



March 9<sup>th</sup> 2023

The Editors,  
Gastrointestinal Disorders

Dear Editors,

**Re: The Role of TGF- $\beta$ , Activin and Follistatin in Inflammatory Bowel Disease. R1**

Thank you for your email dated March 1<sup>st</sup>. We thank the three peer reviewers for their helpful comments regarding the manuscript. Consideration of these has helped to improve the manuscript further.

We will provide responses to these comments in a point-by-point fashion as follows.

We are now pleased to submit the revised version of this manuscript. We will look forward to hearing the outcome of your consideration.

I look forwards to hearing the outcome of the peer review process for this manuscript.

Yours sincerely,

Andrew S Day,  
Paediatric Gastroenterologist,  
Department of Paediatrics, Christchurch Hospital  
Professor, University of Otago, Christchurch

**REVIEWER 1**

We thank the reviewer for their complimentary comments

## REVIEWER 2

Comment 1: As suggested, the CONCLUSION of the manuscript has been shortened substantially.

Comment 2: The word fully has been added to this sentence as suggested (amended word in red)

Comment 3: We have maintained the formatting in the INTRODUCTION with three paragraphs to ensure optimal readability

Comments 4 and 5: The titles for sections 2.1 and 2.2 have been amended (in red text) Further, a figure has been added (Figure 1)

Comment 6: We agree that single sentences should not make paragraphs. The formatting has been modified accordingly (e.g. line 181, line 232)

Comment 7: The text in the “effect” section of the tables has been modified (reduced). It proved difficult to modify further

Comment 8: The headings for section 3.1 and 4.1 have been amended (red text)

Comment 9: A second figure illustrating key signalling pathways has been added as suggested

Comment 10: The word has been amended as suggested (red text)

Comment 11: Lines 56-57 have been modified slightly to enhance clarity (red text)

Comment 12: The references have been revised as per requirements

Comment 13: Thank you for mentioning typographical errors: these have been amended (red text)

### **REVIEWER 3**

Comment 1: An amendment to the references has been made.

Comment 2: The aim in the INTRODUCTION has been amended as suggested (red text)

Comment 3: Two figures have been added

Comment 4: The tables have been linked from the text of the manuscript.

Comment 5: IBD has been retained in the title of table 2. Whilst the majority of the included studies exclusively evaluated patients with CD, reference 74 did also include children with UC. The table has not been expanded, as this was not intended to review all studies utilising this protein, but to illustrate with representative studies.

Comment 6 and 7: We agree that there is not yet human data to support the efficacy of these agents in the IBD. However, the preclinical data does support a role in gut inflammation, suggesting potential roles for IBD as well. Further statements have been made to indicate this for both sections

Comment 8: The conclusion has been shortened as suggested.

Comment 9: thank you for the suggestion to check the clinical trial registry. Unfortunately, no relevant trials were identified.