

ANSWERING REVIEWERS

January 21st, 2014



Jin-Lei Wang
Director, Editorial Office, World Journal of Gastroenterology

Dear director,

Thank you for reviewing our manuscript.

Title: Trefoil factors in inflammatory bowel disease

Authors: Aamann L, Vestergaard EM, and Grønbaek H.

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 5838

We have considered the comments and improved the manuscript according to the reviewers suggestions. Please for details see our comments below.

According to your advise, the manuscript has been edited by American Journal Experts.
Certificate verification key: C545-3988-B7DC-CDA9-6DD0

The material is original research, has not been previously published and has not been submitted for publication elsewhere while under consideration.

Conflict of interest statement: None declared

All sources of support of the work have been acknowledged.

For future correspondence please contact:

Professor Henning Grønbaek, M.D., Ph.D.

Department of Hepatology & Gastroenterology

Aarhus University Hospital

Nørrebrogade 44, DK-8000 Aarhus C, Denmark

E-Mail: henngroe@rm.dk

Telephone: (+45) 2167 9281 Fax: +45 78462820

Reviewed by 01587889:

This is a well written paper and references are up to date. **It should be accepted in its current form.** This review describes the TFF family and the role of peptide family in relation to IBD and also summarizes the current knowledge on their expression, possible function and pharmacological role in INBD. Since the discovery of the TFFs, a number of animal studies and studies on UC and CD patients have shown the peptides to be linked with inflammatory conditions in the gut. Although a significant role in mucosal protection and repair has been established for the TFFs, the full knowledge of their biological functions in IBD remains elusive. The quantitative measurements of the peptides in patients with IBD have been less promising due to large inter-individual variations and their future as biomarkers in IBD is uncertain. Clearly, the authors believe that future studies may show if the peptides have a potential as a novel therapeutic in IBD and the further identification of regulatory mechanisms that can affect TFF expression may aid in the development of new drugs in IBD.

Response:

Thank you for the positive comments to our manuscript.

Reviewed by 00009417:

In the excellent review trefoil factors in IBD are addressed. The current knowledge is reviewed and important details are addressed. The ms is in the scope of the WJG. The ms **could be improved by a scheme to summarize current knowledge about TFFs in IBD. Important pathways should be highlighted.**

Response:

Thanks for the positive comments to the MS. We agree that a scheme may improve the manuscript and have included a figure that highlights the potential role and pathways of TFFs in IBD.

Reviewed by 00227403:

-Although this is a descriptive review the authors should **report the method** used (for example medline research, from....to..., using the terms".....") -The authors should **report the references in the text and at the end of the text** (in the specific section). This is a crucial point. -**The title should explain that at the moment the involvement of Trefoil factor in IBD is unclear**

1. Method used.

Response:

For this review we have searched PubMed/Medline for “trefoil factors” AND “inflammatory bowel disease”, OR “ulcerative colitis”, OR “Crohn's disease”.

2. Report references in the text and at the end of the text.

Response:

References are reported in the text and listed according to the requirements of World journal of Gastroenterology.

3. The title

Response:

The title of the review is open and does not tell that the involvement of TFF in IBD is clear. We believe the title covers the subject of the MS and thus should not be changed.

Reviewed by 00722601.

It's an interesting and novel topic in IBD. The review is in some points unclear and not well organized. I think that it's needed a deep revision and restructuration of the review to expose the data clearly: definition of TFF, actions, general experience, experience in IBD... without mix points. I think that this review should not be accepted for publication.

Response:

This review consists of a thorough introduction and description of the TFFs and their role in IBD. It represents the existing knowledge about TFF and IBD – from the beginning when Wright and co-workers in the early 1990'ies defined the pattern of trefoil peptide gene expression in the ulceration-associated cell lineage (UACL) and the nearby mucosa in Crohn's disease and till present. As concluded in the review the full knowledge of the TFFs biological functions in IBD is complex and remains elusive. The authors have expert scientific and clinical knowledge on IBD and in the field of trefoil factors with a number of publications on this subject.

Thank you for publishing our review in The World Journal of Gastroenterology.

Yours sincerely,

A handwritten signature in blue ink, appearing to read 'Luise Aamann', with a stylized flourish at the end.

Luise Aamann, M.D.

Department of Hepatology & Gastroenterology

Aarhus University Hospital

Nørrebrogade 44,
DK-8000 Aarhus C, Denmark
E-Mail: luise_aa@yahoo.dk