Thessaloniki, 18th December 2019

Dear Professor Lian-Sheng Ma,

Founder and Chief Executive Officer,

We are pleased to submit the revision of our invited manuscript (ID: 03476752), titled "Diagnostic and clinical significance of antigen-specific pancreatic antibodies in inflammatory bowel diseases: a meta-analysis."

In the revised version we have considered all queries raised by the editorial office and the reviewers. A detailed response to the reviewers' comments is attached.

Concerning the comments raised by the editorial office, we can verify that we have adhered to all. In further detail:

1. The English language has been revised and approved by native English speakers.
2. An audio file for the core tip has been submitted in mp3 format.
3. Regarding the file containing all figures in editable format, although we have included this file in the submission, the figures cannot be editable as they are produced from different statistical programs. We apologize for that but it is beyond our control.
4. Our manuscript should be prepared with Word-processing Software, using 12 pt Book Antiqua font and 1.5 line spacing with ample margins. Unfortunately, in the Tables this was not always feasible.
5. All authors affiliations are rearranged as suggested, including postal codes! Author contributions have been changed, as suggested! In the abstract, abbreviations and acronyms are defined the first time they are used. We omitted all abbreviations from the keywords. Within the core tip, abbreviations and acronyms are defined the first time they are used. Throughout the manuscript text, abbreviations and acronyms are defined the

first time they are used within the main text and then used throughout the remainder of the manuscript. Three levels of subtitles were included, as suggested.

6. Article highlights have been included before the references.
7. In the references, the PMIDs and DOIs were inserted in all references. Two references however did not have a PMID (Lalkhen AG, McCluskey A. Clinical tests: sensitivity and specificity. Contin Educ Anaesth Crit Care Pain 2008;8:221–3 [DOI: 10.1093/bjaceaccp/mkn041] and Al Fattani AG, Aljoudi A. Sources of bias in diagnostic accuracy studies. J Appl Hematol 2015;6:178 [DOI: 10.4103/1658-5127.171991]). Additionally, we checked the reference list for repeated references.
8. In the figures, distinct colors were selected, with comparable visibility. However, not all colors are available as the figures are produced by other statistical programs. Additionally, we could not avoid the use of red and green in Figure 2, as these signs included are the default format of the RoB graph. No abbreviations exist in the title of the figures/tables and all abbreviations are explained in the figure/table legends as full name (abbreviation).
9. Every superscript with *, #, was replaced with superscript numbers for illustration.
10. No supplementary files are submitted in this manuscript.

Thank you in advance for considering our manuscript and wish you a Happy New Year!

Yours sincerely,

Dimitrios P. Bogdanos,

Professor of Immunopathology,

The Dame Sheila Sherlock Medalist

Chair & Director

The authors would like to thank both reviewers for taking the time to review our manuscript.

We wish you a Merry Christmas and a Happy New Year!

Best regards,

The authors

Reviewer 1	
Comment 1	This is a great meta-analysis looking at the utility of biomarkers for the diagnosis of CD, specifically Anti-GP2. The specificity of this test of 97% is exceptional. The authors' caution is appreciated in recommending wide-spread use of this test, mainly because of it's low sensitivity. This study does, however, really support a potential utility for its very high negative predictive value.
Response 1	Thank you very much for your comments! We have highlighted the potential utility for the high negative predictive value in the discussion!
Reviewer 2	
Comment 1	This meta-analysis is remarkably thorough and meticulous. The conclusion that anti-GP2 is not an ideal diagnostic marker of CD seems justified. If my interpretation of Table 4 is not oversimplified, it seems to me that it could be interpreted as hypothetically showing that 98-99% of all positive tests are false positives! If this observation is correct, then it should perhaps be emphasized more strongly in the Abstract and the text.
Response 1	Thank you very much for your comments! We have included one more sentence in the abstract, as kindly suggested stating that: “In this hypothetical cohort, for 81.3% of the positive cases diagnosis would be missed.”