

Dear Lian-Sheng Ma, Company Editor-in-Chief,

**Re: "Origin and genomic characteristics of SARS-CoV-2 and its interaction with ACE2 receptors, focusing on gastrointestinal tract"**

On behalf of my co-Authors, I would like to thank you and the reviewers very much for reviewing our manuscript entitled: *"Origin and genomic characteristics of SARS-CoV-2 and its interaction with ACE2 receptors, focusing on gastrointestinal tract"*, and considering it for publication in *"World Journal of Gastroenterology"*, following the amendments that we have made, based on Editor-in-Chief and Reviewers' comments. Please see below, a point-by-point response, to the Reviewers' comments. The appropriate changes have also been made in the revised manuscript.

**As part of our revised version:**

**A) Please see below a point-by-point reply to the Editor-in-Chief and Reviewers' comments.**

Their comments are shown in red color and our answers are shown in blue color :

**Reviewer #1:**

Comments to the manuscript: The origin and genomic characteristics of SARS-CoV-2 and its interaction with ACE2 receptors, focusing on gastrointestinal tract, by the authors Galanopoulos M et al. The aim of this review was to analyze some key elements about the SARS-CoV-2 genome and its general characteristics, in addition to the role of ACE2 receptor in SARS-COV-2 replication and pathogenesis, especially in the GI tract. It is an article of great scientific interest due to the topicality of the subject, and due to its application to the problem experienced worldwide (Pandemic by COVID-19). Furthermore, the study of ACE2 receptor in SARS-COV-2 replication and pathogenesis, especially in the GI tract, makes it particularly original. Title: It

is appropriate. Abstract: It is appropriate Background: The introduction is adequate and allows a proper understanding of the problem of study and the first-degree hypothesis (verification hypothesis). Methods and Results: Authors are recommended to present a clearer description of the following aspects: 1. The sources of information they used. 2. The inclusion and exclusion criteria of the scientific articles that were consulted to carry out this review. 3. The total number of articles that were consulted, and the number of articles that did not meet the inclusion criteria, and finally the number of articles on which they based the current review. Results Figure 2 is very interesting, although authors are recommended to make a clearer description of it in the section: Transmission of SARS-CoV-2 In the section on ACE2 and gastrointestinal lumen, authors are encouraged to submit more information (more scientific articles) on ACE2 expression in the epithelial cells of the gut for maintaining ecology of the gut microbiome.

We would like to thank the Reviewer for his important comments. Regarding the “Methods and Results” section, all the requested comments have been added, as well as a new figure, namely “Figure 1”, in the Figure Legend section of the main manuscript. As concerns the comment for Figure 2, a detailed description has been added in the respective figure legend after been renamed to “**Figure 3 Transmission cycle of SARS-CoV-2**”. Finally, based on the 3<sup>rd</sup> comment regarding the addition of more scientific articles for microbiome and dysbiosis in the section on “ACE2 and gastrointestinal lumen”, even though there is scarce evidence due to this novel disease, 4 additional refs have been inserted combined with the respective parts into the above section.

**Reviewer # 2:**

I suggest to publish the Mini-Review article after minor polishing Abstract and conclusion. Rich information, challenges & issue not much covered, language OK, reference OK, in short, original and up to the mark as a Mini-Review.

We would like to thank the Reviewer for his important comments. The appropriate changes have been made in Abstract and conclusion parts.

