxonomically identify the bacteria present in study samples (for example, in stools and intestinal mucosa). The «rrs» gene, also known as 16S ribosomal DNA or 16S rDNA, as mentioned in table 3 of our article, encodes 16S rRNA. Even though there are limitations in sequencing based on 16S rRNA, it continues to be the gold standard due to the extensive databases based

on this marker. Illumina belongs to the «next generation» sequencing technologies that are limited by the length of the sequences they can provide, and so specific regions of the 16S rRNA gene must be selected in the analysis.<sup>3</sup> Other sequencing strategies and equipment currently exist that were designed for completion and correction.

Thirdly, the inability to absolutely establish the microbiota that is characteristic of IBS due to the factors mentioned by García-Mazcorro et al. is a fundamental aspect of our review. In fact, that was why we reached the conclusion that even though there is evidence that the intestinal microbiota is different in persons with IBS from that of normal subjects (level 3b evidence, grade B recommendation), it is not possible to establish a microbial composition that is specific for this disorder (level 3b evidence, grade B recommendation).

On the other hand, we agree that the taxonomic levels found were not mentioned in some cases, but some of the studies reviewed only reported the differences in microbial groups. And finally, we agree that our already extensive review fell short of analyzing the use of probiotics, prebiotics, and even synbiotics, in the treatment of IBS, but we felt these topics should be the subject of another review. As a matter of fact, a very recent systematic review of the literature has reported that probiotics were superior to placebo due to a lower frequency of IBS symptom persistence (55.8% vs. 73.1%).4 In addition, probiotics were shown to be superior to placebo in the improvement of overall symptoms, abdominal pain, subjective abdominal bloating, and flatulence. Specifically, it was Bifidobacterium spp that showed a tendency toward the improvement of overall symptoms and abdominal pain, but determining which strain(s) will be the effective one(s) has yet to be established. The authors also found that there were very few studies on prebiotics and synbiotics. Another review found that B. infantis 35624 was effective in improving subjective bloating in IBS in general and B. animalis DN-173 010 in patients with constipation predominant IBS (IBS-C).5 Furthermore, the relation between diet and the microbiota should also be analyzed. For example, low FODMAP (Fermentable Oligosaccharides Disaccharides, Monosaccharides, And Polyols) diets that improve IBS symptoms also appear to reduce the concentration and proportion of bifi-

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