

Dr. Lian-Sheng Ma,  
Founder and Chief Executive Officer  
*World Journal of Gastroenterology*

Dear Dr. Lian-Sheng Ma:

I wish to resubmit a Frontier article titled “Biomarkers in autoimmune pancreatitis and IgG4-related disease” for publication (ID64203) in the *World Journal of Gastroenterology*. The paper was coauthored by Akane Hara, Kosuke Minaga, Tomoe Yoshikawa, Ken Kamata, and Masatoshi Kudo.

We appreciate the comments from the reviewers and editors. We revised the manuscript in accordance with the suggestion raised by the reviewers. We addressed all of the comments from the reviewers.

The science editor required us to reduce the numbers of self-cited references. We tried to decrease the numbers of self-cited references. In this revision, the number of self-cited references was decreased down to 9 (Reference No.4, 25, 26, 27, 31, 32, 34, 36, 53). These self-cited references are indispensable and necessary for the readers to understand the progress of biomarkers in autoimmune pancreatitis and IgG4-RD. This is because major papers regarding innate immune responses in autoimmune pancreatitis and IgG4-related disease are published by our group. We believe that our revised manuscript is suitable for the publication of *World Journal of Gastroenterology*.

We look forward to hearing from you.

Sincerely,  
Tomohiro Watanabe, MD, PhD  
Associate Professor  
Department of Gastroenterology and Hepatology  
Kindai University Faculty of Medicine  
377-2 Ohno-Higashi

## Responses to the reviewers' comments

Reviewer #1:

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade A (Priority publishing)

**Conclusion:** Accept (General priority)

**Specific Comments to Authors:** Dear authors, First of all, thank you for submitting your manuscript to the World Journal of Gastroenterology. Congratulations on writing an interesting, comprehensive and fluent article. IgG4-RD is a newly recognised disease, information about its diagnostic markers is lacking. The manuscript contains the newest data about existing biomarkers and pathogenesis. It would be clearer and more memorable if you summarized the existing biomarkers in the table and provide some illustrative components while discussing pathogenesis.

Reply; We appreciate positive evaluation from this reviewer. We agree that the table is important and necessary for the readers to understand the relationship between the existing biomarkers and immuno-pathogenesis. In this revision, we added Table 1, in which the readers can see the biomarkers and references. As for the pathogenesis, please see the Figure 1 and Figure 2 in the original manuscript in which the immuno-pathogenesis of autoimmune pancreatitis and IgG4-related disease are clearly visualized.

Reviewer #2:

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Minor revision

**Specific Comments to Authors:** The Frontiers manuscript "Biomarkers in autoimmune pancreatitis and IgG4-related disease" is overall well-written and an important work. My minor suggestions/comments are as follows: -The sentence "AIP and IgG4-RD are newly established disease entities proposed by Japanese physicians[2-4]." in the conclusion section seems out of place and of questionable value; please consider deleting/heavily revising. -I would strongly suggest adding an algorithm (e.g. for the diagnostic workup of possible/suspected AIP) as a clinically useful figure. This is particularly important

*in those who have normal or only minimally elevated serum IgG4 levels (can pose a diagnostic conundrum).*

Reply; We appreciate positive evaluation from this reviewer. In response to the initial comment, we have rewritten the introduction and conclusion section. These changes are highlighted in red colors. In response to the second comment, we added an algorithm as Figure 3 in the revised manuscript, in which the readers can see how to use serum biomarkers for the diagnosis of autoimmune pancreatitis and IgG4-related disease. As you can see, Figure 3 is focusing on the diagnostic conundrum upon encounter with patients displaying normal serum concentrations of IgG4.

### **Reviewer #3**

**Conclusion:** Accept (General priority)

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade B (Minor language polishing)

Overall the manuscript is well written and addresses an important topic. It is applicable/salient for clinicians and researchers. No major concerns. Some of the phrasing may be revised for attention to detail, objectivity, and accuracy. For instance, "Autoimmune pancreatitis (AIP) and immunoglobulin G4-related disease (IgG4-RD) are new disease entities characterized by enhanced IgG4 antibody responses."; are these really "new disease entities", or are they "recently recognized"?

Reply; We appreciate positive evaluation from this reviewer. As for this comment, we think that AIP and IgG4-RD are recently established and recognized disease entities since new findings regarding the immuno-pathogenesis and clinical manifestation are accumulating rapidly. Therefore, we think that the wordings pointed out by the reviewer are adequate.