### **Editorial Office's comments**

#### ***Science Editor:***

Scientific quality: This is a minireview of the SARS-CoV-2 and its interaction with ACE2 receptors focusing on gastrointestinal tract. The topic is within the scope of the WJG. (1) Classification: Grade B and Grade B; (2) Summary of the Peer-Review Report: The aim of this review was to analyze some key elements about the SARS-CoV-2 genome and its general characteristics, in addition to the role of ACE2 receptor in SARS-COV-2 replication and pathogenesis, especially in the GI tract. It is an article of great scientific interest due to the topicality of the subject, and due to its application to the problem experienced worldwide. Furthermore, the study of ACE2 receptor in SARS-COV-2 replication and pathogenesis, especially in the GI tract, makes it particularly original. The inclusion and exclusion criteria of the scientific articles that were consulted to carry out this review. The questions raised by the reviewers should be answered; and (3) Format: There are 5 figures. A total of 51 references are cited, including 24 references published in the 2020. There are no self-citations. 2 Language evaluation: Classification: Grade A and Grade B. 3 Academic norms and rules: The authors provided the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement. No academic misconduct was found in the Bing search. The CrossCheck results showed the similarity to be high. According to our policy, the overall similarity index should be less than 30%, and the single-source similarity

should be less than 5%. Please rephrase these repeated sentences. 4  
Supplementary comments: This is an invited manuscript. The study is  
without financial support. The topic has not previously been published in the  
WJG. The corresponding author has published 1 article in the BPG. 5 Issues  
raised: (1) I found the authors did not provide the original figures. Please  
provide the original figure documents. Please prepare and arrange the figures  
using PowerPoint to ensure that all graphs or arrows or text portions can be  
reprocessed by the editor; and (2) I found the authors did not add the PMID  
and DOI in the reference list. Please provide the PubMed numbers and DOI  
citation numbers to the reference list and list all authors of the references.  
Please revise throughout. 6 Re-Review: Required. 7 Recommendation:  
Conditionally accepted.

We would like to thank the Science Editor for the significant comments. We  
feel that our answer to Reviewers' #1 & #2 comments also addresses the first  
comment ("the questions raised by the reviewers should be answered").  
Regarding the comment "The CrossCheck results showed the similarity to be  
high... Please rephrase these repeated sentences.", we feel that 39% similarity  
index that was found by your crosscheck software is indeed significant, even  
though we had already used software "Grammarly" before submission and  
the similarity index had been under 10% excluding bibliography (the report is  
attached). Nevertheless, and in keeping with your valuable comments we  
have managed to rephrase most of the sentences but not all, due to the  
molecular nature of the paper and as such, it is difficult to change some terms  
such as DNA or RNA expression and also some terms about the molecular  
mechanisms of this review. Furthermore, the appropriate changes have been  
implied based on comments "I found the authors did not add the PMID and  
DOI in the reference list. Please provide the PubMed numbers and DOI  
citation numbers to the reference list and list all authors of the references.  
Please revise throughout." Finally, regarding the comment "I found the  
authors did not provide the original figures. Please provide the original figure

documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor”, we prepared the figures using PPT and you may find these attached. At this point, we want to underline the fact that figures 5&6 were not able to be made completely in PPT format due to their molecular nature. The figures were constructed using the illustration program BioRender. This program offers the option to export the illustration either as PNG, JPG file or as a PDF file. We think that the PNG file is the best format in order to be editable. Would this be acceptable to you? If not, please feel free to exclude these 2 figures.

***Editorial Office Director:***

I have checked the comments written by the science editor.

We would like to thank the Editorial Office Director for the comment.

***Company Editor-in-Chief:***

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office’s comments and the Criteria for Manuscript Revision by Authors.

We would like to thank the Company Editor-in-Chief for the comment.

**B) Regarding the special requirements for figures:**

As it was aforementioned, we prepared the figures using PPT and you may find these attached.

**C) Regarding the special requirements for references:**

We added the PMID numbers anywhere needed.

We hope that you will find this revised draft of our manuscript, as suitable for publication in **“World Journal of Gastroenterology”**. Thank you very much for your co-operation.

Yours sincerely,

**Michail Galanopoulos, M.D., PhD, FEBSGH**

**Consultant Gastroenterologist**

**Department of Gastroenterology, 401 General Military Hospital of Athens,  
138 Mesogeion Avenue and Katechaki Street, Athens-GR 11525, Greece.**

**[galanopoulosdr@gmail.com](mailto:galanopoulosdr@gmail.com)**