

Reviewer 1

Thank you for the opportunity to review the manuscript titled "Genetic actors that predict response and failure of biological therapy in IBD". This review emphasizes genetic factors that predict patient response and failure to biologic therapy in IBD, thereby enhancing clinical results and promoting personalized treatment strategies. The literature review is comprehensive and well-explored.

- *Authors` reply:* We would like to thank the reviewer for the opportunity to improve our manuscript. We appreciate the positive feedback regarding the comprehensiveness of our literature review and are grateful for the constructive comments provided.

However, several specific questions and concerns need to be addressed to enhance the clarity and depth of the study. Title needs to be modified. Also, avoid abbreviations (IBD) in the main title of the study. The main title of the manuscript is crucial as it provides readers with an immediate understanding of the paper's content and focus.

- *Authors` reply:* We agree that the title should be modified for clarity and have revised it to eliminate the abbreviation "IBD," ensuring that it accurately reflects the content and focus of the study. We considered the following title - Genetic factors that predict response and failure of biologic therapy in Inflammatory Bowel Disease: genetic variations in drug metabolism and treatment resistance, however, there is a limitation of 18 words, therefore, we chose Genetic factors that predict response and failure of biologic therapy in Inflammatory Bowel Disease.

Abstract is too brief. A scientific abstract should typically in range between 200 to 250 words. To address this, it is recommended to include background information on IBD, outlining its pathophysiology and disease burden. Additionally, incorporate a discussion of current therapeutic strategies, highlighting recent advancements and their clinical implications in the management of IBD.

- *Authors` reply:* We acknowledge the concern regarding the brevity of the abstract. We have expanded it to include background information on inflammatory bowel disease (IBD), outlining its pathophysiology and

disease burden, as well as a discussion of current therapeutic strategies and recent advancements.

It is suggested to add a comprehensive discussion of the pathophysiological mechanisms underlying IBD, substantiated by both preclinical and clinical evidence.

- **Authors` reply:** We have added a comprehensive paragraph on the pathophysiological mechanisms underlying IBD. We acknowledge how important is to include both preclinical and clinical evidence, to enhance the understanding of biologic therapy rationale for use in IBD. However, we limited this paragraph because the topic of the paper is different and we want to focus on genetic factors predicting response and failure to biologics in IBD patients in order to improve their clinical management.

The author should include a detailed comparison of traditional gold standard methods and advanced techniques for diagnosing IBD, emphasizing their respective advantages and limitations.

- **Authors` reply:** We included also the standard methods and advanced techniques for diagnosing IBD, emphasizing their respective advantages and limitations as much as possible.

Furthermore, the discussion should highlight which diagnostic approach is most effective for the early prediction of IBD, providing evidence to support the recommended method.

- **Authors` reply:** Additionally, we highlighted the crucial need for early prediction of IBD, emphasizing that this will improve the patient outcome and prognosis.

Abbreviation rules should be considered properly, full names should be mentioned once followed by abbreviations according to the abbreviation rule.

- **Authors` reply:** We have ensured that abbreviation rules are properly applied throughout the manuscript, mentioning full names followed by their abbreviations as recommended.

There are many typos and grammatical errors, authors should proofread the article for English and rephrase the overall sentence structure. Overall formatting is required. Updated references need to be cited.

- *Authors` reply: We thoroughly proofread the manuscript to correct typographical and grammatical errors, rephrasing sentences for clarity. Overall formatting has also been updated, and we have ensured that all references are current and correctly cited.*
- *We appreciate the reviewer's insights, which have significantly contributed to enhancing the quality of our manuscript. We are confident that these revisions address the concerns raised and improve the clarity and depth of our study. Thank you again for your valuable feedback.*