

Dear Editorial Board of *World Journal of Clinical Cases*,

It's a great pleasure to resubmit our revised version of the manuscript entitled "***Autoimmunity as the comet tail of COVID-19 pandemic***", to be considered for publication as an opinion review in Your Journal.

We have accepted the comments of the Referee and Editors and modified our manuscript accordingly. All the changes to the previous version of the manuscript have been highlighted in the text.

Below You can find, detailed point by point, our answers to the comments of Editors and Referee.

Referee's comments:

1. Autoimmunity as the comet tail of COVID-19 pandemic. A good manuscript and provides current knowledge on the additional complications of SARS-CoV-2 infection APL antibodies: they appear transiently in most of the infections and do not indicate autoimmune response. Follow-up is important to ensure whether response was transient or autoimmune response.

Authors' answer: We agree with the comment of the Referee. This information has been better detailed in the revised version of the manuscript and two new refs (120, 121) added and discussed in section 3.1.

2. Please discuss PIMS or MIS-C and include relevant references like: PMID: 32410760, 32499548, 32418446, 32598831, 32598830, 32493739, 32511692, 32527868, 32524957

Authors' answer: We thank the Referee for suggesting those references. Suggested papers were searched, added and discussed in the text (see section 3.6, refs: 164, 167, 168, 172-178) and in table 1.

3. Low incidence of severe COVID-19 in DMARDs-treated patients also suggest those molecules have potential therapeutic applications for the patient management. Some of the currently explored immunotherapies for COVID-19 like IL-6, IL-1 neutralization by

monoclonal antibodies or intravenous immunoglobulin (IVIG) are also used for the management of autoimmune and inflammatory responses highlighted by the authors. These points could be discussed for the therapies. Some of the references include PMID: 32562483, 32376394, 32574265, 32499548, 32482597, [https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913\(20\)30173-9/fulltext](https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(20)30173-9/fulltext)

Authors' answer: We thank the Referee for the comment. The overlapping COVID-19 morbidity and mortality rates between rheumatic patients and general population were already explained in the original manuscript on the base of a "*concomitant therapeutic background able to counteract the excessive activation of the immune system*" (section 4). However, following the Referee's comment, we discussed in more detail this view in the section 5 (concluding discussion) and added the suggested references (144, 145, 172, 192-194).

4. Include a discussion on why autoimmune responses (either rheumatic, hematologic or neurologic) appear following COVID-19.

Authors' answer: As suggested, we implemented section 5 (concluding discussion), by adding a new part of text resuming the immunologic cascades triggered by SARS-CoV-2 in infected individuals, which were already detailed in previous paragraphs, and describing the associations between these pathways and the specific immune-mediated clinical manifestations occurring during COVID-19.

5. ITP has been reported and need to be discussed (PMID: 32294340). Also, autoimmune haemolytic anaemia (PMID: 32374906, 32460350, 32542444) and Evans Syndrome (PMID: 32420629)

Authors' answer: We thank the Referee for the comment. With the exception of the refs. PMID: 32294340 and PMID: 32374906, which were already cited in the original version of our manuscript, we implemented the section 3.3 *Immune-mediated blood*

***disorders* and table 1 by adding and discussing the other suggested references (refs 141-143).**

Editorial Office's comments:

1. Scientific quality: The manuscript describes an opinion review of the autoimmunity as the comet tail of COVID-19 pandemic. The topic is within the scope of the WJCC. (1) Classification: Grade B; (2) Summary of the Peer-Review Report: A good manuscript and provides current knowledge on the additional complications of SARS-CoV-2 infection APL antibodies: they appear transiently in most of the infections and do not indicate autoimmune response. Follow-up is important to ensure whether response was transient or autoimmune response. The questions raised by the reviewers should be answered;

Authors' answer: All the questions raised by the Referee have been addressed in the revised version of the manuscript.

and (3) Format: There are 1 table and 2 figures. A total of 172 references are cited, including 52 references published in the last 3 years. There is 1 self-citation. 2 Language evaluation: Classification: Grade A. 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 CrossCheck detection and 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 WJCC. 5 Issues raised: (4) The “Author Contributions” section is missing. Please provide the author contributions;

Authors' answer: The section “Author Contributions” was already provided in the previous version of the manuscript following the section "Acknowledgements". However, following the Journal's instruction, the order has been changed and this section has been moved to the title page, and now it follows the authors' affiliations. Please note that, in order to answer Referee's comments, the total number of refs is now 194.

(2) The authors did not provide original pictures. 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;

Authors' answer: Figure 1 and figure 2 have been supplied as PPT files. Please note that, as we were not able to separately submit the PPT figures as image files, both the two images have been provided in two slides of a single PPT file submitted as a supplemental material.

(3) PMID and DOI numbers are missing 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.

Authors' answer: References have been changed throughout the manuscript according to the suggested style.

6 Re-Review: Required. 7 Recommendation: Conditional acceptance.

Yours Sincerely,

Rossella Talotta, MD, PhD

University of Messina, Rheumatology Unit, Department of Clinical and Experimental Medicine,
Azienda Ospedaliera “Gaetano Martino”, via Consolare Valeria 1, 98100, Messina, Italy

Mail: talotta1@virgilio.it; Phone: 0039-0902211; FAX: 0039-0902935162