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Manuscript Type: REVIEW

Type: Invited manuscript ID 03967085

No: 65115

Title: Hypotheses and facts for genetic factors related to severe COVID-19

Short title: Genetics and severe COVID-19

Authors: Stanislav Kotsev, Dimitrina Miteva, Stanislava Krayselska, Martina Shopova, Maria Pishmisheva, Spaska Stanilova, Tsvetelina Velikova

Dear Editor,

Dear Reviewers,

Thank you for your time to revise our Manuscript ID 65114, **Hypotheses and facts for genetic factors related to severe COVID-19**.

We took into account all the comments and suggestions the reviewers made. We have made the respective changes in the manuscript according to your remarks. Those changes are highlighted within the manuscript in red color. Please see below, in blue, for a point-by-point response to the reviewers' comments.

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (High priority)

Specific Comments to Authors: Congratulations on the completeness of the review: all the major genetic studies carried out have been treated and summarized in a very complete and exhaustive way.

- Thank you for your high evaluation of our work!

Describing HLA genes system you could have explained the connection about autoimmune diseases and susceptibility to infectious disease, and the predisposition to autoimmune disease in the same loci identified by GWA that you describe in HLA paragraph (multiple sclerosis or diabetes e.g.).

- Thank you for this remark. We have made the necessary changes and information about autoimmune diseases and HLA-association have been added in the HLA-paragraph.

This is very interesting also for the protection that steroids and interferons or other immunomodulatory therapies should give to autoimmune diseases patients or high evolution risk patients in the initial phase of SARS-COV-2 infection.

- Thank you for the valuable note. It is really intriguing for us as physicians, as well. We have made a brief comment on the autoimmune agents in patients with such diseases and the role of the immunomodulators in the development of cytokine storm.
- Additionally, we have corrected some other minor issues to improve the clarity and logical flow of the paper (highlighted in yellow).

4 LANGUAGE QUALITY

Please resolve all language issues in the manuscript based on the peer review report. Please be sure to have a native-English speaker edit the manuscript for grammar, sentence structure, word usage, spelling, capitalization, punctuation, format, and general readability, so that the manuscript's language will meet our direct publishing needs.

- We have corrected all the language issues that we have spotted, and according to a bilingual colleague of us.

5 EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) Science editor: 1 Scientific quality: The manuscript describes a review of the hypotheses and facts for genetic factors related to severe COVID-19. The topic is within the scope of the WJV. (1) Classification: Grade B; (2) Summary of the Peer-Review Report: All the major genetic studies carried out have been treated and summarized in a very complete and exhaustive way. However, the questions raised by the reviewer should be answered; and (3) Format: There is 1 table. (4) References: A total of 126 references are cited, including 79 references published in the last 3 years; (5) Self-cited references: There are 2 self-cited references. The self-referencing rates should be less than 10%. Please keep the reasonable self-citations that are closely related to the topic of the manuscript, and remove other improper self-citations. If the authors fail to address the critical issue of self-citation, the editing process of this manuscript will be terminated; and (6) References recommend: The authors have the right to refuse to cite improper references recommended by peer reviewer(s), especially the references published by the peer reviewer(s) themselves. If the authors found the peer reviewer(s) request the authors to cite improper references published by themselves, please send the peer reviewer's ID number to the editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation: Classification: Grade A. 3 Academic norms and rules: No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an invited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJV. 5 Recommendation: Conditional acceptance.

➤ We have taken into account all the notes made by the editor.

(2) Editorial office director:

(3) 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 Virology, 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 have taken into account all the notes made by the editor.